

# Complex associations among modifiable determinants of circadian syndrome among employed people in southwestern China

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## Abstract

**Background:** Circadian syndrome (CircS) may be closely linked to lifestyle, psychological, and occupational factors, but evidence is lacking. This study aimed to explore complex associations between lifestyle, psychological and occupational factors and CircS among employed people in southwestern China.

**Methods:** In this study, network analysis was used to identify complex associations between lifestyle, psychological and occupational factors and CircS in employed people from the Chinese Cohort of Working Adults (CCWA). The centrality of each variable was estimated by strength centrality index, which was calculated by the sum of edge weights connected to the variable. Bridge in the network was identified as the variables in the top 80<sup>th</sup> percentile of overall bridge strength, which was defined as the most strongly connected variables across lifestyle, psychological and occupational factors and CircS. The differences were assessed in network structures between subgroups divided by the median score of the variable with the strongest bridge strength.

**Results:** Among 31,105 participants from CCWA, 5213 (16.76%) had CircS. In the constructed network, anxiety (edge weights: 0.28), smoking (edge weights: 0.15), drinking (edge weights: 0.10), perceived noise at work (edge weights: 0.08), and implicit health attitude (edge weights: -0.02) were directly related to CircS, with 83.31% of the variance for CircS explained by these neighboring factors. Anxiety was the most central variable (strength centrality: 1.20) in the network and the strongest bridge (bridge strength: 0.84) connecting all domains of variables. A stronger association between anxiety and CircS was observed in the network of participants with more severe anxiety (edge weight: 0.23) than those with less severe anxiety (edge weight: 0.03).

**Conclusion:** Anxiety had the strongest association with CircS and was the central factor with the highest strength centrality, also the bridge with the highest bridge strength in the network.

**Keywords:** Circadian syndrome; Employed people; Network analysis; Lifestyle; Psychological factor; Occupational factor; Anxiety

## Introduction

Circadian syndrome (CircS) is an emerging syndrome linking metabolic syndrome (MetS) components such as obesity, hypertension, dyslipidemia, and impaired glucose tolerance with circadian disruptions, sleep disorders, and depression.<sup>[1]</sup> While MetS serves as an early indicator of cardiovascular diseases (CVDs), the inclusion of circadian and mental health factors in CircS offers a more comprehensive pathophysiological model for CVD risk prediction.<sup>[2,3]</sup> Research has shown that circadian

disruption and depression are associated with CVDs, such as heart failure and ischemic stroke,<sup>[4,5]</sup> and contribute to poorer cardiovascular outcomes.<sup>[6]</sup> In a cohort study of 9360 adults, prevalence of CircS (39.0%) was lower than MetS (44.7%), yet the 5-year CVD risk (15.1%) of CircS patients was higher than MetS patients, suggesting that CircS may hold greater public health implications for CVD prevention.<sup>[2]</sup>

Understanding modifiable determinants of CircS, including lifestyle and psychological factors, is crucial.<sup>[1]</sup>

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Sedentary behavior, sleep deprivation, and poor dietary habits would increase both MetS and CircS risk,<sup>[7,8]</sup> while psychological factors like anxiety exacerbate sleep disorders and depression.<sup>[9,10]</sup> Occupational factors, especially irregular work schedules, may disproportionately impact employees, elevating their CircS risk.<sup>[11,12]</sup> Despite the known impact of lifestyle and psychological factors on MetS, research specifically targeting CircS determinants remains sparse. In addition, CircS may conversely affect lifestyle and psychological factors, which has made their complex associations become a system of reciprocal interactions.

The complexity of interactions among lifestyle, psychological, and occupational factors requires advanced analytical methods. Network analysis, which captures multifaceted associations within complex systems, offers a promising approach.<sup>[13]</sup> Previous studies have employed this method to explore behavioral and psychological factors in relation to health outcomes, revealing reciprocal relationships and highlighting central variables.<sup>[14–16]</sup> This study aimed to apply network analysis to explore the associations between these factors and CircS among employed people, provide insights for targeted interventions and policy-making to reduce CircS risk and the burden of non-communicable diseases in the workforce.

## Methods

### Ethical approval

This study was approved by the Ethics Committee of West China Fourth Hospital and West China School of Public Health, Sichuan University (No. Gwl2021064). All participants provided informed consent on the cover page of the online questionnaire before taking part.

