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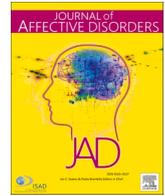
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Research paper

How do men and women differ in their depressive symptomatology? A gendered network analysis of depressive symptoms in a French population-based cohort

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ABSTRACT

Background: The experience of depressive manifestations and the presentation of symptoms in clinical settings may differ in men and women. Despite the extensive literature, it remains unclear how depressive manifestations interact at symptom levels in men and women. First, we aimed to describe and compare depressive networks by sex. Second, we examined symptom connections to Clinical depression and Functional Limitations as a proxy of self-recognition of a depressive episode.

Methods: We estimated networks from the 20 CES-D items in men and women from a large population-based French cohort. We computed centrality measures and ran comparisons. Then, we re-estimated two networks in men and women separately, adding, on the one hand, Clinical Depression and, on the other hand, Limitations due to a depressive episode.

Results: Over 200,000 participants were included in this study. Women were twice as likely to have a previous diagnosis of depression. Sex-ratio was less pronounced (1,7:1) for Limitations due to depression. Centrality measures revealed similar symptom patterns. However, network structures differed between men and women. We found some symptom connections to Clinical depression and Limitations to be non-invariant according to sex.

Limitations: Cross-sectional data does not capture the direction of the connections between symptoms and an eventual diagnosis. We lacked data about the diagnosis's context and could not account for other factors influencing depressive symptomatology.

Conclusions: Network structures differed, suggesting gender-specific mechanisms in activating symptoms and depressive states. Addressing central symptoms evoking depressed moods with tailored interventions may serve to tackle depressive states in men and women.

1. Introduction

The gender gap in depression rates is among the most consistent findings in epidemiological and survey data across Western countries. Women are twice as likely as men to have depression over their lifetime (Kuehner, 2003). The literature on this subject is extensive. Even if differences in socioeconomic, intrapersonal, and biological factors may partly account for this gender gap (Kuehner, 2017), unresolved questions still deserve further understanding. In particular, there is a possible gender difference in the experience of depressive manifestations and the

detection of depression, which may be underdiagnosed in men.

Indeed, research has shown that women tend to experience traditional symptoms (i.e., somatic symptoms, depressed mood), while men experience what is commonly known as 'male-typical symptoms' (i.e., risky behaviors, substance abuse, anger) (Cochran and Rabinowitz, 1999). These patterns are often attributed to gender norms and gender role expectations (Addis, 2008). However, recent research supports that neither women nor men experience depression as a uniform syndrome (Martin et al., 2013), meaning these patterns do not suppose strong homogeneity assumptions within each gender group. Closely related to

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the experience of depressive symptoms is their perception and self-recognition, which can be considered the first stage of the help-seeking pathway (Möller-Leimkühler, 2002). Some authors suggest that men can sometimes deny their mental health symptoms or adopt coping strategies because admitting them might contradict their normative male role, thus leading to delay or avoiding help-seeking (Möller-Leimkühler, 2002). Others consider that we need further understanding of whether and how masculinity norms shape men's help-seeking process and men's symptom disclosure to clinicians (Addis, 2008).

From a clinical perspective, identifying depressive symptoms and accurate diagnosis can be challenging. Several factors (e.g., clinician's experience, symptom heterogeneity, underreported symptoms, differential diagnosis) can impact this process. In particular, research has documented that patients' characteristics, like sex or race/ethnicity, can influence clinicians' identification of mental health problems and clinical judgment (Borowsky et al., 2000), with men being less diagnosed than women even when meeting diagnostic criteria (Afifi, 2007; Bertakis et al., 2001; Garb, 2021).

Many sex-comparative studies have examined depressive symptomatology by looking at item endorsement rates and differences in total sum scores (i.e., adding up endorsement scores and classifying individuals as depressed or not depressed at a certain threshold). This approach, known as the 'common-cause hypothesis', considers items or symptoms as equally good indicators of an underlying disorder and understands them as interchangeable (Fried and Nesse, 2015a). Even if this approach has contributed to shedding light on associated risk factors, recent research has shown that depressive symptoms are rather heterogeneous, involving different structures, mechanisms, and etiology (Fried and Nesse, 2015b). Alternatively, a symptom-level approach is needed to study the relationships between individual symptoms. Scholars suggest that psychometric networks offer a way forward to understanding symptom-level mechanisms (Fried et al., 2017). This approach considers mental health disorders as complex dynamic systems of interacting symptoms. Accordingly, if one symptom becomes active in a network, it will likely activate others and vice-versa (Cramer, 2016).

Prior works investigating sex differences in depressive networks are scarce, and results are mixed. Two studies reported no statistical differences in men's and women's networks. In both cases, sampling included subjects diagnosed with Major Depression (MD) (Steen et al., 2021) or a treatment-seeking population (Vetter et al., 2021). Considering studies based on the general adult population, two studies were conducted in Hong Kong. In both cases, networks were estimated using the Patient Health Questionnaire-9 (PHQ-9). One did find sex differences in a certain number of symptom connections (Jin et al., 2022), and the other one did not (Cheung et al., 2021). However, these studies were conducted in the post-Covid19 pandemic context in Asia, limiting the generalization to other populations. Yet, unraveling how depressive manifestations interact within a network separately in men and women from the general population could give meaningful insight into identifying symptoms that healthcare providers may target. Also, prevention interventions could be designed from a gender perspective, leading to more effective results. Moreover, it could provide information on the gender mechanisms related to an MD diagnosis and self-recognition of a depressive episode.

This paper addresses one main aim and two subsidiaries. First, we aim to describe and compare depressive symptom networks in men and women from a large population-based French cohort. Second, we aim to study potential sex differences in the connections between depressive symptoms within a network and Clinical depression and explore possible sex differences in the associations between depressive symptoms and functional limitations. We distinguish gender, a social construct encompassing many dimensions (Bauer, 2023), from biological sex. While the latter was used during data collection, we used "gender" as an analytical category to interpret our results. This dimension of "gender"

refers to social structures and hierarchical relations that inequitably distribute resources across genders/sexes (Lee et al., 2023). Our gendered perspective, therefore, intends to articulate the representations between sexes, norms, power relationships, and health-related outcomes.

