

Cross-Talk Between Sleep Quality and HRQoL in CKD: Insights from Network and Cost–Utility Analysis

Saumya Saumya

Jamia Hamdard

Mohammad Ahmed Khan

`drm.ahmedkhan@jamiahamdard.ac.in`

Jamia Hamdard

Avinash Ignatius

Noble Hospitals and Research Centre Pune

Research Article

Keywords: Sleep quality, Health related quality of life, Chronic kidney disease, Network analysis, Cost utility

Posted Date: September 29th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10955895/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License.
[Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Objective

To explore the relationship between sleep quality and health-related quality of life (HRQoL) in chronic kidney disease (CKD) patients using network analysis, and to evaluate the cost-utility of targeted insomnia intervention.

Methods

A cross-sectional study was conducted among 150 CKD patients recruited from a tertiary care center in India. Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI), and HRQoL was evaluated using the European Quality of Life-5 Dimensions (EQ-5D-5L) questionnaire, supplemented by its Visual Analogue Scale (VAS). Separate symptom networks were estimated for early CKD (stage 1–3) and late CKD (stage 4–5) patients using regularized partial correlations. Central and bridge symptoms were identified using Expected Influence (EI) and Bridge Expected Influence (BEI). A cost-utility analysis simulated quality-adjusted life years (QALYs) gained through cognitive behavioral therapy for insomnia (CBT-I) and calculated the incremental cost-effectiveness ratio (ICER).

Results

In early-stage CKD, daytime dysfunction (C7) showed the highest centrality, while sleep disturbance (C5), anxiety/depression (E5), and self-care (E2) were the primary bridge symptoms connecting sleep quality and HRQoL. In late-stage CKD, sleep duration (C3) was both the most central and bridging symptom, followed by E5. Cost-utility simulation revealed the incremental cost-effectiveness ratio (ICERs) of ₹13,767/QALY (early CKD) and ₹34,419/QALY (late CKD), both well below India's cost-effectiveness threshold (₹197,000–₹591,000/QALY).

Conclusion

Network analysis identified stage-specific central and bridge symptoms connecting sleep quality and HRQoL in CKD. Targeting these symptoms through CBT-I may offer significant clinical benefits and represent a cost-effective intervention strategy in the Indian healthcare context.

1. Introduction

Chronic kidney disease (CKD) imposes a major and increasing global health burden, with prevalence estimates suggesting that approximately 13.4% of the worldwide population is affected; equating to over 843 million individuals globally [1–3]. India and China contribute disproportionately to this burden, together accounting for nearly one-third of all CKD cases, with India alone responsible for an estimated

115.1 million cases [4]. In the Indian context, mortality associated with kidney failure has increased significantly, with a 38% rise documented between 2001–2003 and 2010–2013 [5]. In addition to its high mortality and economic costs, CKD is characterized by a substantial and progressive decline in health-related quality of life (HRQoL) [6–8].

The relationship between CKD severity and HRQoL impairment has been well established, with evidence indicating that even modest reductions in estimated glomerular filtration rate (eGFR) are significantly associated with poorer quality of life [9–13]. Among the numerous factors influencing HRQoL in individuals with CKD, sleep disturbances have emerged as a critical and modifiable contributor. Sleep-related problems are highly prevalent across all stages of CKD and are independently associated with adverse clinical outcomes, including increased cardiovascular risk, faster progression to end-stage renal disease, and heightened all-cause mortality [14–16].

The burden of sleep disturbances is particularly relevant in Asian populations, where average sleep durations tend to be shorter compared to Western countries [17]. In India, survey data reveal declining satisfaction with sleep quality among adults, with rates dropping from 76% in 2020 to 67% in 2021 [18]. Sleep disturbances in CKD are driven by a multifaceted interplay of metabolic dysregulation, nocturnal symptoms, and comorbidities such as obstructive sleep apnea (OSA), which affects over 40% of patients and becomes increasingly prevalent with disease progression [19–21]. Pathophysiological mechanisms, including intermittent hypoxia, heightened sympathetic activity, oxidative stress, and systemic inflammation contribute to both sleep disruption and renal deterioration, accounting for a complex bidirectional relationship between sleep quality and kidney function [22–24].

Despite increasing recognition of sleep disruption and poor HRQoL in CKD, most studies assess these outcomes in isolation. Traditional linear models fail to capture the interconnected nature of symptoms in chronic illness. Network analysis offers a novel approach by mapping inter-symptom relationships, identifying central and bridge symptoms whose treatment may yield broader improvements [25–27].

Given the substantial economic burden of CKD care, particularly in low- and middle-income countries like India, there is a critical need for symptom-targeted interventions that are not only clinically effective but also economically sustainable. Cost-utility analysis, which quantifies treatment value in terms of quality-adjusted life years (QALYs), serves as a robust tool for guiding such resource-efficient healthcare decisions [28–30].

In this study, we applied symptom network analysis to sleep quality and HRQoL in CKD patients, identifying key intervention targets using regularized partial correlation networks. Also conducted a cost-utility simulation to estimate QALY gains and ICERs for treating these central symptoms. To our knowledge, this is the first study to integrate network analysis with economic modeling in a CKD population.

2. Methodology

2.1 Study structure

This research followed a cross-sectional design and it was carried out over a one-year duration from June 2023 to June 2024, in the Nephrology outpatient department of a tertiary care hospital in Pune, Maharashtra, India. The research protocol received approval from the Institutional Ethics Committee of the respective hospital. To ensure confidentiality and anonymity, informed consent was obtained from all participants prior to their enrollment in the study.

2.2 Research cohort

The patient selection process adhered to the following predetermined criteria.

Inclusion criteria: (a) patients who were 18 years or above, of either gender; (b) consent to participate and sign an informed consent form; (c) confirmed cases of chronic renal disease based on estimated glomerular filtration rate and/or albuminuria level.

Exclusion criteria: (a) pregnant subjects; (b) patients with tumors, infections, and cerebrovascular illness; (c) patients with an active urinary tract infection, psychosis, and (d) history of sleep related issues.

Detailed demographic information (age, gender, education, smoking and drinking habits, and family history) was collected using a case record form (CRF). Socioeconomic status was evaluated using an adapted version of Kuppuswamy's scale, classifying participants into five distinct categories: upper, upper-middle, lower-middle, upper-lower, and lower. These categories were determined based on variables including the education level, occupation of the household head, and monthly household income.

