



# Contribution of Personality Traits, Psychological Factors, and Health-Related Quality of Life to Medication Adherence in Patients with Rheumatoid Arthritis

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**Purpose:** This study sought to investigate the associations between personality traits and medication adherence and to identify predictors of good medication adherence in rheumatoid arthritis (RA) patients.

**Materials and Methods:** A total of 207 RA patients using disease-modifying anti-rheumatic drugs were invited for an interview and questionnaire study. Medication adherence was measured using the Compliance Questionnaire for Rheumatology (CQR). Personality traits were analyzed with the five-factor model of the Korean version of the Big Five Inventory 10. Psychological factors were assessed with the Patient Health Questionnaire-9, Generalized Anxiety Disorder-7, and British Columbia Cognitive Inventory. Health-related Quality of Life (HRQoL) and functional disability were evaluated with the EuroQoL-5 dimension questionnaire and Health Assessment Questionnaire. Multivariate logistic regression analyses were performed to investigate predictors of good medication adherence.

**Results:** Nonadherence to medication was reported by 66.7%. The number of daily prescribed pills was higher in the medication adherence group than in the nonadherence group. Concomitant oral glucocorticoid doses were associated with medication adherence. A high level of conscientiousness and diabetes mellitus comorbidity were associated with better medication adherence [odds ratio (OR), 2.11; 95% confidence interval (CI), 1.01–4.38 and OR, 3.00; 95% CI, 1.12–8.07, respectively]. There were no significant differences in psychological factors or HRQoL between medication adherence and nonadherence groups.

**Conclusion:** The personality trait of conscientiousness was associated with medication adherence among the five personality traits evaluated. Patients with diabetes mellitus also showed higher medication adherence than those without this comorbidity.

**Key Words:** Medication adherence, patient compliance, rheumatoid arthritis, personality

## INTRODUCTION

Adherence to medication is generally defined as “the extent to

which patients take medication as prescribed by their health care providers.”<sup>1</sup> Long-term medication adherence is required for positive clinical outcomes for many chronic conditions,

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including rheumatoid arthritis (RA). Effective treatment of RA is determined by medication adherence and drug efficacy with disease-modifying anti-rheumatic drugs (DMARDs), corticosteroids, and nonsteroidal anti-inflammatory drugs. Nonadherence to DMARDs results in inadequate disease control as reflected by progressive joint destruction, poorer quality of life, and increased mortality.

The reported rate of medication adherence in RA patients varies from 30% to 99% based on the definition of adherence and how medication adherence is measured.<sup>2</sup> However, there is no gold standard with which to measure adherence to medication in RA patients. Assessment of adherence can be broken down into direct methods that measure the concentration of a drug or its metabolites in blood or urine and indirect methods, such as pill counts, survey of pharmacy records, and administering survey questionnaires.<sup>1</sup> Among methods to detect adherence, self-reports are useful in terms of ease, minimal burden for patients, and low cost. To date, there is one validated rheumatology-specific adherence questionnaire known as the Compliance Questionnaire for Rheumatology (CQR).<sup>3</sup>

Medication adherence is influenced by various factors. Numerous specific factors have been shown to be associated with nonadherence to DMARD therapy, including belief in medication and illness perception,<sup>4</sup> self-efficacy,<sup>5</sup> and sociodemographic, psychological, and clinical factors related to adherence. However, factors associated with adherence in RA patients are inconsistent across studies.<sup>2</sup>

Personality is defined as a set of traits and psychological schemes that affect interactions and adaptation to environment.<sup>6</sup> Personality traits are relatively stable over time, particularly during midlife.<sup>7</sup> To describe personality traits, the Big Five personality traits, known as the five-factor model of personality, is commonly used in clinical and health psychology settings. The five traits are “extroversion,” “agreeableness,” “conscientiousness,” “neuroticism,” and “openness to experience.” Extroversion describes the degree of interpersonal interactions and the traits of being talkative, sociable, and friendly. Agreeableness is a characteristic of comfortable and harmonious interpersonal relationships, while conscientiousness estimates the desire to preserve social principles and norms. Neuroticism reflects an individual’s degree of emotional stability, while openness indicates a person’s preferences for diversity, change, and intellectual stimulation.<sup>8</sup> Personality traits have been found to be associated with RA symptoms, especially extra-articular symptoms, such as fatigue, aching, malaise, and insomnia.<sup>9</sup>

Previous studies have suggested that adherence can be related to personality traits in specific conditions, such as hemodialysis, HIV disease, cholesterol lowering treatment, and multiple sclerosis.<sup>10-13</sup> Less, however, is known about associations between medication adherence and personality traits in RA patients. One previous study involving RA patients showed that a high level of neuroticism was associated with aggressive

treatment.<sup>14</sup> In a recent study, personality traits were found to have a strong influence on the impact of RA and the patient’s ability to adjust to having RA.<sup>15</sup>

In this study, we sought to examine whether the Big Five personality traits, in addition to demographic factors, clinical factors, psychological factors, and factors related to health-related Quality of Life (HRQoL), are associated with medication adherence as assessed by the CQR questionnaire, which is the only validated self-report questionnaire available to assess medication adherence in RA patients.