### Study design and participants

The Chinese Cohort of Working Adults (CCWA) was established based on the staff in the Chengdu Bureau of the National Railway Administration of China, a giant system covering about 120 kinds of occupations in China,<sup>[11]</sup> including officers, engineers, drivers, doctors, nurses, railway policemen, field workers, and service workers. These employed people mainly resided in the Sichuan, Chongqing, and Guizhou Provinces of southwest China. A systematic random sampling method was used to recruit the participants, using unique job identification numbers as the sampling frame. In the baseline survey between October 1, 2021 and December 31, 2021, 39,926 participants out of 119,780 staff were invited for an investigation. The investigation was conducted with reference to the Checklist for Reporting Results of Internet E-Surveys.<sup>[17]</sup> Briefly, an online questionnaire was designed by an expert panel to collect participants' demographic, lifestyle, psychological, and occupational characteristics. The usability and technical functionality of the electronic questionnaire were tested with 50 participants before deploying it. The questionnaire items were designed with logical branching (e.g., participants with a smoking history would not be further asked about

the duration of smoking cessation), and the response values were restricted within reasonable ranges (e.g., the daily sleep time cannot be entered with a value greater than 16 h). The questionnaire was distributed through the personnel management website information system and required about 25–35 min to complete. During the survey process, health management personnel at each site encouraged participants to complete the questionnaire. To assess the validity of the collected questionnaires, three commonsense questions (e.g., which city is the capital of China?) were placed at the beginning, middle, and end of the questionnaire, and only those with all three questions correctly answered were considered valid.

Finally, 31,105 people participated in the CCWA, with a response rate of 77.91% (31,105/39,926) and all complete questionnaires were valid. All of them also received a physical examination at the designated health care centers run by the Chengdu Bureau of the National Railway Administration of China, which had unified medical examination equipment and clinical laboratory tests. An overview of data collection is shown in Supplementary Figure 1, <http://links.lww.com/CM9/C352>.

### CircS definition

CircS was defined based on the joint statement “Harmonizing the Metabolic Syndrome”.<sup>[18]</sup> Considering the potential association between circadian rhythm disruption and MetS, Zimmet *et al*<sup>[1]</sup> further proposed the term “circadian rhythm syndrome”. According to previous studies,<sup>[1–3,19,20]</sup> the CircS was defined as the presence of four or more of the following seven symptoms/conditions: (1) obesity, defined as body mass index (BMI)  $\geq 25$  kg/m<sup>2</sup>;<sup>[21]</sup> (2) elevated blood pressure, defined as systolic  $\geq 130$  mmHg and/or diastolic  $\geq 85$  mmHg; (3) high fasting blood glucose (FBG), defined as FBG  $\geq 100$  mg/dL; (4) decreased high-density lipoprotein cholesterol (HDL-C), defined as HDL-C  $< 40$  mg/dL in men or  $< 50$  mg/dL in women; (5) elevated triglycerides (TG), defined as TG  $\geq 150$  mg/dL; (6) short sleep, defined as sleep time  $< 6$  h/day; and (7) depression, defined as moderate, moderately severe, or severe depression, defined as the depression score  $\geq 10$ .<sup>[2,18,22]</sup> Among them, body weight and height used to calculate BMI were measured in light clothing and barefoot. Blood pressure was averaged over the three measurements made at a resting state. FBG, HDL-C, and TG were measured in venous blood samples collected after fasting for at least 8 h at night. Sleep time was measured by one item, i.e., “How many hours of actual sleep at night did you get on average in the past month?” The depression score was calculated from the Patient Health Questionnaire-9 (PHQ-9),<sup>[22]</sup> a self-administered version of the Primary Care Evaluation of Mental Disorders diagnostic instrument for common mental disorders.

### Candidate determinants of CircS

According to the previous literature,<sup>[2,19]</sup> we selected a comprehensive set of lifestyles, psychological, and occupational factors as candidate determinants of CircS [Supplementary Table 1, <http://links.lww.com/CM9/C352>].

