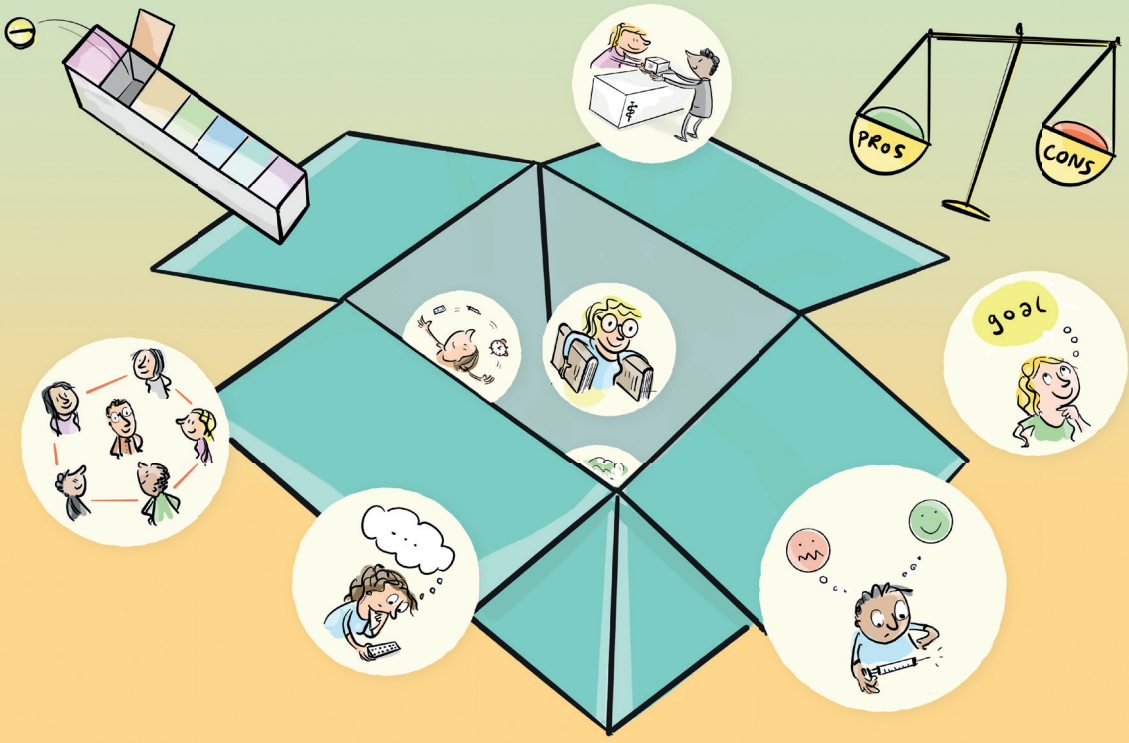
UNPACKING MEDICATION ADHERENCE

An Investigation of Barriers and Facilitators to DMARD Use in Inflammatory Arthritis: Patient and Healthcare Professional Perspectives and Communication



Marieke Voshaar

Stellingen

behorende bij het proefschrift:

Unpacking medication adherence

An investigation of barriers and facilitators to DMARD use in inflammatory arthritis: patient and healthcare professional perspectives and communication

1. In established rheumatoid arthritis, the patient is not merely the recipient of care, but a member of the multidisciplinary treatment team (based on this thesis)

2. Medication adherence cannot be improved by correcting patients; it requires understanding the capability, opportunity and motivation underlying their behaviour (based on this thesis)

3. What matters most for DMARD adherence is not remembering the medication, but having a reason to take it (based on this thesis)

4. Awareness of patients' medication barriers has little clinical value unless healthcare professionals invite patients to discuss them (based on this thesis)

5. Patient priorities should inform the selection of targets for adherence support, because the barriers most visible to healthcare professionals may differ from those most important to patients (based on this thesis)

6. Good medication communication requires meeting both the patient's need to understand and the patient's need to be understood (based on this thesis)

7. The absence of an adherence discussion during a consultation cannot be interpreted as evidence that the patient experiences no difficulties with medication use (based on this thesis)

8. "The most important thing in communication is hearing what is not being said." (Peter F. Drucker)

9. "I can't change the direction of the wind, but I can adjust my sails to always reach my destination." (Jimmy Dean) (Even when four supervisors issue four different weather reports)

10. "I love deadlines. I love the whooshing noise they make as they go by." (Douglas Adams)

Marieke Voshaar, 11 december 2026

UNPACKING MEDICATION ADHERENCE

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UNPACKING MEDICATION ADHERENCE

An investigation of Barriers and Facilitators to DMARD Use in Inflammatory Arthritis: Patient and Healthcare Professional Perspectives and Communication

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in het openbaar te verdedigen op

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UNPACKING MEDICATION ADHERENCE

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to be defended in public on

Friday, December 11, 2026,
at 12.30 pm

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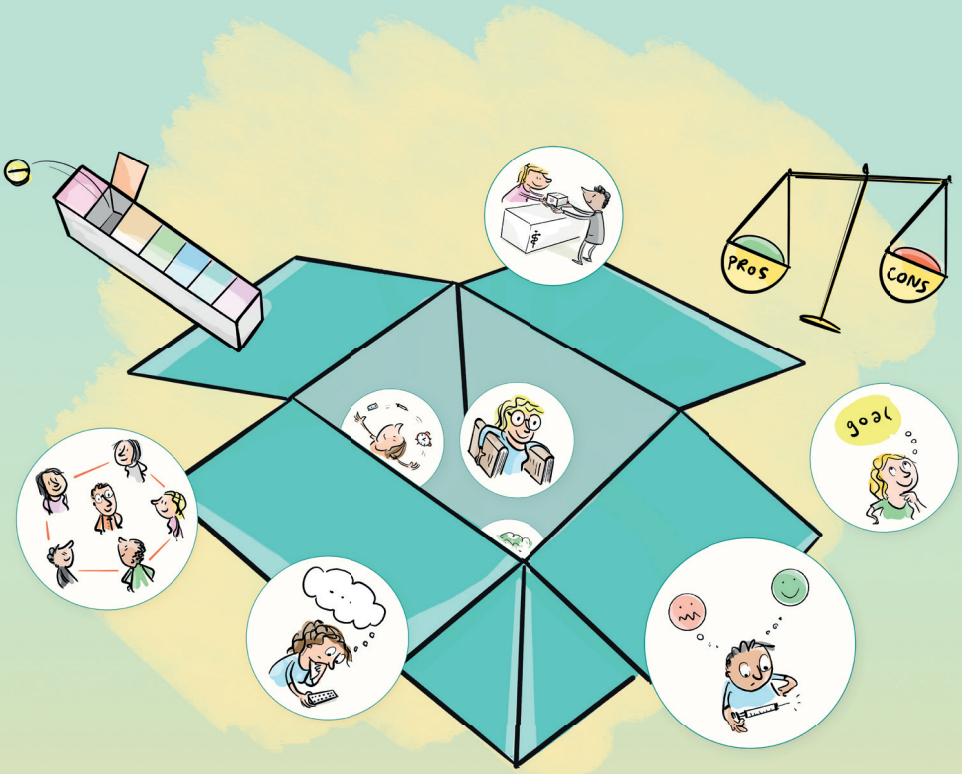
Prof. dr. J.M.W. Hazes (Erasmus MC)

“We cannot control every circumstance, but we can choose how to respond to it”

Inspired by Epictetus

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PROS
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Chapter 1

General introduction

RHEUMATOID ARTHRITIS (RA)

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disorder primarily characterized by inflammation of the synovial joints, leading to pain, swelling, and progressive joint destruction, fatigue, and decreased physical abilities.[1,2] Affecting approximately 0.5–1% of the global population, RA significantly compromises quality of life, resulting in disability and economic burden if untreated.[3,4] The clinical presentation of RA includes joint stiffness, especially in the morning or after periods of inactivity, and symmetrical joint involvement in areas such as the wrists, knees, and small joints of the hands.[5] Extra-articular manifestations, including cardiovascular disease, interstitial lung disease, amyloidosis and vasculitis, further contribute to the disease's morbidity.[6,7] RA can manifest at any age, from newborns to the elderly. The median age of RA symptom onset is approximately 45 years for women and 50 years for men, with a wide range, indicating that many individuals develop RA well before reaching old age.[8,9] RA is more common in women than in men, with an approximate female-to-male ratio of 3:1.[10] Early diagnosis and pharmacological treatment are critical for preventing irreversible joint damage and improving long-term outcomes.[11,12]

DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS (DMARDS)

Up to the last decades of the 20th century, the treatment of RA was symptomatic, providing pain relief and comfort to the affected patients, who apart from impaired functionality and dependency, were confronted with a considerable early mortality. Over the past decades parallel to more insight in the pathogenesis of the diseases, potential curative treatments were developed and improved. Presently, the key to treat RA effectively is early pharmacological treatment with disease-modifying anti-rheumatic drugs (DMARDs). They are classified into conventional synthetic DMARDs (csDMARDs), biologic DMARDs (bDMARDs), and targeted synthetic DMARDs (tsDMARDs), each with distinct mechanisms of action.[13,14] Early initiation and monitoring of DMARD therapy are pivotal to reach target or sustained remission and to prevent progression of structural damage.[15–17] Patients need to follow treatment regimens closely to fully benefit from DMARD therapy. Obviously the efficacy of DMARDs to control disease activity and prevent damage and late-complications is mediated by adherence.[2,18] Moreover, optimal DMARD

adherence correlates with improved patient-reported outcomes, such as reduced pain and enhanced physical functioning.[19] Nevertheless, RA patients' adherence to DMARDs is often suboptimal, ranging from 25% (underdosing) to 107% (overdosing), depending on the measurement method and population.[20–23]

MEDICATION NON-ADHERENCE IN RA

Medication adherence, defined by the World Health Organization (WHO), as "the extent to which a person's behaviour, taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a healthcare provider" is critical in RA management.[24] It is a multidimensional phenomenon shaped by patient-, therapy-, condition-, social/economic, and healthcare system–related factors. Several of these factors (i.e., patient perceived barriers and/or facilitators) have been linked to medication (non-) adherence although the associations are often weak and/or inconsistent (Figure 1).[21,23,28,50] In RA, (non-) adherence to DMARDs significantly impacts disease outcomes.[26–28] Non-adherence is associated with increased disease activity, greater healthcare utilization, and poorer functional outcomes.[7,23] Non-adherence is further linked to higher rates of irreversible joint damage, reduced productivity, and increased comorbidities, including cardiovascular and pulmonary complications.[29] Healthcare system and Social and Economic factors are also linked to medication non-adherence in chronic conditions, including rheumatoid arthritis.[30–38]

Medication non-adherence can be intentional or nonintentional. Nonintentional is often considered simply forgetting to perform the behaviour. Other examples of nonintentional non-adherence are when patients cannot afford the medication or medication is not available. Some patients are not able to swallow or inject the prescribed medications. In contrast, intentional non-adherence is related to purposeful deviation of the behaviour defined as "involving self-conscious planning and evaluations (beliefs about what is good or bad)".[39] Although they stem from different sources of motivation, both forms of non-adherence are not mutually exclusive, and thus often exist in any individual prescribed chronic disease treatment over the course of treatment.[40,41]

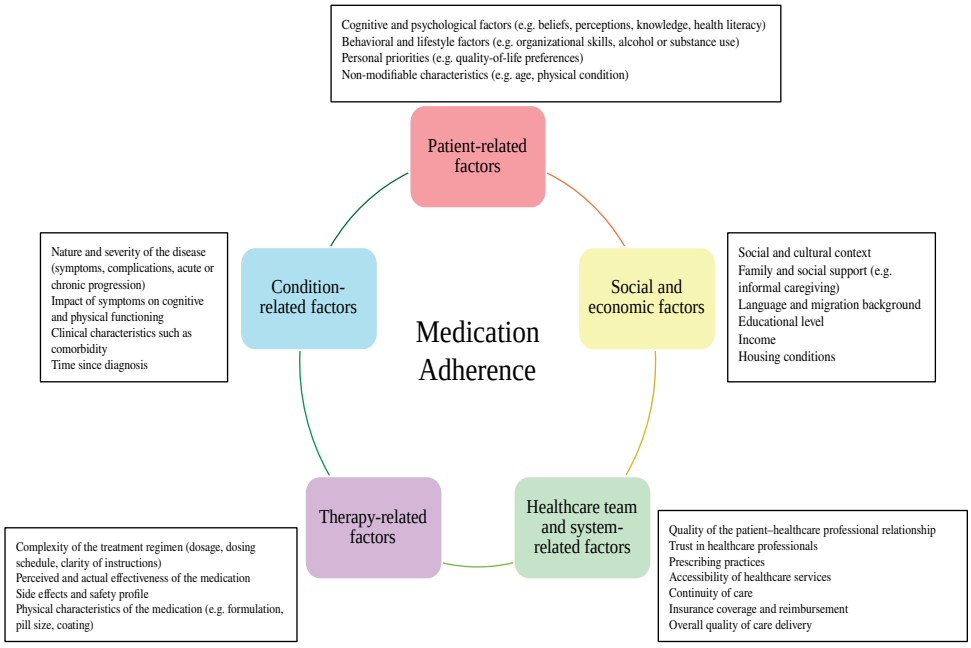


Figure 1. Barriers and Facilitators to Medication Adherence [24]

According to the Necessity-Concerns Framework of Horne and Weinman, intentional non-adherence is based on the assumption that patient's decision to take medication is driven by a cost-benefit assessment (see Figure 2).[42] Herein, personal beliefs about the necessity of taking the medication for maintaining or improving health are balanced against concerns about the potential adverse effects of taking the medication.[42,43] Many studies underline the importance of addressing these necessity beliefs and concerns about medication to improve adherence.[44-53] Mostly, stronger necessity beliefs were associated with better medication adherence, whereas concern beliefs were associated with decreased medication adherence.[46, 47, 48, 53] Therefore, necessity beliefs can be seen as facilitators and concerns as barriers to optimal medication adherence.

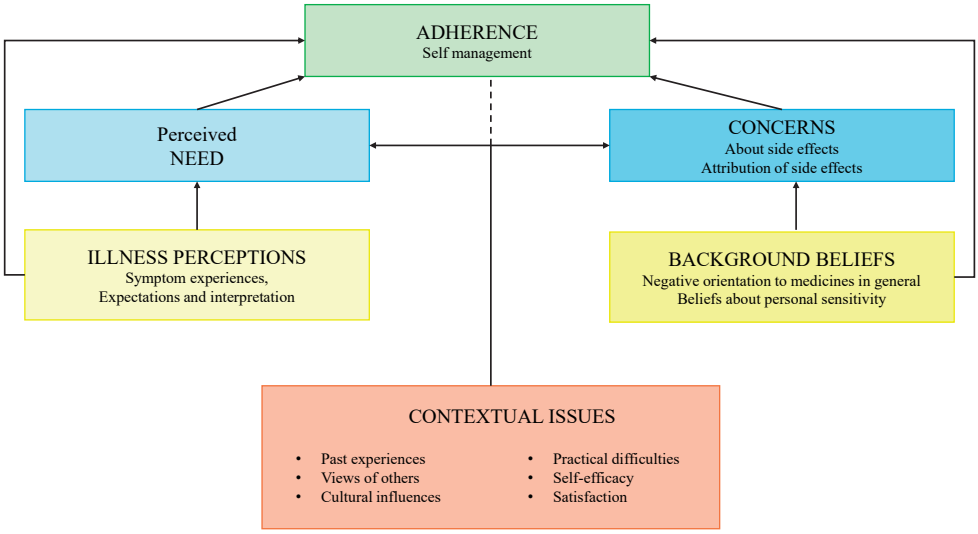


Figure 2. Patient adherence to medication is influenced by a number of factors relating to how the patient judges the necessity of their treatment relative to their concerns.[42]

BARRIERS AND FACILITATORS TO MEDICATION ADHERENCE

Understanding barriers and facilitators to DMARD use is critical to address medication adherence in RA.[53] Theory-informed qualitative research can help to gain more insight into these barriers and facilitators and provide targets for behavioural change strategies.

Barriers

Several studies explored barriers and facilitators to medication use, in general or RA-specific.

Salt and Frazier (2010) conducted a narrative review highlighting the identification of multiple factors influencing adherence, including patients' beliefs about medications, concerns regarding adverse effects, and the quality of communication with HCPs.[53] Notably, fears about side effects were found to be a major reason for non-adherence. Psychosocial factors also play a crucial role. Depression and anxiety, prevalent among patients with chronic illnesses, have been linked to lower adherence rates. A lack of social support further exacerbates this issue, as patients without encouragement from family or peers may struggle with medication routines. Barriers within the healthcare system include

inadequate patient education from HCPs, insufficient follow-up, and lack of shared decision-making. Patients who do not feel involved in their treatment decisions are less likely to remain adherent. Furthermore, the complexity of treatment regimens, requiring multiple daily doses or injectable medications, can contribute to non-adherence.

The authors noted that while issues like side effects are commonly addressed, other barriers such as cultural beliefs, health literacy, and socioeconomic status are often overlooked, partly because of the scarcity of focused research on these topics.

Similarly, Sanderson et al. (2010) conducted a qualitative study exploring patients' experiences with DMARDs.[54] Their findings revealed that patients often perceived DMARDs as powerful drugs with potentially severe side effects, contributing to a heightened awareness of their disease. This perception led to increased distress, uncertainty, and doubts about treatment efficacy, ultimately negatively affecting adherence.

Furthermore, Scheiman-Elazary et al. (2016) conducted a systematic review and meta-analysis, demonstrating that non-adherence to DMARDs is common among patients with rheumatoid arthritis.[19] The study emphasized that delayed onset of drug effectiveness and fear of side effects are significant barriers to adherence.

A review by Pasma et al. (2013) showed that a significant barrier to medication adherence is patients' lack of understanding about the necessity and benefits of DMARDs, leading to intentional non-adherence.[50] Patients who perceive their condition as mild or experience asymptomatic periods may be less inclined to adhere to long-term medication regimens. Additionally, medication side effects, such as gastrointestinal distress, fatigue, or immunosuppression, deter patients from consistent use. Other identified factors influencing medication adherence in rheumatoid arthritis patients were: patients' beliefs about medication, the complexity of treatment regimens, and the quality of patient-HCP communication.

However, the review also highlighted that certain barriers, particularly those related to individual patient perceptions and socioeconomic factors, are not thoroughly understood due to limited research in these areas.[50]

Economic factors, such as high medication costs and limited insurance coverage, are significant barriers in healthcare systems, where medication costs are not (fully) reimbursed. Patients facing financial constraints may ration their medication or forgo treatment altogether.[33,35] Additionally, disparities in healthcare access due to geographic location or transportation difficulties can further impede adherence.

While various studies have identified facilitators and barriers to DMARD adherence, there remains a need for more comprehensive research identifying and prioritizing these factors to develop targeted interventions.[55,56] Patient-centred strategies that promote education, enhance patient-HCP communication, and address psychosocial and economic barriers are crucial for improving adherence rates. Future research should focus on barriers, important to individual patient needs, to optimize medication adherence and, consequently, treatment outcomes. This thesis will add knowledge about which barriers and facilitators are important for patients, and which are *most* important to them. The outcomes can contribute to the development of useful routine clinical care to enhance adherence.

Facilitators

Facilitators to medication use may enhance adherence. In this thesis, barriers and facilitators will be taken into account. Some facilitators have been identified in previous studies.

A strong patient-provider relationship, characterized by open and understandable communication and shared decision-making, is one of the most effective facilitators of medication adherence. Patients who receive clear explanations about their medication's benefits and potential side effects are more likely to adhere to treatment plans.[53]

Social support from family, friends, and patient advocacy groups has been identified as a key facilitator. Encouragement from a support network can reinforce the importance of medication adherence and provide practical assistance, such as medication reminders or help with managing side effects.[25,53]

Other facilitators that may improve adherence have been mentioned in the study of Harrold and Andrade (2009). Simplifying medication regimens by reducing dosing frequency or utilizing combination therapies can significantly improve adherence. Fixed-dose combinations and

long-acting formulations help reduce the burden of treatment, making adherence more manageable for patients.[21]

The Role of HCPs in Addressing Patient Barriers and Facilitators to DMARD Adherence

HCPs play a critical role in identifying and addressing modifiable patient-specific barriers and facilitators to optimize adherence to DMARDs. To enhance adherence, HCPs must continuously assess and adapt their communication strategies to meet individual patients' evolving needs.[57,58] A misalignment between patients' perceived challenges and facilitators and the attending HCP's professional assessment can negatively impact adherence, ultimately reducing treatment efficacy and clinical outcomes.[46,48, 59]

Research indicates that HCPs often underestimate concerns regarding side effects and dependency on DMARDs compared to patients, leading to discrepancies in treatment priorities.[60] While patients primarily focus on maintaining normalcy and engaging in valued activities, HCPs tend to emphasize clinical outcomes and lifestyle modifications.[61] Understanding these differing perspectives is essential for improving adherence, as it allows for patient-centred care that aligns with both medical and personal goals.

As these different perspectives of barriers are categorized in the WHO domains, several examples can be given:

Patient-Related Factors: Individual beliefs about medication efficacy, self-management abilities, and coping mechanisms significantly influence adherence. HCPs must assess these factors and provide tailored support to address concerns and enhance adherence.[50]

Therapy-Related Factors: Many patients experience challenges related to DMARD side effects and the delayed onset of therapeutic benefits, which can discourage adherence. Transparent communication regarding treatment timelines and effective management of side effects is crucial for mitigating these concerns.[53]

Social and Economic Factors: External factors, including financial constraints, limited healthcare access, and inadequate social support, can pose significant barriers to adherence. Recognizing these contextual

influences enables HCPs to implement targeted interventions that improve adherence outcomes.[50]

Ultimately, patients are responsible for adhering to prescribed medication regimens. However, HCPs can play a pivotal role in fostering adherence through personalized education, shared decision-making, behavioural interventions, and social support mechanisms. By identifying, exploring and handling medical and personal barriers, HCPs can contribute to improved disease management and better health outcomes for patients with rheumatoid arthritis (RA).

Theoretical framework to identify barriers and facilitators to DMARD use

Although previous studies have explored barriers to medication use, a robust theoretical framework is needed to comprehensively and systematically identify and ultimately address barriers and facilitators to DMARD use. Different models and theories help systematically explore non-adherence drivers and identify targeted interventions.[50,51,62] However, existing approaches have not sufficiently identified adherence barriers.[49,51,63-68] This may be because models like the Health Belief Model[64] , Theory of Reasoned Action[67], Theory of Planned Behaviour[65], and Social Cognitive Theory[66] were designed to explain or predict behaviours rather than drive adherence interventions. Effective adherence models must incorporate behavioural change elements, such as skills[70] and environment[71], which some theories overlook.

The Theoretical Domains Framework (TDF)[69] , derived from 33 health behaviour theories, addresses this gap by encompassing 12 theoretical domains. The Theoretical Domains Framework (TDF) provides a theory-informed approach to identify determinants of behaviour, grouped into domains, relevant for behavioural change and implementation strategies.[70,72,73] In addition to the TDF, the Behaviour Change Wheel helps categorize identified barriers and facilitators under the three components of the Behaviour Change Wheel (COM-B): capability, opportunity, and motivation. The COM-B can be effectively used in a process of designing and implementing intervention tools.[71]

Interventions based on COM-B and TDF effectively target specific behavioural barriers.[71,72] So far, the TDF has been applied to medication adherence only in cardiovascular disease, leading to an adapted version, the Identification of Medication Adherence Barriers Model (IMAB), which

includes ten of the original 12 TDF domains[74] (see Fig. 3). It covers both individual and organizational theories, reducing the risk of omitting key adherence factors, particularly in DMARD treatment.

In this thesis the IMAB will be applied to identify both facilitators and barriers of DMARD use by patients and by HCPs. Although the IMAB was developed to identify medication adherence *barriers*, the studies in this thesis will focus on identifying *facilitators* as well using the same domains of this model.

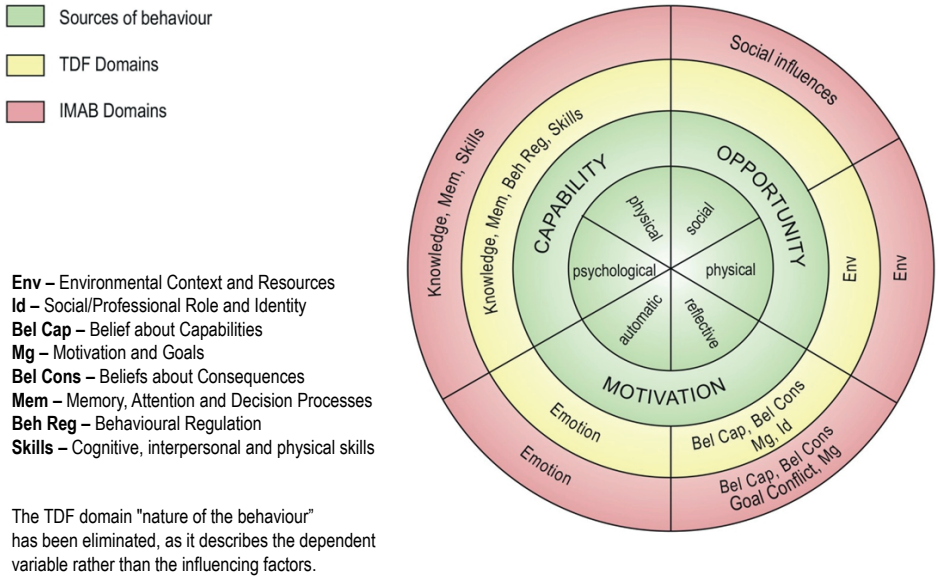


Figure 3. COM-B, derived from the Behaviour Change Wheel[71], TDF[69], and IMAB[74]

Patient-centred communication

Patients need to feel safe to express their (non-)adherence, as this can be a delicate subject. The communication style should therefore be open and non-judgemental.

Although a robust patient–HCP relationship is vital for adherence, systemic barriers, including inadequate organisational infrastructure (e.g. at pharmacies)[78] poor insurance coverage [34], fragmented medication distribution [35], insufficient HCP training [36], overburdened HCPs, limited consultation times [37] and gaps in patient education and follow-up [38],

undermine this relationship. Patient-centred communication improves adherence by fostering trust and shared responsibility.[55] Notably, effective patient–HCP communication increases adherence; a meta-analysis by Zolnierek and DiMatteo[55] found that optimal communication improved adherence by 19%, with further gains of 12% when communication skills were enhanced by offering physicians communication training.

Effective patient-HCP communication is a two-way dialogue. In that dialogue, both parties listen and speak without (being) interrupting; they ask clarifying questions, express their concerns and opinions, exchange information, and grasp entirely and understand what the others mean.[36,75] Thus, effective communication requires at least two active participants ("it takes two to tango"): an informed and activated patient and a prepared and pro-active HCP. [61, 76] Healthcare professionals should be aware and open to understand patients' barriers to medication use. While prominent obstacles such as side effects and concerns about long-term medication consequences are well-documented, other barriers remain less apparent and are not as extensively investigated. These findings suggest that there is a significant gap in the literature concerning the full spectrum of barriers to medication adherence. This gap underscores the need for more comprehensive research to inform patient-centred communication strategies. Exploring whether HCPs are well informed about the potentially broad variation of barriers and facilitators to DMARD use in patients with RA, and to what extent and how barriers to DMARD use are discussed in routine clinical consultations is warranted.

Besides the HCPs, patients also have an active role to foster the communication about their medication use and the barriers they experience. To stimulate this active role, five different PCC activities can be distinguished:(1) patient education, about medication (use) (2) patient involvement/shared decision-making when a drug is prescribed, (3) patient empowerment/self-management, (4) involvement of family and friends and (5) physical and emotional support. Scholl et al.'s Patient-Centred Care (PCC) model stimulates collaborative consultations that tailor interventions to individual needs through education, shared decision-making, and support.[77]

AIM AND OUTLINE OF THIS THESIS

The aim of this thesis is to add knowledge about which barriers and facilitators influence DMARD use in patients with inflammatory arthritis (predominantly rheumatoid arthritis). This is relevant, as facilitators and barriers can impact (non-) adherent behaviour and, consequently, treatment outcomes and quality of life. Involving the patient as an individual, with unique needs, concerns and preferences has a relevant impact on treatment outcomes (safety, effectiveness and costs). Patient centred care (PCC) empowers patients to take greater personal responsibility for their own treatment; this approach is discussed in Chapter 2. This narrative review summarizes the existing evidence on patient-centred care (PCC) in rheumatoid arthritis (RA), a healthcare approach that emphasises patients' preferences, needs and values, with particular attention to medication adherence.

Given the complexity of non-adherent behaviour, this thesis reports on two studies conducted to explore the barriers and facilitators to medication use reported by patients (Chapter 3), as well as the barriers and facilitators that patients consider most important (Chapter 4). In Chapter 3, barriers and facilitators to DMARD use were assessed using focus groups and questionnaires. The COM-B model and an adapted Theoretical Domains Framework (TDF) were used to categorize these barriers and facilitators. In Chapter 4, the patient-reported barriers and facilitators to DMARD use identified in Chapter 3 were prioritized by patients using maximum difference scaling (also known as best-worse scaling).

