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Depression and anxiety symptom networks in hemorrhoid patients: evidence from the UK biobank

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Abstract

Background Hemorrhoidal disease is highly prevalent and associated with significant psychological distress. However, the interplay between depression and anxiety symptoms and their variation across subgroups remains uncharacterized. This study identifies the key symptoms contributing to distress in these patients and explores subgroup differences to optimize mental health interventions.

Methods We analyzed data from 10,482 hemorrhoid patients in the UK Biobank and constructed Gaussian Graphical Models (GGMs) based on PHQ-9 and GAD-7 symptom scores. Network estimation was carried out using EBIC graphical lasso regularization, and centrality metrics including strength, betweenness, and closeness were calculated using the qgraph package. Subgroup comparisons by gender, smoking history, age, and time interval were performed using the NetworkComparisonTest with 1,000 bootstrap iterations.

Results The symptom network showed high stability ($CS = 0.75$), with "Sad mood" (*strength* = 1.41) and "Too much worry" (*betweenness* = 2.54) acting as central bridges between depressive and anxiety symptoms. Gender differences were pronounced: male and female networks differed significantly in both global strength ($S = 0.19$, $p = 0.03$) and structure ($M = 0.10$, $p = 0.01$), with women showing stronger emotion-cognition connections and men emphasizing somatic-behavioral linkages. Patients assessed ≥ 20 years after hemorrhoid diagnosis exhibited increased global connectivity ($S = 0.23$, $p = 0.02$) despite stable core architecture ($M = 0.07$, $p = 0.73$).

Conclusions "Sad mood" and "Too much worry" are key treatment targets in hemorrhoid-related psychopathology. Gender-stratified approaches, such as emotion-focused therapies for women and behavioral activation for men, may help disrupt the pain-distress cycle. Applying principles of network psychiatry could optimize integrated care for this underserved population.

Keywords Depression, Anxiety, Network Analysis, Hemorrhoids, UK Biobank

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Introduction

The bidirectional relationship between physical and mental health is increasingly acknowledged, with chronic physical conditions often exacerbating psychological distress, while mental disorders can, in turn, intensify physical symptoms [1, 2]. Among these conditions, Hemorrhoidal disease presents a distinctive case due to its high prevalence and limited understanding of psychological burden. It offers a paradigmatic model for exploring the psychosomatic interface, as it is characterized by a high global prevalence (approximately 40% in adults [3]) and the poorly investigated mental health sequelae linked to its chronic pathophysiology. Persistent pain and social stigma associated with anorectal disorders frequently contribute to depressive symptoms and anxiety, further exacerbated by patients' reluctance to seek support due to embarrassment and shame [4–8]. Beyond acute symptomatic phases characterized by pain, pruritus, and bleeding, the condition's histopathological basis in venous plexus hypertrophy and stromal degradation establishes a persistent vulnerability state, fostering anticipatory anxiety about symptom recurrence even during clinical quiescence [9, 10]. Notably, the temporal dimension of hemorrhoidal disease (e.g., duration) may differentially modulate symptom network architectures — a critical gap in current research. Despite growing evidence of this psychological toll, traditional research approaches have struggled to unravel the complex interplay of symptoms, often treating depression and anxiety as homogeneous constructs rather than dynamic networks of interacting elements.

Depression and anxiety in hemorrhoid patients are closely intertwined, sharing mechanisms such as maladaptive cognitive patterns and dysregulated stress responses [11, 12]. However, conventional methodologies reliant on aggregate symptom scores suffer from critical limitations in characterizing the nuanced interdependencies among discrete symptoms (e.g., Sad Mood or Excessive Worry) that collectively sustain psychological distress. This methodological constraint becomes particularly salient in populations with multifactorial psychological burdens, such as patients with hemorrhoidal disease, where psychopathology emerges not only from nociceptive signaling but also from socially mediated mechanisms — particularly stigma-induced self-isolation and avoidance of medical care. Network analysis — a novel methodological framework — provides a paradigm shift by mapping symptom-to-symptom interactions and identifying central nodes that may act as drivers of psychopathology [13]. By contrast to traditional models, this approach conceptualized mental disorders as systems of mutually reinforcing symptoms, thereby identifying potential pathways through which targeted interventions might disrupt the entire network [14]. For example, targeting a highly central symptom such as "Sad Mood" might alleviate broader depressive symptoms by weakening their interconnections.

Despite its transformative potential, network analysis remains unexplored in the study of mental health in hemorrhoid populations. To address this, we utilized data from the UK Biobank to construct the first symptom network of depression and anxiety for individuals with hemorrhoids. We employ GGMs to identify core symptoms and bridge edges and examine the variations of network characteristics across subgroups stratified by gender, age, smoking history, and the time interval between hemorrhoid diagnosis and mental health assessment. Through this approach, we aim to (1) elucidate mechanisms underlying psychological distress in this population, (2) prioritize intervention targets based on symptom centrality, and (3) advance the application of network theory in chronic disease research — a critical step toward personalized, mechanism-driven mental healthcare.

Methods

Study design and population

The UK Biobank is a large-scale prospective cohort study that enrolled 502,536 participants aged 37–73 years between 2006 and 2010, with longitudinal follow-ups spanning over a decade [15]. For the present analysis, we selected a subsample of 10,482 participants who met the inclusion criteria for investigating the association between hemorrhoidal disease and depression-anxiety symptom networks (Fig. S1).

Symptom assessment

Depression and anxiety symptoms were assessed using the Patient Health Questionnaire-9 (PHQ-9) and Generalized Anxiety Disorder-7 (GAD-7), two psychometrically robust instruments with well-established validity and reliability in both clinical and population-based studies [16, 17]. Participants rated the frequency of each symptom over the preceding two weeks on a 4-point Likert scale: 0 (not at all), 1 (several days), 2 (more than half the days), and 3 (nearly every day). Total scores ranged from 0 to 27 for the PHQ-9 (depression severity) and 0 to 21 for the GAD-7 (anxiety severity). Symptom-level data were extracted from questionnaires administered between October 2016 and July 2017, ensuring temporal alignment with hemorrhoidal disease diagnoses recorded in the UK Biobank.

Statistical analysis

Network analysis

All analyses were conducted in R (version 4.0.3). To address potential biases in estimating partial correlations caused by the ordinal nature of the PHQ-9 and GAD-7 items (e.g., Likert-scale responses with nonnormal

distributions), we constructed the network using Spearman's rank-order correlations [18]. Spearman's method is robust to non-normality and appropriately handles the rank-based structure of ordinal data, avoiding strong parametric assumptions required for Pearson correlations [19]. Networks were estimated and visualized using the qgraph and bootnet packages [20, 21]. Following established methodologies [22–24], we quantified the informational value of each item using its average standard deviation and assessed potential item redundancy via the "networktools" package's goldbricker function. A redundancy threshold of 0.25 was applied, and statistical significance was set at $p < 0.01$ to control for Type I error.

Given the continuous nature of symptom severity scores, a GGM was implemented using the extended Bayesian Information Criterion (EBIC) graphical lasso [25]. The primary analysis used $\gamma = 0.5$, following recommendations for psychological symptom networks [26]. Sensitivity analyses with γ values of 0 and 0.25 further confirmed the robustness and stability of the results. This approach employs regularization to shrink trivial partial correlations to zero, producing a sparse and interpretable network. Within the GGM framework, nodes represent individual symptoms (e.g., PHQ2 ["Sad Mood"], GAD3 ["Too Much Worry"]), while edges denote conditional dependencies between symptoms after adjusting for all other nodes. Edge colors encode directionality: blue for positive correlations, red for negative correlations, with thickness proportional to effect size (absolute partial correlation coefficient).

