#### ORIGINAL RESEARCH

## The Inter-Relationships Between Depressive Symptoms and Suicidality Among Macau Residents After the "Relatively Static Management" COVID-19 Strategy: A Perspective of Network Analysis

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**Background:** Suicidality is a global public health problem which has increased considerably during the coronavirus disease 2019 (COVID-19) pandemic. This study examined the inter-relationships between depressive symptoms and suicidality using network analysis among Macau residents after the "relatively static management" COVID-19 strategy.

**Methods:** An assessment of suicidal ideation (SI), suicide plan (SP), suicide attempt (SA) and depressive symptoms was conducted with the use of individual binary response items (yes/no) and Patient Health Questionnaire (PHQ-9). In the network analysis, central and bridge symptoms were identified in the network through "Expected Influence" and "Bridge Expected Influence", and specific symptoms that were directly associated with suicidality were identified via the flow function. Network Comparison Tests (NCT) were conducted to examine the gender differences in network characteristics.

**Results:** The study sample included a total of 1008 Macau residents. The prevalence of depressive symptoms and suicidality were 62.50% (95% CI = 59.4-65.5%) and 8.9% (95% CI = 7.2-10.9%), respectively. A network analysis of the sample identified SI ("Suicidal ideation") as the most central symptom, followed by SP ("Suicide plan") and PHQ4 ("Fatigue"). SI ("Suicidal ideation") and PHQ6 ("Guilt") were bridge nodes connecting depressive symptoms and suicidality. A flow network revealed that the strongest connection was between S ("Suicidality") and PHQ6 ("Guilt"), followed by S ("Suicidality") and PHQ 7 ("Concentration"), and S ("Suicidality") and PHQ3 ("Sleep").

**Conclusion:** The findings indicated that reduction of specific depressive symptoms and suicidal thoughts may be relevant in decreasing suicidality among adults. Further, suicide assessment and prevention measures should address the central and bridge symptoms identified in this study.

Keywords: COVID-19, depression, suicidality, adults, network analysis

### Introduction

Suicidality is a major public health problem globally.<sup>1</sup> Every year, more than 700,000 people die by suicide, and it is estimated that one person dies every 40 seconds. The coronavirus disease 2019 (COVID-19) pandemic is one of the major risk factors impacting on suicidality.<sup>2–5</sup> Since the start of the COVID-19 pandemic, mental health professionals have been concerned about rising suicide rates, with warnings such as "Suicide epidemic triggered by COVID-19"<sup>6</sup> and

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"Dual pandemic of suicide and COVID-19".<sup>7</sup> A meta-analysis examining suicidality during the COVID-19 pandemic found an increase rate for suicidal ideation (SI) (10.81%), suicide attempts (SA) (4.68%), and self-harm (9.63%) when compared to studies conducted prior to COVID-19 pandemic.<sup>8</sup> Another meta-analysis revealed that the prevalence rate of SI among hospitalized and non-hospitalized populations was 1.134 (95% CI: 1.048–1.227) to 1.142 times (95% CI: 1.018–1.282) higher, while the prevalence of SA was also 1.14 times higher (95% CI: 1.053–1.233) to 1.32 (95% CI: 1.17–1.489) than the corresponding figures during the pre-pandemic period.<sup>9</sup> Suicide is not only a leading cause of death among the general population,<sup>10</sup> but also places a heavy burden on affected families, communities, and societies worldwide.<sup>1</sup> Therefore, suicide prevention has become a global imperative especially during the COVID-19 pandemic. Furthermore, the mass lockdowns, social isolation, and economic consequences of the pandemic<sup>11–13</sup> might have resulted in an increase of physical and mental (ie, depression), behavioral (ie, panic buying), financial (ie, unemployment) and psychosocial (ie, racism) problems which could contribute to the risk of suicidality.<sup>3,8,14</sup> Therefore, understanding the association between mental health problems (eg, depression) and suicidality during the pandemic is essential for developing the relevant public health strategies and guidelines to address these problems.<sup>15</sup>