In Chapter 5, the HCPs perspectives on the barriers and facilitators to medication use experienced by patients were explored using the adapted TDF framework. The final study (Chapter 6) examined whether, and which, barriers were addressed in real-life outpatient rheumatology consultations, as well as how HCPs responded when patients mentioned a barrier, with specific focus on communication behaviour. This thesis concludes with a summary of all findings and a general discussion (Chapter 7 and Chapter 8).

REFERENCES

1. Firestein, G. S. (2003). Evolving concepts of rheumatoid arthritis. *Nature, 423*(6937), 356–361.
2. Smolen, J. S., Landewé, R., Bijlsma, J., et al. (2020). EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological DMARDs: 2019 update. *Annals of the Rheumatic Diseases, 79*(6), 685–699. https://doi.org/10.1136/annrheumdis-2019-216655
3. Cooper, N. J. (2000). Economic burden of rheumatoid arthritis: A systematic review. *Rheumatology, 39*(1), 28–33.
4. Hsieh, P.-H., Wu, O., Geue, C., McIntosh, E., McInnes, I. B., & Siebert, S. (2020). Economic burden of rheumatoid arthritis: A systematic review of literature in biologic era. *Annals of the Rheumatic Diseases, 79*(6), 771–777. https://doi.org/10.1136/annrheumdis-2019-216243
5. Aletaha, D., Neogi, T., Silman, A. J., et al. (2010). 2010 rheumatoid arthritis classification criteria: An American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Annals of the Rheumatic Diseases, 69*(9), 1580–1588. https://doi.org/10.1136/ard.2010.138461
6. Turesson, C., & Matteson, E. L. (2014). Extra-articular features of rheumatoid arthritis and systemic involvement. *Rheumatic Disease Clinics of North America, 40*(4), 547–562.
7. Aviña-Zubieta, J. A., Thomas, J., Sadatsafavi, M., Lehman, A. J., & Lacaille, D. (2012). Risk of incident cardiovascular events in patients with rheumatoid arthritis: A meta-analysis of observational studies. *Annals of the Rheumatic Diseases, 71*(9), 1524–1529.
8. Wasserman, A. M. (2011). Diagnosis and management of rheumatoid arthritis. *American Family Physician, 84*(11), 1245–1252
9. Myasoedova, E., Crowson, C. S., Kremers, H. M., Therneau, T. M., & Gabriel, S. E. (2010). Is the incidence of rheumatoid arthritis rising? Results from Olmsted County, Minnesota, 1955–2007. *Arthritis & Rheumatism, 62*(6), 1576–1582.
10. Gabriel, S. E. (2001). The epidemiology of rheumatoid arthritis. *Rheumatic Disease Clinics of North America, 27*(2), 269–281.
11. van Nies, J. A. B., Tsonaka, R., Gaujoux-Viala, C., Fautrel, B., & van der Helm-van Mil, A. H. M. (2015). Evaluating relationships between symptom duration and persistence of rheumatoid arthritis: Does a window of opportunity exist? Results on the Leiden Early Arthritis Clinic and ESPOIR cohorts. *Annals of the Rheumatic Diseases, 74*(5), 806–812. https://doi.org/10.1136/annrheumdis-2014-206047
12. Smolen, J. S., Aletaha, D., & McInnes, I. B. (2016). Rheumatoid arthritis. *The Lancet, 388*(10055), 2023–2038. https://doi.org/10.1016/S0140-6736(16)30173-8
13. Smolen, J. S., Breedveld, F. C., Burmester, G. R., et al. (2016). Treating rheumatoid arthritis to target: 2014 update of the recommendations of an international task force. *Annals of the Rheumatic Diseases, 75*(1), 3–15. https://doi.org/10.1136/annrheumdis-2015-207524
14. O'Shea, J. J., Kontzias, A., Yamaoka, K., Tanaka, Y., & Laurence, A. (2013). Janus kinase inhibitors in autoimmune diseases. *Annals of the Rheumatic Diseases, 72*(Suppl 2), ii111–ii115. https://doi.org/10.1136/annrheumdis-2012-202576

15. Aletaha, D., & Smolen, J. S. (2018). Diagnosis and management of rheumatoid arthritis: A review. *JAMA, 320*(13), 1360–1372. https://doi.org/10.1001/jama.2018.13103

16. Nell, V. P. K., Machold, K. P., Eberl, G., Stamm, T. A., Uffmann, M., & Smolen, J. S. (2004). Benefit of very early referral and very early therapy with disease-modifying anti-rheumatic drugs in patients with early rheumatoid arthritis. *Rheumatology, 43*(7), 906–914. https://doi.org/10.1093/rheumatology/keh199

17. van Vollenhoven, R. (2019). Treat-to-target in rheumatoid arthritis - are we there yet? *Nature Reviews. Rheumatology*, *15*(3), 180–186. https://doi.org/10.1038/s41584-019-0170-5.

18. Contreras-Yáñez, I., Ponce De León, S., Cabiedes, J., Rull-Gabayet, M., & Pascual-Ramos, V. (2010). Inadequate therapy behavior is associated to disease flares in patients with rheumatoid arthritis who have achieved remission with disease-modifying antirheumatic drugs. *The American Journal of the Medical Sciences*, *340*(4), 282–290. https://doi.org/10.1097/MAJ.0b013e3181e8bcb0

19. Scheiman-Elazary, A., Duan, L., Shourt, C., et al. (2016). The rate of adherence to antiarthritis medications and associated factors among patients with rheumatoid arthritis: A systematic literature review and meta-analysis. *The Journal of Rheumatology, 43*(3), 512–523. https://doi.org/10.3899/jrheum.141371

20. de Klerk, E., van der Heijde, D., Landewé, R., van der Tempel, H., Urquhart, J., & van der Linden, S. (2003). Patient compliance in rheumatoid arthritis, polymyalgia rheumatica, and gout. *The Journal of Rheumatology*, *30*(1), 44–54.

21. Harrold, L. R., & Andrade, S. E. (2009). Medication adherence of patients with selected rheumatic conditions: A systematic review of the literature. *Seminars in Arthritis and Rheumatism, 38*(5), 396–402. https://doi.org/10.1016/j.semarthrit.2008.01.011

22. Wabe, N., Wojciechowski, J., Wechalekar, M. D., Cleland, L. G., McWilliams, L., Lee, A., Proudman, S., & Wiese, M. D. (2017). Disease activity trajectories in early rheumatoid arthritis following intensive DMARD therapy over 3 years: association with persistence to therapy. *International Journal of Rheumatic Diseases*, *20*(10), 1447–1456. https://doi.org/10.1111/1756-185X.13184

23. Neame, R., & Hammond, A. (2005). Beliefs about medications: A questionnaire survey of people with rheumatoid arthritis. *Rheumatology, 44*(6), 762–767. https://doi.org/10.1093/rheumatology/keh587

24. World Health Organization. (2003). *Adherence to long-term therapies: Evidence for action*. Geneva, Switzerland: World Health Organization.

25. DiMatteo, M. R. (2004). Social support and patient adherence to medical treatment: A meta-analysis. *Health Psychology, 23*(2), 207–218. https://doi.org/10.1037/0278-6133.23.2.207

26. Waimann, C. A., Marengo, M. F., de Achaval, S., et al. (2013). Electronic monitoring of oral therapies in ethnically diverse and economically disadvantaged patients with rheumatoid arthritis: Consequences of low adherence. *Arthritis & Rheumatism, 65*(6), 1421–1429. https://doi.org/10.1002/art.37917

27. de Thurah, A., Nørgaard, M., Harder, I., & Stengaard-Pedersen, K. (2010). Compliance with methotrexate treatment in patients with rheumatoid arthritis: Influence of patients' beliefs about the medicine. *Rheumatology International, 30*(11), 1441–1448. https://doi.org/10.1007/s00296-009-1160-8

28. van den Bemt, B. J. F., Zwikker, H. E., & van den Ende, C. H. M. (2012). Medication adherence in patients with rheumatoid arthritis: A critical appraisal of the existing literature. *Expert Review of Clinical Immunology, 8*(4), 337–351. https://doi.org/10.1586/eci.12.23
29. Osterberg, L., & Blaschke, T. (2005). Adherence to medication. *New England Journal of Medicine, 353*(5), 487–497. https://doi.org/10.1056/NEJMra050100
30. Nieuwlaat, R., Wilczynski, N., Navarro, T., et al. (2014). Interventions for enhancing medication adherence. *Cochrane Database of Systematic Reviews*, (11), CD000011. https://doi.org/10.1002/14651858.CD000011.pub4
31. Horne, R., & Weinman, J. (1999). Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. *Journal of Psychosomatic Research, 47*(6), 555–567.
32. Zangi, H. A., Ndosi, M., Adams, J., et al. (2015). EULAR recommendations for patient education for people with inflammatory arthritis. *Annals of the Rheumatic Diseases, 74*(6), 954–962. https://doi.org/10.1136/annrheumdis-2014-206807
33. Bigdeli, M., Jacobs, B., Tomson, G., et al. (2013). Access to medicines from a health system perspective. *Health Policy and Planning, 28*(7), 692–704. https://doi.org/10.1093/heapol/czs108
34. Mackintosh, M., Channon, A., Karan, A., Selvaraj, S., Cavagnero, E., & Zhao, H. (2016). What is the private sector? Understanding private provision in the health systems of low-income and middle-income countries. *Lancet (London, England)*, *388*(10044), 596–605. https://doi.org/10.1016/S0140-6736(16)00342-1
35. Cameron, A., Ewen, M., Ross-Degnan, D., Ball, D., & Laing, R. (2009). Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis. *Lancet (London, England)*, *373*(9659), 240–249. https://doi.org/10.1016/S0140-6736(08)61762-6
36. Street, R. L., Jr., Makoul, G., Arora, N. K., & Epstein, R. M. (2009). How does communication heal? Pathways linking clinician–patient communication to health outcomes. *Patient Education and Counseling, 74*(3), 295–301.
37. Shanafelt, T. D., Boone, S., Tan, L., Dyrbye, L. N., Sotile, W., Satele, D., West, C. P., Sloan, J., & Oreskovich, M. R. (2012). Burnout and satisfaction with work-life balance among US physicians relative to the general US population. *Archives of Internal Medicine*, *172*(18), 1377–1385. https://doi.org/10.1001/archinternmed.2012.3199
38. Lorig, K. R., & Holman, H. (2003). Self-management education: History, definition, outcomes, and mechanisms. *Annals of Behavioral Medicine, 26*(1), 1–7.
39. Lehane, E., & McCarthy, G. (2007). Intentional and unintentional medication non-adherence: A comprehensive framework for clinical research and practice? A discussion paper. *International Journal of Nursing Studies*, *44*(8), 1468–1477. https://doi.org/10.1016/j.ijnurstu.2006.07.
40. Gadkari, A. S., & McHorney, C. A. (2012). Unintentional non-adherence to chronic prescription medications: how unintentional is it really? *BMC Health Services Research*, *12*, 98. https://doi.org/10.1186/1472-6963-12-98
41. Easthall, C., & Barnett, N. (2017). Using Theory to Explore the Determinants of Medication Adherence; Moving Away from a One-Size-Fits-All Approach. *Pharmacy (Basel, Switzerland)*, *5*(3). https://doi.org/10.3390/pharmacy5030050

42. Horne, R. (2006). Compliance, adherence, and concordance: Implications for asthma treatment. *Chest, 130*(1 Suppl), 65S–72S.

43. Horne, R. (1999). Patients' beliefs about treatment: The hidden determinant of treatment outcome? *Journal of Psychosomatic Research, 47*(6), 491–495.

44. Elliott, R. A. (2008). Poor adherence to medication in adults with rheumatoid arthritis: Reasons and solutions. *Disease Management & Health Outcomes, 16*(1), 13–29. https://doi.org/10.2165/00115677-200816010-00003

45. Clifford, S., Barber, N., & Horne, R. (2008). Understanding different beliefs held by adherers, unintentional nonadherers, and intentional nonadherers: Application of the Necessity-Concerns Framework. *Journal of Psychosomatic Research, 64*(1), 41–46. https://doi.org/10.1016/j.jpsychores.2007.05.004

46. Menckeberg, T. T., Bouvy, M. L., Bracke, M., et al. (2008). Beliefs about medicines predict refill adherence to inhaled corticosteroids. *Journal of Psychosomatic Research, 64*(1), 47–54. https://doi.org/10.1016/j.jpsychores.2007.07.016

47. Clifford, S., Barber, N., Elliott, R., Hartley, E., & Horne, R. (2006). Patient-centred advice is effective in improving adherence to medicines. *Pharmacy World & Science, 28*(3), 165–170. https://doi.org/10.1007/s11096-006-9026-6

48. van Steenis, M., Driesenaar, J., Bensing, J., et al. (2014). Relationship between medication beliefs, self-reported and refill adherence, and symptoms in patients with asthma using inhaled corticosteroids. *Patient Preference and Adherence, 8*, 83–91. https://doi.org/10.2147/PPA.S44185

49. Treharne, G. J., Lyons, A. C., & Kitas, G. D. (2004). Medication adherence in rheumatoid arthritis: Effects of psychosocial factors. *Psychology, Health & Medicine, 9*(3), 337–349. https://doi.org/10.1080/13548500410001721909

50. Pasma, A., van 't Spijker, A., Hazes, J. M. W., Busschbach, J. J. V., & Luime, J. J. (2013). Factors associated with adherence to pharmaceutical treatment for rheumatoid arthritis patients: A systematic review. *Seminars in Arthritis and Rheumatism, 43*(1), 18–28. https://doi.org/10.1016/j.semarthrit.2012.12.001

51. Brus, H., van de Laar, M., Taal, E., Rasker, J., & Wiegman, O. (1999). Determinants of compliance with medication in patients with rheumatoid arthritis: The importance of self-efficacy expectations. *Patient Education and Counseling, 36*(1), 57–64.

52. van den Bemt, B. J., van den Hoogen, F. H., Benraad, B., Hekster, Y. A., van Riel, P. L., & van Lankveld, W. (2009). Adherence rates and associations with nonadherence in patients with rheumatoid arthritis using disease modifying antirheumatic drugs. *The Journal of Rheumatology, 36*(10), 2164–2170. https://doi.org/10.3899/jrheum.081204

53. Salt, E., & Frazier, S. K. (2010). Adherence to disease-modifying antirheumatic drugs in rheumatoid arthritis patients: A narrative review of the literature. *Orthopaedic Nursing, 29*(4), 260–275. https://doi.org/10.1097/NOR.0b013e3181e5c2c9

54. Sanderson, T., Morris, M., Calnan, M., Richards, P., & Hewlett, S. (2010). What outcomes from pharmacological treatments are important to people with rheumatoid arthritis? Creating the basis of a patient core set. *Arthritis Care & Research, 62*(5), 640–646. https://doi.org/10.1002/acr.20034

55. Zolnierek, K. B. H., & DiMatteo, M. R. (2009). Physician communication and patient adherence to treatment: A meta-analysis. *Medical Care, 47*(8), 826–834.

56. Mathijssen, E. G. E., van den Bemt, B. J. F., Wielsma, S., van den Hoogen, F. H. J., & Vriezekolk, J. E. (2020). Exploring healthcare professionals' knowledge, attitudes and experiences of shared decision making in rheumatology. *RMD Open, 6*(1), e001121. https://doi.org/10.1136/rmdopen-2019-001121

57. Nota, I., Drossaert, C. H., Taal, E., & van de Laar, M. A. (2014). Arthritis patients' motives for (not) wanting to be involved in medical decision-making and the factors that hinder or promote patient involvement. *Clinical Rheumatology, 35*(5), 1225–1235.

58. Zwikker, H. E., Lesuis, N., den Broeder, A. A., et al. (2017). Rheumatologists' beliefs about medication barely differ from patients' medication beliefs. *European Journal for Person Centered Healthcare, 5*(3), 308–314.

59. Ferguson, K., & Bole, G. G. (1979). Family support, health beliefs, and therapeutic compliance in patients with rheumatoid arthritis. *Patient Counselling and Health Education, 1*(3), 101–105.

60. Lorish, C. D., Richards, B., & Brown, S. (1989). Missed medication doses in rheumatic arthritis patients: Intentional and unintentional reasons. *Arthritis Care and Research, 2*(1), 3–9.

61. Schoenthaler, A., Basile, M., West, T. V., & Kalet, A. (2018). It takes two to tango: A dyadic approach to understanding the medication dialogue in patient-provider relationships. *Patient Education and Counseling, 101*(8), 1500–1505. https://doi.org/10.1016/j.pec.2018.02.009

62. Park, D. C., Hertzog, C., Leventhal, H., et al. (1999). Medication adherence in rheumatoid arthritis patients: Older is wiser. *Journal of the American Geriatrics Society, 47*(2), 172–183.

63. Viller, F., Guillemin, F., Briançon, S., et al. (1999). Compliance to drug treatment of patients with rheumatoid arthritis: A 3-year longitudinal study. *The Journal of Rheumatology, 26*(10), 2114–2122.

64. Rosenstock, I. M. (1966). Why people use health services. *Milbank Memorial Fund Quarterly, 44(3)*, 94–127.

65. Ajzen, I. (1991). The theory of planned behavior. *Organizational Behavior and Human Decision Processes, 50*(2), 179–211.

66. Bandura, A. (2001). Social cognitive theory of mass communication. *Media Psychology, 3*(3), 265–299. https://doi.org/10.1207/S1532785XMEP0303_03

67. Fishbein, M. (2008). A reasoned action approach to health promotion. *Medical Decision Making, 28*(6), 834-844

68. Prochaska, J. O., & DiClemente, C. C. (1992). Stages of change in the modification of problem behaviors. *Progress in Behavior Modification, 28*, 183–218.

69. Michie, S., Johnston, M., Abraham, C., Lawton, R., Parker, D., & Walker, A. (2005). Making psychological theory useful for implementing evidence based practice: A consensus approach. *Quality & Safety in Health Care, 14*(1), 26–33. https://doi.org/10.1136/qshc.2004.011155

70. Cane, J., O'Connor, D., & Michie, S. (2012). Validation of the theoretical domains framework for use in behaviour change and implementation research. *Implementation Science, 7*, 37. https://doi.org/10.1186/1748-5908-7-37

71. Michie, S., van Stralen, M. M., & West, R. (2011). The behaviour change wheel: A new method for characterising and designing behaviour change interventions. *Implementation Science, 6*(1), 1–12.

72. Atkins, L., Francis, J., Islam, R., et al. (2017). A guide to using the Theoretical Domains Framework of behaviour change to investigate implementation problems. *Implementation Science, 12*(1), 77, 1–18. https://doi.org/10.1186/s13012-017-0605-9

73. Patey, A. M., the Canada PRIME Plus Team, Islam, R., Francis, J. J., Bryson, G. L., & Grimshaw, J. M. (2012). Anesthesiologists' and surgeons' perceptions about routine pre-operative testing in low-risk patients: application of the Theoretical Domains Framework (TDF) to identify factors that influence physicians' decisions to order pre-operative tests. *Implementation Science*, *7*(1), 1–13. https://doi.org/10.1186/1748-5908-7-52

74. Easthall, C., Taylor, N., Bhattacharya, D. (2019). Barriers to medication adherence in patients prescribed medicines for the prevention of cardiovascular disease: a conceptual framework. *The International Journal of Pharmacy Practice, 27*(3), 223–231

75. Boykins, A. D. (2014). Core communication competencies in patient-centered care. *The ABNF Journal : Official Journal of the Association of Black Nursing Faculty in Higher Education, Inc*, *25*(2), 40–45.

76. Bensing, J. M., Deveugele, M., Moretti, F., et al. (2011). How to make the medical consultation more successful from a patient's perspective? Tips for doctors and patients from lay people in the United Kingdom, Italy, Belgium and the Netherlands. *Patient Education and Counseling, 84*(3), 287–293. https://doi.org/10.1016/j.pec.2011.06.008

77. Scholl, I., Zill, J. M., Härter, M., & Dirmaier, J. (2014). An integrative model of patient-centeredness - A systematic review and concept analysis. *PLOS ONE, 9*(9), e107828. https://doi.org/10.1371/journal.pone.0107828

78. Hughes, T. D., Cutrell, S., Minshew, L. M., Brown, P., & Ferreri, S. P. (2022). An exploration of barriers, facilitators, and practical solutions for adopting medication synchronization into community pharmacies: A qualitative analysis. *Exploratory Research in Clinical and Social Pharmacy, 5*, 100111. https://doi.org/10.1016/j.rcsop.2022.100111


"I can do this!"
Education
Empowerment
Involvement
Support

Chapter 2

Patient-centred care in established rheumatoid arthritis

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Review of the evidence on patient-centred care (PCC) in rheumatoid arthritis (RA) shows that involving the patient as an individual – with unique needs, concerns and preferences – has a relevant impact on treatment outcomes (safety, effectiveness and costs). This approach empowers patients to take personal responsibility for their treatment.

Because healthcare professionals (HCPs) are only able to interact personally with their patients just a few hours per year, patients with a chronic condition such as RA should be actively involved in the management of their disease. To stimulate this active role, five different PCC activities can be distinguished: (1) patient education, (2) patient involvement/shared decision-making, (3) patient empowerment/ self-management, (4) involvement of family and friends and (5) physical and emotional support. This article reviews the existing knowledge on these five PCC activities in the context of established RA management, especially focused on opportunities to increase medication adherence in established RA.

Abstract

PATIENT-CENTRED CARE IN ESTABLISHED RHEUMATOID ARTHRITIS

In line with rapid changes in our society, health care changes too. Fortunately, the efficacy, efficiency and effectiveness of treatments for chronic diseases more and more result in improvements in the quality of life and survival. Individuals increasingly prefer an active role in shaping their own lives, including how a chronic disease affects them. This process is catalysed by the rapid growth of the Internet, which offers convenient access to a wide range of health information, with interactive communication platforms [1]. Patients increasingly search the Internet for medical information, wish to have open communication channels with their health professionals, and are eager to actively participate in making important medical decisions [2].

Shift from physician-centred care to patient-centred care

These developments are influencing today's health-care systems. For decades, health-care systems were mainly organised from the biomedical perspective. Consequently, the needs of the healthcare professional (HCP) and the system took priority in the delivery of care to patients. In this model, the health professional was at the centre of the system – he or she had exclusive access to knowledge – and the patient was expected to comply with the instructions given by health professionals [3].

Further, the view on how to provide high-quality health care has altered [1,2].

Respecting patient's autonomy is not only ethically ‘the right thing to do’, it is essential, as it is the patient who has to live with the daily discomforts, the challenges of RA and the threat of disability.

High-quality care is now considered to be a collaboration of professionals and patients jointly working on restoring or maintaining the patient's health status [4,5]. Educated and empowered, patients will better manage their disease. Where professionals must stimulate and educate patients, they must feel obligated to work as partners with health professionals to optimise health (‘participatory medicine’).

In short, health care is changing from physician-centred care to patient-centred care (PCC), in which the health professional and the patient together decide what the best care will be [1].

Patient as part of the multidisciplinary care team

PCC is defined by the Institute of Medicine (a division of the National Academy of Sciences in the United States) as: *'providing care that is respectful of, and responsive to, individual patient preferences, needs, and values, ensuring that patient values guide all clinical decisions'* [6]. PCC places each patient at the centre of the health-care system, and it recognises the patient as a whole person with physical, psychological and social needs. Contrary to common belief, patient-centredness requires more than a respectful attitude towards patients or a personalised style of clinical interviewing. PCC is guiding patients with complete and *unbiased* information based on sharing the best available evidence and considering patients' cultural traditions, personal preferences and values, family situations, social circumstances and lifestyles. These individual characteristics may shine a different light on risks and benefits. As a consequence, patient's individual vision/experiences and physicians' visions (based on intensive education and experiences with many other patients) should be exchanged and integrated into treatment plans [7].

Bottom line; the underlying philosophy of PCC is the overall respect for patients as unique living beings in their specific social world, which implicates that patients should be treated as autonomous individuals who need to be viewed as full members of the multidisciplinary care team in order to assure that their wishes should be respected.

Patients need knowledge, skills and power

By definition of being the owner of their illness, RA patients typically cope with their illness on their own, in their own environment, most of the time in the absence of a HCP. Consequently, they need knowledge, skills, as well as power to be able to monitor and manage their symptoms on a daily basis, and to partner with health professionals in optimising their health [1–3] as follows:

- Patients need knowledge about the disease and symptoms, treatment options and possible outcomes and knowledge about personal values and preferences
- They need skills to self-manage their disease, and to participate in medical decision-making (e.g., health literacy, self-monitoring, self-management and decision-making skills)

- Finally, they need power to believe in their capacity to self-manage their disease, and to be able to influence the treatment decision-making (i.e., self-efficacy) [1–3]. This includes factors such as believing that they have permission to participate and ask questions, having confidence in the value of own knowledge and ability to acquire medical knowledge, and self-efficacy to use self-management and decision-making skills.

Thus, besides knowledge and skills, the patients also have to be empowered to increase his/her self-efficacy, one of the main elements in Bandura's social cognitive theory [8]. Bandura defined self-efficacy as one's belief in one's ability to succeed in specific situations. Self-efficacy beliefs are cognitions that determine whether health behaviour change will be initiated, how much effort will be expended, and how long they will persevere in the face of difficulties [8].

Therefore, in light of this theory, it is essential to stimulate the perceived self-efficacy of patients to make them valuable partners in their own care. Patients need to be explicitly invited by the health professional to participate [9]. Improving self-efficacy also requires new skills for both patients and healthcare professionals [10]. This will require improving knowledge to patients and their families; improving health literacy; and finding effective means to facilitate skills essential for shared decision-making (SDM), goal setting, coaching and problem solving between health professionals and patients [11]. Education should finally also be focused on changing attitudes of both doctors and patients to overcome the power imbalance between doctors and patients in the clinical setting [12].

In this article, all examples to strengthen/stimulate PCC are based on knowledge, skills and power. These three elements are essential for the patient to be a valuable partner in his/her care process [1–3].

Evidence for effectiveness of PCC

Reviews on the effectiveness of PCC compared with more traditional health care show that the degree to which patients are more involved in their care has a significant impact on the quality of their treatment with regard to safety and effectiveness [7]. It might also benefit the health-care system in terms of financial performance [7]. Summary analyses of studies on interventions to better inform and involve patients in their care show improved experience with health care, lower dependence

on health services, better adherence to treatment and, in some cases, measurable improvements in health outcomes [7,13,14]. This approach is agreed upon by the WHO (World Health Organisation) [15], which emphasises the importance of PCC.

PCC might also increase patient safety

PCC not only improves patient outcomes and satisfaction rate but might also improve patient safety. Although health care in general improves health of patients significantly, sizable numbers of patients are harmed each year because of medical errors [16]. An important contributor to medical errors is inadequate transitional care [17,18]. Patients with chronic conditions receive care that is often fragmented, incomplete, inefficient and, consequently, less effective [18]. Particularly in patients with established RA, this complexity is compounded by co-morbidities. Most patients with established RA acquire relationships with multiple professionals and institutions. Professionals should therefore collaborate across disciplines to make coordinated decisions, but should also encourage the patient to actively coordinate their care as constant factor in the health-care system. Patients can, for example, bring their own medication list, ask questions and involve themselves in test results.

Barriers for PCC

Although it is widely advocated that PCC should be incorporated in usual care, there are also barriers, which slow down the uptake of PCC in clinical care. Firstly, although PCC seems logically and morally well founded, and the evidence to support PCC is growing, still more evidence is necessary to demonstrate the (cost-) effectiveness of PCC. Secondly, terminology can be a barrier in the implementation of PCC. PCC is a 'container concept' for multiple different elements that refer to different medical processes in the medical consultation. This makes PCC difficult to operationalise in implementable and measurable elements [4,19,20]. PCC also requires additional competencies from the healthcare professional. Healthcare professionals should be able to judge the extent to which patients would like to be involved, and/or would like to make a shared decision. Finally, time constraints are often reported to be an important barrier to PCC [21]. A shortage of health staff leads to rituals and routines of practice, which impede the development of PCC in hospitals [22]. Surprisingly, although time constraints are commonly perceived as a barrier for the adoption of PCC in clinical practice, there is no evidence for a negative impact of PCC on the length of consultation or increase health-care costs [23].

Applying patient-centred care to improve medication adherence

As illustrated in this publication, patient-centred care (PCC) improves clinical quality and outcomes, and it might also decrease health-care costs. Besides, PCC might also decrease one of the underlying problems for poor health-care outcomes: medication adherence [24,25].

As in all chronic diseases, medication adherence is poor in patients with rheumatoid arthritis (RA). Although disease-modifying antirheumatic drugs (DMARDs) have proven to decrease the disease activity and radiological progression, adherence to DMARDs is not optimal and ranges from 22% (underuse) to 107% (overuse) [26]. This DMARD non-adherence has proven negative outcome results such as increased disease activity, radiological damage, loss of function and a lower quality of life [27]. Interventions to increase patient's medication adherence are therefore warranted.

At the moment, however, there is limited research on adherence interventions in rheumatic diseases, and the published studies showed inconsistent effect on adherence or disease outcome [28]. Patient-centred approaches may represent a foundation upon which to develop new medication adherence interventions and to enhance those that exist, but with the intent of also improving clinical outcomes, patient experience and satisfaction with medication use [29].