## MATERIALS AND METHODS

### Study population and data collection

Patients with RA currently using traditional or biologic DMARDs were recruited through the rheumatology outpatient clinic of Bucheon St. Mary’s Hospital in South Korea. We enrolled 207 consecutive patients with RA between November 2018 and January 2019. Inclusion criteria were age above 18 years and an established diagnosis of RA according to the 1987 ACR classification criteria for RA or 2010 ACR/EULAR classification criteria. Patients completed the questionnaire and clinical interview. Patients were excluded if they rejected participation or had a mental disorder that resulted in linguistic difficulties preventing adequate understanding and completion of the questionnaires. All patients signed a written informed consent form prior to inclusion, and this study was approved by the Institutional Review Board of The Catholic University of Korea, Bucheon St. Mary’s Hospital (approval number HC18OESI0078). Data collection was carried out by direct interviews, physical examination, and review of medical history. Demographic data, educational level, working status, smoking, alcohol status, marital status, and monthly net income were obtained. Clinical factors measured were duration of RA, use of medication for RA, doses of methotrexate and corticosteroids, experience with adverse drug events, C-reactive protein (CRP) levels, erythrocyte sediment rate (ESR), and number of other medications taken. Etanercept, infliximab, tocilizumab, abatacept, and adalimumab were categorized as biologic DMARDs (bDMARDs). Tofacitinib was categorized as targeted synthetic kinase inhibitors (tsDMARDs). Assessment of RA disease activity was evaluated by disease activity score using 28 joints (DAS-28) calculated using ESR and CRP concentration, clinical disease activity index (CDAI), and simplified disease activity index (SDAI).<sup>16</sup> With respect to medication used for treatment of RA, we collected data relating to number of oral medications and total number of pills per day.

### Measures

Functional disability was assessed using the Korean version of the Health Assessment Questionnaire (HAQ).<sup>17</sup> The HAQ has exhibited good criterion validity, as well as test-retest reliability.

HRQoL was assessed by the EuroQoL-5 dimension questionnaire (EQ-5D) using the transformed weighted health state index score.<sup>18</sup>

The British Columbia Cognitive Complaints Inventory (BC-CCI) is a 6-item scale that measures perceived cognitive problems, including concentration, memory, trouble expressing thoughts, word selection, slow thinking, and difficulty solving problems.<sup>19</sup> Depressive symptoms were measured using the validated Korean version of the Patient Health Questionnaire-9 (PHQ-9).<sup>20</sup> Anxiety was assessed using the validated Korean version of the Generalized Anxiety Disorder-7 (GAD-7).<sup>21</sup>

Medication adherence was evaluated using the CQR, a 19-item questionnaire developed and validated in RA patients, compared with an electronic medication event monitoring system.<sup>3</sup> Patients rated their agreement with 19 statements using a 4-point Likert scale with a score from 1 to 4. The adjusted total score ranged from 0 to 100 and was used as a continuous scale. A cut-off of 80% has been used to define the behavior of patients as adherent ( $\geq 80\%$ ) or non-adherent ( $< 80\%$ ).<sup>3</sup> The CQR has been translated, and back-translation of the original CQR with modification for use in Koreans revealed that this measure has good reliability in RA patients.<sup>22</sup>

Personality traits were assessed with the validated Korean version of the 10-item short version of the Big Five Inventory-10 (K-BFI-10). The BFI-10 is a short-form of the Big Five Personality Inventory that consists of two items for each of the five personality traits, namely extraversion, agreeableness, conscientiousness, neuroticism, and openness to experience.<sup>23</sup> BFI-10 is a relative measure, wherein higher scores represent a higher level of each personality trait. Personality traits were treated as dichotomous variables, with lower scores (score for each trait  $< 4$ ) used as the referent category and higher scores (score  $\geq 4$ ) as the outcome. The BFI-10 has been translated and validated in Korean.<sup>8</sup>

### Statistical analysis

Continuous variables with a normal distribution are reported as means  $\pm$  standard deviations, while continuous variables with a non-normal distribution are reported as medians and interquartile ranges. Categorical variables are presented as frequencies (%). Student's *t* test or Wilcoxon rank sum test was used to compare continuous variables, while the chi-square test or Fisher's exact test, as appropriate, was used to compare categorical variables between groups. Adherence was measured with the CQR, with an 80% cut-off point used to define nonadherence. Multiple logistic regression models were used to identify factors associated with medication adherence. Variables that showed a *p* value less than 0.2 in univariate regression were entered into multiple logistic analysis. To quantify the strength of the multivariate associations, we used odds ratios with 95% confidence intervals. An association with a *p* value less than 0.05 was considered statistically significant. R software (version 3.4.4, The R Project for Statistical Comput-

ing, [www.r-project.org](http://www.r-project.org)) was used for statistical analysis.

