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Comparison of workplace impairment and daily activity impairment in acute and chronic insomnia disorder: a study of Chinese adults

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Abstract: Background: Insomnia is a common condition that adversely affects work productivity, and a significant proportion of individuals with acute insomnia disorder (AID) eventually develop chronic insomnia disorder (CID). However, it remains unclear whether workplace impairment and daily activity impairment occur early in the course of insomnia. Methods: This cross-sectional study included 295 AID and 305 CID participants. Multiple linear regression was used to assess associations between insomnia, workplace and daily activity impairment, and related factors (daytime sleepiness, depressive and anxiety symptoms). Restricted cubic spline (RCS) analysis was also conducted to explore nonlinear relationships. Mediation analysis was performed to assess the potential mediating effects of daytime sleepiness and depressive and anxiety symptoms between insomnia and workplace and daily activity impairment. Results: No significant differences were found between the AID and CID groups in presenteeism or productivity-loss costs (P>0.05). Insomnia severity, daytime sleepiness, and depressive and anxiety symptoms were the correlated factors of workplace and daily activity impairment (P<0.05). A nonlinear relationship between depressive symptoms and presenteeism, as well as between daytime sleepiness and daily activity impairment, was identified in both groups ($P_{overall}$<0.01, $P_{nonlinearity}$<0.05). Mediation analysis showed that in the AID group, depressive symptoms mediated the effects on absenteeism and daily activity impairment (mediation proportions: 37.02% and 28.61%, respectively). In the CID group, anxiety symptoms had a greater mediating effect on presenteeism and daily activity impairment (mediation proportions: 53.01% and 31.70%, respectively). Conclusions: Presenteeism and productivity-loss costs occur in AID and are comparable with those resulting from CID. Depressive and anxiety symptoms are also important mediators of workplace and daily activity impairment in AID. We recommend investing in portable and effective interventions to improve work productivity.

Key words: Insomnia; Workplace impairment; Daily activity impairment; Presenteeism; Absenteeism

1 Introduction

Insomnia is a highly prevalent mental disorder that imposes a substantial economic burden, largely due to work productivity loss (Natsky et al., 2020; Sutton, 2021; van Someren, 2021). Previous research has found that individuals with insomnia face employment-related challenges, including workplace impairment (presenteeism: reduced work performance; absenteeism: time lost from work) and daily activity impairment (functional limitations in daily activities outside work) (Espie et al., 2018; Streatfeild et al., 2021; Espel-Huynh et al., 2022; Chalet et al., 2023). However, most studies focus on insomnia symptoms in general, rather than distinguishing between different stages of an insomnia disorder.

Distinguishing between acute insomnia disorder (AID) and chronic insomnia disorder (CID) is crucial for both clinical practice and public health policy. AID is a significant subtype of insomnia with a high annual incidence of 36.6% (Ohayon and Reynolds, 2009;

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Boyle et al., 2024). It is common, and 40% of individuals with AID (i.e., 3 d to 3 months) transition to CID (i.e., 3 months or longer) (Ellis et al., 2012, 2014). However, both stages of insomnia disorder are associated with symptoms such as daytime sleepiness, anxiety, and depression (Passarella and Duong, 2008; Khachatryan, 2021; Yang et al., 2023; Zhang et al., 2023), which may further impact work performance, social interactions, and overall quality of life (Khachatryan, 2021). The progression from AID to CID represents not only a temporal extension of symptoms but also an escalation in severity, comorbidity, and functional impairment (Boyle et al., 2024). However, the specific contributions of these symptoms to workplace and daily activity impairment at different stages of insomnia disorder have not been systematically examined.

To address these gaps, our aim in this study was to investigate the associations between different stages of insomnia disorder (AID group vs. CID group) and impairment in both workplace and daily activity. We also explored the roles of daytime sleepiness and depressive and anxiety symptoms. On the basis of prior related studies, we propose the following hypotheses: (1) individuals with AID already experience workplace and daily activity impairment; (2) insomnia-related symptoms of daytime sleepiness, depression, and anxiety are significantly associated with workplace and daily activity impairment in both groups; (3) insomnia-related symptoms of daytime sleepiness, depression, and anxiety mediate the relationship between insomnia and impairment in workplace and daily activity, with potential differences between AID and CID.