The association between suicidality and mental health problems, particularly depression, has been well established. For instance, depressive symptoms were positively associated with suicidality,<sup>16,17</sup> and were among the most prominent predictive factors for SI, suicide plan (SP)<sup>18</sup> and SA.<sup>17</sup> It is estimated that suicide is 25 times more likely to occur in people with depression than in the general population.<sup>19</sup> Meanwhile, a significant increase in depressive symptoms was also observed during the COVID-19 pandemic.<sup>20</sup> Increased depressive symptoms can be associated with fear of being infected with COVID-19, social distancing, and changing economic conditions.<sup>12,21,22</sup> A meta-analysis of 162,639 participants across 17 counties found that the overall prevalence of depressive symptoms was 28% during the COVID-19 pandemic.<sup>13</sup> The more intense the lockdown measures, the higher the risk of depression. For instance, a study of 55,589 participants from 40 countries found that with increasing lockdown intensity, the risk of developing depressive symptoms increased by more than 1.7 times.<sup>21</sup> The greater the depressive symptoms, the higher the probability of suicidal thoughts and behaviors emerging during the COVID-19 pandemic.<sup>3,23,24</sup>

The Macau Special Administrative Region of China (Macau SAR), located on the west of the Pearl Delta River estuary in southern China, heavily depends upon international visitors to sustain its social and economic existence. The long-term persistence of COVID-19-related travel restrictions and quarantine prevention policy caused intense economic damage in Macau.<sup>25</sup> However, Macau SAR implemented stringent restriction and quarantine policy during the sixth wave of the pandemic in the Region, dubbed "618" wave, which occurred from June 18 to August 7, 2022, and resulted in 705 new confirmed cases (38.7%) and 1116 asymptomatic infections (61.3%). Macau SAR authorized a "relatively static management" for 12 days, closing down public institutions such as schools, casinos, and cinemas<sup>26</sup> to control the sources of infection and cut off the channels of transmission. These measures, as well as the "dynamic zero COVID" prevention policy taken by Macau and mainland China, were very successful in reducing the spread of COVID-19.<sup>27,28</sup> However, the economy was adversely affected and has not yet recovered to its pre-pandemic levels.<sup>29</sup> As a result, there has been an increase rate of psychological problems,<sup>30</sup> such as depression and suicidality. For example, previous studies found that the prevalence of depressive symptoms and SI among Macau residents were 38.5% and 13.5%, respectively,<sup>31</sup> which were substantially higher than the initial wave of COVID-19 outbreak in UK and Brazil in 2020.<sup>32</sup> Moreover, suicide rates increased during the COVID-19 pandemic.<sup>33</sup> In 2020, suicide cases (n=69) increased by 23% over 2019 (n=50), while suicide cases in Macau during the first three quarters of 2022 (n=65) were 70% higher than in the same period in 2021.<sup>34</sup> During both significant outbreaks of COVID-19 in 2020 and 2022, the overall suicide rates in Macau were 9.8 and 9.67 per 100,000 individuals,<sup>34,35</sup> respectively, which was higher than the global suicide rate in 2019 (9.0 per 100,000 people).<sup>36</sup> Thus, it is imperative to investigate the inter-relationships between suicidality and depression after the "relatively static management" COVID-19 strategy in Macau.

Network analysis (NA) offers a novel perspective for investigating psychiatric problems conceptualized as a causal interplay between symptom systems.<sup>37</sup> In network theory, the symptoms as variables are represented by nodes, the connection between the nodes are represented by edges,<sup>38</sup> and the central node is the most influential symptom with a large number of connection in a network which is linked to other symptoms.<sup>38,39</sup> NA provides a perspective into how

symptoms of a syndrome interact with each other and can help identify which symptoms are most influential or central to a syndrome, which can be prioritized for intervention.<sup>40</sup>

Although NA was widely applied to various psychiatric disorders among numerous subgroups of the population during the COVID-19 pandemic,<sup>31,41,42</sup> there is a lack of research on the specific interrelationship between depressive symptoms and suicidality in the general population. For instance, prior network analyses focused on depressive symptoms among Hong Kong residents<sup>43</sup> and mental health symptoms and suicidality among young adults aged 10–35 years during the COVID-19 pandemic.<sup>44</sup> Another network analysis study examined psychiatric symptoms (eg, anxiety and depression) and suicidality among adolescents in Macau<sup>45</sup> and college students in China.<sup>46</sup> Most studies also focused on young populations, as suicide is a leading cause of death in this subpopulation.<sup>1</sup> To date, no studies have examined the specific correlates of suicidality among Macau adult residents, particularly during the pandemic, despite the upward trend of suicide in this population. Understanding the relationship between depressive symptoms and suicidality is crucial to reducing suicide risks. Hence, this study examined the inter-relationships between depressive symptoms and suicidality using network analysis among Macau adult residents after the "relatively static management" COVID-19 strategy.