To assess node centrality, we used the centralityPlot function from the qgraph package to compute strength, betweenness, and closeness [21]. Strength centrality reflects a node's direct influence within the network, calculated as the sum of absolute edge weights connected to it. Betweenness centrality identifies bridging symptoms by measuring how frequently a node lies on the shortest path between other node pairs. Closeness centrality, defined as the inverse of the average shortest path length from a node to all others, indicates symptom propagation efficiency. Node predictability, defined as the proportion of variance explained by neighboring nodes (R^2), was estimated using the mgm package to evaluate symptom interdependence [27].

Estimation of network accuracy and stability

Network robustness was evaluated using non-parametric bootstrapping procedures in the bootnet package [21]. Edge weight accuracy was evaluated by generating 95% confidence intervals (CIs) from 1,000 bootstrap samples. Narrow CIs indicate greater estimation precision, while intervals that include zero suggest non-significant edges [28]. Centrality stability was examined through case-dropping bootstrap (1,000 permutations) to calculate the correlation stability coefficient (*CS-C*). This metric quantifies the maximum proportion of cases that can be removed while maintaining a correlation ≥ 0.70 between original and subset centrality estimates [29]. Following established guidelines, *CS-C* values ≥ 0.50 were considered acceptable, with values ≥ 0.75 indicating high stability.

Community detection algorithms

Based on prior comparisons evaluating community detection methods, we selected three algorithms that demonstrate high accuracy and low bias [30]. Community detection aims to identify cohesive subgroups within the network by grouping similar nodes, thereby uncovering latent structures [31]. However, the definitions and evaluation criteria for community detection remain contested within the academic field [32]. To address this complexity, algorithm selection was informed by their complementary strengths in capturing different network characteristics. Accordingly, we applied three widely used community detection algorithms: Louvain [33], Walktrap [34], and Fast Greedy [35].

Comparison of network characteristics

Subgroup analyses examined the moderating effects of demographic and clinical factors [36], including gender (male/female), smoking history (yes/no), age (< 65/≥65 years), and time interval (< 6 months/≥6 months, < 1 year/≥1 year, < 5 years/≥5 years, < 10 years/≥10 years, < 20 years/≥20 years). Network comparisons were conducted by using the NetworkComparisonTest package [37], evaluating global strength (sum of absolute edge weights) and edge-wise differences via 1,000 permutation tests.

Consistent with previous research [38], significant differences between the two networks were assessed separately using a two-tailed significance level of $P < 0.05$.

Results

Descriptive statistics and correlation analyses

Among the 10,482 included participants (mean age = 63.7 years, *SD* = 7.42; 52.85% female), the mean total scores for depressive and anxiety symptoms were 2.97 (*SD* = 3.93) on the PHQ-9 and 2.21 (*SD* = 3.49) on the GAD-7, indicating subclinical severity overall (Table 1). Individual symptom analysis revealed that "Sad Mood" (PHQ2: *M* = 0.52, *SD* = 0.79) and "Nervous" (GAD1: *M* = 0.47, SD = 0.72) were the most frequently endorsed symptoms (Table S1). Spearman correlation analyses (Fig. 1) demonstrated significant positive associations among all PHQ-9 and GAD-7 items (adjusted $p < 0.001$ after Bonferroni correction for 120 comparisons).

Table 1 Demographic characteristics of the study sample ($n = 10,482$)

Variables	
Age, mean (SD)	63.7 (7.42)
Sex, n (%)	
Male	4942 (47.15%)
Female	5540 (52.85%)
Smoking history, n (%)	
Yes	4507 (43.0%)
No	5975 (57.0%)
Time interval, n (%)	
< 6 months	571 (5.45%)
6 months to < 1 year	170 (1.62%)
1 year to < 5 years	1558 (14.86%)
5 years to < 10 years	2266 (21.62%)
10 years to < 20 years	3456 (32.97%)
≥ 20 years	2461 (23.48%)
PHQ-9 total, mean (SD)	2.97 (3.93)
GAD-7 total, mean (SD)	2.21 (3.49)

PHQ-9: nine-item Patient Health Questionnaire; GAD-7: seven-item Generalized Anxiety Disorder scale.

Network estimation

The Goldbricker analysis (redundancy threshold = 0.25, $p < 0.01$) confirmed the distinctiveness of all PHQ-9 and GAD-7 symptoms, with no redundant items identified. Figure 2 illustrates the GGM of the depression-anxiety symptom network, characterized by an average node predictability (R^2) of 0.49. Within the depressive symptom community, the strongest connection was observed between "Anhedonia" (PHQ1) and "Sad Mood" (PHQ2) (edge weight = 0.47), followed by "Sleep" (PHQ3) and "Energy" (PHQ4) (0.30), and "Sad Mood" (PHQ2) and "Guilt" (PHQ6) (0.21). In the anxiety community, the most prominent edges linked "Nervous" (GAD1) to "Restless" (GAD5) (0.41), followed by "Nervous" (GAD1) and "Afraid" (GAD7) (0.30), and "Control Worry" (GAD2) to "Too Much Worry" (GAD3) (0.24). A moderate cross-community bridge was identified between "Motor" (PHQ8) and "Control Worry" (GAD2) (0.17), suggesting a distinct pathway between psychomotor symptoms and anxiety-related cognitive processes.

Network centrality

Centrality metrics highlighted distinct symptom roles within the network (Fig. 3; Table 2). "Sad Mood" (PHQ2) demonstrated the highest strength centrality (1.41), followed by "Nervous" (GAD1: 1.33) and "Too Much Worry" (GAD3: 1.24), indicating their strong direct influence on the network. "Too Much Worry" (GAD3) emerged as the primary bridging symptom, evidenced by its highest betweenness centrality (2.54), while "Sad Mood" (PHQ2) and "Anhedonia" (PHQ1) showed the highest closeness centrality (1.37 and 1.35, respectively), reflecting rapid symptom propagation. In contrast, "Suicide" (PHQ9) exhibited the lowest strength (-1.81) and betweenness centrality (-1.44), underscoring its peripheral role in the network.

Network accuracy and stability

Bootstrap analyses confirmed robust network estimation. Edge weight accuracy was supported by narrow 95% confidence intervals across all connections (Figure S2), while case-dropping bootstrap revealed strong centrality stability, with correlation stability coefficients of 0.75 for strength and betweenness centrality (Figure S3). This indicates that 75% of the sample could be removed while maintaining over 70% correlation with original centrality rankings. Bootstrapped difference tests identified significant statistical distinctions between the strongest and weakest edges (Figure S4), as well as between the highest and lowest centrality indices (Figure S5). Sensitivity analyses across $\gamma = 0$, 0.25, and 0.5 confirmed the robustness of centrality estimates, with minimal variability observed across specifications. Key hub nodes (e.g., PHQ2, GAD3) retained consistent rankings, and the median range of centrality metrics was near zero (Table S4).

Network comparisons

Figures S6-S13 present subgroup comparisons of network centrality indices. The Network Comparison Test (NCT) revealed significant differences in both global strength ($S = 0.19$, $p = 0.03$) and network structure between males and females ($M = 0.10$, $p = 0.01$). Compared to the male network, the female network displayed increased edge weights for Anhedonia – Sad Mood ($diff = 0.09$, $p = 0.001$) and Energy – Appetite ($diff = 0.06$, $p = 0.007$), indicating stronger associations between these symptoms in females. Similarly, higher edge weights were observed in females for Energy – Suicide ($diff = 0.005$, $p = 0.023$), Energy – Nervous ($diff = 0.014$, $p = 0.008$), Motor – Control worry ($diff = 0.10$, $p = 0.003$), Control worry – Relax ($diff = 0.05$, $p = 0.042$), and Relax – Irritable ($diff = 0.06$, $p = 0.011$).