2 Results

2.1 Sample characteristics

Of the eligible patients, 86.61% (634/732) provided informed consent. A total of 34 participants were missing social demographic information and were excluded from the analyses, resulting in a final sample size of 600 (Fig. 1). Of these, 295 were classified as AID and 305 as CID. Overall, 56.00% were employed full-time or part-time, 39.17% were students, and 4.83% were unemployed. Compared with participants with CID, those with AID were generally younger and more educated, and fell into the demographic of workers and students with lower income (Table 1).

The range of Insomnia Severity Index (ISI) scores was 8 to 28 for both groups. There was no significant difference in insomnia severity between the two groups. Compared to patients with CID, those with AID showed less depression but more anxiety. Presenteeism and daily activity impairment were similar across groups, although absenteeism was higher in the CID group. Productivity-loss costs were also comparable between groups (USD 578.08±3491.30 for CID vs. USD 494.61±1746.07 for AID; Table 1).

2.2 Linear regression of overall workplace and daily activity impairment in multiple models

Based on the results of Spearman's rank correlation (Fig. S1), we adjusted for covariates and used multiple linear regression analyses to test the relationship between insomnia and impairment in both workplace and daily activity. We set subclinical insomnia as the reference, and found that greater severity of insomnia was associated with greater impairment in daily activities and with presenteeism and absenteeism. The presence of daytime sleepiness significantly influenced the relationship between insomnia severity and both presenteeism (β=0.05, 95% confidence interval (CI): 0.02–0.09, P<0.01) and daily activity impairment (β=0.04, 95% CI: 0.01–0.08, P<0.05). Furthermore, hyper-anxiety moderated the association between insomnia severity and both presenteeism (β=0.11, 95% CI: 0.03–0.18, P<0.01) and daily activity impairment (β=0.14, 95% CI: 0.07–0.22, P<0.001). Meanwhile mild depression (β=0.06, 95% CI: 0.01–0.10, P<0.05), moderate depression (β=0.11, 95% CI: 0.05–0.17, P<0.001), and severe depression (β=0.11, 95% CI: 0.01–0.22, P<0.05) moderated the relationship between insomnia severity and daily activity impairment.

There were no significant differences between the AID and CID groups in terms of presenteeism (β=6.00×10^{-4}, 95% CI: -3.37×10^{-2}–3.50×10^{-2}, P=0.813) or absenteeism (β=−0.01, 95% CI: −0.03–0.01, P=0.455). However, participants with AID showed significantly less daily activity impairment than those with CID (β=−0.04, 95% CI: −0.08–0.01, P<0.05). These results are presented in Table S1.