PCC to improve medication adherence

The principles of PCC are already embedded in the changes in terminology with respect to medication adherence. The oldest term to describe non-adherence was non-compliance. This term was intended to be a neutral alternative to earlier descriptions of patients who did not follow the healthcare professionals' advice, such as 'untrustworthy', 'uncooperative' or as proposed by Hippocrates, patients who lie about taking treatment. In short, compliance is a paternalistic conceptualisation of medication-taking behaviour, which disregards patients' perceptions on medication-taking [29]. Compliance is now replaced by adherence (the extent to which a patient's medication-intake behaviour corresponds with agreed recommendations of their healthcare professional) in an effort to put the therapeutic relationship in its proper perspective. The concept of adherence places emphasis on a process, in which

the appropriate treatment is based on a shared decision between the HCP and the patient and in which the patient's autonomy is respected. The difference between refusal of treatment and non-adherence is the patient's involvement in the decision-making process [30]. Thus, non-adherence occurs only if the patient does not follow treatment recommendations that are mutually agreed upon [31].

Unintentional and intentional non-adherence

Recently, two types of non-adherence have been conceptualized as 'unintentional' (e.g., forgetting medicines and miscommunication) and 'intentional'. Unintentional non-adherence reflects a person's absence of ability and skills for taking medicines, including forgetting or poor manual dexterity, whereas intentional non-adherence is driven by a decision not to take medicines as prescribed [32–34].

Factors associated with adherence

Knowledge of factors associated with medication adherence in RA could provide possible targets for (improved) adherence interventions, and it might also help to identify patients who would benefit from an intervention. However, non-adherent RA patients seem hard to characterize by its (socio)demographic-, therapy- and condition-related factors [35]. These findings are confirmed in studies in other chronic diseases [36].

Although (socio)demographic-, therapy- and condition-related factors are not well associated with medication adherence, patients seem to adhere better when the treatment regimen makes sense to them: when the treatment seems effective, when the benefits seem to exceed the risks/ costs (both financial, emotional and physical) and when they feel they have the ability to succeed at the regimen (self-efficacious) [25]. Thus, patients' knowledge, skills and power indeed seem to influence adherence behaviour.

According to the Necessity-Concerns Framework of Horne and Weinman [32–34], it is assumed that patient's decision to take medication is driven by a cost-benefit assessment. Herein, personal beliefs about the necessity of taking the medication for maintaining or improving health are balanced against concerns about the potential adverse effects of taking the medication [32–34].

Many studies underline the importance of addressing these necessity beliefs and concerns about medication to improve adherence. In RA, several studies assessed associations between medication non-adherence and necessity and concern beliefs about medication (measured with the Beliefs about Medicines Questionnaire (BMQ)). Mostly, stronger necessity beliefs were associated with better medication adherence, whereas some studies suggest that stronger concern beliefs were associated with decreased medication adherence [37–39].

Interventions to improve medication adherence should target these feelings. However, first, patients must feel safe to express their (non-)adherence, as this can be a delicate subject. The communication style must be open and non-judgemental, compliant to PCC and SDM. Motivational interviewing might be suitable to explore patients' medication needs, concerns and practical barriers. Then, patient's individual feelings about the necessity of the drug, patient's concerns and possible practical barriers can be explored. Possible barriers for adherence (not feeling the advantages of the medication, having concerns about the medication or experiencing practical barriers) can be explored with the patient (possibly using Fig. 1). To increase adherence, practical barriers can be resolved, and interventions to increase patient's beliefs about the necessity of the drug and to decrease patients concerns about the medication can be initiated. These interventions might be organised in the healthcare setting, although e-health solutions can also be an alternative.

At the moment, there are no published studies on the effectiveness of an e-health intervention on medication adherence in RA. Studies in other chronic conditions show promising results [40,41]. However, the interventions are often complex, and the effect size is moderate. In case of forgetfulness, electronic reminders, especially SMS reminders, have been proven effective. Though long-term effects remain unclear, it seems logical that improving adherence can lead to optimised health outcomes [40].

In fact, when a patient does not reach his/her treatment target, a rheumatologist should always consider whether the patient is a non-responder or a non-adherer. In order to detect non-adherent patients, a rheumatologist can use electronic devices to measure patient's adherence (relatively costly) or use a validated

questionnaire (e.g., Compliance Questionnaire on Rheumatology). Besides, HCPs can always discuss with the patients whether he/she experiences practical barriers (problems with taking the medication and forgetting medication), has doubts about the necessity of the drugs and/or concerns about their medication.

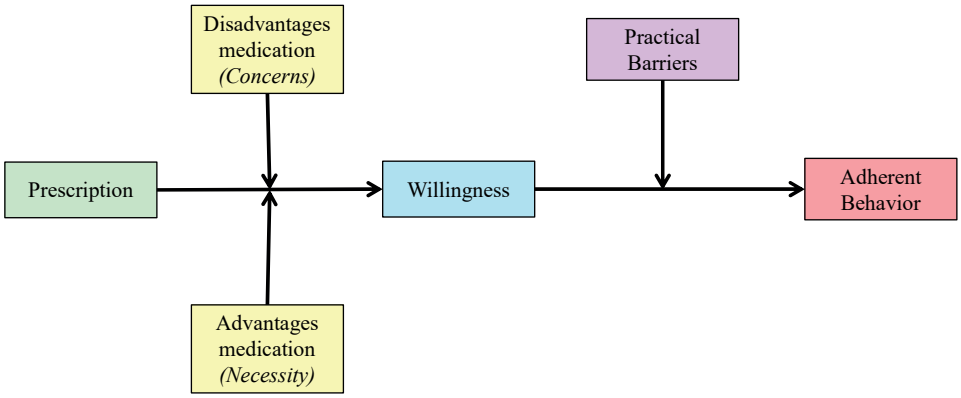


Figure 1. Simplified model to concordantly discuss patient's main barriers for medication adherence: (a) intentional due to an imbalance between perceived benefits and concerns and (b) unintentional due to practical barriers. During this discussion, patient's expertise and beliefs are completely valued [26].

Operationalisation of the concept of PCC

Multiple models and frameworks have been developed for describing PCC, with many overlapping elements [4,18,20]. This variety of frameworks leads to a heterogeneous use of the term PCC and measures to objectify PCC. Therefore, Scholl et al. have in 2014 synthesised the different dimensions of PCC, and they integrated these dimensions in a model [18]. This model describes the four main principles of PCC as essential prerequisite activities and essential enablers to implement PCC in daily clinical care. The main principles and activities are the focus of this article, and they are depicted in Fig. 2.

This model distinguishes four main principles of PCC:

1. *The patient is a unique person (Each patient has his/her own needs, preferences, feelings, cognitions, expectations and skills).*
2. *Competent HCPs (they need specific competencies for PCC such as being respectful, empathic, tolerant, accountable and committed to the patient).*
3. *The patient–HCP relationship is the central component for PCC (Patients and HCPs should have a partnership based on trust and mutual caring).*

4. *Biopsychosocial perspective (Understanding patient's illness within a broader framework by exploring the patient with his/her unique biological, psychological and social context).*

Based on these four principles, five PCC activities can be distinguished.

1. Patient information/education
2. Patient involvement/shared decision-making
3. Patient empowerment/self-management
4. Family and friends involvement
5. Physical and emotional support

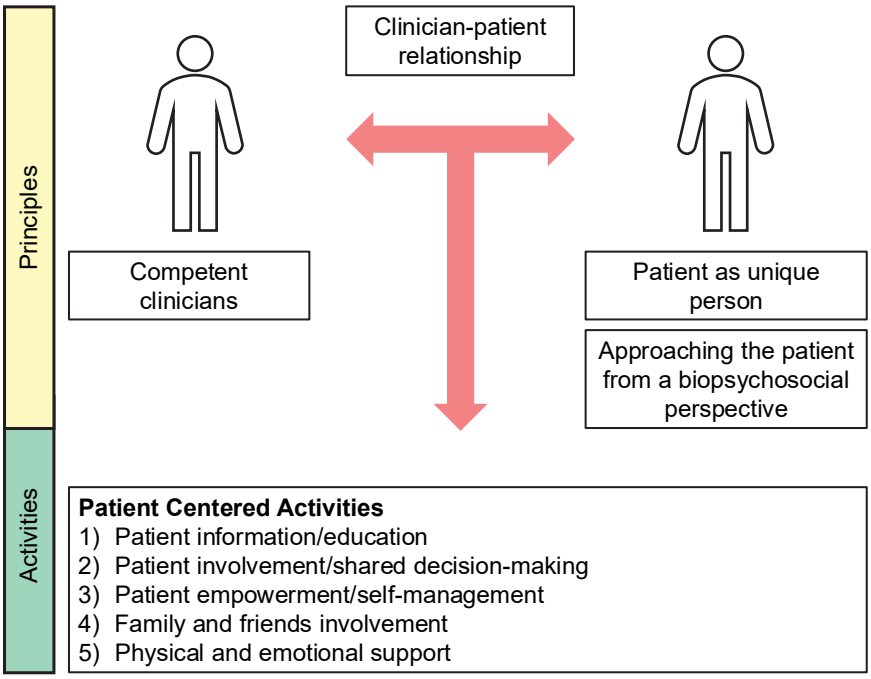


Figure 2. Principles and activities of patient-centredness (adapted from Scholl [18]).

In this article, these five PCC activities will be elucidated in more detail.

(1) Patient information/education

Informing RA patients about the (consequences of the) disease and treatment options is a key element of providing health care. Especially, the uncertain disease progression, erratic course of exacerbations and remissions, the variable effects of rest, exercise and emotion, the

management of often complex medication regimes, and the uncertainty of the prognosis and long-term are essential items to be addressed. In addition, patients should be informed about how to access medical, psychosocial, physical and financial support [18]. Information provision is not only relevant at the beginning of the disease to explain the diagnosis but also relevant throughout the course of the disease in order to control the impact of the disease and its treatment on everyday life.

Recent studies have shown that RA patients have a high need for information, and that often these needs are not being met [42–44]. Patients state that information provision should not be limited to information about the disease and treatment but should also include emotional aspects and the impact on everyday life and focus on individual needs [44,45].

Physicians can only tailor information to the individual patient's needs, when patients are invited to share information (e.g., regarding symptoms and their impact on daily life, questions and concerns). With this mutual information exchange, the creation of the patient-HCP partnership begins. Possible questions to invite patients to share their thoughts are as follows:

- Which symptoms bother you most? Why?
- Can you tell me in your own words what you have understood and then, if necessary, I can help clarify

An example of integrating the view of the patients with regard to his/her condition is the application of PROs (Patient-Reported Outcomes), with disease-specific instruments as there is the RAID [46] (rheumatoid arthritis impact of disease) or generic instruments such as the SF-36 [47]. Online communication between patients and professionals is gaining popularity, and it helps to overcome a barrier to be able to reach the specialist at certain times [48].

The educational needs assessment tool (ENAT) can also support health professionals in assessing patient information needs. It is a self-completion questionnaire, which allows patients to prioritise their educational needs. The ENAT was developed by arthritis patients and their physicians, and it comprises the following domains: pain management, movement, feelings, arthritis process, treatments, self-help measures and support systems. It can be used to prepare a consultation in order

to provide patient-centred and tailored education [45]. The ENAT can be obtained from the website http://www.leeds.ac.uk/acumen/pages/research/ENAT.html.

Interventions developed in the last decade also try to acknowledge this need for tailored information; there is a trend towards a more holistic and tailored approach with a greater focus on behavioural, cognitive and emotional aspects [49]. In addition, information provision is more directly linked to educate skills to patients that enable them to monitor and manage their symptoms on a daily basis, that is, it is more integrated in self-management interventions and interventions to support SDM. This fits within the approach of PCC.

Low health literacy: a barrier to deliver information to patients

A barrier to PCC is low health literacy among patients [50–52]. Health literacy is 'the degree to which individuals can obtain, process and understand the basic health information and services they need to make appropriate health decisions and function effectively in the healthcare environment'. In order to be able to accomplish this, a constellation of skills including the ability to interpret documents and read and write prose (printed literature), use quantitative information (numeracy) and speak and listen effectively (oral literacy) is required [53]. Low health literacy is a significant problem, and it has been linked to poorer health outcomes [54] and medical costs [55,56].

In order to identify patients with low health literacy, various measurements are available such as the Rapid Estimate of Adult Literacy in Medicine (REALM) [57], the Test of Functional Health Literacy in Adults (TOFHLA) [58], the Newest Vital Sign [59], the functional, communicative and critical health literacy scales assessment by Ishikawa et al. [60] and the Health Literacy Skills Instrument by McCormack [61]. An easy-to-administer self-assessment instrument that combines the measurement of computer skills with health literacy skills is the eHealth Literacy Scale (eHEALS) by Norman and Skinner [62].

Interventions for individuals with low health literacy are summarised by Sheridan and Haun [54,63]. Several discrete design features of the health literacy interventions that improved patient comprehension were, for example, presenting essential information by itself or first, presenting information so that the higher number is better, presenting numerical information in tables rather than in text, adding icon arrays to numerical

information and adding video to verbal narrative. Furthermore, improving health literacy by focusing on self-management reduced emergency department visits, hospitalisations and disease severity.

Patient information and e-health

Although patient information is often provided as verbal and written instructions and demonstrations, patient information may also be provided online. The increasing accessibility and availability of the Internet, social media and related computer technologies provide new opportunities for the communication and delivery of information. More and more RA patients search the Internet for a diagnosis or treatment before consulting their physician [64,65]. In addition, also after consultation, patients search the Internet for confirmation, additional information and for information about the available treatment options [64,65]. Patients state that they visit the Internet in order to be an active participant in their health care, and also to be a responsible informed patient [64]. However, patients are hesitant to discuss their search for information with their rheumatologist because they fear it may be perceived as challenging by their physician [64].

Recent research demonstrated that seeking medical information with common search engines and simple search terms is quite complex and not always efficient, despite the increased use of Internet. Although the accuracy of the information provided is generally good, high health literacy levels are required, and key information is poorly covered and inconsistent [65–67]. Many patients perceive that online health information is confusing, and they have difficulties with formulating proper search strategies and evaluating the relevance and reliability [64,68]. Health-care organisations such as hospitals but also patient organisations could play a role in this by developing (online) tools that identify reliable and valuable information (i.e., carefully selected information). This information should be written on a level that is understandable for the majority of the population. Some arthritis foundations have reliable information online about treatments for RA, especially written for patients (e.g., www.reumafonds.nl and http://www.rheumatology.org/Learning-Center/Glossary).

Despite these emerging novel communication channels, only limited studies in rheumatology have focused on the use of these innovative information technologies. Rittberg, Dissanayake and Katz performed a qualitative analysis of publicly available methotrexate self-injection

education videos on YouTube [69]. This study demonstrated that only a minority of videos is useful for teaching how to self-inject methotrexate. However, in a follow-up pilot study, using a self-developed web-based video to teach patients to self-inject methotrexate followed by further in-person nurse education showed that the video was a very efficient manner of informing patients. The results of the video equal the standard teaching practice with regard to patient satisfaction, confidence for self-injection and knowledge while decreasing teaching time by 25% [70]. The video is available at http://www.youtube.com/watch? v=jTn9YaQZn1U.

Another method to provide information-using technology is to share audio recordings of the consultation with patients. Although studies regarding audio-recorded consultations have their focus in oncology and paediatrics, this technology can be a valuable innovation for rheumatology as well. A recent review noted that patients who received audio recordings have better information recall, clearer understanding and more active engagement in treatment decisions [71]. Furthermore, patients and their families value an audible record, because it allows them to share and reflect on what has been said. Nowadays, patients have also started to audio record their consultations using their phones, which has elicited strong reactions by some physicians [29]. HCPs have mixed perceptions regarding the benefits, values and risks. Some HCPs accept and understand the benefits for the patient, whereas others see this as a threat and a consequence of distrust. A legitimate concern of HCPs regards sharing the recording with a wider audience or goes viral on the Internet. This virgin territory requires a new policy [72]. This new policy should incorporate recommendations such as (1) the HCP should be informed before, (2) the recordings will not be distributed and/or altered and (3) if the HCP wants, he/she might receive a copy of the recordings.

(2) Patient involvement/SDM

SDM is defined as a patient-centred approach in which the HCP and the patient go through all phases of the decision-making process together. Based on the best available evidence, the HCP informs the patient on all treatment options and their harms and benefits. The patient expresses his/ her values and preferences regarding these options. Together, they come to an agreement on what the best way is to proceed for this individual patient [73,74].

The benefits of SDM

Patient involvement in decision-making is considered beneficial, because patients have the right to self-determination [75], and the successful treatment of RA relies heavily on patients' self-management. However, situations can occur that patients and rheumatologists are not agreeing on the best treatment. There are four possibilities: the patient and the rheumatologist agree to a certain treatment or they agree to not follow a certain treatment. In these two cases, consensus has been reached about an optimal treatment in an SDM process. The problem occurs when the patient exercises the right to self-determination of which he/she is entitled to: he/she does not want a certain treatment proposed by the rheumatologist. In most cases, the proposed treatment will not be given, although some physicians would feel perhaps irritated as physicians might experience this patient (from a physician-centred view) as a non-cooperative patient. The fourth possibility in clinical practice can be described as follows: the patient proposes a certain treatment, such as different medication/dose or a scan, but the rheumatologist does not agree. Then, it is essential that guidelines are followed, and best available evidence is discussed and explained to the patient to clarify the rejection and to avoid an unhappy patient. Care should be given within the boundaries of best clinical practice. Therefore, the treatment needs to closely fit in with the patient's values and lifestyle [76]. Furthermore, patient involvement is associated with better health outcomes, such as health status, self-management, adherence, coping behaviour and satisfaction with care [43,77–82]. The results are especially promising in chronic care [78] where the doctor–patient relationship is potentially a long-term one, and it requires partnership [83]. Finally, patient participation is important because studies show that patients' and rheumatologists' beliefs about illness and treatment may differ. This includes how they rank the potential benefits and side effects of available treatment options, how they prioritise long-term outcomes and how they approach the escalation of treatment [84,85]. Therefore, high-quality patient–physician communication about the choice of treatment is important. The importance of SDM in rheumatology is confirmed by the 2013 European League Against Rheumatism (EULAR) recommendations, which state that ‘treatment of RA patients must be based on a shared decision between the patient and the rheumatologist’ [86]. Importantly, the EULAR international task force developing RA treatment recommendations noted that ‘decision-sharing by patient and rheumatologist is of such overwhelming importance that it should spearhead the recommendations’ [86].

Implementation of SDM

Although desirable, implementing SDM in daily clinical practice is challenging for both doctors and patients. Previous studies with questionnaires report that 30–40% of adults with RA report suboptimal SDM communication with their HCP. Younger and more educated patients seem to be more likely involved in medical decision-making [43,80,81,87]. In addition, patients with limited health literacy, limited language proficiency and lower trust in physician are associated with suboptimal SDM communication [87].

For patients, it can be difficult to recognise that a decision needs to be made, and to actively participate in the process to come to an informed value-based decision [9,12,88]. They often have low confidence in their capacity to participate, a (perceived) lack of medical knowledge, are uncertain about which questions to ask and, above all, they perceive inequity in their relationship with their doctor.

HCPs, on the other hand, may not desire or be comfortable with patient involvement due to a lack of time, self-efficacy and skills or due to indifference towards decision support tools [89–91]. Moreover, HCPs may overestimate their actual level of SDM [92], and some believe that patients do not want to participate in medical decision-making [93]. However, several studies have shown that RA patients have a high information need, and they want to be more actively involved in medical decision-making [9,43,80,81,94–98].

In daily clinical care, rheumatologists (and other team members) can facilitate SDM. As stated before, few patients are active participants by nature; most RA patients are not even aware of having a choice, and they are reluctant to participate due to a perceived power imbalance in the doctor–patient relationship. Therefore, the HCP, as an expert in complex medical decision-making and the one who is emotionally detached, should guide the decision-making process [99]. This process can roughly be divided into three phases (Table 1):

1. Firstly, the patient has to be informed that there is a decision to be made, what the options are and that the patient can have a role in the decision-making process (i.e., acknowledging the relevance of patient participation and supporting patients in becoming involved to increase their confidence/self-efficacy to fulfil that role). This might be the most important step to take. The patient needs to know that there is often no single best choice, that his/her preference is of relevance (e.g., for increased adherence) and that, if relevant, doing nothing or keeping the status quo is also an option [100,101].
2. The second phase is information exchange. This includes the HCP describing all treatment options, the clinical harms and benefits of these options, and the possible impact on daily life. In this stage, it is important to give patients time to process all the information. Furthermore, patients need support in assessing how the treatment may affect their daily life, and in developing and expressing preferences, values, expectations and worries about the treatment. In this phase of information exchange, patient decision aids (PtDAs) may be helpful (see subsequently).
3. Finally, when all relevant influencing factors are clear to all parties, the options can be deliberated, and a decision can jointly be made.

Table 1. Shared decision-making in three steps.

1. Initiating shared decision-making (SDM)
• Stating the decision (and its options)
• Explaining SDM and the relevance of patient participation
• Exploring patient's preferred role in the SDM process and need for information
2. Mutual information exchange
• Detailed description of treatment options (benefits/harms/impact in daily life)
• Eliciting patient's preferences (based on values, expectations and worries)
• Determining patient's preferred role in the SDM process
3. (Shared) deliberation of the options and (shared) decision-making

Exploring patient's role

During this decision-making process, the patient's preferred role should be explored. Research shows that most, but not all RA patients, want to participate. Most patients want to go through the full decision-making process with their physician, and others want to engage with the information but do not necessarily want to be involved in deliberation and decision-making [9,94,102–109]. What makes it even more complex is that patient's preference for involvement may change over time, and it may vary according to the situation he/she is in [9]. Moreover, patients

who initially may be reluctant to participate may change their mind after the options have been presented [110]. Therefore, preference elicitation should be done at each decision and after presenting the options. This task requires empathic attention to the situation of the patient, and to the verbal and non-verbal cues the patient offers as the HCP invites the patient into the deliberative process [99]. If the patient decides to leave the decision-making to his/her doctor, the patient's values and preferences are still valuable to enhance the chance of success of treatment. Then, the doctor has the challenging task to decide in the patient's best interest; deciding which treatment fits in with the patient's personal values and lifestyle.

SDM also covers shared responsibility [101]. This specific aspect may be attractive to some patients and frightening to others [9]. Unexpected responsibility can be a burden, which is not desirable. To prevent patients from feeling abandoned to have to decide on their own, HCPs will need to make explicit that it is a shared process and not a derogation of responsibility [111].

Patient decision aids

To facilitate SDM, PtDAs can be implemented. In contrast to standard patient information materials, PtDAs state the decision to be made, and they help patients weigh the pros and cons of all relevant options. Furthermore, PtDAs help patients to clarify their values and preferences, and to prepare them for the SDM encounter. PtDAs come in many forms: on paper, video and/or (interactive) websites. They can be used before, during and in between clinical encounters – depending on the decision at stake and the patient's pathway. It is not yet clear which format is best. For a wide variety of treatment and screening decisions, PtDAs have repeatedly shown to have a positive impact on patients' knowledge about options, patients' risk perceptions and patients' feelings of being informed [82]. Moreover, PtDAs have improved patients' involvement in medical decision-making, and they lead to decisions that are more in line with patients' personal values [82]. PtDAs can have a positive impact on patients' satisfaction with decision-making, anxiety, adherence or health outcomes [82]. Although there is a clear need for increased patient involvement in RA, only a few studies on PtDAs in rheumatology have been reported, and the effects of the PtDAs have not yet been thoroughly determined [112–115].

Recently, a PtDA about RA medications, for use during the clinical encounter, was developed specifically for patients with limited health literacy [114]. By using five issue cards, the PtDA focuses less on reading and more on conversation and verbal exchange of information. A field test proved the PtDA to be effective in promoting a conversation and exchange of experience on the part of the HCP and values and preferences on the part of the patient.

As stated before, PtDAs come in many forms, including (interactive) websites. Web-based PtDAs have the advantage of being easily adjustable, which is especially relevant in RA where new treatments evolve rapidly. Furthermore, on websites, the information can be provided in portions, adapting the amount and complexity of information to individual needs. In recent years, three studies on web-based PtDAs for RA have been reported [112,113,115], all with a different focus. One PtDA used animated videos and a value-clarification exercise to support treatment decision-making in RA patients who were prescribed methotrexate, but were unsure about starting it [112]. This PtDA focused on two options: to take methotrexate as prescribed or to refuse methotrexate and talk to the doctor about other treatment options. A pilot study among 30 participants reported improvement in patients' decisional conflict and knowledge after using this PtDA.

Fraenkel et al. recently developed a PtDA aimed to inform RA patients with ongoing active disease about the risks and benefits related to biologic therapy [113]. This tool is an interactive, web-based, computerised educational module with voiceovers. The main focus of this PtDA is on supporting accurate risk perceptions when patients face the decision to initiate a biological DMARD. Preliminary evidence showed that this tool increased patients' knowledge, patients' willingness to escalate care and the likelihood of making an informed value-concordant choice. The most recent study reports the effects of a PtDA that enables patients to compare multiple DMARDs on clinical aspects and possible impact on daily life [115]. This PtDA provides patients the opportunity to compare multiple specific DMARDs, perform exercises to gain insight in their preferences, worries and questions, and endorses patients to express these feelings and questions to the health professionals. A quasi-experimental study showed that users perceived a more active role in decision-making, and they perceived the final choice to be more consistent with their personal values.

All PtDA studies described earlier provide data that support the potential value of PtDAs in RA decision-making. All web-based PtDA studies report high acceptance rates; patients value the opportunity to process all the information at their own time and pace, as compared with during the medical encounter. However, the results should be interpreted as preliminary evidence – there is a need for controlled clinical trials to examine the impact of these tools in clinical practice.

Despite their promising effects, just implementing PtDAs is not enough to guarantee SDM to happen. Without a (natural) empathic doctor–patient interaction and evolvement into partnership, a successful SDM process will not occur.

(3) Patient empowerment/self-management

In order to evolve from being a passive recipient of care to an active partner in health care, patients should develop knowledge, skills and power (see Table 2).

Table 2. Characteristics of an empowered activated patient.

An empowered activated patient:
• Understands his/her health condition and its effects
• Feels able to participate in decision-making with their (his/her) health professional
• Feels able to make informed choices about treatment
• Understands the need to make necessary changes to his/her lifestyle for managing the condition
• Is able to challenge and ask questions to the health professionals providing him/her care
• Takes responsibility for his/her health, and actively seeks care only when necessary

Source: 1st European conference on patient empowerment [116].

This can be established in self-management programmes. The programmes give patients with RA strategies and tools to better cope with the disease. Although self-management is often linked to patient education, patient education offers only information, whereas self-management interventions are more problem focused, action oriented and emphasise patient-generated care plans [117,118]. Self-management is therefore often defined as 'the individual's ability to manage the symptoms, treatment, physical and psychosocial consequences and lifestyle changes inherent in living with a chronic condition and to affect the cognitive, behavioural and emotional responses necessary to maintain a satisfactory quality of life' [119]. Successful self-management interventions for patients with a chronic illness require an integrated

approach with not only active involvement of the patient and the health professional but also active involvement of the social environment of the patient: family, friends and colleagues [119–121].

Self-management in RA

The first self-management interventions in RA were introduced in the 1980s with the implementation of the Arthritis Self-Management Program (ASMP) [118]. This programme showed persistent reduction in pain and physician visits after 4 years. Self-efficacy was also increased in the self-management group [8,122,123]. Reviews of RA self-management programmes have shown that the explicit use of social cognitive therapy and cognitive behavioural therapy led to short-term significant improvements in function [124–126], although effects are rarely sustained. This might be a result of the fact that the need for support is very diverse.

Despite the potential effectiveness of self-management interventions, many patients have difficulty managing their chronic illness properly [119]. The access to self-management support might be hampered for various individual reasons such as depression, weight problems, difficulty exercising, fatigue, poor physician communication, low family support, physical symptoms, lack of awareness, transportation problems and cost/lack of insurance coverage [127]. Taking these different individual barriers into account, the conclusion is that each patient needs self-management support based on individual's needs.

Provision of self-management interventions

There are different types of self-management programmes, such as peer-led, lay-led and health professionals-led programmes, or a combination of these programmes. Most research with regard to self-management interventions evaluates group programmes delivered face to face, in contrast to the one-to-one approach by health professionals, which is the least evaluated delivery method.

Lay-led self-management programmes are becoming widespread in the attempt to promote selfcare for people with chronic conditions. However, only small, short-term improvements in patients' self-efficacy, self-rated health, cognitive symptom management and frequency of exercise were published [128]. Arthritis self-management interventions provided by lay leaders (voluntary arthritis patients) showed positive changes

both in the lay leaders and in course participants: less pain and more willingness 'to get on with life' was reported [129].

New technologies, such as Internet-based interventions, have shown positive results in health status measures (health distress, activity limitation, self-reported global health and pain) and in self-efficacy for up to 1 year [130]. An online peer-led self-management programme appeared to decrease symptoms, improve health behaviours, self-efficacy and satisfaction with the health-care system, and to reduce health-care utilisation up to 1 year [131].

Another possible viable solution is exploiting the potential of smartphone technology. Smartphone applications can be utilised without special training, often contain user-friendly visual graphics and voiceover animations. They can be provided in all languages with minor modifications to the intervention, and they are available at almost any place (including rural and remote areas) at any preferred time (so patients who work full time can also be reached). Nevertheless, the use of this technology is likely limited by age, gender and/or socio-economic levels, and its continuous utilisation may result in several problems, such as addictive use of the smartphone [132]. Furthermore, the existing medical applications available in online application stores developed for rheumatic diseases were not evaluated in any step of application development or discussed in the medical literature so far, which results in lack of scientific evidence on the effectiveness of such interventions [132].

