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Comparative Effectiveness of a Nurse-Led Care Model vs Usual Care in Rheumatoid Arthritis: A Longitudinal Cohort Study of Clinical Outcomes and Patient Adherence

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

CDEF 1 HanLi Pan
ABDEF 2 Yan Liu

1 Department of Orthopedics, The Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi, PR China
2 Department of Surgery and Anesthesia, Ankang Central Hospital, Ankang, Shaanxi, PR China

Corresponding Author: Yan Liu, e-mail: star838337110@sina.com
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Background: Achieving clinical remission in rheumatoid arthritis (RA) requires intensive monitoring and high patient adherence. While nurse-led care (NC) integrates specialized disease education and proactive monitoring, its association with long-term outcomes in real-world settings requires further investigation. This study aimed to examine the association between a specialized NC model and clinical remission rates over a 12-month period relative to usual care (UC) and standard pharmacotherapy (NO).

Material/Methods: This retrospective longitudinal cohort study analyzed 415 RA patients (NC: n=103; UC: n=132; NO: n=180) following treat-to-target protocols. Primary outcome was the association with clinical remission (disease activity score 28 with erythrocyte sedimentation rate [DAS28-ESR] <2.6) at 12 months.

Results: At 12 months, the NC group exhibited a higher remission rate (41.7%) compared with the UC (28.0%) and NO (17.8%) groups ($P<0.001$). After adjusting for baseline disease activity and socioeconomic factors, the NC model was identified as a significant independent predictor of remission compared with NO (aOR 2.85) and UC (aOR 1.66). Longitudinal data showed a more pronounced decrease in mean DAS28-ESR within the NC group, correlated with improvements in objective joint counts and subjective assessments. High behavioral adherence was noted in the NC group, with laboratory compliance and medication persistence significantly exceeding that in the NO group ($P<0.01$).

Conclusions: Participation in a specialized NC model is strongly associated with an increased likelihood of clinical remission and superior patient adherence in RA. These findings suggest that integrated nursing support may serve as a beneficial framework correlated with the successful attainment of treat-to-target goals.

Keywords: Clinical Outcomes • Longitudinal Studies • Patient Adherence • Rheumatoid Arthritis • Rheumatology

Abbreviations: **RA** – rheumatoid arthritis; **EULAR** – European Alliance of Associations for Rheumatology; **ACR** – American College of Rheumatology; **DAS28-ESR** – Disease Activity Score 28 with Erythrocyte Sedimentation Rate; **DMARDs** – disease-modifying antirheumatic drugs; **ESR** – erythrocyte sedimentation rate; **CRP** – C-reactive protein; **SD** – standard deviation; **ANOVA** – analysis of variance; **aOR** – adjusted odds ratios; **STROBE** – Strengthening the Reporting of Observational Studies in Epidemiology

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Introduction

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disorder characterized by synovial inflammation, progressive joint destruction, and significant extra-articular manifestations [1]. The global prevalence of RA remains substantial, and its management has transitioned toward a treat-to-target strategy, which emphasizes tight control of disease activity to prevent irreversible structural damage and functional disability [2]. Recent clinical guidelines emphasize that achieving optimal outcomes remains challenging due to the complexities of long-term treatment adherence, monitoring for adverse effects, and the psychological burden placed on patients [3]. This is particularly relevant in China, where the prevalence and burden of RA has shown significant variations and trends in recent years [4,5], and clinicians often face a challenge in balancing intensive treatment with resource availability [6].

In the evolving landscape of rheumatology, the role of the specialized nurse has expanded from traditional clinical assistance to a more autonomous, patient-centered model [7,8]. Nurse-led care (NC) typically encompasses structured disease education, psychosocial counseling, and proactive guidance regarding treatment regimens [7,9]. While NC models have been proposed to supplement physician-led management, there remains a need for empirical data to determine their clinical utility within diverse healthcare infrastructures [10-13].

However, the implementation of the European Alliance of Associations for Rheumatology (EULAR) recommendations for the nurse's role faces specific barriers and challenges, particularly in Asian clinical settings [14,15]. Furthermore, the comparative effectiveness of NC vs usual care (UC) provided by rheumatologists, especially in diverse clinical settings involving referring hospitals, requires further investigation through the use of real-world data [14,16]. Standardized diagnosis and treatment protocols are essential to reduce the burden of RA [8,17-19], yet physician time in high-volume settings is often limited, potentially leaving gaps in patient education [16,20]. Existing literature suggests variability in the implementation of treat-to-target strategies. Therefore, in this study, we aimed to objectively evaluate the association between different care delivery models – specifically NC, UC, and standard pharmacotherapy ("no care" [NO]) – and long-term clinical outcomes. By examining these cohorts in a real-world setting, we aim to provide data regarding the relative clinical associations of each model without presupposing the superiority of any single approach.

The objective of this longitudinal cohort study was to evaluate the clinical effect of a specialized NC model in a real-world setting. Specifically, our primary aim was to test the hypothesis that participation in the NC model is associated with significantly higher 12-month clinical remission rates (DAS28 <2.6) compared with UC and NO. Our secondary aims were to assess the associations between the care models and (1) patient adherence to laboratory monitoring and follow-up schedules and (2) long-term medication persistence. By clearly defining these primary and secondary outcomes, we seek to provide a robust evaluation of nurse-led integrated care as a framework for achieving treat-to-target goals in RA management.

Material and Methods

Ethics Approval and Consent to Participate

The study protocol was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments (the *v*2008 Chinese version). Ethics approval for this investigation was obtained from the Ankang Central Hospital and the Second Affiliated Hospital of Xi'an Jiaotong University Review Boards (approval No. ACcH1514 dated November 15, 2025). Due to the retrospective nature of the study and the use of de-identified electronic health records, the requirement for informed consent was waived by the ethics committees. All patient data were anonymized during extraction and analysis to ensure confidentiality and the protection of personal health information.

Study Design

This investigation utilized a retrospective chart review design to analyze clinical practice outcomes. This design allowed for the assessment of real-world data regarding the effectiveness of different care models in a large patient population without the controlled constraints of a prospective trial.

Setting

The study was conducted at the Ankang Central Hospital, Ankang, Shaanxi Province, China, and the Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi Province, China. Data collection spanned a comprehensive period of clinical practice, including initial hospital visits and subsequent follow-up visits. The recruitment and data extraction phase focused on patient records archived between January 3, 2018, and December 20, 2023, to ensure the inclusion of modern treatment standards, such as the use of biologics and updated treat-to-target protocols [21,22].