3. Outcome measures

3.1 Assessment of sleep quality using PSQI

"PSQI is a widely recognized instrument designed to assess multiple aspects of sleep quality over the past month" [31]. "It includes questions on subjective sleep quality, sleep latency, sleep duration, sleep efficiency, disturbances, and daytime dysfunction. Each rated on a range from 0 to 3" [31]. "The cumulative of all provides an overall PSQI (0–21). Higher scores (PSQI $\geq$ 5) reflect poorer sleep quality" [31]. In this study, participants were classified into two categories; one with poor sleep quality (PSQI $\geq$ 5) and another with good sleep quality (PSQI < 5), on the basis of their global PSQI.

3.2 HRQoL measurement using the EQ-5D-5L

EQ-5D-5L instrument used for the assessment of HRQoL, which consists of two parts:

1. "Quality of health is evaluated through the descriptive system across the above dimensions: (1) mobility, (2) self-care, (3) usual activities, (4) pain/discomfort, and (5) anxiety/depression. Each of these is rated on a scale with five levels, ranging from no problem to extreme problem" [32].

“Patients indicate their current health status by selecting the statement that best describes their condition for each dimension. These choices are converted into a single-digit score for each dimension, which are then combined to create a five-digit code representing the individual’s overall health state” [32]. Using the Crosswalk Index Value Calculator, this health state further transformed into a EQ-5D index score [33, 34].

2. “Patients use the EQ 5D VAS to provide a personal assessment of their health, marking their evaluation on a vertical visual analogue scale. The endpoints of this scale offer a numerical insight into health outcomes through the individual’s perspective ranging from 0 (worst health status) to 100 (best health status)” [32].

3.3 Symptom network analysis

3.3.1 Network construction and estimation

To examine the interrelations between sleep quality and HRQoL in patients with CKD, we constructed separate symptom networks for patients in early-stage CKD (Stages 1–3) and late-stage CKD (Stages 4–5). Each network incorporated 12 nodes, including seven components from the PSQI: subjective sleep quality (C1), sleep latency (C2), sleep duration (C3), habitual sleep efficiency (C4), sleep disturbances (C5), use of sleep medication (C6), and daytime dysfunction (C7) and five domains from the EQ-5D-5L instrument: mobility (E1), self-care (E2), usual activities (E3), pain/discomfort (E4), and anxiety/depression (E5).

The networks were estimated using regularized partial correlation models based on the graphical Least Absolute Shrinkage and Selection Operator (LASSO). Model selection was guided by the extended Bayesian information criterion (EBIC) with the hyperparameter γ set to 0.5, promoting a sparse and interpretable structure by shrinking trivial edges to zero. Spearman correlations were used due to the ordinal nature of the items. Nodes were partitioned into two conceptual communities: the sleep quality community (PSQI) and the HRQoL community (EQ-5D-5L). Network estimation and visualization were implemented in Python.

3.3.2 Centrality and bridge metrics

To assess the importance of each symptom within the networks, we calculated Expected Influence (EI), a centrality measure that sums the edge weights of all connections associated with a given node, retaining the sign of the correlations.

Additionally, Bridge Expected Influence (BEI) was calculated to quantify each node’s connectivity across the two symptom communities. BEI represents the sum of edge weights linking a given node to all nodes in the opposing community, thus identifying bridge symptoms that may mediate relationships between PSQI and HRQoL domains.

Nodes with the highest EI values were interpreted as central symptoms, whereas those with the highest BEI values were interpreted as bridge symptoms.

Although formal bootstrapping for stability was not performed, our approach aligns with prior network psychometric methods. Centrality metrics such as Expected Influence (EI) and Bridge EI (BEI) were interpreted qualitatively. As suggested by Epskamp et al. [35], a correlation stability (CS) coefficient > 0.25 is typically acceptable, and we used visual inspection and ranked plots to support the robustness and interpretability of our findings.

3.4 Cost utility analysis

A cost-utility analysis (CUA) was conducted from the healthcare provider's perspective to evaluate the economic value of sleep-focused interventions in patients with CKD. The analysis considered only direct medical costs, and intervention strategies were modeled on established behavioral therapies, particularly cognitive behavioral therapy for insomnia (CBT-I). Cost inputs were obtained from Indian published sources and adjusted using purchasing power parity (PPP) where applicable.

3.4.1 Estimation of life expectancy by CKD stage

Stage-specific life expectancy was estimated based on published literature. Drawing on the study by Neild GH (2016) [36], which examined stage-wise survival patterns in CKD populations stratified by age, an average life expectancy of 15 years was assumed for early-stage CKD, and 6 years for late-stage CKD, corresponding to the study cohort's mean age of approximately 59 years [36].

3.4.2 Utility gain estimation

HRQoL outcomes were measured using the EQ-5D-5L instrument. Utility scores were derived using the EQ-5D-5L Crosswalk Index Value Calculator. A mean utility gain of 0.045 was applied, based on evidence from prior studies evaluating sleep interventions, including internet-based CBT-I and pharmacologic treatments. These studies reported EQ-5D utility gains ranging from + 0.026 to + 0.059 across randomized and real-world settings [37, 38].

QALY calculation:

QALYs were calculated using the standard formula:

QALYs gained = Utility gain × Life expectancy

Early-stage CKD: QALY = $0.045 \times 15 = 0.675$, Late-stage CKD: QALY = $0.045 \times 6 = 0.270$

Cost estimation

The cost of intervention was modeled at ₹9,293 per patient, based on a global average therapy session cost of \$460 USD, converted to Indian rupees using a 2023 PPP conversion rate of 20.2 ($₹9,293 = \$460 \times 20.2$) [39, 40].

ICER calculation

The incremental cost-effectiveness ratio (ICER) was computed as:

$$\text{ICER} = \frac{\text{Cost Intervention} - \text{Cost Standard Care}}{\text{QALY Intervention} - \text{QALY Standard}}$$

Given that sleep interventions are not part of routine CKD care, baseline costs and QALY gains were assumed to be negligible.

Cost-effectiveness threshold

In accordance with the World Health Organization's (WHO) cost-effectiveness guidance, interventions are considered cost-effective if the cost per QALY gained is less than one to three times a country's per capita GDP [41]. As per the Union Budget 2023–24 presented by the Government of India, the estimated per capita income is ₹197,000 [42]. Based on this, the willingness-to-pay (WTP) threshold for cost-effective interventions in India ranges from ₹197,000 to ₹591,000 per QALY.

