

The backbone symptoms of depression: a network analysis after the initial wave of the COVID-19 pandemic in Macao

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ABSTRACT

Background: The coronavirus disease 2019 (COVID-19) pandemic disrupted the working lives of Macau residents, possibly leading to mental health issues such as depression. The pandemic served as the context for this investigation of the network structure of depressive symptoms in a community sample. This study aimed to identify the backbone symptoms of depression and to propose an intervention target. **Methods:** This study recruited a convenience sample of 975 Macao residents between 20th August and 9th November 2020. In an electronic survey, depressive symptoms were assessed with the Patient Health Questionnaire-9 (PHQ-9). Symptom relationships and centrality indices were identified using directed and undirected network estimation methods. The undirected network was constructed using the extended Bayesian information criterion (EBIC) model, and the directed network was constructed using the Triangulated Maximally Filtered Graph (TMFG) method. The stability of the centrality indices was evaluated by a case-dropping bootstrap procedure. Wilcoxon signed rank tests of the centrality indices were used to assess whether the network structure was invariant between age and gender groups. Results: Loss of energy, psychomotor problems, and guilt feelings were the symptoms with the highest centrality indices, indicating that these three symptoms were backbone symptoms of depression. The directed graph showed that loss of energy had the highest number of outward projections to other symptoms. The network structure remained stable after randomly dropping 50% of the study sample, and the network structure was invariant by age and gender groups. Conclusion: Loss of energy, psychomotor problems and guilt feelings constituted the three backbone symptoms during the pandemic. Based on centrality and relative

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influence, loss of energy could be targeted by increasing opportunities for physical activity.

Subjects Psychiatry and Psychology, Public Health, Mental Health, COVID-19 **Keywords** Depression, Survey, Network analysis, COVID-19, Macao

INTRODUCTION

At the end of 2019, China first reported novel coronavirus pneumonia cases in Wuhan (World Health Organization, 2020b) and it was named the coronavirus disease 2019 (COVID-19) in February 2020 (World Health Organization, 2020a). In order to contain the COVID-19 outbreak and control health-related hazards rapidly and effectively, governments at national and regional levels implemented some travel bans and quarantine regulations (Centers for Disease Control & Prevention, 2021; GOV.UK, 2021; TRAVELBANS, 2021). For cities reliant on tourism, travel restrictions and quarantine regulations would inevitably lead to large-scale economic difficulties and labor market rigidity (Mulder, 2020; Sbai, 2020; Uğur & Akbıyık, 2020; World Tourism Organization, 2020). As the casino capital of the world, Macao may have suffered more than other cities (Direcção dos Serviços de Estatística e Censos, 2021a, 2021b). Economic disruptions are known to trigger mental health problems such as depression (Ennis, Hobfoll & Schröder, 2000; Madianos et al., 2011), anxiety (Crayne, 2020), or post-traumatic stress symptoms (Ennis, Hobfoll & Schröder, 2000).

An online survey of Macao residents reported that 7.7% of the participants suffered from significant financial losses and 11.5% of them had severe depressive symptoms (*Macao Daily News, 2021b*). It has been confirmed that even without meeting the diagnostic criteria for major depressive disorder (MDD), having depressive symptoms is associated with adverse consequences, such as increased dysfunction (*Geiselmann & Bauer, 2000*), lower quality of life (*Bertha & Balázs, 2013*), and an increased risk for suicidal behaviors (*Balázs et al., 2013*; *Hegerl, 2016*). For example, a street survey in Macao reported that about 26% of young participants had suicidal ideation in the past 3 months (*Macao Daily News, 2021a*). The COVID-19 pandemic served as the context for this study of depressive symptoms ("depression" hereinafter) among residents in Macao, with the aim of identifying a possible intervention target.

Traditionally, research about the epidemiology and etiology of major depression follows the latent factor approach (*Everett*, 2013). This approach postulates that depression is the unobserved entity that is manifested by observable symptoms called indicators (*Schmittmann et al.*, 2013). In this view, depression is the common cause of the observed symptoms, and without it, the symptoms would have zero correlations with each other (*Brown*, 2006; *Everett*, 2013; *Schmittmann et al.*, 2013). This is contradicted by the finding that anhedonia, hopelessness or tiredness usually correlated with each other even when the diagnostic criteria for MDD were not fulfilled (*Borsboom*, 2008; *Santos et al.*, 2017). This implies that the traditional approach may inadequately describe the complexity and dynamics of depression (*Marchetti*, 2018; *Mullarkey, Marchetti & Beevers*, 2019).

An alternative approach, called network analysis, focuses instead on symptoms and their relations, without assuming that a latent factor causes the symptoms (*Borsboom & Cramer, 2013*). Unlike the latent variable approach, the symptoms are considered "active ingredients of mental disorders" instead of mere by-products (*Borsboom & Cramer, 2013*). Although the debate regarding the pros and cons of each approach continues (*Epskamp, Rhemtulla & Borsboom, 2017*; *Guyon, Falissard & Kop, 2017*), network analysis provides insight into how these symptoms are associated and interconnected, and what symptoms can serve as prevention or intervention targets (*Borsboom & Cramer, 2013*; *Cramer et al., 2016*; *Cramer et al., 2010*; *Epskamp, Rhemtulla & Borsboom, 2017*).

Although several studies using the network approach have probed the association patterns of various psychiatric conditions among different subpopulations during the COVID-19 pandemic (*Bai et al.*, 2021; *Di Blasi et al.*, 2021; *Li et al.*, 2022; *Wang et al.*, 2020), few have focused on tourism-dependent areas like Macao. Previous studies revealed that the network structure of mental health symptoms in various subpopulations might differ by age, gender, or health status (*Hartung et al.*, 2019; *Shim et al.*, 2020; *Wang et al.*, 2020). For this reason we examined age and gender as factors for subgroup analyses.

Examining the interaction of depression symptoms was undertaken with three specific aims: (1) to describe directional relationships among depressive symptoms; (2) to compare the pattern of symptoms across gender and age groups; and (3) to identify potential prevention or intervention targets.

METHODS

Setting and participants

This cross-sectional study was conducted from August 20 to November 9, 2020, after the initial wave of the COVID-19 pandemic in Macao. The initial wave is defined as the interval between the first recorded COVID-19 case (January 22, 2020) and the last recorded local case of the first wave (March 28, 2020). (*Macau Daily, 2020*; *Tencent, 2021*). From March 29, 2020 to August 2, 2021, there were no local infection but only imported cases (*BBC News, 2021*; *Macau Daily, 2021*). Participants were invited to participate in an online survey through advertisements in major social network platforms (specifically: WeChat, Facebook, and Instagram). To be eligible, participants had to be: (1) residing in Macao during the COVID-19 pandemic; (2) 18 years of age or above; (3) able to read and understand Chinese; and (4) provided informed consent. The study protocol was approved by the Institutional Review Board (IRB) of Beijing Anding Hospital, Capital Medical University.