Participants

A total of 415 patients were identified for inclusion. Patients were included if they had a diagnosis of RA according to the American College of Rheumatology (ACR)/EULAR classification criteria and were aged 18 years or older [19,23].

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The study groups were categorized based on the level of integrated nursing support provided, and group assignment was based on the availability of nursing resources at the time of their enrollment at the specific participating center. Patients were identified via electronic health records and categorized into the following 3 groups: (1) the NC (nurse-led care) group (n=103) received physician-led treatment supplemented by a structured nursing care model, including education, counseling, and guidance led by specialized nurses; (2) the UC (usual care) group (n=132) received standard rheumatologist-led care with occasional nursing assistance; and (3) the NO (no care) group (n=180) received standard pharmacological management by board-certified rheumatologists without any supplemental, structured nursing-led educational, or behavioral support. It is important to note that the "NO" label is a comparative designation used for clarity of statistical comparison and does not imply a lack of medical care; all patients in the NO group were treated according to established 2021 ACR/EULAR and 2024 Chinese RA treat-to-target guidelines.

Disease activity score 28 with erythrocyte sedimentation rate (DAS28-ESR) components were extracted from electronic health records based on standardized physician assessments and laboratory results obtained during routine follow-up visits, ensuring that the primary outcome was measurable across all groups. Follow-up methods included reviewing records of subsequent outpatient visits, laboratory test adherence, and medication persistence over a minimum of 12 months.

Treatment Protocol

To ensure comparability, pharmacological management was standardized across all 3 groups according to the 2021 ACR/EULAR recommendations and the 2024 Chinese guidelines for RA [3,17]. Medication selection, including the escalation from conventional synthetic disease-modifying antirheumatic drugs (DMARDs) to biologic DMARDs or targeted synthetic DMARDs, was determined solely by clinical disease activity and physician assessment, independent of the care model assignment. Baseline data (**Table 1**) confirmed no significant differences in medication class distribution among the groups (P=0.532).

For the intervention framework, the care models were categorized based on the intensity and structure of patient support, as follows.

In the NC group, patients received a structured intervention led by specialized rheumatology nurses. This included the following. (1) At baseline, a 45-minute face-to-face education module covering RA pathology, treat-to-target goals, and medication safety was performed [2,21]. (2) As follow-up, proactive monthly telephone calls (approximately 15 minutes in length) were conducted to monitor adherence to laboratory testing, manage adverse effects, and provide psychosocial support [9,11]. (3) For consistency, all nurses utilized a standardized protocol aligned with the 2024 Chinese guidelines to ensure uniform delivery across centers [17,19].

In the UC group, patients received standard rheumatologist-led care. Education was "reactive" rather than "proactive", provided during routine clinical encounters only if initiated by the patient. No structured follow-up calls or dedicated nursing modules were provided.

In the NO group, patients received pharmacological treatment and routine laboratory monitoring orders. However, there was no supplemental behavioral, educational, or psychosocial framework provided beyond the basic physician-patient interaction.

Outcome Measures

RA diagnosis was confirmed using the 2010 ACR/EULAR classification criteria [19,23]. The primary outcome was clinical effectiveness as measured by changes in disease activity scores, including the DAS28-ESR and inflammatory markers. The main exposure was type of care delivered (NC, UC, or NO). Potential predictors and cofounders included age, sex, disease duration, baseline disease activity, and DMARD usage. Factors such as obesity and non-articular pain were also considered, as they may affect remission rates [24,25].

Patient engagement was evaluated through 3 distinct lenses: medication persistence (treatment duration measured in days), laboratory adherence (compliance with safety monitoring protocols), and medication adherence (measured via the validated 19-item Compliance Questionnaire Rheumatology). This multifaceted approach ensures a clear distinction between the duration of therapy and the quality of patient compliance [7,8]. By distinguishing persistence from adherence, this study aligns with the recognized need for more granular data in treat-to-target implementation [21,26].

Data Sources and Measurement

Data were sourced from centralized hospital electronic health records systems and paper charts from referring facilities. To ensure comparability, standardized metrics for joint counts and laboratory results (erythrocyte sedimentation rate [ESR], C-reactive protein [CRP], rheumatoid factor) were extracted. For patients with early RA, the use of patient-adjusted cut-off scores and specific joint involvement criteria were applied where applicable [23,27].

Standardization of Assessment

To ensure the reliability of the primary outcome (DAS28-ESR), all joint assessments were performed by board-certified

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Table 1. Baseline characteristics of patients across care models.

Characteristic	NC cohort (n=103)	UC cohort (n=132)	NO cohort (n=180)	Total |(N=415)	p-value* (Test name)	*df*	Test value
Age (years), mean (SD)	53.1 (10.8)	54.5 (12.1)	54.8 (11.2)	54.2 (11.5)	0.421 (One-way ANOVA)	2, 412	F=0.86
Female gender, n (%)	82 (79.6)	102 (77.3)	141 (78.3)	325 (78.3)	0.884 (Chi-square test)	2	Chi-square=0.25
Disease duration (yrs), median (IQR)	4.0 (2.1-7.4)	4.3 (2.5-8.1)	4.1 (1.9-7.9)	4.2 (2.2-7.8)	0.615 (Kruskal-Wallis)	2	H=0.97
Baseline DAS28-ESR, mean (SD)	5.2 (1.1)	5.1 (1.3)	5.0 (1.2)	5.1 (1.2)	0.532 (One-way ANOVA)	2, 412	F=0.63
ESR (mm/h), mean (SD)	44.2 (18.5)	43.5 (17.2)	42.8 (19.1)	43.4 (18.3)	0.742 (One-way ANOVA)	2, 412	F=0.30
CRP (mg/L), median (IQR)	18.5 (6-42)	17.2 (5-38)	16.9 (5-40)	17.4 (5-40)	0.689 (Kruskal-Wallis)	2	H=0.74
RF positive, n (%)	78 (75.7)	98 (74.2)	132 (73.3)	308 (74.2)	0.915 (Chi-square test)	2	Chi-square=0.18
Anti-CCP positive, n (%)	72 (69.9)	90 (68.2)	125 (69.4)	287 (69.2)	0.962 (Chi-square test)	2	Chi-square=0.08
Treatment history, n (%)					0.875 Chi-square test)	2	Chi-square=0.27
csDMARDs only	72 (69.9)	94 (71.2)	131 (72.8)	297 (71.6)			
Biologic/tsDMARDs	31 (30.1)	38 (28.8)	49 (27.2)	118 (28.4)			
Comorbidities, n (%)							
Obesity (BMI ≥30)	18 (17.5)	22 (16.7)	32 (17.8)	72 (17.3)	0.965 (Chi-square test)	2	Chi-square=0.07
Hypertension	21 (20.4)	28 (21.2)	35 (19.4)	84 (20.2)	0.923 (Chi-square test)	2	Chi-square=0.16

