Biopsychosocial determinants and gender disparities in health-related quality of life among rheumatoid arthritis patients: a nationwide multicentre study in China

Y. Zhu[1], H. Xu[1], L. Zhang[2], Y. Huo[3], R. Wu[4], L. Wu[5], L. Lei[6], L. Geng[7], C. Tan[8], X. Li[9], R. Li[1], Y. Su[1,10], and the Women's Rheumatoid Arthritis Research Collaborative Group

[1]Department of Rheumatology and Immunology, Peking University People's Hospital, Beijing; [2]Third Hospital of Shanxi Medical University, Shanxi Bethune Hospital, Shanxi Academy of Medical Sciences, Tongji Shanxi Hospital, Taiyuan, Shanxi; [3]Department of Rheumatology and Immunology, The Fifth People's Hospital of Datong, Datong, Shanxi; [4]Department of Rheumatology and Immunology, The First Affiliated Hospital, Jiangxi Medical College, Nanchang University, Nanchang, Jiangxi; [5]Department of Rheumatology and Immunology, People's Hospital of Xinjiang Uygur Autonomous Region, Urumqi, Xinjiang; [6]Department of Rheumatology and Immunology, The First Affiliated Hospital of Guangxi Medical University, Nanning, Guangxi; [7]Department of Rheumatology and Immunology, The Drum Tower Clinical Medical School of Nanjing Medical University, Nanjing, Jiangsu; [8]Department of Rheumatology and Immunology, West China Hospital, Sichuan University, Chengdu, Sichuan; [9]Department of Rheumatology and Immunology, The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, Anhui; [10]Department of Rheumatology and Immunology, Peking University People's Hospital, Qingdao, Shandong, China.

Abstract

Objective

This study aimed to investigate the gender-specific factors influencing health-related quality of life (HRQoL) among rheumatoid arthritis (RA) patients within biopsychosocial framework and the interacting effects of these factors.

Methods

A prospective multi-centre cross-sectional study was conducted. Binary logistic regression and subsequent stratified analyses were used to analyse the determinants of HRQoL among RA patients and how they interacted.

Results

Female patients (83.85%) exhibited earlier onset (45.68 vs. 50.85 years), longer disease duration (60.00 vs. 36.00 months), lower Clinical Disease Activity Index (CDAI) (19.00 vs. 22.00), and less glucocorticoid use (39.55% vs. 47.75%). Multivariable analysis suggested that better HRQoL was linked to urban residence and higher education. Worse HRQoL was related to older age at onset, higher financial burden, glucocorticoid use, elevated CDAI, irregular follow up, longer follow-up intervals, comorbidities, anxiety/depressive symptoms, poor sleep satisfaction, and fatigue. Stratified analysis revealed significant interactions among CDAI and financial burden, anxiety/depressive symptoms and sleep satisfaction.

Conclusion

These findings highlight the biopsychosocial factors affecting HRQoL, emphasising the need for gender-specific strategies and targeted interventions focusing on financial burden, anxiety/depressive symptoms and sleep satisfaction in RA patients with moderate-to-high disease activity.

Key words

rheumatoid arthritis, health-related quality of life, EQ-5D-5L, Clinical Disease Activity Index, gender

*Yin Zhu, BMed**
*Haojie Xu, MMed**
Liyun Zhang, MD
Yuehong Huo, MD
Rui Wu, MD
Lijun Wu, MD
Ling Lei, MD
Linyu Geng, MD
Chunyu Tan, MD
Xiaomei Li, MD
Ru Li, MD
Yin Su, MD, PhD

**Contributed equally.*

Please address correspondence to:
Yin Su
Department of Rheumatology and Immunology,
Peking University People's Hospital,
11 Xizhimen South Street,
Beijing 100044, China.
E-mail: suyin@pkuph.edu.cn

and to:
Ru Li: doctorliru123@163.com

Received on September 27, 2025; accepted in revised form on January 19, 2026.

Funding: the study was supported by grants from the National Natural Science Foundation of China (92374101, 82230121), Beijing Science and Technology Planning Project (Z191100006619111) to Y. Su. This work was conducted under the framework of the Women's Rheumatoid Arthritis Research Collaborative Group established by the Chinese Association of Women in Rheumatology and Immunology.

Competing interests: none declared.

Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune disorder characterised by persistent synovitis and systemic inflammation, leading to pain, disability, multisystem comorbidities, and significant impairment of health-related quality of life (HRQoL) (1, 2). The prevalence of RA varies across geographic regions (3, 4). According to the Global Burden of Disease (GBD) 2017 data, RA prevalence ranged from 0.10% to 0.38%, with higher rates observed in developed countries (4). In China, approximately 0.28% of the population is affected, with a higher prevalence in women compared to men (2~3:1) (5).

Compared to the general population, patients with RA exhibited significantly impaired HRQoL (6-9). Previous studies have linked demographic and clinical characteristics, such as age (10), education (11), financial burden (11, 12), disease activity (13, 14), follow-up adherence (15), and comorbidities (16), to HRQoL in RA patients. The biopsychosocial model, pioneered by Engel *et al*., provides a powerful paradigm for understanding health and illness by acknowledging the intricate interplay of biological (*e.g*. disease duration, comorbidities), psychological (*e.g*. symptoms of anxiety/depression), and social factors (*e.g*. income, education) (17). Gender, as a risk factor that play an essential role in the treatments, outcomes and HRQoL of RA patients, inherently operates across and interacts with all three biopsychosocial domains, significantly influencing HRQoL (18, 19). Social, biological and psychological aspects of gender may all impact HRQoL of RA patients through mechanisms that are yet to be fully explored. Growing awareness of gender disparities in HRQoL has prompted researchers to advocate for incorporating these distinctions into RA management and treatment protocols.

The EuroQol Five-Dimensional Five-Level Questionnaire (EQ-5D-5L) was one of the most widely used preference-based instruments for assessing HRQoL globally, owing to its multidimensional nature and applicability across different cultural contexts (20). It has been broadly employed in studies of various chronic diseases, including RA (21). The EQ-5D-5L measures health utility through five dimensions: mobility (MO), self-care (SC), usual activities (UA), pain/discomfort (PD), and anxiety/depression (AD), with five levels of severity for each (no/slight/moderate/severe/extreme problems). In addition, the EQ-5D-5L includes the EQ visual analogue scale (EQ-VAS), which assesses self-reported health status on a scale of 0 (worst imaginable health) to 100 (best imaginable health) (22).