Table 3. Interventions with respect to family and friends' involvement.

1. Involvement of informal carers in decision-making processes regarding health policy and services.
2. Provide official recognition, financial support and social security benefits to informal carers.
3. Provide professional home visits and regular communication between professionals and informal carers, including assessment of health and safety conditions and technical aids.
4. Use the informal carers' experience of the cared-for individual in the training of professional carers.
5. Provide mental health protection measures for informal carers such as possibilities for flexible and part-time work, peer support, self-help, training and tools to evaluate carers' own mental health needs.

Source: 1st European conference on patient empowerment [116].

(4) Family and friends' involvement

Patients with RA must cope with pain, stiffness, physical activity restrictions and also the psychological impact of their disease on their lives. Many of these adaptive challenges require help from others. Thus, rheumatic disease patients need an available and satisfying network of interpersonal relations on which they can rely for both emotional sustenance and practical support. However, a rheumatic disease also has an inevitable impact on the patient's family, social network and work. They also need to cope with disruptions in social life and work productivity.

Therefore, it is not only important to empower patients but to support families and other informal caregivers as well [133]. Examples of interventions to involve family and friends are depicted in table 3. This empowerment of informal caregivers should be done by either the health provider or the empowered patient him/herself.

Informal caregivers may carry a large share of care provision. Supporting their role, training, and protecting their well-being have led to positive outcomes for the health of carers and the people they care for [116,134]. Informal caregivers can also be empowered by being invited to participate in meetings between the patient and the health professional. Furthermore, networks in local communities can empower informal caregivers (often families). Here, they have the opportunity to share knowledge, experiences and worries with other informal caregivers in terms of psychosocial support and training [116].

Informal caregivers often involve family. Although patients rely most on close family members as support (strong ties), weaker ties (less intimate, more distanced contacts) appeared more durable and less liable to loss over time than stronger ties [135]. Weak ties are especially useful when help from a stronger tie would be inconvenient, impractical or unwanted. Whereas intimate relationships with close ties decrease patient's feeling of independence, weak ties mostly less implicate burden or stigma about the receipt of help [135]. Moreover, weak ties are often based on reciprocating actions (payment, being friends), and therefore rendering the dependence/independence balance, which is experienced as less stressful, more durable and sustainable than other ties [135].

(5) Physical and emotional support

Besides informing, empowering and giving patients the right skills in order to participate in decision-making, PCC must also pay attention to patient's physical and emotional issues. The level of physical comfort that patients report has a tremendous impact on their experience of being ill [136]. In addition, emotional problems can be as debilitating as the physical effects of RA. Patients with RA are more likely to suffer from anxiety, depression and low self-esteem, and they have high levels of associated mortality and suicide, compared with the healthy population. The loss of the ability to carry out daily functions due to RA is also associated with the onset of depressive symptoms. Furthermore, the psychological effects of RA can extend to the partners, families, informal carers and patient's working environment [137].

Physical and emotional support interventions aim to support patient's physical state (pain management, foot care), emotional state (fatigue, depression), patient's lifestyle (nutrition, exercise, smoking), social functioning (work and social network), but also patient's safety (adverse events reporting, clean medical facilities, transitional care) [18,138].

Patient's physical and emotional status can also be improved by involvement in self-monitoring. In a British randomised clinical trial with 100 RA and psoriatic arthritis patients, patients received a training session where they were taught how to monitor their blood test results and which symptoms and side effects to report. In this study, the introduction of a self-monitoring programme resulted in half the number of appointments with the rheumatology nurse with no detrimental effects to their clinical status of the patient (pain, fatigue, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), disease activity) and with no increase in visits to the rheumatologist or general practitioner (GP). Patients with RA and PsA demonstrated that they can successfully understand and interpret their blood test results, and use this information along with reports of their symptoms and side effects [139].

CONCLUSION

PCC integrates the perspectives, understanding and preferences of patients into the delivery of health care. Essential for PCC is an effective patient-HCP partnership in which the HCP's recommendations are informed by an understanding of the individual patient's values, needs

and life context (e.g., home life, job and family relationships). In addition, PCC takes into account the perspectives of the patient's family and other informal caregivers, when appropriate.

For the implementation of collaborative PCC, patients need knowledge (about treatment options available and of personal preferences and goals), skills (such as interventions to overcome low health literacy) and power (e.g., the believed ability to use this knowledge to influence decision-making in the encounter with the doctor). Patients will benefit when they are involved in their care, both at home and in clinical settings. Health information materials, PtDAs, self-management action plans and other 'technologies' to stimulate patient engagement are most effective when they supplement or augment, rather than replace, interactions between patients and professionals [140]. As patients take on new roles in health care, ongoing support from health professionals may become even more important.

PCC requires time and often a change in the mindset of both professionals and patients. Patient-centredness was associated with better outcomes and higher cost [141], although Stewart et al. imply that patient-centred practice improved health status, and it increased the efficiency of care by reducing diagnostic tests and referrals [142]. For either the short run or the long run, managers, patients and purchasers should determine whether the improvement in outcomes and patient satisfaction associated with becoming patient-centred is worth the investment in costs.

For successful implementation, Scholl et al. describe five enablers [18] as follows:

- Patient-HCP communication *(adequate competencies for patient-centred communication)*
- Integration of medical and non-medical care *(recognition and integration of non-medical aspects of care in health-care services)*
- Teamwork and team building *(importance of interdisciplinary and multi-skilled teams)*
- Access to care *(timely access to conveniently accessible care)*
- Coordination and continuity of care *(coordinated continuity of care)*

Once implemented, it is expected that PCC may help improve the quality and safety of care, and it may help ensure an affordable health-care system for the next generations.

Vignette 1

In the Netherlands, a web portal was designed, which not only offers information on rheumatic diseases, treatments, available aids and support but also contains a personal secure login section, where patients can find their diagnosis, current medication and medication history, blood results, actual and previous disease activity, and outcomes on the quality of life-related instruments. All data are accompanied by written information and (where possible) charts and graphs to show the fluctuation in scores along a timeline using colours to compare the data to norm scores (www.reumacentrumtwente.nl).

Patients who were using this portal reported that they felt more involved in their treatment, and they had more knowledge about their treatment. One patient reported *It would mean more involvement in myself. It concerns information about me, so I would like that very much (insight in electronical medical records)*' (male, 59 years, RA) [143,144].

Vignette 2

Researchers and HCPs from Canada developed a PtDA called the Animated, Self-serve, Web-based Research tool (ANSWER) for patients considering methotrexate for RA (http:// answer.arccanada.org/). This instrument aimed to provide unbiased information on benefits and risks of methotrexate for RA, and to guide users through thinking if this is the right' treatment for them based on the information and their personal preferences. In a proof-ofconcept study, this decision tool improved patients' decision comfort and knowledge. However, there was no effect on patient's perceptions of their ability to effectively manage and participate in their health care. One of the participants stated ...*I had done a lot of research about methotrexate on my own beforehand and I was really quite reluctant to use it. And the whole process helped me to, it didn't convince me to, I wouldn't say it convinced me, but what I would say is it helped me accept it was the best choice. (Lucy)*' [112].

Practice points

- Patient education should not only be focused on general information about the disease and treatment but should also be more tailored to patient's individual needs. An education needs assessment tool can facilitate the exploration of patient's information needs.
- Although shared decision-making (SDM) is considered beneficial and is recommended by the EULAR, the implementation of SDM in clinical practice is suboptimal. HCPs should guide the patient in the decision-making process as few patients are active participants by nature. This process can be facilitated with patient decision aids.
- Many RA patients have difficulty to manage their chronic illness properly. New technologies, such as Internet and mobile phones, seem to be promising tools to improve patient's self-management.
- Rheumatic disease patients need an available and satisfying network for emotional and practical support. Interventions to involve patient's family and friends are therefore essential.
- Health information materials should supplement, rather than replace interactions between patients and HCPs.
- For the optimal implementation of PCC, patients need knowledge (e.g., about disease, treatment options, personal values and preferences), skills to manage their disease and to participate in medical decision-making and finally power to believe in their capacity to self-manage their disease.
- There is no evidence for a negative impact of PCC on the length of consultation or increase in health-care costs.

Research agenda

- Future research on PCC is essential to further develop, optimise and evaluate PCC. Aspects that should be covered are as follows:
- Research focusing on the methodological aspects of PCC research aiming to standardise outcome measures and develop/validate instruments to assess these outcome measures
- Research focusing on the (cost-) effectiveness of PCC interventions
- Research that identifies optimal interventions to improve patient-centred care
- Research that identifies specific populations and contextual considerations that would benefit most from a greater degree of PCC
- Research on the implementation of PCC in clinical practice, including the education of healthcare professionals on this topic

REFERENCES

1. van der Eijk M, Nijhuis FA, Faber MJ, et al. Moving from physician-centred care towards patient-centred care for Parkinson's disease patients. Parkinsonism & Related Disorders 2013;19(11):923–7.
2. Hibbard JH. Moving toward a more patient-centred healthcare delivery system. Health Affairs [Millwood] 2004. Suppl Variation: var 133–5.
3. Kremer JA, Van Der Eijk M, Aarts JW, et al. The individual formerly known as patient, TIFKAP. Minerva Medica 2011; 102(6):505.
4. Bensing J. Bridging the gap. The separate worlds of evidence-based medicine and patient-centred medicine. Patient Education and Counseling 2000;39(1):17–25.
5. Sevin C, Moore G, Shepherd J, et al. Transforming care teams to provide the best possible patient-centred, collaborative care. The Journal of Ambulatory Care Management 2009;32(1):24–31.
6. Weinberg DB, Cooney-Miner D, Perloff JN, et al. Building collaborative capacity: promoting interdisciplinary teamwork in the absence of formal teams. Medical Care 2011;49(8):716–23.
7. Coulter A, Ellins J. Effectiveness of strategies for informing, educating, and involving patients. British Medical Journal 2007;335(7609):24–7.
8. Bandura A. Health promotion by social cognitive means. Health Education & Behavior 2004;31(2):143–64.
9. Nota I, Drossaert CHC, Taal E, van de Laar MAFJ. Arthritis patients' motives for (not) wanting to be involved in medical decision-making and the factors that hinder or promote patient involvement. Clin Rheumatol. 2016;35(5):1225–35. doi:10.1007/s10067-014-2820-y
10. Zangi HA, Ndosi M, Adams J, et al. EULAR recommendations for patient education for people with inflammatory arthritis. Annals of the Rheumatic Diseases 2015;74(6):954–62.
11. Bechtel C, Ness DL. If you build it, will they come? Designing truly patient-centered health care. Health Affairs (Millwood) 2010;29(5):914–20.
12. Joseph-Williams N, Elwyn G, Edwards A. Knowledge is not power for patients: a systematic review and thematic synthesis of patient-reported barriers and facilitators to shared decision making. Patient Education and Counseling 2014;94(3):291–309.
13. Frampton S, Guastello S, Brady C, et al. Patient-centred care improvement guide. Derby, Connecticut: Planetree; October 2008.
14. Elwyn G, Laitner S, Coulter A, et al. Implementing shared decision-making in the NHS. British Medical Journal 2010; 341:c5146.
15. People-centred health care. Bulletin of the World Health Organization 2014;92(10). 701–701.
16. Institute of Medicine [US] Committee on Quality of Healthcare in America, Kohn LT, Corrigan JM, Donaldson MS, editors. To err is human: building a safer health system. Washington [DC]: National Academies Press [US]; 2000.
17. Howard R, Avery A, Bissell P. Causes of preventable drug-related hospital admissions: a qualitative study. Quality & Safety in Health Care 2008;17(2):109–16.

18. Scholl I, Zill JM, Härter M, Dirmaier J. An integrative model of patient-centeredness - a systematic review and concept analysis. PLoS One. 2014;9(9):e107828. doi:10.1371/journal.pone.0107828
19. Nelson S, Gordon S. The complexities of care: nursing reconsidered. Ithaca, New York: ILR Press London; 2006.
20. Davies PG. Patient centredness. Journal of Epidemiology & Community Health 2007;61(1):39.
21. Pelzang R, Wood B, Black S. Nurses' understanding of patient-centred care in Bhutan. Br J Nurs. 2010;19(3):186–93. doi:10.12968/bjon.2010.19.3.46541
22. Kelly J. Barriers to achieving patient-centered care in Ireland. Dimensions of Critical Care Nursing 2007;26(1):29–34.
23. Légaré F, Stacey D, Turcotte S, et al. Interventions for improving the adoption of shared decision making by healthcare professionals. The Cochrane Database of Systematic Reviews 9. 2014 Sep 15. https://doi.org/10.1002/14651858.CD006732.pub3
24. Beach MC, Sugarman J, Johnson RL, et al. Do patients treated with dignity report higher satisfaction, adherence, and receipt of preventive care? Annals of Family Medicine 2005;3(4):331–8.
25. Schneider J, Kaplan SH, Greenfield S, et al. Better physician-patient relationships are associated with higher reported adherence to antiretroviral therapy in patients with HIV infection. Journal of General Internal Medicine 2004;19(11): 1096–1103.
26. van den Bemt BJ, Zwikker HE, van den Ende CH. Medication adherence in patients with rheumatoid arthritis: a critical appraisal of the existing literature. Expert Review of Clinical Immunology 2012;8(4):337–51.
27. Waimann CA, Marengo MF, de Achaval S, et al. Electronic monitoring of oral therapies in ethnically diverse and economically disadvantaged patients with rheumatoid arthritis: consequences of low adherence. Arthritis and Rheumatism 2013;65(6):1421–9.
28. Galo JS, Mehat P, Rai SK, et al. What are the effects of medication adherence interventions in rheumatic diseases: a systematic review. Annals of the Rheumatic Diseases 2016;75(4):667-673.
29. Kuntz JL, Safford MM, Singh JA, et al. Patient-centered interventions to improve medication management and adherence: a qualitative review of research findings. Patient Education and Counseling 2014;97(3):310–26.
30. Resnik DB. The patient's duty to adhere to prescribed treatment: an ethical analysis. Journal of Medicine and Philosophy 2005;30(2):167–88.
31. Cameron C. Patient compliance: recognition of factors involved and suggestions for promoting compliance with therapeutic regimens. Journal of Advanced Nursing 1996;24(2):244–50.
32. Horne R, Weinman J, Barber N, et al. Concordance, adherence and compliance in medicine taking. Report for the National Coordinating Centre for NHS Service Delivery and Organization R & D [NCCSDO] Available at. 23 February 2008. http://www.sdo.lshtm.ac.uk/files/project/76-final-report.pdf.

33. Horne R. Representations of medication and treatment: advances in theory and assessment. In: Petrie KJ, Weinman J, editors. Perceptions of health and illness. Chur [Switzerland]: Harwood; 1997. p. 155–88.
34. Horne R, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. Journal of Psychosomatic Research 1999;47:555–67.
35. Clifford S, Barber N, Horne R. Understanding different beliefs held by adherers, unintentional nonadherers, and intentional nonadherers: application of the necessity-concerns framework. Journal of Psychosomatic Research 2008; 64:41–6.
36. Pasma A, van't Spijker A, Hazes JM, et al. Factors associated with adherence to pharmaceutical treatment for rheumatoid arthritis patients: a systematic review. Seminars in Arthritis and Rheumatism 2013 Aug;43(1):18–28.
37. World Health Organisation. Adherence to long-term therapies: evidence for action Geneva. World Health Organisation; 2003.
38. Neame R, Hammond A. Beliefs about medications: a questionnaire survey of people with rheumatoid arthritis. Rheumatology [Oxford] 2005;44(6):762–7.
39. van den Bemt BJ, van den Hoogen FH, Benraad B, et al. Adherence rates and associations with nonadherence in patients with rheumatoid arthritis using disease modifying antirheumatic drugs. The Journal of Rheumatology 2009; 36(10):2164–70.
40. Zwikker HE, van Dulmen S, den Broeder AA, van den Bemt BJ, van den Ende CH. Perceived need to take medication is associated with medication non-adherence in patients with rheumatoid arthritis. Patient Prefer Adherence. 2014;8:1635-45. doi:10.2147/PPA.S66849
41. Linn AJ, Vervloet M, van Dijk L, et al. Effects of eHealth interventions on medication adherence: a systematic review of the literature. Journal of Medical Internet Research 2011 Dec 5;13(4):e103.
42. Dragoi RG, Ndosi M, Sadlonova M, et al. Patient education, disease activity and physical function: can we be more targeted? A cross sectional study among people with rheumatoid arthritis, psoriatic arthritis and hand osteoarthritis. Arthritis Research & Therapy 2013;15:R156.
43. Kjeken I, Dagfinrud H, Mowinckel P, et al. Rheumatology care: involvement in medical decisions, received information, satisfaction with care, and unmet healthcare needs in patients with rheumatoid arthritis and ankylosing spondylitis. Arthritis Care & Research 2006;55(3):394–401.
44. Nota I, Drossaert CH, Taal E, van de Laar MA. Patients' considerations in the decision-making process of initiating disease modifying anti rheumatic drugs. Arthritis Care & Research 2015;67(7):956–64.
45. Hardware B, Lacey E, Shewan J. Towards the development of a tool to assess educational needs in patients with arthritis. Clinical Effectiveness in Nursing 2004;8:111–7.
46. Gossec L, Paternotte S, Aanerud GJ, et al. Finalisation and validation of the rheumatoid arthritis impact of disease score, a patient-derived composite measure of impact of rheumatoid arthritis: a EULAR initiative. Annals of the Rheumatic Diseases 2011;70(6):935–42.

47. Aaronson NK, Acquadro C, Alonso J, et al. International quality of life assessment (IQOLA) project. Quality of Life Research : An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation 1992;1(5):349–51.

48. Mittal MK, Dhuper S, Siva C, et al. Assessment of email communication skills of rheumatology fellows: a pilot study. Journal of the American Medical Informatics Association 2010;17(6):702–6.

49. Zangi HA, Ndosi M, Adams J, et al. EULAR recommendations for patient education for people with inflammatory arthritis. Annals of the Rheumatic Diseases 2015;74(6):954–62.

50. Peters E, Hibbard J, Slovic P, et al. Numeracy skill and the communication, comprehension, and use of risk-benefit information. Health Affairs (Millwood) 2007;26(3):741–8.

51. Fiscella K, Epstein RM. So much to do, so little time: care for the socially disadvantaged and the 15-minute visit. Archives of Internal Medicine 2008;168(17):1843–52.

52. Epstein RM, Street Jr RL. The values and value of patient-centered care. Annals of Family Medicine 2011;9(2):100–3.

53. Institute of Medicine Committee on Health, L.. In: Nielsen-Bohlman L, Panzer AM, Kindig DA, editors. Health literacy: a prescription to end confusion. US: National Academies Press; 2004. Copyright 2004 by the National Academy of Sciences. All rights reserved.: Washington (DC).

54. Sheridan SL, Halpern DJ, Viera AJ, et al. Interventions for individuals with low health literacy: a systematic review. Journal of Health Communication 2011;16(Suppl. 3):30–54.

55. Jordan JE, Buchbinder R, Osborne RH. Conceptualising health literacy from the patient perspective. Patient Education and Counseling 2010;79(1):36–42.

56. Paasche-Orlow MK, Parker RM, Gazmararian JA, et al. The prevalence of limited health literacy. Journal of General Internal Medicine 2005;20(2):175–84.

57. Davis TC, Long SW, Jackson RH, et al. Rapid estimate of adult literacy in medicine: a shortened screening instrument. Family Medicine 1993;25(6):391–5.

58. Parker RM, Baker DW, Williams MV, et al. The test of functional health literacy in adults: a new instrument for measuring patients' literacy skills. Journal of General Internal Medicine 1995;10(10):537–41.

59. Weiss BD, Mays MZ, Martz W, et al. Quick assessment of literacy in primary care: the newest vital sign. Annals of Family Medicine 2005;3(6):514–22.

60. Ishikawa H, Takeuchi T, Yano E. Measuring functional, communicative, and critical health literacy among diabetic patients. Diabetes Care 2008;31(5):874–9.

61. McCormack L, Bann C, Squiers L, et al. Measuring health literacy: a pilot study of a new skills-based instrument. Journal of Health Communication 2010;15(Suppl. 2):51–71.

62. Norman CD, Skinner HA. eHEALS: the eHealth literacy scale. Journal of Medical Internet Research 2006;8(4):e27.

63. Haun JN, Valerio MA, McCormack LA, et al. Health literacy measurement: an inventory and descriptive summary of 51 instruments. Journal of Health Communication 2014;19(Suppl. 2):302–33.

64. Hay MC, Cadigan RJ, Khanna D, et al. Prepared patients: internet information seeking by new rheumatology patients. Arthritis Care & Research 2008;59(4):575–82.

65. van der Vaart R, Drossaert CH, Taal E, et al. Patient preferences for a hospital-based rheumatology interactive health communication application and factors associated with these preferences. Rheumatology 2011;50(9):1618–26.

66. Ansani NT, Vogt M, Henderson BAF, et al. Quality of arthritis information on the internet. American Journal of Health- System Pharmacy 2005;62(11):1184–9.

67. Berland GK, Elliott MN, Morales LS, et al. Health information on the Internet: accessibility, quality, and readability in English and Spanish. Journal of the American Medical Association 2001;285(20):2612–21.

68. Van der Vaart R, Drossaert CH, de Heus M, et al. Measuring actual eHealth literacy among patients with rheumatic diseases: a qualitative analysis of problems encountered using health 1.0 and health 2.0 applications. Journal of Medical Internet Research 2013;15(2).

69. Rittberg R, Dissanayake T, Katz SJ. A qualitative analysis of methotrexate self-injection education videos on YouTube. Clinical Rheumatology 2015:1–5.

70. Katz SJ, Leung S. Teaching methotrexate self-injection with a web-based video maintains patient care while reducing healthcare resources: a pilot study. Rheumatology International 2015;35(1):93–6.

71. Tsulukidze M, Durand M-A, Barr PJ, et al. Providing recording of clinical consultation to patients – a highly valued but underutilized intervention: a scoping review. Patient Education and Counseling 2014;95(3):297–304.

72. Tsulukidze M, Grande SW, Thompson R, et al. Patients covertly recording clinical encounters: threat or opportunity? A qualitative analysis of online texts. PLoS One 2015;10(5):e0125824.

73. Charles C, Gafni A, Whelan T. Decision-Making in the physician-patient encounter: revisiting the shared treatment decision-making model. Social Science & Medicine 1999;49(5):651–61.

74. Frosch DL, Kaplan RM. Shared decision-making in clinical medicine: past research and future directions. American Journal of Preventive Medicine 1999;17(4):285–94.

75. Kassirer JP. Incorporating patients' preferences into medical decisions. New England Journal of Medicine 1994; 330(26):1895–6.

76. O'Connor AM, et al. Knowledge translation for patients: methods to support patients participation in decision-making about preference sensitive treatment options in Rheumatology. In: Tugwell P, et al., editors. Evidence-based rheumatology. London: BMJ Publishing Group; 2004.

77. Ward MM, Sundaramurthy S, Lotstein D, et al. Participatory patient-physician communication and morbidity in patients with systemic lupus Erythematosus. Arthritis Care & Research 2003;49(6):810–8.

78. Joosten EAG, DeFuentes-Merillas L, de Weert GH, et al. Systematic review of the effects of shared decision-making on patient satisfaction, treatment adherence and health status. Psychotherapy and Psychosomatics 2008;77(4):219–26.

79. Wilson SR, Strub P, Buist AS, et al. Shared treatment decision-making improves adherence and outcomes in poorly controlled asthma. American Journal of Respiratory and Critical Care Medicine 2010;181(6):566–77.

80. Nota I, Drossaert CH, Taal E, et al. Patient participation in decisions about disease modifying anti-rheumatic drugs: a cross-sectional survey. BMC Musculoskeletal Disorders 2014;15:333.

81. Brekke M, Hjortdahl P, Kvien TK. Involvement and satisfaction: a Norwegian study of health care among 1,024 patients with rheumatoid arthritis and 1,509 patients with chronic noninflammatory musculoskeletal pain. Arthritis and Rheumatism 2001;45(1):8–15.

82. Stacey D, L_egar_e F, Col NF, Bennett CL, Barry MJ, Eden KB, et al. Decision aids for people facing health treatment or screening decisions. Status and date: Edited [no change to conclusions], published in. 2014[1].

83. Montori VM, Gafni A, Charles C. A shared treatment decision-making approach between patients with chronic conditions and their clinicians: the case of diabetes. Health Expectations 2006;9(1):25–36.

84. Spoorenberg A, Van Tubergen A, Landewe R, et al. Measuring disease activity in ankylosing spondylitis: patient and physician have different perspectives. Rheumatology 2005;44(6):789–95.

85. Suarez-Almazor ME, Conner-Spady B, Kendall CJ, et al. Lack of congruence in the ratings of patients' health status by patients and their physicians. Medical Decision-Making 2001;21(2):113–21.

86. Smolen JS, Landewe R, Breedveld FC, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. Annals of the Rheumatic Diseases 2014;73(3):492–509.

87. Barton JL, Trupin L, Tonner C, et al. English language proficiency, health literacy, and trust in physician are associated with shared decision-making in rheumatoid arthritis. The Journal of Rheumatology 2014;41(7):1290–7.

88. Fraenkel L, McGraw S. Participation in medical decision-making: the patients perspective. Medical Decision-Making 2007;27:533–8.

89. Elwyn G, Scholl I, Tietbohl C, et al. “Many miles to go...”: a systematic review of the implementation of patient decision support interventions into routine clinical practice. BMC Medical Informatics and Decision-Making 2013;13(Suppl. 2): S14.

90. Gravel K, Legare F, Graham I. Barriers and facilitators to implementing shared decision-making in clinical practice: a systematic review of health professionals' perceptions. Implementation Science 2006;1(1):16.

91. Zong JY, Leese J, Klemm A, et al. Rheumatologists' views and perceived barriers to using patient decision aids in clinical practice. Arthritis Care & Research [Hoboken] 2015;67(10):1463–70.

92. Heisler M, Tierney E, Ackermann RT, et al. Physicians' participatory decision-making and quality of diabetes care processes and outcomes: results from the triad study. Chronic Illness 2009;5(3):165–76.

93. Hanson JL. Shared decision-making: have we missed the obvious? Archives of Internal Medicine 2008;168(13): 1368–70.

94. Neame R, Hammond A, Deighton C. Need for information and for involvement in decision-making among patients with rheumatoid arthritis: a questionnaire survey. Arthritis Care & Research 2005;53(2):249–55.

95. Schildmann J, Grunke M, Kalden JR, et al. Information and participation in decision-making about treatment: a qualitative study of the perceptions and preferences of patients with rheumatoid arthritis. Journal of Medical Ethics 2008;34(11):775–9.

96. Deber RB, Kraetschmer N, Urowitz S, et al. Do people want to be autonomous patients? Preferred roles in treatment decision-making in several patient populations. Health Expectations 2007;10(3):248–58.

97. Garfield S, Smith F, Francis SA, et al. Can patients' preferences for involvement in decision-making regarding the use of medicines be predicted? Patient Education and Counseling 2007;66(3):361–7.

98. Fraenkel L, Bogardus S, Concato J, et al. Preference for disclosure of information among patients with rheumatoid arthritis. Arthritis Care & Research 2001;45(2):136–9.

99. Montori VM, Hargraves I, LeBlanc A. For empathic decision-making. KER unit blog. Rochester, USA: Mayo Clinic Shared Decision-Making National Resource Center; 2015.

100. Elwyn G, Edwards A, Kinnersley P, et al. Shared decision-making and the concept of equipoise: the competences of involving patients in healthcare choices. The British Journal of General Practice 2000;50(460):892–9.

101. Towle A, Godolphin W, Grams G, et al. Putting informed and shared decision-making into practice. Health Expectations 2006;9(4):321–32.

102. Levinson W. Not all patients want to participate in decision-making. A national study of public preferences. Journal of General Internal Medicine 2005;20(6):531–5.

103. Arora NK, McHorney CA. Patient preferences for medical decision-making: who really wants to participate? Medical Care 2000;38(3):335–41.

104. Ende J, Kazis L, Ash A, et al. Measuring patients' desire for autonomy. Journal of General Internal Medicine 1989;4(1): 23–30.

105. Beisecker AE, Beisecker TD. Patient information-seeking behaviors when communicating with doctors. Medical Care 1990;28(1):19–28.

106. Charles C, Gafni A, Whelan T. Shared decision-making in the medical encounter: what does it mean?[or it takes at least two to tango]. Social Science & Medicine 1997;44(5):81–92. 6.

107. Charles C, Gafni A, Whelan T. Decision-Making in the physician-patient encounter: revisiting the shared treatment decision-making model. Social Science & Medicine 1999;49(5):651–61.

108. Edwards A, Elwyn G. Inside the black box of shared decision-making: distinguishing between the process of involvement and who makes the decision. Health Expectations 2006;9(4):307–20.

109. Bhavnani V, Fisher B. Patient factors in the implementation of decision aids in general practice: a qualitative study. Health Expectations 2010;13(1):45–54.

110. van Tol-Geerdink JJ, Stalmeier PF, van Lin EN, et al. Do patients with localized prostate cancer treatment really want more aggressive treatment? Journal of Clinical Oncology 2006;24(28):4581–6.

111. Stiggelbout AM, Van der Weijden T, De Wit MP, et al. Shared decision-making: really putting patients at the centre of healthcare. British Medical Journal 2012;27(344):e256.