Conversely, males exhibited stronger edge weights for Appetite – Motor ($diff = 0.06$, $p = 0.021$), Sad Mood – Suicide ($diff = 0.05$, $p = 0.029$), Sleep – Control worry ($diff = 0.03$, $p = 0.015$), Sad Mood – Restless ($diff = 0.06$, $p = 0.002$), Suicide – Too Much Worry ($diff = 0.007$, $p = 0.050$), Energy – Control worry ($diff = 0.04$, $p = 0.003$), and Appetite – Restless ($diff = 0.004$, $p = 0.038$).

Comparisons based on time interval (< 20 years vs. ≥20 years) revealed a significant difference in global strength ($S = 0.23$, $p = 0.02$), while network structure differences were not significant ($M = 0.07$, $p = 0.73$). The < 20-year network exhibited stronger edge weights for Sleep – Energy ($diff = 0.05$, $p = 0.036$) and Guilt – Motor ($diff = 0.06$, $p = 0.047$). Conversely, the ≥ 20-year network revealed increased edge weights for Appetite – Restless

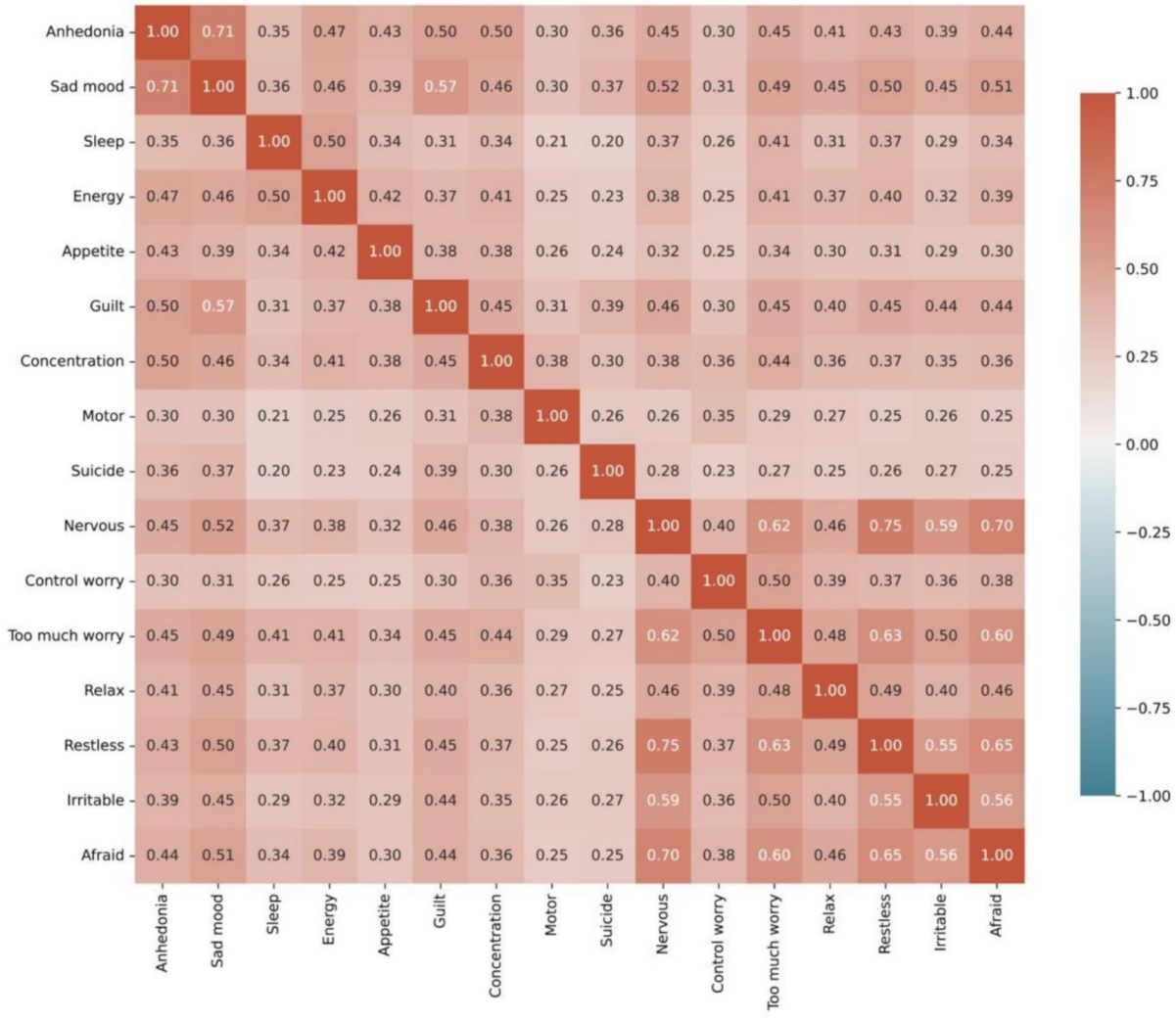


Fig. 1 Heatmap of the Spearman correlation matrix. The number in each box is the Spearman correlation coefficient. Only significant coefficients are presented after the Bonferroni correction test ($p < 0.05/(16*15/2)$)

(*diff* = 0.07, $p = 0.003$), Relax – Irritable (*diff* = 0.06, $p = 0.038$), and Guilt – Nervous (*diff* = 0.06, $p = 0.013$). These findings suggest that while the overall network structure remains stable over time, specific symptom associations shift, potentially reflecting evolving psychopathological mechanisms across time since diagnosis.

Discussion

This study represents the first application of network analysis to elucidate the structural relationships between depressive and anxiety symptoms in hemorrhoid patients. By leveraging a large-scale cohort from the UK Biobank, we identified distinct symptom clusters, core drivers of psychological distress, and gender-specific network configurations. These findings deepen our understanding of psychosomatic dynamics in chronic anorectal conditions and offer actionable insights for personalized mental health interventions. Moreover, they challenge traditional symptom aggregation approaches that may obscure critical mechanistic pathways.

Beyond direct physical discomfort, hemorrhoid patients face unique psychosocial challenges that may amplify emotional distress. The intimate nature of anorectal symptoms often evokes profound shame and perceived stigma, particularly in cultures where bowel dysfunction remains a taboo subject [39]. This stigma can lead to delayed help-seeking, social withdrawal, and maladaptive coping behaviors (e.g., avoiding defecation), creating a vicious cycle where physiological symptoms exacerbate psychological distress and vice versa. Lifestyle disruptions, such as impaired work productivity due to pain or avoidance of physical and social activities, further compound the emotional burden. These latent psychosocial mechanisms (shame, stigma, lifestyle interference)