However, large-scale multicentre studies are still lacking in validating the interaction effects of biopsychosocial variables, particularly regarding gender-specific differences in HRQoL and the interplay between financial burden, psychiatric symptoms, and disease activity. This study aims to: 1. characterise the HRQoL status and gender disparities in RA patients; 2. identify determinants of HRQoL through multivariable regression model; 3. explore the independent or interactive roles of biopsychosocial factors through stratified analyses.

Methods

Study population

This was a multi-centre, prospective, cross-sectional study. Participants were recruited from 330 hospitals in all provinces of Chinese mainland (Supplementary Table S1). Eligible voluntarily patients registered from July and September 2023, resulting in 16,170 collected questionnaires. Inclusion criteria were: fulfillment of the 1987 American College of Rheumatology (ACR) criteria (23) or 2010 ACR/European Alliance of Associations for Rheumatology (EULAR) classification criteria for RA (24); age ≥18 years; informed consent and completion of all questionnaire items. Exclusion criteria included the presence of severe cognitive impairment or communication barriers, and >10% missing key data. The study protocol was approved by the Institutional Review Board of Peking University People's Hospital (IRB Approval no.: 2023PHB048-001; Date: 7 February 2023). The data cleaning process was as follows: 7 questionnaires were excluded for invalid answers; 328 were removed

due to a deficiency of over 10% in key data. The final data of analysis was comprised of 15,835 valid questionnaires.

Biopsychosocial framework and study variables

Data were collected via electronic questionnaires (https://www.wjx.cn/). Guided by the biopsychosocial model (17), this study conceptualises HRQoL as an outcome dynamically influenced by interactions among biological, psychological, and social factors. Variables were operationalised according to this framework and presented in the following logical sequence: 1. demographic and social factors: gender, age, onset age, education, residence, financial burden, and annual household income; 2. clinical/biological parameters: swollen/tender joint counts, Patient/Physician Global Assessment of Disease Activity, disease activity, disease duration, adherence to scheduled follow-up, follow-up interval, medication use (glucocorticoids, conventional synthetic DMARDs, biologic/targeted synthetic DMARDs), and comorbidities; 3. psychological factors: anxiety/depressive symptoms, sleep satisfaction and fatigue score; 4. outcome indicator: HRQoL.

Instrument

Disease activity was evaluated using the Clinical Disease Activity Index (CDAI), calculated from 28-Swollen Joint Count (SJC-28), 28-Tender Joint Count (TJC-28), Patient Global Assessment of Disease Activity (PtGA), and Physician Global Assessment of Disease Activity (PhGA). Total scores range from 0 to 76, categorised as remission (CDAI ≤2.8), low (2.8 < CDAI ≤10), moderate (10 < CDAI ≤22), or high disease activity (CDAI >22) (25). HRQoL was assessed using the Chinese version of the EQ-5D-5L, which evaluates MO, SC, UA, PD, and AD (1–5 levels) and responses were converted into a population-specific health utility value (range: -0.33–1) (22). Anxiety and depressive symptoms were measured using the 4-item Patient Health Questionnaire-4 (PHQ-4) (26), which is composed of the 2-item Generalized Anxiety Disorder Screener (GAD-2) (27) and the 2-item Patient Health Questionnaire (PHQ-2) (28). The PHQ-4 consists of the questions about the frequency of the depressive symptoms and the anxiety symptoms over the last two weeks. The answers to each question are 'not at all', 'several days', 'more than half the days', and 'nearly every day', corresponding to 0, 1, 2, and 3 points respectively. A GAD-2 or PHQ-2 score of 3 or higher is commonly used as a cut-off to indicate probable major depressive disorder or generalised anxiety disorder respectively, but these scores alone do not constitute a clinical diagnosis (29). Thus, we defined a GAD-2 or PHQ-2 score of 3 or higher as anxiety symptoms and depressive symptoms respectively in our research. Sleep satisfaction was self-rated as 'very poor', 'poor', 'good', and 'very good', dichotomised into 'poor' (very poor/poor) and 'good' (good/very good) for analysis. Fatigue was measured using a visual analogue scale (VAS; 0–100, with higher scores indicating greater severity).

Quality control

The questionnaire design was based on the *Chinese Practice guidelines for RA patients* (30), *Expert Recommendations for RA Management* (31), and EQ-5D-5L standards, with revisions by Women's Rheumatoid Arthritis Research Collaborative Group. The electronic questionnaire incorporated logic checks and mandatory fields to ensure data accuracy. Each participating institution was assigned a unique QR code, and IP addresses were restricted to one submission. Manual verification procedures ensured that data consistency exceeded 95%.

Statistical analysis

Baseline characteristics were compared between male and female patients. Continuous variables underwent normality testing via the Kolmogorov-Smirnov test and were analysed using Student's t-tests (for normally distributed data) or non-parametric tests (for non-normally distributed data). Categorical variables were assessed by chi-square tests. Missing data on disease duration were substituted with median values. Logistic regression models identified associations between sociodemographic/clinical/psychological factors and HRQoL. Subgroup analyses evaluated the interactions between CDAI and financial burden, anxiety symptoms, depressive symptoms and sleep satisfaction. All analyses were performed in R software (v. 4.3.2, R Foundation for Statistical Computing, Vienna, Austria), with statistical significance set at $p<0.001$.

Results

Sociodemographic profile: younger-onset females shouldering greater financial burden

A total of 15,835 RA patients were enrolled in this study, with 83.85% (13,278/15,835) being female. The mean age of the participants was 53.69±12.93 years, and the median onset age was 46.51±13.24 years. Both mean age and mean onset age were significantly younger in female patients (both $p<0.001$). Among the participants, 51.12% (8,095/15,835) received an education of junior high school or below, and 62.92% (9,963/15,835) resided in urban areas ($p>0.001$). Regarding financial burden, 47.67% (7,548/15,835) reported a moderate burden, 24.05% (3,809/15,835) a substantial burden, and 8.34% (1,321/15,835) a minimal burden. Female patients reported a statistically significant higher financial burden, with 27.62% of females reporting a "substantial/severe" burden compared to 26.20% of males ($p<0.001$). In terms of annual household income, 40.90% (6,477/15,835) earned ≤50,000 China Yuan (CNY), while only 2.19% (346/15,835) reported an income of >300,000 CNY ($p>0.001$) (Table I).