## Methods

### Participants and Procedure

This was a cross-sectional study using snowball sampling method conducted from July 26 to September 9, 2022, during which Macau SAR government implemented the "relatively static management" of the sixth wave of the pandemic. Face-to-face interviews were not possible during the COVID-19 outbreaks due to lockdowns and social distancing. Following previous studies,<sup>31,47,48</sup> participants were invited to participate in this survey on an anonymous and voluntary basis through a Quick Response code (QR code) that was linked to an invitation and assessment instruments on key social network platforms' advertisements such as WeChat, Instagram, and Facebook. To be eligible, participants were (1) local residents who lived in Macau during the 618 COVID-19 wave and experienced the "relatively static management" COVID-19 strategy; (2) aged 18 years or above; (3) able to understand the purpose and content of the survey. The study was approved by the Institutional Review Board of the University of Macau (Ethnics approval number: SSHRE22-APP05-FHS) which adhered to the principles of the Declaration of Helsinki. Participants are provided electronic written informed consent.

### Measures

Basic socio-demographic data were collected, including age, gender, marital status, living situation, education level, and employment status. A number of variables related to COVID-19 were also recorded, including concern about COVID-19, quarantine status during the COVID-19 pandemic, fear of infection, economic loss caused by the pandemic, monthly income, regular physical activity, chronic physical illness, and psychiatric disorders during the outbreak.

The validated Chinese version of the self-report Patient Health Questionnaire (PHQ-9) was used to measure depression.<sup>49,50</sup> The PHQ-9 consists of nine items referring to the past two weeks which is based on the Diagnostic and Statistical Manual of Disorders-IV (DSM-IV) criteria for depression,<sup>50</sup> with each item scoring between 0 ("not at all") and 3 ("nearly every day"); the PHQ-9 total score ranges from 0 to 27, with a higher total score indicating more depressive symptoms.<sup>51</sup> The PHQ-9 items include: anhedonia (PHQ1), sad mood (PHQ2), sleep (PHQ3), fatigue (PHQ4), appetite (PHQ5), guilt (PHQ6), concentration (PHQ7), motor disturbance (PHQ8), and suicidal ideation (PHQ9).<sup>52</sup>

In this study, suicidality in the past week consists of SI, suicide plan (SP), and SA.<sup>53,54</sup> SI refers to having thoughts or wishes about ending one's own life but not making plans for death;<sup>53,55</sup> SP refers to preparing to use a specific method to end one's own life;<sup>56</sup> SA is defined by the act of self-injury to end one's own life.<sup>53,55</sup> Following previous studies,<sup>45,57</sup> the item on Suicidal ideation (PHQ9) was excluded from the network analysis as it was duplicating the suicidal ideation (SI) component of suicidality. Standard questions on suicidality with (yes/no) responses were used as recommended in previous studies;<sup>45,58,59</sup> the SI was evaluated with the question, "During the '618 COVID-19 outbreak', have you had thoughts that you would be better off dead?". SP was assessed with the question, "During the '618 COVID-19 outbreak',

have you made a plan for suicide?" while SA was measured with the question, "During the '618 COVID-19 outbreak', have you attempted suicide?". A participant was defined as "having suicidality" if he or she answered "yes" to any of the three questions. For those in need of mental health services, information regarding mental health resources (eg, contact information for helplines and hotline services) was provided at the end of the survey.

### Data Analysis

### Network Estimation

For statistical analyses, R software<sup>60</sup> was used to conduct the network analysis. In the network model, each node is represented as an individual symptom; each edge is regarded as the association between two nodes. Stronger correlations were represented by thicker edges, while a positive correlation was indicated with a green edge and a negative correlation with a red edge.<sup>61</sup> To assess the polychoric correlations between all survey items in the network model, a Graphical Gaussian Model (GGM) with graphic least absolute shrinkage and selection operator (LASSO) and an Extended Bayesian Information Criterion (EBIC) model were adopted,<sup>62</sup> which could enhance prediction accuracy, interpretability and optimality of the network model.<sup>63</sup> Due to the skewed distribution of mean scores on study items, non-parametric correlations were computed using nonparanormal transformations.<sup>64</sup> An evaluation of network estimation was performed using the "estimateNetwork" function in R packages "bootnet" with "EBICglasso" as the default method.<sup>62</sup> A network visualization was conducted using the R packages' qgraph'<sup>62</sup> and "ggplot2" was used to optimize its visual representation.<sup>62,65</sup>