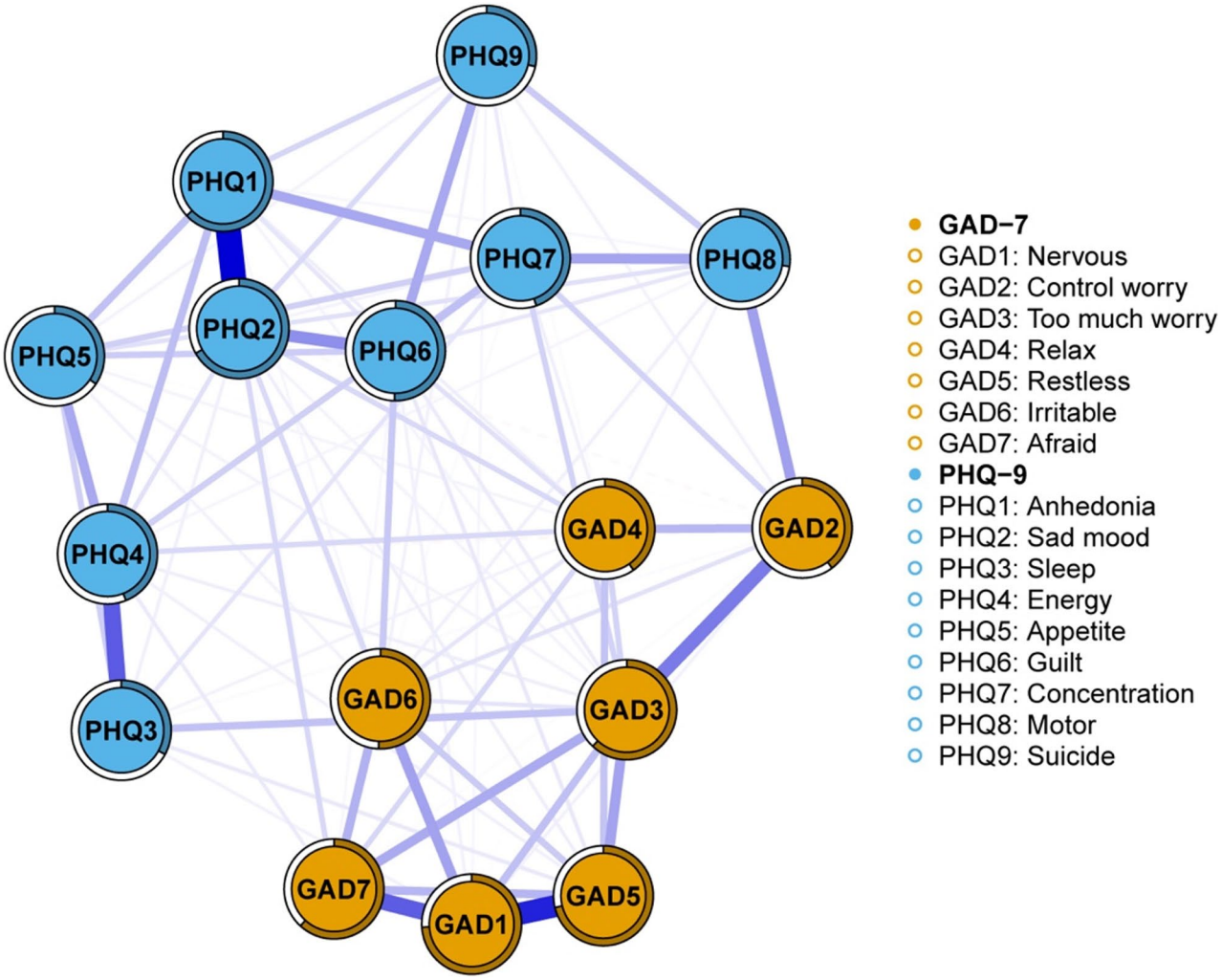


Fig. 2 Network model of depression and anxiety in patients with hemorrhoids. Blue lines are positive connections. The thickness of the line represents the connection strength. Colored areas in the rings surrounding the nodes represent the node predictability (percentage of the variance of a given node explained by surrounding nodes)

likely contribute to the prominence of sad mood and excessive worry observed in our network, suggesting that interventions should address both physical symptoms and their psychosocial sequalae.

Community detection algorithms identified two primary symptom clusters: depression (PHQ-9 items) and anxiety (GAD-7 items), a division that aligns with established diagnostic taxonomies. While the Louvain and Fast Greedy methods produced clinically interpretable groupings, the Walktrap algorithm uniquely isolated PHQ-8 ("Motor") into a separate community, highlighting a critical nuance. Psychomotor symptoms, typically regarded as behavioral manifestations of depression, may play a dual role in hemorrhoid patients by contributing to pain-related functional impairment. Specifically, reduced physical activity associated with motor retardation could exacerbate venous congestion in the rectal area, potentially creating a feedback loop in which psychological distress amplifies physiological pathology. This interpretation is consistent with recent neuroimaging studies showing that psychomotor slowing in depression is linked to reduced connectivity within the motor cortex-basal ganglia circuits, which overlap with pain modulation networks [40]. Future research integrating actigraphy data could help determine whether targeted motor rehabilitation (e.g., graded exercise) can disrupt this maladaptive cycle.

Centrality analyses identified PHQ2 ("Sad Mood"), GAD1 ("Nervous"), and GAD3 ("Too Much Worry") as the network's core nodes. PHQ2's dominance across strength and closeness centrality underscores its dual role as both a primary driver and rapid propagator of distress — a finding consistent with its designation as a diagnostic cornerstone for major depressive disorder in DSM-5 and

