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# Are Health Care Professionals' Implicit and Explicit Attitudes Toward Conventional Disease-Modifying Antirheumatic Drugs Associated With Those of Their Patients?

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**Objective.** It is generally unknown how the attitudes and beliefs of health care professionals (HCPs) might affect the attitudes, beliefs, and medication-taking behavior of patients with rheumatoid arthritis (RA). This study aims 1) to examine the attitudes, health-related associations (both implicit and explicit), and beliefs of HCPs about conventional disease-modifying antirheumatic drugs, and 2) to assess whether these attitudes, health-related associations, and beliefs of HCPs are associated with those of their patients, with their patients' medication-taking behavior, and disease activity.

**Methods.** HCPs were recruited from 2 centers that specialized in rheumatology across The Netherlands, and patient recruitment followed. In this observational study, implicit outcomes were measured with single-category implicit association tests, whereas explicit outcomes were measured with a bipolar evaluative adjective scale and the Beliefs About Medicines Questionnaire–Specific. Spearman's rank correlations were used to describe correlations between implicit and explicit measures of the attitudes of HCPs. Multilevel, mixed-effects linear models were used to examine the association of HCP-related characteristics, including the implicit and explicit outcomes of HCPs, with those of their patients, their medication-taking behaviors, and disease activity.

**Results.** Of the 1,659 initially invited patients, 254 patients with RA (mean age 62.8 years, mean disease duration 11.8 years, and 68.1% of the patients were female) who were treated by 26 different HCPs agreed to participate in this study. The characteristics, attitudes, health-related associations, and beliefs about medicines of HCPs were not significantly associated with those of their patients, nor with their medication-taking behaviors or disease activity scores.

**Conclusion.** This study demonstrated that the attitudes, health-related associations (as measured both implicitly and explicitly), and beliefs of HCPs were not significantly associated with the attitudes, beliefs, medication-taking behavior, and disease activity of patients with RA.

## INTRODUCTION

Disease-modifying antirheumatic drugs (DMARDs) are recommended to patients with rheumatoid arthritis (RA) to suppress the inflammatory response, and consequently, to decrease disease activity and reduce radiologic damage (1,2). Despite the beneficial

effects of DMARDs, previous studies have reported major issues regarding medication-taking behavior of RA patients, with adherence rates varying from 30% to 107% depending on the measurement method used (3–5). Nonadherence to medication can lead to worsening of clinical outcomes (i.e., high disease activity, radiologic progression, and a decrease in physical functioning and

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No potential conflicts of interest relevant to this article were reported.

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### SIGNIFICANCE & INNOVATIONS

- It is unknown whether the attitudes and beliefs of health care professionals (HCPs) might affect attitudes, beliefs, and medication-taking behavior of patients with rheumatoid arthritis (RA).
- This study demonstrated that sociodemographic characteristics, implicit and explicit attitudes and health-related associations, and the beliefs of HCPs about medicines were not associated with those of their patients with RA nor with patients' medication-taking behavior and disease activity scores.
- These findings provide some first insights into the potential (and the lack thereof) of implicit and explicit perceptions of medication of HCPs in relation to patients' medication adherence and disease activity.

quality of life) and increased health care expenditures (6–8). There have been several attempts to explore effective intervention strategies and targets for improving medication-taking behavior in this population (9). However, so far, adherence-improving interventions were only partly effective in changing medication-taking behavior.

An explanation for the ineffectiveness of adherence-improving interventions might be that previous studies have largely focused on the perspective of patients rather than the perspective of health care professionals (HCPs) (9–12). Several studies suggest that the attitudes and beliefs of HCPs might be associated with the attitudes and beliefs of their patients (Zwicker et al, submitted for publication) (13–15). It can, therefore, be assumed that during clinic visits, the attitudes and beliefs of HCPs might affect patients' medication-taking behavior as well. However, targeting the concerns of patients and their beliefs about the need for medication (16), and making HCPs aware of patients' suboptimal medication intake (17), does not improve patients' medication-taking behavior. New insights into processes that may underlie patients' non-adherent medication-taking behavior, or that may influence the patient–provider interaction, are therefore required.