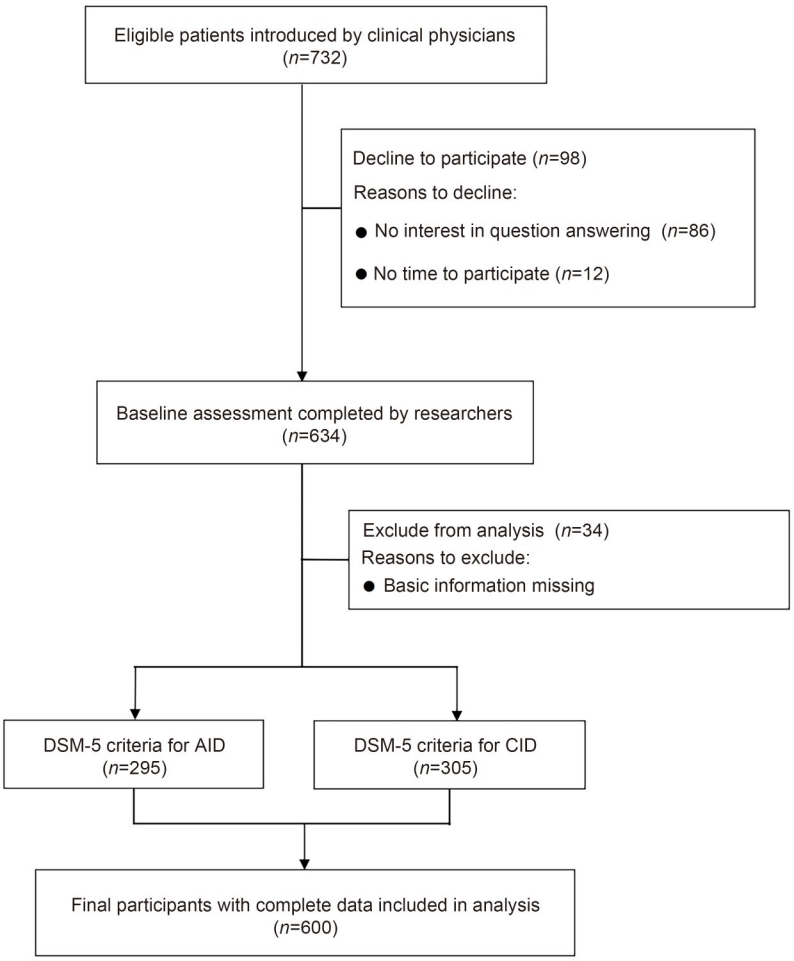

Fig. 1 Flowchart of the study. AID: acute insomnia disorder; CID: chronic insomnia disorder; DSM-5: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition.

2.3 Nonlinear relationships between insomnia-related symptoms and workplace and daily activity impairment

When Epworth Sleepiness Scale (ESS), 9-item Patient Health Questionnaire (PHQ-9), and 7-item Generalized Anxiety Disorder Questionnaire (GAD-7) scores were evaluated as continuous variables, positive correlations between these factors and impairment in both workplace and daily activities persisted. The reference thresholds for the restricted cubic spline (RCS) analysis were selected based on widely accepted clinical cutoffs: ESS score=10, PHQ-9 score=5, GAD-7 score=5, and ISI score=15.

Interestingly, the RCS curve model effectively captured the nonlinear associations between ESS scores and daily activity impairment in both groups ($P_{overall}$<0.001, $P_{nonlinearity}$<0.01), with the impact of sleepiness accelerating sharply when ESS scores exceeded a threshold of 10. The CID curves were consistently positioned above the AID curves (Fig. 2c). Similarly, PHQ-9 scores demonstrated a strong inverted U-shaped association with presenteeism in both groups ($P_{overall}$<0.001, $P_{nonlinearity}$<0.001), with the positive correlation peaking at scores of 5 to 10 and diminishing beyond 10 (Fig. 2d). Linear relationships were observed between ESS scores and both presenteeism ($P_{overall}$<0.001, $P_{nonlinearity}$=0.436; Fig. 2a) and absenteeism ($P_{overall}$<0.001, $P_{nonlinearity}$=0.778; Fig. 2b). In addition, there was a significant positive linear correlation between PHQ-9 scores and absenteeism ($P_{overall}$<0.001, $P_{nonlinearity}$=0.774; Fig. 2e), as well as daily activity impairment ($P_{overall}$<0.001, $P_{nonlinearity}$=0.051; Fig. 2f). However, we did not find a nonlinear relationship between ISI or GAD-7 scores and impairment in either workplace or daily activity (all $P_{nonlinearity}$>0.05; Figs. S2 and S3).