Measures

Depressive symptoms were assessed with the self-rated Patient Health Questionnaire - 9 items (PHQ-9), Chinese version (*Wang et al., 2014; Xu, Wu & Xu, 2007*). The PHQ-9 asks about nine symptoms: anhedonia, sadness, sleep, energy, appetite, guilt, concentration, psychomotor changes, and suicidal ideation (*Kroenke, Spitzer & Williams, 2001; Spitzer, Kroenke & Williams, 1999*). These are rated from 0 (not at all) to 3 (nearly every day), with higher scores indicating more severe symptoms. The Chinese version of PHQ-9 is

psychometrically validated and has good properties (*Xu, Wu & Xu, 2007*; *Yu et al., 2012*). PHQ-9 was the chosen instrument because its items directly correspond to the symptoms of the Diagnostic and Statistical Manual of Mental Disorders (DSM).

Network analysis

First, the data were verified if they are suitable for network analysis by checking item distributions. All items were not normally distributed so partial polychoric correlations were calculated (Beard et al., 2016). These partial correlations were used to estimate a directed, and weighted network using the Triangulated Maximally Filtered Graph (TMFG) method (Massara, Di Matteo & Aste, 2017). TMFG method distinguishes influencing and influenced nodes based on the concept of node dependence (Jacob et al., 2016). To identify important symptoms, three centrality measures were examined: strength, betweenness, and closeness. For each symptom, the outgoing and incoming strength were compared (Kenett et al., 2010; Kenett et al., 2011). The difference between outgoing and incoming strength is known as node influence (or relative importance), with higher values indicating greater influence (Christensen, 2018). Subsequently, the stability of the centrality indices was checked by dropping between 30-50% of cases. Finally, the indices were checked if they were invariant by age group (≤ 28 years vs. ≥ 29 years) and gender (*Epskamp*, Borsboom & Fried, 2018). Please refer to Table 1 for a description of the network properties of interest, what they represent, and how they are calculated. The pattern of symptom relations in the directed network was further validated by comparing it to an undirected network estimated by the extended Bayesian information criterion (EBIC) graphical lasso (glasso) method. Figure 1 shows the procedure flow of this study.

All analytical procedures were performed in the R language (*R Core Team, 2020*) using the packages bootnet, networktools, NetworkToolbox, psych, and qgraph (*Christensen, 2018; Epskamp, Borsboom & Fried, 2018; Epskamp et al., 2012; Jones, 2020; Revelle, 2020*).

RESULTS

In all, 975 persons participated (women: 65.0%, 31.1 ± 11.5 years; men: 35.0%, 27.8 ± 10.0 years) in the survey. Most participants were well-educated (*i.e.*, undergraduate/college or higher: 78.5%) and were unmarried (61.4%).

Node centrality and node influence

Loss of energy, psychomotor problems, and guilt feelings were identified as the central items in strength (outgoing and incoming), betweenness, and closeness. The same symptoms had the most influence except that concentration difficulty was ranked higher than guilt feelings (Table 2). Loss of energy, psychomotor problems, guilt feelings, difficulty in concentration had positive relative influence values (Table 2). Figure 2A displays the undirected network of PHQ-9 symptoms, and Figure 2B displays the directed network of PHQ-9 symptoms. The directed graph showed that loss of energy had the highest number of outward projections to other symptoms (Figure 2B).

Table 1 Directed Network properties and their calculation.								
Network property	Intuitive meaning	Calculation						
1. Node centrality	More important nodes are central, less important nodes are peripheral							
a. In-(out-) strength	How well a node is directly connected to other nodes (Epskamp, Borsboom & Fried, 2018)	(an edge with direction) <i>ending</i> in a given node (<i>Guo et al.</i> , 2011). Out-strength: the sum of the weighted number of arcs						
b. Betweenness	How often a node lies in the shortest path between pairs of nodes (<i>Freeman</i> , 1978) or being "in the middle" of other nodes (<i>Hansen</i> , <i>Shneiderman & Smith</i> , 2011).	starting from a given node (<i>Guo et al.</i> , 2011). Betweenness of node X is: 1/(n-1)(n-2) × sum of number of shortest arcs/ number of arcs that pass through node X (<i>Rubinov & Sporns</i> , 2010).						
c. Closeness	How easy it is for a given node to reach other nodes without relying on intermediary nodes (<i>Leavitt</i> , 1951)	Closeness of node X is: The reciprocal of the average distance (with direction) between X and all other nodes (<i>Rubinov & Sporns</i> , 2010).						
2. Relative influence	The relative degree of incoming and outgoing edges	Positive values indicate higher outgoing strength relative to incoming strength. Negative values indicate higher incoming strength relative to outgoing strength (<i>Christensen</i> , 2018).						
3. Stability of centrality indices	How well the network structure is preserved when taking subsets of cases.	Subsamples of 70%, 60% and 50% were randomly drawn from the full sample, each with 1,000 replications. The ranking of centrality indices was averaged over replications and correlated to their ranking in the full sample (<i>Epskamp</i> , <i>Borsboom & Fried</i> , 2018).						
4. Invariance of centrality indices by age (28 years and below <i>vs.</i> 29 and above) and gender groups	Whether the important symptoms differ by age or gender	Separate networks were developed by age group and gender. Then, the hypothesis that the ranks of the PHQ-9 symptoms were similar between groups was tested using the paired Wilcoxon sign rank test.						

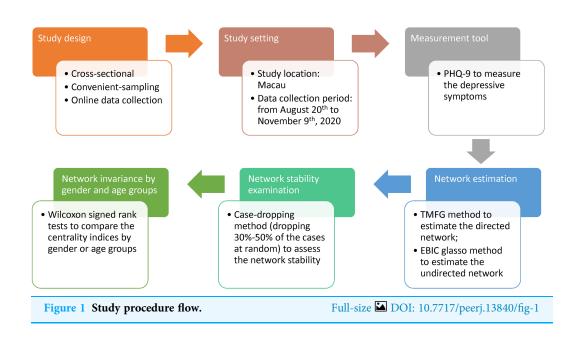


Table 2 Centrality measures of the nine depressive symptoms (sorted in descending order of outgoing strength).

PHQ-9 symptom	Strength		Betweenness	Closeness	
	Outgoing	Incoming	Relative influence		
D4: Loss of energy	3.05	2.61	0.08	12	4.09
D8: Psychomotor problems	2.82	2.60	0.04	6	4.14
D6: Guilt feelings	2.43	2.35	0.02	8	3.88
D7: Difficulty in concentration	2.09	1.95	0.04	2	3.55
D2: Sad mood	1.61	1.66	-0.02	2	3.35
D5: Appetite change	1.48	1.67	-0.06	0	3.43
D1: Anhedonia	1.22	1.317	-0.04	0	3.13
D3: Sleep problems	1.06	1.25	-0.08	0	3.16
D9: Suicidal ideation	0.98	1.324	-0.15	0	3.20

		the case-dropping n	

	70% subsample retained	60% subsample retained	50% subsample retained
In-strength	0.75	0.76	0.76
Out-strength	0.93	0.93	0.93
Betweenness	0.95	0.94	0.95
Closeness	0.71	0.71	0.72

Stability of centrality indices

The correlation of the symptom ranks in each centrality index between the subsamples and the full sample was 0.71 or higher (Table 3), indicating that the network structure remained stable after randomly dropping up to 50% of the study sample. (*Epskamp*, *Borsboom & Fried*, 2018)

Invariance of centrality indices

The Wilcoxon signed rank tests showed that outgoing strength, incoming strength, betweenness, and closeness did not vary by age or gender groups (all *p* values > 0.05; Tables 4 and 5). Figure 2 shows that the central symptoms are the same in undirected and directed networks (Figure 2A and 2B). Figures 3 and 4 show the z-score-transformed centrality indices of PHQ-9 symptoms by gender and by age group.