Theoretical and empirical contributions in the field of psychology provide abundant evidence that only a small part of behavior originates from conscious or reflective thought processes and largely depends on subconscious or automatic processes (18–21). These dual process theories assume that subconscious or automatic processes explain a unique part of behavior that cannot be explained by conscious thought (18–21). By extending these findings to adherence research, these dual process theories provide a plausible explanation as to why the often-measured and explicitly reported attitudes and beliefs about medicines may give insufficient insight into the processes underlying adherence. These theories also pinpoint automatic processes, and specifically, implicit attitudes, as potentially essential elements in understanding the communication of HCPs and patients' medication-intake behavior (18–21). In this study, we define implicit attitudes as automatically activated associations, which are based on past

experiences and mediate favorable or unfavorable feelings that individuals might not be aware of, whereas explicit attitudes are defined as deliberate or conscious evaluations of medication (19–21). Few studies have investigated patients' implicit attitudes and their association with medication-taking behavior in rheumatic diseases (22,23). However, studies on the implicit attitudes of HCPs toward medication in the field of rheumatology are lacking. The implicit attitudes of HCPs might be involved in the patient–provider interaction (e.g., communication between HCPs and patients), which then might affect patients' attitudes as well as patients' medication-taking behavior. It is unknown whether the implicit attitudes and beliefs of HCPs about medication might be associated with patients' implicit attitudes and beliefs about medication, patients' medication-taking behavior, and patients' disease activity in the field of rheumatic diseases (15,22).

Therefore, the aim of this study is 1) to examine the implicit and explicit attitudes of HCPs and the health-related associations with conventional DMARD use, together with HCPs' explicitly reported beliefs about medicines, and 2) to assess whether these attitudes are associated with those of their patients, patients' medication-taking behavior, and patients' disease activity scores.

## SUBJECTS AND METHODS

**Study design and setting.** An observational study was performed in 2 of the largest centers that specialize in rheumatology across The Netherlands (i.e., covering ~20% of all patients with RA): Sint Maartenskliniek (Nijmegen) and Reade (Amsterdam). Rheumatologists and physician assistants (PAs) were recruited between July 5, 2016 and January 23, 2017, and patients were recruited between July 5, 2016 and November 30, 2017. This project resulted in a large data set, including measures of implicit and explicit attitudes and beliefs toward medication of both patients and HCPs. Van Heuckelum et al focused on the patient data only (a detailed description on the measurement of patients' implicit and explicit attitudes, medication-taking behavior, and clinical variables published previously) (23). The current study focuses on the implicit and explicit attitudes of HCPs and explores their associations with patient data. An overview of the study is presented in Table 1. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for observational studies and the ESPACOMP Medication Adherence Reporting Guideline (EMERGE) were used as guidance for adequate reporting in this study (24,25).

### Ethics approval and patient and public involvement.

This study was conducted according to the Ethical Principles for Medical Research as stated in the Declaration of Helsinki (64th World Medical Association General Assembly, Fortaleza, Brazil, October 2013) and was approved by the Medical Research Ethics Committee of Arnhem-Nijmegen (File 2016–2410). Two patient

**Table 1.** Study overview and measurements of health care professionals and rheumatoid arthritis patients at baseline and follow-up\*

Baseline	Follow-up
Health care professionals Implicit attitudes and health-related associations Sociodemographics Explicit attitudes and health-related associations Beliefs about medicines (i.e., necessity and concern beliefs about cDMARDs)	Not applicable
Patients Implicit attitudes and health-related associations Sociodemographics Explicit attitudes and health-related associations Beliefs about medicines (i.e., necessity and concern beliefs about cDMARDs) Self-reported medication-taking behavior Disease activity score (i.e., DAS28-CRP)	Medication-taking behavior measured with Medication Event Monitoring System (Aardex) for a minimum period of 3 months.

\* Inclusion and performing baseline measurements of health care professionals were completed before inclusion and performing baseline measurements of patients with rheumatoid arthritis. The maximum follow-up period for patients was 9 months. cDMARDs = conventional disease-modifying antirheumatic drugs; DAS28-CRP = Disease Activity Score in 28 joints using the C-reactive protein level.

research partners were involved in the design phase of this study. The patient research partners pretested the Single-Category Implicit Association Tests (SC-IATs) and assessed the comprehensibility of the hardcopy questionnaire for patients with RA.

**Eligibility criteria and selection procedures.** All rheumatologists, residents, and PAs working in the rheumatology departments at Sint Maartenskliniek and Reade with a minimum employment contract period of 9 months were asked to participate in this study. Written information about the study protocol (an adapted version for patients was used) and an informed consent form were attached to an email sent to all rheumatologists and PAs. After the rheumatologists and PAs agreed to the study via email, a research appointment was made to sign the informed consent form. Subsequently, patients were assessed for eligibility. All consecutive adult patients (age  $\geq 18$  years) with a clinical diagnosis of RA and treated with at least 1 conventional DMARD (cDMARD) for a minimum period of 1 year were invited to participate in this study. No additional inclusion and exclusion criteria were defined for patient selection. Written information about the study protocol and an informed consent form were sent by mail to all consecutive patients 4 weeks before the planned regular consultation with their treating clinician. After the patient's agreement to participate, the researcher made a research appointment before the planned regular consultation in order to sign the informed consent form.