3.5 Statistical Assessment

Statistical analysis was performed as follows: categorical variables were summarized using frequencies and percentages, whereas continuous data were expressed as the mean $\pm$ standard deviation (SD). Group comparisons were made using Chi-square (χ^2) tests and Student's t-tests. To compare multiple groups, a one-way analysis of variance (ANOVA) was employed. Logistic regression analysis was used to assess the relationship between quality of sleep and variables associated with CKD. All statistical analyses were performed using SPSS software, with $p < 0.05$ for determining statistical significance. For network modeling, Python was used to compute and visualize regularized partial correlation networks via Graphical LASSO with EBIC model selection.

4. Results

4.1 Sociodemographic profile

A total of 150 CKD patients were enrolled based on predefined inclusion and exclusion criteria. The cohort had a mean age of 58.92 ± 7.82 years and included 51.3% males. Poor sleep quality was reported by 77.33% of participants, with a marginally higher prevalence among females. Advanced or late CKD (stages 4–5) accounted for 40% of the sample, all of whom reported poor sleep quality. Socioeconomically, 46.66% of patients belonged to the upper-middle group, followed by 28.66% lower-middle, 22.66% upper-lower, and 2% lower class. Additionally, 19.33% reported a family history of CKD, and 22.66% reported substance use. The majority (90.66%) were literate. Further details are summarized in Table 1.

Table 1
Sociodemographic profile

Parameters	All CKD Patients 150	PSQI < 5 (Good Sleeper) 34 (22.66%)	PSQI > 5 (Poor Sleeper) 116 (77.33%)
Gender (n, %)	77 (51.30)	21 (61.76)	56 (48.27)
Male	73 (48.66)	13 (38.23)	60 (51.72)
Female			
Age (years $\pm$ SD)	58.92 $\pm$ 7.82	58.64 $\pm$ 7.7	59.00 $\pm$ 7.8
CKD stage (n, %)	60 (40)	34 (100)	26 (17.33)
1–3	90 (60)	00 (00)	90 (77.58)
4–5			
Socioeconomic status (n, %)	70 (46.66)	11 (32.35)	59 (50.86)
Upper middle	43 (28.66)	7 (20.58)	36 (31.03)
Lower middle	34 (22.66)	14 (41.17)	20 (7.24)
Upper lower	3 (2)	2 (5.88)	1 (0.86)
Lower			
Family history of CKD (n, %)	29 (19.33)	5 (14.70)	24 (20.68)
Yes	121 (80.66)	29 (85.29)	92 (79.31)
No			
Substance use (n, %)	34 (22.66)	7 (20.58)	27 (23.27)
Yes	116 (77.33)	27 (79.41)	89 (76.72)
No			
Education (n, %)	136 (90.66)	30 (88.23)	106 (91.37)
Literate	14 (9.33)	4 (11.76)	10 (8.62)
Illiterate			

SD: standard deviation.

Group-wise comparisons between good and poor sleepers revealed significant differences in several domains. Poor sleepers had longer CKD duration (5.70 vs. 4.20 years; $p < 0.001$), higher PSQI global scores (8.28 vs. 2.50; $p < 0.001$), longer sleep latency, reduced sleep efficiency, and shorter sleep duration. PSQI domain scores (C1–C7) were consistently higher among poor sleepers, indicating more

severe sleep disturbances. Although EQ-5D index values were comparable across groups, EQ-5D VAS scores were significantly lower in poor sleepers (69.08 vs. 71.44; $p = 0.043$), indicating reduced perceived health status. These findings underscore the close link between sleep quality and overall functional health in the CKD population. Full clinical comparisons are presented in Table 2..

Table 2
Overview of anthropometric and biochemical parameters

Variable (mean ± SD)	All CKD Patients (n = 150)	Good sleeper (n = 34)	Poor sleeper (n = 116)	P Value
Age (years)	58.92 ± 7.82	58.64 ± 7.7	59.00 ± 7.8	0.812
Height (cm)	162.85 ± 7.25	164.4 ± 6.89	162.39 ± 7.33	0.146
Weight(kg)	62.71 ± 8.03	66.7 ± 7.21	65.40 ± 8.26	0.359
BMI (kg/m2)	24.85 ± 3.40	24.76 ± 2.99	24.87 ± 3.52	0.853
Systolic blood pressure (mmhg)	138.90 ± 13.84	137.95 ± 13.70	139.18 ± 13.93	0.648
Diastolic blood pressure (mmhg)	84.10 ± 9.98	83.25 ± 9.19	84.35 ± 10.22	0.552
Duration of CKD	5.36 ± 2.32	4.20 ± 1.73	5.70 ± 2.37	< 0.001 ^{***}
C1	1.25 ± 1.08	0.17 ± 0.38	1.5 ± 0.75	< 0.001 ^{***}
C2	1.71 ± 1.00	0.73 ± 0.66	2.0 ± 0.90	< 0.001 ^{***}
C3	0.84 ± 0.66	0.29 ± 0.46	1.00 ± 0.62	< 0.001 ^{***}
C4	0.08 ± 0.27	0.02 ± 0.17	0.09 ± 0.29	0.106
C5	1.15 ± 0.48	0.76 ± 0.43	1.26 ± 0.44	< 0.001 ^{***}
C6	0.77 ± 0.95	0.05 ± 0.23	0.98 ± 0.98	< 0.001 ^{***}
C7	1.20 ± 0.69	0.44 ± 0.50	1.43 ± 0.57	< 0.001 ^{***}
Total PSQI	6.97 ± 3.51	2.50 ± 1.21	8.28 ± 2.82	< 0.001 ^{***}
Sleep duration (hrs)	6.70 ± 0.89	7.44 ± 0.55	6.49 ± 0.86	< 0.001 ^{***}
Sleep efficiency (%)	90.65 ± 5.30	83.33 ± 5.25	89.30 ± 4.50	< 0.001 ^{***}
Sleep latency (min)	39.86 ± 18.04	24.11 ± 8.20	44.48 ± 17.53	< 0.001 ^{***}