Table 1 Demographic characteristics of participants between AID and CID

Parameter	Total (*n*=600)	AID (*n*=295)	CID (*n*=305)	*t* or χ^2	*P*
Age (years)	35.01±11.52	33.30±11.55	36.59±11.23	3.61[a]	<0.001***
BMI (kg/m^2)	21.94±3.39	22.12±4.20	21.93±3.35	−0.04[a]	0.326
Sex				0.13[b]	0.792
Male	177 (29.50)	89 (30.17)	88 (28.85)		
Female	423 (70.50)	206 (69.83)	217 (71.15)		
Education				19.65[b]	<0.001***
College or above	495 (82.50)	264 (89.49)	231 (75.74)		
Senior high schools or below	105 (17.50)	31 (10.51)	74 (24.26)		
Occupation				15.42[b]	<0.001***
Full- or part-time job	336 (56.00)	144 (48.81)	192 (62.95)		
Students	235 (39.17)	139 (47.12)	96 (31.48)		
No jobs	29 (4.83)	12 (4.07)	17 (5.57)		
Marital status				22.57[b]	<0.001***
Married	321 (53.50)	129 (43.73)	192 (62.95)		
Divorce or others	24 (4.00)	13 (4.41)	11 (3.61)		
Unmarried	255 (42.50)	153 (51.86)	102 (33.44)		
Income (CNY)				37.10[b]	<0.001***
<5000	317 (52.83)	180 (61.02)	137 (44.92)		
5000–10 000	156 (26.00)	44 (14.92)	112 (36.72)		
10 000–15 000	72 (12.00)	40 (13.56)	32 (10.49)		
>15 000	55 (9.17)	31 (10.51)	24 (7.87)		
ISI				2.90[b]	0.235
Subclinical insomnia	265 (44.17)	123 (41.69)	142 (46.56)		
Moderate insomnia	270 (45.00)	143 (48.47)	127 (41.64)		
Hyper-insomnia	65 (10.83)	29 (9.83)	36 (11.80)		
ESS				6.10[b]	0.018*
No drowsiness	442 (73.67)	204 (69.15)	238 (78.03)		
Drowsiness	158 (26.33)	91 (30.85)	67 (21.97)		
PHQ-9				13.65[b]	0.003**
No depression	148 (24.67)	54 (18.31)	94 (30.82)		
Mild depression	266 (44.33)	147 (49.83)	119 (39.02)		
Moderate depression	165 (27.50)	83 (28.14)	82 (26.89)		
Severe depression	21 (3.50)	11 (3.73)	10 (3.28)		
GAD-7				19.17[b]	<0.001***
No anxiety	208 (34.67)	127 (43.05)	81 (26.56)		
Mild anxiety	257 (42.83)	115 (38.98)	142 (46.56)		
Moderate anxiety	87 (14.50)	35 (11.86)	52 (17.05)		
Severe anxiety	48 (8.00)	18 (6.10)	30 (9.84)		
Presenteeism	0.17±0.23	0.16±0.22	0.19±0.24	1.60[a]	0.110
Absenteeism	0.04±0.11	0.03±0.09	0.07±0.17	1.39[a]	<0.001***
Overall workplace impairment	0.20±0.25	0.18±0.24	0.22±0.26	2.04[a]	0.042*
Daily activity impairment	0.39±0.23	0.37±0.21	0.41±0.25	1.75[a]	0.082
Productivity-loss costs (USD)	537.03±2772.05	494.61±1746.07	578.08±3491.30	0.37[a]	0.713

Data are expressed as mean±SD or number (percentage). [a] χ^2 value; [b] *t* value. * *P*<0.05; ** *P*<0.01; *** *P*<0.001. AID: acute insomnia disorder; CID: chronic insomnia disorder; BMI: body mass index; ESS: Epworth Sleepiness Scale; ISI: Insomnia Severity Index; PHQ-9: 9-item Patient Health Questionnaire; GAD-7: 7-item Generalized Anxiety Disorder Questionnaire; SD: standard deviation.