The four lifestyle factors were selected. Drinking status (never, current, or former) and smoking status (never, current, or former) were defined according to the China Kadoorie Biobank Study.<sup>[23,24]</sup> Dietary pattern was measured by a food frequency questionnaire (FFQ) scale with a healthy eating index, with a higher score indicating more healthy dietary behavior.<sup>[25,26]</sup> Physical activity (PA) was measured by the total value of the metabolic equivalent for tasks (METs) for occupational, traffic-related, chore, and leisure-time activities, with a higher score indicating a higher level of PA one was engaged in.<sup>[27]</sup>

The three psychological factors were selected. Well-being was assessed by a Short Scales of Flourishing and Positive and Negative Feelings,<sup>[28]</sup> with a total score ranging from 8 to 56 and a higher score indicating better well-being. Anxiety was evaluated by a 7-item self-reported Generalized Anxiety Disorder (GAD-7),<sup>[29]</sup> with a total score from 0 to 21 and a higher score indicating a higher level of anxiety. The implicit health attitudes, representing one's attitude toward his/her health based on implicit assessment strategies,<sup>[30]</sup> were evaluated by a Lay Theory of Health Measure,<sup>[31]</sup> with a total score from 6 to 36 and a higher score indicating a stronger health-promoting intention.

The two occupational factors were selected. The regularity of work was categorized as irregular and regular. The perceived noise at work was measured by the three items designed in previous research<sup>[32,33]</sup>: "The noise in your work environment is too loud", "The noise in your work environment has affected your physical health", and "The noise in your work environment has affected your mental health". A five-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree) was used to rate each item, with a total score from 3 to 15 and a higher score indicating a higher level of perceived noise at work.

Some sociodemographic characteristics were considered the covariates or confounders, according to the previous studies,<sup>[2,12]</sup> including age, sex (male, female), ethnicity (Chinese Han, minorities), marital status (unmarried, married/cohabitation, separated/divorced/widowed), living status (living alone, living with non-family members, and living with family members), educational level (senior high school or below, junior college, bachelor degree or above), and monthly household income (<CNY 6000 yuan, CNY 6000–9999 yuan, ≥CNY 10,000 yuan).

## Statistical analyses

### Descriptive statistics

Continuous and categorical variables were summarized by  $n$  (%) or mean  $\pm$  standard deviation (SD), respectively, with values compared by Student's  $t$ -test or chi-squared test. Multiple imputation with chained equations on 25 sets was applied to handle missing values before modeling.<sup>[34]</sup> R software version 4.1.0 (R Foundation for Statistical Computing, Vienna, Austria) was used to conduct all statistical analyses, and the statistical significance was defined as  $P < 0.05$ .

## Network construction and estimation

Network analysis based on mixed graphical models (MGM) was conducted to identify connections (edges) among variables (nodes).<sup>[35]</sup> In the network, edge thickness represented the strength of association (i.e., absolute partial correlation coefficient), with green and red edges indicating positive and negative correlations, respectively [Supplementary Figure 2, <http://links.lww.com/CM9/C352>]. A least absolute shrinkage and selection operator (LASSO) was applied to minimize spurious edges, resulting in a sparse, interpretable network.<sup>[36]</sup> An extended Bayesian Information Criterion (EBIC) with a tuning parameter of 0.5 selected the model,<sup>[37]</sup> and a Fruchterman–Reingold algorithm visualized the network. The strength centrality index was used to evaluate the centrality of factors in the network,<sup>[37]</sup> defined as the sum of edge weights connected to a variable.

The bridge in the network was defined as the most strongly connected variable in different domains (i.e., lifestyle, psychological, and occupational factors and CircS domains).<sup>[38]</sup> Bridges can impact network structure and may be related to the spread of intervention effects among domains.<sup>[38]</sup> The bridge strength was calculated by summing the absolute values of all edge weights connecting a given variable with variables in different domains. Bridges were identified with the top 80<sup>th</sup> percentile of the overall bridge strengths, i.e., variables for which deactivation would result in preventing the activation of variables in the other domains. Besides, we divided the strongest bridge into two subgroups by the median score of the bridge to explore network structure differences.

Network stability was analyzed using non-parametric bootstrapping (1000 times) with confidence intervals (CIs) to test the reliability of edge weights.<sup>[37]</sup> A correlation stability coefficient was used to evaluate the stability of the strength centrality, with values  $>0.5$  indicating a well-fitting model.<sup>[37]</sup> In addition, we calculated the percentage of explained variance ( $R^2$ ) for each node in the network by predictability index.<sup>[38]</sup> An overview of network construction and estimation is shown in Supplementary Figure 1, <http://links.lww.com/CM9/C352>.