Variable (mean ± SD)	All CKD Patients (n = 150)	Good sleeper (n = 34)	Poor sleeper (n = 116)	P Value
Mobility	2.16 ± 0.92	2.08 ± 0.83	2.18 ± 0.95	0.574
Self-care	2.14 ± 0.88	2.05 ± 0.77	2.17 ± 0.91	0.512
Usual activities	2.17 ± 0.87	2.05 ± 0.73	2.20 ± 0.90	0.386
Pain/discomfort	2.52 ± 0.80	2.50 ± 0.61	2.53 ± 0.84	0.825
Anxiety/depression	2.1 ± 0.84	1.88 ± 0.80	2.16 ± 0.85	0.089
EQ-5D Index	0.65 ± 0.29	0.71 ± 0.20	0.63 ± 0.31	0.105
EQ-5D VAS	69.62 ± 7.83	71.44 ± 5.73	69.08 ± 8.29	0.043 [§]

SD: Standard deviation; **: $p < 0.01$; *: $p < 0.05$. BMI: Body mass index; C1: Subjective sleep quality; C2: Sleep latency; C3: Sleep duration; C4: Sleep efficiency; C5 : Sleep disturbance; C6 :Use of sleeping medication; C7:Daytime dysfunction; PSQI: Pittsburgh Sleep Quality Index; EQ-5D: European Quality of Life-5 Dimensions; VAS: visual analogue scales.

4.2 Association between sleep quality and CKD

Logistic regression revealed significant correlation between poor sleep quality (the dependent variable) and two key factors of CKD. CKD stage showed a strong relationship (OR = 0.01; 95% CI: 0.0013 to 0.0772, $p < 0.01$). Similarly, CKD duration was significantly associated with poor sleep quality, with an odds ratio of 0.266 and a 95% CI of 0.1190 to 0.5933 ($p < 0.01$). (Table 3).

Table 3
Association between sleep quality and CKD

Variables	Odds Ratio	95% CI	P Value
Systolic blood pressure (mmhg)	0.459	(0.2077, 1.0137)	0.054
Diastolic blood pressure (mmhg)	1	(0.4656, 2.1478)	1
CKD Stage	0.01	(0.0013, 0.0772)	0.0001**
CKD Duration (years)	0.266	(0.1190, 0.5933)	0.0001**
** $p < 0.01$			

4.3 Symptom network structure

Two separate networks were constructed to compare early-stage CKD and late-stage CKD in terms of interrelations between sleep quality (PSQI domains) and HRQoL (EQ-5D-5L dimensions). Each network included 12 nodes and was regularized using graphical LASSO with EBIC selection ($\gamma = 0.5$). Edge thickness in the network graphs reflected the magnitude of the regularized partial correlations.

In both networks, clear clustering was observed, corresponding to the two predefined communities : PSQI components and EQ-5D-5L dimensions.

4.3.1 Central symptoms and expected influence for early-stage CKD

The network model for early CKD ($n = 90$) comprised 12 nodes and 35 non-zero edges, visualized using regularized partial correlations. Nodes from both sleep (C1–C7) and HRQoL domains (E1–E5) were moderately interconnected, indicating symptom interdependency. Notably, C7 (Daytime Dysfunction) emerged as the most central symptom, with the highest EI = 1.038. Other prominent symptoms included E3 (Usual Activities) and C5 (Sleep Disturbance). Higher BEI scores indicate stronger bridging roles between the sleep and HRQoL symptom communities. In early-stage CKD, key bridge symptoms identified include sleep disturbance (C5), anxiety/depression (E5), and self-care (E2). Visual representations of the early-stage CKD network and bridge centrality metrics are shown in Fig. 1(a) and Fig. 1(b), respectively.

Figure 1. Symptom network model of sleep quality (C1–C7) and HRQoL (E1–E5) in early-stage CKD: (a): Nodes represent individual components of the PSQI (blue) and EQ-5D-5L (orange) dimensions. Edges represent partial correlations between nodes, with blue indicating positive associations and red indicating negative associations. The thickness and intensity of edges reflect the magnitude of the correlation, and node size is scaled according to Expected Influence (EI). **(b):** Bridge Expected Influence (BEI) values for all symptoms. C1 = Subjective sleep quality; C2 = Sleep latency; C3 = Sleep duration; C4 = Habitual sleep efficiency; C5 = Sleep disturbance; C6 = Use of sleep medication; C7 = Daytime dysfunction. E1 = Mobility; E2 = Self-care; E3 = Usual activities; E4 = Pain/discomfort; E5 = Anxiety/depression.

4.3.2 Central symptoms and expected influence for late-stage CKD

The network for late CKD ($n = 60$) was denser, with stronger associations between nodes (42 non-zero edges). In contrast to the early-stage group, C3 (Sleep Duration) emerged as the most central symptom (EI = 1.155), indicating that insufficient sleep length had the greatest influence on the broader symptom network.

BEI values were computed for all nodes. The highest BEI scores were observed for C3 (sleep duration), E5 (anxiety/depression), and E2 (self-care), highlighting their prominent roles in linking sleep disturbances with impaired HRQoL in this population. The late-stage network and associated bridge centrality profiles are illustrated in Fig. 2(a) and Fig. 2(b).

Figure 2. Symptom network model of sleep quality (C1–C7) and HRQoL (E1–E5) in late-stage CKD. (a): Nodes represent individual components of the PSQI (blue) and EQ-5D-5L (orange) dimensions. Edges represent partial correlations between nodes, with blue indicating positive associations and red

indicating negative associations. The thickness and intensity of edges reflect the magnitude of the correlation, and node size is scaled according to Expected Influence (EI). **(b):** Bridge Expected Influence (BEI) values for all symptoms. C1 = Subjective sleep quality; C2 = Sleep latency; C3 = Sleep duration; C4 = Habitual sleep efficiency; C5 = Sleep disturbance; C6 = Use of sleep medication; C7 = Daytime dysfunction. E1 = Mobility; E2 = Self-care; E3 = Usual activities; E4 = Pain/discomfort; E5 = Anxiety/depression.

4.4 Cost–Utility Analysis Results

To evaluate the economic feasibility of intervening on network-identified central symptoms, a stage-stratified cost–utility analysis was conducted. QALYs were estimated by multiplying utility gains (derived from EQ-5D-5L) by modeled life expectancy for each CKD stage group.

For early-stage CKD (target node: C7), with a utility gain of 0.045 and life expectancy of 15 years, the estimated QALY gain was 0.675. For late-stage CKD (target node: C3), with an equivalent utility gain and a life expectancy of 6 years, the QALY gain was 0.270.