2. Methods

2.1. Settings and participants

The present study analyzed baseline data from CONSTANCES (Zins and Goldberg, 2015), a nationwide population-based cohort of adults living in Metropolitan France. During the inclusion period (February 2012 to September 2021), >200,000 volunteers aged 18–69 were enrolled in the cohort. At the time of inclusion, volunteers responded to a self-administered questionnaire covering socio-demographic characteristics and health data. They ran medical examinations and para-clinical tests in one participating Health Screening Center (HSC). During follow-up, participants fill out an annual questionnaire and attend an HSC on a 4-year periodic basis.

Participants enrolled in 2020 and 2021 were excluded from this study because, as is well known, mental health was heavily impacted by the Covid-19 pandemic. Since this study is primarily exploratory, we retained all participants without age restriction.

2.2. Measures

2.2.1. Depressive symptomatology

For the sake of simplicity, in this study, we use 'symptoms' to refer to affective states or manifestations even if these terms slightly differ in their definition (i.e., severity). Participants self-administered the French version of the Center for Epidemiologic Studies Depression Scale (CES-D) at baseline based on the frequency they experienced each symptom over the last week. A previous study validated this version and demonstrated the full measurement invariance across gender (Morin et al., 2011), meaning that items are interpreted similarly in men and women from the general population. The scale comprises 20 items structured in 4 main sub-scales. Three dimensions represent the underlying 'negative' affect (depressive affect, somatic and interpersonal), while the fourth represents the 'positive' affect. Items belonging to this positive dimension are positively worded and were reverse coded before analysis. Items are presented on a Likert-scale with four options, with 0 corresponding to Rarely or Never and three corresponding to Mostly all the time. A final score ranges from 0 to 60 by adding the sub-scale scores, with a higher score indicating more severe depressive symptomatology. We retained a cut-off point at 19 for identifying men and women at risk of depression (Morin et al., 2011).

2.2.2. Clinical Depression

Participants responded to a medical questionnaire during their visit to an HSC covering personal and family medical history, including 'Personal history of Treated Depression' (yes or no, and age at diagnosis). We renamed this variable as 'Clinical Depression', signifying that participants were diagnosed with depression by a clinician in the past.

2.2.3. Limitations associated with a depressive episode

At baseline, participants self-responded to a question regarding the global activity limitation indicator (GALI) in the past six months with four intensity options (from strongly limited to not limited). In case of limitation, they specified the health reasons contributing to it, which included a 'Depressive state' option. We recoded this variable as 'Limitations associated with a depressive episode' if participants answered Yes (whatever the intensity) and selected 'Depressive state'. This variable served as a proxy of self-recognition of a depressive episode for two reasons. First, because self-reporting functional limitations allowed a direct assessment of participants' own perception, and second, its

limited time scope mitigated recall bias.

2.3. Statistical analysis

2.3.1. Estimation of Networks based on the Gaussian Graphical Model (GGM)

This study was conducted in two steps. First, we estimated network models in men and women separately, wherein the nodes indicated symptoms measured by the 20 CES-D items, and the edges represented weighted undirected connections between two symptoms (Epskamp et al., 2018). We used Spearman's Rank Correlation matrices as the inputs of our models and handled missing values with complete pairwise observations. We used a regularization technique, the graphical least absolute shrinkage and selection operator (gLasso), which limits the estimation of weak and spurious edges by shrinking some to 0, leading to parsimonious networks (Epskamp and Fried, 2018). We used the Extended Bayesian Information Criterion for model selection.

We examined each node's associations with all others, computing three centrality measures: strength, betweenness, and closeness. Strength quantifies how well a node is directly connected to other nodes taking the absolute sum of edge weights connected to this node. Betweenness quantifies how often a node lies on the shortest path connecting two nodes. Closeness quantifies how well a node is indirectly connected to others taking the inverse of the sum of the distance from a node to all other nodes (Borsboom et al., 2021; Deserno et al., 2022).

We assessed the accuracy of the edge weights by computing bootstrapped confidence intervals (BCI) and the stability of symptoms' strength by correlating this measure from the original sample with subsequent subsets of samples with fewer cases. This case-drop bootstrap procedure gives the Correlation Stability coefficient (CS-C) that reflects the proportion of cases that can be dropped to obtain a high correlation with the original sample (i.e., good stability of strength index).

We plotted women's and men's networks using the same layout based on the Fruchterman and Reingold algorithm that places nodes with higher centrality towards the center. We ran statistical tests to compare networks by sex using the Network Comparison Test (van Borkulo et al., 2017), a non-parametric method. First, we tested the invariance of the network structures, meaning that under the null hypothesis, each pair of edges in the women's and the men's networks is equal. We examined which pair of edges differed in post hoc tests (i.e., edge invariance tests) after controlling for multiple tests using the Holm-Bonferroni method as previously recommended (Fried et al., 2022). Second, we tested for the invariance of the global strength, meaning that under the null hypothesis, both networks have the same level of connectivity (i.e., the absolute sum of all edge weights is equal across networks).

Second, we re-estimated networks in men and women from the 20 CES-D items and included Clinical depression as a binary node indicating the presence versus absence of the diagnosis. In this step, the analyses focused on specific edge comparison tests according to sex to examine each connection between a symptom and this external node, and for simplification purposes, centrality measures were not examined. Holm-Bonferroni correction was applied. Additionally, we re-estimated networks in men and women and included Limitations associated with a depressive episode, indicating the presence versus absence of this variable.

2.3.2. Sensitivity analysis

To account for potential cofounders in the depressive networks, we re-estimated networks from the 20 CES-D items and incorporated five external nodes referring to socio-demographic characteristics. These additional networks were also compared by sex to assess the robustness of our comparisons. The external nodes were coded 0 vs. 1, with 1 defining the exposition. These were: age (<50 years vs. 50 years or above), educational level (higher education vs. up-to-completed high

school French diploma or equivalent), occupation (high-skilled workers vs. low-skilled workers, based on the most occupied position over the life and on the French official professional ranking position), financial difficulties (has never vs. has already encountered this challenge) and employment status (employed vs. unemployed/retired/in training/unable to work/another situation).