DISCUSSION

This study found that loss of energy, psychomotor problems, and guilt feelings are the most important symptoms among Macao residents after the initial wave of COVID-19. The results remained the same even when the following factors were varied: (i) sample size, (ii) age or gender, or (iii) estimation method (directed or undirected).

The finding that loss of energy has the highest strength centrality, indicates that it is the nexus of depressive symptoms in community-based setting, which is consistent with

Table 4	Centrality	indices	of PHQ	9-9 syı	mptoms	by s	gender.
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	Outgoing strength		Incoming strength		Betweenness		Closeness	
	Males	Females	Males	Females	Males	Females	Males	Females
D1: Anhedonia	1.57	1.60	1.74	1.68	0	2	3.47	3.38
D2: Sad mood	2.58	1.18	2.42	1.31	8	0	3.97	3.10
D3: Sleep problems	1.17	1.00	1.26	1.24	0	0	2.93	3.13
D4: Loss of energy	2.53	3.12	2.35	2.56	10	13	3.90	4.01
D5: Appetite change	1.09	1.49	1.31	1.63	0	0	3.22	3.38
D6: Guilt feelings	1.74	2.40	1.66	2.33	4	7	3.49	3.84
D7: Difficulty in concentration	2.93	2.06	2.70	1.97	8	2	4.27	3.53
D8: Psychomotor problems	2.48	2.79	2.33	2.58	2	6	3.90	4.09
D9: Suicidal ideation	1.03	0.97	1.36	1.30	0	4	3.05	3.15
Wilcoxon's signed rank test W ⁺			$W^{+} = 23$		$W^{+} = 13$		$W^{+} = 18$	
	$W^{-} = 23$		$W^{-} = 22$		$W^{-} = 15$		$W^{-} = 27$	
	p = 1.0		p = 1.0		p = 1.0		p = 0.64	

Note:

W⁺: the sum of positive differences between male and female scores, W⁻: the sum of negative differences between male and female scores.

Table 5	Centrality	indices	of PHQ-9	symptoms	by age group.
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	Outgoing strength		Incoming strength		Betweenness		Closeness	
	Ages 18-28	Ages 29-68	Ages 18-28	Ages 29-68	Ages 18-28	Ages 29-68	Ages 18-28	Ages 29-68
D1: Anhedonia	1.10	2.62	1.31	2.56	0	8	3.03	4.15
D2: Sad mood	1.82	3.12	1.93	2.84	4	12	3.44	4.46
D3: Sleep problems	0.98	1.57	1.22	1.72	0	0	2.93	3.56
D4: Loss of energy	2.70	2.12	2.05	2.23	8	4	3.43	3.94
D5: Appetite change	1.43	1.14	1.62	1.31	2	0	3.26	2.90
D6: Guilt feelings	1.38	2.56	1.56	2.01	2	8	3.22	3.58
D7: Difficulty in concentration	2.48	2.36	2.48	2.11	4	2	3.94	3.66
D8: Psychomotor problems	2.87	1.52	2.41	1.82	10	0	3.83	3.29
D9: Suicidal ideation	1.02	1.00	1.19	1.39	0	0	2.92	3.31
Wilcoxon's signed rank test	$W^{+} = 18$		$W^{+} = 14$		$W^{+} = 13$		$W^+ = 9.5$	
	$W^{-} = 27$		$W^{-} = 31$		$W^{-} = 15$		$W^- = 35.5$	
	p = 0.64		p = 0.34		p = 0.93		p = 0.12	

Note:

W⁺: the sum of positive differences between male and female scores, W⁻: the sum of negative differences between male and female scores.

another network analysis conducted in mainland China (*Wang et al., 2020*). Loss of energy refers to a feeling of tiredness, fatigue or having little energy (*Billones, Kumar & Saligan, 2020*), and it is a very prevalent symptom in depression (*Angst & Dobler-Mikola, 1984*; *Buchwald & Rudick-Davis, 1993*; *Corfield, Martin & Nyholt, 2016*; *Pae et al., 2007*; *Reyes-Gibby et al., 2006*), especially in people who somatize their depressive symptoms, a tendency found in East Asians (*Stahl, 2002*). The *Hinz et al.* (*2016*) study revealed that loss of energy had the highest factor loading in the PHQ-9, confirming that loss of energy is a core symptom of depression. Previous neuronal pathway studies also showed that chronic

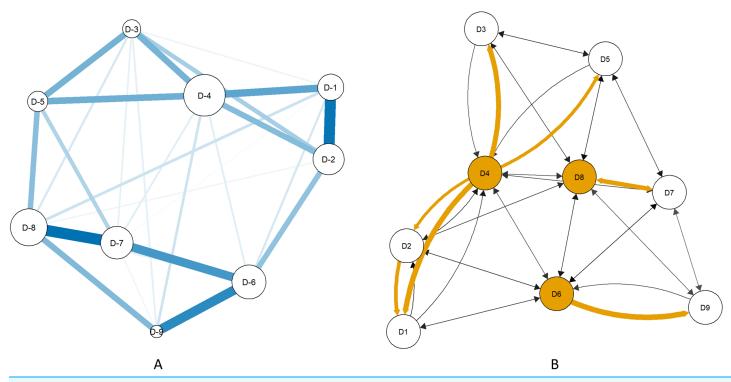


Figure 2 PHQ-9 symptom networks estimated by the extended Bayesian information criterion graphical lasso method (A) and the Triangulated Maximally Filtered Graph method (B). Key: D1: Anhedonia; D2: Sad mood; D3: Sleep problems; D4: Loss of energy; D5: Appetite change; D6: Guilt feelings; D7: Difficulty in concentration; D8: Psychomotor problems; D9: Suicidal ideation. Figure 2A: Node size indicates strength centrality and edge thickness indicates weight. Figure 2B: Shaded nodes have the highest outgoing strength. Arrows indicate the direction of influence. Yellow arrows indicate strong associations.

Full-size LOS DOI: 10.7717/peerj.13840/fig-2

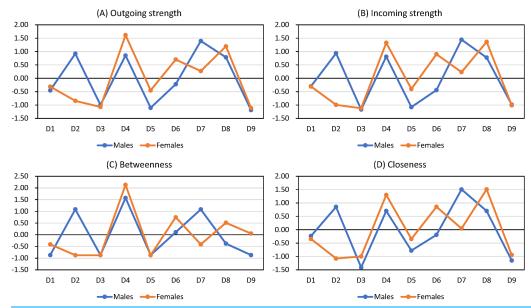
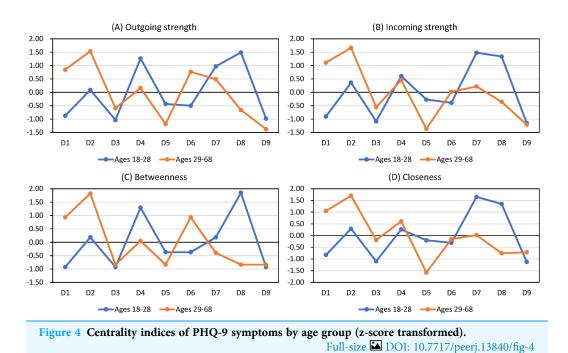


Figure 3 Centrality indices of PHQ-9 symptoms by gender (z-score transformed).