**Procedures of data collection.** At baseline, the implicit and explicit attitudes and health-related associations of HCPs, combined with sociodemographic data (i.e., age, sex, current position, years of working experience, and mean hours of patient contact per week) and explicit beliefs about medicines, were assessed. Implicit data were collected prior to completing the hardcopy questionnaires in order to prevent contamination effects

of explicit measures with implicit measures. The same procedures were applied to patients at baseline, supplemented with a hardcopy questionnaire to assess self-reported medication-taking behavior. Electronic monitoring of medication-taking behavior was continued for a minimum period of 3 months after the patient's inclusion in the study. At the patient's follow-up visit, Medication Event Monitoring System (MEMS) read-outs were used to assess medication-taking behavior over the previous months. The patient's disease activity score (measured by the Disease Activity Score in 28 joints using the C-reactive protein level [DAS28-CRP]) was assessed in conformity with treatment protocols as part of the standard care.

**Measurement instruments.** *SC-IATs.* SC-IATs were used to measure 2 concepts of automatic associations in this study: implicit attitudes (i.e., positive versus negative), and implicit health-related associations (i.e., health versus sickness) with medication. The SC-IAT is considered a reliable and valid instrument to measure implicit associations with a single attitude object (i.e., antirheumatic drugs) (26). Each concept was assessed in 3 rounds: 1 practice round of 20 trials, followed by 2 experimental rounds of 40 trials each. Trials displayed various positive/health-related, negative/sickness-related, and medicine-related words and pictures in a computerized categorization task in which automatic associations were measured based on the response times of HCPs and patients. The response times in the experimental rounds served as a proxy for association strength, where faster responses represented stronger associations. In other words, if HCPs were on average faster in categorizing trials coupling drug stimuli and negative (versus positive) stimuli, then this reflects a relatively negative (versus positive) automatic association with cDMARDs. SC-IATs for rheumatologists/PAs included 5 generic pictures of cDMARDs (i.e., methotrexate,

leflunomide, hydroxychloroquine, sulfasalazine, and azathioprine), whereas SC-IATs for patients were personalized based on their personal cDMARD treatment. Supplementary Appendix A, available on the *Arthritis Care & Research* website at <http://onlinelibrary.wiley.com/doi/10.1002/acr.24186/abstract>, provides a more detailed description of the SC-IAT procedures used in this study.

**Bipolar evaluative adjective scale.** For both HCPs and patients, a bipolar evaluative adjective scale was used to assess explicit medication attitudes (10 semantic differential scaled items, e.g., "I think [name of cDMARD(s)] is 1 negative–5 positive") and explicit health-related associations (8 semantic differential scaled items, e.g., "To what extent do you associate [cDMARD] with the following terms, 1 dead–5 alive"). Items in this questionnaire represented the same associations with cDMARDs as measured with the SC-IATs (see Supplementary Appendix B, available on the *Arthritis Care & Research* website at <http://onlinelibrary.wiley.com/doi/10.1002/acr.24186/abstract>).

**Beliefs About Medicines Questionnaire–Specific (BMQ-Specific).** HCPs filled out the BMQ-Specific (10 Likert-scaled items) adapted to the perspective of HCPs (e.g., "Without the medicines my patients would be very ill"), whereas patients filled out the original validated BMQ-Specific (e.g., "Without the medicines I would be very ill"). Item scores varied from 1 (strongly disagree) to 5 (strongly agree), which resulted in sum scale scores of 5 to 25 for each subscale (necessity beliefs versus concern beliefs) (12,27).

**Compliance Questionnaire on Rheumatology (CQR) and MEMS.** Self-reported medication-taking behavior of patients was measured with the validated CQR (19 Likert-scaled items, ranging from 1 to 4). MEMS (Aardex) were used as electronic monitors to measure medication-taking behavior based on device usage. A diary was given to patients to register unintended openings of the MEMS. Medication-taking behavior was operationalized as correct dosing, which is defined as the percentage of days in which the correct number of doses was taken.

**Clinical (laboratory) outcomes.** Clinical characteristics (i.e., serology, disease duration, type and current number of DMARD(s), and disease activity scores [i.e., the DAS28-CRP]) were extracted from patients' medical files by the local researchers.

**Study size.** Assuming a sample size requirement of 10 patients per variable, a study sample of 240 patients is sufficient to build a reliable linear model including a maximum of 8 independent variables. Taking into account a 15% loss to follow-up, a sample size of 275 patients was required.