112. Li LC, Adam PM, Backman CL, et al. Proof-of-concept study of a web-based methotrexate decision aid for patients with rheumatoid arthritis. Arthritis Care & Research [Hoboken] 2014;66(10):1472–81.

113. Fraenkel L, Peters E, Charpentier P, et al. Decision tool to improve the quality of care in rheumatoid arthritis. Arthritis Care and Research 2012;64(7):977–85.

114. Barton JL, Koenig CJ, Evans-Young G, et al. The design of a low literacy decision aid about rheumatoid arthritis medications developed in three languages for use during the clinical encounter. BMC Medical Informatics and Decision Making 2014 November 25;14(1):104.

115. Nota I, Drossaert C, Taal E, et al. The evaluation of a patient decision aid for anti-rheumatic drugs. EULAR 2014:175. Paris; 2014.

116. The European Network on Patient Empowerment. Patient Empowerment – Living with a chronic disease. http://www. enope.eu/.

117. Coulter A, Collins A. Making shared decision-making a reality: no decision about me, without me. London: The Kings Fund; 2011. Available at: http://www.kingsfund.org.uk/publications/nhs_ decisionmaking.html [accessed 11.07.15].

118. Lorig KR, Holman H. Self-management education: history, definition, outcomes, and mechanisms. Annals of Behavioral Medicine 2003;26(1):1–7.

119. Barlow J, Wright C, Sheasby J, et al. Self-management approaches for people with chronic conditions: a review. Patient Education and Counseling 2002;48(2):177–87. (a) Newman S, Steed L, Mulligan K. Self-management interventions for chronic illness. Lancet 2004 October 23–29; 364(9444):1523–37.

120. Holman H, Lorig K. Patient self-management: a key to effectiveness and efficiency in care of chronic disease. Public Health Reports 2004;119(3):239–43.

121. Carryer J, Budge C, Hansen C, et al. Providing and receiving self-management support for chronic illness: patients' and health practitioners' assessments. Journal of Primary Health Care 2010;2(2):124–9.

122. Dures E, Hewlett S. Cognitive-behavioural approaches to self-management in rheumatic disease. Nature Reviews Rheumatology 2012;8(9):553–9.

123. Garnefski N, Kraaij V, Benoist M, et al. Effect of a cognitive behavioral self-help intervention on depression, anxiety, and coping self-efficacy in people with rheumatic disease. Arthritis Care & Research [Hoboken] 2013;65(7):1077–84.

124. Niedermann K, Fransen J, Knols R, et al. Gap between short- and long-term effects of patient education in rheumatoid arthritis patients: a systematic review. Arthritis and Rheumatism 2004;51(3):388–98.

125. Riemsma RP, Taal E, Kirwan JR, et al. Systematic review of rheumatoid arthritis patient education. Arthritis and Rheumatism 2004;51(6):1045–59.

126. Nuñez DE, Keller C, Ananian CD. A review of the efficacy of the self-management model on health outcomes in community-residing older adults with arthritis. Worldviews on Evidence-Based Nursing 2009;6(3):130–48.

127. Jerant AF, von Friederichs-Fitzwater MM, Moore M. Patients' perceived barriers to active self-management of chronic conditions. Patient Education and Counseling 2005;57(3):300–7.

128. Foster G, Taylor SJ, Eldridge SE, et al. Self-management education programmes by lay leaders for people with chronic conditions. Cochrane Database of Systematic Reviews 2007;4. Cd005108.

129. Hainsworth J, Barlow J. Volunteers' experiences of becoming arthritis self-management lay leaders: "It's almost as if I've stopped aging and started to get younger!". Arthritis and Rheumatism 2001;45(4):378–83.

130. Lorig KR, Ritter PL, Laurent DD, et al. The internet-based arthritis self-management program: a one-year randomized trial for patients with arthritis or fibromyalgia. Arthritis and Rheumatism 2008;59(7):1009–17.

131. Lorig KR, Ritter PL, Dost A, et al. The expert patients programme online, a 1-year study of an internet-based self-management programme for people with long-term conditions. Chronic Illness 2008;4(4):247–56.

132. Azevedo AR, de Sousa HM, Monteiro JA, et al. Future perspectives of smartphone applications for rheumatic diseases self-management. Rheumatology International 2015;35(3):419–31.

133. Revenson TA. The role of social support with rheumatic disease. Baillière's Clinical Rheumatology 1993;7(2):377–96.

134. Pickard S. The 'good carer': moral practices in late modernity. Sociology 2010;44(3):471–87.

135. Rogers A, Brooks H, Vassilev I, et al. Why less may be more: a mixed methods study of the work and relatedness of 'weak ties' in supporting long-term condition self-management. Implementation Science 2014;9:9.

136. Kroenke K, Spitzer RL, Williams JBW, et al. Physical symptoms in primary care predictors of psychiatric disorders and functional impairment. Archives of Family Medicine 1994;3:774–9.

137. Gettings L. Psychological well-being in rheumatoid arthritis: a review of the literature. Musculoskeletal Care 2010; 8(2):99–106.

138. Dissanayake RK, Bertouch JV. Psychosocial interventions as adjunct therapy for patients with rheumatoid arthritis: a systematic review. International Journal of Rheumatic Diseases 2010;13(4):324–34.

139. McBain H, Shipley M, Olaleye A, et al. A self-monitoring and patient-initiated follow-up service for patients with rheumatoid or psoriatic arthritis: a randomized controlled trial. EULAR 2014. Paris: Abstract OP0086-HPR.

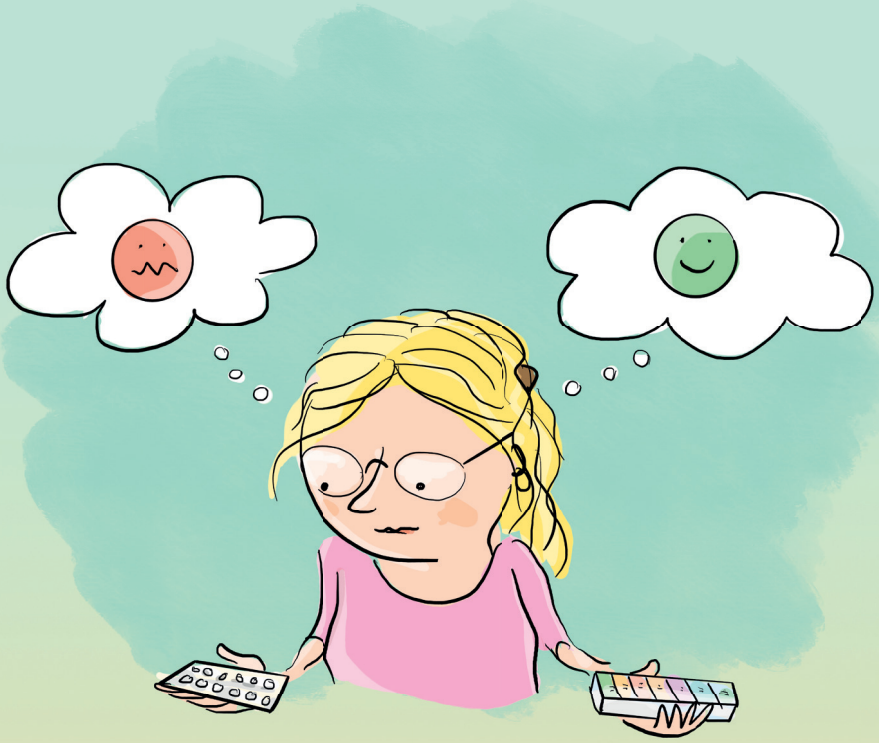
140. Coulter A, Ellins J. Effectiveness of strategies for informing, educating, and involving patients. BMJ: British Medical Journal 2007;335(7609):24–7.

141. Bechel D, Myers WA, Smith DG. Does patient-centered care pay off? Joint Commission Journal on Quality and Patient Safety 2000;26(7):400–9.

142. Stewart M, Brown JB, Donner A, et al. The impact of patient-centered care on outcomes. The Journal of Family Practice 2000;49(9):796–804.

143. van der Vaart R, Drossaert CH, Taal E, et al. Experiences and preferences of patients regarding a rheumatology interactive health communication application: a qualitative study. International Journal on Advances in Life Sciences 2010;2(3&4):143–53.

144. van der Vaart R, Drossaert CH, Taal E, et al. Impact of patient-accessible electronic medical records in rheumatology: use, satisfaction and effects on empowerment among patients. BMC Musculoskeletal Disorders 2014;26(15):102.



Chapter 3

Barriers and facilitators to disease-modifying antirheumatic drug use in patients with inflammatory rheumatic diseases: a qualitative theory-based study

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Abstract

Background: Although disease-modifying anti-rheumatic drugs (DMARDs) are the cornerstone of treatment for inflammatory rheumatic diseases, medication adherence to DMARDs is often suboptimal. Effective interventions to improve adherence to DMARDs are lacking, and new targets are needed to improve adherence. The aim of the present study was to explore patients' barriers and facilitators of optimal DMARD use. These factors might be used as targets for adherence interventions.

Methods: In a mixed method study design, patients (n = 120) with inflammatory arthritis (IA) completed a questionnaire based on an existing adapted Theoretical Domains Framework (TDF) to identify facilitators and barriers of DMARD use. A subgroup of these patients (n = 21) participated in focus groups to provide insights into their facilitators and barriers. The answers to the questionnaires and responses of the focus groups were thematically coded by three researchers independently and subsequently categorized.

Results: The barriers and facilitators that were reported by IA patients presented large inter-individual variations. The identified barriers and facilitators could be captured in the following domains based on an adapted TDF: *(i)* knowledge, *(ii)* emotions, *(iii)* attention, memory, and decision processes, *(iv)* social influences, *(v)* beliefs about capability, *(vi)* beliefs about consequences, *(vii)* motivation and goals, *(viii)* goal conflict, *(ix)* environmental context and resources, and *(x)* skills.

Conclusions: Patients with IA have a variety of barriers and facilitators with regard to their DMARD use. All of these barriers and facilitators could be categorized into adapted domains of the TDF. Interventions that address individual facilitators and barriers, based on capability, opportunity, and motivation, are needed to develop strategies for medication adherence that are tailored to individual patient needs.

BACKGROUND

Inflammatory arthritis (IA) is a long-term autoimmune disease that is characterized by pain, swollen joints, bone damage, and disability [1–3]. The most common conditions of IA are rheumatoid arthritis (RA), ankylosing spondylitis (AS), and psoriatic arthritis (PsA). Inflammatory arthritis, especially RA and PsA, can cause joint damage without proper and early treatment, and early guided treatment with disease-modifying anti-rheumatic drugs (DMARDs) is often recommended [4–8]. The new paradigm in inflammatory arthritis, is to treat to target (T2T), involving regular disease activity monitoring, ideally using the most recently described composite measures and remission criteria [9, 10]. The full benefits of DMARDs can be achieved if patients strictly follow drug regimens [11–14]. However, rates of adherence to prescribed medications in patients with IA are suboptimal and vary widely from 3 to 93 % [15–22]. Therefore, interventions to improve medication adherence are warranted, but current interventions to improve adherence are often complex and not very effective [12, 23]. To discover possible intervention targets, more insights into patients' motivations to take or not take their medications are essential [24, 25].

Theoretical models may be useful for systematically exploring possible drivers of non-adherence and finding corresponding intervention strategies that target these drivers [26–28]. Although different models have been applied to medication adherence, none of these individual models have been satisfactory for identifying barriers that result in non-adherence [28–33]. A possible explanation might be that the applied models, such as the Health Belief Model [34], Theory of Reasoned Action [35], Theory of Planned Behaviour [36], and Social Cognitive Theory [37], were developed to *understand*, *explain*, or *predict* behaviours. However, to develop useful interventions for adherence, other models or theoretical constructs are needed that are particularly relevant to *changing* behaviour. This means that some essential domains, such as skills [38] or the environment [39], may be overlooked by some theories. To develop a model that contains many domains that could be associated with different behaviour theories, including theories that focus on behavioural change, the Theoretical Domains Framework (TDF) could be helpful. The TDF [40] poses 12 theoretical domains that are based on 33 health behaviour theories (see Additional file 1). The TDF covers a broad spectrum of individual and organisational theories. Thus, it limits the risk of omitting important areas when exploring factors that may impact adherence to

DMARD treatment. With regard to medication adherence, the TDF has only been applied in a study of barriers to medication adherence in cardiovascular disease. This resulted in an adapted version of the TDF that contains ten of the 12 original TDF domains [25], the Identification of Medication Adherence Barriers Model (IMAB; see Fig. 1).

To obtain more insights into patients' drivers that result in adherence and non-adherence, the aim of the present study was to identify both facilitators and barriers of DMARD use in IA patients using an adapted version of the TDF that was designed for medication adherence (IMAB). Although the IMAB was developed to identify medication adherence *barriers*, the present study focused on identifying *facilitators* as well using the same domains of this model.

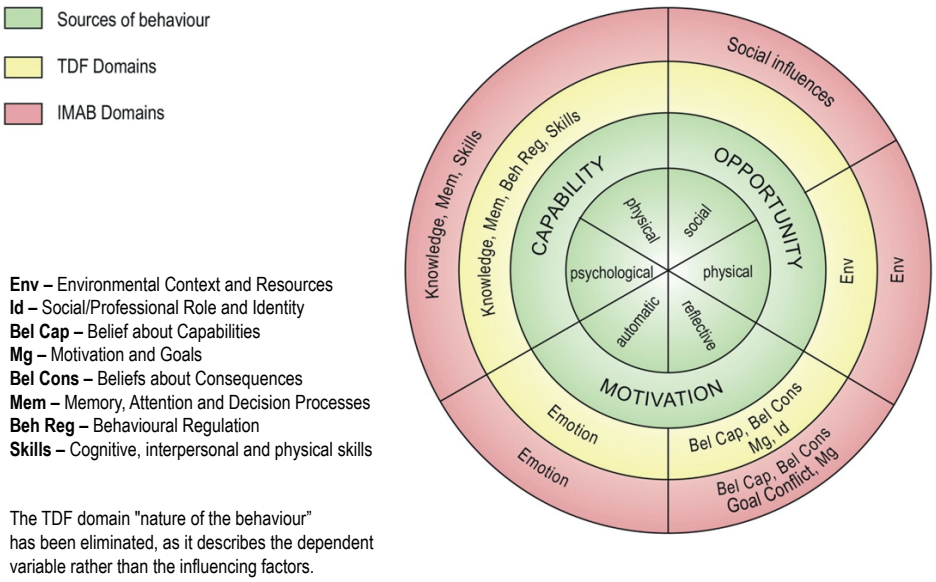


Figure 1. COM-B, derived from the Behaviour Change Wheel [45], TDF [40], and IMAB [25]

METHODS

The results of this mixed method study are reported according to the Consolidated criteria for reporting qualitative research (COREQ) [41].

Design

The study consisted of two phases: (1) a cross sectional survey using a questionnaire that assessed facilitators and barriers of medication use in patients with IA who were using DMARDs, and (2) focus groups with a subgroup of Phase 1 patients to provide in-depth understanding of the identified facilitators and barriers. The aim was to first identify barriers and facilitators of DMARD use in a large group of IA patients by sending out questionnaires and then use these answers in smaller focus group sessions (10–15 patients) to discuss, elaborate upon, and deepen the understanding of the raised barriers and facilitators, until thematic saturation occurred.

Participants

Patients (n = 285) who were registered in the outpatient pharmacy of the Sint Maartenskliniek (Nijmegen, The Netherlands) were invited by mail to participate in this study according to a random sampling method. The inclusion criteria were the following: (1) adult (>18 years old) IA patients who used DMARDs and (2) ability to read and write in Dutch. No exclusion criteria were applied. Both early and established IA patients were eligible to participate in the study. The written invitation consisted of a letter with a description of the study, a questionnaire with open-ended questions, and an invitation to participate in the focus groups. To assess the adherence of the patients to DMARDs, the Compliance Questionnaire on Rheumatology (CQR) was applied. Self-addressed stamped envelopes were provided for the patients to return the questionnaires.

Procedure

Phase 1: questionnaires in patients with IA who used DMARDs

The questionnaire comprised 18 open-ended questions that covered the ten IMAB domains, derived from the TDF (Table 1). The questions were formulated by the researchers (MV, BvdB, and SvD) and pilot-tested through a think-aloud procedure [42] by seven patients with IA, ten people without IA, and two psychologists. The questionnaire allowed the patients to add new domains in cases in which a construct did not fit in any of the existing domains ("Is there anything that influences the use of your medication that is not represented by one of the presented domains?").

Table 1. Summary of questions with corresponding IMAB domains

Domain	Interview question
Knowledge	What would you like to know about your medication to take them (or inject them) as prescribed by your physician?
Emotions	Which emotions are evoked by the use of your medication?
Attention, memory, and decision process	Are you preoccupied with your medication? Do you sometimes, on purpose or accidently, forget your medication? Do you feel sufficiently involved in the decision-making process surrounding your medication?
Social influences	In which way does your physician play a role in the use of your medication, other than prescribing them? Does any other health professional (like your pharmacist or your RA nurse practitioner) play a role in the use of your medication? Does your family or do your friends play a role in the use of your medication? Does your work environment (colleagues or supervisors) influence your medication use?
Beliefs about capabilities	In which situations do *you* find it difficult to use your medication?
Beliefs about consequences	According to you, what could be the consequences of taking (or injecting) your medication? According to you, what could be the consequences of NOT taking (or injecting) your medication?
Motivation and goals	What is an important goal (or an important personal motivation) for you to take (or inject) your medication? What is an important goal (or an important personal motivation) for you NOT to take (or inject) your medication?
Goal conflict	What is helpful to you in daily life to be able to take or inject your medication the right way? Which daily hassles prevent you sometimes from taking (or injecting) your medication?
Environmental context and resources	Is the use of your medication sometimes influenced by the ordering, retrieving, delivery, prescribing, and/or reimbursement of your medication?
Skills	According to you, what is important for a patient with RA to be able (physically as well as mentally) to take (or inject) the medication well?

Phase 2: focus groups with a subgroup of phase 1 patients

All of the patients who participated in the focus groups had previously completed the questionnaire in Phase 1, and were already sensitized to the research topic and IMAB domains. This so-called sensitization process was meant to enhance the quality and quantity of the patients' contributions in the later focus group sessions [43]. The patients who accepted this invitation were randomly selected to participate in one of the focus groups. A pilot focus group was not conducted, since patients were involved in the development of the questions and sensitized by filling out the questionnaire. The duration of the focus group sessions was 2 h, and they were conducted at Sint Maartenskliniek. Two researchers led each focus group. In the first focus group, one female researcher (AH) facilitated plenary conversations, and another female researcher (MV) studied the group process and took notes. Two breakout sessions were led by two female researchers (MO and AH). The second focus group was organised similarly, with the exception that the breakout sessions were led by one female researcher (AH) and one male researcher (BvdB). After introducing all of the participants in the focus group, the aim of the group discussion was clarified, namely to identify potential barriers and facilitators of DMARD use. After the domains of the model were introduced and explained, the group was divided into two breakout groups. Each subgroup was given 45 min to explore five of the ten domains of the IMAB, with a focus on identifying barriers and facilitators for each domain. In the plenary session, after the breakout session, all of the barriers and facilitators that were identified in the subgroups were discussed. The patients were then asked if they could think of any additional barriers or facilitators that did not fit in one of the presented domains, such that new domains could be added.

Analysis

Both focus groups were audiotaped with consent from all of the patients and transcribed verbatim. Descriptive statistics were computed (means, standard deviations, and frequencies where appropriate). To ensure the patients' privacy, all identifying information was anonymised. All patients in the focus group read the transcripts and were given the opportunity to discuss changes they felt were needed before coding the transcripts (member check). The answers of the questionnaire and the content of the transcripts were then thematically analysed [44] to identify themes and subthemes that reflected facilitators and barriers for adherence and non-adherence. The notes that were taken during the breakout sessions were also analysed. Three researchers (MV, JV, and BvdB) independently

coded the data and categorized the codes into themes and subthemes using the IMAB model. The coding process was discussed until consensus was reached among the researchers.

To facilitate a future implementation process, the barriers and facilitators that were identified with the corresponding IMAB domains were categorized according to the components of the Behaviour Change Wheel [45]: Capability, Opportunity, and Motivation (COM). In this behaviour system, these three components interact to generate Behaviour (COM-B; Fig. 1).

RESULTS

One hundred twenty of the 285 patients (42 %) returned the questionnaire. The mean age of the patients that returned the questionnaire was 59.6 years (SD = 15.4 years), and 60 % of the patients were female. Most of the patients had RA (71 %). DMARD adherence according to the CQR was 68 % (Table 2).

Table 2. Patient characteristics

	Patients
	(*n* = 285)[a]
Age, years (SD)	59.6 (±15.4)
Female, *n* (%)	171 (60%)
Diagnosis:	
Rheumatoid arthritis	201 (71%)
Rheumatoid factor (RF positive+)	140 (70%)
Anti-citrullinated Protein antibodies Positive(Anti-CCP+)	114 (57%)
Psoriatic arthritis	49 (17%)
Juvenile idiopathic arthritis	12 (4%)
Other diagnoses	23 (8%)
Pharmacological therapy, n (%)	
Methotrexate	239 (84%)
Sulphasalazine	7 (2%)
Leflunomide	8 (3%)
Hydroxychloroquine	52 (18%)
Glucocorticosteroid	29 (10%)
Biological DMARDs	81 (28%)

Note: Questionnaires were processed anonymously. The patient characteristics that are presented in the table were gathered from the patients that filled out the questionnaire

The subgroup of patients in the focus groups was comparable with regard to mean age (59.4 years, SD = 9.4 years). Of the patients in the focus groups, 86 % were female, and the majority of the patients had RA. DMARD adherence according to the CQR was 43 %.

Table 3 summarizes the identified barriers and facilitators for IA patients (by the respondents of the questionnaire and the participants of both focus groups) with regard to DMARD use, categorized according to the IMAB model and COM-B core components that were derived from the Behaviour Change Wheel [45]. The Attention, Memory, and Decision Process domain was split into two separate domains based on consensus between the three researchers ("Memory and Attention" and "Decision-making process") to accommodate the categorization of all of the identified barriers and facilitators. Several of the identified barriers and facilitators were categorized into more than one IMAB domain because of the multifaceted nature of these factors. All of the barriers and facilitators that were collected could be categorized in the presented domains. No new, additional domains were mentioned by the focus groups, which supported the data received from the respondents of the questionnaire.

Table 3. IMAB domains and corresponding facilitators and barriers categorized according to COM-B components

COM-B	Domain	Facilitators	Barriers
CAPABILITY	Knowledge	Knowledge of treatment effect Information about necessity Information about alternative medication Information about experiences from others Knowledge of how to administer medication	Knowledge of side effects Knowledge of cost of medication
	Skills	Cognitive abilities Coping strategies Communication skills Fine motor skills	Insufficient cognitive, communicative, or physical skills to understand and/or administer medication
	Memory and Attention	Treatment effect Aids (to remember) Social support Embedded in daily routine	Lack of daily routine Experiencing side effects Forgetting to take medication Change of appearance of medication Impact on lifestyle Lack of treatment effect

Table 3. Continued

COM-B	Domain	Facilitators	Barriers
	Decision-making process	Self-management (patient decides) Satisfying relationship with health professional (communication and trust)	Lack of involvement of health professional (health professional decides, no shared decision- making) Doubting own knowledge Influence of health insurance companies
OPPORTUNITY	Environmental context and resources	Logistics (having medication in stock) Access to health professionals	Quality of product (needle) Logistics (medication storage temperature, pharmacy has no stock) Cost of medication Travelling (clearing injectable medications through customs) Change of name or appearance of medication
	Social influences	Health professionals (rheumatologist, pharmacist, nurse, general practitioner): capabilities, trust, and empathy Health insurance company: reimburses medication, provides clear information Family and friends: support adherence, support in choices of medication, instrumental support Colleagues: support, understanding	Lack of support from colleagues (incomprehension, negative reactions)
MOTIVATION	Beliefs about capabilities	Aids (to use, to remember) Self-efficacy Good (overall) health status	Difficulty in adherence because of social and work events Lack of daily routine Worse health status Difficult to inject Experience of side effects Doubting own knowledge with regard to medication (as barrier to adherence)

Table 3. Continued

COM-B	Domain	Facilitators	Barriers
	Beliefs about consequences	Belief of treatment effect Belief of being able to better participate (social, work)	Experience of (long- and short-term) side effects Belief that medication will be harmful: higher disease activity Lack of belief in efficacy Dependency on medication Less acceptance of (long-term) medication Non-acceptance of diagnosis
	Emotions	Joy Gratitude Hope Confidence	Anxiety Sadness Anger Dependency on medication Irritation Incomprehension Disparity Powerlessness/ helplessness Insecurity Feeling overwhelmed Feeling crestfallen Grief Embarrassment Regret Stress Disappointment Desolation Despair Agitation
	Motivation and Goals	Improvement of Quality of Life Treatment effect Social participation (including work) Improvement of life expectancy Better relationship with health professional Maintain autonomy	Worse health status/ wellbeing Side effects Comorbidity Complexity of regimen Resistance of need for medication Denial of existence of illness Difficulty administering medication Lack of daily routine

Table 3. Continued

COM-B	Domain	Facilitators	Barriers
	Goal conflict	Embedded in daily routine Treatment effect leading to active social participation (e.g., work) Instrumental support (aids, information) Social support Method of administration (intravenous or low frequency) Stock (always available)	Experiencing side effects Restrictions due to using medication (no alcohol) Worse well-being (mentally and/or physically) Not able to participate (social, work) Distracted from taking medication Lack of social support

Capability

Capability, the first COM-B component, reflects the individual's psychological and physical capacity to engage in the activity concerned [45]. Capability encompassed the following domains: Knowledge, Skills, Memory and Attention, and Decision-making Process.

Knowledge

Knowledge about DMARD use was considered both a barrier and a facilitator of adherence. Information about how to administer the medication, general information (also about alternative medications), and information about necessity and the time to onset of effect of DMARD use were mentioned frequently as facilitators of DMARD use. Knowledge of side effects and the cost of some of the medications were perceived as barriers. Some patients sometimes felt guilty using expensive medications, and they felt that they were a burden to society. Thoughts and doubts about how precisely the medication acts on the body were also mentioned as a potential barrier:

> *"....You do not know how these medications exactly act in your body. Yes, they tend to decrease the disease activity, but you need to know how the medication works. It maybe goes beyond my knowledge, but surely it must be achievable to translate this information in a simple way. I think that would help to accept that you can take or inject this medication...".*
> Female, 63 years, diagnosed with RA in 2015

Clear and understandable instruction inserts were found to facilitate adherence.

Skills

Patients mentioned that having acquired appropriate coping skills to manage the disease and its medication were facilitators for medication adherence. Examples were given, such as being able to accept the fact that they had to use their medication probably for the rest of their lives. Cognitive abilities were also reported by the patients as facilitators, such as being able to dose their medication, understand which day of the week they need to take certain medications, or being able to distinguish between different medications. Lacking these abilities was seen as a barrier to medication adherence. Several barriers, such as how to open the package of the medication or difficulties with opening the tap to get water for medication, were also mentioned. These physical abilities were referred to as "fine motor skills." Communication skills were considered to be crucial, such as being able to communicate in a timely manner with the rheumatologist about side effects when these side effects prevented patients from using the prescribed medication.

Memory and attention

Patients mentioned that incorporating the intake of their medication in their daily routines was a great help. Aids, such as an alarm on their smartphone or help from a family member to remind them to take the medication, were sometimes used. Experiencing beneficial effects of the medication facilitated adherence to medication use.

> *"They prescribed it, I took it and it went very well. Then I have something to hold on to. If I continue, then all will be great. That is what happened."*
> Female, 75 years, diagnosed with RA in 2009

Social support was mentioned as a facilitator as well. Support from family, friends, and colleagues was considered very essential by all of the patients.

Several barriers of DMARD use were mentioned by the patients, including the absence of a daily routine, experiencing side effects of the medication, forgetting to take the medication, and a lack of efficacy of the medication. Another barrier was related to the appearance or name of the medication. For example, changing the colour or name of the medication was considered confusing and potentially dangerous. The patients also considered the impact of the medication as intruding on their lifestyle, such as not being able to consume alcohol on certain days because of the medication, which was felt as patronizing and limiting social activities.

Decision-making process

The patients mentioned that the physician plays an important role as a facilitator for adherence, specifically in the decision-making process. A good relationship with the treating physician was considered crucial for trust and communication about disease management, including adherence. The patients reported that if they have self-management skills, then a shared decision-making process was considered a natural process, subsequently leading to a more equal relationship with the physician and better adherence. However, potential barriers to adherence were mentioned by the patients, such as a lack of interest and lack of competence by the physician to involve the patient in the treatment regimen or a lack of competence and lack of interest by the patient, which would hamper the patient's involvement as a partner in the treatment.

> *"You need to be taken seriously. A little bit of interaction. Of course you need to trust the abilities of your physician, but it wouldn't hurt to be critical in a positive way..."* Male, 47 years, diagnosed with RA in 2011

The influence of health insurance companies was also mentioned as a potential barrier by the patients, specifically the possibility of a changing reimbursement policy that may influence the adherence or non-adherence to DMARDs.

Opportunity

Opportunity, the second COM-B component, reflects all of the factors that lie outside the individual that make the behaviour possible or prompt it [45]. Opportunity encompassed the following domains: Environmental Context and Resources and Social Influences.