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fatigue and depression shared the same neurobiological mechanisms (*Berman et al.*, 1999; *Chaves-Filho et al.*, 2019).

In a community-based setting, previous studies reported that loss of energy is an early-endorsed symptom when people encounter some depressing or stressful life events (Fava & Tossani, 2007; Pae et al., 2007; Robinson et al., 2015), and loss of energy is predictive for an increased risk of future depression (Demyttenaere, De Fruyt & Stahl, 2005), which could explain the high centrality of energy loss in this study. However, in psychiatric samples, the top-ranked central symptom is usually sad mood (Beard et al., 2016; van Rooijen et al., 2018), which is different from the finding in this study. This suggests a discrepancy between psychiatric and community samples. Also, Borsboom's group ran network analysis with the nine DSM depression symptoms combined with 19 other non-DSM symptoms of depression in a group of depressed outpatients (Fried et al., 2016). Interestingly, loss of energy was the most central symptom by strength in their expanded list of symptoms, suggesting that loss of energy could be a symptom that transcends cultural boundaries. Since the present study was conducted during the pandemic, energy loss is probably related to the physical inactivity induced by the lockdown experience (McIlvenny et al., 2000; Stewart et al., 1998), and the worries brought about by unemployment and reduced income (Sharpe & Wilks, 2002).

What the present study adds to the literature is that targeting loss of energy may prevent full-blown major depression or alleviate it if already diagnosed. In particular, the results show that appetite change, sleep problems, anhedonia, and sadness are more strongly influenced by loss of energy than any other symptoms. This implies that treating loss of energy, whether by lifestyle changes or medications, may sever the backbone that projects to four other symptoms. Given that loss of energy is very prevalent in major depression (Angst & Dobler-Mikola, 1984; Buchwald & Rudick-Davis, 1993; Corfield, Martin &

Nyholt, 2016; Pae et al., 2007; Reyes-Gibby et al., 2006), targeting loss of energy may have substantial payoff.

Engaging in physical activity during the pandemic was inversely related to major depression symptoms in older adults (*Callow et al., 2020*). Similarly, adolescents in China who engaged in more than 30 mins of physical activity daily were less prone to depressive symptoms (*Kang et al., 2021*). This highlights one of the numerous trade-offs between infection control and mental health during the COVID-19 pandemic.

Psychomotor disturbance was the second most central symptom in this study and this is consistent with previous studies (*Ge et al.*, 2019; *Wang et al.*, 2020). Psychomotor abnormalities, such as slowing down in thought, motor retardation, restlessness or fidgeting, are manifestations of concentration difficulty, anxiety or mental tension (*Bennabi et al.*, 2013). Slowness in thoughts and behaviors is one of the primary manifestations in depression according to the DSM 5th edition (*American Psychiatric Association*, 2013). Fried et al. (2015) showed that when people deal with stressful events, they tend to endorse psychomotor disturbance the highest, although this symptom is not very frequently endorsed in depression (*Lamers et al.*, 2012).

It is also notable that loss of energy and psychomotor disturbance were the two most central symptoms. Both the International Classification of Diseases (ICD) and the DSM systems consider sadness and anhedonia as the two core symptoms (*Kennedy*, 2008), implying that depression is primarily a cognitive and affective disorder (*Demyttenaere*, *De Fruyt & Stahl*, 2005). This suggests that if sadness and anhedonia were treated, psychomotor disturbances and loss of energy will resolve. However, loss of energy tends to linger as a residual symptom after the emotional symptoms have resolved (*Demyttenaere*, *De Fruyt & Stahl*, 2005). It was also shown that psychomotor retardation responds to high frequency repetitive transcranial magnetic stimulation (rTMS) independently of overall clinical response (*Baeken et al.*, 2010). Psychomotor retardation is associated with high levels of interleukin 6 (IL-6), and decreasing IL-6 levels improved psychomotor retardation (*Belge et al.*, 2021; *Goldsmith et al.*, 2016). In this broader context, the results in this study suggest a treatment (or prevention) regimen that targets energy and motor symptoms.

Guilty feelings had the third highest centrality and is the top-ranked affective symptom. Guilt was described by *Klass (1987)* as a state that includes a cognitive component of having done something wrong and an affective component of shame even though neither wrongful actions nor other people are passing judgment. Previous studies found that guilt is one of the most useful discriminating symptoms of depression (*Ghatavi et al., 2002*; *Jarrett & Weissenburger, 1990*). Excessive guilt could lead to problematic outcomes such as impaired motivation and self-care, possibly evolving to depression (*Luck & Luck-Sikorski, 2020*; *Tilghman-Osborne, Cole & Felton, 2010, 2012*). The directed network analysis implies that "people do not feel guilty because they are thinking of suicide (*i.e.*, a big sin)" but rather "people are thinking of suicide because they feel they have fallen short of some standard (*i.e.* guilt)." This fits logically with *Joiner's (2005)* theory of perceived burdensomeness to loved ones as a motive for suicide. In his theory, suicidal people think of themselves as a liability, so they are better off dead.

Using factor analysis, *Berrios et al.* (1992) found that guilt consists of cognitive and affective factors. Importantly, they reported that the cognitive factor—the negative self-appraisal was correlated with psychomotor retardation. Although the results in this study showed that guilt and psychomotor problems were not very strongly correlated, their earlier finding and the present study could be the basis for speculating that by targeting motor symptoms, feelings of guilt might also alleviate. There has been much work suggesting that dopaminergic treatments for psychomotor retardation, although the hypothesized downstream benefit is for anhedonia (*Argyropoulos & Nutt, 2013; Kapur & Mann, 1992*). Guilt has received less attention compared to other emotions such sadness, anxiety, and anger, so it would be important to further study its role in major depression.

The advantages of this study consist of a relatively large sample size and a novel approach (network analysis) in a community whose main economic activity was shut down by the pandemic (Direcção dos Serviços de Estatística e Censos, 2021a, 2021b). However, this study is subject to several limitations. First, as a cross-sectional study it lacks a time dimension for validating the predicted direction among symptoms. Hence, the symptom relations of the network cannot be interpreted as causal. In addition, changes in the pattern of depressive symptoms pre- and post-pandemic could not be studied. Therefore, this study remains exploratory and future longitudinal studies are necessary. Second, both network estimation methods in this study rely on symptoms that are rated on an ordinal scale. These ordinal variables are assumed to be thresholds of a normally distributed variable. However, suicidal ideation (D9), may not be normally distributed in the population (Glashouwer et al., 2010). Third, the analysis in this study limited its scope to the nine canonical symptoms of depression, so including depressive symptoms outside of them might produce a different pattern of relationships. Fourth, this study was conducted in a community sample, hence it cannot be generalized to special populations such as adolescents, the elderly, or psychiatric samples.