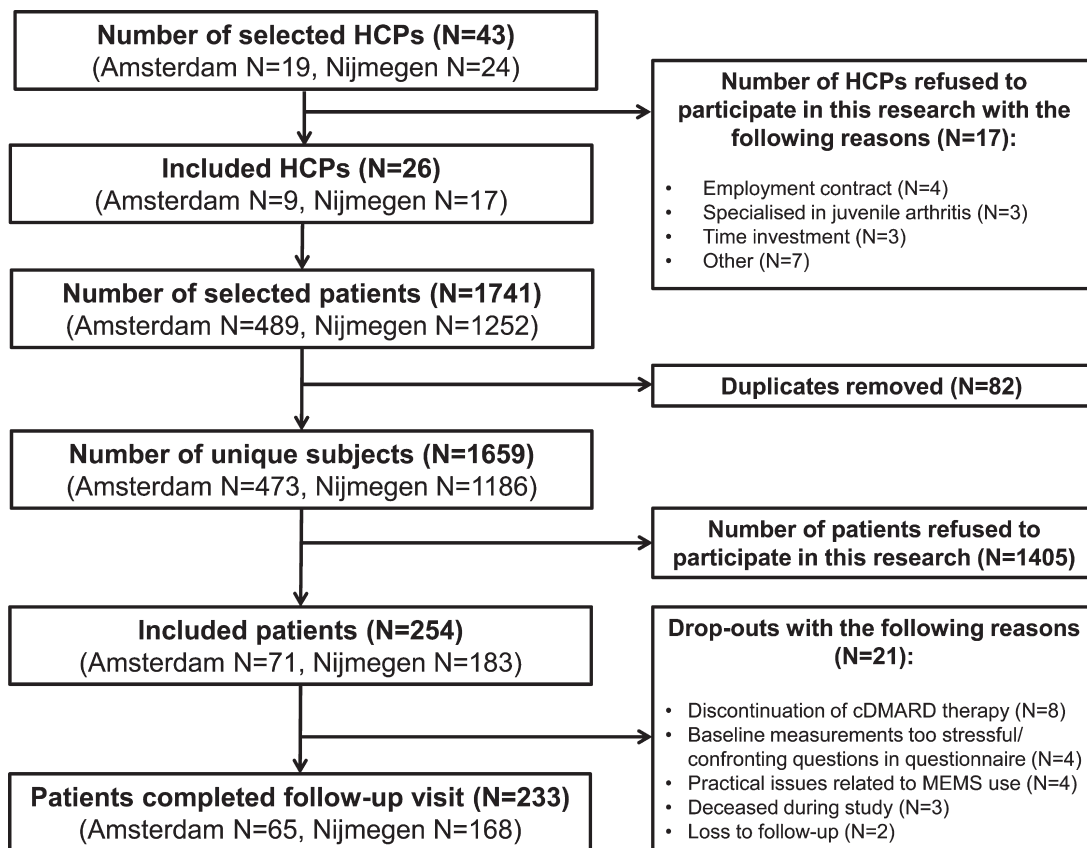
**Statistical analysis.** Statistical analyses were performed with Stata, version 13.1. Descriptive statistics were used for describing the characteristics of HCPs and patients. Data were presented as percentages in case of proportions. *P* values less than or equal to 0.05 were considered statistically significant.

Data obtained from the SC-IATs were expressed as response times in milliseconds (ms). The improved IAT scoring algorithm described by Greenwald and Nosek was used to calculate the *D* measure for strength of automatic associations (see Supplementary Table 1, available on the *Arthritis Care & Research* website at <http://onlinelibrary.wiley.com/doi/10.1002/acr.24186/abstract>, for a detailed description on calculating *D* measures) (28). *D* measures above zero indicated that HCPs or patients had relatively faster responses on the positive categorization rounds than on negative categorization rounds and were interpreted as a relatively more positive than negative implicit attitude toward cDMARDs, or a relatively more health-related association than a sickness-related association, and vice versa.

For explicit medication attitudes and associations, mean scale scores with SDs were calculated. Beliefs about medicines were operationalized as sum scale scores for necessity beliefs, sum scale scores for concern beliefs, and necessity–concerns differential (NCD) scores. NCD scores were calculated by subtracting the sum of the item scores for concerns from the sum of item scores for necessity beliefs. A positive NCD indicated that necessity beliefs dominate concern beliefs, and vice versa (27,29). Medication-taking behavior was operationalized as correct dosing (i.e., proportion of days with the correct number of doses taken). Self-reported, medication-taking behavior was calculated with the discriminant function for CQR items as described by de Klerk et al (30,31). Correct dosing measured with MEMS was calculated over a period of 3 months follow-up based on device usage.