Gender-specific clinical patterns: longer disease duration but reduced disease activity, glucocorticoid utilisation, and comorbidity burden in female patients

Female RA patients exhibited lower values than males in the following clinical indicators: TJC-28 (4.00 [1.00–10.00] *vs*. 6.00 [2.00–12.00]), SJC-28 (2.00 [0.00–6.00] *vs*. 4.00 [1.00–9.00]), PtGA (55.00 [30.00–70.00] *vs*. 60.00 [40.00–78.00]), PhGA (54.00 [30.00–70.00] *vs*. 60.00 [40.00–75.00]), and CDAI (19.00 [12.00–29.00] *vs*. 22.00 [14.50–34.00], all $p<0.001$). The median disease du-

Table I. Demographic data of 15,835 RA patients and gender disparities.

Demographic data		Male (n=2557)	Female (n=13278)	t/χ^2	*p*
Age (years) (M ± SD)		56.43 ± 13.00	53.16 ± 12.85	11.77 [a]	<0.001
Onset age (years) (M ± SD)		50.85 ± 13.16	45.68 ± 13.09	18.27 [a]	<0.001
Education n (%)	Junior high school and below	1243 (48.61)	6852 (51.60)	7.68 [b]	0.006
	Senior high school and above	1314 (51.39)	6426 (48.40)		
Residence n (%)	rural	933 (36.49)	4939 (37.20)	0.46 [b]	0.497
	urban	1624 (63.51)	8339 (62.80)		
Financial burden n (%)	minimal	272 (10.64)	1049 (7.90)	25.08 [b]	<0.001
	mild	448 (17.52)	2180 (16.42)		
	moderate	1167 (45.64)	6381 (48.06)		
	substantial	590 (23.07)	3219 (24.24)		
	severe	80 (3.13)	449 (3.38)		
Annual household income (ten thousand) n (%)	≤5	1003 (39.23)	5474 (41.23)	11.97 [b]	0.018
	5-10	905 (35.39)	4542 (34.21)		
	10-15	464 (18.15)	2144 (16.15)		
	15-30	138 (5.40)	819 (6.17)		
	>30	47 (1.84)	299 (2.25)		

[a] student t-test was adopted; [b] Chi-square test was adopted. RA: rheumatoid arthritis; M: mean; SD: standard deviation.

Table II. Clinical features of 15,835 RA patients and gender disparities.

Clinical features		Male (n=2557)	Female (n=13278)	Z/χ^2	*p*
TJC-28 (IQR)		6.00 (2.00, 12.00)	4.00 (1.00, 10.00)	-11.90 [a]	<0.001
SJC-28 (IQR)		4.00 (1.00, 9.00)	2.00 (0.00, 6.00)	-11.77 [a]	<0.001
PtGA (IQR)		60.00 (40.00, 78.00)	55.00 (30.00, 70.00)	-5.10 [a]	<0.001
PhGA (IQR)		60.00 (40.00, 75.00)	54.00 (30.00, 70.00)	-5.97 [a]	<0.001
CDAI (IQR)		22.00 (14.50, 34.00)	19.00 (12.00, 29.00)	-11.79 [a]	<0.001
Disease duration (months) (IQR)		36.00 (12.00, 84.00)	60.00 (24.00, 120.00)	-12.16 [a]	<0.001
Irregular follow-up n (%)		431 (16.86)	2027 (15.27)	4.13 [b]	0.042
Follow-up interval (months) n (%)	≤6	2251 (88.03)	11661 (87.82)	0.09 [b]	0.765
	>6	306 (11.97)	1617 (12.18)		
Glucocorticoid therapy n (%)		1221 (47.75)	5251 (39.55)	59.72 [b]	<0.001
csDMARDs n (%)		2423 (94.76)	12470 (93.91)	2.73 [b]	0.098
b/tsDMARDs n (%)		1097 (42.90)	5429 (40.89)	3.59 [b]	0.058
Comorbidities n (%)		1584 (61.95)	7025 (52.91)	70.63 [b]	<0.001

[a] Z test was adopted; [b] Chi-square test was adopted.
IQR: interquartile range; TJC-28: 28-tender joint count; SJC-28: 28-swollen joint count; PtGA: Patient global assessment of disease activity; PhGA: Physician global assessment of disease activity; csDMARDs: conventional synthetic disease-modifying anti-rheumatic drugs; b/tsDMARDs: biologic/targeted synthetic disease-modifying anti-rheumatic drugs; CDAI: Clinical Disease Activity Index.

ration among RA patients was 60.00 months [24.00–120.00], with females having a significantly longer disease duration compared to males (60.00 months [24.00–120.00] *vs*. 36 months [12.00–84.00], $p<0.001$). Regarding treatment patterns, 15.52% (2,458/15,835) of patients missed regular follow-up appointments, and 12.14% (1,923/15,835) had follow-up intervals exceeding six months. Among the patients, 94.05% (14,893/15,835) used csDMARDs, and 41.21% (6,526/15,835) used b/tsDMARDs (both $p>0.001$). Female patients were less likely to use glucocorticoids (39.55% *vs*. 47.75%, $p<0.001$). Comorbidities were present in 54.37% (8,609/15,835) of patients, with significantly fewer females reporting comorbidities compared to males (52.91% *vs*. 61.95%, $p<0.001$) (Table II).

Gender-specific disparities in quality of life: diminished sleep satisfaction but enhanced health utility in female RA patients

Overall, 20.03% (3171/15,835) of patients reported anxiety symptoms, and 20.06% (3176/15,835) reported depressive symptoms. There were no significant gender differences in the proportion of patients with anxiety and depressive symptoms ($p>0.001$). Poor sleep satisfaction was reported by 36.05% (5,709/15,835) of patients, with a higher proportion of females experiencing poor sleep satisfaction compared to males (36.88% *vs*. 31.76%, $p<0.001$). The median fatigue VAS score was 50.00 [30.00–70.00], with no significant gender differences observed ($p>0.001$). In the EQ-5D-5L dimensions, males exhibited greater limitations in MO, SC, and UA than females (mild or worse issues: 55.89% *vs*. 49.03%; 47.28% *vs*. 40.08%; 54.83% *vs*. 49.62%, respectively, all $p<0.001$). No significant gender differences in PD and AD ($p>0.001$). The median health utility value of EQ-5D-5L was 0.17 [0.06–0.32], and the median EQ-VAS score was 70.00 [60.00–80.00]. Female patients reported a slightly higher health utility value than males (0.83 *vs*. 0.78, $p<0.001$), while EQ-VAS scores were comparable between genders ($p>0.001$) (Table III).

Table III. Quality of life in 15,835 RA patients and gender disparities.