Environmental context and resources

Access to the rheumatologist when needed was felt as an essential facilitator for the patients. Another facilitator that was discussed by the patients was logistics. The prescribed medication should be in stock in the pharmacy. Logistics was also mentioned as a barrier in cases in which the pharmacy did not have the medication in stock. Another barrier was the quality of the products, such as the needles for injections. The patients complained that the needles were too blunt. Additionally, clearing injectable medications through customs while travelling abroad and situations in which the storage temperature could not be controlled were also perceived as barriers.

> *"Going on holiday, taking your injections with you, and the temperature should not exceed above 25 C, that is a disaster. Then I think: the pharmacist should provide a little cool box with these kind of medications"……* Female, 63 years, diagnosed with RA in 2015

The cost of medication was also mentioned as a barrier, but the patients stated that they would be willing to pay a small amount for the medication if it was not covered by their insurance in order to obtain them.

Social influences

Support from the social environment of the patient was mentioned as a facilitator. One example that was related to the private environment was mentioned in one of the focus groups:

> *"Sometimes, when I am feeling good, I think, 'I just skip my medication.' but my husband always pushes me: 'You have to take your medication just as usual.' But, still, I find it difficult (to take my medication always)…"* Female, 64 years, diagnosed with RA in 2000

Therefore, the patients reported that support from family and friends could be helpful to stimulate adherence. This support could be provided by discussing treatment options or by giving instrumental support, such as helping administer the medication.

The patients experienced an understanding of their disease from their social network. They indicated that they received support from their work environment, especially when they showed an open and transparent attitude with regard to their condition. Concerning their treating health professionals (i.e., physician, pharmacist, nurse, and general practitioner), their capabilities, mutual trust, and empathy were considered crucial for treatment. Especially in long-term conditions, bonding with health professionals was found by the patients to be beneficial and recommended with regard to adherence. Furthermore, reimbursement and clear information about the medication that is provided by the health insurance companies were mentioned as facilitators of adherence. As a barrier, the patients mentioned a lack of support, specifically incomprehension by colleagues and subsequent negative reactions.

Motivation

Motivation, the third COM-B component, reflects brain processes that energize and direct behaviour [45]. Motivation encompassed the following domains: Beliefs about Capabilities, Beliefs about Consequences, Emotions, and Motivation and Goals.

Beliefs about capabilities

This domain represents the patients' beliefs about their own capabilities, such as believing they are able to manage their condition (self-efficacy). Having good overall health status (apart from IA) and using aids (to remember to take their medication) were mentioned as facilitators to strengthen their belief in their ability to use DMARDs. Social and work events, a lack of a daily routine, worse health status, difficulties administering the medications (such as how to inject them), experiencing side effects, and doubting their own knowledge about their medications were mentioned as barriers.

Beliefs about consequences

Strong beliefs about the beneficial effects of treatment and believing that they are able to participate better in social activities and work were mentioned as facilitators to medication adherence. The following items were mentioned as barriers: fear, feelings of doubt of efficacy of medication, feelings of desire to stop treatment to be free of the ongoing dependency on medication, feelings of insecurity about the long-term effects, and nonacceptance of the IA diagnosis.

Emotions

In contrast to the basic negative emotions (fear, anger, and sadness) and other negative feelings (Table 3) that were often mentioned as barriers to medication adherence, positive emotions (joy, feelings of gratitude, hope, and confidence) were rarely mentioned with regard to DMARD use.

> *"I am worried about my organs, such as my heart, my liver and my kidneys. It is toxic, everything I need to take. I cannot imagine that my body can tolerate it for many years. So, that is my biggest fear...."* Female, 51 years, diagnosed with RA in 2014

Motivation and goals

Facilitators of adherence that were mentioned in this domain, were experiencing a positive effect of the medication and being able to maintain autonomy, social participation, and work participation, leading

to improvements in quality of life. The patients were well aware that treatment options have significantly better health outcomes these days, which motivates them to take their medications. Moreover, being able to hold grandchildren, being able to do volunteer work, or being able to keep their jobs were essential facilitators as well. Patients were taking their medication to please their physician to strengthen the relationship. A longer life expectancy was also considered a facilitator with regard to adherence. Patients expressed feeling resistant toward taking their medication, especially patients who already felt down because of the long-term nature of their condition. More practical issues surfaced as barriers, such as a lack of a daily routine, worse health status (not feeling well, besides the IA), fear of side effects, and difficulty administering the medication (use of injections). Especially the elderly patients expressed that their regimen was sometimes perceived as too complex, resulting in non-adherence.

Goal conflicts arose in situations in which the taking of DMARDs interfered with the patients' valued goals. The barriers that were identified with regard to goal conflict included experiencing side effects (and therefore sometimes not being able to participate socially or in a work environment), not being able to consume alcohol while taking their medication (and therefore sometimes feeling restricted in social contexts), not feeling well physically and mentally (besides the IA) and therefore not willing to take the medication, perceiving a lack of social support, and being distracted from taking the medication. Especially during holidays, of which the goal is to relax and enjoy, when there is a lack of a routine, adhering to treatment was found to be difficult, and could lead to ambivalent feelings:

> *"...I always eat my breakfast before the intake of my medication. During holidays, the routine is gone, so a holiday is always positive and nice, but also a little bit negative...."* Male, 51 years, diagnosed with Psoriasis and RA in 2001

However, some facilitators accommodated the intake of DMARDs without interfering with the patients' goals. When taking the medication was firmly embedded in a daily routine, it was easier to adhere to DMARD use. Instrumental support, such as aids (week boxes or a phone alarm), to stimulate adherence was considered helpful. Social support from family, friends, health professionals, and colleagues also strengthened adherence behaviour. Social relatives may emphasize the importance of continuing

to use the medications despite interfering with a goal that is set by the patient and especially the long term benefits. Patients mentioned that an easy way to administer their medication, such as intravenously, or a low frequency of use, helped them to be adherent without causing goal conflicts. The less effort the patient has to expend is associated with a higher probability of adherent behaviour.

DISCUSSION

The barriers and facilitators that were reported by IA patients in the present study presented large inter-individual variations. The barriers and facilitators were identified using the following domains of the existing adapted version of the TDF for medication adherence [25, 40]: *(i)* knowledge, *(ii)* emotions, *(iii)* attention, memory, and decision processes, *(iv)* social influences, *(v)* beliefs about capability, *(vi)* beliefs about consequences, *(vii)* motivation and goals, *(viii)* goal conflict, *(ix)* environmental context and resources, and *(x)* skills. These domains, originally developed to identify medication adherence barriers, appear to be useful for also identifying medication adherence facilitators. In the present study, in addition to using the adapted domains of the TDF, the Behaviour Change Wheel helped categorize all the identified barriers and facilitators under the three elements of the Behaviour Change Wheel (COM-B). Patients should have the *opportunity* to take their medication, should be *motivated* to take their medication, and be *capable* of taking their medication. Because the Behaviour Change Wheel can be effectively used in a process of designing and implementing intervention tools [45], categorization of the identified barriers and facilitators using the domains of an adapted TDF and the Behaviour Change Wheel elements may enhance the future development and implementation of an intervention for adherence.

Most facilitators and barriers that were found in the present study were comparable to factors that were related to adherent and non-adherent behaviour in other studies of long-term diseases. Two recently published reviews summarized quantitative data on facilitators and barriers in patients with RA [16, 26], and some similarities with the present results were found. A good patient-healthcare professional relationship, knowledge about treatment, the absence of negative effects, an easy treatment regimen, patients' belief that they are able to fulfil the therapy, and an appropriate amount of information that is provided

by the healthcare professional appear to improve adherence. Consistent with these two previous reviews, barriers that resulted in non-adherence in the present study included not believing in the necessity of antirheumatic medication, a busy lifestyle, and receiving contradictory information from the healthcare professional. In contrast, the finding that poorly developed health services with inadequate or non-existent reimbursement may stimulate non-adherent behaviour was not evident in our study. The latter might be explained by the fact that good health insurance is available to all patients in The Netherlands.

According to our qualitative study, barriers and facilitators that were mentioned by the patients as related to adherence and non-adherence but were found not to be statistically significant in the previous reviews were coping, immediacy of side-effects, perceived effectiveness of the medication (outcome expectation), lack of belief in benefit, number of medications, level of methotrexate dose, change in appearance of the medication, social support, and improvement in quality of life.

One explanation for the different findings between the present study and the previous reviews may be related to the type of study (i.e., qualitative vs. quantitative research). In the present qualitative study, the patients were free to write down their own experiences as answers to open-ended questions. In the focus groups, discussions that were based on individual opinions were held freely, which contributed to a variety of answers and reflected barriers and facilitators to medication adherence. The previous reviews consisted of quantitative studies, in which different factors were mentioned as statistically related or unrelated to adherence and non-adherence.

The present study provided an overview of many different barriers and facilitators with regard to DMARD use in IA patients. Such various opinions were attributable to the fact that we used an adapted Theoretical Domains Framework with all its domains, thus offering patients the opportunity to identify many different factors that may influence their adherence and non-adherence. Most of the patients' barriers and facilitators were captured by the TDF, which may contribute to developing useful, effective, tailor-made interventions for individual IA patients to stimulate adherence.

All barriers or facilitators that the patients mentioned could be categorized under one of the domains of the adapted TDF, suggesting

that this framework is helpful for identifying barriers and facilitators of medication adherence. Another strength of the TDF is the combination of cognitive and behavioural constructs with appropriate implementation strategies from the Behaviour Change Wheel [45]. The Behaviour Change Wheel comprises three elements—capability, opportunity, and motivation—that may help identify types of interventions that may be suitable for addressing the barriers and facilitators of medication adherence in future studies.

A few limitations of the present study should be mentioned. First, selection bias could have occurred because non-adherent patients might have been less willing to participate in the study. To determine whether selection bias occurred, all of the respondents (n = 120) completed the CQR to assess medication adherence. The rate of adherence was 67.5 %. This represents a comparable rate of adherent and non-adherent respondents compared with previous studies on medication adherence in RA, which limits the possibility of selection bias [15–17].

Second, the response rate for the questionnaire was modest, 42 %. A possible explanation for this modest response could be that it was rather time consuming to complete the questionnaire with open-ended questions and the CQR. Because of the applied methodology, it was not possible to examine whether responders of the questionnaire differed from the non-responders in this study nor whether this could have influenced our findings. This approach was chosen to guarantee anonymity, to emphasize the aim of this study to identify barriers and facilitators to DMARD use, and to keep the already long questionnaire feasible to fill out.

Third, the present study may have limited generalizability. We only included Caucasian patients from one region in The Netherlands. None of the participants were from other ethnic backgrounds or represented various religions. Therefore, potential difficulties in taking medications because of cultural or religious reasons (e.g., Ramadan) were not mentioned in this study. Future studies should include patients with different ethnicities and different religions and from different regions to confirm the present findings.

Fourth, the domains that were used in the present study were previously established. One point of criticism may be that the domains that were introduced to the patients may have led them to specific responses.

However, in the design of our study, we anticipated this possible shortcoming and added an extra question: "Is there anything that influences the use of your medication that is not represented by one of the presented domains?" Some of the patients mentioned additional barriers and facilitators, but these could be categorized under one of the existing domains. The fact that all of the barriers and facilitators could be categorized into one of the domains of the TDF indicates the usefulness of this framework for capturing all barriers and facilitators that are important for IA patients in the use of DMARDs.

Fifth, patterns or relationships between the theoretical domains of the TDF are not specified within the TDF framework, in contrast to other theoretical models of behaviour, such as the Theory of Planned Behaviour [36]. The use of the TDF framework in the present study was specifically meant to capture as many barriers and facilitators as possible with regard to adherence, without exploring the relationships between domains or weight of individual domains. Future studies should explore these relationships and their relative weight with regard to barriers and facilitators of medication adherence. Because we used a different approach, the present study was not an attempt to replace existing behavioural theories.

CONCLUSIONS

The patients in the present study identified a large variety of barriers and facilitators of DMARD use. All the identified facilitators and barriers fit in the domains of an existing adapted version of the TDF. Therefore, the TDF appears to be an appropriate framework for systematically assessing drivers that influence adherence and non-adherence to the use of DMARDs. However, further research is necessary to provide insights into (i) the frequency and impact of different barriers and facilitators on adherence, (ii) the development of tools to detect facilitators and barriers in individual patients, and (iii) the extent of modifiability of barriers and reinforcement of facilitators. This is essential before an intervention can be designed, implemented, and evaluated for IA patients with regard to DMARD use.

Practice implications

The present study was one step toward developing an intervention to optimize DMARD use in IA patients. Given the fact that the nature of

the identified facilitators and barriers of medication adherence is very heterogeneous, interventions that improve adherence should consist of an inventory of patient's individual barriers and facilitators, followed by an intervention that is tailored to individual patient needs. The Behaviour Change Wheel may be beneficial as a guiding model in this process. Furthermore, the present study shows that the TDF framework is a useful tool for assessing patients' individual facilitators and barriers.

Abbreviations

AS: Ankylosing spondylitis; CQR: Compliance Questionnaire on Rheumatology; DMARDs: Disease-modifying anti-rheumatic drugs; IMAB: Identification of Medication Adherence Barriers Model; PsA: Psoriatic arthritis; RA: Rheumatoid arthritis; TDF: Theoretical Domains Framework.

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APPENDIX 1. THEORIES USED IN THE THEORETICAL DOMAINS FRAMEWORK

Motivation theories

- Theory of planned behaviour (+ theory of reasoned action)
- Protection motivation theory, health belief model
- Social cognitive theory
- Locus of control theories
- Social learning theory
- Social comparison theory
- Cognitive adaptation theory
- Social identity theory
- Elaboration likelihood model
- Goal theories
- Intrinsic motivation theories
- Self-determination theory
- Attribution theory
- Decision-making theories (e.g., social judgment theory, "fast and frugal" model, systematic *vs*. heuristic decision-making)
- Fear arousal theory

Action theories

- Learning theory
- Operant theory
- Modelling
- Self-regulation theory
- Implementation theory/automotive model
- Goal theory
- Volitional control theory
- Social cognitive theory
- Cognitive behaviour therapy
- Transtheoretical model
- Social identity theory

Organisation theories

- Effort-reward imbalance
- Demand-control model
- Diffusion theory
- Group theory (e.g., group minority theory)
- Decision–making theory
- Goal theory
- Social influence
- Person situation contingency models

REFERENCES

1. Bykerk V, Emery P. Delay in receiving rheumatology care leads to long-term harm. Arthritis Rheum. 2010;62(12):3519–21.
2. American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines. Guidelines for the management of rheumatoid arthritis: 2002 update. Arthritis Rheum. 2002;46(2):328–46.
3. Klareskog L, Catrina AI, Paget S. Rheumatoid arthritis. Lancet. 2009;373(9664): 659–72.
4. Mottonen T, et al. Delay to institution of therapy and induction of remission using single-drug or combination-disease-modifying antirheumatic drug therapy in early rheumatoid arthritis. Arthritis Rheum. 2002;46(4):894–8.
5. Weinblatt ME. Rheumatoid arthritis in 2003: where are we now with treatment? Ann Rheum Dis. 2003;62(Suppl 2):ii94–6.
6. Wolfe F, Michaud K. Resistance of rheumatoid arthritis patients to changing therapy: discordance between disease activity and patients' treatment choices. Arthritis Rheum. 2007;56(7):2135–42.
7. Smolen JS, et al. Treating rheumatoid arthritis to target: recommendations of an international task force. Ann Rheum Dis. 2010;69(4):631–7.
8. Smolen JS, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs. Ann Rheum Dis. 2010;69(6):964–75.
9. Smolen JS. Treat-to-target as an approach in inflammatory arthritis. Curr Opin Rheumatol. 2016;28(3):297–302.
10. Smolen JS, et al. Treating rheumatoid arthritis to target: 2014 update of the recommendations of an international task force. Ann Rheum Dis. 2016;75(1):3–15.
11. Newsome G. Guidelines for the management of rheumatoid arthritis: 2002 update. J Am Acad Nurse Pract. 2002;14(10):432–7.
12. Chambers SA, Rahman A, Isenberg DA. Treatment adherence and clinical outcome in systemic lupus erythematosus. Rheumatology (Oxford). 2007; 46(6):895–8.
13. Darmawan J, Rasker JJ, Nuralim H. Reduced burden of disease and improved outcome of patients with rheumatoid factor positive rheumatoid arthritis compared with dropouts. A 10 year observational study. J Rheumatol Suppl. 2003;67:50–3.
14. Julian LJ, et al. Depression, medication adherence, and service utilization in systemic lupus erythematosus. Arthritis Rheum. 2009;61(2):240–6.
15. Costedoat-Chalumeau N, et al. Adherence to treatment in systemic lupus erythematosus patients. Best Pract Res Clin Rheumatol. 2013;27(3):329–40.
16. van den Bemt BJ, Zwikker HE, van den Ende CH. Medication adherence in patients with rheumatoid arthritis: a critical appraisal of the existing literature. Expert Rev Clin Immunol. 2012;8(4):337–51.
17. Garcia-Gonzalez A, et al. Treatment adherence in patients with rheumatoid arthritis and systemic lupus erythematosus. Clin Rheumatol. 2008;27(7):883–9.

18. Doyle DV, et al. The long-term use of D-penicillamine for treating rheumatoid arthritis: is continuous therapy necessary? Br J Rheumatol. 1993; 32(7):614–7.
19. Owen SG, et al. Determinants of compliance in rheumatoid arthritic patients assessed in their home environment. Br J Rheumatol. 1985;24(4):313–20.
20. Pullar T, et al. The use of a pharmacological indicator to investigate compliance in patients with a poor response to antirheumatic therapy. Br J Rheumatol. 1988;27(5):381–4.
21. Taal E, et al. Health status, adherence with health recommendations, self-efficacy and social support in patients with rheumatoid arthritis. Patient Educ Couns. 1993;20(2–3):63–76.
22. Salt E, Frazier S. Adherence to Disease Modifying Anti-Rheumatic Drugs in Rheumatoid Arthritis Patients: A Narrative Review of the Literature. Orthop Nurs. 2010;29(4):260–75.
23. Galo JS, et al. What are the effects of medication adherence interventions in rheumatic diseases: a systematic review. Ann Rheum Dis. 2016;75(4):667–73.
24. de Achaval S, Suarez-Almazor ME. Treatment adherence to disease-modifying antirheumatic drugs in patients with rheumatoid arthritis and systemic lupus erythematosus. Int J Clin Rheumtol. 2010;5(3):313–26.
25. Easthall C. Developing the Identification of Medication Adherence Barriers (IMAB) instrument; a novel application of behaviour change theoretical frameworks. 2012.
26. Pasma A, et al. Factors associated with adherence to pharmaceutical treatment for rheumatoid arthritis patients: a systematic review. Semin Arthritis Rheum. 2013;43(1):18–28.
27. Brus H, et al. Determinants of compliance with medication in patients with rheumatoid arthritis: the importance of self-efficacy expectations. Patient Educ Couns. 1999;36(1):57–64.
28. Treharne GJ, Lyons AC, Kitas GD. Medication adherence in rheumatoid arthritis: Effects of psychosocial factors. Psychol Health Med. 2004;9(3):337–49.
29. Ferguson K, Bole GG. Family support, health beliefs, and therapeutic compliance in patients with rheumatoid arthritis. Patient Couns Health Educ. 1979;1(3):101–5.
30. Lorish CD, Richards B, Brown S. Missed medication doses in rheumatic arthritis patients: intentional and unintentional reasons. Arthritis Care Res. 1989;2(1):3–9.
31. Neame R, Hammond A. Beliefs about medications: a questionnaire survey of people with rheumatoid arthritis. Rheumatology (Oxford). 2005;44(6):762–7.
32. Park DC, et al. Medication adherence in rheumatoid arthritis patients: older is wiser. J Am Geriatr Soc. 1999;47(2):172–83.
33. Viller F, et al. Compliance to drug treatment of patients with rheumatoid arthritis: a 3 year longitudinal study. J Rheumatol. 1999;26(10):2114–22.
34. Rosenstock I. Why people use health services. Milbank Mem Fund Q. 1966; 44:94–127.
35. Fishbein M, Ajzen I. Belief, attitude, intention, and behaviour: an introduction to theory and research. Reading: Addison-Wesley; 1975.
36. Ajzen I. The theory of planned behavior. Organ Behav Hum Decis Process. 1991;50(2):179–211.

37. Bandura A. Prentice-Hall series in social learning theory. In: Social foundations of thought and action: A social cognitive theory. Englewood Cliffs: Prentice-Hall, Inc; 1986.

38. Fishbein M, et al. Factors influencing behaviour and behaviour change. In: Handbook of health psychology. Mahwah: Lawrence Erlbaum Associates; 2001.

39. Prochaska JO, DiClemente CC. Stages of change in the modification of problem behaviors. Prog Behav Modif. 1992;28:183–218.

40. Michie S, et al. Making psychological theory useful for implementing evidence based practice: a consensus approach. Qual Saf Health Care. 2005;14(1):26–33.

41. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. Int J Qual Health Care. 2007;19(6):349–57.

42. Willis GB, Royston P, Bercini D. The use of verbal report methods in the development and testing of survey questionnaires. Appl Cogn Psychol. 1991;5(3):251–67.

43. Kamberelis G, Dimitriadis G. Focus groups: Strategic articulations of pedagogy, politics, and inquiry. In: Denzin NK, Lincoln YS, editors. Collecting and interpreting qualitative materials. 3rd ed. Thousand Oaks: Sage Publications, Inc; 2008. p. 375–402.

44. Boyatzis RE. Transforming qualitative information: Thematic analysis and code development. Thousand Oaks: Sage Publications, Inc; 1998.

45. Michie S, van Stralen MM, West R. The behaviour change wheel: A new method for characterising and designing behaviour change interventions. Implement Sci. 2011;6(1):42–53.


TOP 3:
1. Feeling Better
2. Staying Independent
3. Being Involved
patients

Chapter 4

Ranking facilitators and barriers of medication adherence by patients with inflammatory arthritis: a maximum difference scaling exercise

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Abstract

Introduction: Facilitators and barriers of adherence to disease-modifying anti-rheumatic drugs (DMARDs) have been identified by patients with inflammatory arthritis earlier. However, the relative importance from the patients' perspective of these factors is unknown. Knowledge on this ranking might guide the development of interventions and may facilitate targeted communication on adherence. This study aims to examine 1) the relative importance patients attach to facilitators and barriers for DMARDs adherence, and 2) the relationship between patient characteristics and ranking of these factors.

Methods: One hundred twenty-eight outpatients with inflammatory arthritis; (60% female, mean age 62 years (SD = 12), median disease duration 15 years, IQR (7, 23) participated in a Maximum Difference scaling exercise and ranked 35 items based upon previously identified facilitators and barriers to medication adherence. Hierarchical Bayes estimation was used to compute mean Rescaled Probability Scores (RPS; 0–100) (i.e. relative importance score). Kendall's coefficient of concordance was used to examine a possible association between patients' characteristics (i.e. age, sex and educational level) and ranking of the items.

Results: The three most important items ranked by patients were: Reduction of symptoms formulated as "Arthritis medications help to reduce my symptoms" (RPS = 7.30, CI 7.17–7.44), maintaining independence formulated as "I can maintain my independence as much as possible" (RPS = 6.76, CI 6.54–6.97) and Shared decision-making formulated as "I can decide –together with my physician- about my arthritis medications" (RPS = 6.48, CI 6.24–6.72). No associations between patient characteristics and ranking of factors were found.

Conclusions: Reducing symptoms, maintaining independence and shared decision-making are patients' most important factors for DMARDs adherence. This knowledge might guide the development of interventions and may facilitate communication between health professionals and their patients on medication adherence.

BACKGROUND

Inflammatory arthritis (IA), including rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS), is characterized by inflammation, impaired physical function, and ultimately progressive joint damage. New pharmacological treatments have led to improved outcomes and prevention of disability over the last decades. Obviously, disease-modifying antirheumatic drugs (DMARDs) only work if taken by a patient in accordance with the prescription. According to the World Health Organization (WHO): 'Across diseases, adherence is the most important modifiable factor that compromises treatment outcomes'. Indeed, adherence to DMARDs is still suboptimal. Non-adherence estimates between 30 and 90% [1–3], and consequently has been shown to have a negative impact on outcomes of the disease [4–6]. Adherence to treatment reflects the extent to which medication is taken as prescribed and the full benefits of DMARDs can be achieved if patients follow drug regimens [7–11]. Multiple factors have been identified that may affect medication adherence in patients with inflammatory arthritis (e.g. RA). Whereas medication beliefs, self-efficacy and the patient-HCP relationship are consistently related to medication adherence [12–16], other factors such as age, disease duration, and complexity of medication regimen show conflicting results [2, 17, 18]. Understanding which potentially modifiable factors are most important to patients and whether these factors are related to patient's characteristics is needed to develop targeted adherence interventions [2, 18–20].

In a previous qualitative study [20], we identified facilitators and barriers to DMARDs use in patients with inflammatory arthritis using an adapted version of the Theoretical Domains Framework (TDF) [21, 22]. However, the *relative* importance of the identified facilitators and barriers of adherence for patients with inflammatory arthritis are unknown. The ranking by patients of these factors might help communication between physicians and their patients with regard to the initiation and follow up of a DMARD-treatment. Even more, a relation between the ranking of the facilitators and barriers and patient characteristics needs to be addressed; this may be useful for the development of targeted adherence interventions.

Therefore, the aim of this study is to study the ranking by arthritis patients themselves of facilitators and barriers for DMARDs adherence,

using a preference scaling methodology. In addition we aim to examine whether this ranking is associated with demographic characteristics.

METHODS

Design

This study is a cross-sectional study, ranking the importance of previously identified facilitators and barriers for adherence to DMARDs in patients suffering from inflammatory arthritis using a Maximum Difference Scaling (MaxDiff) exercise [20]. A MaxDiff exercise (or best-worst scaling) is a method that simplifies the ranking tasks for participants and provides insight into trade-offs in the decision-making process (Sawtooth Software (2013) The MaxDiff system/version 8 Technical Paper. Sequim: WA, Sawtooth Software). The MaxDiff method was proved to be efficacious in similar studies in rheumatology [23–25]. This study took place in 2018–2019.

Preparatory work

For this study, facilitators and barriers for DMARD use, as identified in a previous qualitative study using focus groups and a questionnaire in patients with inflammatory rheumatic diseases was used [20]. In that study, 82 facilitators and barriers were identified, collated in the 11 domains from the adjusted Theoretical Domain Framework (TDF) [21, 22], and subsequently grouped into the higher order components Capability, Opportunity, and Motivation of the Behaviour Change Wheel (BCW) [22]. Factors were selected from these three COM components by three researchers (MV, JV, BvdB), yielding a feasible, neutrally phrased, and representative set of 35 items related to the originally identified facilitators and barriers. The 35 items were used as input for the Maximum Difference Scaling exercise. (see Table 1).

Table 1. Items grouped according to TDF domains and COM components

COM-B	Domain	Item
CAPABILITY		
1	Knowledge	• My knowledge about my arthritis medication is sufficient (e.g. how the medications work, when and how often I need to take my medications) • I understand what my treatment with medications encompasses • The reimbursement of my arthritis medications by the health insurance company • The way I have to administer my arthritis medications (injection or tablet)
2	Skills	• I can cope with my inflammatory arthritis • I have accepted my disease • I have accepted the need for my arthritis medications • I can open the medication packaging • I have good communication skills (e.g. to discuss my arthritis medications)
3	Memory and attention	• The support from family and/or friends • I can incorporate my arthritis medications into daily routines • The name and/or appearance (colour, shape) of my arthritis medications does not change • The support from my colleagues/supervisor in the workplace • The availability of aids (reminders such as electronic messages) in order to take the arthritis medications as prescribed by the physician
4	Decision-making process	• I can decide – together with my physician – about my arthritis medications • The relationship with my physician • The reimbursement of my arthritis medications by the health insurance company • I have good communication skills (e.g. to discuss my arthritis medications) • The relationship with my pharmacist
OPPORTUNITY		
5	Environmental context and resources	• I can get to my physician (accessibility, availability, timely access/when needed) • The reimbursement of my arthritis medications by the health insurance company • My arthritis medications are easy to use (e.g. the size of the tablet) • The name and/or appearance (colour, shape) of my arthritis medications does not change

Table 1. Continued

COM-B	Domain	Item
		• It is easy to travel with my arthritis medication, e.g. to go abroad (able to keep my arthritis medications at a low temperature, clearance from customs/airline • My arthritis medications are expensive (a burden to society) • I can get to the pharmacy (e.g. accessibility, e.g. my arthritis medication is in stock)
6	Social influences	• The relationship with my physician • The reimbursement of my arthritis medications by the health insurance company • The support from family and/or friends • The support from my colleagues/supervisor in the workplace • The experiences of other patients with these arthritis medications • The relationship with my pharmacist
MOTIVATION		
7	Beliefs about capabilities	• My general health (apart from my inflammatory arthritis) • There are no side effects from my arthritis medications • I can cope with my inflammatory arthritis • I have accepted my disease • I have accepted the need for my arthritis medications • I have another chronic condition (apart from my inflammatory condition) • I can incorporate my arthritis medications into daily routines • My arthritis medications are easy to use (e.g. the size of the tablet) • The way I have to administer my arthritis medications (injection or tablet) • The availability of aids (reminders such as electronic messages) in order to take the arthritis medications as prescribed by the physician
8	Beliefs about consequences	• Arthritis medications help to reduce my symptoms • I can maintain my independence as much as possible • I *expect* the arthritis medications will help to reduce my symptoms • There are no side effects from my arthritis medications • I have accepted my disease • I *expect* to be more able to participate in social activities • I have accepted the need for my arthritis medications
9	Emotions	• I am glad arthritis medications are available • I am anxious about how my arthritis medications affect my body • I am sad I have to take my arthritis medications throughout my life • I am angry I have to take my arthritis medications throughout my life

Table 1. Continued

COM-B	Domain	Item
10	Motivation and goals	• Arthritis medications help to reduce my symptoms • I can maintain my independence as much as possible • My general health (apart from my inflammatory arthritis) • There are no side effects from my arthritis medications • The relationship with my physician • I have accepted my disease • I have accepted the need for my arthritis medications • I have another chronic condition (apart from my inflammatory condition) • I can open the medication packaging • I can incorporate my arthritis medications into daily routines • My arthritis medications are easy to use (e.g. the size of the tablet) • The way I have to administer my arthritis medications (injection or tablet) • The support from my colleagues/supervisor in the workplace • What the medication regimen for my arthritis medications includes (simple or complex drug regimen) • The relationship with my pharmacist
11	Goal conflict	• My general health (apart from my inflammatory arthritis) • The support from family and/or friends • I have another chronic condition (apart from my inflammatory condition) • I can incorporate my arthritis medications into daily routines • My arthritis medications are easy to use (e.g. the size of the tablet) • The support from my colleagues/supervisor in the workplace • The experiences of other patients with these arthritis medications • The availability of aids (reminders such as electronic messages) in order to take the arthritis medications as prescribed by the physician

Note: Some determinants were grouped by patients under more than one domain

Pilot testing

The maximum difference scaling exercise was pilot tested among a small group of patients and care providers (patients with inflammatory arthritis, n = 4; psychologists, n = 2; and pharmacists, n = 2). Based on the pilot results, small changes in the wording of the items and the instructions were made to avoid misinterpretation.