RECOMMENDATIONS

The findings would be important for policy makers and mental health service providers to balance pandemic control regulations with opportunities to engage in physical activity. The promotion of mental health by a more active lifestyle should be encouraged. Targeting loss of energy may help relieve the other depressive symptoms.

CONCLUSION

Loss of energy, psychomotor problems and guilt feelings constituted the three backbone symptoms during the pandemic. Based on centrality and relative influence, loss of energy could be targeted by increasing opportunities for physical activity.

ADDITIONAL INFORMATION AND DECLARATIONS

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Competing Interests

The authors declare that they have no competing interests.

Author Contributions

- Yan-Jie Zhao performed the experiments, analyzed the data, prepared figures and/or tables, authored or reviewed drafts of the article, and approved the final draft.
- Wei Bai performed the experiments, analyzed the data, prepared figures and/or tables, and approved the final draft.
- Hong Cai performed the experiments, analyzed the data, prepared figures and/or tables, and approved the final draft.
- Sha Sha performed the experiments, analyzed the data, authored or reviewed drafts of the article, and approved the final draft.
- Qinge Zhang performed the experiments, analyzed the data, authored or reviewed drafts of the article, and approved the final draft.
- Si Man Lei conceived and designed the experiments, performed the experiments, authored or reviewed drafts of the article, and approved the final draft.
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Human Ethics

The following information was supplied relating to ethical approvals (*i.e.*, approving body and any reference numbers):

The Institutional Review Board (IRB) of Beijing Anding Hospital, Capital Medical University, approved the study.

Data Availability

The following information was supplied regarding data availability: Raw data and code are available in the Supplemental Files.

Supplemental Information

Supplemental information for this article can be found online at http://dx.doi.org/10.7717/peerj.13840#supplemental-information.

REFERENCES

- **American Psychiatric Association. 2013.** *Diagnostic and statistical manual of mental disorders* (DSM-5®). Washington, D.C.: American Psychiatric Pub.
- **Angst J, Dobler-Mikola A. 1984.** The definition of depression. *Journal of Psychiatric Research* **18(4)**:401–406 DOI 10.1016/0022-3956(84)90029-3.
- **Argyropoulos SV, Nutt DJ. 2013.** Anhedonia revisited: is there a role for dopamine-targeting drugs for depression? *Journal of Psychopharmacology* **27(10)**:869–877 DOI 10.1177/0269881113494104.
- Baeken C, De Raedt R, Santermans L, Zeeuws D, Vanderhasselt MA, Meers M, Vanderbruggen N. 2010. HF-rTMS treatment decreases psychomotor retardation in medication-resistant melancholic depression. *Progress in Neuro-Psychopharmacology and Biological Psychiatry* 34(4):684–687 DOI 10.1016/j.pnpbp.2010.03.021.
- Bai W, Zhao Y, An F, Zhang Q, Sha S, Cheung T, Cheng CP, Ng CH, Xiang YT. 2021. Network analysis of insomnia in Chinese mental health professionals during the COVID-19 pandemic: a cross-sectional study. *Nature and Science of Sleep* 13:1921–1930 DOI 10.2147/NSS.S326880.
- Balázs J, Miklósi M, Keresztény A, Hoven CW, Carli V, Wasserman C, Apter A, Bobes J, Brunner R, Cosman D, Cotter P, Haring C, Iosue M, Kaess M, Kahn JP, Keeley H, Marusic D, Postuvan V, Resch F, Saiz PA, Sisask M, Snir A, Tubiana A, Varnik A, Sarchiapone M, Wasserman D. 2013. Adolescent subthreshold-depression and anxiety: psychopathology, functional impairment and increased suicide risk. *Journal of Child Psychology and Psychiatry* 54(6):670–677 DOI 10.1111/jcpp.12016.
- **BBC News. 2021.** New local COVID-19 cases confirmed in Macau, and the anti-pandemic "top students" face challenges (in Chinese). *Available at https://www.bbc.com/zhongwen/simp/chinese-news-58083265*.
- Beard C, Millner AJ, Forgeard MJ, Fried EI, Hsu KJ, Treadway MT, Leonard CV, Kertz SJ, Bjorgvinsson T. 2016. Network analysis of depression and anxiety symptom relationships in a psychiatric sample. *Psychological Medicine* 46(16):3359–3369 DOI 10.1017/S0033291716002300.
- Belge JB, Van Diermen L, Sabbe B, Moens J, Morrens M, Coppens V, de Timary P, Constant E, Vansteelandt K, Sienaert P, Schrijvers D. 2021. Improvement of psychomotor retardation after electroconvulsive therapy is related to decreased IL-6 levels. *Progress in Neuro-Psychopharmacology and Biological Psychiatry* 105(Suppl. 20):110146

 DOI 10.1016/j.pnpbp.2020.110146.
- Bennabi D, Vandel P, Papaxanthis C, Pozzo T, Haffen E. 2013. Psychomotor retardation in depression: a systematic review of diagnostic, pathophysiologic, and therapeutic implications. *BioMed Research International* 2013(1):1–18 DOI 10.1155/2013/158746.