## RESULTS

### Demographic and clinical characteristics

A total of 207 patients with RA was enrolled in this study, of which three were excluded due to an incomplete questionnaire. Baseline demographics and clinical characteristics are summarized in Tables 1 and 2, respectively. The study participants were 83.3% female, and the median age was 58 years. Most participants were married (72.5%); only a few were single (5.9%), widowed (11.8%), or separated/divorced (9.8%). Almost half of the participants had attained a high school education. More than half of the participants had a household monthly income greater than 2 million Korean won. Based on CQR, 68 participants (33.3%) were adherent given a cut-off score of 80% or greater. The median age was 59 years for the medication adherence group and 57 years for the medication nonadherence group. Age, sex, BMI, smoking status, alcohol status, marital status, employment status, education level, and household income did not differ significantly between medication nonadherence and adherence groups. The median disease duration of patients was 6.8 years, and 20.1% of patients reported side effects. The median DAS-28 (CRP) score was 3.1, indicating low disease activity. Median CDAI and SDAI values were 11.0 and 11.3, respectively, indicating moderate disease activity. Sixty-one percent of patients had comorbidities, including hypertension (27.9%), osteoporosis (21.6%), and dyslipidemia (20.1%). Demographic and clinical factors were examined for possible associations with medication adherence and nonadherence (Tables 1 and 2). Age, sex, marital status, education level, smoking, alcohol, employment status, household income, comorbidities, presence of adverse events, disease activity, and laboratory data were not significantly associated with medication adherence.

### Personality traits, depression, anxiety, and cognitive decline in the study group

Scores for the five personality traits in the medication adherence and nonadherence groups are presented in Table 2. The median score for "extroversion" was 3.0 (2.5-3.5), that for "agreeableness" was 4.0 (3.5-4.5), for "conscientiousness" 4.0 (3.5-4.5), for "neuroticism" 2.5 (2.0-3.5), and for "openness to experience" 3.0 (2.5-3.5). There were no significant differences in the scores of each domain of personality between the medication adherence and nonadherence groups.

Average PHQ-9 and GAD-7 scores were 4.0 and 2.0, respectively, indicating no depressive symptoms or anxiety in the RA patients. There were 18.6% of patients with depression and 9.8% with anxiety, showing no significant difference between nonadherence and adherence groups (Table 2).

The median BC-CCI score was 5.0, which indicated mild

**Table 1.** Demographic Characteristics of the Rheumatoid Arthritis Patients (n=204)

	Total (n=204)	Medication nonadherence (n=136)	Medication adherence (n=68)	p value
Sex				
Female	170 (83.3)	112 (82.4)	58 (85.3)	0.740
Age (yr)	58.0 (52.5–63.0)	57.0 (51.5–62.0)	59.0 (53.0–65.0)	0.145
BMI (kg/m <sup>2</sup> )	23.2 (21.4–25.5)	23.2 (21.4–25.5)	23.1 (21.4–25.8)	0.997
Smoking status				0.142
Never smoker	166 (81.4)	109 (80.7)	57 (82.6)	
Current smoker	26 (12.7)	21 (15.4)	5 (7.4)	
Ex-smoker	12 (5.9)	6 (4.4)	6 (8.8)	
Alcohol user	57 (27.9)	37 (27.2)	20 (29.4)	0.869
Marital status				0.639
Single	12 (5.9)	9 (6.6)	3 (4.4)	
Married	148 (72.5)	101 (74.3)	47 (69.1)	
Separated/divorced	20 (9.8)	12 (8.8)	8 (11.8)	
Widower/widow	24 (11.8)	14 (10.3)	10 (14.7)	
Employment				0.168
Employed	93 (45.6)	68 (50.0)	25 (36.8)	
Unemployed	105 (51.5)	65 (47.8)	40 (58.8)	
Retired	6 (2.9)	3 (2.2)	3 (4.3)	
Education level				0.069
Elementary	36 (17.6)	18 (13.2)	18 (26.5)	
Middle	34 (16.7)	21 (15.4)	13 (19.1)	
High	93 (45.6)	67 (49.3)	26 (38.2)	
College	36 (17.6)	25 (18.4)	11 (16.2)	
Graduate	5 (2.5)	5 (3.7)	0 (0.0)	
Household income (won/per month)				0.066
<500000	22 (12.0)	10 (8.1)	12 (19.7)	
500000–1500000	10 (5.4)	4 (3.3)	6 (9.8)	
1500000–20000000	22 (12.0)	14 (11.4)	8 (13.1)	
20000000–30000000	37 (20.1)	28 (22.8)	9 (14.8)	
30000000–50000000	44 (23.9)	32 (26.0)	12 (19.7)	
≥50000000	49 (26.6)	35 (28.5)	14 (23.0)	
Comorbidities (yes)	126 (61.8)	85 (62.5)	41 (60.3)	0.879
Diabetes mellitus	25 (12.3)	12 (8.8)	13 (19.1)	0.035*
Hypertension	57 (27.9)	35 (25.7)	22 (32.4)	0.408
Osteoporosis	44 (21.6)	30 (22.1)	14 (20.6)	0.951
Dyslipidemia	41 (20.1)	28 (20.6)	13 (19.1)	0.879

BMI, body mass index.