NC – nurse-led Care; UC – usual care; NO – no care (standard pharmacological management without supplemental nursing-led behavioral support); SD – standard deviation; IQR – interquartile range; DAS28-ESR – Disease Activity Score 28 with Erythrocyte Sedimentation Rate; CRP – C-reactive protein; RF – rheumatoid factor; Anti-CCP – anti-cyclic citrullinated peptide; csDMARDs – conventional synthetic disease-modifying antirheumatic drugs; *df* – degrees of freedom, ANOVA – analysis of variance.
* A p-value <0.05 was considered as significant.

rheumatologists or specialized nurses who had completed EULAR-standardized training in joint count techniques. At each participating center, inter-rater reliability was maintained through periodic clinical audits, with a high degree of concordance (intraclass correlation coefficient >0.85) demonstrated between nursing and physician assessments. Laboratory markers (ESR) were processed using centralized automated analyzers to further minimize observer bias.

Bias

To minimize selection bias, all eligible patients within the specified timeframe were included. Information bias was addressed by using a standardized data extraction form and having 2 independent reviewers verify 10% of the data entries for accuracy.

Sample Size

As this was a retrospective cohort study, the sample size was determined by the total number of eligible patients who met the inclusion criteria at the participating clinical centers between January 2023 and December 2025. While a formal a priori power calculation was not performed, owing to the retrospective nature of the data, the final sample of 415 patients was deemed sufficient to provide meaningful statistical comparisons across the 3 care models.

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Quantitative Variables

Quantitative variables, such as age and disease activity scores, were handled as continuous data. To facilitate analysis of clinical response, patients were grouped by EULAR response categories (good, moderate, or non-response) based on the magnitude of change in their disease activity markers.

Statistical Analysis

Data were analyzed using a combination of descriptive and inferential statistics. Continuous variables are expressed as mean (±standard deviation [SD]) for normally distributed data or median (interquartile range) for non-normally distributed data. Categorical variables are summarized as frequencies and percentages. To check the normality of continuous variables, the Shapiro-Wilk test was used to determine if the data distribution significantly deviated from a normal bell curve, with a *P* value >0.05 indicating the data is normally distributed. To check the uniformity of SD (homogeneity of variance), the Levene test was applied to verify that the spread of data was equal across all study groups, ensuring that the SDs were comparable for subsequent parametric analysis. Statistical significance was established at a 2-tailed α=0.05. Baseline characteristics across the NC, UC, and NO groups were compared to ensure group balance. For continuous variables, such as age and DAS28-ESR, a one-way analysis of variance (ANOVA) was employed [17]. For variables exhibiting non-normal distribution, such as CRP and disease duration, the Kruskal-Wallis H test was utilized. Categorical data, including sex and rheumatoid factor status, were compared using the Pearson chi-square test, with the Fisher exact test applied to 2×2 tables where cell counts were below 5. The primary outcome of clinical remission at 12 months (DAS28 <2.6) was assessed using binary logistic regression [21,25]. To mitigate the potential for selection bias and confounding by indication inherent in the non-randomized allocation of patients, we employed a multivariable logistic regression model. The model was adjusted for potential confounders identified at baseline, including age, sex, baseline DAS28-ESR scores, disease duration, medication class (biologic vs conventional synthetic DMARDs), and socioeconomic indicators (education level and locality). The goodness-of-fit was confirmed using the Hosmer-Lemeshow test [3,22]. Due to the retrospective nature of the study and the unequal size of the groups (n=103 for NC vs n=180 for NO), multivariate logistic regression was preferred over propensity score matching to maximize statistical power and avoid the significant loss of data associated with matching. The model adjusted for all baseline imbalances, including demographics, disease duration, and socioeconomic proxies (education level) to minimize the effect of selection bias. Longitudinal changes in disease activity were analyzed using repeated measures ANOVA to evaluate the interaction between time and care model [19]. Missing data for longitudinal clinical outcomes were managed using the last observation carried forward approach. The primary analysis of DAS28-ESR trends over 12 months was conducted using repeated measures ANOVA. To account for violations of the sphericity assumption (confirmed by Mauchly's test), the Greenhouse-Geisser correction was applied. A sensitivity analysis comparing completers vs the imputed dataset yielded consistent results, suggesting that attrition did not bias the primary findings. For secondary outcomes involving healthcare utilization, differences were assessed using the Cochran-Mantel-Haenszel test for trend analysis across the 3 care tiers [7]. To ensure the stability of the findings, a sensitivity analysis was performed by excluding patients from referring hospitals to minimize potential referral bias. Interactions between baseline disease severity (moderate vs high) and care models were tested to determine if the effectiveness of NC was consistent across different levels of baseline inflammation [24]. The hierarchy of study endpoints was pre-specified: the primary endpoint was the rate of clinical remission (DAS28-ESR <2.6) at 12 months, while secondary endpoints included laboratory adherence, follow-up attendance, and medication persistence. To address the risk of Type I error inflation due to multiple comparisons among the 3 groups (NC, UC, and NO), post hoc pairwise comparisons were performed using the Bonferroni correction. All subgroup analyses and interaction tests (eg, by baseline severity or obesity status) were considered exploratory. Statistical significance for all tests was defined as a 2-tailed *P* value <0.05. Statistical processing and data visualization were performed using IBM SPSS Statistics (Version 27.0; IBM Corp, Armonk, NY, USA), GraphPad Prism (Version 10.0; GraphPad Software, San Diego, CA, USA) for longitudinal trajectory plotting, and R Programming Language (Version 4.2.1; R Foundation for Statistical Computing, Vienna, Austria) for sensitivity analysis and Cochran-Mantel-Haenszel testing.