Depending on the distribution and type of variables, independent samples *t*-tests, Pearson's chi-square tests, Fisher's exact tests, and proportion tests were performed to test for significant differences in the characteristics of HCPs between study sites. Spearman's rank correlations were used to describe the correlation between implicit and explicit HCP outcomes. Because of the explorative (rather than the hypothesis-testing) character of this study, no multiple testing corrections were performed over the separate correlational analyses.

Due to the hierarchical structure of data (i.e., patients were nested in the sample of HCPs), linear multilevel regression models were built to assess the association of the characteristics, implicit and explicit attitudes and health-related associations of HCPs, and beliefs about medicines with the following: patients' implicit attitudes and health-related associations, patients' explicit attitudes and health-related associations, patients' necessity and concern beliefs, correct dosing measured with both self-report and MEMS, and disease activity scores. Bivariate analyses were performed to select the most important predictors to prevent overfitting of the model due to the large number of variables measured in this study. Determinants with *P* values <0.2 were entered in the final models. These final models were adjusted for the following patient-related variables: age, sex, level of education, household situation (i.e., living alone versus living together with at least 1 person), disease duration, anti-cyclic citrullinated peptide status, hospital, and biologic DMARD use. Final models for correct



**Figure 1.** Flow chart of health care professionals (HCPs) and their patients with rheumatoid arthritis. cDMARDs = conventional disease-modifying antirheumatic drugs; MEMS = Medication Event Monitoring System.

dosing and disease activity scores were additionally adjusted for the patient's necessity and concern beliefs.

## RESULTS

**Study sample characteristics.** Of the 43 initially invited rheumatologists and PAs, 26 HCPs agreed to participate in this study (overall response rate 60.5%; Amsterdam response rate 47.4%; and Nijmegen response rate 70.8%) (Figure 1). The majority of participants (92.3%) had a current position as a rheumatologist and were male (69.2%). Participating HCPs had a mean  $\pm$  SD age of  $49.7 \pm 8.3$  years with an average of  $16.4 \pm 9.4$  years of

working experience. See Table 2 for a complete overview of HCP characteristics. Of the nonparticipating HCPs, 30.8% were male, and 71.4% had a current position as a rheumatologist. A total of 254 patients treated by these 26 different HCPs (overall response rate 15.3%; Amsterdam response rate 15.0%; and Nijmegen response rate 15.4%) agreed to participate in this study, which resulted in several patients per HCP, varying from 3 to 19 patients. Patients had a mean age of  $62.8 \pm 11.2$  years, 68.1% were female, 32.7% of the patients was highly educated, and 22.0% were living alone. Biologic DMARDs were prescribed to 32.7% of the patients, and the mean  $\pm$  SD disease duration of patients was  $11.8 \pm 9.0$  years. A more detailed description of all patient

**Table 2.** Characteristics of health care professionals in the field of rheumatology participating in the study\*

Characteristics of health care professionals	Nijmegen (n = 17)	Amsterdam (n = 9)	Overall (n = 26)	P
Age, mean $\pm$ SD years	48.5 $\pm$ 8.7	52.1 $\pm$ 7.4	49.7 $\pm$ 8.3	0.31
Female	7 (41.2)	1 (11.1)	8 (30.8)	0.11
Current position				0.28
Rheumatologist	15 (88.2)	9 (100)	24 (92.3)	
Physician assistant	2 (11.8)	0 (0.0)	2 (7.7)	
Working experience, mean $\pm$ SD years	14.9 $\pm$ 9.6	19.2 $\pm$ 8.7	16.4 $\pm$ 9.4	0.27
Patient contact per week, mean $\pm$ SD hours	18.4 $\pm$ 8.0	25.3 $\pm$ 10.7	20.8 $\pm$ 9.4	0.07
Right-handed	15 (88.2)	5 (55.6)	20 (76.9)	0.06

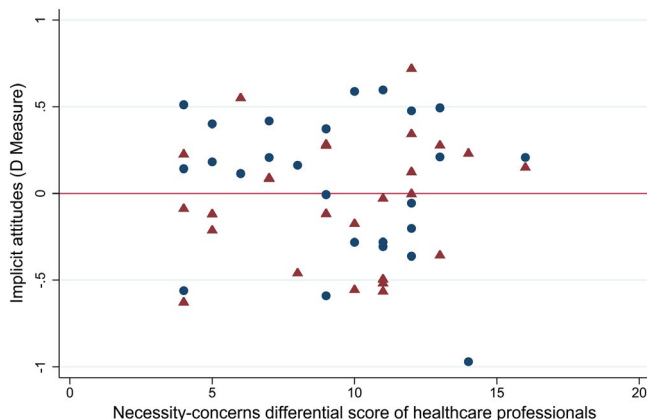
\* Values are the number (%) unless indicated otherwise.

characteristics can be found in Supplementary Table 1, available on the *Arthritis Care & Research* website at <http://onlinelibrary.wiley.com/doi/10.1002/acr.24186/abstract>.