Quality of life		Male (n=2557)	Female (n=13278)	χ^2/Z	*p*
Anxiety symptoms n (%)		570 (22.29)	2601 (19.59)	9.78 [a]	0.002
Depressive symptoms n (%)		560 (21.9)	2616 (19.7)	6.47 [a]	0.011
Sleep satisfaction n (%)	good	1745 (68.24)	8381 (63.12)	24.42 [a]	<0.001
	poor	812 (31.76)	4897 (36.88)		
Fatigue VAS (IQR)		52.00 (30.00,70.00)	50.00 (30.00,70.00)	-3.04 [b]	0.002
MO n (%)	no problems	1128 (44.11)	6768 (50.97)	50.61 [a]	<0.001
	slight problems	945 (36.96)	4318 (32.52)		
	moderate problems	336 (13.14)	1457 (10.97)		
	severe problems	122 (4.77)	521 (3.92)		
	unable to/extreme problems	26 (1.02)	214 (1.61)		
SC n (%)	no problems	1348 (52.72)	7956 (59.92)	60.10 [a]	<0.001
	slight problems	812 (31.76)	3702 (27.88)		
	moderate problems	270 (10.56)	1047 (7.89)		
	severe problems	105 (4.11)	400 (3.01)		
	unable to/extreme problems	22 (0.86)	173 (1.30)		
UA n (%)	no problems	1155 (45.17)	6689 (50.38)	37.8 [a]	<0.001
	slight problems	952 (37.23)	4664 (35.13)		
	moderate problems	331 (12.94)	1324 (9.97)		
	severe problems	99 (3.87)	441 (3.32)		
	unable to/extreme problems	20 (0.78)	160 (1.21)		
PD n (%)	no problems	503 (19.67)	2782 (20.95)	13.23 [a]	0.010
	slight problems	1318 (51.54)	7056 (53.14)		
	moderate problems	539 (21.08)	2537 (19.11)		
	severe problems	166 (6.49)	708 (5.33)		
	unable to/extreme problems	31 (1.21)	195 (1.47)		
AD n (%)	no problems	1060 (41.45)	5364 (40.40)	5.24 [a]	0.263
	slight problems	1105 (43.21)	6010 (45.26)		
	moderate problems	289 (11.30)	1430 (10.77)		
	severe problems	81 (3.17)	353 (2.66)		
	unable to/extreme problems	22 (0.86)	121 (0.91)		
Health utility value of quality of life (IQR)		0.78 (0.65,0.94)	0.83 (0.69,0.94)	-5.04 [b]	<0.001
EQ-VAS (IQR)		70.00 (60.00,80.00)	75.00 (60.00,81.00)	-2.03 [b]	0.043

[a] Chi-square test was adopted; [b] Z test was adopted. MO: mobility; EQ: EurolQol; SC: self-care; UA: usual activities; PD: pain/discomfort; AD: anxiety/depression; VAS: visual analogue scale; IQR: interquartile range.

Biopsychosocial determinants affecting HRQoL: gender was not independently associated with HRQoL

Patients were grouped into 'good' or 'poor' quality of life based on the median EQ-5D-5L health utility value. Significant differences were observed between these groups in the following biopsychosocial factors: gender, onset age, education, financial burden, residence, use of glucocorticoids, use of b/tsDMARDs, disease duration, follow-up adherence, follow-up interval, comorbidities, anxiety/depressive symptoms, sleep satisfaction, and fatigue VAS (all $p<0.001$, Table IV).

Multivariable regression analysis revealed that receiving senior high school education and above (adjusted OR=0.86, 95%CI: 0.80–0.94, $p<0.001$) and urban residence (adjusted OR=0.86, 95%CI: 0.79–0.93, $p<0.001$) were independently associated with good HRQoL. Financial burden was associated with poor HRQoL, with increasing financial burden corresponding to a greater likelihood of poor HRQoL (adjusted OR=2.79, 95%CI: 2.34–3.31 for mild burden; adjusted OR=6.58, 95%CI: 4.95–8.76 for severe burden, $p<0.001$). Use of glucocorticoids was also associated with poor HRQoL (adjusted OR=1.41, 95%CI: 1.31–1.53, $p<0.001$). Additionally, CDAI (adjusted OR=3.37, 95%CI: 3.01–3.76, $p<0.001$), anxiety symptoms (adjusted OR=2.70, 95%CI: 2.31–3.15), depressive symptoms (adjusted OR=2.32, 95%CI: 1.99–2.71) and poor sleep satisfaction (adjusted OR=2.29, 95%CI: 2.11–2.48) were major factors related to poor HRQoL (all $p<0.001$). Longer follow-up intervals (adjusted OR=1.44, 95%CI: 1.26–1.64, $p<0.001$) and older age at onset (45–59 and ≥ 60 *vs.* ≤44 years: adjusted OR=1.21, 95%CI: 1.12–1.32, $p<0.001$; adjusted OR=1.61, 95%CI: 1.43–1.81, $p<0.001$) were also associated with poor HRQoL (Table V).

Female RA patients showed better HRQoL than Male RA patients (Table III). While in the multivariable regression analysis, gender was not independently associated with HRQoL (Table V). To further address potential confounding, we performed 1:2 propensity score matching on key covariates (age, financial burden, income, disease duration) (Suppl. Table S3). In the matched cohort, the association between gender and HRQoL remained non-significant ($p=0.003$).

Synergistic interaction of risk factors: combined effects of anxiety/depressive symptoms, impaired sleep satisfaction, elevated financial burden, and moderate-to-high disease activity on HRQoL deterioration

In multivariable logistic regression, financial burden (*e.g.* severe burden: adjusted OR=6.58, 95%CI: 4.95-8.76), CDAI (adjusted OR=3.37, 95%CI: 3.01–3.76), anxiety symptoms (adjust-

Table IV. Comparison between good quality of life and poor quality of life groups.