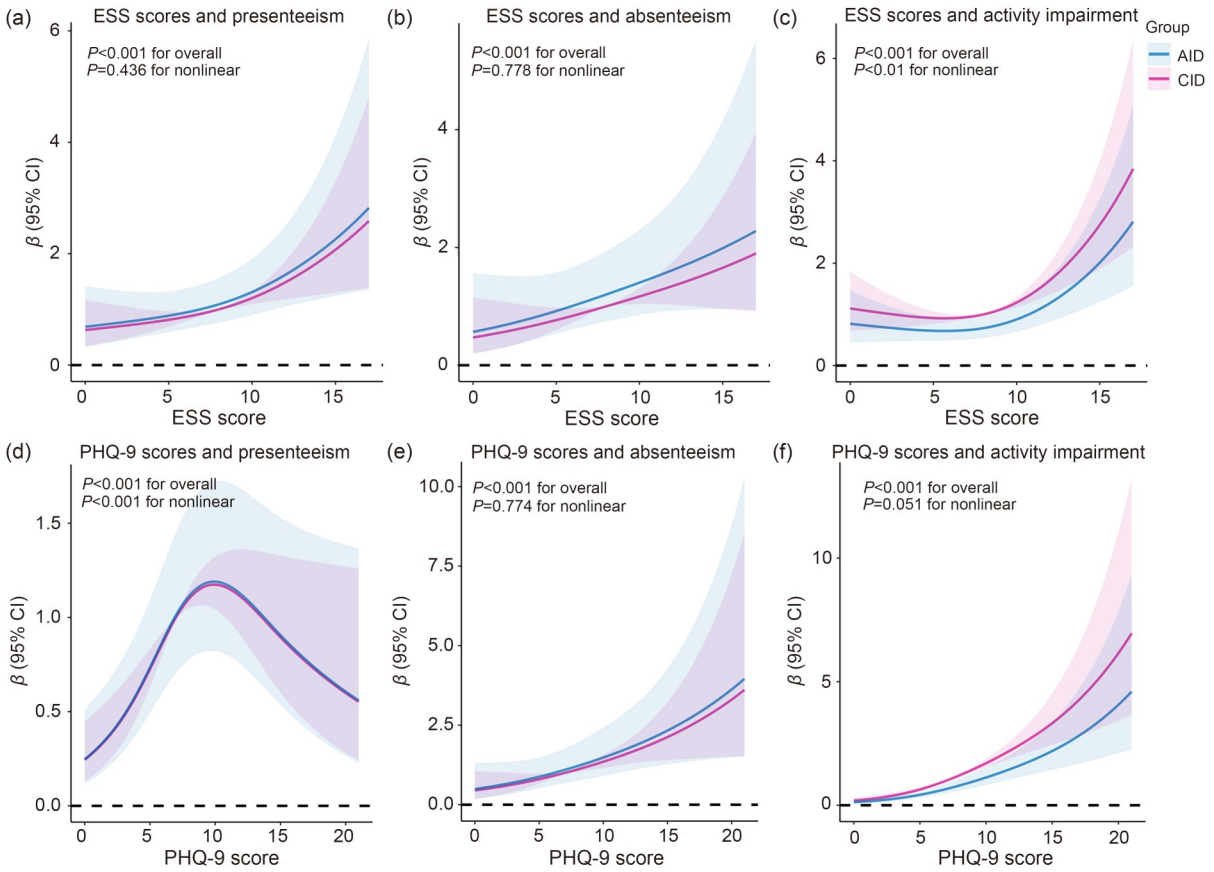

Fig. 2 Restricted cubic spline (RCS) analysis of workplace and daily activity impairment. The analyses were adjusted for potential confounders including sex, age, BMI, occupation, income, and marital status. (a–c) Relationships between ESS scores and presenteeism (a), absenteeism (b), and activity impairment (c). Given that an ESS score of ≥10 indicates clinically significant daytime sleepiness, an ESS score of 10 was set as the reference threshold. (d–f) Relationships between PHQ-9 scores and presenteeism (d), absenteeism (e), and activity impairment (f). Given that a PHQ-9 score of ≥5 indicates clinically relevant depressive symptoms, a PHQ-9 score of 5 was set as the reference threshold. AID: acute insomnia disorder; CID: chronic insomnia disorder; BMI: body mass index; ESS: Epworth Sleepiness Scale; PHQ-9: 9-item Patient Health Questionnaire; CI: confidence interval.

2.4 Mediation analysis for associations of factors with workplace and daily activity impairment

Based on the correlation and multiple linear regression analysis results, we were able to determine that ESS, PHQ-9, and GAD-7 were likely acting as mediators. In the AID group, PHQ-9 scores did not significantly mediate the relationship between ISI scores and presenteeism (β=0.002, P=0.218; Fig. 3a), but served as the primary mediator between ISI scores and absenteeism, accounting for 37.02% of the total effect (β=1.85×10^{-3}, P<0.05; Fig. 3b). PHQ-9 also significantly mediated the association between ISI scores and daily activity impairment (28.61% of the effect, β=0.007, P<0.001; Fig. 3c). In the CID group, PHQ-9 did not mediate the relationship between ISI scores and either presenteeism (β=0.001, P=0.692; Fig. 3d) or absenteeism (β=0.21×10^{-3}, P=0.810; Fig. 3e), but did mediate the relationship between ISI scores and daily activity impairment (30.25% of the effect, β=0.006, P<0.001; Fig. 3f).

GAD-7 scores did not significantly mediate the relationship between ISI scores and either presenteeism (β=0.003, P=0.140) or absenteeism (β=0.001, P=0.168) in the AID group, but were a significant mediator for daily activity impairment (20.70% of the effect, β=0.005, P<0.001). In the CID group, GAD-7 significantly mediated the relationship between ISI scores and presenteeism (53.01% of the effect, β=0.003, P<0.05), and also mediated the relationship between ISI scores and daily activity impairment (31.70% of the effect, β=0.006, P<0.001). These results are presented in Fig. S4.