## Sensitivity analyses

We estimated the network excluding participants with missing data and compared it with the network including all participants to assess robustness. Spearman correlations of edge weights and strength centrality were computed to assess similarity.<sup>[39,40]</sup> Besides, permutation tests were used to estimate differences between networks in their global strength (the sum of absolute values of all edge weights).<sup>[39]</sup> We also used *post-hoc* analysis to test edge weight differences with the false discovery rate (FDR) corrected  $P$  values.<sup>[41]</sup>

## Results

### Basic characteristics of the participants

A total of 31,105 employed adults were included, with an overall CircS prevalence of 16.76% (5213/31,105) [Table 1].

**Table 1: Basic characteristics of all participants in the CCWA.**

Variables	Overall (n = 31,105)	Non-CircS (n = 25,892)	CircS (n = 5213)	P value
Demographic characteristics				
Age (years)	36.64 ± 10.49	35.64 ± 10.30	41.48 ± 10.07	<0.001
Sex				<0.001
Male	25,518 (82.04)	20,632 (79.68)	4886 (93.73)	
Female	5587 (17.96)	5260 (20.32)	327 (6.27)	
Ethnicity				0.021
Chinese Han	28,969 (93.13)	24,075 (92.98)	4894 (93.88)	
Minorities	2136 (6.87)	1817 (7.02)	319 (6.12)	
Marital status				<0.001
Unmarried	8217 (26.42)	7494 (28.94)	723 (13.87)	
Married/cohabitation	21,194 (68.14)	17,072 (65.94)	4122 (79.07)	
Separated/divorced/widowed	1694 (5.45)	1326 (5.12)	368 (7.06)	
Living status				<0.001
Living alone	5573 (17.92)	4602 (17.77)	971 (18.63)	
Living with non-family members	5256 (16.90)	4537 (17.52)	719 (13.79)	
Living with family members	20,276 (65.19)	16,753 (64.70)	3523 (67.58)	
Educational level				<0.001
Senior high school or below	9329 (29.99)	6878 (26.56)	2451 (47.02)	
Junior college	14,218 (45.71)	12,269 (47.39)	1949 (37.39)	
Bachelor's degree or above	7558 (24.30)	6745 (26.05)	813 (15.60)	
Monthly household income (Chinese yuan)				<0.001
<6000	11,369 (36.55)	9326 (36.03)	2040 (39.13)	
6000–9999	13,774 (44.28)	11,465 (44.28)	2309 (44.29)	
≥10,000	5962 (19.17)	5098 (19.69)	864 (16.57)	
Lifestyle characteristics				
Drinking				<0.001
Never	12,836 (41.27)	11,371 (43.92)	1465 (28.10)	
Current or former	18,269 (58.73)	14,521 (56.08)	3748 (71.90)	
Smoking				<0.001
Never	14,226 (45.74)	12,744 (49.22)	1482 (28.43)	
Current or former	16,879 (54.26)	13,148 (50.78)	3731 (71.57)	
Dietary pattern				<0.001
Poor	1227 (3.94)	922 (3.56)	305 (5.85)	
Average	18,135 (58.30)	14,943 (57.71)	3192 (61.23)	
Ideal	11,743 (37.75)	10,027 (38.73)	1716 (32.92)	
PA intensity				<0.001
Low level	9338 (30.02)	7659 (29.58)	1679 (32.21)	
Medium level	10,961 (35.24)	9239 (35.68)	1722 (33.03)	
High level	10,806 (34.74)	8994 (34.74)	1812 (34.76)	
Psychological factors				<0.001
Well-being	36.50 ± 10.57	36.94 ± 10.50	34.34 ± 10.62	<0.001
Anxiety	5.55 ± 5.57	5.09 ± 5.29	7.87 ± 6.30	<0.001
Implicit health attitude	25.04 ± 5.99	25.19 ± 6.04	24.31 ± 5.68	<0.001
Occupational characteristics				
Regularity of work				<0.001
Irregular	17,626 (56.67)	14,799 (57.16)	2827 (54.23)	
Regular	13,479 (43.33)	11,093 (42.84)	2386 (45.77)	
Perceived noise at work	10.30 ± 2.69	10.14 ± 2.66	11.10 ± 2.69	<0.001
Components of CircS				
Obesity	11,292 (36.30)	9405 (36.32)	1887 (36.20)	0.875
High blood pressure	9852 (31.67)	8177 (31.58)	1675 (32.13)	0.446
Elevated blood glucose	6502 (20.90)	5367 (20.73)	1135 (21.77)	0.094
Decreased HDL-C	4047 (13.01)	3343 (12.91)	704 (13.50)	0.255
Elevated TG	12,862 (41.35)	10,708 (41.36)	2154 (41.32)	0.973
Short sleep	7057 (22.69)	5856 (22.62)	1201 (23.04)	0.519
Depression	9382 (30.16)	7805 (30.14)	1577 (30.25)	0.891