Sample size

A standard method for sample size calculations for discrete-choice experiments is lacking [26]. Neither is there a guidelines for sample size calculations when using a maximum difference scaling method [27]. Previous MaxDiff studies reported that a minimum of 100 respondents results in a reliable assessment of preferences with the MaxDiff exercise [25]. For our study, we therefore chose to recruit a convenience sample of at least 100 consecutive patients with IA from one clinic.

Patients and measures

Patients were recruited from the rheumatology clinic (Arthritis Centre Twente, Medisch Spectrum Twente, Enschede in the Netherlands). Inclusion criteria were: 18 years or older; a diagnosis of inflammatory arthritis; using one or more DMARDs; the ability to communicate in Dutch; and informed consent. Patients with a planned visit to their rheumatologist at the hospital, were informed about this study by their rheumatologist or rheumatology nurse. If they showed interest and fulfilled the inclusion criteria, they received a letter explaining the study in more detail. The letter comprised an internet link that led them to the web-based Maximum Difference Scaling exercise, which they could complete at home. This study protocol (K17–08) was presented to the Medical Ethical Committee of the Medisch Spectrum Twente Hospital in Enschede, the Netherlands. Formal ethical approval for this study is not required under Dutch Law. Still, in accordance with the Personal Data Protection Act, informed consent was sought before the start of the Maximum Difference Scaling exercise. Taking into account an expected response rate of 20–30% [28], invitation letters were sent by mail to 450 outpatients with inflammatory arthritis using one or more DMARDs.

Online survey

The Sawtooth software's Lighthouse Studio MaxDiff 500 SSI Web version 8 was used to develop an online survey comprising a MaxDiff exercise (Sawtooth Software Inc. 2013) and a questionnaire to collect patient characteristics. In the MaxDiff exercise participants are shown several

subsets of the possible items pertaining to medication adherence and are asked to indicate the most and least important item in each subset. In this study, each subset contained four items related to adherence.

Part 1 of the online survey assessed the following patient characteristics: sex, age, diagnosis, level of education, disease duration, and DMARDs use (which type of DMARD).

Part 2 of the online survey comprised the choice task using the maximum difference scaling method: 27 subsets were presented. Each subset contained four items related to DMARD use (Fig. 1). This approach simplifies the ranking tasks for participants, enables discrimination between ratings of different items involved in complex decisions and is not influenced by scale related biases [29]. Sawtooth software creates an optimal design of subsets based on 20,000 iterations of the exercise to ensure variation in the combination of items. An open link was created to be disseminated to the patients.

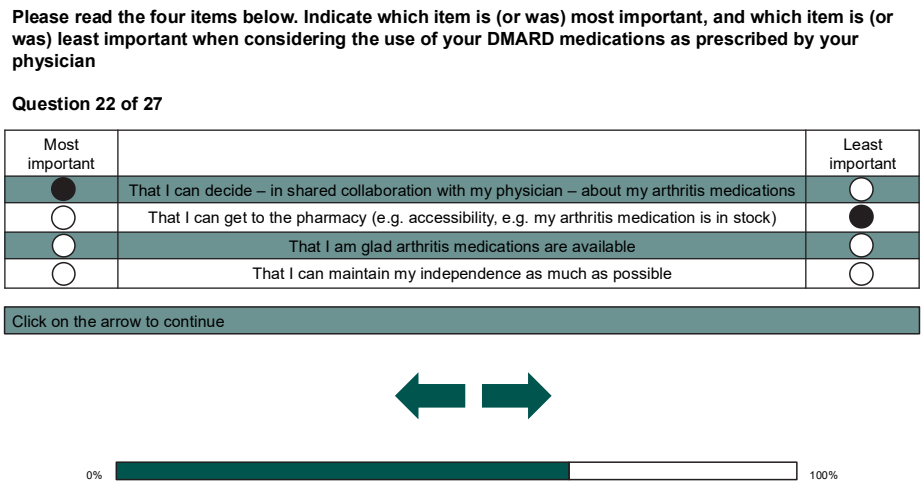


Figure 1. Example of a MaxDiff question

Each of the subsets had a different order of various items, to ensure that every participant would rank the item three times (27 × 4/35 = 3) and to avoid that higher importance was given to the first mentioned item. Participants were asked to choose the most important and the least important item, by answering the question: "In order to take my arthritis medication as prescribed by my physician, which item is/was most/least important to me?"

Statistical analysis

Descriptive analyses were used to describe patient characteristics. Where appropriate, mean and standard deviation (normally distributed continuous variables), median and interquartile range (25th–75th percentile; not normally distributed continuous variables), or percentages (binary variables) were calculated. Level of education was categorized according to the International Standard Classification of Education (ISCED). To enhance international comparability, three broad groups of educational categories were constructed: no or pre-primary education, primary education and lower secondary education (ISCED 0–2); upper secondary education (ISCED 3–4); and tertiary education (ISCED 5–6). Age was grouped into tertiles (0–58/59–68/69–84 years old). The rank order and the relative importance of each item were generated by the Sawtooth software's Lighthouse Studio, using hierarchical Bayes modelling. To facilitate interpretation, the scores were rescaled to a Rescaled Probability Score (RPS) on a scale from 0 to 100: the higher the score, the more important the item. (Sawtooth Software (2013) The MaxDiff System/version 8 Technical Paper. Sequim: WA, Sawtooth Software, 2013). The rescaled probability scores added up to a value of 100, which reflects the relative importance of the item. Patients that gave inconsistent answers on the maximum difference scaling exercise (Root Likelihood below the recommended cut-off of 0.336) were excluded from the analysis. To explore a possible association between the ranking of the RPS scores and patients' characteristics (i.e., sex, age, educational level), Kendall's coefficient of concordance (Kendall's W) was computed [30]. Kendall's W, a non-parametric statistic, is used to determine the degree of agreement between groups when working with ranked data at an ordinal level of measurement. It is a normalization of the statistic of the Friedman test, and can be used for assessing agreement among raters. *Kendall's W* ranges from 0 (no agreement) to 1 (complete agreement). A p-value < 0.05 allows to reject the null hypothesis that there is no agreement in ranking between groups. SPSS version 24.0 was used.

RESULTS

A total of 128 patients took part in the maximum difference exercise (response rate 28%). Three patients had a RLH below 0.336 and were therefore excluded from the analyses. Table 2 shows the characteristics of the participants. Most participating patients were women (60%) and most participating patients had rheumatoid arthritis (89%). The median disease duration was 15 years, IQR (7, 23). These patient characteristics were not significantly different from the former study in which the items were identified [20].

Table 2. Sample characteristics

	IA Patients (*N*=125)
Age, years (mean, SD)	62.7 (±12)
Sex	
Female	75 (60%)
Diagnosis	
Rheumatoid arthritis	111 (88.8%)
Ankylosing Spondylitis	4 (3.2%)
Psoriatic Arthritis	7 (5.6%)
Other diagnoses	3 (2.4%)
Level of education	
Up to lower secondary education	38 (30.6%)
Upper secondary education	42 (33.9%)
Tertiary education	44 (35.5%)
Disease duration, years (median, IQR)	15 (7, 23)
Pharmacotherapy	
Methotrexate (subcutaneous)	22 (17.6%)
Methotrexate (oral)	64 (51.2%)
Leflunomide	3 (2.4%)
Hydroxychloroquine	29 (23.2%)
Sulfasalazine	13 (10.4%)
Gold (oral)	1 (0.8%)
Infliximab	2 (1.6%)
Etanercept	15 (12 %)
Adalimumab	7 (5.6%)
Rituximab	6 (4.8%)
Abatacept	5 (4 %)
Tocilizumab	11 (8.8%)

IA Inflammatory arthritis; SD Standard deviation

In Table 3, the 35 items with their relative probability score are displayed and grouped according to the COM-B model. The five highest ranked items were: "Arthritis medications help to reduce my symptoms" (RPS = 7.30, CI 7.17–7.44), "I can maintain my independence as much as possible" (RPS = 6.76, CI 6.54–6.97) "I can decide –together with my physician- about my arthritis medications" (RPS = 6.48, CI 6.24–6.72), "My general health (apart from IA)" (RPS = 6.42, CI 6.08–6.76), and "I *expect* the arthritis medications will help to reduce my symptoms" (RPS = 6.32, CI 6.10–6.55).

The five least important items were: "What the medication regimen for my arthritis medications includes (simple or complex drug regimen)" (RPS = 0.55, CI 0.46–0.64), "I am sad I have to take my arthritis medications throughout my life" (RPS = 0.34, CI 0.24–0.45), "I am angry that I have to take my arthritis medications throughout my life" (RPS = 0.26, CI 0.18–0.33), "The relationship with my pharmacist" (RPS = 0.24, CI 0.15–0.33), "The availability of aids (reminders such as electronic messages) in order to take the arthritis medications as prescribed by the physician" (RPS = 0.23, CI 0.17–0.29).

Table 3. Ranking of items based on Rescaled Probability Score (RPS)

Ranking	Description	COM component (numbers: see table 1)	RPS	CI lower	CI upper
1	Arthritis medications help to reduce my symptoms	Motivation: 8/10	7.30	7.17	7.44
2	I can maintain my independence as much as possible	Motivation: 8/10	6.76	6.54	6.97
3	I can decide – together with my physician - about my arthritis medications	Capability: 4	6.48	6.24	6.72
4	My general health (apart from my inflammatory arthritis)	Motivation: 7/10/11	6.42	6.08	6.76
5	I expect the arthritis medications will help to reduce my symptoms	Motivation: 8	6.32	6.10	6.55
6	I am glad arthritis medications are available	Motivation: 9	6.16	5.93	6.40
7	There are no side effects from my arthritis medications	Motivation: 7/8/10	5.46	5.11	5.82
8	I can cope with my inflammatory arthritis	Capability and Motivation: 7/2	5.43	5.11	5.76
9	The relationship with my physician	Capability, Opportunity and Motivation: 4/6/10	5.38	5.10	5.66
10	I can get to my physician (accessibility, availability, timely access/when needed)	Opportunity: 5	4.87	4.54	5.19
11	My knowledge about my arthritis medications is sufficient (e.g. how the medications work, when and how often I need to take my medications)	Capability: 1	4.16	3.87	4.46
12	I have accepted my disease	Capability and Motivation: 7/8/10/2	3.99	3.60	4.38

Table 3. Continued

Ranking	Description	COM component (numbers: see table 1)	RPS	CI lower	CI upper
13	I understand what my treatment with medications encompasses	Capability: 1	3.79	3.49	4.09
14	I am anxious about how my arthritis medications affect my body	Motivation: 9	3.00	2.59	3.40
15	I expect to be more able to participate in social activities	Motivation: 8	2.90	2.59	3.22
16	The reimbursement of my arthritis medications by the health insurance company	Capability and Opportunity: 1/4/6/5	2.75	2.30	3.20
17	I have accepted the need for my arthritis medications	Capability and Motivation: 7/8/10/2	2.41	2.14	2.67
18	The support from family and/or friends	Capability, Opportunity and Motivation: 3/6/11	2.37	2.03	2.72
19	I have another chronic condition (apart from my inflammatory condition)	Motivation: 7/10/11	1.74	1.43	2.05
20	I can open the medication packaging	Capability and Motivation: 10/2	1.63	1.36	1.91
21	I can incorporate my arthritis medications into daily routines	Capability and Motivation: 3/7/10/11	1.45	1.24	1.66
22	My arthritis medications are easy to use (e.g. the size of the tablets)	Capability, Opportunity and Motivation:7/10/11/5	1.15	0.92	1.38
23	The name and/or appearance (color, shape) of my arthritis medications does not change	Capability and Opportunity 3/5	0.97	0.64	1.31
24	It is easy to travel with my arthritis medications, e.g. go abroad (able to keep my arthritis medications at a low temperature, clearance from customs/airline)	Opportunity: 5	0.93	0.67	1.19

Table 3. Continued

Ranking	Description	COM component (numbers: see table 1)	RPS	CI lower	CI upper
25	My arthritis medications are expensive (a burden to society)	Opportunity: 5	0.90	0.67	1.12
26	I can get to the pharmacy (e.g. accessibility, e.g. my arthritis medication is in stock)	Opportunity: 5	0.84	0.69	1.00
27	I have good communication skills (e.g. to discuss my arthritis medications)	Capability: 4/2	0.82	0.69	0.95
28	The way I have to administer my arthritis medications (injection or tablet)	Capability and Motivation: 1/7/10	0.76	0.61	0.90
29	The support from my colleagues/supervisor in the workplace	Capability, Opportunity and Motivation: 6/10/11	0.63	0.47	0.79
30	The experiences of other patients with these arthritis medications	Capability, Opportunity and Motivation: 6/11	0.62	0.47	0.76
31	What the medication regimen for my arthritis medications includes (simple or complex drug regimen)	Motivation: 10	0.55	0.46	0.64
32	I am sad I have to take my arthritis medications throughout my life	Motivation: 9	0.34	0.24	0.45
33	I am angry that I have to take my arthritis medications throughout my life	Motivation: 9	0.26	0.18	0.33
34	The relationship with my pharmacist	Capability, Opportunity and Motivation: 4/6/10	0.24	0.15	0.33
35	The availability of aids (reminders such as electronic messages) in order to take the arthritis medications as prescribed by the physician	Capability and Motivation: 3/7/11	0.23	0.17	0.29

RPS Rescaled Probability Score; *CI* Confidence Interval

Agreement in ranking between patient subgroups

Kendall's W analyses showed that all subgroups ranked the items at a high level of agreement (Kendall's W ranged from .97 to .99; $p < .001$ for sex and age, and $p = .001$ for level of education)) indicating that no significant difference based on sex, age or level of education, in ranking the relative importance of items important to adherence were found. *Kendall's W* ranges from 0 (no agreement) to 1 (complete agreement). A p-value < .05 allows to reject the null hypothesis that there is no agreement in ranking between groups.

DISCUSSION

This study ranked the earlier identified facilitators and barriers of adherence to arthritis medication by patients. The five highest ranked items are "Arthritis medications help to reduce my symptoms", "I can maintain my independence as much as possible", "I can decide -together with my physician- about my arthritis medications", "My general health (apart from IA)", and "I expect the arthritis medications will help to reduce my symptoms". All these factors are related to reducing symptoms, maintaining independence and shared decision-making. The five least important ranked items were: "What the medication regimen for my arthritis medications includes (simple or complex drug regimen)", "I am sad I have to take my arthritis medications throughout my life", "I am angry that I have to take my arthritis medications throughout my life", "The relationship with my pharmacist", "The availability of aids (reminders such as electronic messages) in order to take the arthritis medications as prescribed by the physician", suggesting practical issues are least important for arthritis patients in order to adhere to medication in this study. Categorising patients' top five items according to the COM-B model reveals that four of the five highest ranked items are related to patient's *motivation*, whereas one determinant is related to patient's *capabilities*.

Our results are in line with a recently published qualitative focus group study using nominal group technique [31]. Although this latter study had an inductive approach and was consequently not based on a theoretical model, several findings were comparable. Items like the importance of patient-physician interaction and efficacy of medication were ranked high. Our study also indicated the absence of a relation between ranking

of factors pertaining to adherence and demographics: sex, age and education.

Our study also confirmed that patients prefer to discuss and decide the choice of medications in close collaboration with their physician [32–34]. Patients are also more likely to adhere to a treatment that matches their preferences [35]. Tailoring treatment to patients' medication preferences shows to be a promising strategy to improve adherence [28]. Therefore, providing the patient with unambiguous, high quality information [36] creates optimal circumstances for adherence to medication. Although practical issues such as the availability of aids to facilitate adherence were in this study ranked relatively low, such aids (e.g., application of electronic messages or reminders) can have a significant effect on adherence [37].

Strengths and limitations

This study is the first patient oriented and theory-based study ranking facilitators and barriers for adherence that can help for the development of targeted interventions to improve adherence. These findings are helpful information for healthcare professionals to guide the conversation on adherence with their patients. The mentioned factors influencing adherent behaviour can be used as a checklist for both the health professional and the patient to discuss potential adherence problems when needed. The factors ranked as most important were related to patients' motivation, indicating that motivational support, such as motivational interviewing, could be useful to enhance adherence [38]. Furthermore, the findings of this study can be used for the development of future adherence interventions. There are some limitations in this study. The first limitation is that a selection bias in the recruitment process could have occurred. One may assume that more motivated patients, and more adherent patients were inclined to participate in this study. However, our study sample was representative for patients with inflammatory arthritis using DMARDs in the Netherlands. The second limitation is that all items related to facilitators and barriers needed to be rephrased. Obviously, rephrasing was necessary to reduce bias by using neutral wordings taking away any positive or negative valence of each facilitators and barriers [39, 40]. Most patients included in this mono centre study had rheumatoid arthritis, used conventional synthetic DMARDs (csDMARDs) or biological DMARDs (bDMARDS), and had a long disease duration, limiting the generalization of our findings. Furthermore, patients with

different levels of disease activity, with different routes of administration or with comorbidities may also rank these items differently.

To examine whether the outcome of the ranking process differs in subgroup of patients (e.g., other rheumatic conditions, other DMARDs such as targeted synthetic DMARDs (tsDMARDs), patients with short disease duration, patients with different levels of disease activity) or in other countries (e.g., with different healthcare systems and insurances), future research is warranted.

Conclusions

Our study showed the ranking of adherence-related factors by patients with inflammatory arthritis. Reducing symptoms, maintaining independence and shared decision-making are considered most important for DMARDs adherence by patients. This finding can be of value to enhance communication between healthcare professionals and patients. When health professionals give attention to these items in their conversation with patients, adherence might be enhanced. Furthermore, the results are useful information for the development of interventions to optimize DMARDs adherence in IA patients. Since most highly ranked items are related to motivation according to the COM-B model, it might be useful to focus on the development of adherence interventions that capture motivational components.

Abbreviations

DMARDs: Disease-modifying anti-rheumatic drugs; TDF: Theoretical domains framework; IA: Inflammatory arthritis; RA: Rheumatoid arthritis; MaxDiff: Maximum difference scaling exercise; RPS: Rescaled probability score; BCW: Behaviour change wheel; COM-B model: Capability, opportunity and motivation-behaviour model (based on the behaviour change wheel); Kendall's W: Kendall's coefficient of concordance; SPSS: Statistical package for the social sciences; RLH: Root likelihood; SD: Standard deviation; CI: Confidence interval

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REFERENCES

1. Harrold LR, Andrade SE. Medication adherence of patients with selected rheumatic conditions: a systematic review of the literature. Semin Arthritis Rheum. 2009;38(5):396–402. https://doi.org/10.1016/j.semarthrit.2008.01.011.
2. Pasma A, van't Spijker A, Hazes JM, Busschbach JJ, Luime JJ. Factors associated with adherence to pharmaceutical treatment for rheumatoid arthritis patients: a systematic review. Semin Arthritis Rheum. 2013;43(1):18– 28. https://doi.org/10.1016/j.semarthrit.2012.12.001.
3. van den Bemt BJ, Zwikker HE, van den Ende CH. Medication adherence in patients with rheumatoid arthritis: a critical appraisal of the existing literature. Expert Rev Clin Immunol. 2012;8(4):337–51. https://doi.org/10. 1586/eci.12.23.
4. Bluett J, Morgan C, Thurston L, Plant D, Hyrich KL, Morgan AW, Barton A. Impact of inadequate adherence on response to subcutaneously administered anti-tumour necrosis factor drugs: results from the biologics in rheumatoid arthritis genetics and genomics study syndicate cohort. Rheumatology (Oxford). 2015;54(3):494–9. https://doi.org/10.1093/ rheumatology/keu358.
5. Viller F, Guillemin F, Briancon S, Moum T, Suurmeijer T, van den Heuvel W. Compliance to drug treatment of patients with rheumatoid arthritis: a 3 year longitudinal study. J Rheumatol. 1999;26(10):2114–22.
6. Waimann CA, Marengo MF, de Achaval S, Cox VL, Garcia-Gonzalez A, Reveille JD, Suarez-Almazor ME. Electronic monitoring of oral therapies in ethnically diverse and economically disadvantaged patients with rheumatoid arthritis: consequences of low adherence. Arthritis Rheum. 2013; 65(6):1421–9. https://doi.org/10.1002/art.37917.
7. Chambers SA, Rahman A, Isenberg DA. Treatment adherence and clinical outcome in systemic lupus erythematosus. Rheumatology (Oxford). 2007; 46(6):895–8. https://doi.org/10.1093/rheumatology/kem016.
8. Darmawan J, Rasker JJ, Nuralim H. Reduced burden of disease and improved outcome of patients with rheumatoid factor positive rheumatoid arthritis compared with dropouts. A 10 year observational study. J Rheumatol Suppl. 2003;67:50–3.
9. Julian LJ, Yelin E, Yazdany J, Panopalis P, Trupin L, Criswell LA, Katz P. Depression, medication adherence, and service utilization in systemic lupus erythematosus. Arthritis Rheum. 2009;61(2):240–6. https://doi.org/10.1002/ art.24236.
10. Newsome G. Guidelines for the management of rheumatoid arthritis: 2002 update. J Am Acad Nurse Pract. 2002;14(10):432–7.
11. Smolen JS, Landewe R, Bijlsma J, Burmester G, Chatzidionysiou K, Dougados M, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis. 2017;76(6):960–77. https://doi.org/10. 1136/annrheumdis-2016-210715.
12. de Thurah A, Norgaard M, Harder I, Stengaard-Pedersen K. Compliance with methotrexate treatment in patients with rheumatoid arthritis: influence of patients' beliefs about the medicine. A prospective cohort study. Rheumatol Int. 2010;30(11):1441–8. https://doi.org/10.1007/s00296-009-1160-8.

13. Hope HF, Hyrich KL, Anderson J, Bluett J, Sergeant JC, Barton A, et al. The predictors of and reasons for non-adherence in an observational cohort of patients with rheumatoid arthritis commencing methotrexate. Rheumatology (Oxford). 2020;59(1):213–23. https://doi.org/10.1093/ rheumatology/kez274.

14. Neame R, Hammond A. Beliefs about medications: a questionnaire survey of people with rheumatoid arthritis. Rheumatology (Oxford). 2005;44(6):762–7. https://doi.org/10.1093/rheumatology/keh587.

15. Treharne GJ, Lyons AC, Kitas GD. Medication adherence in rheumatoid arthritis: effects of psychosocial factors. Psychol Health Med. 2004;9(3):337–49. https://doi.org/10.1080/13548500410001721909.

16. van den Bemt BJ, van den Hoogen FH, Benraad B, Hekster YA, van Riel PL, van Lankveld W. Adherence rates and associations with nonadherence in patients with rheumatoid arthritis using disease modifying antirheumatic drugs. J Rheumatol. 2009;36(10):2164–70. https://doi.org/10.3899/jrheum. 081204.

17. Curtis JR, Bykerk VP, Aassi M, Schiff M. Adherence and persistence with methotrexate in rheumatoid arthritis: a systematic review. J Rheumatol. 2016;43(11):1997–2009. https://doi.org/10.3899/jrheum.151212.

18. Wong PK. Medication adherence in patients with rheumatoid arthritis: why do patients not take what we prescribe? Rheumatol Int. 2016;36(11):1535–42. https://doi.org/10.1007/s00296-016-3566-4.

19. Delestras S, Roustit M, Bedouch P, Minoves M, Dobremez V, Mazet R, et al. Comparison between two generic questionnaires to assess satisfaction with medication in chronic diseases. PLoS One. 2013;8(2):e56247. https://doi.org/ 10.1371/journal.pone.0056247.

20. Voshaar MJH, Vriezekolk J, van Dulmen S, van den Bemt B, van de Laar M. Barriers and facilitators to disease-modifying antirheumatic drug use in patients with inflammatory rheumatic diseases: a qualitative theory-based study. BMC Musculoskelet Disord. 2016;17(1):442. https://doi.org/10.1186/ s12891-016-1289-z.

21. Easthall, C. (2012). Developing the identification of medication adherence barriers (IMAB) instrument; a novel application of behaviour change theoretical frameworks.

22. Michie S, Johnston M, Abraham C, Lawton R, Parker D, Walker A. Making psychological theory useful for implementing evidence based practice: a consensus approach. Qual Saf Health Care. 2005;14(1):26–33. https://doi.org/ 10.1136/qshc.2004.011155.

23. Meyfroidt S, Hulscher M, De Cock D, Van der Elst K, Joly J, Westhovens R, Verschueren P. A maximum difference scaling survey of barriers to intensive combination treatment strategies with glucocorticoids in early rheumatoid arthritis. Clin Rheumatol. 2015;34(5):861–9. https://doi.org/10.1007/s10067- 015-2876-3.

24. van Hulst LT, Kievit W, van Bommel R, van Riel PL, Fraenkel L. Rheumatoid arthritis patients and rheumatologists approach the decision to escalate care differently: results of a maximum difference scaling experiment. Arthritis Care Res (Hoboken). 2011;63(10):1407–14. https://doi.org/10.1002/ acr.20551.

25. Verhoef LM, Selten EMH, Vriezekolk JE, de Jong AJL, van den Hoogen FHJ, den Broeder AA, Hulscher ME. The patient perspective on biologic DMARD dose reduction in rheumatoid arthritis: a mixed methods study. Rheumatology (Oxford). 2018;57(11):1947–55. https://doi.org/10.1093/ rheumatology/key205.

26. de Bekker-Grob EW, Donkers B, Jonker MF, Stolk EA. Sample size requirements for discrete-choice experiments in healthcare: a practical guide. Patient. 2015;8(5):373–84. https://doi.org/10.1007/s40271-015-0118-z.

27. Cheung KL, Wijnen BF, Hollin IL, Janssen EM, Bridges JF, Evers SM, Hiligsmann M. Using best-worst scaling to investigate preferences in health care. Pharmacoeconomics. 2016;34(12):1195–209. https://doi.org/10.1007/ s40273-016-0429-5.

28. van Heuckelum M, Mathijssen EG, Vervloet M, Boonen A, Hebing RC, Pasma A, et al. Preferences of patients with rheumatoid arthritis regarding disease modifying antirheumatic drugs: a discrete choice experiment. Patient Prefer Adherence. 2019;13:1199–211. https://doi.org/10.2147/ppa.s204111.

29. Muhlbacher AC, Kaczynski A, Zweifel P, Johnson FR. Experimental measurement of preferences in health and healthcare using best-worst scaling: an overview. Health Econ Rev. 2016;6(1):2. https://doi.org/10.1186/ s13561-015-0079-x.

30. Legendre P. Species associations: the Kendall coefficient of concordance revisited. J Agric Biol Environ Stat. 2005;10(2):226–45. https://doi.org/10. 1198/108571105X46642.

31. Kelly A, Tymms K, de Wit M, Bartlett SJ, Cross M, Dawson T, et al. Patient and caregiver priorities for medication adherence in gout, osteoporosis and rheumatoid arthritis: nominal group technique. Arthritis Care Res (Hoboken). 2019. https://doi.org/10.1002/acr.24032.

32. Levinson W, Kao A, Kuby A, Thisted RA. Not all patients want to participate in decision making. A national study of public preferences. J Gen Intern Med. 2005;20(6):531–5. https://doi.org/10.1111/j.1525-1497.2005.04101.x.

33. Nota I, Drossaert CH, Taal E, van de Laar MA. Arthritis patients' motives for (not) wanting to be involved in medical decision-making and the factors that hinder or promote patient involvement. Clin Rheumatol. 2016;35(5): 1225–35. https://doi.org/10.1007/s10067-014-2820-y.