**HCPs' attitudes, health-related associations, and beliefs.** The mean  $\pm$  SD *D* measure for implicit attitudes of HCPs was  $0.045 \pm 0.41$ , whereas the mean  $\pm$  SD *D* measure for implicit health-related associations was  $-0.037 \pm 0.36$ . The mean  $\pm$  SD scale score for explicit attitudes (i.e., positive–negative) was similar to the mean  $\pm$  SD scale score for explicit health-related associations ( $3.8 \pm 0.45$  and  $3.9 \pm 0.34$ , respectively). Regarding beliefs about medicines (necessity and concern beliefs), the mean sum scale score for the necessity beliefs of HCPs ( $20.9 \pm 1.77$ ) was higher than the mean sum scale for concern beliefs ( $11.5 \pm 2.19$ ). This resulted in a mean NCD-score for HCPs of  $9.4 \pm 3.35$ , which indicates that necessity beliefs outweigh concern beliefs about cDMARDs.

No significant correlation was found between the implicit attitudes and implicit health-related associations of HCPs nor between the implicit and explicit attitudes and health-related associations of HCPs. The same applied for implicit attitudes/associations and NCD scores ( $\rho = -0.10$ ,  $P = 0.63$ , and  $\rho = 0.22$ ,  $P = 0.29$ , respectively). This lack of association is illustrated in Figure 2. However, a significant correlation was found between the explicit attitudes of HCPs toward cDMARDs and their explicit health-related associations ( $\rho = 0.48$ ,  $P = 0.01$ ).

**Association of the attitudes and beliefs of HCPs about medicines with attitudes and beliefs of their patients.** Table 3 provides an overview of the final multilevel linear regression models with patients' implicit and explicit outcomes as dependent variables. HCP-related factors, including sociodemographic characteristics, implicit and explicit attitudes, and health-related associations combined with explicit beliefs



**Figure 2.** Lack of association between implicit measures (i.e., single-category implicit association test [SC-IAT] concept for attitudes and health-related associations) and differential scores of health care professionals' necessity concerns. Circles represent SC-IAT concept attitudes (positive–negative). Triangles represent SC-IAT concept associations (health–sickness).

about medicines were not significantly associated with patients' implicit and explicit outcomes. Only a few patient-related factors were significantly associated with patients' implicit and explicit outcomes. A high level of education of patients was significantly associated with more positive implicit attitudes toward cDMARDs, compared to patients with a low to medium level of education (coefficient 0.11 [95% confidence interval (95% CI) 0.001, 0.22]). The patient's age was significantly associated with their explicitly reported attitudes and health-related associations (coefficient 0.01 [95% CI 0.002, 0.02] and coefficient 0.01 [95% CI 0.001, 0.02], respectively), where older patients reported explicitly more positive attitudes and health-related associations than younger patients. Biologic DMARD users reported significantly higher sum scale scores for necessity beliefs than patients who were currently not treated with biologic DMARDs (coefficient 1.25 [95% CI 0.30, 2.20]). Patients who were living alone (coefficient  $-1.25$  [95% CI  $-2.40$ ,  $-0.11$ ]) or with a longer mean disease duration (coefficient  $-0.07$  [95% CI  $-0.12$ ,  $-0.02$ ]) reported significantly fewer concern beliefs than patients who were living together or who had a short mean disease duration.

#### Association of the attitudes, associations, and beliefs of HCPs with medication adherence and disease activity scores.

HCP-related factors, including sociodemographic characteristics, implicit and explicit attitudes, and health-related associations combined with beliefs about medicines were not significantly associated with correct dosing and disease activity scores (see Supplementary Table 2, available on the *Arthritis Care & Research* website at <http://onlinelibrary.wiley.com/doi/10.1002/acr.24186/abstract>). However, the patients' age, necessity beliefs, and concern beliefs were significantly associated with self-reported correct dosing (coefficient 0.02 [95% CI 0.01, 0.04], coefficient 0.10 [95% CI 0.06, 0.15], and coefficient  $-0.05$  [95% CI  $-0.09$ ,  $-0.002$ ], respectively). Higher age and higher necessity beliefs were associated with higher scores for self-reported correct dosing, whereas higher concern beliefs were associated with lower scores for self-reported correct dosing. Patients' disease duration and necessity beliefs were significantly associated with correct dosing measured with MEMS (coefficient  $-0.26$  [95% CI  $-0.48$ ,  $-0.04$ ] and coefficient 0.61 [95% CI 0.04, 1.17], respectively). A relatively longer disease duration was associated with lower scores for MEMS correct dosing, whereas higher necessity beliefs were associated with higher scores for MEMS correct dosing. Sum scale scores for patients' concern beliefs were significantly associated with disease activity scores (coefficient 0.04 [95% CI 0.003, 0.09]), where more concerns were associated with higher disease activity scores.