Cost modeling applied a base intervention cost of ₹9,293, derived from a global session cost of \$460 USD adjusted for PPP as per IMF data [39, 40]. The corresponding ICERs) were ₹13,767 per QALY for early-stage CKD and ₹34,419 per QALY for late-stage CKD.

All ICERs remained substantially below the widely accepted Indian cost-effectiveness threshold of ₹197,000 to ₹591,000 per QALY ($3 \times$ per capita GDP) [42], supporting the high economic value of targeted sleep interventions across CKD stages. (Table 4).

Table 4
Cost–utility outcomes of sleep intervention across CKD stages

Cost (₹)	CKD stage	QALY gained	ICER
9293	Early	0.675	13767
9293	Late	0.270	34419

CKD: Chronic kidney disease; QALY: Quality adjusted life year; ICER: Incremental Cost-Effectiveness Ratio.

5. Discussion

Our study reveals a high burden of sleep disturbance and poor quality of life in CKD patients. Consistent with prior reports, roughly half of our cohort screened positive for poor sleep (PSQI ≥ 5) [43]. Previous studies in CKD have found poor sleep prevalence ranging 37–97% across settings, and low-quality sleep is known to exacerbate disease and impair quality of life [43]. In parallel, EQ-5D VAS scales in our sample were markedly below general population norms, reflecting diminished HRQoL in CKD. Indeed, systematic

reviews show that CKD patients experience significantly worse HRQoL than healthy individuals, with the lowest scores seen in advanced (dialysis-dependent) disease [44]. These findings underscore that CKD imposes a substantial symptom and HRQoL burden.

Network analysis highlighted stage-specific differences in the symptom structure associating sleep quality and HRQoL in patients with CKD. In early-stage CKD, daytime dysfunction (PSQI: C7) and usual activities (EQ-5D 5L: E3) emerged as the most central symptoms based on EI, indicating their high level of interconnectedness with other symptoms. This finding is consistent with previous network studies where daytime dysfunction has been identified as a core node influencing sleep-related distress and functional impairment [46, 47].

However, our BEI analysis identified a distinct set of bridge symptoms that connect the sleep and HRQoL domains. Specifically, in early CKD, the most prominent bridge symptoms were sleep disturbance (C5), anxiety/depression (E5), and self-care impairment (E2). This differs from existing literature that predominantly highlights daytime dysfunction as the key bridge [48–49], suggesting that in CKD, the propagation of dysfunction across domains may be more strongly driven by sleep fragmentation, psychological distress, and functional limitations related to disease self-management.

In late-stage CKD, the network shifted substantially. Sleep duration (C3) became the most central symptom, indicating that in more advanced disease stages, sleep quantity plays a dominant role in symptom interconnectivity. Importantly, sleep duration (C3) also exhibited the highest bridge centrality, followed by anxiety/depression (E5), pointing to these as the key connectors between poor sleep and reduced quality of life in advanced CKD. This pattern underscores the role of sleep deprivation and psychological burden in mediating functional decline at later stages of disease progression.

These network-level findings carry significant clinical implications. Central and bridge symptoms are theorized to exert disproportionate influence over the symptom network, and targeting them may yield widespread improvements. In early CKD, interventions focusing on improving sleep continuity, addressing emotional distress, and enhancing self-care behaviors may reduce symptom burden across both sleep and quality-of-life domains. In contrast, in late CKD, restoring adequate sleep duration and managing psychological distress may be key to preserving patient functionality. Overall, our findings suggest that C5, E5, and E2 in early CKD, and C3 and E5 in late CKD, should be considered high-impact, stage-specific targets for symptom-focused interventions aiming to improve HRQoL outcomes.

We integrated these findings into a cost-utility analysis of CBT-I in CKD. Assuming a modest utility gain ($\Delta QALY = 0.045$) consistent with published estimates for digital CBT-I interventions [37, 38] and applying stage-specific life expectancies (15 years for early-stage and 6 years for late-stage CKD) derived from large cohort data [36], the intervention cost was modeled at ₹9,293 per patient. This estimate was based on a global average CBT-I session cost of \$460 USD, converted to Indian rupees using a 2023 PPP exchange rate of 20.2 ($₹9,293 = \$460 \times 20.2$) [39, 40].

The resulting ICERs were highly favorable: approximately ₹13,767 per QALY for early-stage CKD and ₹34,419 per QALY for late-stage CKD. These ICERs are substantially below conventional WTP thresholds in India. According to WHO guidelines, cost-effective interventions are generally defined as those falling below 1–3 times a country's per capita GDP [41], translating to a range of approximately ₹197,000 to ₹591,000 per QALY in India [42]. Against these thresholds, our estimated ICERs fall one to two orders of magnitude lower, indicating that CBT-I would be considered highly cost-effective in the CKD population.

These findings are consistent with broader evidence supporting the cost-effectiveness of CBT-I and digital CBT-I across populations. Recent evaluations have shown that CBT-I not only provides QALY gains but also achieves long-term health improvements at sustainable costs [50].

5.1 Limitations and Future Directions

A key strength of this study is its novel integration of symptom network analysis with cost-utility modeling in a CKD population, offering a multidimensional understanding of sleep-quality of life relationships. Stratification by CKD stage allowed identification of stage-specific central and bridge symptoms, and the use of validated instruments (PSQI, EQ-5D-5L) enhances measurement reliability. The cost-effectiveness analysis was contextualized using real-world cost data and established willingness-to-pay thresholds, strengthening its policy relevance.

However, certain limitations are also observed. The network analysis was cross-sectional and correlational, limiting causal inference. All measures were self-reported, which may introduce bias. Cost-utility estimates relied on assumptions drawn from general populations rather than CKD-specific data, and factors such as discounting and adherence were not modeled. True societal willingness-to-pay in India remains uncertain despite use of standard thresholds.

Future research should validate these findings through longitudinal or interventional designs, including randomized trials of CBT-I in CKD with concurrent cost-effectiveness evaluations. Temporal network modeling and qualitative exploration of patient experiences could further enhance understanding, while real-world implementation data would improve the robustness of economic estimates.