2.3.3. Statistical packages

We used R version 4.4 for all analyses. The bootnet package version 1.5 (Epskamp et al., 2018) and the qgraph package version 1.9.4 (Epskamp et al., 2012) were used to estimate and plot the networks. Comparisons across networks were made with the NCT package version 2.2.2 (van Borkulo et al., 2017).

2.4. Ethics

Data from CONSTANCES cohort obtained authorization from the French National Commission for Information Technology and Liberties (CNIL) and the National Institute for Medical Research (Inserm) institutional review board. All studies using the CONSTANCES cohort data have received approval from a scientific committee. All participants have given written consent to use their data for scientific research.

3. Results

3.1. Sample characteristics

Overall, 201,952 volunteers of CONSTANCES were eligible and included in the present study, of whom 108,391 (54 %) were women. Women reported having a diagnosis of clinical depression significantly more often than men (20 % and 11 %, respectively) and also had a higher median CES-D score (10 [Interquartile range (IQR) 4, 15] and 7 [IQR 5, 16], respectively). Differences in item-endorsement rates were significant, with women reporting depressive symptoms more frequently than men. The participants' main characteristics are shown in Supplemental materials (Table S1), and the means and distribution of items are shown in Table 1. Of all 20 CES-D items included in the network analysis, missing ratings ranged from 4,7 % to 9,2 % in women and 3,8 % to 6,9 % in men. A comparison of profiles with incomplete questionnaires (at least four missing items) is provided in Table S2.

3.2. Network estimation, inference, and comparison from the 20 CES-D items

Networks are displayed in Fig. 1. Men's network was slightly denser than the women's, with 161 edges estimated using gLasso of 190 possible and 152 of 190, respectively. The mean weight edge was 0.0448 and 0.0455 in men and women, respectively. The estimation procedure yielded accurate edges in men and women, with very narrow BCIs (Supplementary materials Fig. S1).

In both networks, the strongest connection was found between '12. (not) Happy – 16. (not) Enjoyed life' (coefficients of edge weights are shown in Table S2). Both men's and women's networks showed strong connections between the following symptoms: '15. People unfriendly' – '19. People disliked me', '4. (not) Felt as good as others' – '8. (not) Felt hopeful', '6. Felt depressed' – '3. Could not shake the blues' and '6. Felt depressed' – '18. Felt sad'.

Centrality indices are shown in Fig. 2. Strength index values were stable after dropping many cases (CS-C = 0.75). Within each network, '6. Felt depressed' and '18. Felt sad' were the most highly connected symptoms with others (highest strength values). '18. Felt sad' also played an important role by activating other parts within each network (highest betweenness values) and by its ability to affect other symptoms quickly (highest closeness value). There were, however, some sex differences in other symptoms' importance. For example, in men, the second most relevant symptom in activating other parts of the network was '9. Life

Table 1
Distributions of the 20 CES-D items by sex.

Items	Women				Men			
	Rarely (%)	Some of the time (%)	Occasionally (%)	Most or all of the time (%)	Rarely (%)	Some of the time (%)	Occasionally (%)	Most or all of the time (%)
1. Bothered by things	70,280 (69 %)	23,389 (23 %)	6061 (6 %)	1742 (1,7 %)	67,120 (76 %)	16,798 (19 %)	3571 (4.0 %)	1122 (1.3 %)
2. Poor appetite	83,586 (81 %)	15,447 (15 %)	3683 (3,6 %)	971 (0,9 %)	78,853 (88 %)	8717 (9.7 %)	1671 (1.9 %)	473 (0.5 %)
3. Could not shake the blues	84,152 (82 %)	12,131 (12 %)	4839 (4,7 %)	1916 (1,9 %)	78,395 (88 %)	7347 (8.2 %)	2554 (2.9 %)	1037 (1.2 %)
4. Felt as good as others	35,491 (36 %)	32,357 (33 %)	14,726 (15 %)	16,558 (17 %)	39,127 (45 %)	23,138 (27 %)	8415 (9.7 %)	15,965 (18 %)
5. Had trouble keeping mind on task	49,994 (49 %)	36,130 (35 %)	12,789 (12 %)	3905 (3,8 %)	52,936 (59 %)	26,412 (30 %)	7575 (8.5 %)	2216 (2.5 %)
6. Felt depressed	62,671 (61 %)	27,743 (27 %)	9220 (9 %)	3380 (3,3 %)	65,969 (74 %)	16,866 (19 %)	4630 (5.2 %)	1759 (2.0 %)
7. Everything was an effort	62,972 (61 %)	26,600 (26 %)	9591 (9,3 %)	3583 (3,5 %)	63,923 (72 %)	18,245 (20 %)	4990 (5.6 %)	1878 (2.1 %)
8. Felt hopeful	30,478 (30 %)	37,411 (37 %)	20,113 (20 %)	13,182 (13 %)	31,498 (36 %)	30,789 (35 %)	13,998 (16 %)	11,848 (13 %)
9. Life was a failure	82,012 (80 %)	13,978 (14 %)	4555 (4,4 %)	2163 (2,1 %)	74,496 (84 %)	10,259 (12 %)	2865 (3.2 %)	1434 (1.6 %)
10. Felt fearful	70,621 (69 %)	21,720 (21 %)	7092 (7 %)	2369 (2,3 %)	71,661 (81 %)	12,773 (14 %)	3103 (3.5 %)	1097 (1.2 %)
11. Restless sleep	32,667 (32 %)	35,584 (34 %)	22,338 (22 %)	12,984 (13 %)	37,479 (42 %)	30,738 (34 %)	14,490 (16 %)	6832 (7.6 %)
12. Happy	37,935 (37 %)	40,350 (40 %)	17,442 (17 %)	5959 (5,9 %)	35,158 (40 %)	33,705 (38 %)	13,039 (15 %)	6495 (7.3 %)
13. Talked less	66,771 (66 %)	25,542 (25 %)	7298 (7,2 %)	1874 (1,8 %)	60,497 (68 %)	21,246 (24 %)	5167 (5.8 %)	1468 (1.7 %)
14. Felt lonely	63,454 (62 %)	24,378 (24 %)	10,210 (9,9 %)	4648 (4,5 %)	65,006 (73 %)	15,474 (17 %)	5817 (6.5 %)	2624 (3.0 %)
15. People unfriendly	83,395 (82 %)	13,664 (13 %)	3134 (3,1 %)	1062 (1 %)	75,224 (85 %)	10,280 (12 %)	2089 (2.4 %)	829 (0.9 %)
16. Enjoyed life	33,347 (33 %)	36,775 (36 %)	22,409 (22 %)	8831 (8,7 %)	32,195 (36 %)	31,411 (36 %)	17,190 (19 %)	7491 (8.5 %)
17. Crying spells	77,498 (75 %)	18,094 (18 %)	5423 (5,3 %)	1889 (1,8 %)	82,359 (93 %)	5114 (5.7 %)	1121 (1.3 %)	417 (0.5 %)
18. Felt sad	51,931 (50 %)	36,955 (36 %)	10,664 (10 %)	3480 (3,4 %)	60,611 (68 %)	22,081 (25 %)	4913 (5.5 %)	1491 (1.7 %)
19. People disliked me	82,823 (81 %)	14,538 (14 %)	3798 (3,7 %)	1403 (1,4 %)	76,967 (87 %)	9281 (10 %)	2009 (2.3 %)	705 (0.8 %)
20. Could not get going	46,640 (45 %)	41,048 (40 %)	11,711 (11 %)	3397 (3,3 %)	49,696 (56 %)	30,432 (34 %)	6946 (7.8 %)	1854 (2.1 %)