Data are presented as number (%) or median (IQR).

\* $p < 0.05$ .

cognitive decline. There was no significant difference in this score between nonadherence and adherence groups (Table 2).

### Associations between medication characteristics and medication adherence

Most participants were treated with methotrexate (75%), while less than 10% were treated with biologic DMARDs. However, medication adherence and nonadherence patients did not differ with regard to number of total prescribed pills, number of DMARDs, types of DMARDs, dose of methotrexate or non-steroidal anti-inflammatory drugs, or dietary supplement use

(Table 3). Interestingly, adherent patients were prescribed a larger number of daily pills ( $4.2 \pm 1.4$  vs.  $3.7 \pm 1.5$ ). They also more frequently used prednisolone (44.1% vs. 30.1%) and were prescribed a higher dose of prednisolone than non-adherent patients, as illustrated in Table 3.

### Associations between personality characters, psychological characters, HRQoL, and medication adherence

Median total scores on PHQ-9 and GAD-7 were 1.8- and 4.5-fold higher, respectively, in higher neuroticism than lower neu-

roticism individuals ( $p=0.024$  and  $p<0.001$ ), indicating that RA patients with high neuroticism are more depressed and anxious. No other characters were significantly different between

the two groups (Table 4).

Patients with high conscientiousness were significantly older and had lower PHQ-9 and higher CQR scores than those

**Table 2.** Clinical and Psychological Characteristics of the RA Patients (n=204)

	Total (n=204)	Non-adherent (n=136)	Adherent (n=68)	p value
<b>Clinical characteristics</b>				
Disease duration (yr)	6.8 (2.5–12.0)	6.0 (2.5–12.0)	8.0 (2.1–13.0)	0.413
RA duration (≤5 yr)	56 (27.5)	43 (31.6)	13 (19.1)	0.370
RA duration (>6 yr, ≤10 yr)	53 (26)	37 (27.2)	16 (23.5)	0.693
RA duration (>10 yr, ≤20 yr)	53 (26)	33 (24.35)	20 (29.4)	0.535
RA duration (>20 yr)	11 (5.4)	5 (3.7)	6 (8.8)	0.185
Early RA (≤1 yr)	31 (15.25)	18 (13.2)	13 (19.1)	0.370
Adverse events, yes	41 (20.1)	27 (19.9)	14 (20.6)	>0.999
Admission due to RA flare, yes	33 (16.2)	19 (14.0)	14 (20.6)	0.313
<b>Disease activity</b>				
DAS-28 (ESR)	3.8±1.3	3.8±1.2	3.9±1.5	0.464
DAS-28 (CRP)	3.1 (2.1–3.9)	3.1 (2.1–4.0)	2.9 (2.2–3.9)	0.931
Tender joint count	2.0 (0.0–5.0)	2.0 (0.0–5.0)	2.0 (0.0–4.0)	0.574
Swollen joint count	0.0 (0.0–1.0)	0.0 (0.0–1.5)	1.0 (0.0–1.0)	0.329
PGA	3.0 (2.0–5.0)	3.0 (2.0–4.0)	3.0 (2.0–5.0)	0.109
VAS	5.0 [3.0–6.0]	4.5 [3.0–5.0]	5.0 [3.0–6.0]	0.196
ESR (mm/hr)	28.0 (15.5–49.0)	27.5 (14.0–49.0)	28.0 (17.0–46.0)	0.988
CRP (mg/L)	2.6 (0.9–7.7)	2.3 (0.8–7.2)	3.0 (1.5–10.7)	0.254
CDAI	11.0 (6.0–16.2)	10.0 (5.0–16.2)	11.0 (7.5–16.5)	0.761
SDAI	11.3 (6.2–17.7)	11.3 (6.0–17.7)	11.4 (7.8–18.3)	0.690
Low disease activity (DAS 28<3.2)	94 (46.1)	65 (47.8)	29 (42.6)	0.585
<b>Laboratory data</b>				
White blood cell (10 <sup>9</sup> cells/L)	6.545 (5.795–7.910)	6.455 (5.795–7.700)	6.710 (5.795–8.320)	0.299
Hemoglobin (g/dL)	13.0±1.3	13.1±1.3	12.9±1.2	0.206
Platelet (10 <sup>9</sup> /L)	270.4±62.8	266.6±56.0	278.4±74.4	0.245
eGFR (mL/min/1.73 m <sup>2</sup> )	92.0 (79.0–102.5)	93.0 (81.0–102.0)	89.5 (77.0–105.0)	0.457
RF positivity	183 (91.0)	124 (92.5)	59 (88.1)	0.432
ACPA positivity	128 (82.6)	84 (80.8)	44 (86.3)	0.453
<b>Psychological characters</b>				
PHQ-9 score	4.0 (2.0–8.0)	4.0 (2.0–7.0)	4.0 (2.0–9.5)	0.683
Depression (PHQ-9≥10)	38 (18.6)	21 (15.4)	17 (25.0)	0.144
GAD-7 score	2.0 (0.0–4.0)	2.0 (1.0–4.0)	1.0 (0.0–3.5)	0.553
Anxiety (GAD-7≥10)	20 (9.8)	12 (8.8)	8 (11.8)	0.677
BC-CI score	5.0 (2.0–7.0)	5.0 (3.0–8.0)	5.0 (2.0–7.0)	0.273
<b>HRQoL and functional disability</b>				
EQ-5D-5L index value	0.8 (0.7- 0.9)	0.8 (0.7- 0.9)	0.8 (0.7- 0.9)	0.174
EQ-5D VAS, 0–100	70.0 (50.0–80.0)	70.0 (50.0–80.0)	70.0 (50.0–80.0)	0.798
HAQ score	0.4 (0.0–0.9)	0.4 (0.0–0.9)	0.5 (0.1–1.1)	0.121
<b>Personality traits</b>				
Extroversion score	3.0 (2.5–3.5)	3.0 (2.5–3.5)	3.0 (2.5–3.8)	0.913
Agreeableness score	4.0 (3.5–4.5)	4.0 (3.5–4.2)	4.0 (3.5–4.5)	0.416
Conscientiousness score	4.0 (3.5–4.5)	4.0 (3.5–4.5)	4.0 (3.5–4.5)	0.067
Neuroticism score	2.5 (2.0–3.5)	2.5 (2.0–3.5)	2.8 (2.0–3.0)	0.646
Openness to experience score	3.0 (2.5–3.5)	3.0 (2.5–3.5)	3.0 (2.5–3.5)	0.302