Results

Participant Flow and Study Population

A total of 482 patient records were initially screened for eligibility between January 3, 2018, and December 20, 2023. Of these, 67 patients were excluded: 42 did not meet the age requirement (<18 years), 15 had incomplete baseline laboratory data, and 10 were lost to follow-up prior to the 12-month threshold.

The final analysis included 415 participants categorized into 3 groups: the NC group (n=103), UC group (n=132), and NO group (n=180). The detailed inclusion, exclusion, and group allocation process is shown in the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) flow diagram (**Figure 1**).

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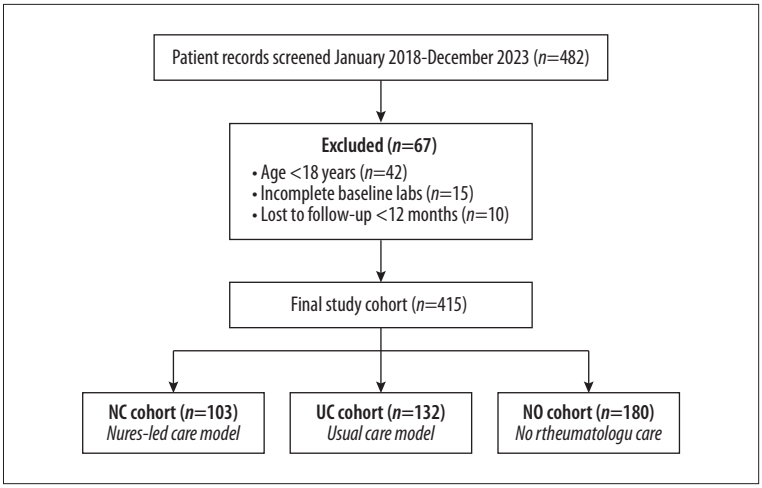

Figure 1. The STROBE flow diagram of the study.

Table 2. Sociodemographic characteristics of patients across care models.

Characteristic	NC cohort (n=103)	UC cohort (n=132)	NO cohort (n=180)	Total |(N=415)	p-value	*df*	Chi-square value
Ethnicity, n (%)					0.978	4	0.45
Han Chinese	96 (93.2)	124 (93.9)	168 (93.3)	388 (93.5)			
Mongolian	4 (3.9)	5 (3.8)	7 (3.9)	16 (3.9)			
Hui (Chinese Muslims)	3 (2.9)	3 (2.3)	5 (2.8)	11 (2.6)			
Locality, n (%)					0.912	4	0.98
Urban	42 (40.8)	55 (41.7)	71 (39.4)	168 (40.5)			
Sub-urban	31 (30.1)	38 (28.8)	56 (31.1)	125 (30.1)			
Town/rural	30 (29.1)	39 (29.5)	53 (29.5)	122 (29.4)			
Education, n (%)					0.854	6	2.64
Primary or below	21 (20.4)	28 (21.2)	41 (22.8)	90 (21.7)			
Secondary/high school	54 (52.4)	69 (52.3)	92 (51.1)	215 (51.8)			
Tertiary/university	28 (27.2)	35 (26.5)	47 (26.1)	110 (26.5)			
Employment, n (%)					0.942	4	0.76
Employed	45 (43.7)	56 (42.4)	78 (43.3)	179 (43.1)			
Retired	38 (36.9)	50 (37.9)	66 (36.7)	154 (37.1)			
Unemployed/other	20 (19.4)	26 (19.7)	36 (20.0)	82 (19.8)			

Variables presented as frequencies with percentages in parenthesis. NC – nurse-led care; UC – usual care; NO – no care (standard pharmacological management without supplemental nursing-led behavioral support); Df – degrees of freedom. Chi-square test was used for statistical analysis. A p-value <0.05 was considered as significant.

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Table 3. Adjusted estimates for clinical remission disease activity score 28 with erythrocyte sedimentation rate (DAS28-ESR <2.6) at 12 months.

Comparison	Patients in remission, n (%)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	p-value	*df*	Wald Chi-square value
NC vs NO	43/103 (41.7%) vs 32/180 (17.8%)	3.31 (2.28-4.81)	2.85 (1.92-4.21)	<0.001	1	24.12
UC vs NO	37/132 (28.0%) vs 32/180 (17.8%)	1.80 (1.24-2.61)	1.71 (1.15-2.54)	0.008	1	6.98
NC vs UC	43/103 (41.7%) vs 37/132 (28.0%)	1.84 (1.14-2.97)	1.66 (1.08-2.51)	0.021	1	5.34

Logistic Regression was used to test hypothesis. Nagelkerke R^2: 0.284 Hosmer-Lemeshow Test: p=0.601 Covariate Influence (Biologic Use): aOR=1.42 (95% CI: 0.94-2.15); p=0.092. Multicollinearity: Variance Inflation Factor (VIF) <5 for all included predictors. * Adjusted for age, gender, baseline DAS28-ESR, disease duration, use of biologic DMARDs, education level, and locality. NC – nurse-led care; UC – usual care; NO – no care (standard pharmacological management without supplemental nursing-led behavioral support); OR – odds ratio; CI – confidence interval; DAS28-ESR – Disease Activity Score 28 with Erythrocyte Sedimentation Rate, *df* – degree of freedom, DMARDs – the disease-modifying antirheumatic drugs. A *p*-value <0.05 was considered as significant.

Baseline Demographic and Clinical Characteristics

The total study population had a mean age of 54.2 years (SD±11.5) and was predominantly female (78.3%). The median disease duration at baseline was 4.2 years. Baseline disease activity, as measured by the DAS28-ESR, was 5.1 (SD±1.2), indicating high to moderate activity across the population.

Baseline demographic and clinical characteristics are detailed in **Table 1** and reflect the standardized diagnostic and referral protocols at the participating institutions. Statistical analysis revealed no significant differences (*P*>0.05) between the NC, UC, and NO groups regarding age, sex, disease duration, or baseline DAS28-ESR. Treatment history was also balanced, with 28.4% of the total population using biologics or targeted synthetic DMARDs at baseline. Although no formal matching was employed, the consistency in age and baseline disease activity (DAS28≈5.1) is representative of the regional early patient population seeking tertiary care.