Note: All tests comparing distributions between men and women were significant with p-values <0.001.

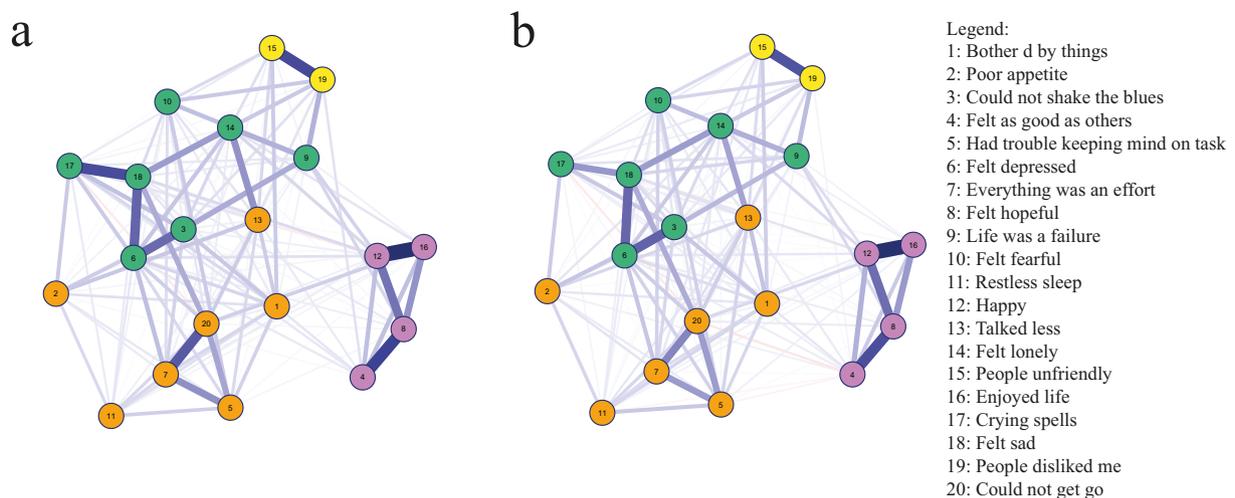


Fig. 1. Estimated symptom networks from Graphical Gaussian Models (GGM) with Spearman's Rank Correlations. Panel 'a': women (n=108,391). Panel 'b': men (n=93,561). Blue edges represented positive partial correlations, and red ones negative partial correlations. The strongest absolute edge weights were displayed as the widest and most saturated. Items were colored by dimensions (factors); Green: depressive affect, Purple: positive affect; Orange: somatic; Yellow: interpersonal. In both models, the edge weight between '12.Happy – 16. Enjoyed life' was the strongest (0.418 BCI [0.412; 0.424], 0.432 BCI [0.426; 0.439] in women and men, respectively).

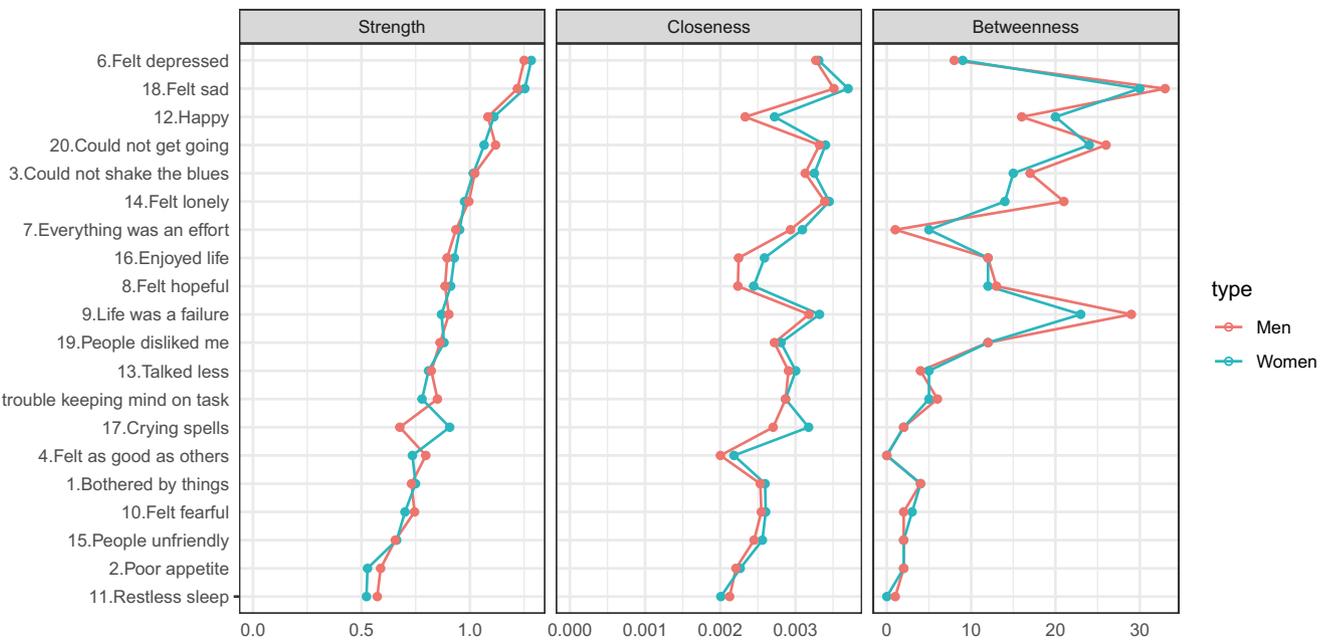


Fig. 2. Centrality indices of the 20 CES–D items in women and men.