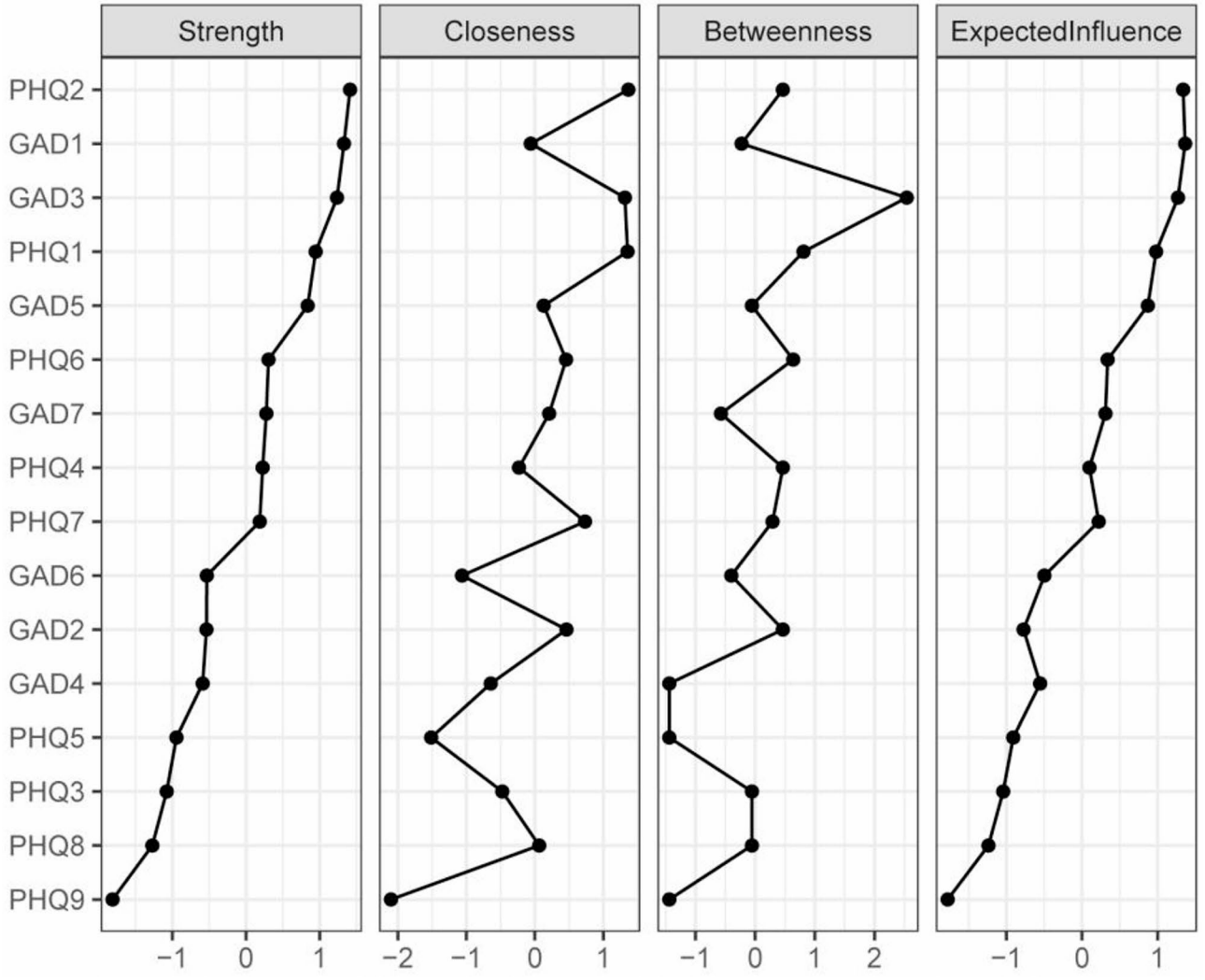


Fig. 3 Centrality measures of depression and anxiety symptoms within the symptom network among hemorrhoid patients. The figure displays centrality metrics (i.e., strength, betweenness, closeness, and expected influence) of depression and anxiety symptoms in the network (z-scores)

ICD-10 [41, 42]. Importantly, these emotional symptoms likely interact with comorbid physical sequelae of hemorrhoidal disease. Chronic pain and bleeding can directly disrupt sleep architecture via nociceptive signaling to arousal centers [43], while fear of symptom exacerbation may promote social withdrawal — both established risk factors for depression and anxiety. Moreover, somatic mediators such as pelvic floor hypertonicity (exacerbated by anxiety-related muscle tension) [44] and gut microbiome alterations (linked to stress-induced dysbiosis) [45] could further bridge psychological distress and anorectal pathology. Future studies should explicitly model these comorbidities to disentangle their causal roles in symptom networks.

Existing research highlights a strong association between pain-related symptoms and suicidal ideation, particularly in cases of severe disease and diminished quality of life, suggesting that suicidal ideation may become more prominent as symptom severity escalates [46]. However, in our study, PHQ-9 ("Suicide") exhibited a peripheral network influence. This finding is not entirely unexpected, as hemorrhoidal disease, while distressing, does not typically reach the pain severity levels linked to heightened suicide risk in conditions such as cancer or neuropathic pain syndromes [47].

We propose that the peripheral role of suicidal ideation in our cohort reflects both clinical and contextual moderators. Clinically, hemorrhoidal symptoms rarely produce the unremitting, high-intensity pain associated with suicidal crises in terminal conditions. Contextually, the UK Biobank population ($M = 63.7$ years) may possess greater psychosocial resilience through established social support networks and coping strategies. However, this does not preclude suicide risk in specific subgroups, particularly those experiencing severe functional impairment, social isolation, or comorbid psychiatric conditions.

Table 2 List of nodes, their predictability, and their centrality Estimation

Nodes	Symptom	Predictability (R^2)	Centrality			
			Betweenness	Closeness	Strength	ExpectedInfluence
PHQ1	Anhedonia	0.63	0.81	1.35	0.95	0.98
PHQ2	Sad mood	0.67	0.46	1.37	1.41	1.34
PHQ3	Sleep	0.33	-0.05	-0.48	-1.08	-1.04
PHQ4	Energy	0.44	0.46	-0.23	0.23	0.10
PHQ5	Appetite	0.34	-1.44	-1.51	-0.94	-0.91
PHQ6	Guilt	0.50	0.64	0.46	0.31	0.34
PHQ7	Concentration	0.45	0.29	0.73	0.19	0.22
PHQ8	Motor	0.27	-0.05	0.06	-1.27	-1.24
PHQ9	Suicide	0.29	-1.44	-2.10	-1.81	-1.78
GAD1	Nervous	0.74	-0.23	-0.06	1.33	1.36
GAD2	Control worry	0.40	0.46	0.46	-0.54	-0.77
GAD3	Too much worry	0.62	2.54	1.32	1.24	1.27
GAD4	Relax	0.40	-1.44	-0.64	-0.59	-0.55
GAD5	Restless	0.71	-0.05	0.13	0.84	0.87
GAD6	Irritable	0.51	-0.40	-1.06	-0.53	-0.50
GAD7	Afraid	0.62	-0.57	0.21	0.28	0.31

Qualitative studies report that patients with "embarrassing" chronic illnesses often describe feeling like a burden, which can exacerbate hopelessness [48]. Future research should incorporate quality-of-life measures (e.g., SF-36) and social connectedness metrics to identify vulnerable individuals in whom suicidal ideation may become central. Patient narratives could further clarify how disease-related shame transitions into hopelessness in severe cases. Furthermore, cultural and psychosocial factors likely influence symptom reporting [49]. In populations where mental health stigma persists, individuals may underreport suicidal ideation despite experiencing latent risk. Traditional self-report measures might, therefore, underestimate the true prevalence of suicidal thoughts. Future research should consider multimodal assessments incorporating implicit cognitive measures, such as attentional bias tasks, to capture underlying risk more accurately.

The high betweenness centrality of "Too much worry" (GAD3) underscores its bridging function within the symptom network, likely due to worry's broad impact on both emotional and physiological processes. Chronic worry is known to amplify responses to adverse events such as pain and bleeding, thereby intensifying subjective distress [50]. Similarly, "Nervous" (GAD1) may exacerbate discomfort in hemorrhoid patients by increasing sympathetic nervous system activity, leading to vasoconstriction and local ischemia [44]. These interactions suggest that targeting core symptoms like worry could improve both psychological and physical well-being.

From a neurobiological perspective, worry serves as both a cognitive amplifier and a somatic stressor. Chronic worry dysregulates prefrontal-amygdala circuits, heightening threat perception and sympathetic arousal [51] — mechanisms that may contribute to vasoconstriction and ischemic pain in hemorrhoidal disease. Conversely, nociceptive signals from inflamed tissues may sustain anxiety via interoceptive pathways, creating a bidirectional feedback loop [52]. This interplay suggests that interventions targeting worry, such as metacognitive therapy or mindfulness-based stress reduction, could disrupt these self-reinforcing cycles. Indeed, a review of studies on irritable bowel syndrome (IBS) patients found that cognitive-behavioral therapy aimed at reducing worry not only alleviated anxiety but also decreased visceral hypersensitivity, suggesting its potential transdiagnostic applicability to populations with hemorrhoidal conditions [53].

The gender-specific symptom architectures uncovered here offer critical insights into the paradox of hemorrhoid epidemiology [54, 55]. While men constitute over 80% of clinical cases due to cultural stigma deterring women from seeking care for "embarrassing" anorectal conditions [39], our network analysis reveals that women experience a more tightly woven tapestry of emotional and cognitive symptoms. Specifically, women showed significantly stronger associations between Anhedonia and Sad Mood ($diff = 0.09$, $p = 0.001$), and between Motor symptoms and Control Worry ($diff = 0.10$, $p = 0.003$). These patterns align with gender-specific distress expression: women tend to internalize psychological suffering through affective-cognitive channels, potentially mediated by estrogen's neuromodulatory effects on limbic-prefrontal circuits [56, 57]. Conversely, men's stronger Appetite – Motor ($diff = 0.06$, $p = 0.021$) and Sad Mood – Restless ($diff = 0.06$, $p = 0.002$) connections reflect an externalizing phenotype, where distress manifests via somatic and behavioral pathways. This divergence may

stem from socialization processes that encourage emotional expression in women but stigmatize vulnerability in men [58], as well as androgen-mediated integration of metabolic and motor systems [59, 60]. Clinically, these differences necessitate tailored approaches: women may benefit more from emotion-focused therapies (e.g., mindfulness), while men may respond better to behavioral activation targeting somatic symptoms.