Data are shown as mean ± standard deviation or n (%). CCWA: Chinese Cohort of Working Adults; CircS: Circadian syndrome; HDL-C: High-density lipoprotein cholesterol; PA: Physical activity; TG: Triglycerides.

The prevalence of CircS symptoms/conditions ranged from 13.01% (4047/31,105, decreased HDL-C) to 41.35% (12,862/31,105, elevated TG). The participants had a mean age of  $36.64 \pm 10.49$  years, with 82.04% (25,518/31,105) being male. Less than half (43.33%, 13,479/31,105) of the participants had regular work. The perceived noise at work scored  $10.30 \pm 2.69$  on average. More than half of them were current or former drinkers (58.73%, 18,269/31,105) and smokers (54.26%, 16,879/31,105). Most participants had an average diet quality (58.30%, 18,135/31,105) and a medium level of PA (35.24%, 10,961/31,105). The mean scores for well-being, anxiety, and implicit health attitude were  $36.50 \pm 10.57$ ,  $5.55 \pm 5.57$ , and  $25.04 \pm 5.99$ , respectively.

**Association among variables in networks**

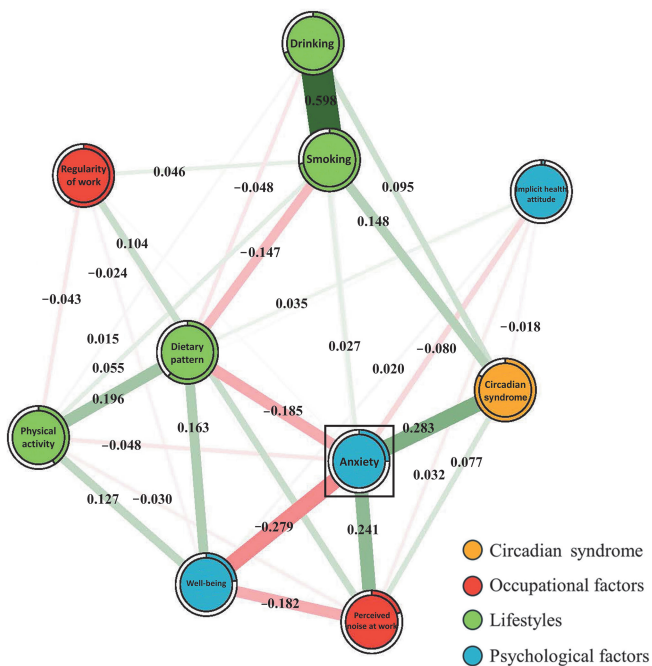
The MGM-identified network [Figure 1] and the corresponding adjacency matrix of edge weights [Supplementary Figure 3, <http://links.lww.com/CM9/C352>], based on all participants, were shown. We found that anxiety (edge weight: 0.28), smoking (0.15), drinking (0.10), perceived noise at work (0.08), and implicit health attitude (-0.02) were directly associated with CircS. The nodewise predictability showed that 83.31% of the variance for CircS could be interpreted by these directly associated variables [Supplementary Table 2, <http://links.lww.com/CM9/C352>]. Lifestyle, psychological, and occupational factors interacted with one another, with strong associations observed between perceived noise at work and anxiety (edge weight: 0.241), between perceived noise at work and

well-being (-0.182), and between dietary pattern and anxiety (-0.185). The edge weights of the network in all participants were close to bootstrapped values of edge weights, with narrower CIs of edge weights indicating better accuracy of the results [Supplementary Figure 4, <http://links.lww.com/CM9/C352>].