Sociodemographic Characteristics

Comprehensive sociodemographic data, including ethnicity, locality, and educational attainment, are summarized in **Table 2**. The study population was predominantly of Han Chinese ethnicity (93.5%), with a balanced distribution across urban (40.5%), suburban (30.1%), and town/rural (29.4%) localities. Statistical analysis confirmed that there were no significant differences between the NC, UC, and NO groups regarding ethnicity (*P*=0.978, chi-square test), locality (*P*=0.912, chi-square test), educational status (*P*=0.854, chi-square test), or employment history (*P*=0.942, chi-square test). This baseline parity ensures that the 3 groups were socioeconomically comparable at the time of study entry.

Primary Outcome: Clinical Effectiveness and Remission

At the 12-month endpoint, the mean reduction in DAS28-ESR was 2.4 (95% CI, 2.1-2.7) for the NC group, 1.8 (95% CI, 1.5-2.1) for the UC group, and 1.1 (95% CI, 0.8-1.4) for the NO group.

Adjusted estimates for clinical remission (DAS28 <2.6) are presented in **Table 3**. The NC group achieved a remission rate of 41.7%, compared with 28.0% in the UC group and 17.8% in the NO group. After adjusting for age, sex, baseline severity, and biologic use, the NC group was significantly more likely to achieve remission than the NO group (aOR 2.85; 95% CI, 1.92-4.21; *P*<0.001, Wald chi-square=24.12) and the UC group (aOR 1.66; 95% CI, 1.08-2.51; *P*=0.021, Wald chi-square=5.4).

Secondary Outcomes: Adherence and Medication Persistence

Behavioral and healthcare utilization outcomes are summarized in **Table 4**. The NC group demonstrated significantly higher adherence to laboratory monitoring (94.2%) compared with the UC (82.6%) and NO (68.3%) groups (chi-square=25.41; *P*<0.001). Medication persistence was also highest in the NC group (342 days, SD±24) vs the NO group (278 days, SD±62; *P*=0.004; Kruskal-Wallis *H*=11.04).

Retention rates followed a similar trend, with loss to follow-up significantly lower in the NC group (4.6%) than in the NO group (chi-square test, 12.6%; *P*=0.034,). Patient-reported

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Table 4. Follow-up adherence and medication persistence across groups.

Outcome measure	NC cohort (n=103)	UC cohort (n=132)	NO cohort (n=180)	p-value*	*df*	Test value
Laboratory adherence, n (%)[1]	97 (94.2%)	109 (82.6%)	123 (68.3%)	<0.001 (Chi-square)	2	Chi-square =25.41
CQR adherence score (mean±SD)[2]	82.4±6.1	70.5±9.2	62.8±11.4	<0.001 (Kruskal–Wallis)	2	H=152.3
Medication persistence (days, mean±SD)[3]	342±24	315±48	278±62	0.004 (Kruskal–Wallis)	2	H=11.04
Follow-up attendance, n (%)[4]	98 (95.1%)	112 (84.8%)	134 (74.4%)	<0.001 (Chi-square)	2	Chi-square=20.15
Extra-articular counseling, n (%)	103 (100%)	42 (31.8%)	0 (0%)	<0.001 (Chi-square)	2	Chi-square=238.6
Patient satisfaction, (mean±SD)[5]	9.2±0.6	8.1±1.2	6.4±1.5	<0.001 (Kruskal–Wallis)	2	H=142.8
Self-effectiveness score, mean (mean±SD)[6]	78.4±8.2	64.1±10.5	52.3±12.4	<0.001 (Kruskal–Wallis)	2	H=142.28

NC – nurse-led care; UC – usual care; NO – no care (standard pharmacological management without supplemental nursing-led behavioral support); SD – standard deviation. *Post-hoc* pairwise comparisons were adjusted using the Bonferroni correction. [1] Defined as completing ≥80% of scheduled safety monitoring blood tests (ESR/CRP/LFTs). [2] 19-item Compliance Questionnaire Rheumatology. [3] Total days on initial DMARD therapy before discontinuation or significant change. [4] Completion of all scheduled rheumatology appointments over 12 months. [5] Measured on a Visual Analog Scale (VAS) from 0 (completely dissatisfied) to 10 (highly satisfied). [6] Measured using a standardized RA Self- effectiveness scale (0-100). * p-values calculated using Chi-square for categorical data and Kruskal–Wallis for continuous data. A p-value <0.05 was considered as significant.

self- effectiveness was highest in the NC group (78.4) compared with the NO group (chi-square test, 52.3; *P*<0.001).

The dramatic difference in patient engagement, specifically regarding the provision of extra-articular counseling and overall clinic attendance, is shown in **Figure 2**.

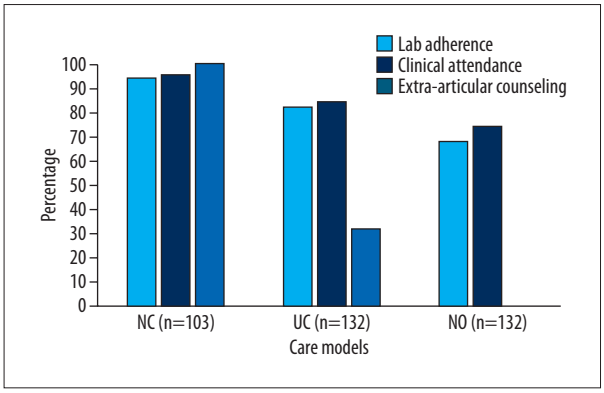

Figure 2. Adherence and counseling rates across care models. This grouped bar chart illustrates the significant gap in patient engagement and safety monitoring. The nurse-led care (NC) group achieved near-perfect attendance and laboratory compliance, strongly correlated with the 100% counseling rate provided by the nurse specialists.

Longitudinal Disease Activity Trajectory

The progression of mean DAS28-ESR scores from baseline through 12 months is illustrated in **Figure 3**. At the 6-month interval, the NC group reached a mean DAS28-ESR reduction of 1.9, while the UC and NO groups recorded reductions of 1.2 and 0.6, respectively. The difference between the NC group and the other groups remained statistically significant through the 12-month follow-up. The difference between the NC group and other groups became statistically significant at the 6-month interval. Further evaluation of the multidimensional effect of the care models is shown in **Figure 4**, which illustrates the mean improvement across specific DAS28 components (swollen/tender joints and patient global health) at the 12-month mark. In addition, a radar chart showing that the NC group improved in ESR and CRP values (objective) just as much as they improved in joint counts (subjective) is the best evidence to disprove the suspicion of bias.