was a failure’ while in women it was ‘20.Could not get going’. Also, ‘17. Crying spells’ had the 10th strongest position in women, while in men, the 16th. All in all, ‘6.Felt depressed’, ‘18.Felt sad’, ‘9.Life was a failure’ and ‘20.Could not get going’ played the most important role in the depressive symptomatology among participants.

The Network Comparison Test revealed that network structures were significantly different ($p < 0.00019$), meaning that some pairs of edges were non-invariant in men and women. Indeed, 32 edges had significantly different weights according to sex (all corrected $p < 0.04$, details in Table S3). For example, in women, the connections ‘17.Crying spells’ – ‘18.Felt sad’, ‘6.Felt depressed’ – ‘17.Crying spells’, ‘11.Restless sleep’ – ‘17.Crying spells’, ‘13.Talked less’ – ‘14.Felt lonely’, ‘20.Could not get going’ – ‘7.Everything was an effort’ were significantly stronger than in

men. In men, the connections ‘3.Could not shake the blues’ - ‘6.Felt depressed’, ‘4.(not) Felt as good as others’ - ‘12.(not) Happy’, ‘9.Life was a failure’ - ‘18.Felt sad’, ‘13.Talked less’ - ‘18.Felt sad’ and ‘2.Poor appetite’ - ‘14.Felt lonely’ were significantly stronger than in women. In contrast, the test comparing global strength was not significant.

3.3. Network estimation including clinical depression as an external factor

Networks showing all edges across the 21 nodes are available in Fig. S2. Networks highlighting the connections between symptoms and Clinical depression are plotted in Fig. 3. In both men’s and women’s networks, the node ‘Clinical depression’ was connected to almost the

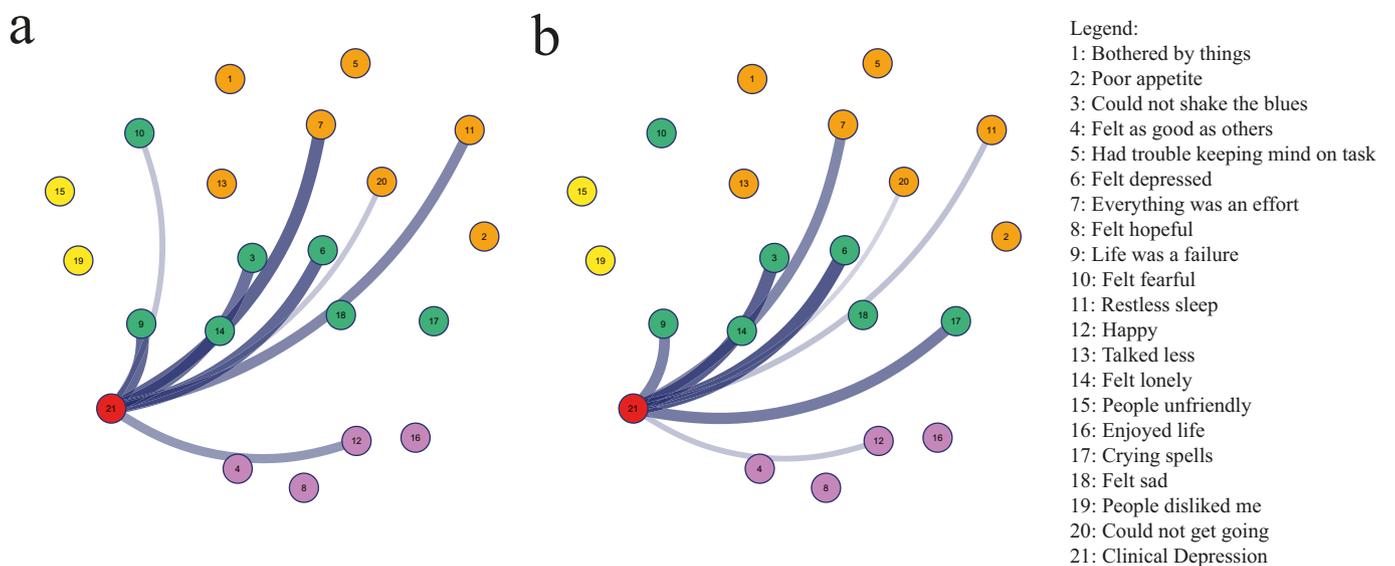


Fig. 3. Connections between depressive symptoms and Clinical Depression as an external factor (node 21). Panel ‘a’: women ($n=108,391$). Panel ‘b’: men ($n=93,561$). Edges’ widths were scaled to the closest higher value than any absolute edge weight in order to facilitate comparisons across sexes. Edges were curved to avoid overlapping. Items were colored by dimensions (factors); Green: depressive affect, Purple: positive affect; Orange: somatic; Yellow: interpersonal.

same symptoms, although these connections were relatively unstable (wide BCIs, not shown). In women, ‘7.Everything was an effort’ (0.052) had the strongest connection with this node, while in men, it was ‘6.Felt depressed’ (0.057). This node did not play a crucial role in the networks as it had the least strength, betweenness, and closeness values in men and women (not shown). The edge invariance test revealed that men and women presented non-invariance in three edges (corrected $p < 0.004$): in women, ‘11.Restless sleep’ and ‘12.(not) happy’ had stronger connections to ‘21.Clinical depression’ than in the men’s network. In men, ‘17.Crying spells’ was strongly connected to ‘21.Clinical depression’, which was absent in women.