RA, Rheumatoid arthritis; DAS-28, Disease Activity Score using 28 joints; ESR, Erythrocyte Sediment Rate; CRP, C-reactive protein; PGA, Physician Global Assessment; VAS, Visual Analog Scale; CDAI, Clinical Disease Activity Index; SDAI, Simplified Disease Activity Index; eGFR, Estimated Glomerular Filtration Rate; RF, rheumatoid factor; ACPA, anti-citrullinated protein antibody; PHQ-9, Patient Health Questionnaire-9; GAD-7, Generalized Anxiety Disorder-7; BC-CI, The British Columbia-Cognitive Complaints Inventory; HRQoL, health-related Quality of Life; EQ-5D, EuroQoL-5 dimension questionnaire; HAQ, Health Assessment Questionnaire. Data are presented as number (%), mean±SD, or median (IQR).

**Table 3.** Differences between Medication Characteristics of Adherent and Non-Adherent Patients

	Non-adherent (n=136)	Adherent (n=68)	p value
Number of prescription drugs	4.6 (1.8)	5.1 (1.6)	0.057
Number of daily prescription drugs	3.7 (1.5)	4.2 (1.4)	0.030*
Numbers of cDMARDs			0.329
None	9 (6.6)	5 (7.4)	
1	78 (57.4)	32 (47.1)	
2	49 (36.0)	31 (45.6)	
Weekly methotrexate	101 (74.3)	52 (76.5)	0.864
Leflunomide	24 (17.6)	10 (14.7)	0.740
Sulfasalazine	7 (5.1)	6 (8.8)	0.478
Hydroxychloroquine	4 (2.9)	1 (1.5)	0.873
Tacrolimus	31 (22.8)	17 (25.0)	0.861
bDMARDs or tsDMARDs	10 (7.4)	8 (11.8)	0.432
Methotrexate dose (mg/week)	7.8 (4.58)	7.8 (4.68)	0.405
Prednisolone use	41 (30.1)	30 (44.1)	0.069
Dose of prednisolone (mg/day)	1.2 (2.1)	1.9 (2.5)	0.027*
Dose of prednisolone (mg/month)	33.8 (61.0)	56.8 (75.7)	0.027*
NSAID use	92 (67.6)	46 (67.6)	>0.999
Dietary supplements use	49 (36.0)	32 (47.1)	0.172
DMARDs change history within 6 months	54 (39.7)	27 (39.7)	>0.999
Frequency of DMARDs change within 6 month			0.951
1	30 (22.1)	15 (22.1)	
2	14 (10.3)	9 (13.2)	
3	8 (5.9)	3 (4.4)	
4	1 (0.7)	0 (0)	
Prednisolone change history within 6 months	42 (30.9)	31 (45.65)	0.056