- Berman RM, Narasimhan M, Miller HL, Anand A, Cappiello A, Oren DA, Heninger GR, Charney DS. 1999. Transient depressive relapse induced by catecholamine depletion: potential phenotypic vulnerability marker? *Archives of General Psychiatry* 56(5):395–403 DOI 10.1001/archpsyc.56.5.395.
- Berrios G, Bulbena A, Bakshi N, Dening T, Jenaway A, Markar H, Martin-Santos R, Mitchell S. 1992. Feelings of guilt in major depression. Conceptual and psychometric aspects. *The British Journal of Psychiatry* 160(6):781–787 DOI 10.1192/bjp.160.6.781.
- Bertha EA, Balázs J. 2013. Subthreshold depression in adolescence: a systematic review. *European Child & Adolescent Psychiatry* 22(10):589–603 DOI 10.1007/s00787-013-0411-0.
- **Billones RR, Kumar S, Saligan LN. 2020.** Disentangling fatigue from anhedonia: a scoping review. *Translational Psychiatry* **10(1)**:1–11 DOI 10.1038/s41398-020-00960-w.
- **Borsboom D. 2008.** Psychometric perspectives on diagnostic systems. *Journal of Clinical Psychology* **64(9)**:1089–1108 DOI 10.1002/jclp.20503.
- **Borsboom D, Cramer AO. 2013.** Network analysis: an integrative approach to the structure of psychopathology. *Annual Review of Clinical Psychology* **9(1)**:91–121 DOI 10.1146/annurev-clinpsy-050212-185608.
- Brown TA. 2006. Confirmatory factor analysis for applied research. New York: Guilford Press.
- **Buchwald AM, Rudick-Davis D. 1993.** The symptoms of major depression. *Journal of Abnormal Psychology* **102(2)**:197–205 DOI 10.1037/0021-843X.102.2.197.
- Callow DD, Arnold-Nedimala NA, Jordan LS, Pena GS, Won J, Woodard JL, Smith JC. 2020. The mental health benefits of physical activity in older adults survive the COVID-19 pandemic. *The American Journal of Geriatric Psychiatry* **28(10)**:1046–1057 DOI 10.1016/j.jagp.2020.06.024.
- Centers for Disease Control and Prevention. 2021. Travelers prohibited from entry to the United States. *Available at https://www.cdc.gov/coronavirus/2019-ncov/travelers/from-other-countries.html* (accessed 9 April 2021).
- Chaves-Filho AJM, Macedo DS, de Lucena DF, Maes M. 2019. Shared microglial mechanisms underpinning depression and chronic fatigue syndrome and their comorbidities. *Behavioural Brain Research* 372(2):111975 DOI 10.1016/j.bbr.2019.111975.
- **Christensen AP. 2018.** Network toolbox: methods and measures for brain, cognitive, and psychometric network analysis in R. *The R Journal* **10(2)**:422–439 DOI 10.32614/RJ-2018-065.
- Corfield EC, Martin NG, Nyholt DR. 2016. Co-occurrence and symptomatology of fatigue and depression. *Comprehensive Psychiatry* 71:1–10 DOI 10.1016/j.comppsych.2016.08.004.
- Cramer AO, van Borkulo CD, Giltay EJ, van der Maas HL, Kendler KS, Scheffer M, Borsboom D. 2016. Major depression as a complex dynamic system. *PLOS ONE* 11(12):e0167490 DOI 10.1371/journal.pone.0167490.
- Cramer AO, Waldorp LJ, van der Maas HL, Borsboom D. 2010. Comorbidity: a network perspective. *Behavioral and Brain Sciences* 33(2–3):137–150 DOI 10.1017/S0140525X09991567.
- Crayne MP. 2020. The traumatic impact of job loss and job search in the aftermath of COVID-19. *Psychological Trauma Theory Research Practice and Policy* 12(S1):S180-s182 DOI 10.1037/tra0000852.
- **Demyttenaere K, De Fruyt J, Stahl SM. 2005.** The many faces of fatigue in major depressive disorder. *International Journal of Neuropsychopharmacology* **8(1)**:93–105 DOI 10.1017/S1461145704004729.
- Di Blasi M, Gullo S, Mancinelli E, Freda MF, Esposito G, Gelo OCG, Lagetto G, Giordano C, Mazzeschi C, Pazzagli C, Salcuni S, Lo Coco G. 2021. Psychological distress associated with the

- COVID-19 lockdown: a two-wave network analysis. *Journal of Affective Disorders* **284**:18–26 DOI 10.1016/j.jad.2021.02.016.
- Direcção dos Serviços de Estatística e Censos. 2021a. Incoming tourists (in Chinese). *Available at https://www.dsec.gov.mo/ts/#!/step2/KeyIndicator/zh-MO/243* (accessed 29 April 2021).
- **Direcção dos Serviços de Estatística e Censos. 2021b.** Time series database employment of local residents (in Chinese). *Available at https://www.dsec.gov.mo/ts/#!/step1/zh-MO* (accessed 18 April 2021).
- Ennis NE, Hobfoll SE, Schröder KE. 2000. Money doesn't talk, it swears: how economic stress and resistance resources impact inner-city women's depressive mood. *American Journal of Community Psychology* 28(2):149–173 DOI 10.1023/A:1005183100610.
- **Epskamp S, Borsboom D, Fried EI. 2018.** Estimating psychological networks and their accuracy: a tutorial paper. *Behavior Research Methods* **50(1)**:195–212 DOI 10.3758/s13428-017-0862-1.
- **Epskamp S, Cramer AO, Waldorp LJ, Schmittmann VD, Borsboom D. 2012.** qgraph: network visualizations of relationships in psychometric data. *Journal of Statistical Software* **48(4)**:1–18 DOI 10.18637/jss.v048.i04.
- **Epskamp S, Rhemtulla M, Borsboom D. 2017.** Generalized network psychometrics: combining network and latent variable models. *Psychometrika* **82(4)**:904–927 DOI 10.1007/s11336-017-9557-x.
- **Everett B. 2013.** An introduction to latent variable models. Berlin: Springer Science & Business Media
- **Fava GA, Tossani E. 2007.** Prodromal stage of major depression. *Early Intervention in Psychiatry* **1(1)**:9–18 DOI 10.1111/j.1751-7893.2007.00005.x.
- **Freeman LC. 1978.** Centrality in social networks conceptual clarification. *Social Networks* **1(3)**:215–239 DOI 10.1016/0378-8733(78)90021-7.
- Fried EI, Epskamp S, Nesse RM, Tuerlinckx F, Borsboom D. 2016. What are 'good' depression symptoms? Comparing the centrality of DSM and non-DSM symptoms of depression in a network analysis. *Journal of Affective Disorders* 189(1):314–320 DOI 10.1016/j.jad.2015.09.005.
- **Fried EI, Nesse RM, Guille C, Sen S. 2015.** The differential influence of life stress on individual symptoms of depression. *Acta Psychiatrica Scandinavica* **131(6)**:465–471 DOI 10.1111/acps.12395.
- Ge F, Yuan M, Li Y, Zhang J, Zhang W. 2019. Changes in the network structure of posttraumatic stress disorder symptoms at different time points among youth survivors: a network analysis. *Journal of Affective Disorders* 259(5):288–295 DOI 10.1016/j.jad.2019.08.065.
- **Geiselmann B, Bauer M. 2000.** Subthreshold depression in the elderly: qualitative or quantitative distinction? *Comprehensive Psychiatry* **41(2 Suppl 1)**:32–38 DOI 10.1016/S0010-440X(00)80006-1.
- **Ghatavi K, Nicolson R, MacDonald C, Osher S, Levitt A. 2002.** Defining guilt in depression: a comparison of subjects with major depression, chronic medical illness and healthy controls. *Journal of Affective Disorders* **68(2–3)**:307–315 DOI 10.1016/S0165-0327(01)00335-4.
- Glashouwer KA, de Jong PJ, Penninx BWJH, Kerkhof AJFM, van Dyck R, Ormel J. 2010. Do automatic self-associations relate to suicidal ideation? *Journal of Psychopathology and Behavioral Assessment* 32(3):428–437 DOI 10.1007/s10862-009-9156-y.
- Goldsmith DR, Haroon E, Woolwine BJ, Jung MY, Wommack EC, Harvey PD, Treadway MT, Felger JC, Miller AH. 2016. Inflammatory markers are associated with decreased psychomotor speed in patients with major depressive disorder. *Brain Behavior and Immunity* 56:281–288 DOI 10.1016/j.bbi.2016.03.025.