3.4. Network estimation including Limitations associated with a depressive episode as an external factor

Networks showing the connections between symptoms and Limitations are in Fig. 4. The gLasso procedure yielded relatively stable connections between ‘21.Limitations’ and nine and eleven symptoms in men and women, respectively (BCIs not shown). Fig. S3 displays networks with all edges across the 21 nodes. In both networks, ‘3.Could not shake the blues’ had the strongest connection with Limitations (0.135 and 0.144 in women and men, respectively). Men and women presented non-invariance in three edges: In men, ‘17.Crying spells’ and ‘6.Felt depressed’ were more strongly connected to ‘Limitations’ than women ($p < 0.004$ and $p < 0.05$, respectively). In women, ‘5.Had trouble keeping in mind’ was strongly connected to ‘Limitations’ ($p < 0.004$) while this connection was absent in men’s network.

3.5. Sensitivity analyses

After re-estimating the symptom networks accounting for socio-demographic variables, the network structures were statistically different by sex (corrected p -value < 0.0005) (Fig. S4). Specifically, 30 edges were non-invariant by sex, of which 23 were the same as in the main analyses (colored in Table S4). Nine edges that were statistically different by sex in the comparison without accounting for sociodemographic characteristics were no longer different, meaning that they were explained by this adjustment.

4. Discussion

4.1. Summary of key findings

This study described and compared depressive symptomatology of men and women from the general adult population living in France. Our results revealed that symptom network structures differed, with 32 connections being non-invariant by sex. In contrast, when examining individual symptoms’ relevance, we found similar patterns with ‘Felt sad’ and ‘Felt depressed’ playing a key role in activating other depressive symptoms in both sexes. To our knowledge, this is the first study to link depressive symptoms with a diagnosis of Clinical depression from a network perspective. In men, presenting ‘Crying spells’ may play an important role in a clinician’s judgment when diagnosing depression. Similarly, in women, ‘Restless sleep’ and ‘(not) happy’ may act as red flags in detecting depression in clinical settings. Furthermore, we identified eleven and nine symptoms, in women and men, respectively, that are likely to be implied in the self-recognition process of a depressive episode. Three of them were non-invariant by sex; specifically, in men ‘Felt depressed’ and ‘Crying spells’ were strongly associated with self-reporting limitations in the past six months, while in women, it was ‘Having troubles keeping things in mind’.

4.2. Comparison with the literature

Regarding centrality measures within each network, in our study, ‘Felt sad’ and ‘Felt depressed’ were the most central symptoms for both men and women. Comparison with other studies may be limited since few articles have analyzed networks in the general population by sex from the CES–D. Despite different contexts, populations, and measurement tools, these results are consistent with other works. For example, one Brazilian study in which authors used a revised version of the CES–D in a youth sample found that these two symptoms were the most central (Manfro et al., 2021). Similarly, although using the EURO–D scale, one Finnish study found that ‘Depressed mood’ was the most central symptom among older European adults (Savelieva et al., 2021). Another study comparing depressive networks between oncological patients and the general population found that ‘Depressed mood’ was the most central symptom in the latter (Hartung et al., 2019). Other

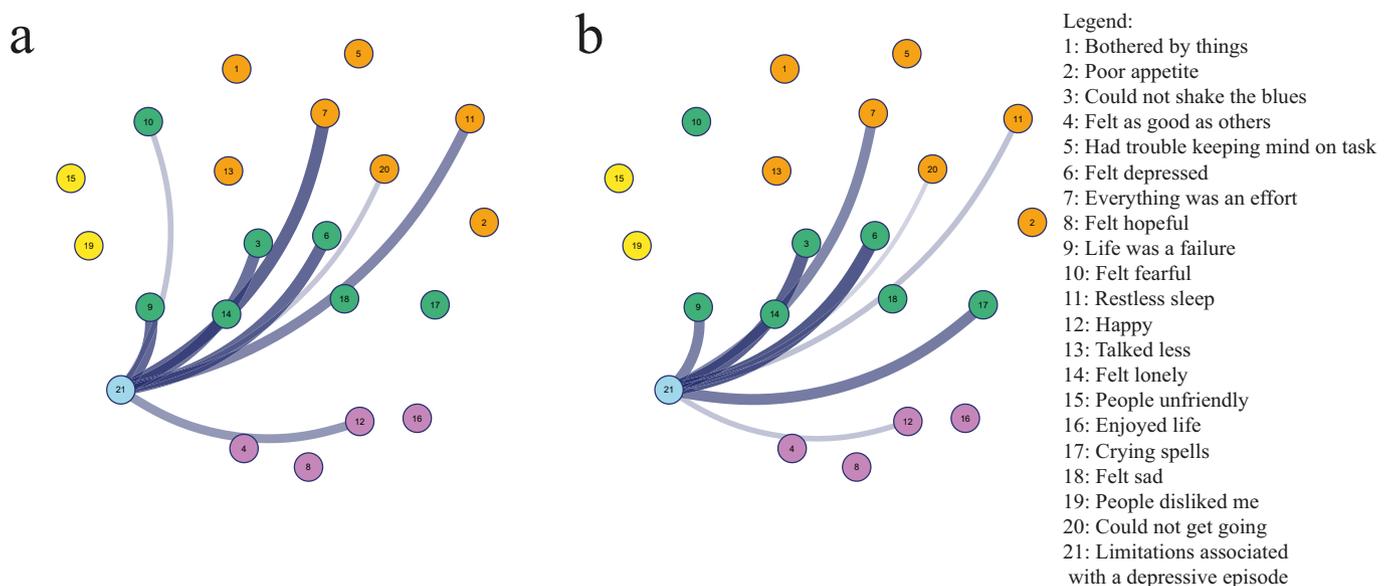


Fig. 4. Connections between depressive symptoms and Limitations associated with a depressive episode as an external factor (node 21). Panel ‘a’ women ($n=108,391$). Panel ‘b’: men ($n=93,561$). Edges’ widths were scaled to the closest higher value than any absolute edge weight to facilitate comparisons across sexes. Edges were curved to avoid overlapping. Items were colored by dimensions (factors); Green: depressive affect, Purple: positive affect; Orange: somatic; Yellow: interpersonal.

studies based on clinical samples have also found symptoms evoking ‘Depressed mood’ as the most central (van Borkulo et al., 2015), suggesting that men and women from the general population report depressive symptomatology similarly to clinical populations. This is also in line with a systematic review that analyzed depressive symptoms according to gender and found no significant differences in reported symptoms in studies that included community versus clinical samples (Cavanagh et al., 2017).