### Centrality and Stability

The network structure's expected influence (EI) was calculated using the R package qgraph<sup>61</sup> to evaluate the importance of each node in the network model. Compared with traditional centrality indices such as node strength, EI is particularly suitable for networks that could distinguish between positive and negative edges.<sup>66</sup> In the network model, the nodes with a greater EI were deemed more important and influential.<sup>31</sup> To identify bridge symptoms in the network model that associate with two or more psychiatric syndromes,<sup>67</sup> the "bridge" function of the R package "networktools" (version 1.5.0) was used to calculate the bridge expected influence.<sup>68</sup> Compared to bridge symptoms with lower expected influence values, those with higher expected influence values were associated with a higher risk of contagion between different communities of symptoms.<sup>69</sup> Predictability of each node<sup>70</sup> and control of confounding effects in basic demographic data<sup>71,72</sup> in the network model were estimated using the R package "mgm". The value of predictability is indicated as the linkage between its neighboring node.<sup>31</sup> Moreover, the "flow" function in the R package "qgraph" was used to examine particular depressive symptoms that were directly related to suicidality.<sup>61</sup>

In addition, the stability and accuracy of network model were assessed using the "bootnet" function in R package (Version 1.4.3)<sup>62</sup> with 1000 permutations of case dropping bootstrap procedure for each node. A correlation stability coefficient (CS-coefficient) was used to assess the network's stability. A correlation greater than 0.7 indicated that a maximum proportion of cases could be dropped, representing a 95% probability that original centrality indices correlate with the centrality of subset networks.<sup>62</sup> Following previous studies,<sup>31,45,62</sup> a CS-coefficient value of above 0.25 was regarded as stable in the network model, while a value of above 0.5 was regarded as preferable stable A non-parametric bootstrapped difference test was performed to assess the difference between pairs of nodes and edges. The difference between two nodes or edges was significant if zero was excluded from the 1000-bootstrap 95% confidence interval (CI). Bootstrapped 95% CI was used to estimate edge accuracy, with a narrower CI representing a more trustworthy network.<sup>62</sup>

### Network Comparison Test

As recommended previously,<sup>45</sup> to test the differences in depression and suicidality network models between genders, an analysis of gender differences in network structure and global strength was performed using Network Comparison Test (NCT), with "NetworkComparisonTest" in R package (Version 2.2.1)<sup>73</sup> with 1000 permutations.

In total, 1020 Macau residents were invited to participate in the study, and 1008 met the inclusion criteria and completed the assessment, representing a participation rate of 98.82%. The mean age of participants was 38.4 years (standard deviation (SD)=11.5 years) and 26.7% of participants (n=269) were male. The prevalence rates of depression (PHQ-9  $\geq$  5) and overall suicidality during the 618 COVID-19 wave were 62.5% (95% CI = 59.4–65.5%) and 8.9% (95% CI = 7.2–10.9%), respectively, while the rates of SI, SP, and SA were 8.4% (95% CI = 6.8–10.3%), 3.5% (95% CI = 2.4–4.8%), and 3.3% (95% CI = 2.3–4.6%), respectively. The PHQ and suicidality assessments are presented in Supplementary Table S1, which shows means, standard deviations, skewness, and kurtosis.

### Network Structure and Centrality measures Analysis

Figure 1 presents the network structure of depression and suicidality among Macau residents after the "relatively static management" COVID-19 strategy conducted by EBICglasso model. The mean predictability in this sample was 0.511, representing on average 51.1% of each node's variance that could be explained by its neighboring nodes. In the network model, the connection with the strongest positive edge was SP ("Suicide plan") - SA ("Suicide attempt"), followed by PHQ7 ("Concentration") - PHQ8 ("Motor disturbance"), and PHQ1 ("Anhedonia") - PHQ4 ("Fatigue"). The correlation between PHQ item and suicidality are shown in <u>Supplementary Table S2</u>. Additionally, the flow network of suicidality with PHQ items is presented in Figure 2. The S ("Suicidality") - PHQ 6 ("Guilt") was the strongest edge, followed by S ("Suicidality") – PHQ7 (Concentration), and S ("Suicidality")-PHQ3 ("Sleep").