**Key variables in the network**

We found that anxiety was the most central variable (with the highest strength centrality of 1.20) in the network [Figure 2]. Among all lifestyle, psychological, and occupational variables directly related to CircS, anxiety (strength: 1.20), smoking (strength: 1.02), and drinking (strength: 0.83) ranked top three in strength centrality. The strength centrality indices remained highly stable [Supplementary Figure 5, <http://links.lww.com/CM9/C352>]. In the network, we found anxiety (bridge strength: 0.84) was the strongest bridge connecting lifestyle, psychological, and occupational factors and CircS [Figure 1], indicating that anxiety may be the most important variable impacting network structure and influencing the spread of intervention effects across domains. The specific bridge strength of each variable can be found in Figure 2.

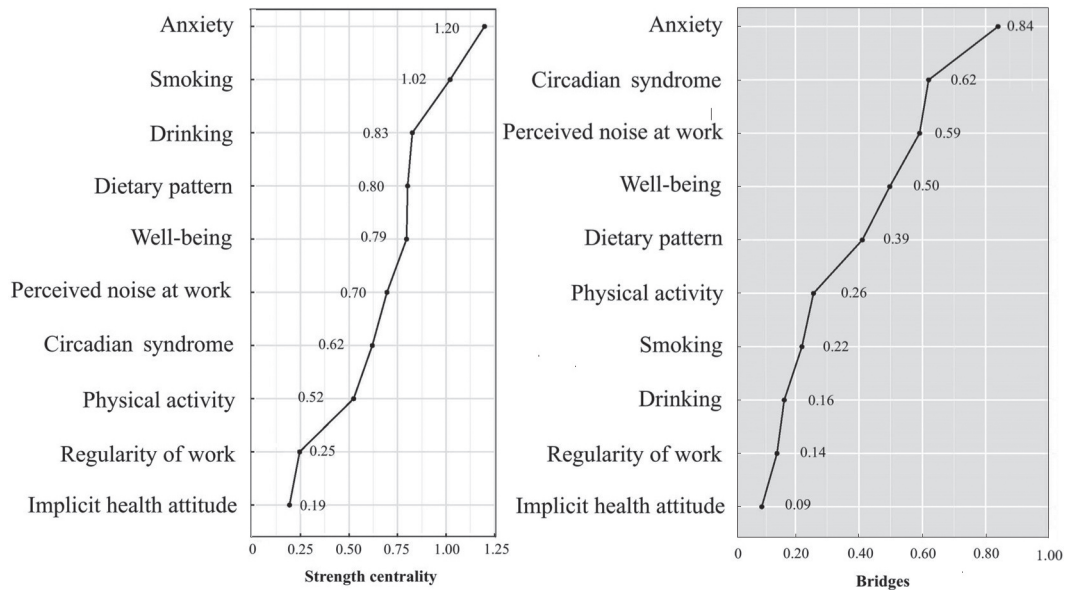
Since anxiety was the strongest bridge in the network, we proceeded to compare network structures among participants with less and more severe anxiety, as determined by the median score of anxiety (median value = 5) [Figure 3]. The edge weights of the two networks were close to their respective bootstrapped values of edge weights [Supplementary Figure 6, <http://links.lww.com/CM9/C352>]. We found that perceived noise at work, drinking, smoking, well-being, and anxiety were directly associated with CircS in the networks [Figure 3], and the edge weight between anxiety and CircS in participants with more severe anxiety (edge weight: 0.23) was stronger than that in participants with less severe anxiety (edge weight: 0.03) [Supplementary Tables 3 and 4, <http://links.lww.com/CM9/C352>]. Besides, anxiety (strength: 1.51) was the most central variable in the network of participants with less severe anxiety, with well-being as the strongest bridge; smoking (strength: 1.63) was the most central variable in the network of participants with more severe anxiety, with anxiety as the strongest bridge (except for CircS). The specific strength centrality and bridge strength can be found in Supplementary Figure 7, <http://links.lww.com/CM9/C352>. The strength centrality indices remained highly stable [Supplementary Figure 8, <http://links.lww.com/CM9/C352>].