DMARDs, disease-modifying anti-rheumatic drugs; bDMARDs, biologic DMARDs; tsDMARDs, targeted synthetic DMARDs; cDMARDs, conventional DMARDs; NSAID, nonsteroidal anti-inflammatory drugs.  
Data are presented as number (%) or mean±SD.

with low conscientiousness. Patients with both high extroversion and agreeableness had low PHQ-9 and GAD-7 scores, compared to those with both low extroversion and agreeableness. In other words, individuals with low extroversion, conscientiousness, and agreeableness scores exhibited more depressive symptoms ( $p<0.05$ ) (Table 4). Patients with high openness had a lower BC-CCI score, which indicates cognitive decline. There were no significant differences among the remaining factors, such as HAQ and EQ-5D, between individuals that scored high and low for the five personality traits (Table 4). Medication adherence was significantly higher only in patients with a high conscientiousness score based on CQR score ( $p<0.05$ ) (Table 4).

**Multivariate analysis of variables associated with medication adherence**

Binary logistic regression of CQR as an independent variable was used to calculate the odds of factors associated with med-

**Table 4.** Clinical Characteristics of the Sample Based on Personality Profile (n=204)

	Extroversion		p value	Agreeableness		p value	Conscientiousness		p value	Neuroticism		p value	Openness		p value
	High (n=49)	Low (n=155)		High (n=109)	Low (n=94)		High (n=119)	Low (n=85)		High (n=24)	Low (n=180)		High (n=46)	Low (n=158)	
Sex, female, n (%)	40 (81.6)	130 (83.9)	0.883	88 (80.7)	81 (86.2)	0.398	93 (78.2)	77 (90.6)	0.031*	22 (91.7)	148 (82.2)	0.382	39 (84.8)	131 (82.9)	0.940
Age (yr)	57.0 (52.0-64.0)	58.0 (53.0-62.5)	0.912	59.0 (53.0-64.0)	57.5 (52.0-62.0)	0.337	59.0 (53.5-65.5)	56.0 (47.0-61.0)	0.001*	56.0 (50.5-58.5)	58.0 (53.0-63.5)	0.062	58.5 (47.0-64.0)	58.0 (53.0-63.0)	0.967
PHQ-9	3.0 (1.0-5.0)	4.0 (2.0-8.0)	0.008*	3.0 (1.0-7.0)	5.0 (3.0-9.0)	0.017*	3.0 (1.0-7.0)	5.0 (3.0-8.0)	0.003*	7.5 (2.5-14.5)	4.0 (2.0-7.0)	0.024*	4.0 (2.0-7.0)	4.0 (2.0-8.0)	0.583
GAD-7	1.0 (0.0-2.0)	2.0 (1.0-5.0)	0.008*	1.0 (0.0-3.0)	2.0 (1.0-6.0)	0.011*	2.0 (0.0-3.0)	2.0 (1.0-5.0)	0.073	4.5 (2.0-11.0)	1.0 (0.0-3.0)	<0.001*	1.0 (0.0-3.0)	2.0 (0.0-4.0)	0.277
BC-CCI	4.0 (2.0-7.0)	5.0 (3.0-8.0)	0.072	5.0 (2.0-8.0)	3.0 (3.0-7.0)	0.863	4.0 (2.0-7.0)	6.0 (4.0-9.0)	0.017	4.0 (3.0-6.5)	5.0 (2.0-7.5)	0.916	3.5 (2.0-6.0)	5.0 (3.0-8.0)	0.012*
HAQ	0.2 (0.0-0.8)	0.5 (0.0-1.0)	0.127	0.5 (0.1-0.9)	0.4 (0.0-1.0)	0.521	0.4 (0.0-0.9)	0.6 (0.0-1.0)	0.314	0.7 (0.0-1.1)	0.4 (0.0-0.9)	0.867	0.2 (0.0-0.8)	0.5 (0.0-1.0)	0.098
EQ-5D	0.8 (0.7-0.9)	0.8 (0.7-0.9)	0.158	0.8 (0.7-0.9)	0.8 (0.7-0.9)	0.581	0.8 (0.7-0.9)	0.8 (0.7-0.8)	0.314	0.8 (0.6-0.9)	0.8 (0.7-0.9)	0.341	0.8 (0.8-0.9)	0.8 (0.7-0.9)	0.340
CQR	75.4 (66.7-84.2)	75.4 (64.9-80.7)	0.517	77.2 (66.7-84.2)	74.6 (64.9-80.7)	0.397	77.2 (66.7-84.2)	71.9 (63.2-78.9)	0.025*	73.7 (61.4-80.7)	75.4 (66.7-82.5)	0.209	74.6 (63.2-82.5)	75.4 (64.9-82.5)	0.595

BC-CCI, The British Columbia Cognitive Complaints Inventory; CQR, Compliance Questionnaire for Rheumatology; EQ-5D, EuroQoL-5 dimension questionnaire; GAD-7, Generalized Anxiety Disorder-7; HAQ, Health Assessment Questionnaire; PHQ-9, Patient Health Questionnaire-9.  
Data represent medians±interquartile ranges.  
\*  $p<0.05$ .