In terms of network centrality measured by EI, the three nodes with the highest EI centrality were SI ("Suicidal ideation"), SP ("Suicide plan") and PHQ4 ("Fatigue"), whereas PHQ 3 ("Sleep"), SA ("Suicide attempt"), and PHQ5 ("Appetite") had the lowest EI centrality (Figure 1). As shown in Figure 3, the two key bridge symptoms examined by bridge EIs linking PHQ-8 and suicidality communities were SI ("Suicidal ideation") and PHQ6 ("Guilt").

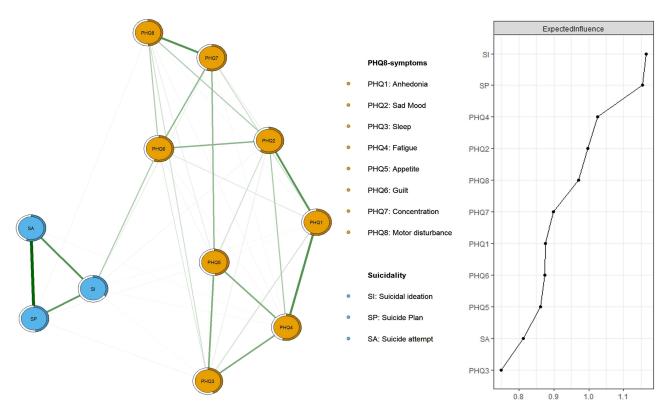


Figure I The network structure of depressive symptoms and suicidality among Macau residents shortly after the "relatively static management" COVID-19 strategy.

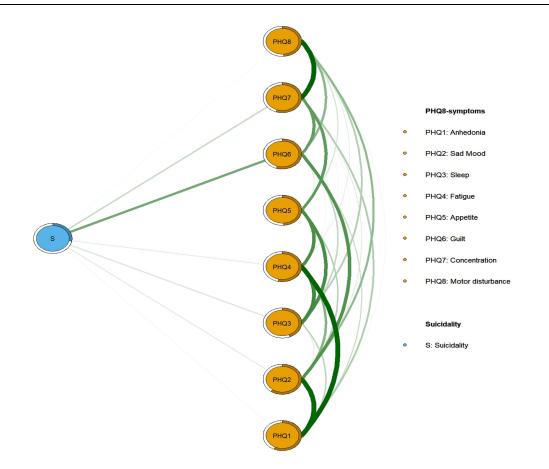


Figure 2 Flow network of suicidality.

Figure 4 illustrates the assessment of network stability; the network structure is stable with a CS-coefficient of EI of 0.361, which indicates that 36% of the sample can be dropped without significantly affecting the network structure. In terms of the accuracy of the network, bootstrap 95% CIs for estimated edge weights revealed a narrow range, as shown in <u>Supplementary Figure S1A</u>. As most of the edge weights were non-zero, the majority of the edges were considered accurate and stable. Additionally, most comparisons of edge weights were statistically significant according to bootstrapped difference tests as presented in <u>Supplementary Figure S1B</u>, suggesting that the network model was reliable.

# The Confounding Effects of Basic Demographic Data on Depressive Symptoms and Suicidality

Demographic factors such as gender, age, marital status, and level of education were found to be significantly associated with depressive symptoms and suicidality in previous studies.<sup>74–77</sup> Marriage, for instance, was both a risk and protective factor of depression in different studies.<sup>75,78</sup> Lower education and females were associated with higher risk of depression,<sup>78</sup> while women were also more likely to have suicidal behaviors.<sup>79</sup> It is likely that lower level of education could adversely affect depression through interfering with cognitive development,<sup>80</sup> while the lower social position for women in some areas<sup>78</sup> could also increase the risk of depression. Previous research has found that age might serve as a mediator between certain mental problems (eg, anorexia and bulimia nervosa) and SA.<sup>81</sup> Moreover, age showed a negative relationship with emotional distress, which could be attributed to higher levels of optimism and external control among older adults.<sup>82</sup> A study found that during the COVID-19 pandemic, age was negatively associated with suicidal thoughts among residents in Mexico<sup>83</sup> and China.<sup>84</sup> In contrast, another study found that male gender was a risk factor for suicidal thoughts among the general population.<sup>83</sup> Therefore, to examine the inter-relationship between depressive symptoms and suicidality, it is important to minimize the confounding effects caused by basic demographic