## DISCUSSION

This study demonstrated that HCP-related factors, including sociodemographic characteristics, implicit and explicit attitudes, and health-related associations combined with explicit

**Table 3.** Results of the multivariate, multilevel, linear regression models and predictors for patients' implicit and explicit attitudes, health-related associations, and beliefs about medicines\*

	Patient's implicit attitudes	Patient's implicit health-related associations	Patient's explicit attitudes	Patient's explicit health-related associations	Patient's necessity beliefs about medicines	Patient's concern beliefs about medicines
<b>HCP-related factors</b>						
Age, years	†	†	†	†	†	†
Sex, female (yes/no)	†	†	†	†	†	†
Current position rheumatologist (yes/no)	†	†	-0.13 (-0.54, 0.29)	0.19 (-0.32, 0.71)	†	-0.55 (-2.27, 1.17)
Working experience, years	†	†	-0.005 (-0.015, 0.006)	†	†	†
Mean hours of patient contact per week	†	†	†	†	0.04 (-0.01, 0.10)	†
<b>HCP's implicit and explicit attitudes and health-related associations</b>						
Implicit attitudes, mean <i>D</i> measure	†	†	†	†	†	†
Implicit health-related associations, mean <i>D</i> measure	†	†	-0.19 (-0.46, 0.07)	-0.01 (-0.34, 0.32)	†	†
Explicit attitudes, mean scale score	†	†	0.09 (-0.20, 0.38)	0.24 (-0.12, 0.60)	0.34 (-0.86, 1.33)	-0.55 (-1.78, 0.69)
Explicit health-related associations, mean scale score	†	†	0.12 (-0.20, 0.43)	0.11 (-0.29, 0.50)	1.02 (-0.31, 2.34)	†
<b>HCP's beliefs about medicines</b>						
Necessity beliefs, sum scale scores	†	†	-0.05 (-0.10, 0.007)	-0.02 (-0.09, 0.04)	0.10 (-0.16, 0.36)	†
Concern beliefs, sum scale scores	†	†	†	†	†	†
<b>Patient-related factors</b>						
Age, years	†	0.004 (-0.0004, 0.008)	0.01 (0.002, 0.02)‡	0.01 (0.001, 0.02)‡	†	†
Sex, female (yes/no)	†	†	†	†	†	†
High level of education (yes/no)	0.11 (0.001, 0.22)‡	0.08 (-0.02, 0.18)	†	†	†	†
Household situation, alone (yes/no)	†	0.08 (-0.03, 0.19)	†	†	†	-1.25 (-2.40, -0.11)‡
Disease duration, years	†	†	†	†	0.04 (-0.01, 0.09)	-0.07 (-0.12, -0.02)‡
Anti-CCP positive (yes/no)	†	†	†	†	†	†
Biologic DMARD (yes/no)	-0.06 (-0.17, 0.05)	†	-0.06 (-0.25, 0.14)	-0.14 (-0.38, 0.09)	1.25 (0.30, 2.20)‡	†
Hospital Nijmegen (yes/no)	†	†	†	†	†	-0.87 (-2.05, 0.31)

\* Values are the coefficient (95% confidence interval). Reference level was "no" for predictors with "yes/no" categories. Anti-CCP = anti-cyclic citrullinated peptide; DMARD = disease-modifying antirheumatic drug; HCP = health care professional.

† Covariate not included in the final multivariate model due to the level of significance of this covariate in bivariate analysis ( $P \geq 0.2$ ).

‡ Predictor remained significant in the multivariate, multilevel, regression models.



beliefs about medicines were not significantly associated with patients' implicit and explicit attitudes and associations, as well as patients' medication-taking behavior and disease activity scores. Only a few patient-related factors were significantly associated with the outcome measures in this study: the patient's age (outcome measures: self-reported correct dosing and the patient's explicit attitudes and health-related associations), level of education (outcome measure: the patient's implicit attitudes), household situation (outcome measure: the patient's concern beliefs about medicines), disease duration (outcome measures: MEMS correct dosing and the patient's concern beliefs about medicines), biologic DMARD use (outcome measure: the patient's necessity beliefs about medicines), sum scale scores for the patient's necessity beliefs (outcome measure: MEMS correct dosing and self-reported correct dosing), and concern beliefs (outcome measures: self-reported correct dosing and the patient's disease activity scores). Regarding medication-taking behavior and disease activity scores, the patient's necessity beliefs and concern beliefs were the only modifiable variables as possible targets for improving medication-taking behavior and disease activity in patients with RA.