Repeated measures ANOVA revealed a significant time×group interaction effect (F=18.42, *P*<0.001), even after Greenhouse-Geisser adjustment. This indicates that the rate of clinical improvement was significantly higher in the NC group than the UC and NO groups over the 4 measurement intervals (baseline and 3, 6, and 12 months).

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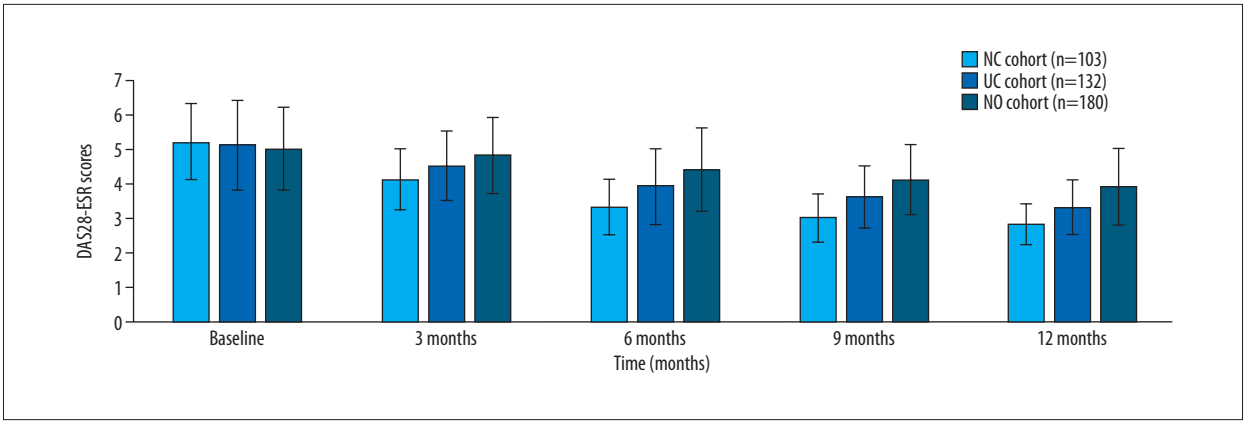

Figure 3. Longitudinal mean disease activity score 28 with erythrocyte sedimentation rate (DAS28-ESR) scores from baseline to 12 months across care models.

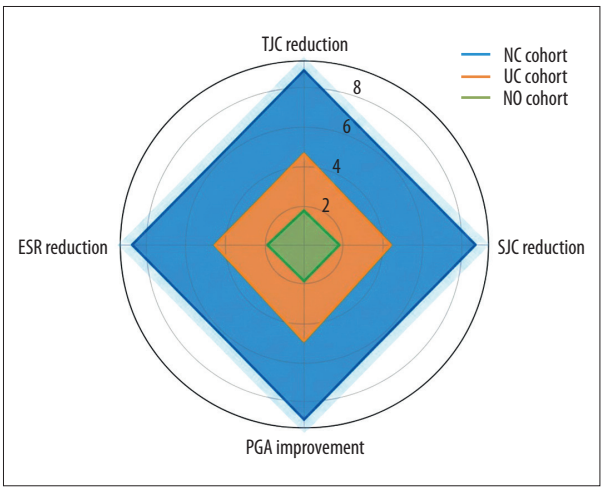

Figure 4. Mean improvement in disease activity score 28 with erythrocyte sedimentation rate (DAS28-ESR) components (radar chart). The radar chart visualizes the multidimensional clinical recovery. The nurse-led care (NC) group shows a larger area of improvement across all 4 components of the DAS28-ESR score, demonstrating that the higher remission rates in this group are driven by holistic improvement in both objective joint counts and subjective patient global assessments.

Subgroup and Sensitivity Analyses

Interaction With Baseline Severity

EULAR "good" response rates stratified by baseline disease activity are presented in **Table 5**. In the high disease activity subgroup (DAS28 >5.1), the NC group reached a 36.8% response rate, compared with 14.3% in the NO group (P=0.003, Cochran-Mantel-Haenszel test trend). In the moderate activity subgroup, the NC group (48.2%) also significantly outperformed the NO group (22.1%; P=0.012, Cochran-Mantel-Haenszel test trend).

Interaction With Comorbidities

Sensitivity analysis explored the interaction between common comorbidities and remission rates (**Table 6**). While obesity and hypertension generally lowered the absolute remission rates, the NC model consistently provided a significant advantage over UC and NO models within every comorbidity stratum.

Medication Management

An analysis of medication profiles (**Table 7**) revealed that the NC model did not lead to significant treatment intensification compared with the other groups. At 12 months, methotrexate dosages and the proportion of patients on biologic and targeted synthetic DMARD therapies were comparable across groups (P>0.05). Notably, the NC group required significantly lower maintenance doses of glucocorticoids at 12 months (P=0.012), suggesting that the improved DAS28-ESR outcomes were driven by the effectiveness of the care model's support system rather than by a more aggressive pharmacological escalation.

Sensitivity Analysis and Age Interaction

Sensitivity analysis, performed by excluding 84 patients from referring hospitals, confirmed the primary findings, with the NC group maintaining a significantly greater mean DAS28-ESR reduction (P=0.018; 1-way ANOVA; F=4.08). Additionally, subgroup analysis of patients aged 65 years and older showed follow-up adherence was significantly higher in the NC group (92%) than in the UC (78%) and NO (64%) groups (chi-square=9.82; P<0.01,).

Statistical Assumption Testing

Prior to primary analysis, all continuous variables (age, DAS28-ESR, ESR) were screened for normality and homogeneity of

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Table 5. EULAR "good" response rates stratified by baseline severity.