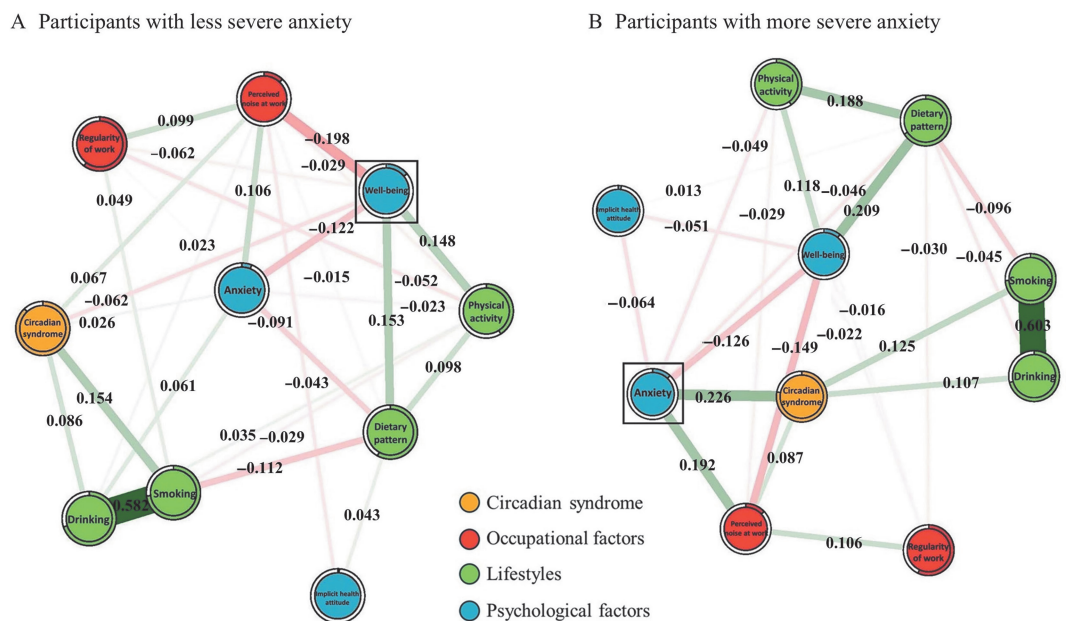
**Figure 1:** Network of all participants in the Chinese Cohort of Working Adults. Green edges indicate positive relationships, while red edges indicate negative relationships. The thickness of the edges is proportional to the absolute value of the edge weights. Rings around colored parts display prediction functions, including explained variance for continuous variables and correct classification for categorical variables. The variable framed by the square is the strongest bridge (with the highest bridge strength) among all lifestyle, psychological and occupational factors. Demographics were adjusted in the networks while were not plotted.

**Replicability of the findings**

After excluding 6916 participants with at least one missing variable, the remaining 24,189 participants were used for replicability of the findings. The basic information can be found in Supplementary Table 5, <http://links.lww.com/CM9/C352>. Network structure, adjacency matrix, strength centrality, and bridges based on the participants without missing data can be found in Supplementary Figures 9–11, <http://links.lww.com/CM9/C352>. The network of participants without missing data was robust,



**Figure 2:** Strength centrality indices and bridge strength of variables in the network of all participants in the Chinese Cohort of Working Adults.



**Figure 3:** Networks of participants with less severe and more severe anxiety. The network structure constructed by circadian syndrome and lifestyle, psychological, and occupational factors in participants with anxiety scores equal to or below the median (A) and above the median (B). Green edges indicate positive correlations, while red edges indicate negative correlations. The thickness of the edges is proportional to the absolute value of the edge weights. Rings around colored parts display prediction functions, including explained variance for continuous variables and correct classification for categorical variables. The variable framed by the square is the strongest bridge (with the highest bridge strength) among all lifestyle, psychological, and occupational factors. Demographics were adjusted in the networks while were not plotted.

with high correlation stability coefficients of strength centrality [Supplementary Figures 12 and 13, <http://links.lww.com/CM9/C352>]. Besides, a high correlation was observed in strength centrality ( $r = 0.97$ ) and bridge strength ( $r = 0.99$ ) between networks of all participants and of those without missing data. The permutation test showed no significant differences in the two networks' global strengths (test statistic  $S = 0.01$ ,  $P = 0.93$ ). Among 136 non-zero edges, *post-hoc* comparison showed that only 10 (7.35%) were significantly different between

these two networks, which meant that the networks were generally similar.