- GOV.UK. 2021. Coronavirus (COVID-19): red list travel ban countries. *Available at https://www.gov.uk/guidance/transport-measures-to-protect-the-uk-from-variant-strains-of-covid-19* (accessed 9 April 2021).
- Guo SZ, Lu ZM, Chen Z, Luo H. 2011. Strength-strength and strength-degree correlation measures for directed weighted complex network analysis. *IEICE Transactions on Information and Systems* E94d(11):2284–2287 DOI 10.1587/transinf.E94.D.2284.
- **Guyon H, Falissard B, Kop JL. 2017.** Modeling psychological attributes in psychology an epistemological discussion: network analysis vs. latent variables. *Frontiers in Psychology* **8**:475 DOI 10.3389/fpsyg,2017.00798.
- Hansen DL, Shneiderman B, Smith MA. 2011. Calculating and visualizing network metrics. Analyzing social media networks with nodexl: insights from a connected world. 69–78. Available at https://www.webofscience.com/wos/woscc/full-record/WOS:000317276100008? SID=EUW1ED0D13p5VGCxDRbDgaVp3m5eu.
- **Hartung TJ, Fried EI, Mehnert A, Hinz A, Vehling S. 2019.** Frequency and network analysis of depressive symptoms in patients with cancer compared to the general population. *Journal of Affective Disorders* **256**:295–301 DOI 10.1016/j.jad.2019.06.009.
- **Hegerl U. 2016.** Prevention of suicidal behavior. *Dialogues in Clinical Neuroscience* **18(2)**:183–190 DOI 10.31887/DCNS.2016.18.2/uhegerl.
- Hinz A, Mehnert A, Kocalevent R-D, Brähler E, Forkmann T, Singer S, Schulte T. 2016. Assessment of depression severity with the PHQ-9 in cancer patients and in the general population. *BMC Psychiatry* **16(1)**:1–8 DOI 10.1186/s12888-016-0728-6.
- Jacob Y, Winetraub Y, Raz G, Ben-Simon E, Okon-Singer H, Rosenberg-Katz K, Hendler T, Ben-Jacob E. 2016. Dependency network analysis (D(EP)NA) reveals context related influence of brain network nodes. *Scientific Reports* 6:27444 DOI 10.1038/srep27444.
- Jarrett RB, Weissenburger JE. 1990. Guilt in depressed outpatients. *Journal of Consulting and Clinical Psychology* 58(4):495 DOI 10.1037//0022-006x.58.4.495.
- Joiner TE. 2005. Why people die by suicide. Cambridge, Massachusetts: Harvard University Press.
- **Jones P. 2020.** networktools: tools for identifying important nodes in networks. R package version 1.2.3. *Available at https://CRAN.R-project.org/package=networktools*.
- Kang S, Sun Y, Zhang X, Sun F, Wang B, Zhu W. 2021. Is physical activity associated with mental health among Chinese adolescents during isolation in COVID-19 pandemic? *Journal of Epidemiology and Global Health* 11(1):26–33 DOI 10.2991/jegh.k.200908.001.
- **Kapur S, Mann JJ. 1992.** Role of the dopaminergic system in depression. *Biol Psychiatry* **32(1)**:1–17 DOI 10.1016/0006-3223(92)90137-O.
- Kenett YN, Kenett DY, Ben-Jacob E, Faust M. 2011. Global and local features of semantic networks: evidence from the hebrew mental lexicon. *PLOS ONE* **6(8)**:e23912 DOI 10.1371/journal.pone.0023912.
- Kenett DY, Tumminello M, Madi A, Gur-Gershgoren G, Mantegna RN, Ben-Jacob E. 2010. Dominating clasp of the financial sector revealed by partial correlation analysis of the stock market. *PLOS ONE* 5(12):e15032 DOI 10.1371/journal.pone.0015032.
- **Kennedy SH. 2008.** Core symptoms of major depressive disorder: relevance to diagnosis and treatment. *Dialogues in Clinical Neuroscience* **10(3)**:271–277 DOI 10.31887/DCNS.2008.10.3/shkennedy.
- **Klass ET. 1987.** Situational approach to assessment of guilt: development and validation of a self-report measure. *Journal of Psychopathology and Behavioral Assessment* **9(1)**:35–48 DOI 10.1007/BF00961630.

- **Kroenke K, Spitzer RL, Williams JB. 2001.** The PHQ-9: validity of a brief depression severity measure. *Journal of General Internal Medicine* **16(9)**:606–613 DOI 10.1046/j.1525-1497.2001.016009606.x.
- Lamers F, Burstein M, He J-P, Avenevoli S, Angst J, Merikangas KR. 2012. Structure of major depressive disorder in adolescents and adults in the US general population. *The British Journal of Psychiatry* 201(2):143–150 DOI 10.1192/bjp.bp.111.098079.
- **Leavitt HJ. 1951.** Some effects of certain communication patterns on group performance. *Journal of Abnormal and Social Psychology* **46(1)**:38–50 DOI 10.1037/h0057189.
- Li W, Zhao N, Yan X, Xu X, Zou S, Wang H, Li Y, Du X, Zhang L, Zhang Q, Cheung T, Ungvari GS, Ng CH, Xiang YT. 2022. Network analysis of depression, anxiety, posttraumatic stress symptoms, insomnia, pain, and fatigue in clinically stable older patients with psychiatric disorders during the COVID-19 outbreak. *Journal of Geriatric Psychiatry and Neurology* 35(2):196–205 DOI 10.1177/08919887221078559.
- **Luck T, Luck-Sikorski C. 2020.** Feelings of guilt in the general adult population: prevalence, intensity and association with depression. *Psychology, Health & Medicine* **26(9)**:1–11 DOI 10.1080/13548506.2020.1859558.
- Macao Daily News. 2021a. A street survey revealed that 26% students wanted to end their lives (in Chinese). Available at https://appimg.modaily.cn/amucsite/web/index.html#/detail/9771368 (accessed 14 April 2021).
- Macao Daily News. 2021b. Survey: most of the interviewees are mentally stable at the late-stage of COVID-19 (in Chinese). *Available at https://appimg.modaily.cn/amucsite/web/index.html#/detail/9772244* (accessed 14 April 2021).
- **Macau Daily. 2020.** First COVID-19 case confirmed in Macao (in Chinese). *Available at https://mp.weixin.qq.com/s/bx7ZXkrNu81i1bXOPIy83Q*.
- **Macau Daily. 2021.** Macau has no local confirmed cases for 365 consecutive days (in Chinese). *Available at https://mp.weixin.qq.com/s/TcvON-QzDrDJnHC068bTrA*.
- Madianos M, Economou M, Alexiou T, Stefanis C. 2011. Depression and economic hardship across Greece in 2008 and 2009: two cross-sectional surveys nationwide. *Social Psychiatry and Psychiatric Epidemiology* **46(10)**:943–952 DOI 10.1007/s00127-010-0265-4.
- **Marchetti I. 2018.** Hopelessness: a network analysis. *Cognitive Therapy and Research* **43(3)**:611–619 DOI 10.1007/s10608-018-9981-y.
- Massara GP, Di Matteo T, Aste T. 2017. Network filtering for big data: triangulated maximally filtered graph. *Journal of Complex Networks* 5(2):161–178 DOI 10.1093/comnet/cnw015.
- McIlvenny S, DeGlume A, Elewa M, Fernandez O, Dormer P. 2000. Factors associated with fatigue in a family medicine clinic in the United Arab Emirates. *Family Practice* 17(5):408–413 DOI 10.1093/fampra/17.5.408.
- **Mulder N. 2020.** The impact of the COVID-19 pandemic on the tourism sector in Latin America and the Caribbean, and options for a sustainable and resilient recovery. *Available at https://www.cepal.org/sites/default/files/publication/files/46502/S2000751_en.pdf* (accessed 9 April 2021).
- Mullarkey MC, Marchetti I, Beevers CG. 2019. Using network analysis to identify central symptoms of adolescent depression. *Journal of Clinical Child & Adolescent Psychology* 48(4):656–668 DOI 10.1080/15374416.2018.1437735.
- Pae C-U, Lim H-K, Han C, Patkar AA, Steffens DC, Masand PS, Lee C. 2007. Fatigue as a core symptom in major depressive disorder: overview and the role of bupropion. *Expert Review of Neurotherapeutics* 7(10):1251–1263 DOI 10.1586/14737175.7.10.1251.
- **R Core Team. 2020.** *R: a language and environment for statistical computing.* Vienna, Austria: The R Foundation for Statistical Computing. *Available at https://www.R-project.org.*