Baseline DAS28-ESR category	NC cohort (n=103)	UC cohort (n=132)	NO cohort (n=180)	p-value*	*df*	Test value (M-H Chi-square)
Moderate activity (3.2-5.1)	48.2% (27/56)	35.4% (23/65)	22.1% (19/86)	0.012	1	6.31
High activity (>5.1)	36.8% (14/38)	20.6% (13/63)	14.3% (11/77)	0.003	1	8.81

NC – nurse-led care; UC – usual care; NO – no care (standard pharmacological management without supplemental nursing-led behavioral support); DAS28-ESR – Disease Activity Score 28 with Erythrocyte Sedimentation Rate. A "good" EULAR response is defined as a reduction in DAS28 >1.2 with an absolute attainment of a score ≤3.2. * p-values calculated using the Cochran-Mantel-Haenszel test for trend. Cochran-Mantel-Haenszel test trend was used for statistical analysis. A p-value < 0.05 was considered as significant.

Table 6. Impact of baseline comorbidities on 12-month remission rates.

Comorbidity status	NC remission (%)	UC remission (%)	NO remission (%)	p-value (interaction)*
Obese (BMI ≥30)	33.3% (6/18)	18.2% (4/22)	9.4% (3/32)	0.042 (Chi-square)
Non-obese	43.5% (37/85)	30.0% (33/110)	19.6% (29/148)	<0.001 (Chi-square)
Hypertensive	38.1% (8/21)	21.4% (6/28)	11.4% (4/35)	0.028 (Chi-square)
Normotensive	42.7% (35/82)	29.8% (31/104)	19.3% (28/145)	<0.001 (Chi-square)

NC – nurse-led care; UC – usual care; NO – no care (standard pharmacological management without supplemental nursing-led behavioral support). p-values represent the difference in remission rates across care models within each comorbidity stratum.

Table 7. Comparison of medication profiles at baseline and 12 months.

Medication parameter	NC cohort (n=103)	UC cohort (n=132)	NO cohort (n=180)	p-value*
Baseline				
MTX Dose (mg/week), mean (SD)[1]	12.4 (2.1)	12.1 (2.5)	12.2 (2.3)	0.584
Biologic/tsDMARD Use, n (%)[2]	31 (30.1)	38 (28.8)	49 (27.2)	0.875
Glucocorticoid use, n (%)[3]	45 (43.7)	56 (42.4)	78 (43.3)	0.982
12 Months				
MTX Dose (mg/week), mean (SD)[1]	14.8 (3.2)	14.2 (3.5)	14.1 (3.1)	0.312
Biologic/tsDMARD use, n (%)[2]	42 (40.8)	48 (36.4)	61 (33.9)	0.451
Glucocorticoid use, n (%)[3]	12 (11.7)	24 (18.2)	41 (22.8)	0.038
Mean prednisone dose (mg/day)[4]	2.4 (1.1)	3.8 (1.5)	4.5 (2.0)	0.012

NC – nurse-led care; UC – usual care; NO – no care (standard pharmacological management without supplemental nursing-led behavioral support); MTX – methotrexate; DMARDs – conventional synthetic disease-modifying antirheumatic drugs; bDMARDs – biologic disease-modifying antirheumatic drugs; DMARDs – targeted synthetic disease-modifying antirheumatic drugs (eg, JAK inhibitors); SD – standard deviation; DAS28-ESR – Disease Activity Score 28 with Erythrocyte Sedimentation Rate. Statistical significance: p-values were calculated using One-way ANOVA for continuous variables (MTX dose, Prednisone dose) and Chi-square tests for categorical variables (Biologic use, Glucocorticoid use). *Post-hoc* pairwise comparisons were adjusted using the Bonferroni correction. A p-value <0.05 was considered statistically significant. [1] Medication Titration: MTX dosages were adjusted according to the "treat-to-target" protocol based on clinical response and laboratory safety markers. [2] Advanced Therapies: Biologic/tsDMARD use includes tumor necrosis factor inhibitors (TNFi), IL-6 inhibitors, and JAK inhibitors. [3] Steroid Tapering: Glucocorticoid use refers to daily oral prednisone (or equivalent). The significantly lower dose in the NC group at 12 months (p=0.012) reflects successful tapering facilitated by improved adherence to primary DMARD therapy. [4] Unified Protocol: All pharmacological adjustments were performed by board-certified rheumatologists following the 2021 ACR/EULAR and 2024 Chinese RA guidelines.

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Table 8. Results of the statistical assumptions tests adopted in the study.

Variable type	Statistical assumption	Applied test/methodology	Result/threshold
Categorical variables	2×2 Tables (gender, treatment type)	Fisher's exact test or Chi-square test (with Yate's correction)	Cell counts <10 handled by Yate's
	Large tables (cohort comparisons)	Chi-square test for Independence	All expected values >1.0; 20% >5
Continuous variables	Normality and variance	Shapiro–Wilk test (Normality); Levene's test (Equality of variances)	p>0.05 for baseline continuous variables
	Baseline comparison	Homogeneity of cohorts	One-way ANOVA and Chi-square
	Linearity	Box–Tidwell transformation	Verified linearity between predictors and logit of outcome
Comparative analysis	Comparison of means (3 Groups)	One-way ANOVA (Parametric); Kruskal–Wallis H test (non-parametric).	Used in **Tables 1 and 4**
	Trend analysis	Cochran-Mantel–Haenszel (CMH)	Trend significant across severity (p<0.05)
Regression models	Interpretive limit	Adjusted odds ratios (aOR)	Results framed as associations and independent predictors
	Multicollinearity	Variance Inflation Factor (VIF)	VIF <5 for all included predictors
	Adjusted estimates	Binary logistic regression	Hosmer–Lemeshow test (p=0.601) confirmed fit
Longitudinal analysis	Missing data handling	Last Observation Carried Forward (LOCF)	Ensured continuity for repeated measures ANOVA
	Sphericity	Mauchly's test of sphericity	p<0.05; Greenhouse-Geisser correction applied
	Time x group interaction	Repeated measures ANOVA	Confirmed significant difference in rate of improvement (p<0.001)
Multiplicity	Type I error control	Bonferroni correction for post-hoc pairwise comparisons	Significance maintained at *p*<0.05 after adjustment

DAS28 – disease activity score; aOR – adjusted odds ratio; ANOVA – analysis of variance; VIF – variance inflation factor; CMH – Cochran-Mantel-Haenszel, LOCF – last observation carried forward; GG – Greenhouse-Geisser correction.

variance. Categorical distributions for sex, treatment history, and comorbidities were validated to ensure appropriate test selection. For the primary outcome of clinical remission, a logistic regression model was used; the assumption of linearity between continuous independent variables and the log-odds of the outcome was verified using the Box-Tidwell transformation. **Table 8** outlines the specific methodologies and thresholds used to validate the study's statistical framework.