6. Conclusion

In summary, CKD patients in our cohort exhibited high rates of poor sleep quality and reduced HRQoL. Symptom network analysis identified daytime dysfunction and usual activity limitations as key drivers in early CKD, while sleep duration dominated in late-stage disease. The economic evaluation further demonstrated that insomnia treatment; modeled as CBT-I, would be highly cost-effective, with ICERs far below national thresholds. A one-time CBT-I program (₹9,293 PPP-adjusted) could yield lasting quality-of-life improvements, particularly through improvements in sleep, emotional distress, and self-care. Given the centrality of sleep disturbance in the symptom network, targeting it may produce broad, cascading benefits, supporting its integration into CKD care as a high-value intervention under Indian economic norms.

Declarations

Conflict of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethics approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Institutional Ethics Committee of Noble Hospital and Research Centre, Pune, Maharashtra, India (Reference: NHIEC/Jun/2023).

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Consent for publication

Not applicable.

Mohammad Ahmed Khan

Conceptualization, Methodology, Formal analysis, Validation, Writing - review & editing, Visualization, Supervision.

Avinash Ignatius

Conceptualization, Methodology, Resources, Investigation, Visualization, Supervision.

Funding

The authors did not receive support from any organization for the submitted work.

Author Contribution

Saumya: Conceptualization, Methodology, Software, Formal analysis, Investigation, Validation, Writing - original draft, Writing - review & editing, Visualization. Mohammad Ahmed Khan: Conceptualization, Methodology, Formal analysis, Validation, Writing - review & editing, Visualization, Supervision. Avinash Ignatius: Conceptualization, Methodology, Resources, Investigation, Visualization, Supervision.

Availability of supporting data

The data that support the findings of this study are not openly available due to reasons of sensitivity and are available from the corresponding author upon reasonable request.

Code Availability

The code used during the current study is available from the corresponding author on reasonable request.

References

1. Provenzano M, Coppolino G, Faga T, Garofalo C, Serra R, Andreucci M. Epidemiology of cardiovascular risk in chronic kidney disease patients: the real silent killer. *Rev Cardiovasc Med*. 2019;20(4):209.
2. Hill NR, Fatoba ST, Oke JL, Hirst JA, O'Callaghan CA, Lasserson DS, et al. Global prevalence of chronic kidney disease – A systematic review and meta-analysis. *PLoS ONE*. 2016;11(7):3–4.
3. Jager KJ, Kovesdy C, Langham R, Rosenberg M, Jha V, Zoccali C. A single number for advocacy and communication: worldwide more than 850 million individuals have kidney diseases. *Kidney Int*. 2019;96(5):1048–50.
4. Bikbov B, Purcell CA, Levey AS et al. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*.
5. Dare AJ, Fu SH, Patra J, Rodriguez PS, Thakur JS, Jha P. Million Death Study Collaborators. Renal failure deaths and their risk factors in India, 2001–2013: nationally representative estimates from the Million Death Study. *Lancet Glob Health*. 2017;5(1):e89–95.
6. Perlman RL, Finkelstein FO, Liu L, Roys E, Kiser M, Eisele G. Quality of life in chronic kidney disease (CKD): a cross-sectional analysis in the Renal Research Institute-CKD study. *Am J Kidney Dis*. 2005;45(4):659–64.
7. Porter A, Fischer MJ, Brooks D, Bruce M, Charleston J, Cleveland WH. Quality of life and psychosocial factors in African Americans with hypertensive chronic kidney disease. *Transl Res*. 2012;159(1):5–9.
8. Kontodimopoulos N, Pappa E, Niakas D. Gender-and age-related benefits of renal replacement therapy on health-related quality of life. *Scand J Caring Sci*. 2009;23(4):723–7.
9. Alhaji MM, Tan J, Hamid MRA, Timbuak JA, Naring L, Tuah NA. Determinants of quality of life as measured with variants of SF-36 in patients with pre-dialysis chronic kidney disease. *Saudi Med J*. 2018;39(7):653–9.
10. Porter AC, Lash JP, Xie D, Pan Q, DeLuca J, Kanthety R, et al. Predictors and outcomes of health-related quality of life in adults with CKD. *Clin J Am Soc Nephrol*. 2016;11(7):1154–60.
11. Nguyen NT, Cockwell P, Maxwell AP, Griffin M, O'Brien T, O'Neil C. Chronic kidney disease, health-related quality of life, and their associated economic burden among a nationally representative

- sample of community-dwelling adults in England. PLoS ONE. 2018;13(11).
12. Chin HJ, Song YR, Lee JJ, Lee SB, Kim KW, Na KY, et al. Moderately decreased renal function negatively affects the health-related quality of life among the elderly Korean population: a population-based study. *Nephrol Dial Transpl.* 2008;23(9):2812–5.
 13. Hussien H, Apetrii M, Covic A. Health-related quality of life in patients with chronic kidney disease. *Int J Care Coord.* 2021;24(4):175–84.
 14. Bello AK, Alrukhaimi M, Ashuntantang GE, Basnet S, Rotter RC, Douthat WG, et al. Complications of chronic kidney disease: current state, knowledge gaps, and strategy for action. *Kidney Int Suppl.* 2017;7(2):123–7.
 15. Xu J, Yoon IY, Chin HJ. The effect of sleep apnea on all-cause mortality in non-dialyzed chronic kidney disease patients. *Sleep Med.* 2016;27–28:32–8.
 16. Tang SC, Lam B, Yao TJ, Leung WS, Chu CM, Ho YW, et al. Sleep apnea is a novel risk predictor of cardiovascular morbidity and death in patients receiving peritoneal dialysis. *Kidney Int.* 2010;77(11):1033–7.
 17. Willoughby AR, Alikhani I, Karsikas M, Chua XY, Chee MWL. Country differences in nocturnal sleep variability: observations from a large-scale, long-term sleep wearable study. *Sleep Med.* 2023;104:157–63.
 18. Day WS, The Philips. 2020, 2021 global sleep survey. Philips. 2021 [cited 2024 June 26]. Available from: <https://www.philips.co.in/c-e/smartsleep/campaign/world-sleep-day.html> and, <https://www.philips.com/a-w/about/news/archive/standard/news/press/2021/20210310-philips-survey-reveals-covid-19-s-negative-impact-on-sleep-quality-and-cpap-use.html>
 19. Markou N, Kanakaki M, Myrianthefs P, Hadjiyanakos D, Vlassopoulos D, Damianos A, et al. Sleep-disordered breathing in non-dialyzed patients with chronic renal failure. *Lung.* 2006;184:44–7.
 20. Sakaguchi Y, Shoji T, Kawabata H, Niihata K, Suzuki A, Kaneko T, et al. High prevalence of obstructive sleep apnea and its association with renal function among non-dialysis chronic kidney disease patients in Japan: a cross-sectional study. *Clin J Am Soc Nephrol.* 2011;6:995–9.
 21. Nicholl DDM, Ahmed SB, Loewen AHS, Hemmelgarn BR, Sola DY, Beecroft JM, et al. Declining kidney function increases the prevalence of sleep apnea and nocturnal hypoxia. *Chest.* 2012;141(6):1422–39.
 22. Kinebuchi S, Kazama JJ, Satoh M, Sakai K, Nakayama H, Yoshizawa H, et al. Short-term use of continuous positive airway pressure ameliorates glomerular hyperfiltration in patients with obstructive sleep apnea syndrome. *Clin Sci.* 2004;107(3):317–21.
 23. Hanly PJ, Ahmed SB. Sleep apnea and the kidney: is sleep apnea a risk factor for chronic kidney disease? *Chest.* 2014;146(4):1114–22.
 24. Lin CH, Perger E, Lyons OD. Obstructive sleep apnea and chronic kidney disease. *Curr Opin Pulm Med.* 2018;24(6):549–54.
 25. McNally RJ. Can network analysis transform psychopathology? *Behav Res Ther.* 2016;86:95–104.