Chronic pain-induced prefrontal-amygdala decoupling may drive the externalizing phenotype of male depression through dual synergistic mechanisms. Mechanistically, attenuated dorsolateral prefrontal cortex (DLPFC) regulatory control over the amygdala disrupts emotion regulation, as evidenced by functional connectivity deficits in chronic pain populations [61]. Concurrently, hyperconnectivity between the motor cortex and amygdala facilitates the maladaptive translation of affective distress into motor agitation, a neural signature of pain chronification [62]. This neural reorganization is consistent with the irritable restlessness that characterizes male-specific depression, a phenotype defined by somatic manifestations (e.g., psychomotor restlessness) and a tendency toward anger rather than the prototypical low mood [63].

These divergences underscore the necessity of gender-tailored approaches: for females, interventions that target emotional-cognitive interactions, such as mindfulness-based cognitive therapy or affect regulation strategies, may be particularly effective in addressing the combined effects of anhedonia and worry-related motor symptoms. For males, strategies that engage somatic awareness and behavioral activation, such as structured physical activity or goal-oriented therapy, may better address the externalized nature of mood-related symptoms.

The cross-sectional analysis of symptom networks across time since diagnosis subgroups revealed a complex association between illness chronicity and network topology, challenging conventional phase-based categorizations. In comparisons between shorter time intervals (6 months, 1 year, 5 years, and 10 years post-diagnosis), no significant differences in global strength or overall network structure were observed (all $p > 0.05$). However, individuals with a time intervals of ≥ 20 years exhibited distinct network reorganization compared to those with < 20 years ($S = 0.23$, $p = 0.02$). This pattern suggests that detectable network-level alterations in symptom architecture may emerge only after prolonged exposure to chronic disease processes, aligning with reports of decadal-scale neuroplastic adaptations in conditions like diabetic neuropathy [64] and rheumatoid arthritis [65]. Epidemiological evidence reinforces this chronicity interpretation: in a large clinical cohort of over 21,000 hemorrhoid patients, only 9.3% required surgical intervention [66], while real-world studies report postoperative recurrence rates ranging from 0 to 56.5% depending on procedural type [67]. This natural history implies that our ≥ 20-year cohort likely represents persistent disease trajectories with episodic exacerbations, rather than recovery-oriented pathways — a critical distinction for population health models prioritizing long-term condition management.

Notably, the enhanced Sleep – Energy (*diff* = 0.05, $p = 0.036$) and Guilt – Motor (*diff* = 0.06, $p = 0.047$) connections in the < 20-year cohort may indicate early compensatory mechanisms, while stronger Appetite – Restless (*diff* = 0.07, $p = 0.003$) and Guilt – Nervous (*diff* = 0.06, $p = 0.013$) associations in the ≥ 20-year group could reflect cumulative pathophysiological processes (e.g., central sensitization) interacting with psychosocial stressors over time.

The lack of detectable differences at earlier time points may be due to methodological limitations in current network comparison tools, which may lack the sensitivity to capture subtle or heterogeneous changes in the early stages of illness, as well as the influence of cohort variability and transient symptomatology that may obscure emerging patterns. Alternatively, it could suggest the existence of cumulative pathophysiological thresholds, such as central sensitization or vagal remodeling, that take years to alter network topology significantly.

Clinically, the prominent centrality of PHQ2 ("Sad Mood") and GAD3 ("Too Much Worry") suggests they serve as dual leverage points for psychological intervention in patients with hemorrhoidal disease. To translate this insight into actionable strategies, we propose a multifaceted approach. First, worry-related symptoms may be mitigated using brief cognitive restructuring techniques aimed at reframing catastrophic thoughts, such as "What if this bleeding means something serious?" These interventions could be delivered via mobile applications during symptom flare-ups, offering accessible and timely support. Second, mood disturbance and pelvic dysfunction may be jointly targeted by combining pelvic floor biofeedback with affect regulation strategies, such as diaphragmatic breathing paired with positive mental imagery, aiming to reduce both physiological tension and emotional distress. Third, given the role of inflammation in both hemorrhoidal symptoms and anxiety, dietary protocols incorporating curcumin supplementation alongside soluble fiber may offer dual benefits by attenuating inflammatory cytokines and alleviating gut-brain axis dysregulation [68].

To enhance ecological validity, future studies could apply natural language processing to patient forums or self-reported diaries to identify how core symptoms are expressed in real-world contexts (e.g., "I'm terrified my bleeding means cancer"), thereby refining network models with lived-experience data. Additionally, ecological

momentary assessment (EMA) may enable continuous symptom tracking during hemorrhoidal crises [69, 70], capturing critical fluctuations in mood and worry that indicate windows of vulnerability and present opportunities for just-in-time, adaptive intervention. This integrative symptom-network-informed framework could advance biopsychosocial care models by bridging proctological treatment with psychological precision.

This study possesses several notable strengths. First, by utilizing the UK Biobank's extensive epidemiological data, we systematically characterized the depression-anxiety symptom network in individuals with hemorrhoidal disease, a population that has historically been underrepresented in psychosomatic research. By applying network psychometrics, we identified robust transdiagnostic features (e.g., Sad Mood-Worry interactions) that may serve as stage-specific markers across the illness continuum. Second, our multi-layered validation approach, which includes sensitivity analyses confirming the stability of edge weights and subgroup comparisons stratified by gender, time interval, and smoking, enhances confidence in the replicability of the core network architecture. Crucially, these findings challenge the symptom-equivalence assumption in psychiatric nosology, urging clinicians to prioritize cardinal nodes (PHQ2/GAD3) rather than treating all symptoms as equally pivotal.

Some key limitations should be acknowledged. First, the cross-sectional design precludes causal inference about temporal symptom progression; observed ≥ 20-year network differences might reflect survivor bias rather than actual chronicity effects. Second, reliance on self-report instruments introduces potential measurement biases (e.g., underreporting of stigmatized symptoms like suicidality), though this concern is mitigated by using validated scales (PHQ-9/GAD-7) with established psychometric properties. Third, several potentially important clinical covariates were not available for inclusion in the network models. Specifically, we lacked objective measures of hemorrhoid severity, detailed prior history of diagnosed anxiety or depressive disorders, and information on current medication use (particularly psychotropic medications such as antidepressants or anxiolytics). The absence of these variables is a notable limitation, as they could act as confounding factors or modifiers influencing the observed symptom relationships and network structure. For instance, antidepressant use might attenuate connections involving anxiety or depressive symptoms, while greater hemorrhoid severity might strengthen somatic-psychological symptom links. Future studies incorporating these clinical details are needed to better delineate their roles within the symptom network. Finally, generalizability remains uncertain given the UK-centric sample's age range (40–69 years). Future multinational cohorts incorporating endoscopic staging and digital phenotyping could address these gaps.

This study reveals key structural features of depression-anxiety networks in hemorrhoid patients, identifying "Sad Mood", "Anhedonia" and "Too Much Worry" as central symptoms that exacerbate both psychological distress and physical discomfort. These nodes may serve as psychosomatic bridges, where cognitive-emotional processes interact with pain-signaling pathways. The discovery of sex-specific symptom patterns, with emotional clustering more common in women and behavioral linkages more prominent in men, offers a biological and psychosocial foundation for developing personalized care strategies. By targeting these network hubs through integrated mind-body interventions, clinicians may more effectively disrupt the reinforcing cycle of rectal pain and psychological distress. Our findings advocate for a shift from conventional symptom management to network-informed precision medicine in the treatment of chronic pelvic disorders.