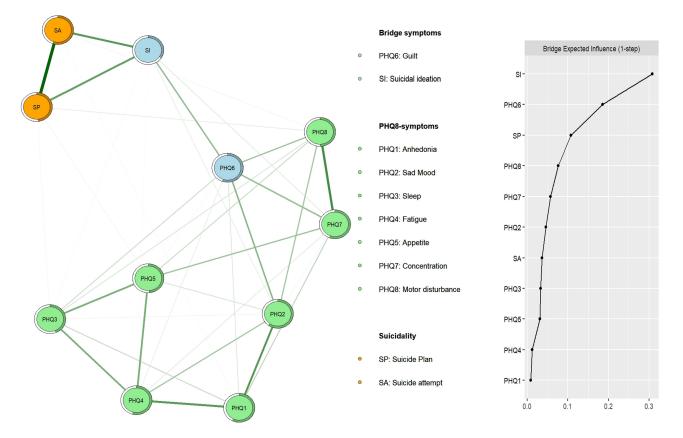


Figure 3 The network structure of depressive symptoms and suicidality with bridge connections among Macau residents shortly after the "relatively static management" COVID-19 strategy.

variables. Following previous research,<sup>72,85,86</sup> the depressive symptoms and suicidality network models, with the structure indexes, were re-evaluated after controlling for age, marital status, gender, and education level (<u>Supplemental Figure S2</u>). Compared to the original network, the re-calculated network model did not find any significant structure change after controlling for the confounding variables (strength:  $r_s = 0.77$  [0.54; 0.95]).

### Gender Differences in Network Models

The comparison of gender differences in network models did not find significant differences in network edge weight (M=0.21, P=0.488), or global strength (network strength: 4.94 in female participants; 5.05 in male participants; S=0.11, P=0.459) (see Supplementary Figures S3–S5).

### Discussion

To the best of our knowledge, this was the first study to explore prevalence of depressive symptoms and suicidality and their inter-relationships using network analysis among Macau residents after the "relatively static management" COVID-19 strategy. Both depressive symptoms and suicidality were common. Network analysis revealed that SI ("Suicidal ideation") was the most central symptom with the highest centrality, followed by SP ("Suicide plan") and PHQ4 ("Fatigue"). In addition, SI ("Suicidal ideation") and PHQ6 ("Guilt") served as bridge nodes linking depressive symptoms with suicidality. Finally, as shown in the Flow network, the strongest connection was between nodes S ("Suicidality") and PHQ 6 ("Guilt"), followed by edges between S ("Suicidality") and PHQ 7 ("Concentration") and S ("Suicidality") and PHQ3 ("Sleep").

SI and SP were the most influential in our sample network which is aligned with previous adults' COVID-19 network analysis.<sup>87</sup> SI was also identified as the bridge symptom. A global survey across 17 countries on the general population found that the lifetime prevalence of SI was 9.2%, while the corresponding prevalence rates of SP and SA were 3.1% and

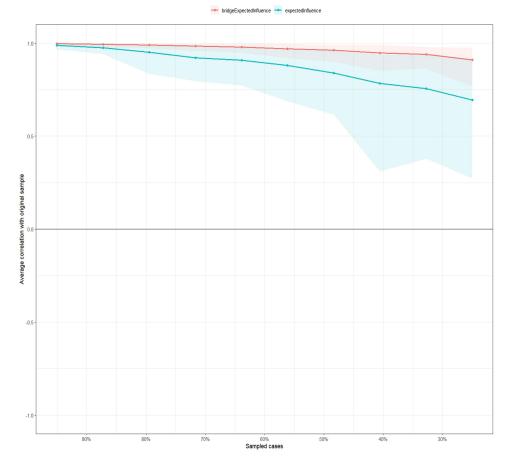


Figure 4 The stability of centrality and bridge centrality indices using case-dropping bootstrap.