**Table 5.** Univariate and Multivariate Logistic Regression Analysis to Identify Factors Contributing to Medication Adherence in Rheumatoid Arthritis Patients

Variable	Univariate regression analysis				Multivariate logistic regression			
	Odds ratio	95% CI		p value	Odds ratio	95% CI		p value
		Lower	Upper			Lower	Upper	
<b>Demographic characters</b>								
Education level	0.68	0.51	0.91	0.010*	0.72	0.49	1.06	0.092
House income	0.78	0.65	0.94	0.010*	0.93	0.73	1.18	0.537
Diabetes mellitus	2.44	1.05	5.69	0.039*	3.00	1.12	8.07	0.030*
<b>Medication characters</b>								
Number of daily prescription drugs	1.25	1.03	1.53	0.026*	1.16	0.89	1.52	0.265
Prednisolone dose	1.16	1.02	1.31	0.025*	1.12	0.94	1.32	0.200
Frequency of DMARDs change	1.88	1.03	3.42	0.914	0.96	0.63	1.46	0.846
<b>Clinical characters</b>								
Early rheumatoid arthritis (≤2 years)	1.29	0.65	2.56	0.454	1.07	0.91	1.26	0.428
DAS-28 (CRP)	1.07	0.84	1.36	0.594	1.02	0.99	1.05	0.220
<b>Personality traits</b>								
High extroversion	1.08	0.55	2.13	0.817	0.88	0.39	2.00	0.763
High agreeableness	1.14	0.64	2.05	0.657	1.23	0.60	2.50	0.577
High conscientiousness	2.27	1.18	4.09	0.013*	2.11	1.01	4.38	0.046*
High neuroticism	1.00	0.41	2.47	1.000	0.71	0.24	2.08	0.532
High openness	0.96	0.48	1.93	0.906	1.10	0.48	2.53	0.821

CI, confidence interval; DMARDs, disease-modifying anti-rheumatic drugs; DAS-28, Disease Activity Score using 28 joints; CRP, C-reactive protein.

\*p<0.05.

ication adherence (Table 5). Factors associated with medication adherence were assessed using multivariable analysis, including education level, household income, diabetes mellitus, number of daily prescription drugs, frequency of DMARDs change during 6 months, prednisolone dose per day, DAS-28, disease duration (early RA), and five personality traits. The multivariate model analysis identified associations between a high level of conscientiousness and medication adherence [odds ratio (OR) 2.11, 95% confidence interval (CI) 1.01–4.38]. Diabetes mellitus was also associated with medication adherence (OR 3.00, 95% CI 1.12–8.07).

## DISCUSSION

This study examined the associations among personality traits, medication adherence, psychological characteristics, and HRQoL in patients with RA. We found that more than 60% of participants exhibited nonadherence. Factors associated with medication adherence were diabetes and corticosteroid dosage. Adherence rates of RA patients vary widely from 30 to 99%.<sup>2</sup> According to the Korean RA cohort KORONA Observational Study Network for Arthritis (KORONA),<sup>24</sup> the prevalence of adherence to RA treatment was 90.4% among 3523 patients using a self-reported questionnaire designed to identify skipped medication days. However, in another Korean study based on a self-reported questionnaire, medication adherence rate was 45.9%.<sup>4</sup> This great variance in the same ethnic

group is likely due to differences in study design, including the definition of adherence and the tools used to assess adherence. The current study differs from previous Korean studies in that we used a validated questionnaire, the CQR, for inflammatory rheumatic disease. We found that 33.3% of patients with RA were adherent based on CQR, which is similar to the results of a few prior studies.<sup>25</sup> To the best of our knowledge, this is the first study to investigate medication adherence and its associated factors in Korean RA patients using a validated self-report questionnaire, the CQR. Because adherence to medication in RA patients can be low, identifying the factors associated with medication adherence is important to develop strategies to increase adherence. However, neither age, sex, level of education, smoking, alcohol, employment status, monthly income, presence of comorbidities nor adverse effects was associated with medication adherence in this study.

One previous study showed that personality traits can impact medication adherence in patients with a chronic disease.<sup>26</sup> The present study is the first to explore associations between the Big Five personality traits and medication adherence in patients with RA. We found that higher extroversion and agreeableness were associated with better psychological health (lower PHQ-9 score and lower GAD-7 score). In contrast, higher neuroticism was associated with poorer psychological health (higher PHQ-9 score and higher GAD-7 score). This finding is consistent with those of previous studies.<sup>11,27</sup> Seto, et al.<sup>27</sup> found that higher neuroticism was associated with anxiety, depression, stress, and worse mental quality of life in fibromyalgia

patients. We demonstrated that lower openness to experience was associated with poor cognitive function. Our results are, therefore, consistent with those of previous studies that reported associations between the Big Five personality traits and cognitive abilities.<sup>28</sup> Personality is a prominent risk factor for cognitive function in old age.<sup>29</sup> Persons higher in extraversion and neuroticism and lower in openness exhibited worse average cognitive function over the follow-up period.<sup>29</sup> Openness refers to the tendency to be creative, curious, imaginative, and open to new ideas and experiences. Thus, individuals with higher openness tend to seek more intellectually stimulating activities, such as reading a book, using a smartphone, and artistic activities that help improve cognitive function.<sup>28</sup> Previous studies have demonstrated an association between openness and cognitive function in older age groups, but we found this association regardless of age. Costa, et al.<sup>30</sup> reported that participants with a high openness score had significantly better pattern analysis performance with no effect of age in a cross-sectional study, consistent with the results of our study.