Supplementary Information

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Supplementary Material 1

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Author contributions

ZH: conceptualization, data curation, formal analysis, data interpretation, writing-original draft; XL: writing-review and editing; YH: writing-review and editing; XY: writing-review and editing; ZY: writing-review and editing; JH: supervision, writing-review & editing; HHEY: writing-review and editing; WM: project administration, supervision, writing-review & editing. All authors reviewed and approved the final version of the manuscript.

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Data availability

The datasets supporting the conclusions of this article are available in the website of the UK Biobank (Application ID: 105783).

Declarations

Ethics approval and consent to participate

All the UK Biobank participants gave written informed consent before data collection. The UK Biobank has full ethical approval from the NHS National Research Ethics Service (reference number:16/NW/0274). The UK Biobank study was conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent to participate in the study. This research was conducted using UK Biobank resource under project number 105783.

Consent for publication

Not applicable.

Competing interests
HHEY reported receiving research grants from the Health Bureau of the Government of the Hong Kong SAR (HMRF) and Viatris, outside the submitted work.

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References

1. Doherty AM, Gaughran F. The interface of physical and mental health. Soc Psychiatry Psychiatr Epidemiol. 2014;49:673–82.
2. Ohrnberger J, Fichera E, Sutton M. The relationship between physical and mental health: A mediation analysis. Soc Sci Med. 2017;195:42–9.
3. Sheikh P, Régnier C, Goron F, Salmat G. The prevalence, characteristics and treatment of hemorrhoidal disease: results of an international web-based survey. J Comp Eff Res. 2020;9(17):1219–32.
4. Huang Z, Huang J, Leung CK, Zhang CJ, Akinwunmi B, Ming W-K. Hemorrhoidal disease and its genetic association with depression, bipolar disorder, anxiety disorders, and schizophrenia: a bidirectional Mendelian randomization study. Hum Genomics. 2024;18(1):27.
5. Kostev K, Konrad M, Smith L, Krieg S. Hemorrhoids are associated with an increased risk of depression in germany: A retrospective cohort study in primary care outpatients. J Psychiatr Res. 2024;175:381–5.
6. Dibley L, Norton C, Whitehead E. The experience of stigma in inflammatory bowel disease: an interpretive (hermeneutic) phenomenological study. J Adv Nurs. 2018;74(4):838–51.
7. Dancey C, Hutton-Young S, Moye S, Devins G. Perceived stigma, illness intrusiveness and quality of life in men and women with irritable bowel syndrome. Psychol Health Med. 2002;7(4):381–95.
8. Diseth TH, Emblem R, Vandvik IH. Adolescents with anorectal malformations and their families: examples of hidden psychosocial trauma. Family Syst Med. 1995;13(2):215.
9. Bayraktar N, Berhuni O, Berhuni MS, Zeki O, Sener ZT, Sertbas G. Effectiveness of lifestyle modification education on knowledge, anxiety, and postoperative problems of patients with benign perianal diseases. J Perianesthesia Nurs. 2018;33(5):640–50.
10. Lohsiriwat V. Hemorrhoids: from basic pathophysiology to clinical management. World J Gastroenterology: WJG. 2012;18(17):2009.
11. Amangalieva G, Ivic-Britt RK, Carmack HJ, Holiday S. Belonging, affirmation, safety, and efficacy (BASE): an integrative model for shame resilience, social support, and humor in r/hemorrhoid. Health Commun 2024:1–12.
12. Cioli V, Gagliardi G, Pescatori M. Psychological stress in patients with anal fistula. Int J Colorectal Dis. 2015;30:1123–9.
13. Luke DA, Harris JK. Network analysis in public health: history, methods, and applications. Annu Rev Public Health. 2007;28(1):69–93.
14. Borsboom D, Cramer AO. Network analysis: an integrative approach to the structure of psychopathology. Ann Rev Clin Psychol. 2013;9(1):91–121.
15. Sudlow C, Gallacher J, Allen N, Beral V, Burton P, Danesh J, Downey P, Elliott P, Green J, Landray M. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. PLoS Med. 2015;12(3):e1001779.
16. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med. 2006;166(10):1092–7.
17. Martin A, Rief W, Klaiberg A, Braehler E. Validity of the brief patient health questionnaire mood scale (PHQ-9) in the general population. Gen Hosp Psychiatry. 2006;28(1):71–7.
18. Zhou Y, Lv X, Wang L, Li J, Gao X. What increases the risk of gamers being addicted? An integrated network model of personality–emotion–motivation of gaming disorder. Comput Hum Behav. 2023;141:107647.
19. Bishara AJ, Hittner JB. Testing the significance of a correlation with nonnormal data: comparison of pearson, spearman, transformation, and resampling approaches. Psychol Methods. 2012;17(3):399.
20. Epskamp S, Cramer AO, Waldorp LJ, Schmittmann VD, Borsboom D. Qgraph: network visualizations of relationships in psychometric data. J Stat Softw. 2012;48:1–18.
21. Epskamp S, Borsboom D, Fried EI. Estimating psychological networks and their accuracy: A tutorial paper. Behav Res Methods. 2018;50:195–212.
22. de Vos JA, Radstaak M, Bohlmeijer ET, Westerhof GJ. The psychometric network structure of mental health in eating disorder patients. Eur Eat Disorders Rev. 2021;29(4):559–74.
23. Mullarkey MC, Marchetti I, Beevers CG. Using network analysis to identify central symptoms of adolescent depression. J Clin Child Adolesc Psychol. 2019;48(4):656–68.
24. Marchetti I. Hopelessness: a network analysis. Cogn Therapy Res. 2019;43(3):611–9.
25. Williams DR. Bayesian Estimation for Gaussian graphical models: structure learning, predictability, and network comparisons. Multivar Behav Res. 2021;56(2):336–52.
26. Epskamp S, Fried EI. A tutorial on regularized partial correlation networks. Psychol Methods. 2018;23(4):617–34.
27. Borgatti SP. Centrality and network flow. Social Networks. 2005;27(1):55–71.
28. Chernick MR. Bootstrap methods: A guide for practitioners and researchers. Wiley; 2011.
29. Costenbader E, Valente TW. The stability of centrality measures when networks are sampled. Social Networks. 2003;25(4):283–307.
30. Christensen AP, Garrido LE, Guerra-Peña K, Golino H. Comparing community detection algorithms in psychometric networks: A Monte Carlo simulation. Behav Res Methods. 2024;56(3):1485–505.
31. Bedi P, Sharma C. Community detection in social networks. Wiley Interdisciplinary Reviews: Data Min Knowl Discovery. 2016;6(3):115–35.
32. Fortunato S, Hric D. Community detection in networks: A user guide. Phys Rep. 2016;659:1–44.
33. Cordeiro M, Sarmento RP, Gama J. Dynamic community detection in evolving networks using locality modularity optimization. Social Netw Anal Min. 2016;6:1–20.
34. Pons P, Latapy M. Computing communities in large networks using random walks. J Graph Algorithms Appl. 2006;10(2):191–218.
35. Clauset A, Newman ME, Moore C. Finding community structure in very large networks. Phys Rev E—Statistical Nonlinear Soft Matter Phys. 2004;70(6):066111.
36. Ravindranath G, Rahul B. Prevalence and risk factors of hemorrhoids: a study in a semi-urban centre. Int Surg J. 2018;5(2):496–9.
37. Jones P, Jones MP. Package 'networktools'. In.: CRAN-R; 2018.
38. Liu R, Chen X, Qi H, Feng Y, Su Z, Cheung T, Jackson T, Lei H, Zhang L, Xiang Y-T. Network analysis of depressive and anxiety symptoms in adolescents during and after the COVID-19 outbreak peak. J Affect Disord. 2022;301:463–71.
39. Haidary AS, Miri SAS, Fayaz Y. Gender disparity in hemorrhoid cases: cultural and Socio-Economic barriers to women's healthcare access. Int J Gen Med 2024:3987–8.
40. Borsook D, Upadhyay J, Chudler EH, Becerra L. A key role of the basal ganglia in pain and analgesia–insights gained through human functional imaging. Mol Pain. 2010;6:27.
41. Edition F. Diagnostic and statistical manual of mental disorders. Am Psychiatric Assoc. 2013;21(21):591–643.
42. ICD W. Classification of mental and behavioural disorders. *Clinical descriptions and diagnostic guidelines Geneve: World Health Organization* 1992.
43. Alexandre C, Miracca G, Holanda VD, Sharma A, Kourbanova K, Ferreira A, Bicca MA, Zeng X, Nassar VA, Lee S. Nociceptor spontaneous activity is responsible for fragmenting non–rapid eye movement sleep in mouse models of neuropathic pain. Sci Transl Med. 2024;16(743):eadg3036.
44. Ziegler MG. Psychological stress and the autonomic nervous system. Primer on the autonomic nervous system. edn.: Elsevier; 2012. pp. 291–3.