- **Revelle W. 2020.** psych: procedures for psychological, psychometric, and personality research. R package version 2.0.9. *Available at https://CRAN.R-project.org/package=psych.*
- Reyes-Gibby CC, Aday LA, Anderson KO, Mendoza TR, Cleeland CS. 2006. Pain, depression, and fatigue in community-dwelling adults with and without a history of cancer. *Journal of Pain and Symptom Management* 32(2):118–128 DOI 10.1016/j.jpainsymman.2006.01.008.
- Robinson RL, Stephenson JJ, Dennehy EB, Grabner M, Faries D, Palli SR, Swindle RW. 2015. The importance of unresolved fatigue in depression: costs and comorbidities. *Psychosomatics* **56(3)**:274–285 DOI 10.1016/j.psym.2014.08.003.
- **Rubinov M, Sporns O. 2010.** Complex network measures of brain connectivity: uses and interpretations. *Neuroimage* **52(3)**:1059–1069 DOI 10.1016/j.neuroimage.2009.10.003.
- Santos H Jr, Fried EI, Asafu-Adjei J, Ruiz RJ. 2017. Network structure of perinatal depressive symptoms in latinas: relationship to stress and reproductive biomarkers. *Research in Nursing & Health* 40(3):218–228 DOI 10.1002/nur.21784.
- **Sbai A. 2020.** How COVID-19 impacted travel & tourism industry globally. *Available at https://infomineo.com/covid-19-impacted-travel-tourism-industry/* (accessed 9 April 2021).
- Schmittmann VD, Cramer AO, Waldorp LJ, Epskamp S, Kievit RA, Borsboom D. 2013.

 Deconstructing the construct: a network perspective on psychological phenomena. *New Ideas in Psychology* 31(1):43–53 DOI 10.1016/j.newideapsych.2011.02.007.
- Sharpe M, Wilks D. 2002. Fatigue. BMJ 325(7362):480-483 DOI 10.1136/bmj.325.7362.480.
- Shim EJ, Ha H, Park JE, Kim BS, Chang SM, Hong JP, Cho MJ, Hahm BJ. 2020. Gender-based examination of the association between individual symptoms of alcohol use disorder, major depressive disorder, and suicidal behaviors: a network analysis of data from the Korean Epidemiologic Catchment Area Study. *Journal of Affective Disorders* 272(10):432–439 DOI 10.1016/j.jad.2020.03.162.
- **Spitzer RL, Kroenke K, Williams JB. 1999.** Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary care evaluation of mental disorders. Patient health questionnaire. *JAMA* **282(18)**:1737–1744 DOI 10.1001/jama.282.18.1737.
- **Stahl SM. 2002.** Does depression hurt? *The Journal of Clinical Psychiatry* **63(4)**:273–274 DOI 10.4088/JCP.v63n0401.
- **Stewart D, Abbey S, Meana M, Boydell KM. 1998.** What makes women tired? A community sample. *Journal of Womens Health* **7(1)**:69–76 DOI 10.1089/jwh.1998.7.69.
- **Tencent. 2021.** Macau has no local confirmed cases for 365 consecutive days (in Chinese). *Available at https://new.qq.com/omn/20210329/20210329A0BOBU00.html*.
- **Tilghman-Osborne C, Cole DA, Felton JW. 2010.** Definition and measurement of guilt: implications for clinical research and practice. *Clinical Psychology Review* **30(5)**:536–546 DOI 10.1016/j.cpr.2010.03.007.
- **Tilghman-Osborne C, Cole DA, Felton JW. 2012.** Inappropriate and excessive guilt: instrument validation and developmental differences in relation to depression. *Journal of Abnormal Child Psychology* **40(4)**:607–620 DOI 10.1007/s10802-011-9591-6.
- **TRAVELBANS. 2021.** Travel ban, new rules and unexpected flying restrictions: what will tourism be like after coronavirus? . *Available at https://travelbans.org/* (accessed 9 April 2021).
- **Uğur NG, Akbıyık A. 2020.** Impacts of COVID-19 on global tourism industry: a cross-regional comparison. *Tourism Management Perspectives* **36**(5):100744 DOI 10.1016/j.tmp.2020.100744.
- van Rooijen G, Isvoranu AM, Kruijt OH, van Borkulo CD, Meijer CJ, Wigman JTW, Ruhe HG, de Haan L, investigators G. 2018. A state-independent network of depressive, negative and

- positive symptoms in male patients with schizophrenia spectrum disorders. *Schizophrenia Research* **193**:232–239 DOI 10.1016/j.schres.2017.07.035.
- Wang W, Bian Q, Zhao Y, Li X, Wang W, Du J, Zhang G, Zhou Q, Zhao M. 2014. Reliability and validity of the Chinese version of the Patient Health Questionnaire (PHQ-9) in the general population. *General Hospital Psychiatry* 36(5):539–544

 DOI 10.1016/j.genhosppsych.2014.05.021.
- Wang Y, Hu Z, Feng Y, Wilson A, Chen R. 2020. Changes in network centrality of psychopathology symptoms between the COVID-19 outbreak and after peak. *Molecular Psychiatry* 25(12):3140–3149 DOI 10.1038/s41380-020-00881-6.
- **World Health Organization. 2020a.** Naming the coronavirus disease (COVID-19) and the virus that causes it. *Available at https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it* (accessed 11 February 2020).
- **World Health Organization. 2020b.** Novel Coronavirus China. *Available at https://www.who.int/csr/don/12-january-2020-novel-coronavirus-china/en/* (accessed 12 January 2020).
- **World Tourism Organization. 2020.** Impact assessment of the covid-19 outbreak on international tourism. *Available at https://www.unwto.org/impact-assessment-of-the-covid-19-outbreak-on-international-tourism* (accessed 9 April 2021).
- **Xu Y, Wu HS, Xu YF. 2007.** The application of Patient Health Questionnaire 9 in community elderly population: reliability and validity (in Chinese). *Shanghai Archives of Psychiatry* **19(5)**:257–259+276 DOI 10.3969/j.issn.1002-0829.2007.05.001.
- Yu X, Tam WW, Wong PT, Lam TH, Stewart SM. 2012. The Patient Health Questionnaire-9 for measuring depressive symptoms among the general population in Hong Kong. *Comprehensive Psychiatry* 53(1):95–102 DOI 10.1016/j.comppsych.2010.11.002.