26. McElroy E, Villadsen A, Patalay P. Systemic comorbidity among common mental disorders: A symptom level network analysis. *Sci Rep*. 2021;11(1):12357.
27. Cornelis S, Bos EH, Zitman FG, et al. Network analysis of depressive and anxiety symptoms in adults with and without chronic physical conditions. *J Affect Disord*. 2018;235:247–56.
28. Liyanage T, Ninomiya T, Jha V, Neal B, Patrice HM, Okpechi I, et al. Global access to renal replacement therapy: a systematic review. *Lancet*. 2015;385(9981):1975–82.
29. Honeycutt AA, Segel JE, Zhuo X, Hoerger TJ, Imai K, Williams D. Medical costs of CKD in the Medicare population. *JASN*. 2013;24(9):1478–83.
30. Ho V, Nguyen N, Lai J, Lee H. The economic burden of CKD and ESRD: implications for health policy. *Health Aff*. 2008;27(3):864–76.
31. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatr Res*. 1989;28(2):193–213.
32. EuroQol Research Foundation. EQ-5D-5L. EuroQol. [cited 2024 June 26]. Available from: <https://euroqol.org/information-and-support/euroqol-instruments/eq-5d-5l/>
33. EuroQol Research Foundation. EQ-5D-5L valuation crosswalk index value calculator. [cited 2024 June 26]. Available from: <https://euroqol.org/eq-5d-instruments/eq-5d-5l-about/valuation-standard-value-sets/crosswalk-index-value-calculator/>
34. Jyani G, Prinja S, Kar SS, Trivedi M, Patro B, Purba F et al. Valuing health-related quality of life among the Indian population: a protocol for the development of an EQ-5D value set for India using an extended design (DEVINE) study. *BMJ Open*. 2020;10(11).
35. Epskamp S, Borsboom D, Fried EI. Estimating psychological networks and their accuracy: A tutorial paper. *Behav Res Methods*. 2018;50(1):195–212.
36. Neild GH. Life expectancy with chronic kidney disease: an educational review. *Pediatr Nephrol*. 2017;32(2):243–8.
37. Sato D, Yoshinaga N, Nagai E, Nagai K, Shimizu E. Effectiveness of Internet-Delivered Computerized Cognitive Behavioral Therapy for Patients With Insomnia Who Remain Symptomatic Following Pharmacotherapy: Randomized Controlled Exploratory Trial. *J Med Internet Res*. 2019;21(4):e12686.
38. Ikeda S, Azuma M, Fujimoto K, Shibahara H, Inoue S, Moline et al. PMH8 EQ-5D Analysis in Patients with Insomnia: Change of Quality of Life in Lemborexant Phase 3 Trial Sunrise 1. *Value in Health*;2020; 23. S585.
39. McCrae CS, Bramoweth AD, Williams J, Roth A, Mosti C. Impact of Brief Cognitive Behavioral Treatment for Insomnia on Health Care Utilization and Costs. *J Clin Sleep Med*. 2014;10(2):127–35.
40. IMF World Economic Outlook Database. (2023). PPP Conversion Rates. <https://www.imf.org/en/Data>
41. Marseille E, et al. Thresholds for the cost–effectiveness of interventions: alternative approaches. *Health Policy Plan*. 2015;30(2):197–204.

42. Government of India. Union Budget 2023–24: Budget at a Glance. Ministry of Finance. New Delhi. 2023. Available from: <https://www.indiabudget.gov.in>
43. Yismaw GY, Workie LL, Wudneh S, Wondim A, Sisay CG, Mohammed SA et al. Poor sleep quality and associated factors among adult chronic kidney disease patients. *Front Med (Lausanne)*. 2024;11.
44. Fletcher BR, Damery S, Aiyegbusi OL, Anderson N, Calvert M, Cockwell P, et al. Symptom burden and health-related quality of life in chronic kidney disease: A global systematic review and meta-analysis. *PLoS Med*. 2022;19(4):e1003954.
45. Spiller TR, Levi O, Neria Y, Suarez-Jimenez B, Lazarov A, Bar-Haim Y. On the validity of the centrality hypothesis in cross-sectional between-subject networks of psychopathology. *BMC Med*. 2020;18:297.
46. Takano Y, Iбата R, Nakano N, Yoshimura M, Ozaki N, Nakagome K. Network analysis to estimate central insomnia symptoms among daytime workers at-risk for insomnia. *Sci Rep*. 2023;13:16406.
47. Robinaugh DJ, Millner AJ, McNally RJ. Identifying highly influential nodes in the complicated grief network. *J Abnorm Psychol*. 2016;125(6):747–57.
48. Yuan S, Wang R, Shi Y, Zhao Y, Tao H, Wu G, et al. Bridge symptoms of insomnia, obsessive-compulsive symptoms, and depression/anxiety: a network analysis. *BMC Psychiatry*. 2025;25(1):570.
49. He Y, Yang T, Guo Q, Wu S, Liu W, Xu T. Innovative analysis of the interconnected network structure between anxiety and sleep quality among college students. *Psychol Res Behav Manag*. 2025;18:607–18.
50. Stokes EA, Stott R, Henry AL, Espie CA, Miller CB. Quality-adjusted life years for digital cognitive behavioural therapy for insomnia (Sleepio): a secondary analysis. *BJGP Open*. 2022;6(4).