**Discussion**

This study used network analysis, from a systematic perspective, to unravel complex associations between lifestyle, psychological, and occupational factors and CircS among employed people. Anxiety, smoking, drinking, perceived noise at work, and implicit health attitude were found

directly associated with CircS in the network, among which anxiety was the most central variable and served as the strongest bridge connecting lifestyle, psychological, and occupational factors and CircS. Furthermore, the association between anxiety and CircS was found stronger in the network of the employed with more severe anxiety than of those with less severe anxiety, also with different central variables and bridges observed in networks.

Some common lifestyle and psychological risk factors of CircS and MetS were observed. For example, smoking and drinking, the two well-known lifestyle risk factors of MetS,<sup>[42,43]</sup> were also found directly associated with CircS. Psychological risk factors of MetS were also strongly associated with CircS, such as anxiety. This was similar to the previous finding that depression was found to be a risk factor of both comorbidities associated with MetS and CircS, as anxiety was considered a predetermined factor or a common syndrome of depression.<sup>[42,43]</sup>

From a practical perspective, lifestyle and psychological variables that played central roles in the network, including anxiety, smoking, and drinking, may deserve special attention for reducing the CircS risk. Central nodes could spread influences of interventions to peripheral nodes of the network, so interventions designed more for central nodes may have the maximum efficiency.<sup>[44,45]</sup> Hence, grouping patterns of variables (i.e., variables connected with wider, also darker, edges in the network) may imply the design of optimal, joint interventions. For example, we found that perceived noise at work was closely associated with well-being and anxiety, which was also consistent with previous findings.<sup>[32,33,46]</sup> Perceived noise at work can measure the personal perception of auditory with consideration of their own noise sensitivity,<sup>[47]</sup> so it may affect CircS through circadian dysfunction, sleep quality, and noise-induced mental health problems. Such mechanisms possibly underlying observed connections in the network should be considered in public health policy-making.

Anxiety was identified as the most important bridge connecting variables in the whole network, which implied that interventions that could reduce anxiety might overall improve related lifestyle and psychological factors and directly and indirectly contribute to CircS prevention.<sup>[48]</sup> It is noted that a stronger association between anxiety and CircS was observed in the network of participants with more severe anxiety than that of participants with less severe anxiety. The observation that the stronger anxiety–CircS association was in the network of those with more severe anxiety suggested that the employed with more severe anxiety disorders were more likely to suffer from CircS than their counterparts with less severe or without anxiety disorders. Thus, further investigation on the effect modification of anxiety on the associations of lifestyle, other psychological, and occupational factors with CircS, also such effect modification of other potential modifying factors, are warranted. Given potential reciprocal relationships between anxiety and CircS, interventions for CircS may also decrease anxiety. In addition, different bridges in networks of the employed with different levels of anxiety implied that bridges may vary during the implementation

of interventions. Therefore, it is vital to maintain dynamic reconstruction and monitoring of the network.

Despite the strong capacity of network analysis in handling various domains of variables and hence proposing the comprehensive design of non-pharmacological interventions, some limitations remain in this study. First, the cross-sectional design may hinder causal inference between determinants and CircS development. For example, those with CircS may feel anxious about their health status, which may result in reverse causality. Therefore, combining network analysis with cohort studies or randomized controlled trials is needed for future researchers seeking solid evidence and efficient interventions on CircS mitigation and prevention. Second, obesity was measured by BMI rather than waist circumference, which may fail to fully estimate cardiometabolic risk. However, a prior study found that BMI and a waist circumference-based score were comparable in terms of predicting the development of type 2 diabetes mellitus and coronary heart disease.<sup>[49]</sup> Third, the data used in this study, although covering a large number of occupations, were collected only from the employed in the three provinces in the southwestern China, so the findings from this study should be generalized to all populations with caution. Fourth, network analysis may obscure differences between individuals, and it is impossible to infer the directionality of associations among the modifiable determinants of CircS. Fifth, some important variables may not be considered due to a lack of information. For example, our study only considered two occupational factors (i.e., regularity of work and perceived noise at work), which may not fully reflect the distinctive risk factors of employed individuals.

In conclusion, this study used network analysis to identify direct associations of anxiety, smoking, drinking, perceived noise at work, and implicit health attitude with CircS. Interventions targeting these preventable and modifiable factors, especially anxiety, a central variable and bridge in the network, may contribute to CircS prevention in employed people.

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### Conflicts of interest

None.

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