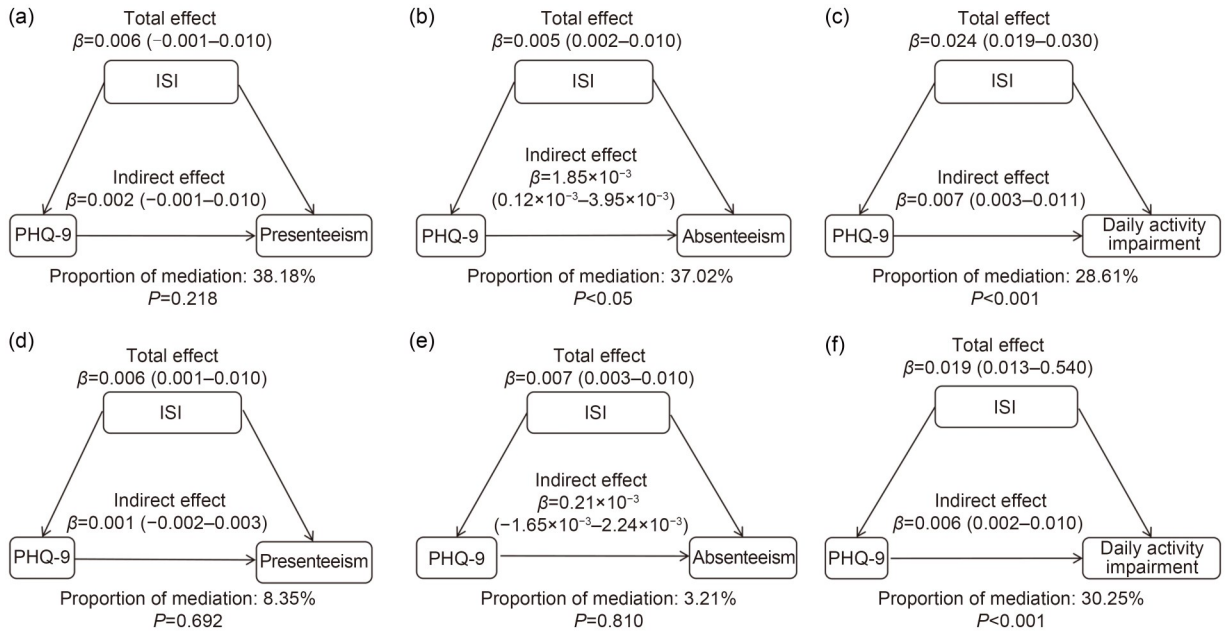

Fig. 3 Mediation analysis models of the relationships between PHQ-9 and workplace and daily activity impairment in the AID and CID groups. (a–c) Mediation analyses in AID group. (d–f) Mediation analyses in CID group. (a, d) Independent variable: ISI score; dependent variable: presenteeism; mediated variable: PHQ-9 score. (b, e) Independent variable: ISI score; dependent variable: absenteeism; mediated variable: PHQ-9 score. (c, f) Independent variable: ISI score; dependent variable: daily activity impairment; mediated variable: PHQ-9 score. The analyses were adjusted for potential confounders, including sex, age, BMI, occupation, income, and marital status. AID: acute insomnia disorder; CID: chronic insomnia disorder; ISI: Insomnia Severity Index; PHQ-9: 9-item Patient Health Questionnaire; BMI: body mass index.

Finally, ESS scores were not a mediating factor of the relationship between ISI scores and workplace/daily activity impairment in either group (Fig. S5). Further subgroup analyses of the categorically mediating factors revealed consistent mediation results (Table S2).

3 Discussion

In this study, there do not appear to be any significant differences between participants with AID and CID in terms of presenteeism and productivity-loss costs. Furthermore, daytime sleepiness, depressive symptoms, and anxiety symptoms are all significantly associated with impairment in both workplace and daily activity. Importantly, depressive and anxiety symptoms play a key mediating role in the relationship between insomnia severity and both workplace and daily activity impairment, with the pattern of mediation differing between AID and CID. These findings highlight the importance of early identification and targeted intervention for insomnia and emotional symptoms to prevent long-term productivity loss.

Our study indicates that insomnia-related productivity-loss costs are similar for individuals with AID and CID, with an average cost of USD 537 over three months without treatment. Currently, assessments of productivity-loss costs for insomnia primarily focus on developed countries (Fang et al., 2024). For instance, Thiart et al. (2016) reported that insomnia patients experience average productivity-loss costs of approximately USD 8142 (original currency: EUR 2900) over a six-month period without treatment. Although the productivity-loss costs among individuals with insomnia in China are lower than those observed in developed countries, they still account for a third of the average three-month wage in China (National Bureau of Statistics of China, 2024). In light of these findings, adapted economic results should be generated using health technology assessment evidence on the quantification and valuation of insomnia-related productivity loss from countries with similar characteristics to the decision-making country (Chauhan et al., 2023). Given the high prevalence of insomnia, it is essential to conduct further investigations into the economic burden of insomnia in developing countries, with large sample sizes.