Variables		Good quality of life (n=7611)	Poor quality of life (n=8224)	χ^2/Z	*p*
Gender n (%)	Male	1107 (14.54)	1450 (17.63)	27.81 [a]	<0.001
	Female	6504 (85.46)	6774 (82.37)		
Onset age (years) n (%)	≤44	3598 (47.27)	3103 (37.73)	185.21 [a]	<0.001
	45-59	3023 (39.72)	3558 (43.26)		
	≥60	990 (13.01)	1563 (19.01)		
Education n (%)	Junior high school and below	3405 (44.74)	4690 (57.03)	238.95 [a]	<0.001
	Senior high school and above	4206 (55.26)	3534 (42.97)		
Financial burden n (%)	Minimal	1024 (13.45)	297 (3.61)	1156.81 [a]	<0.001
	Mild	1491 (19.59)	1137 (13.83)		
	Moderate	3803 (49.97)	3745 (45.54)		
	Substantial	1187 (15.60)	2622 (31.88)		
	Severe	106 (1.39)	423 (5.14)		
Residence n (%)	Rural	2451 (32.20)	3421 (41.60)	149.52 [a]	<0.001
	Urban	5160 (67.80)	4803 (58.40)		
Glucocorticoid therapy n (%)		2436 (32.01)	4036 (49.08)	476.58 [a]	<0.001
csDMARDs n (%)		7165 (94.14)	7728 (93.97)	0.21 [a]	0.649
b/tsDMARDs n (%)		3031 (39.82)	3495 (42.50)	11.66 [a]	<0.001
CDAI n(%)	≤10	2663 (34.99)	730 (8.88)	1600.89 [a]	<0.001
	>10	4948 (65.01)	7494 (91.12)		
Disease duration (years) n (%)	≤1	1820 (23.91)	1612 (19.60)	43.29 [a]	<0.001
	>1	5791 (76.09)	6612 (80.40)		
Irregular follow up n (%)		720 (9.46)	1738 (21.13)	410.76 [a]	<0.001
Follow-up interval(months) n (%)	≤6	7009 (92.09)	6903 (83.94)	246.28 [a]	<0.001
	>6	602 (7.91)	1321 (16.06)		
Comorbidities n (%)		3389 (44.53)	5220 (63.47)	571.86 [a]	<0.001
Anxiety symptoms n (%)		499 (6.56)	2672 (32.49)	1660.02 [a]	<0.001
Depressive symptoms n (%)		507 (6.66)	2669 (32.45)	1640.01 [a]	<0.001
Sleep satisfaction n (%)	good	5919 (77.77)	4207 (51.16)	1214.40 [a]	<0.001
	poor	1692 (22.23)	4017 (48.84)		
Fatigue VAS (IQR)		40.00 (20.00, 70.00)	60.00 (40.00, 75.00)	-30.65 [b]	<0.001

[a] Chi-square test was adopted; [b] Z test was adopted.
csDMARDs: conventional synthetic disease-modifying anti-rheumatic drugs; b/tsDMARDs: biologic/targeted synthetic disease-modifying anti-rheumatic drugs; CDAI: Clinical Disease Activity Index; VAS: visual analogue scale.

ed OR=2.70, 95%CI: 2.31–3.15), depressive symptoms (adjusted OR=2.32, 95%CI: 1.99–2.71), and sleep satisfaction (adjusted OR=2.29, 95%CI: 2.11–2.48) were independently associated with HRQoL (all $p<0.001$) (Table V). A significant interaction was found between CDAI and financial burden (β = -0.29 for sever financial burden, $p<0.001$, Fig. 1, Suppl. Table S2), suggesting these factors jointly affect HRQoL in RA patients. Furthermore, the interaction between CDAI and anxiety symptoms (β = -0.20, $p<0.001$, Fig. 1, Suppl. Table S2) as well as between CDAI and depressive symptoms (β = -0.20, $p<0.001$, Fig. 1, Suppl. Table S2) was also statistically significant, indicating that the impact of CDAI on HRQoL was affected by anxiety and depressive symptoms. Furthermore, the impact of CDAI on HRQoL was amplified by poor sleep satisfaction (β = -0.15, $p<0.001$, Fig. 1, Suppl. Table S2).

Discussion

Drawing on a large, nationally dispersed sample recruited from diverse regions across China, this study provides an in-depth analysis of the sociodemographic characteristics, gender-specific clinical patterns, HRQoL, and influencing factors among RA patients.

This survey adopted Engel's biopsychosocial model (17), incorporating a comprehensive questionnaire covering demographics, clinical characteristics, psychological factors and quality of life. The findings confirmed that the HRQoL of RA patients is influenced by the synergistic interaction of biological, psychological, and social factors. Multivariable regression analysis revealed that older age at onset, higher financial burden, glucocorticoid use, higher CDAI, irregular follow-up, longer follow-up intervals, comorbidities, anxiety symptoms, depressive symptoms, poor sleep satisfaction, and higher fatigue VAS scores were independently associated with impaired HRQoL while receiving senior high school education and above and urban residence were independently associated with good HRQoL. Higher financial burden, anxiety symptoms, depressive symptoms, and poor sleep satisfaction exhibited larger ORs, suggesting that patients with these characteristics may be more prone to poorer quality of life.

Previous studies showed that gender played a significant role in the HRQoL among RA patients, with female generally experiencing worse outcomes than male (32, 33). A meta-analysis using the SF-36 questionnaire, involving over 20,000 RA patients, found that women had significantly lower mental component summary scores and were more prone to anxiety and depression (32). However, in this cohort, significant differences in demographics, clinical characteristics, and HRQoL were found between female and male RA patients, and we observed the phenomenon that

Table V. Univariable and multivariable regression analysis of influencing factors of HRQoL.

Variables		Univariable analysis		Multivariable analysis	
		OR (95%CI)	*p*	OR (95%CI)	*p*
Gender (female *vs*. male)		0.80 (0.73 ~ 0.87)	<0.001	0.89 (0.81 ~ 0.99)	0.030
Onset age (years)	45-59	1.37 (1.28 ~ 1.46)	<0.001	1.21 (1.12 ~ 1.32)	<0.001
	≥60	1.83 (1.67 ~ 2.01)	<0.001	1.61 (1.43 ~ 1.81)	<0.001
Education (Senior high school and above *vs*. Junior high school and below)		0.61 (0.57 ~ 0.65)	<0.001	0.86 (0.80 ~ 0.94)	<0.001
Financial burden	minimal	Reference			
	mild	2.63 (2.26 ~ 3.06)	<0.001	2.79 (2.34 ~ 3.31)	<0.001
	moderate	3.40 (2.96 ~ 3.89)	<0.001	3.28 (2.80 ~ 3.84)	<0.001
	substantial	7.62 (6.58 ~ 8.82)	<0.001	5.17 (4.36 ~ 6.13)	<0.001
	severe	13.76 (10.73~17.65)	<0.001	6.58 (4.95 ~ 8.76)	<0.001
Residence (urban *vs*. rural)		0.67 (0.63 ~ 0.71)	<0.001	0.86 (0.80 ~ 0.93)	<0.001
Glucocorticoid therapy (yes *vs*. no)		2.05 (1.92 ~ 2.18)	<0.001	1.41 (1.31 ~ 1.53)	<0.001
csDMARDs (yes *vs*. no)		0.97 (0.85 ~ 1.11)	0.649		
b/tsDMARDs (yes *vs*. no)		1.12 (1.05 ~ 1.19)	<0.001	0.97 (0.90 ~ 1.05)	0.511
CDAI (>10 *vs*. ≤10)		5.53 (5.05 ~ 6.04)	<0.001	3.37 (3.01 ~ 3.76)	<0.001
Disease duration (months) (>6 *vs*. ≤6)		1.29 (1.20 ~ 1.39)	<0.001	1.05 (0.96 ~ 1.15)	0.327
Regular follow up (no *vs*. yes)		2.57 (2.34 ~ 2.82)	<0.001	1.62 (1.43 ~ 1.82)	<0.001
Follow-up interval (months) (>6 *vs*. ≤6)		2.23 (2.01 ~ 2.47)	<0.001	1.44 (1.26 ~ 1.64)	<0.001
Comorbidities (yes *vs*. no)		2.17 (2.03 ~ 2.31)	<0.001	1.56 (1.44 ~ 1.68)	<0.001
Anxiety symptoms (yes *vs*. no)		6.86 (6.20 ~ 7.59)	<0.001	2.70 (2.31 ~ 3.15)	<0.001
Depressive symptoms (yes *vs*. no)		6.73 (6.08 ~ 7.45)	<0.001	2.32 (1.99 ~ 2.71)	<0.001
Sleep satisfaction (poor *vs*. good)		3.34 (3.12 ~ 3.58)	<0.001	2.29 (2.11 ~ 2.48)	<0.001
Fatigue VAS		1.02 (1.02~1.02)	<0.001	1.01 (1.00 ~ 1.01)	<0.001