2.7%, respectively.<sup>88</sup> SI is a robust predictor of SP and SA<sup>16,89</sup> as 60% of those with SI could transition to SP and SA within 12 months,<sup>88</sup> and with an increase of one unit in the severity of SI, the rate of SA occurrence could increase by 4.4 times.<sup>90</sup> SI and SP also trigger depressive symptoms as bridge symptoms in the network. In accordance with the differential activation theory of suicidality, depression and suicidality could easily be activated by each other because of the configuration formation between SI and depression during early episodes of depression.<sup>91–93</sup> In particular, depression recurrence was significantly related to previous episodes of SI<sup>91</sup> and suicidal symptoms<sup>94</sup> in longitudinal studies of major depression patients, in which more suicidal symptoms were associated with more significant depressive symptoms.<sup>94,95</sup> Similarly, a machine learning study found that suicidality was the top predictor of persistent and recurrent depression over three years.<sup>96</sup> In tandem with those studies, our findings suggest that SI and SP have prominent roles in linking depression and suicidality during the COVID-19 pandemic. Despite the importance of SI and SP, there are still insufficient diagnostic criteria for suicidal ideation and inadequate understanding of passive suicidal behavior.<sup>94</sup> Passive suicidal thoughts was highly related to SA and suicide in a previous study.<sup>97</sup> Meanwhile, the risk factors and assessment of SP are still unclear.<sup>98</sup> Furthermore, most of the treatments that target depression failed to reduce suicidal thoughts and behavior adequately,<sup>99</sup> whereas an earlier meta-analysis reported that prior SI was the strongest predictor of future suicidal thoughts and behaviors.<sup>98,100</sup> Thus, instead of focusing on specific treatment of depressive symptoms, early screening and treatment may need to target central symptoms such as SI and SP in suicide prevention.

"Fatigue" was another prominent central symptom in this network analysis, which is in accordance with previous findings from a depression network among adults and older adults during the COVID-19 outbreak<sup>43,101,102</sup> as well as the network analysis of depression and suicidality among adolescents.<sup>103</sup> The term "Fatigue" refers to a lack of energy, or often referred to as fatigue<sup>104,105</sup> or exhaustion.<sup>106</sup> Fatigue is a crucial influencer of other depressive symptoms, such as

anhedonia,<sup>107,108</sup> hopelessness, and impaired concentration,<sup>109</sup> as well as a contributor to the development of psychiatric disorders (ie, depression and psychotic disorders).<sup>107,108</sup> In addition, fatigue was regarded as a key symptom to influence suicidality in this study. These results also support previous findings that found that greater severity of fatigue could result in a higher risk of suicidality,<sup>59,110</sup> cognitive and functional impairment.<sup>110</sup> On the other hand, the COVID-19 pandemic in itself is a significant risk factor for fatigue that is related to infection<sup>19,111</sup> and restriction of outdoor activities caused by lockdowns.<sup>112</sup> Likewise, persistent fatigue, which is a somatic symptom of depression,<sup>108</sup> is highly prevalent in long COVID,<sup>19,113–115</sup> with prevalence rates of 42.5% according to a meta-analysis study,<sup>116</sup> which may contribute to the risk of suicidal thoughts and behaviors.<sup>115</sup> This may be due to inflammatory impairment of the brain<sup>19</sup> leading to dysregulation of neurotransmitters<sup>3</sup> or cognitive damage.<sup>115</sup> Despite the importance of fatigue in depression and suicidality, fatigue as a screening symptom for depression was considered to be less sensitive than other depressive symptoms, such as anhedonia.<sup>104</sup> Hence, loss of energy should be further addressed in screening and preventive measures for suicidality and depression.

"Guilt" was identified as a bridge symptom in this network model, which is consistent with another study on depression and anxiety of adolescents during the later stages of the COVID-19 pandemic in China. People often experience strong guilt feelings during the COVID-19 pandemic associated with the emergence of anger and blaming towards others (ie, doctors, neighbors, and health authorities),<sup>117</sup> financial loss/worries<sup>111,118</sup> or through witnessing infection or death.<sup>119</sup> In relation to guilt, people often experience worthlessness<sup>105</sup> and negative evaluation or self-blame due to their behavior,<sup>120</sup> which could lead to the development of depressive symptoms. Guilt, or negative self-reflection, can be triggered by depression.<sup>121</sup> A previous study of general adult population found that guilt was strongly linked with depression.<sup>122</sup> Negative self-evaluation due to guilt often leads to painful, overwhelming emotions, while the perception of self-worthlessness can induce suicidality.<sup>123</sup> Moreover, 'Guilt' was the most robust flow connection to suicidality in this network analysis which is consistent with previous studies. For instance, an earlier study reported that feeling worthless due to a traumatic experience was the most significant factor related to SA among 20 depression symptoms in patients with major depressive disorder (MDD).<sup>124</sup> Similarly, guilt was also found to have a significant association with SI among adults who attended mental health services.<sup>125</sup> In addition, the depression network<sup>101</sup> reported that guilt was strongly linked with SI among Wuhan residents during the rowleading the rowleading to COVID-19 pandemic in China.