This study demonstrates that presenteeism during the acute stage of insomnia disorder is as significant as it is during the chronic stage. Specifically, the occurrence of presenteeism is associated with occupational stress factors like heavy job demands and a lack of social support (Janssens et al., 2016; Takano et al., 2023), and these stressors may trigger AID (Kim et al., 2011; Ellis et al., 2012). Furthermore, individuals with AID frequently report more severe distress, sleep disruption, and stress (Ji et al., 2019; Boyle et al., 2024), all of which contribute to distraction in the workplace. In individuals with CID, the persistence of insomnia symptoms over time contributes to continuous declines in work efficiency, concentration, and motivation, which in turn result in sustained presenteeism (Kessler et al., 2011; Takano et al., 2023). However, our results show that patients with CID experience significantly more absenteeism and daily activity impairment than those with AID. A possible explanation is that CID often combines with medical conditions (e.g., cardiometabolic diseases) or mental-health conditions (e.g., depression) (Perlis et al., 2022), which may require individuals to take time off work to recover. Therefore, early intervention for AID is crucial for maintaining workplace productivity and preventing progression to CID, which may lead to severe absenteeism. Treatments such as digital cognitive behavioral treatment for AID could be effective (Yang et al., 2023). Providing digital therapies for use during breaks or after work offers employees convenient treatment without disrupting their work schedules (Espie et al., 2018; Kjørstad et al., 2022).

We demonstrated a positive linear relationship between depressive symptoms and both absenteeism and daily activity impairment among individuals with insomnia, which is consistent with previous findings (Beck et al., 2011; Evans-Lacko and Knapp, 2016; Wang et al., 2020; Eßl-Maurer et al., 2022). Notably, we observed a nonlinear association between depressive symptoms and presenteeism in both AID and CID, with a stronger relationship at low levels of depression that diminished as depression severity increased. This result may be explained by underlying neural mechanisms. With mild depression levels, individuals may experience prefrontal-cortex dysfunction, leading to impaired attention and executive function (Salehinejad et al., 2017), yet still attempt to continue working, resulting in presenteeism. As depressive symptoms worsen, dysregulation of neural circuits involved in motivation and energy (e.g., mesolimbic dopamine pathways) may contribute to greater fatigue and anhedonia (Fox and Lobo, 2019), and this severe depression increases the likelihood of absenteeism rather than presenteeism (Beck et al., 2011; Johnston et al., 2019). Laboratory studies illustrate that both insomnia and depression are associated with altered connectivity in brain regions governing emotional regulation and cognitive control, which may underlie the observed impairment in the workplace (Huang et al., 2012).

Our mediation analysis further reveals that depressive symptoms significantly mediate the relationship between insomnia and both absenteeism and daily activity impairment in AID. In CID, the mediating effect on absenteeism disappears, while the mediating effect on daily activity impairment becomes stronger. This may reflect the fact that AID more strongly triggers daily functional impairment by disrupting sleep-dependent emotional regulation and prefrontal-limbic connectivity (Weng et al., 2025). In contrast, individuals with CID may develop compensatory adaptations in the workplace to cope with their negative emotions (Perogamvros et al., 2020); this could weaken the mediating effect of depression on the relationship between insomnia and absenteeism. Meanwhile, the stronger mediating effect of depressive symptoms on daily activity impairment in the CID group may be attributed to the frequent co-occurrence of other symptoms, such as anxiety, which can amplify the negative impact of chronic insomnia on daily functioning. This aligns with our findings on the mediating effects of anxiety symptoms.

Anxiety symptoms appear to be more positively and linearly associated with workplace and daily activity impairment in AID than in CID. This finding highlights the important role of anxiety symptoms in the onset and development of insomnia in the workplace (Ellis et al., 2021). Anxiety symptoms related to the workplace not only disrupt sleep but also activate the hypothalamic-pituitary-adrenal (HPA) axis (Xue et al., 2025), leading to higher stress responses and further impairments to work productivity and daytime functioning (Xi et al., 2019; Okawara et al., 2024). Compared to AID, mediation analyses in our study revealed that anxiety symptoms play a significantly greater mediating role in the relationship between

CID and absenteeism. This indicates that individuals with CID experience more persistent and severe anxiety in their own right (Dressle et al., 2022), and anxiety-related factors of arousal and avoidance behavior are strong predictors of absenteeism (Hendriks et al., 2015).