Onset age: the adolescents is the reference, adolescents: ≤44 years old, the middle-aged: 45-59 years old, the elderly: ≥60 years old; Financial burden: the extent of perceived financial burden, perceived financial burden being minimal is the reference.
csDMARDs: conventional synthetic disease-modifying anti-rheumatic drugs; b/tsDMARDs: biologic/targeted synthetic disease-modifying anti-rheumatic drugs; CDAI: Clinical Disease Activity Index; VAS: visual analogue scale.

Variables	Total n (%)	EQ-5D-5L (CDAI ≤ 10)	EQ-5D-5L (CDAI > 10)	β (95%CI)	P	P for interaction
All patients	15835 (100.00)	0.89 ± 0.15	0.72 ± 0.26	-0.17 (-0.18 ~ -0.16)	<.001	
Financial Burden						<.001
minimal	1321 (8.34)	0.94 ± 0.10	0.85 ± 0.22	-0.09 (-0.11 ~ -0.07)	<.001	
mild	2628 (16.60)	0.91 ± 0.13	0.79 ± 0.20	-0.12 (-0.13 ~ -0.10)	<.001	
moderate	7548 (47.67)	0.89 ± 0.13	0.75 ± 0.23	-0.15 (-0.16 ~ -0.14)	<.001	
substantial	3809 (24.05)	0.83 ± 0.19	0.63 ± 0.29	-0.20 (-0.22 ~ -0.17)	<.001	
severe	529 (3.34)	0.72 ± 0.26	0.44 ± 0.39	-0.29 (-0.39 ~ -0.18)	<.001	
Anxiety Symptoms						<.001
no	12664 (79.97)	0.90 ± 0.13	0.77 ± 0.22	-0.13 (-0.14 ~ -0.12)	<.001	
yes	3171 (20.03)	0.73 ± 0.24	0.53 ± 0.32	-0.20 (-0.24 ~ -0.16)	<.001	
Depressive Symptoms						<.001
no	12659 (79.94)	0.90 ± 0.13	0.77 ± 0.22	-0.13 (-0.14 ~ -0.12)	<.001	
yes	3176 (20.06)	0.74 ± 0.24	0.54 ± 0.32	-0.20 (-0.24 ~ -0.16)	<.001	
Sleep Satisfaction						<.001
good	10126 (63.95)	0.91 ± 0.13	0.79 ± 0.22	-0.12 (-0.13 ~ -0.11)	<.001	
poor	5709 (36.05)	0.84 ± 0.19	0.61 ± 0.30	-0.22 (-0.24 ~ -0.20)	<.001	

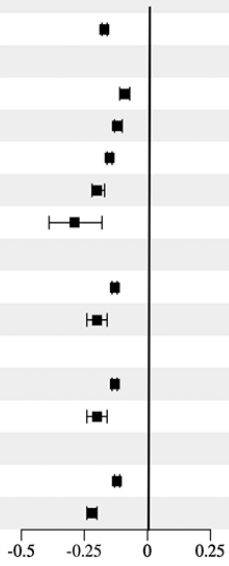

Fig. 1. The forest plot of interaction between CDAI and financial burden, anxiety symptoms, depressive symptoms, sleep satisfaction.

female patients exhibited lower CDAI scores, fewer comorbidities, and better HRQoL despite having earlier disease onset, lower educational and income levels, and higher financial burden. After adjusting for socioeconomic factors, psychological symptoms, treatment regimens, disease duration, and comorbidities in multivariate regression analysis and propensity score matching, this gender-associated difference no longer reached statistical significance. These findings collectively indicate that the initially observed HRQoL difference between genders is likely attributable to confounding variables (*i.e*. socioeconomic conditions, psychological status, disease duration, and comorbidities) rather than gender itself. Thus, gender may not serve as an independent predictor of HRQoL in this population. Overall, these findings emphasise the importance of tailoring RA treatment and support to address gender-specific

differences in social factors, symptoms and psychological health to improve HRQoL for both women and men.

A meta-analysis showed that RA patients have higher prevalence rates of anxiety and depression compared to the general population, and these conditions exacerbate the negative impact of RA on HRQoL (34). This may be related to increased pain, enhanced inflammatory responses, reduced treatment adherence, and lower chances of disease remission (15, 35-37). Multivariable regression confirmed that both anxiety and depressive symptoms were independently associated with poor HRQoL, suggesting that psychological interventions may improve patient outcomes. Interaction analysis suggested that CDAI and psychosocial factors influenced HRQoL through a dynamic, non-linear network. A biological-psychological synergy existed, where higher CDAI strengthened the negative effect of anxiety/depressive symptoms on HRQoL. This might be due to inflammatory states disrupting prefrontal-amygdala emotional regulation circuits (38, 39). Additionally, socioeconomic stress, especially higher financial burden, intensified the link between sleep satisfaction and HRQoL by undermining psychological resilience through chronic stress (40). These findings highlight the interplay of biological, psychological, and social factors, suggesting that holistic biopsychosocial management could enhance RA treatment effectiveness.