Moving to comparisons across networks, contrary to Steen et al. (2021) and Vetter et al. (2021), our study revealed sex differences in network structures and several edges but not in global strength. Both studies differ from ours in their sample size, sample population, and measurement tools, limiting once again comparisons across studies. In particular, Steen et al. used data from 9700 subjects with a Major Disorder Diagnosis and derived network models from DSM and non-DSM symptoms. Vetter et al. used data from a smaller treatment-seeking sample ($n = 590$) who answered the clinician-administered Hamilton Depression Rating Scale.

4.3. Interpretation of our findings

From a clinical perspective, our study allowed us to identify important symptoms in men’s and women’s networks. Sadness and depressed feelings were the two most central symptoms, suggesting that the activation of these two symptoms can trigger or maintain the depressive networks. These two symptoms and ‘Not feeling happy’ evoke one of the two cardinal symptoms of the DSM-V diagnostic criterion, the ‘Depressed Mood’. Therefore, men and women from the general population likely experience this cardinal dimension similarly, implying that, to some extent, the severity of the depressive state depends on the activation of Sadness and depressed feelings. Also, ‘Life was a failure’ played an important role in the men’s network by linking most of the strongest connections between the ‘positive affect’ dimension and the rest of the network. This finding could inform clinicians and patients on how to activate the positive dimension more effectively by targeting the feeling of failure. Similarly, in women, the feeling of ‘Could not get going’ linked information between the somatic complaints dimension (‘Had trouble keeping mind on task’ and ‘Everything was an effort’ in particular) and the ‘depressive affect’ dimension. Therefore, identifying that symptom in women and targeting it with appropriate interventions (e.g., cognitive behavioral therapy) may help to overcome somatic symptoms. Finally, since ‘Felt sad’ had the highest closeness value in men and women, it seems reasonable to affirm that interventions targeting this feeling could quickly impact other depressive symptoms.

From a gendered perspective, the fact that men and women had differences in network structures that were not explained by differences in socio-demographic characteristics at baseline, as the sensitivity analyses demonstrated, is a novel and robust finding and could eventually guide the development of a theoretical framework to explain the underlying symptom mechanisms that relate to gender norms, roles, or attitudes towards depression. For example, we could speculate that there may be a causal pathway in men, different than in women (i.e., based on edges statistically different from women) starting at a central symptom towards more distal symptoms: say, ‘felt sad’ activates a feeling of ‘failure’ which in turn activates a sense of impossibility ‘to keep going’ that strongly affects concentration (‘have trouble keeping in mind’), which in turn activates a negative self-perception (‘not as good as others’). This interpretation does not presume unequivocal directions between symptoms. Instead, these connections must be understood as chains including feedback loops, meaning that the same symptom chain can be read backward. Likewise, the intrapersonal feeling of ‘not as good as others’ (i.e., lack of self-esteem) could be at the onset of the depressive network in men, which can be conceptually related to documented factors associated with an increased risk of depression, such as lack of self-perceived social support (Grav et al., 2012; Grønli et al., 2022). Further qualitative studies are needed to elucidate these possible

activation mechanisms likely shaped by gender roles, norms, or attitudes.

Some interesting clues suggesting gender bias in the diagnosis of Clinical depression deserve further discussion. In the men’s network, we found a significant connection between ‘Crying spells’ and clinical depression. This result is in contrast with what is commonly described by the masculinities literature, that gender socialization and gender norms influence men’s response to distress, reflected in their emotional restriction (i.e., less crying behavior) (Addis, 2008) and in their reluctance to seek help (Johnson et al., 2012). One possible explanation is that whenever a man presents this symptom in consultation, the clinician may interpret this sign as a severe symptom because it is less common. Therefore, disclosing this manifestation may act as a red flag coming from a man. Although women experienced this symptom more frequently than men, it was not connected to Clinical depression in their network, suggesting that either women do not present it in consultation or clinicians overlook it. Either way, these findings indicate that the presentation of ‘Crying spells’ may influence clinical judgment differently depending on whether patients are men or women.

Also, ‘Restless sleep’ was more strongly connected to Clinical depression in the women’s network than in men’s. Interestingly, while this symptom was women’s most frequently endorsed item, it was also the less central symptom within the network structure, meaning that its interconnections with other symptoms were relatively weak (i.e., the share variance between this symptom and others was relatively slight). Thus, women may experience this symptom and present it to their clinician frequently, not presenting any other core depressive symptoms. On the other hand, clinicians may make their diagnosis based almost exclusively on this frequent symptom, indicating different criteria or a wider definition of depression for women relative to men. Another explanation is that other symptoms or factors in the causal pathways between CES-D items and ‘Restless sleep’ may not be measured, leading to spurious connections. Either way, further research is needed to understand the diagnostic context. In particular, whether women are diagnosed based exclusively on somatic complaints without meeting other diagnostic criteria (i.e., suggesting overdiagnosis and medicalization) or over-present these complaints but underestimate others.

Networks including ‘Limitations’ allowed us to distinguish reliably depressive symptoms that may substantiate the recognition of one’s depressive episode. This is a relevant finding that could help understand what triggers men’s and women’s decision-making process to seek help, which, as mentioned before, starts at the intersection of recognizing symptoms and appraising them. In both networks, the same set of symptoms was connected to this external node, with two exceptions: ‘Had trouble keeping in mind’ and ‘Could not get going’ were connected to this node exclusively in women. Also, six symptoms (‘Could not shake out the blues’, ‘Felt depressed’, ‘Everything was an effort’, ‘Life was a failure’, ‘Felt fearful’, and ‘Crying spells’) connected to ‘Limitations’ were also found to be connected to ‘Clinical Depression’ and can be interpreted as those that are likely to be perceived as most severe by men and women who self-recognize their distress. Some of these symptoms were among the most central in both networks, in particular, ‘Felt depressed’, ‘Could not get going’, ‘Could not shake the blues’, ‘Everything was an effort’ and, ‘Life was a failure’ (Fig. 2), confirming their crucial role in activating and maintaining depressive networks.