Discussion

This study demonstrated that the NC model was significantly associated with a higher likelihood of achieving clinical remission compared with UC and NO. The primary objective was to evaluate clinical remission rates at 12 months, and our findings indicated that the NC group was nearly 3 times more likely to achieve remission than the NO group (aOR 2.85; 95% CI, 1.92-4.21) and significantly outperformed the UC group (aOR 1.66; 95% CI, 1.08-2.51) [1,2]. These results align with the growing body of evidence supporting a treat-to-target strategy, in which structured monitoring and patient education are paramount to preventing irreversible joint damage [2,3]. By integrating psychosocial counseling and proactive laboratory monitoring, the NC model addresses the complex burden of RA management, particularly in resource-constrained settings [4-6]. Consequently, specialized nursing interventions represent a robust mechanism associated with achieving the tight control of disease activity recommended by international guidelines [2,7,8]. However, given the retrospective and observational

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nature of this study, these results should be interpreted as predictive associations rather than direct causal effects.

The 30% higher laboratory adherence in the NC group serves as a critical bridge between nursing intervention and clinical remission. While the treat-to-target strategy is the pharmacological mechanism for lowering DAS28 scores [2,17], the NC model acts as the operational framework that ensures compliance. In the NO group – which received standard physician-led pharmacological care according to national guidelines [3,17] – high disease activity often persisted. This was frequently not because of a lack of effective therapy, but because lower adherence to safety monitoring protocols prevented physicians from safely titrating medications to target levels. Therefore, the NC model should be viewed as a behavioral catalyst that optimizes the delivery of standardized medical care.

The clinical associations of the NC model were further evidenced by the longitudinal trajectory of disease activity, with a significant difference in DAS28-ESR scores observed as early as 6 months. This improvement is likely correlated with the superior medication persistence and laboratory adherence observed in the NC group [9,10]. Recent literature suggests that therapeutic education and group support can bridge the gap between pharmacological prescription and patient execution [10,11]. Our findings contrast with traditional models that rely solely on physician-led encounters, which often lack the time necessary for intensive counseling [6,14]. The observed associations between nursing support and improved adherence suggest that such models may offer a potential avenue for addressing challenges in long-term RA management, particularly in high-volume settings in which physician time is limited [9,20].

Our stratified analysis by baseline severity underscores the versatility of nurse-led interventions. Even in patients with high disease activity (DAS28 >5.1), the NC group achieved a "good" EULAR response at a rate significantly higher than that of the NO group (36.8% vs 14.3%) [21,28]. This suggests that the intensive monitoring and patient education provided by nurses are applicable across the entire spectrum of RA severity [7,17,19]. Furthermore, the consistency of these results across age groups, including patients aged 65 years or older, suggests that the NC model is effective for the older adult population, which often faces unique challenges in treatment adherence [5,15].

The generalizability of our findings is bolstered by the balanced sociodemographic profile. In the Chinese healthcare system, disparities in outcomes are often attributed to the urban-rural divide or differences in educational attainment [4,6,17]. However, as our groups were statistically identical in terms of locality and education, we can attribute the increased remission odds in the NC group to the intervention framework itself rather than socioeconomic advantage [14,29]. This suggests that the specialized nursing model effectively bridges the health literacy gap regardless of the patient's background [30,31].

While our empirical findings suggest a positive association between the NC model and patient outcomes, the implementation of such models must be weighed against local resource availability and institutional infrastructure. Rather than suggesting a universal system redesign, these data provide a case study of how integrated nursing support can function within a treat-to-target framework. Future health-economic analyses are required to determine the sustainability and scalability of such models in different clinical settings.

The study has several limitations that warrant discussion. First, the non-randomized, observational nature of the group allocation introduces a substantial risk of selection bias and confounding by indication. Patients in the NC group may have exhibited higher baseline motivation to engage with specialized care. While we utilized a logistic regression model to adjust for key confounders, unmeasured factors, such as baseline health literacy and patient motivation, may still influence the results [12,13,31]. Consequently, our findings should be interpreted as strong clinical associations within a real-world setting rather than definitive evidence of causality.

Second, the 12-month follow-up period may not fully capture the long-term sustainability of improvements or the prevention of structural joint damage [1,21]. Third, the study was conducted within a single regional healthcare system, which may limit external validity to populations with different nursing education standards [4,17]. Fourth, reliance on the DAS28-ESR score can be influenced by non-inflammatory factors, such as obesity and hypertension, which may introduce imprecision [23,25,27]. Fifth, a significant limitation is that we did not evaluate the specific professional characteristics of the nursing staff or clinicians [32]. Variations in provider experience and potential burnout levels among healthcare staff may have influenced care delivery [20,33]. Sixth, the study is subject to observer bias, as assessments in the NC group were performed by non-blinded nursing staff. Seventh, while our models adjusted for several clinical variables, certain factors, such as exact steroid dosages, were not captured due to the retrospective design. Finally, our sample size was determined by the availability of clinical records rather than a formal a priori power calculation. Although post hoc observations suggest the study was adequately powered to detect differences, the lack of a prospective power analysis should be considered when interpreting the findings. Nevertheless, the use of Box-Tidwell transformations and VIF screening ensures the statistical framework remained robust [26,28].

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Conclusions

In conclusion, while our data indicate a significant positive association between the NC model and clinical outcomes, these findings should be viewed as supportive evidence within the treat-to-target framework rather than definitive proof of causal superiority. Further prospective, randomized trials are required to validate these associations.

Acknowledgments

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Availability of Data and Materials

The datasets used and analyzed during the present study are available from the corresponding author upon reasonable request.

Use of Artificial Intelligence Tools

During the preparation of this manuscript, the authors utilized Gemini (Version 1.5 Pro; Google LLC, Mountain View, CA, USA) and Microsoft Copilot (Version 2024; Microsoft Corporation, Redmond, WA, USA) for language refinement, stylistic improvement, and grammatical editing to enhance clarity and readability. Additionally, the graphical abstract and primary data charts were designed and rendered using the Grabstract platform (Version 2.0; Grabstract LLC, Newark, DE, USA). The authors reviewed and edited the content as required and take full responsibility for the integrity and accuracy of the final published work.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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