45. Zhang H, Wang Z, Wang G, Song X, Qian Y, Liao Z, Sui L, Ai L, Xia Y. Understanding the connection between gut homeostasis and psychological stress. J Nutr. 2023;153(4):924–39.
46. Bahk W-M, Park S, Jon D-I, Yoon B-H, Min KJ, Hong JP. Relationship between painful physical symptoms and severity of depressive symptomatology and suicidality. Psychiatry Res. 2011;189(3):357–61.
47. Fishbain DA, Lewis JE, Gao J. The pain suicidality association: a narrative review. Pain Med. 2014;15(11):1835–49.
48. Muse K, Johnson E, David AL. A feeling of otherness: A qualitative research synthesis exploring the lived experiences of stigma in individuals with inflammatory bowel disease. Int J Environ Res Public Health. 2021;18(15):8038.
49. Xiao Y, Lindsey MA. Racial/ethnic, sex, sexual orientation, and socioeconomic disparities in suicidal trajectories and mental health treatment among adolescents transitioning to young adulthood in the USA: A population-based cohort study. Adm Policy Mental Health Mental Health Serv Res. 2021;48(5):742–56.
50. Olatunji BO, Wolitzky-Taylor KB, Sawchuk CN, Ciesielski BG. Worry and the anxiety disorders: A meta-analytic synthesis of specificity to GAD. Appl Prev Psychol. 2010;14(1–4):1–24.
51. Rauch SL, Shin LM, Phelps EA. Neurocircuitry models of posttraumatic stress disorder and extinction: human neuroimaging Research—Past, present, and future. Biol Psychiatry. 2006;60(4):376–82.
52. Berntson GG, Khalsa SS. Neural circuits of interoception. Trends Neurosci. 2021;44(1):17–28.
53. Kinsinger SW. Cognitive-behavioral therapy for patients with irritable bowel syndrome: current insights. Psychol Res Behav Manage 2017:231–7.
54. Riss S, Weiser FA, Schwameis K, Riss T, Mittlböck M, Steiner G, Stift A. The prevalence of hemorrhoids in adults. Int J Colorectal Dis. 2012;27:215–20.
55. Johanson JF, Sonnenberg A. The prevalence of hemorrhoids and chronic constipation: an epidemiologic study. Gastroenterology. 1990;98(2):380–6.
56. Sun Q, Li G, Zhao F, Dong M, Xie W, Liu Q, Yang W, Cui R. Role of Estrogen in treatment of female depression. Aging. 2024;16(3):3021–42.
57. Goldstein I, Giraldi A, Kodigliu A, Van Lunsen H, Marson L, Nappi R, Pfaus A, Salonia A, Traish A, Vardi Y. Physiology of female sexual function and pathophysiology of female sexual dysfunction. Sex Medicine: Sex Dysfunctions Men Women Health Publications Paris 2004:683–748.
58. Chuick CD, Greenfeld JM, Greenberg ST, Shepard SJ, Cochran SV, Haley JT. A qualitative investigation of depression in men. Psychol Men Masculinity. 2009;10(4):302.
59. Asarian L, Geary N. Modulation of appetite by gonadal steroid hormones. Philos Trans R Soc Lond B Biol Sci. 2006;361(1471):1251–63.
60. Jardí F, Laurent MR, Kim N, Khalil R, De Bundel D, Van Eeckhaut A, Van Helleputte L, Deboel L, Dubois V, Schollaert D. Testosterone boosts physical activity in male mice via dopaminergic pathways. Sci Rep. 2018;8(1):957.
61. Apkarian AV, Sosa Y, Sonty S, Levy RM, Harden RN, Parrish TB, Gitelman DR. Chronic back pain is associated with decreased prefrontal and thalamic Gray matter density. J Neurosci. 2004;24(46):10410–5.
62. Bushnell MC, Čeko M, Low LA. Cognitive and emotional control of pain and its disruption in chronic pain. Nat Rev Neurosci. 2013;14(7):502–11.
63. Martin LA, Neighbors HW, Griffith DM. The experience of symptoms of depression in men vs women: analysis of the National comorbidity survey replication. JAMA Psychiatry 2013, 70(10).
64. Abou-El-Hassan H, Dia B, Choucair K, Eid SA, Najdi F, Baki L, Talih F, Eid AA, Kobeissy F. Traumatic brain injury, diabetic neuropathy and altered-psychiatric health: the fateful triangle. Med Hypotheses. 2017;108:69–80.
65. Bekkelund SI, Pierre-Jerome C, Husby G, Mellgren SI. Quantitative cerebral MR in rheumatoid arthritis. AJNR Am J Neuroradiol. 1995;16(4):767–72.
66. Bleday R, Pena JP, Rothenberger DA, Goldberg SM, Buls JG. Symptomatic hemorrhoids: current incidence and complications of operative therapy. Dis Colon Rectum. 1992;35(5):477–81.
67. Lohsiriwat V, Sheikh P, Bandolon R, Ren D-L, Roslani AC, Schaible K, Freitag A, Martin M, Yaltirik P, Godeberge P. Recurrence rates and Pharmacological treatment for hemorrhoidal disease: A systematic review. Adv Therapy. 2023;40(1):117–32.
68. Kaufmann FN, Gazal M, Bastos CR, Kaster MP, Ghisleni G. Curcumin in depressive disorders: an overview of potential mechanisms, preclinical and clinical findings. Eur J Pharmacol. 2016;784:192–8.
69. Colombo D, Fernández-Álvarez J, Patané A, Semonella M, Kwiatkowska M, García-Palacios A, Cipresso P, Riva G, Botella C. Current state and future directions of technology-based ecological momentary assessment and intervention for major depressive disorder: a systematic review. J Clin Med. 2019;8(4):465.
70. Smith KE, Juarascio A. From ecological momentary assessment (EMA) to ecological momentary intervention (EMI): past and future directions for ambulatory assessment and interventions in eating disorders. Curr Psychiatry Rep. 2019;21:1–8.

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