We found that high conscientiousness was associated with medication adherence. This finding is consistent with previous studies, including a meta-analysis.<sup>10-13,26,31</sup> Conscientiousness has been described as “socially prescribed impulse control that facilitates task- and goal-directed behavior.”<sup>32</sup> Therefore, individuals who score high in conscientiousness are often characterized as responsible, reliable, and organized. This tendency may be why highly conscientious individuals comply with medical instructions regarding dosage and timing of medication. Conscientiousness has been found to be an important predictor of all-cause mortality<sup>33</sup> and to have a negative association with risky health behaviors, such as excessive alcohol use, tobacco use, and drug abuse.<sup>34</sup> In turn, it is also positively associated with preventive health behaviors, such as seeing a doctor regularly and exercising.<sup>35</sup> These findings indicate that conscientious people behave in a way to promote good health outcomes,<sup>35</sup> such as adhering to medication. Thus, conscientiousness has plausible direct links to health-related behaviors. In addition, because conscientiousness is associated with improved survival in observational studies, better medication adherence may partly explain this link.<sup>31</sup> High conscientiousness is positively related with age. This could explain why, in our study, older individuals tended to score higher in conscientiousness and were more adherent to RA treatment.

We did not find any association between extroversion, agreeableness, neuroticism, or openness to experience and medication adherence. Previous studies reported a positive and negative association of agreeableness and neuroticism with medication adherence, respectively.<sup>26,36</sup> One possible reason for the difference between previous studies and ours might be selection bias. Because we included only patients who agreed to the clinical trial, it is possible that the patients who disagreed had a high neuroticism score, with neuroticism defined as the tendency to be emotionally unstable, feel negative emotions, and

have anger and depression.

Interestingly, we also found that prednisolone dose and diabetes mellitus were factors that contributed to medication adherence. Similar results were reported in another Korean cohort study in which patients in the nonadherence group were less likely to have diabetes mellitus and used less oral corticosteroids than patients in the adherent group.<sup>24</sup> In a Dutch cohort study, concurrent prednisolone use had a positive effect on methotrexate survival.<sup>37</sup> One explanation for these findings may be the relationship between dose of prednisolone and RA disease activity. Patients with RA who use higher doses of prednisolone are more likely to have higher disease activity. A previous study found that medication adherence decreased with low to moderate disease activity.<sup>38</sup> A UK observational study of 178 RA patients found that patients with high disease activity were more likely to be adherent than those with low disease activity.<sup>39</sup> However, in our study, disease activity as represented by DAS-28, ESR, CRP level, tender joint count, swollen joint count, and visual analog scale were not associated with medication adherence. In fact, conflicting results have been reported for the relationship between medication adherence and disease activity. Some studies, including a recent meta-analysis,<sup>40</sup> found that RA patients with higher medication adherence tended to have lower disease activity. Furthermore, in a meta-analysis, there was no significant difference in swollen joint count, visual analog scale, or CRP level between medication adherent and nonadherent patients,<sup>40</sup> in agreement with our results. These conflicting results could be because of divergent assessment measures of adherence or different definitions of high or low disease activity. Longitudinal studies are needed to fully understand the association between disease activity and medication adherence.

Diabetes mellitus showed a positive effect on adherence in this study. Comorbidities previously have been found to positively impact medication adherence.<sup>24</sup>

This study had several strengths and limitations. The strengths were that we comprehensively evaluated the relationship between medication adherence using CQR and personality traits using a five-factor model, psychological factors, and HRQoL in RA patients. Second, we evaluated medication adherence using the reliable, well-validated, dichotomized CQR, which has been validated in patients with rheumatism, and we assessed personality using a standardized and validated questionnaire and the Big Five personality traits. However, we performed cross-sectional sampling in a general hospital, which limits our ability to generalize our findings, even though we examined a large sample of RA patients using DMARDs. Adherence to medication is a complex and dynamic behavior that can change over time. Because adherence in this study was measured only at the index date, medication adherence should be investigated in a future longitudinal study.

In conclusion, we demonstrated that high conscientiousness is positively associated with medication adherence. This



suggests that measuring conscientiousness in RA patients could help to identify those who may be at risk for nonadherence to medication and who need additional support and education to manage their RA.

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