Figures

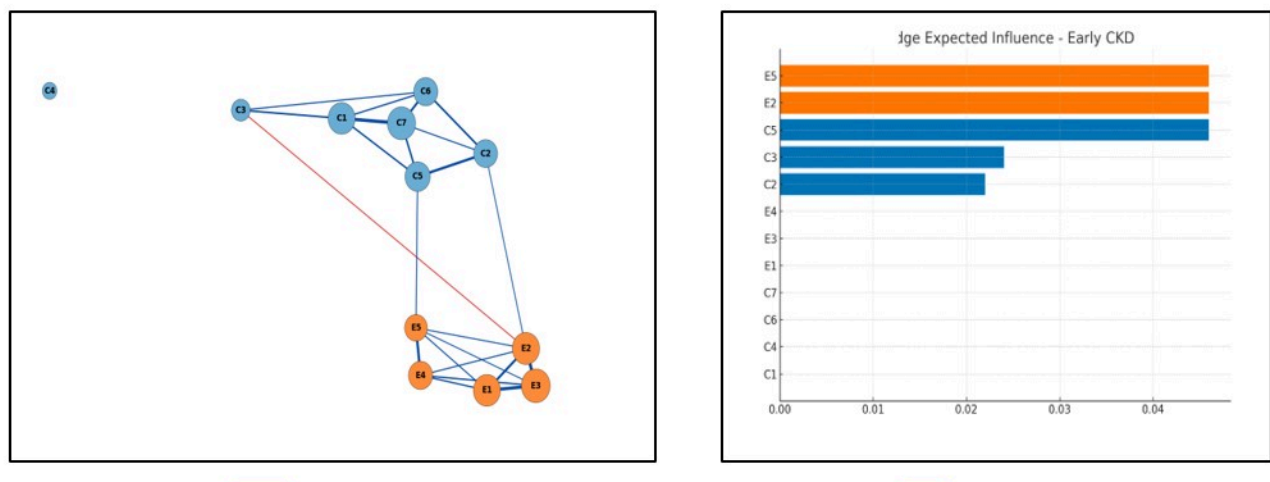


Figure 1

Symptom network model of sleep quality (C1–C7) and HRQoL (E1–E5) in early-stage CKD: (a): Nodes represent individual components of the PSQI (blue) and EQ-5D-5L (orange) dimensions. Edges represent partial correlations between nodes, with blue indicating positive associations and red indicating negative associations. The thickness and intensity of edges reflect the magnitude of the correlation, and node size is scaled according to Expected Influence (EI). (b): Bridge Expected Influence (BEI) values for all symptoms. C1 = Subjective sleep quality; C2 = Sleep latency; C3 = Sleep duration; C4 = Habitual sleep efficiency; C5 = Sleep disturbance; C6 = Use of sleep medication; C7 = Daytime dysfunction. E1 = Mobility; E2 = Self-care; E3 = Usual activities; E4 = Pain/discomfort; E5 = Anxiety/depression.

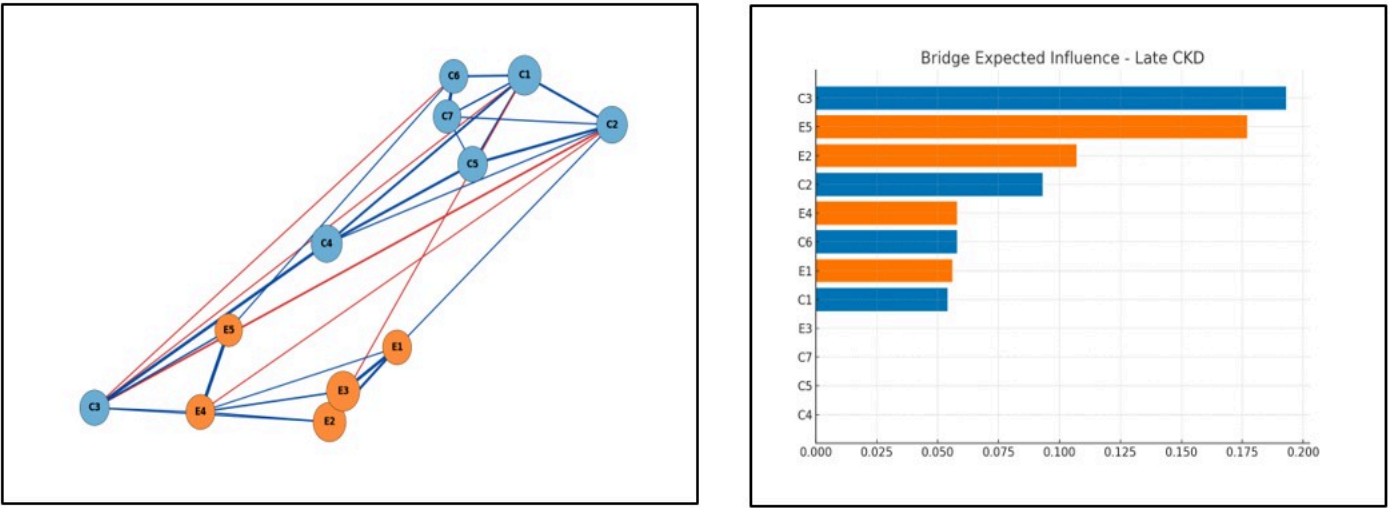


Figure 2

Symptom network model of sleep quality (C1–C7) and HRQoL (E1–E5) in late-stage CKD: (a): Nodes represent individual components of the PSQI (blue) and EQ-5D-5L (orange) dimensions. Edges represent partial correlations between nodes, with blue indicating positive associations and red indicating negative associations. The thickness and intensity of edges reflect the magnitude of the correlation, and node size is scaled according to Expected Influence (EI). (b): Bridge Expected Influence (BEI) values for all symptoms. C1 = Subjective sleep quality; C2 = Sleep latency; C3 = Sleep duration; C4 = Habitual sleep efficiency; C5 = Sleep disturbance; C6 = Use of sleep medication; C7 = Daytime dysfunction. E1 = Mobility; E2 = Self-care; E3 = Usual activities; E4 = Pain/discomfort; E5 = Anxiety/depression.