"Concentration" and "Sleep" were the other strong connection to suicidality, which is in line with previous suicidality and depression network analysis among a community population in Korea.<sup>109</sup> People with depression tend to experience decreased ability to think or make decisions.<sup>105</sup> An earlier study demonstrated that psychosocial dysfunction was predominantly influenced by poor concentration in patients with depression (ie, inability to manage work, household, and relationships, and impairment of social and private activities).<sup>126</sup> Further, impairment of psychosocial function is a risk factor for suicidality as well (Franklin et al, 2017). On the other hand, 'sleep' refers to insomnia or hypersomnia.<sup>105</sup> Insomnia was highly prevalent during the COVID-19 pandemic (Bai et al, 2022b; Li et al, 2020; Morin et al, 2021) associated with COVID-19-related stress, social distancing, and economic burden.<sup>127,128</sup> Sleep dysfunction such as insomnia was strongly associated with suicidality<sup>17</sup> and found to be a significant predictor of SI<sup>129</sup> and SA.<sup>130</sup> In particular, a meta-analysis of longitudinal studies determined that insomnia had the most substantial connection with SI among those with sleep disturbances.<sup>131</sup> Greater levels of insomnia was associated with greater SI intensity,<sup>129</sup> SI maintenance,<sup>131</sup> and SA occurrence.<sup>130</sup> A decrease in serotonin, which is an essential neurotransmitter in the central nervous system that regulates sleep and impulse control,<sup>132,133</sup> may explain the association between sleep problems and suicidality among depression patients. Apart from the biological mechanisms of sleep and suicidality, dysfunctional cognition and attitudes about sleep may also contribute to insomnia and suicidal thoughts.<sup>134</sup> Moreover, concern about current sleeping patterns was the central symptom of depression and insomnia network among the Korean general population during the COVID 19 pandemic.<sup>135</sup>

In this study, "SI", "SP" and "Fatigue" were identified as central symptoms in the depression and suicidality network mode, which are the most influential symptoms that could be targeted in treatment.<sup>40</sup> Thus, early screening and treatment that target SI and SP, as well as those that address lack of energy, should be prioritized for Macau residents in need. Additionally, "Guilt" was identified as a bridge node with the strongest connection to suicidality in this study; therefore, future research should also target feelings of guilt. Mindfulness-based cognitive

therapy, in which depressed patients cultivate a non-judgmental attitude to reduce rumination from negative thinking, could significantly reduce depression and SI.<sup>136</sup> Further, we found that insomnia was also associated with suicidality. Cognitive Behavioral Therapy for Insomnia (CBT-I) is an effective intervention for both insomnia and suicidality, which aims to change sleep maladaptive beliefs and attitudes and dysfunctional sleep cognition.<sup>137</sup> However, most of studies on the association between sleep and suicidality were based on cross-sectional study design, and therefore, causality between them could not be examined.<sup>131,138</sup> Further prospective studies are needed.

The merits of this study included its large sample size and advanced network analysis identifying links between depressive symptoms and suicidality. However, the main limitations should be acknowledged. First, this was a non-experimental, cross-sectional study; hence, causal relationships between suicidality and depressive symptoms could not be determined. It is necessary to conduct future intervention research and longitudinal studies in order to analyze the possible causal relationships and dynamic changes between suicidality and symptoms of depression in adults over time. Second, this study was conducted in the Macau SAR, so the results may not be applicable to other regions because COVID-19 policies and trajectories differ from region to region. Third, due to the risk of COVID-19 infection, snowball sampling via an online survey might have resulted in selection biases which decreased the representativeness of the population. Lastly, biases in recall and social desirability could not be controlled due to the use of self-report assessment in the study.

In conclusion, central symptoms (eg, "Suicidal ideation", "Suicide plan", "Fatigue") and key bridge symptoms (eg, "Suicidal ideation" and "Guilt") identified in this study might serve as crucial targets in the screening, prevention and treatment for adults with depression and suicidality during the pandemic. Future research should prioritize improving assessment and intervention based on central and bridge symptoms for those in need.

## **Data Sharing Statement**

The original contributions presented in the study are included in the article/<u>Supplementary Material</u>. Further inquiries can be directed to the corresponding authors. Requests to access the datasets should be directed to xyutly@gmail.com.

## **Ethics Approval and Consent to Participate**

The study was approved by the Institutional Review Board of the University of Macau (Ethics approval number: SSHRE22-APP05-FHS) which adhered to the principles of the Declaration of Helsinki. Participants are provided electronic written informed consent.

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## **Author Contributions**

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

## Disclosure

The authors report no conflicts of interest in this work.

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