Furthermore, three connections between symptoms and ‘Limitations’ were non-invariant by sex and may shed light on gender mechanisms implied in the self-recognition of a depressive episode. For example, ‘Crying spells’ and ‘Felt depressed’ were more strongly connected to ‘Limitations’ in men’s networks. Consistently with the connection between ‘Crying spells’ and ‘Clinical depression’, if this symptom is commonly attributed to femininity, we could expect these men to be severely depressed since ‘Crying’ can be perceived as a threat to their masculine identity, reinforcing their depressive state. This is in line with the assumption that strong adherence to hegemonic masculine norms puts men at a higher risk of mental health distress (Addis, 2008). On the

contrary, for some men, self-recognizing a depressive episode may indicate poor adherence to hegemonic masculinity. Thus, they may experience and express symptoms from a wide range of manifestations, including those stereotypically considered feminine. Either way, ‘Crying spells’ was strongly connected to both external nodes in men’s networks, indicating a continuum between self-recognition of this symptom, receiving a diagnosis, and adhering to it.

4.4. Limitations

Our study was mainly exploratory and hypothesis-generating; thus, it is important to mention its limitations. First, the CES-D has been designed for screening persons at risk of depression at the population level. Consequently, items only cover a few dimensions of depressive manifestations and probably fail to measure others. Other depressive network studies have shown that combining typical DSM-V and non-DSM-V items leads to clinically relevant networks (Fried et al., 2016). Future research should consider including other items, particularly gendered manifestations (e.g., risky behaviors, substance abuse, anger), that could lead to an in-depth understanding of depressive mechanisms in men and women.

Second, participants were asked about a history of diagnosis of depression, but, except for age at diagnosis, no other information was collected about the diagnostic context (e.g., use of antidepressants, use of psychotherapy, etc.). We made the assumption that the report of a previous diagnosis was accurate and that signs and symptoms of depression persisted in both sex groups. Indeed, symptoms could have evolved throughout the diagnosis and when participants responded to the CES-D. Although research has documented that depressive symptoms can persist for long periods (Colman et al., 2011; Sinkewicz et al., 2022; Tibubos et al., 2019), our conclusions drawn from networks including Clinical depression remain speculative. Likewise, we assumed that the report of Functional impairment associated with a depressive state was accurate and reliable. Even if this question did not strictly presume an MD diagnosis, participants who responded positively were still likely to be in emotional distress by the moment they self-administered the questionnaire because of its narrow time scope (six months).

Third, for the sake of simplicity, we could not account for other well-known factors that could have influenced depressive manifestations (e.g., comorbidities, treatment use, psychotherapy, cognitive variables etc.). Regarding cognitive or emotional variables, previous studies have documented that depressive symptomatology correlates with other cognition measures (Giannouli and Giannoulis, 2023), and specifically, negative affect (measured by the PANAS-X scale) can correlate with intelligence (Giannouli, 2023). Future research should address this gap.

Fourth, we used cross-sectional data, limiting our findings’ causal interpretation. Network analysis should consider longitudinal data when possible since this approach shows promising results in predicting direct associations across time points (Fried et al., 2017). Future research should examine the direction of the connections between the onset of symptoms and the eventual clinical diagnosis in men and women separately. Also, data was highly skewed (not shown). However, using Spearman’s rank correlation matrices as the input for our network estimation method was a robust compromise (i.e., polychoric and Spearman’s rank correlation matrices were highly correlated: 0.91 and 0.94, in men and women, respectively).

Five, missing items were treated with pairwise deletion. This method assumes that data is missing at random. However, participants with incomplete questionnaires were older and had higher levels of depression, although they endorsed fewer answers. This profile of participants could be considered a major violation of the assumption of data missing at random if incomplete questionnaires were related to the severity of the trait. However, the proportion of incomplete questionnaires was low relative to the number of complete questionnaires. Therefore, we considered the risk of selection bias as insignificant.

Last, networks were estimated from large samples. We privileged power (sensitivity), which implied that many edges were estimated. The assumption for sparsity could have been violated (i.e., some weak edges were false positives). Further, it has been reported that when comparing unequal sample sizes, the power of the NCT to detect any differences can be lowered, as it depends on the size of the smallest group (van Borkulo et al., 2017). In our case, men had the smallest group ($n = 93,561$), which we considered notably high.

4.5. Conclusion

Our gendered network analysis provided an overview of different dimensions of depressive symptomatology in men and women from the general population. Network structures differed, suggesting gender-specific mechanisms in activating symptoms and depressive states. Targeting symptoms evoking depressed moods with tailored interventions may serve to tackle depressive states in men and women. Also, our findings suggest that clinical judgment in the diagnosis of depression may not be gender-neutral. This potential gender bias may contribute to the underdiagnosis of depression in men. For instance, when diagnosing men, clinicians may consider symptoms such as ‘Crying spells’, as severe because men are less prone to report stereotypically feminine symptoms. Still, at the same time, they may be overlooking other important symptoms. Likewise, men presenting these stereotypically feminine symptoms in consultation may be indicative of severe depression because they challenge their masculinity. Last, gender differences in symptom connections to limitations associated with a depressive episode inform us about men’s and women’s pathways from the symptom perception to the decision-making process of help-seeking. Unlike women, in men, reporting ‘Crying spells’ is probably a sign of strong adherence to the diagnosis since this manifestation is associated with self-recognition as limited because of a depressive episode and with a previous diagnosis of depression.

Ethics approval and consent to participate

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures were approved by the Institutional Review Board of the French Institute of Health (INSERM). The Constances Cohort study has also been approved by the French Data Protection Authority (“Commission Nationale de l’Informatique et des Libertés”, CNIL). Written informed consent was obtained from all participants.

CRediT authorship contribution statement

Eugenia Alcalde: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Visualization, Writing – original draft, Writing – review & editing, Validation. **Alexandra Rouquette:** Conceptualization, Methodology, Validation, Writing – original draft. **Emmanuel Wiernik:** Conceptualization, Data curation, Validation. **Laurent Rigal:** Conceptualization, Formal analysis, Investigation, Methodology, Supervision, Validation, Writing – original draft, Writing – review & editing.

Declaration of competing interest

None.

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Appendix A. Supplementary data

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