This study has several limitations. The main limitation of a cross-sectional study is its inability to establish causal relationships, and confounding factors can obscure true associations. Consequently, the findings should be interpreted with caution. In addition, the PHQ-4 was a screening tool for anxiety and depression which has limitations and does not equate to a validated diagnostic approach. This methodological choice was to conduct preliminary large-scale screening to draw attention to the frequency of these symptoms in the queue of RA patients, remind doctors to conduct professional evaluations if necessary, but may little overestimate true prevalence. To address these limitations, future research should adopt longitudinal cohort designs to clarify temporal relationships and causal pathways, complemented by interventional clinical trials that test the mechanistic hypotheses generated by the present findings. Furthermore, well-validated and widely recognised instruments should be employed to enhance the comparability and robustness of the findings. Critical confounders, including BMI, occupational exposure, and hormonal status were also expected to be assessed in future research.

Conclusion

This study suggests that a multidimensional management strategy focusing on reducing financial burden and controlling disease activity, combined with psychological interventions and sleep management, may effectively improve HRQoL in RA patients. Reducing financial burden ensures treatment continuity, precise disease activity control improves physical function and systemic symptoms, and integrated psychosomatic management enhances overall recovery. A stepped care model prioritising core biomedical indicators followed by layered psychological and social interventions is recommended. Future research should evaluate the long-term cost-effectiveness of different intervention combinations and explore personalised HRQoL optimisation pathways based on patient stratification.

Acknowledgments

We sincerely appreciate the experts who participated in the compilation and discussion of the survey report. They are listed by their affiliated hospitals as follows:

Liling Xu, Yuan Jia, Ru Li and Yin Su (Dept. of Rheumatology and Immunology, Peking University People's Hospital); Wen Zhang and Wenjie Zheng (Dept. of Rheumatology and Clinical Immunology, Peking Union Medical College Hospital); Lie Dai (Dept. of Rheumatology and Immunology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University); Quan Jiang (Dept. of Rheumatology, Guang'anmen Hospital, China Academy of Chinese Medical Sciences); Jin Lin (Dept. of Rheumatology, The First Affiliated Hospital, Zhejiang University School of Medicine); Xiaomei Li (Dept. of Rheumatology and Immunology, The First Affiliated Hospital of University of Science and Technology of China); Rong Mu (Dept. of Rheumatology and Immunology, Peking University Third Hospital); Lijun Wu (Dept. of Rheumatology and Immunology, People's Hospital of Xinjiang Uygur Autonomous Region); and Miaojia Zhang (Dept. of Rheumatology, The First Affiliated Hospital of Nanjing Medical University).

References

1. GRAVALLESE EM, FIRESTEIN GS: Rheumatoid arthritis - common origins, divergent mechanisms. *N Engl J Med* 2023; 388(6): 529-42. https://doi.org/10.1056/nejmra2103726
2. PEI W, XU L, ZHONG H *et al*.: Clinical features of inflammatory arthritis in daily practice-China's perspective. *Clin Rheumatol* 2025; 44(3): 969-78. https://doi.org/10.1007/s10067-024-07262-2
3. FINCKH A, GILBERT B, HODKINSON B *et al*.: Global epidemiology of rheumatoid arthritis. *Nat Rev Rheumatol* 2022; 18(10): 591-602. https://doi.org/10.1038/s41584-022-00827-y
4. SAFIRI S, KOLAHI AA, HOY D *et al*.: Global, regional and national burden of rheumatoid arthritis 1990-2017: a systematic analysis of the Global Burden of Disease study 2017. *Ann Rheum Dis* 2019; 78(11): 1463-71. https://doi.org/10.1136/annrheumdis-2019-215920
5. LI R, SUN J, REN LM *et al*.: Epidemiology of eight common rheumatic diseases in China: a large-scale cross-sectional survey in Beijing. *Rheumatology* (Oxford) 2012; 51(4): 721-29. https://doi.org/10.1093/rheumatology/ker370
6. BAI B, CHEN M, FU L *et al*.: Quality of life and influencing factors of patients with rheumatoid arthritis in Northeast China. *Health Qual Life Outcomes* 2020; 18(1): 119. https://doi.org/10.1186/s12955-020-01355-7
7. UHLIG T, LOGE JH, KRISTIANSEN IS, KVIEN TK: Quantification of reduced health-related quality of life in patients with rheumatoid arthritis compared to the general population. *J Rheumatol* 2007; 34(6): 1241-47.
8. GONG G, MAO J: Health-related quality of life among Chinese patients with rheumatoid arthritis: the predictive roles of fatigue, functional disability, self-efficacy, and social support. *Nurs Res* 2016; 65(1): 55-67. https://doi.org/10.1097/nnr.0000000000000137
9. KOJIMA M, KOJIMA T, ISHIGURO N *et al*.: Psychosocial factors, disease status, and quality of life in patients with rheumatoid arthritis. *J Psychosom Res* 2009; 67(5): 425-31. https://doi.org/10.1016/j.jpsychores.2009.01.001
10. OGURO N, YAJIMA N, MIWA Y: Age and quality of life in patients with rheumatoid arthritis treated with biologic agents. *Mod Rheumatol* 2020; 30(1): 44-49. https://doi.org/10.1080/14397595.2018.1551274