We found that clinical daytime sleepiness (ESS score≥10) is strongly associated with greater daily activity impairment, compared to non-significant sleepiness (ESS score<10), in both AID and CID. Notably, this association is stronger for daily activity impairment in CID, whereas in AID, daytime sleepiness is more closely related to workplace impairment. Pronounced sleepiness is likely to cause neurocognitive deficits, contributing to daytime functional impairments (Hein et al., 2017). Previous evidence illustrates that insomnia with physiological hyperarousal is more strongly linked to neurocognitive performance deficits (Edinger et al., 2021). According to Spielman's 3P model, AID is widely acknowledged to be initiated by predisposing factors of physical and/or psychological arousal, while CID is thought to be generated by perpetuating factors of long-term negative behaviors and cognitions (Ellis et al., 2021). Therefore, daytime sleepiness among those with AID may reduce workplace performance by causing neurocognitive deficits, while for those with CID it may cause a deterioration in daily activity through wrong behaviors or beliefs due to excessive daytime rest. However, these results should be interpreted with caution, as our findings indicate that daytime sleepiness directly affects both workplace and daily activity impairment, rather than acting as a mediating factor. The complexity of the relationship between daytime sleepiness and workplace or daily activity impairment in individuals with insomnia warrants further investigation.

4 Limitations and future directions

Our study has both strengths and limitations. We used standard clinical criteria to diagnose insomnia disorder in our sample, and this is the first study to explore the relationships between different stages of insomnia and workplace impairment. One limitation of the study is the lack of objective data on presenteeism and absenteeism. Self-assessments of workplace impairment are prone to biases such as recall bias. In addition, the use of a cross-sectional design prevents us from establishing causality between variables. Longitudinal studies would be necessary to examine changes in workplace performance over time and identify causal factors. Finally, our research here focuses on patients with insomnia disorder. This may limit the applicability to broader populations, such as those who have insomnia symptoms caused by other mental conditions or physical conditions.

5 Conclusions

Our study sheds light on workplace impairment in AID, with similar effects found in CID. Early identification of AID provides an opportunity to prevent long-term work productivity loss. Depressive and anxiety symptoms mediate the relationship between insomnia and workplace performance in both AID and CID. Future research should focus on cost-effective and specific strategies for insomnia and negative emotions to inform workplace health policies.

Materials and methods

Detailed methods are provided in the electronic supplementary materials of this paper.

Data availability statement

The dataset used or analyzed during the current study is available from the corresponding authors upon reasonable request.

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Author contributions

Leqin FANG, Shixu DU, Bin ZHANG, and Shufei ZENG designed the study. Leqin FANG, Shixu DU, Hangyi YANG, and Xue LUO collected the data and conducted the statistical analysis. Leqin FANG, Shuqiong ZHENG, and Shufei ZENG interpreted the results. Leqin FANG and Shixu DU wrote the first draft of the manuscript. Hangyi YANG, Xue LUO, Shuqiong ZHENG, Zhiting HUANG, Yuhan ZHAO, Shufei ZENG, and Bin ZHANG revised the manuscript. All authors have read and approved the final version of the manuscript, and therefore, have full access to all the data in the study and take responsibility for the integrity and security of the data.

Compliance with ethics guidelines

Leqin FANG, Shixu DU, Hangyi YANG, Xue LUO, Shuqiong ZHENG, Zhiting HUANG, Yuhan ZHAO, Shufei ZENG, and Bin ZHANG declare that they have no conflicts of interest.

All procedures followed were in accordance with the ethical standards of the Medical Ethics Committee of Nanfang Hospital of Southern Medical University (Ethical Approval No. NFEC-2023-371). Written informed consent was obtained from all participants. All methods were carried out in accordance with relevant guidelines and regulations.

Declaration on the use of generative AI tools

During the preparation of this work, the authors used Claude in order to improve the language of several paragraphs. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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Supplementary information

Materials and methods; Figs. S1–S5; Tables S1 and S2