To our knowledge, this is the first study that investigates the implicit and explicit associations of HCPs with medication in the field of rheumatology. Although some research has been carried out on implicit attitudes of HCPs, previous studies have predominantly focused on implicit attitudes toward other concepts rather than medication or medication-taking behavior (e.g., mental illness, sex, racial bias, and sexuality) (32–35). This makes it challenging to compare our findings with previous work.

Contrary to our expectations, the attitudes, health-related associations, and beliefs of HCPs were not significantly associated with those of their patients, indicating that the perception of HCPs regarding medication seems independent from patients' perceptions and subsequent medication-taking behavior. An explanation for this result might be that patients' attitudes, health-related associations, and beliefs about medicines rely more on previous experiences with medication, whereas the attitudes, health-related associations, and beliefs about medicines of HCPs might rely more on recommendations based on scientific evidence. Another explanation is that if an HCP has a particularly negative implicit or explicit attitude against certain medication it might influence other components of the patient–provider interaction rather than the outcomes measured in this study (e.g., style of communication, trust in the HCP, and patient satisfaction). However, it is possible that the implicit and explicit attitudes and health-related associations or beliefs about medication of HCPs are associated with those of their patients but were not detected in this study due to methodologic limitations. This thought is in line with the study of Fitzgerald et al, which recognized the complexity in studying the involvement of implicit outcomes in the

patient–provider interaction due to methodologic issues and the diversity in characteristics of both patients and HCPs (36).

One of the key strengths of this study is HCP and patient recruitment in 2 of the largest centers that specialize in rheumatology across The Netherlands, combined with the large sample size of patients treated by these HCPs. Another strength is the use of electronic drug monitors to measure medication-taking behavior of patients over a 3-month period in addition to self-reported medication-taking behavior. The use of multiple measurement instruments might, however, have contributed to an overestimation of adherence levels due to the patient's awareness of being monitored and the small amount of variance in adherence measures. Together, with the small amount of variance in explicit measures and the extensive working experience at the level of HCPs, this might have limited the possibility of detecting potential influences of HCPs. The validity of the SC-IATs, used for both study groups, might be questioned because patients might have had limited hand function in contrast with HCPs. This might provide an insufficient contrast between the experimental rounds in the SC-IATs at the patient level and a large contrast between study groups. Also, the design of the SC-IATs (i.e., words and pictures used as stimuli) might have influenced implicit outcomes because it is unclear if those words and pictures are optimally related to the patient's medication use and the prescription of cDMARDs by HCPs. However, pictures were created based on pharmacy records at participating study sites (i.e., manufacturer of the drugs, type of packaging, and appearance of the drug) to increase the ability of patients and HCPs to recognize the cDMARDs at a glance.

All HCPs who participated in this study were working in hospitals that specialized in rheumatology and reported extensive years of work experience. Therefore, caution must be applied for extrapolating our findings to HCPs who were working in more general hospitals or who recently specialized in the field of rheumatology. We have also focused on cDMARDs exclusively. It is, however, conceivable that the implicit and explicit attitudes of HCPs toward biologic DMARDs and recently introduced JAK inhibitors may differ from attitudes toward cDMARDs. On the level of patients, it is assumed that selection bias has occurred due to the large proportion of adherent patients, the small variety in ethnic background, the high percentage of patients who had a high level of education, and a long disease duration. In adherence research, the difficulty of recruiting patients who represent the general population is well recognized and often challenging (37,38).

In conclusion, the implicit and explicit attitudes and health-related associations of HCPs were not significantly associated with each other. Also, the sociodemographic characteristics and the implicit and explicit attitudes, associations, and beliefs about medicines of HCPs were not associated with those of their patients nor with correct dosing and patients' disease activity

scores. These findings provide some first insights into the potential (and the lack thereof) of the implicit and explicit perceptions of medication of HCPs in relation to patients' medication adherence and disease activity.

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## AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Ms van Heuckelum had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study conception and design.** van Heuckelum, Hebing, Vandeberg, Linn, Flendrie, Nurmohamed, van Dulmen, van den Ende, van den Bemt.

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**Analysis and interpretation of data.** van Heuckelum, Vandeberg, van Dulmen, van den Ende, van den Bemt.

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