11. SHEN B, TAN W, FENG G *et al*.: The correlations of disease activity, socioeconomic status, quality of life, and depression/anxiety in Chinese patients with systemic lupus erythematosus. *Clin Dev Immunol* 2013; 2013: 270878. https://doi.org/10.1155/2013/270878
12. HUANG Y, LI J, AGARWAL SK: Economic and humanistic burden of rheumatoid arthritis: results from the US National Survey data 2018-2020. *ACR Open Rheumatol* 2024; 6(11): 746-54. https://doi.org/10.1002/acr2.11728
13. KATCHAMART W, NARONGROEKNAWIN P, CHANAPAI W, THAWEERATTHAKUL P: Health-related quality of life in patients with rheumatoid arthritis. *BMC Rheumatol* 2019; 3: 34. https://doi.org/10.1186/s41927-019-0080-9
14. FENG J, YU L, FANG Y, ZHANG X, LI S, DOU L: Correlation between disease activity and patient-reported health-related quality of life in rheumatoid arthritis: a cross-sectional study. *BMJ Open* 2024; 14(5): e082020. https://doi.org/10.1136/bmjopen-2023-082020
15. HROMADKOVA L, SOUKUP T, VLCEK J: Quality of life and drug compliance: their interrelationship in rheumatic patients. *J Eval Clin Pract* 2015; 21(5): 919-24. https://doi.org/10.1111/jep.12399
16. AN J, NYARKO E, HAMAD MA: Prevalence of comorbidities and their associations with health-related quality of life and healthcare expenditures in patients with rheumatoid arthritis. *Clin Rheumatol* 2019; 38(10): 2717-26. https://doi.org/10.1007/s10067-019-04613-2
17. ENGEL GL: The need for a new medical model: a challenge for biomedicine. *Science* 1977; 196(4286): 129-36. https://doi.org/10.1126/science.847460
18. JAWAHEER D, OLSEN J, HETLAND ML: Sex differences in response to anti-TNF therapy in early and established rheumatoid arthritis - results from the longitudinal Danish DANBIO registry. *J Rheumatol* 2012; 39(1): 46-53. https://doi.org/10.3899/jrheum.110548
19. ZHOU Y, WANG X, AN Y *et al*.: Disability and health-related quality of life in Chinese patients with rheumatoid arthritis: a cross-sectional study. *Int J Rheum Dis* 2018; 21(9): 1709-15. https://doi.org/10.1111/1756-185x.13345
20. HERDMAN M, GUDEX C, LLOYD A *et al*.: Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res* 2011; 20(10): 1727-36. https://doi.org/10.1007/s11136-011-9903-x
21. ZHOU T, GUAN H, WANG L, ZHANG Y, RUI M, MA A: Health-related quality of life in patients with different diseases measured with the EQ-5D-5L: a systematic review. *Front Public Health* 2021; 9: 675523. https://doi.org/10.3389/fpubh.2021.675523
22. LUO N, LIU G, LI M, GUAN H, JIN X, RAND-HENDRIKSEN K: Estimating an EQ-5D-5L value set for China. *Value Health* 2017; 20(4): 662-69. https://doi.org/10.1016/j.jval.2016.11.016
23. ARNETT FC, EDWORTHY SM, BLOCH DA *et al*.: The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis Rheum* 1988; 31(3): 315-24. https://doi.org/10.1002/art.1780310302
24. ALETAHA D, NEOGI T, SILMAN AJ *et al*.: 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis Rheum* 2010; 62(9): 2569-81. https://doi.org/10.1002/art.27584
25. ALETAHA D, SMOLEN J: The Simplified Disease Activity Index (SDAI) and the Clinical Disease Activity Index (CDAI): a review of their usefulness and validity in rheumatoid arthritis. *Clin Exp Rheumatol* 2005; 23 (5 Suppl 39): S100-108.
26. KROENKE K, SPITZER RL, WILLIAMS JB, LÖWE B: An ultra-brief screening scale for anxiety and depression: the PHQ-4. *Psychosomatics* 2009; 50(6): 613-21. https://doi.org/10.1016/S0033-3182(09)70864-3
27. KROENKE K, SPITZER RL, WILLIAMS JBW, MONAHAN PO, LÖWE B: Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. *Ann Intern Med* 2007; 146(5): 317-25. https://doi.org/10.7326/0003-4819-146-5-200703060-00004
28. KROENKE K, SPITZER RL, WILLIAMS JB: The Patient Health Questionnaire-2: validity of a two-item depression screener. *Med Care* 2003; 41(11): 1284. https://doi.org/10.1097/01.mlr.0000093487.78664.3c
29. WICKE FS, KRAKAU L, LÖWE B, BEUTEL ME, BRÄHLER E: Update of the standardization of the Patient Health Questionnaire-4 (PHQ-4) in the general population. *J Affect Disord* 2022; 312: 310-14. https://doi.org/10.1016/j.jad.2022.06.054
30. TIAN X, WANG Q, LI M *et al*.: 2018 Chinese guidelines for the diagnosis and treatment of rheumatoid arthritis. *Rheumatol Immunol Res* 2021; 2(1): 1-14. https://doi.org/10.2478/rir-2021-0002
31. Chronic Disease Management Group of Special Committee on Rheumatology and Immunology of Cross-Straits Medicine Exchange Association. [Expert recommendations for the chronic disease management of rheumatic arthritis]. *Zhonghua Nei Ke Za Zhi* 2023; 62(11): 1256-65. https://doi.org/10.3760/cma.j.cn112138-20221219-00940
32. MATCHAM F, SCOTT IC, RAYNER L *et al*.: The impact of rheumatoid arthritis on quality-of-life assessed using the SF-36: a systematic review and meta-analysis. *Semin Arthritis Rheum* 2014; 44(2): 123-30. https://doi.org/10.1016/j.semarthrit.2014.05.001
33. WEST E, WÅLLBERG-JONSSON S: Health-related quality of life in Swedish men and women with early rheumatoid arthritis. *Gend Med* 2009; 6(4): 544-54. https://doi.org/10.1016/j.genm.2009.12.001
34. DRAKES DH, FAWCETT EJ, YICK JJJ *et al*.: Beyond rheumatoid arthritis: A meta-analysis of the prevalence of anxiety and depressive disorders in rheumatoid arthritis. *J Psychiatr Res* 2025; 184: 424-38. https://doi.org/10.1016/j.jpsychires.2025.03.020
35. STURGEON JA, FINAN PH, ZAUTRA AJ: Affective disturbance in rheumatoid arthritis: psychological and disease-related pathways. *Nat Rev Rheumatol* 2016; 12(9): 532-42. https://doi.org/10.1038/nrrheum.2016.112
36. DIMATTEO MR, LEPPER HS, CROGHAN TW: Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. *Arch Intern Med* 2000; 160(14): 2101-7. https://doi.org/10.1001/archinte.160.14.2101
37. SNOECK HENKEMANS SVJ, VIS M, KOC GH *et al*.: Association between depression and anxiety and inability to achieve remission in rheumatoid arthritis and psoriatic arthritis. *Rheumatology* (Oxford) 2025; 64(5): 2411-21. https://doi.org/10.1093/rheumatology/keae621
38. MUSCATELL KA, DEDOVIC K, SLAVICH GM *et al*.: Greater amygdala activity and dorsomedial prefrontal-amygdala coupling are associated with enhanced inflammatory responses to stress. *Brain Behav Immun* 2015; 43: 46-53. https://doi.org/10.1016/j.bbi.2014.06.201
39. HU P, LU Y, PAN BX, ZHANG WH: New insights into the pivotal role of the amygdala in inflammation-related depression and anxiety disorder. *Int J Mol Sci* 2022; 23(19): 11076. https://doi.org/10.3390/ijms231911076
40. KNEZEVIC E, NENIC K, MILANOVIC V, KNEZEVIC NN: The role of cortisol in chronic stress, neurodegenerative diseases, and psychological disorders. *Cells* 2023; 12(23): 2726. https://doi.org/10.3390/cells12232726