34. Schildmann J, Grunke M, Kalden JR, Vollmann J. Information and participation in decision-making about treatment: a qualitative study of the perceptions and preferences of patients with rheumatoid arthritis. J Med Ethics. 2008;34(11):775–9. https://doi.org/10.1136/jme.2007.023705.

35. Laba TL, Essue B, Kimman M, Jan S. Understanding patient preferences in medication nonadherence: a review of stated preference data. Patient. 2015; 8(5):385–95. https://doi.org/10.1007/s40271-014-0099-3.

36. Mathijssen EG, Vriezekolk JE, Eijsbouts AM, van den Hoogen FH, van den Bemt BJ. Support needs for medication use and the suitability of eHealth technologies to address these needs: a focus group study of older patients with rheumatoid arthritis. Patient Prefer Adherence. 2018;12:349–58. https:// doi.org/10.2147/ppa.s152759.

37. van Heuckelum M, van den Ende CHM, Houterman AEJ, Heemskerk CPM, van Dulmen S, van den Bemt BJF. The effect of electronic monitoring feedback on medication adherence and clinical outcomes: a systematic review. PLoS One. 2017;12(10):e0185453. https://doi.org/10.1371/journal. pone.0185453.

38. Palacio A, Garay D, Langer B, Taylor J, Wood BA, Tamariz L. Motivational interviewing improves medication adherence: a systematic review and meta-analysis. J Gen Intern Med. 2016;31(8):929–40. https://doi.org/10.1007/ s11606-016-3685-3.

39. Pengo MF, Czaban M, Berry MP, Nirmalan P, Brown R, Birdseye A, et al. The effect of positive and negative message framing on short term continuous positive airway pressure compliance in patients with obstructive sleep apnea. J Thorac Dis. 2018;10(Suppl 1):S160–s169. https://doi.org/10.21037/ jtd.2017.07.110.

40. Veldwijk J, Essers BA, Lambooij MS, Dirksen CD, Smit HA, de Wit GA. Survival or mortality: does risk attribute framing influence decision-making behavior in a discrete choice experiment? Value Health. 2016;19(2):202–9. https://doi. org/10.1016/j. jval.2015.11.004.


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Chapter 5

Healthcare professionals' perceptions on barriers and facilitators to DMARD use in rheumatoid arthritis

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Abstract

Background: Disease-modifying anti-rheumatic drugs (DMARDs) are the cornerstone of rheumatoid arthritis (RA) treatment. However, the full benefits of DMARDs are often not realized because many patients are sub-optimally adherent to their medication. In order to optimize adherence, it is essential that healthcare professionals (HCPs) understand patients' barriers and facilitators for medication use. Insight in these barriers and facilitators may foster the dialogue about adequate medication use between HCPs and patients. What HCPs perceive as barriers and facilitators has, so far, scarcely been investigated. This study aimed to identify the perceptions of HCPs on patients' barriers and facilitators that might influence their adherence.

Methods: This qualitative study was performed using semi structured in-depth interviews with HCPs. An interview guide was used, based on an adjusted version of the Theoretical Domains Framework (TDF). Thematic analysis was conducted to identify factors that influence barriers and facilitators to DMARD use according to HCPs.

Results: Fifteen HCPs (5 rheumatologists, 5 nurses and 5 pharmacists) were interviewed. They mentioned a variety of factors that, according to their perceptions, influence DMARD adherence in patients with RA. Besides therapy-related factors, such as (onset of) medication effectiveness and side-effects, most variation was found within patient-related factors and reflected patients' beliefs, ways of coping, and (self-management) skills toward medication and their condition. In addition, factors related to the condition (e.g., level of disease activity), healthcare team and system (e.g., trust in HCP), and social and economic context (e.g. support, work shifts) were reported.

Conclusions: This study provided insights in HCPs' perceptions of the barriers and facilitators to DMARD use patients with RA. Most factors that were mentioned were patient-related and potentially modifiable. When physicians understand patients' perceptions on medication use, adherence to DMARDs can probably be optimized in patients with RA leading to more effectiveness of treatment outcomes.

BACKGROUND

Rheumatoid Arthritis (RA) is a systemic autoimmune condition, presently requiring long-term pharmacological treatment with disease-modifying antirheumatic drugs (DMARDs). Pharmacological treatment, as early as possible, is essential in preventing structural damage of joints and improving functional outcomes and improved quality of life for patients [1, 2]. Medication non-adherence is one of the most recognized factors in RA causing treatment failure, leading to increased disease activity, lower rates of remission and disappointing patient-reported outcomes [3–6]. Adherence rates in RA seem highly variable with a reported range from 30 to 99%, depending on population studied, definition of adherence used and which method of measurement is used [7, 8].

In order to improve medication adherence in patients with RA, identification of barriers and facilitators towards adherence is necessary. A recent study has identified a list of barriers and facilitators that patients experience towards their DMARDs use, such as: insufficient cognitive, communicative, or physical skills to understand and/or administer medication, lack of daily routine and experiencing side effects [9]. The individual patient's barriers and facilitators regarding DMARDs can be discussed with the HCP to provide the room to correct possible misunderstanding, dysfunctional attributions or a lack of knowledge.

According to the World Health Organization (WHO) in 2003, adherence is a multidimensional phenomenon determined by the interplay of five sets of factors of which patient-related factors are just one determinant (World Health Organization, 2003). Also condition related factors, therapy-related factors, healthcare team- and system-related factors, and social and economic factors are determinants for (non)adherence. This emphasizes that healthcare system factors, such as poor drug supply, unclear information about drug administration but also poor HCP-patient communication may have a negative impact on adherence. The quality of communication improves when HCPs tailor their information to the individual patient's needs [10]. Better quality of communication might lead to improved adherence to recommendations and outcomes [11]. HCPs need to be aware of the current needs of their individual patient and adapt their communication accordingly [12, 13]. A mismatch of the individual patient's barriers and facilitators with the perception of the attending HCP, might negatively influence treatment adherence and consequently reduce efficacy and outcomes [14–16]. As HCPs play

an important role in RA management, it is important to explore their insights with regard to medication adherence in order to detect possible mismatches with the patients' perspectives of medication use [17, 18]. However, research about HCPs' perspectives on factors that influence medication non-adherence is scarce [19, 20]. A systematic review and meta-analysis of interventions improving medication adherence showed that interventions focussing on HCPs, significantly improved adherence among patients with chronic conditions [21]. Therefore, knowledge of HCPs' perceptions on the barriers and facilitators regarding medication use of their patients, will help to bridge the different perceptions of both patient and attending HCP and potentially benefit adherence. This study aimed to identify the perceptions of HCPs of the barriers and facilitators to DMARD use in patients with RA.

METHODS

Study design

Semi structured in-depth interviews were held with HCPs involved in the treatment of patients with RA. The Consolidated Criteria for Reporting Qualitative Research (COREQ) checklist was used to ensure complete and transparent reporting [22]. Eligible HCPs were rheumatologists, nurses and pharmacists, experienced in the care for patients with RA. Purposive sampling was used to obtain the perspectives of HCPs with varying professions, sex, age and regions to increase transferability.

Interviews

Based on an adjusted Theoretical Domains Framework (TDF) [23] an interview guide was developed by the researchers to address the perceptions of HCPs on potential barriers and facilitators to DMARDs that influence patients' adherence (see Table 1). Questions were formulated reflecting the following 11 domains: knowledge, emotions, attention/memory, decision-making, social influences, beliefs about capabilities, beliefs about consequences, motivation and goals, goal conflict, environmental context and resources, skills. The interview guide was pilot tested among three HCPs. After the pilot test, no changes to the interview guide were made. Therefore, the data obtained in the pilot test were used for the final study and data analysis. All interviews were conducted by the first female author (MV) who was fully trained and experienced in qualitative interviewing. The interviews were conducted between April and September 2019. A summary of each interview (member check) was

sent to each HCP to ensure their views and beliefs have been interpreted correctly by the researcher.

Table 1. Interview guide

Domain	Interview questions
Knowledge	1. What kind of information do patients need to have in order to take the medication as prescribed by the physician?
Emotions	2. Which emotions can be evoked in patients by the use of the medication?
Attention, memory and decision process	3a. Do you think patients are preoccupied with the medication? Can you elaborate?
	3b. Do you think patients sometimes, on purpose or accidently, forget their medication? Can you elaborate?
	3c. Do you think that patients are sufficiently involved in the decision-making process surrounding their medication? Can you elaborate?
Social influences	4. In which way do HCPs play a role in the use of the medication, other than prescribing them? Can you elaborate?
	5a. Do you think that family and/or friends of patients play a role in the use of the medication (e.g. taking or not taking the medication as prescribed)? Can you elaborate?
	5b. Do you think that the work environment (colleagues or supervisor) can influence the use of medication? Can you elaborate?
Beliefs about capabilities	6. In which situation(s) is it difficult for patients to use the medication as prescribed?
Beliefs about consequences	7. Which beliefs do patients have about the consequences of (not) taking the medication as prescribed by the physician?
Motivation and goals	8a. Which personal goals (or personal motivations) could be important for patients to use the medication as prescribed? Can you elaborate?
	8b. Which personal goals (or personal motivations) could be important for patients to *not* use the medication as prescribed? Can you elaborate?
Goal conflict	9a. What do patients consider helpful to use the medication as prescribed in daily life?
	9b. What would patients consider as barriers in daily life that hamper the use of their medication as prescribed?

Table 1. Continued

Domain	Interview questions
Environmental context and resources	10. Do you think that the ordering, retrieving, delivery, prescribing and/or reimbursement sometimes influence patients' use of medication as prescribed? Can you elaborate?
Skills	11. What is important for patients with RA to be able (physically as well as mentally) to use the medication as prescribed?
	12. Are there other issues important for patients that can influence their medication use?

Recruitment and data collection

Purposive sampling was used to obtain the perspectives of healthcare professionals with varying jobs, sex, regions, age and work experiences to increase transferability. No relationship was established between the interviewer and the participants prior to the study. Participants were invited by e-mail, followed up by a phone call. They were interviewed in their own environment at a time and place of their convenience. Written informed consent to participate as well as to record the interview was obtained prior to the start of the interview. The interviews were audio-recorded and field notes were made during the interviews. Each interview was scheduled for 60 minutes. Data saturation determined the number of interviews. Intermediate analyses were conducted by two researchers (JV, MV) to decide whether new themes had surfaced. Relevant quotes of the participants were selected and translated to support the findings.

Measures

A demographic questionnaire was completed before the start of the interview (age, sex, region, work experience in years, working in Academic/peripheral hospital).

Data analyses

All interview-tapes were transcribed verbatim by a professional agency. The qualitative data analysis software MAXQDA 2018 (MAXQDA, 1989–2018) was used by two independent researchers (JV and MV) to code meaningful fragments in the text, conform the analysis method described by Boeije [24]. This method uses a structured way of coding [25], the principles of constant comparison [26], and in this study, an inductive thematic analysis. This method was chosen because it facilitates a theoretically flexible approach to the coding of these data. Applying

this method to this study implied that the researchers interpreted the data with theoretical sensitivity to the adjusted domains of the TDF framework. Before starting the coding process, the transcripts were read and reread for familiarization with the data. The coding was done in 3 steps: open, axial and selective coding. Open coding is the part of the analysis concerned with identifying, naming, categorizing and describing phenomena found in the transcripts of the HCPs that were interviewed. These open codes were categorized (axial coding). From these axial codes the core themes and interrelatedness between themes were identified (selective coding). To support the coding process, field notes made during the interviews were used. In addition, the researchers made reflective notes about their thoughts and views regarding the identification of themes. Data collection and data analysis alternated in a cyclic process. Throughout this process, 3 authors (MV, BvdB and JV) continuously and repetitively reflected on, compared, discussed, and adjusted the coding in order to carefully determine the number and wording of themes in an iterative design (to ensure confirmability) until consensus was reached (Boeije, 2009).

RESULTS

Fourteen interviews (duration 45–90 min) were held at the hospital and one interview at HCP's home. In Table 2 the participants' characteristics are displayed. Twelve (80%) participants were female and the mean age was 47.4 (range 31–63) years. The mean in employed years was 13.1 (range 3–25) years. Four participants worked in general hospitals, three participants in university hospitals whereas eight participants had work experience in both. Data collection ended after 15 interviews as saturation had been reached after 13 interviews (no new information emerged during two consecutive interviews) [27].

Table 2. Participants' Characteristics

Characteristic	Rheumatologist *N* = 5	Rheumatology nurse *N* = 5	Pharmacist *N* = 5
Mean Age (SD)	54.60 (SD = 7.30)	52.60 (SD = 7.27)	35.00 (SD = 4.64)
Sex (F:M)	3:2	5:0	4:1
Working experience in mean years (SD)	18.20 (SD = 5.36)	12.00 (*SD* = 5.66)	9.20 (*SD* = 4.82)

Table 2. Continued

Characteristic	Rheumatologist *N* = 5	Rheumatology nurse *N* = 5	Pharmacist *N* = 5
Region in the Netherlands (n)	West (2), East (1), South (2)	West (3), East (2), South (0)	West (2), East (0), South (3)
Hospital (n)	Academic (2), Peripheral (0), Academic/ Peripheral (3)	Academic (0), Peripheral (2), Academic/ Peripheral (3)	Academic (1), Peripheral (2), Academic/ Peripheral (2)

SD Standard deviation, *F* Female, *M* Male

Facilitating and hampering factors for medication adherence are listed in Table 3. To present these results in a structured way and thereby enhancing readability, the identified factors were presented according to the taxonomy of medication adherence of the WHO (World Health Organization, 2003). The WHO describes five sets of factors with causes for decreased adherence: Patient-related factors, Condition-related factors, Therapy- related factors, Healthcare team and system-related factors, and Social and economic factors. All identified factors by the HCPs could be placed under these five sets of factors.

Table 3. Adherence factors to medication use according to healthcare professionals in this study

Categories	Facilitators	Barriers
Patient-related	Self-managing medication regimen such as: Embedding medication intake in daily routine; Tapering/dosing/discontinuing temporarily; Managing medication stock at home	Experiencing redefinition of identity
	Personality traits such as openness and conscientiousness	Feeling resistance to become dependent on (lifelong) medication
	Pursuing a solution-oriented approach	Denying the existence of condition
	Pursuing discipline in medication taking	Experiencing inner conflict of medication necessity versus concerns
	Coping with insecurity how future/condition will unfold, having a realistic expectation	Lacking confidence and/or not feeling safe enough to talk about e.g. (non) adherence

Table 3. Continued

Categories	Facilitators	Barriers
	Maintaining autonomy and improving quality of life	Having trouble to understand instruction inserts
	Being able to take care of family	Not believing in prescribed treatment, preferring traditional medication
	Being able to open medication bottles/packages and administer injections/oral medications	Not believing that medication will always be available
	Using aids to remember/motivate adherence	Not believing that condition needs (lifelong) medication
	Believing in positive treatment effect	Believing that the condition can be cured
	Experiencing positive emotions evoked by (positive experience of) medication	Attributing decreased treatment effect due to non-medical switch
		Experiencing negative emotions that are evoked by using medication for a chronic condition
Therapy-related	Experiencing a short-term onset of medication effectiveness	Experiencing side effects
	Experiencing positive treatment effect	Dreading possible interactions (medications, alcohol)
	Employing a dose-reducing strategy	Being confronted with changed appearance of medication
	Aligning patient preferences for medication administration	Perceiving information overload
		Dealing with complexity of instruction inserts
Condition-related	Experiencing high level of disease activity	Perceiving treatment as redundant without a definite diagnosis
		Experiencing a poor general health status e.g. suffering comorbidities (poly pharmacy)
Healthcare team and system-related	Providing tailored information frequently	Imposing limited consultation time to discuss choice of medication
	Discussing reasons for non-adherence before and during therapy	Lacking reimbursement medication

Table 3. Continued

Categories	Facilitators	Barriers
	HCPs are more accessible for patients (by different channels)	
	Offering optimal service logistics medication	
	Creating bond/empathy/trust with patient	
	Physician's positive attitude on medication use	
	Initiating shared decision-making process by HCPs	
Social and Economic	Receiving social and work-related support	Travelling
		Nature of work hindering medication use (shifts)
		Perceiving negative impact of social media/internet
		Perceiving negative experiences/ stories from others about medication
		Interference in medication use because of religious or cultural customs

Some factors reported by the HCPs, reflected opposite pools; for instance, short term versus long term onset of effectiveness, inner conflict of medication necessity versus concerns, and showing an open attitude versus lacking confidence and/or not feeling safe enough to talk about e.g. (non) adherence). Other mentioned factors by the HCPs were interrelated: for instance, embedding medication intake in daily routine and travelling or irregular work shifts, having trouble to understand instruction inserts and dealing with complexity of instruction inserts, personality traits such as openness and conscientiousness (e.g. discipline in medication use) and pursuing a solution oriented approach, and creating bond/empathy/ trust with patient and initiating shared decision-making process by HCPs.

Patient-related factors

Facilitating factors to medication adherence

Patients' strong self-management skills, such as being able to manage medication stock at home, or being able to taper, dose or temporarily discontinue medication on one's own account because of holidays or social events, facilitated medication adherence, according to the HCPs.

Rheumatology nurse (51 years, female): *"Some patients tell us that they have not taken the medication for three months, or that they taper the medication, or that they changed the prescribed dose on their own account (...) and that they choose not to mention this (to their HCPs). If you have to take your medication each week, year in and year out, you will probably think: "It is going so well, why not take a tablet less?"*

To be able to embed medication use in daily routine was stated by most HCPs as very helpful to patients. HCPs mentioned that for some patients this could be a challenge e.g. when the patient works in irregular shifts.

Pharmacist (39 years, male): *"So we accompany someone by the start of using that medicine as best as he/she can. As best as possible in his or her daily life. That is also our great challenge. I always say to our pharmacist assistant: "There is really only one thing you have to do right at the desk and that is find out what someone's daily routine is and respond to it". And, 'mapping expectations': Finding out how a person lives a life when it comes to the use of medicines and then thinking along from: "how can I make sure that someone is fully capable of doing so (medication use as prescribed)."*

Patient's intrinsic motivation to use medication as prescribed was considered highly valuable. According to many HCPs "wanting life back as before" motivated patients to adhere to medication. This motivation for medication adherence would help the patient to set and accomplish realistic work, leisure and family related activities and goals, and ultimately to maintain autonomy and (improve) health-related quality of life. Reasons to be adherent were, according to all HCPs, the experienced treatment effect, ultimately leading to often improvement of quality of life. Another reason which was mentioned frequently was that patients are motivated to use their medication as prescribed, in order to be able to take care of family. This could be in the role of caregiver (taking care of disabled parents or spouse) or in taking care of the children.

HCPs also mentioned that conscientious patients (e.g. having discipline in medication taking, having the patience to wait for a treatment effect), patients with an open attitude that would enhance communication with the HCPs, and patients who are able to successfully cope with insecurity between how their condition will unfold in the future, were considered to better adhere to their medication regime.

HCPs stated that in their experience, besides positive emotions and feelings that could arise from taking medication and experiencing a treatment effect, patients' belief that treatment effects would outweigh side effects, the belief that the use of lifelong medication would improve quality of life, and realistic expectation of how the treatment would affect the condition, contributed to medication adherence.

Practical issues that helped medication use were mentioned by the HCPs as well. For instance to be able to open medication bottles or packages, be able to swallow tablets or to administer injections. Providing aids, such as reminders and pill boxes, were considered as helpful to medication use in case of non-intentional non-adherence.

Barriers to medication adherence

HCPs indicated that patient's negative emotions such as aversion, sadness, anger, and problems with self-image were likely to hamper medication adherence. Problems were described with poorer self-image, describing that patients felt that the use of medication defined them as patients, since living with a lifelong condition meant living with lifelong medication. Patients did not want to be associated with this image all the time. To resist these identity redefinition processes, sometimes denial of the condition was observed and resulted in non-adherent behaviour.

The HCPs thought that many patients did not feel free and safe enough to talk about personal drug-related issues related to their condition, and this affected adherent medication behaviour. For instance, patients' wish to have children that may require a change in medication strategy. According to the HCPs, many patients still feel intimidated by the status of the treating physician, hampering initiating a conversation about changing the medication regimen.

Pharmacist (31 years, female): "*I think that patients admit non-adherence easier to us than to the rheumatologist. They say sometimes: "I am not always taking my medication", or: "While on holiday, I have not used my medication for*

several weeks", or: "When I feel fine, I take less medication than agreed with the rheumatologist"."

HCPs expressed that patients' beliefs and misconceptions about the (long-term) side-effects could hamper medication adherence, as patients can be conflicted about the need for medication versus the concerns they (might) have about the medication they take.

Some HCPs mentioned that some patients mistakenly believed that the condition could be cured by taking medication or that the rheumatic condition would not require (life-long) medication. Other patients refused medication as they were unsure about the availability of medication in the future and they fear to be dependent on one particular medication. Some patients do not believe in the prescribed medication and they prefer traditional medication instead. Some HCPs stated that patients have difficulties to understand the instruction inserts of their medications. One HCP mentioned that after a non-medical switch (prescribing a biosimilar after the prescription of a biological), the patient attributed the decreased treatment effect to the biosimilar, and in turn hampered willingness to take the medication.

Rheumatologist (45 years, female): *"We put a lot of people on biosimilars at the time. We've talked to our patients about that at length. It's the same drug. Well, yes, you're now experiencing that it works less. It can, it may, indeed, that it works less. The effect of the drug is becoming less and that could have happened with that other drug as well. I don't know if we should give people a lot of information about that right now, if it's really the same drug in the end?"*

Therapy-related factors

Facilitating factors to medication adherence

According to the HCPs, a short term to onset of effect of the medication was one of the therapy-related factors facilitating adherence. An experienced positive treatment effect contributed to better adherence as well. HCPs considered the option for tapering medication as a motivation for the patient in order to adhere to the treatment plan. Explaining and discussing the choice in how medication can be administered, especially at the start or when a change is required in the medical treatment, was also considered important to adherence to take away fear and anxiety, according to the HCPs.

Rheumatology nurse (51 years, female): *"What do you like more: once a week an injection – you have to do that yourself – or an IV … I have a number of patients who say, "I think it's – actually – fine. A few hours here in that chair, just reading my paper. That's really a relaxing moment"."*

Barriers to medication adherence

The HCPs reported that the barrier most often mentioned by patients, was experiencing side effects of their medication use. Dreading possible interactions, such as using concomitant medications that patients fear to be contraindicated, or using medication in combination with alcohol or certain drugs, were also given as reasons that patients may be less adherent to their prescribed medication for their rheumatic condition. Another presumed barrier for adherence according to the HCPs, is the change of the appearance of medication, such as colour or packaging boxes. With regard to therapy related information for patients, many instruction inserts are sometimes too complex and too long, risking misinterpretations and information overload. According to the HCPs, communication is key to prevent or overcome these potential barriers.

Condition-related factors

A facilitating factor to medication adherence

A condition-related factor that may positively influence patients' medication use according to some HCPs, was the level of disease activity. When the disease activity was high, patients were more willing to use their medication as prescribed.

Barriers to medication adherence

Most HCPs stated that a poor general health status, such as health problems beside the rheumatic condition, can hamper medication use. For instance, comorbidities that require poly pharmacy, or temporarily health issues, such as having a cold resulting in less wellbeing. They felt that without proper informative communication about the necessity of different medications for different conditions, patients are less inclined to use these. The absence of a definite diagnosis was mentioned as a barrier that would make the patient reluctant to follow a proposed treatment plan.

Rheumatologist (50 years, male): *"I say to my patient; "Of course, it doesn't always matter if you have symptoms, to come to a diagnosis (…). The symptoms are the complaints and you can have them without a diagnosis. Rheumatism is*

all about medicine for the first year. (..) The second year is very often about "it lands", that you feel that your body is not like before. That it is no longer real to demand that you will be as before. And that doesn't come until the second year. And then, of course, you still have all the stages of life". And that's what I mean: you have to look a little bit at what stage someone is in (with regard to a prescribed medication regimen)."

Healthcare team and system-related factors

Facilitating factors to medication adherence

Providing the same information by different HCPs, tailored to the patient and repeated when necessary, would benefit the patient according to the HCPs. Especially after diagnosis when medication is commenced or when a change in medication strategy is required, clarity and information about treatment could help with the acceptance of a lifelong condition and subsequently of life-long medication use.

Some HCPs mentioned that barriers to adherence should be discussed before and during therapy, since non-disclosure for non-adherent behaviour can lead to unnecessary decisions for treatment change (other medication or different dose). They stated that creating easier access for patients to the HCP when needed, for instance through e-mail, would most likely facilitate adherence.

Rheumatology nurse (51 years, female): *"We (colleagues) have already defined the important topics that need to be addressed with the patients, before they come for their first visit. One of these points is the need for probably long-time use of medication. We also explain that we have a schedule to start, use and maybe taper the medication with the focus on best results with as less medication as possible. But, yes, it is a shock for them ... I understand. When you have to use medication year in, year out, that is sad information. It must always "land"."*

Some HCPs mentioned that improvements of the service level with regard to medication logistics could facilitate medication use, e.g. delivering medication at home, an easy way to get a refill at the pharmacy and patient-friendly packaging of medication.

A few HCPs stated that adherence to medication can sometimes be attributed to the attitude of the physician towards medication use. According to these HCPs, a strong positive attitude with regard to

certain medication can influence the willingness of patients to use this medication as prescribed.

The HCPs also expressed that creating a bond with the patients, specifically in chronic conditions, may lead to more mutual empathy and trust and subsequently to more room for discussion, providing and receiving information about more sensitive topics such as barriers to adherence to medication.

Rheumatologist (55 years, female): *"For me it is really important to feel whether patients are taking their medication or not, because only then I can judge whether they are effective or not. Nothing can be as bad as prescribing a higher dose when the condition is progressing, when ultimately it turns out, no matter what the cause is, that the patient was non-adherent (for a while). It would be crazy to change the dose in this case. It is not effective".*

The HCPs stated that for most patients, shared decision- making is essential for adherence to a treatment plan. In their view, the HCP should initiate this process, in collaboration with the patient and if applicable, the rheumatology nurse.

Rheumatologist (50 years, male)*: "I think that doctors are still trained in the way of 'thinking in lists'. Symptoms lead to a diagnosis. This diagnosis leads to a treatment plan and the patient has to conform to it. The involvement of the patient is mainly in the implementation phase. I think it is only in recent years that we have come to realise that this is a very limited model. (..) If you ask someone to perform, it only works well, if that patient knows why they should do so and is better informed about it. I think we know much better by now, that the quality of care and the effect of care is really only good, if someone is involved in decision-making at all stages and thinking along in the various steps of the treatment plan."*

Subsequently, the opposite was highlighted as well, many HCPs felt that patients were often not given a choice between eligible medication strategies, partly because some HCPs do not want to take the patient's decision into account, or because of the prescribed protocols that need to be followed, leaving no room for shared decision-making.

Pharmacist (31 years, female): *"We think patients will start using their medicines better, if they feel that they can decide in: "What are we going to do about it now?" As caregivers, we are inclined to think, "This is our protocol. (...)*

This is step one of the protocol and so we are going to do it this way." I think it's shifting a little bit, but how is it going to be a joint decision? I think that's kind of hard for doctors, of course, to have a protocol on the one hand, (...) whereas that patient might have something else in mind. It is a difficult dilemma".

Barriers to medication adherence

Factors that were mentioned by the HCPs as barriers in medication use, were, e.g., limited consultation time imposed by regulatory authorities: this was considered too short to discuss extensively the medication strategy. Some HCPs stated that costs of medication and (lack of) reimbursement of medication are sometimes reasons for patients not to collect their medication at the pharmacy, leading to non-adherence. This was remarkably mostly mentioned about less expensive drugs, since, e.g., bDMARDS are reimbursed by insurance in the Netherlands.

Rheumatology nurse (55 years, female): *"Then they're not going to use the drugs that aren't being reimbursed anymore, and then they're going to be in a lot of pain. Then they actually want other painkillers, which are reimbursed. But those often have other side effects".*

HCPs reported that another reason for patients to stop their prescribed medication was awareness about the high costs for medication such as biologics. Patients felt that this money could be spend more useful e.g. for environmental friendly projects or to development projects in poor countries.

Rheumatologist (45 years, female): *"Another great example – I think – patients didn't want to use biologicals anymore, because they are so expensive. She thought that the money should go to a project in India. That's one. There's been another one, who also said, "This is too expensive. We, as a society, should not want this." Yes, she just didn't want to. Really, they said, "From an economic point of view, I just don't want this"."*

One HCP felt that their considerations about the choice of medication with regard to costs, can be shared and explained to patients in order to gain understanding resulting to improved adherent behaviour.

Rheumatologist (63 years, female): *"What I also mean here: as a doctor, you take the costs into account, so why do we want to keep that away from our patients so constrainedly. In fact, I think we can be transparent about it (that*

sometimes costs also determines our choice (room for options))…. As long as we can justify that preference in relation to the health gain, it's fine, isn't it?"

Social and economic factors

Facilitating factors to medication adherence

According to some HCPs, most patients rely on social support with regard to their medication use. This social support not only includes support from family and friends, but support from their work environment as well, such as support from the employer and colleagues. This support can be the understanding, empathy, or help with physical or cognitive challenges, such as dividing work load and offering adjusted working hours (support at work) or assisting in administering the medication or reminding medication intake (social support). As opposite, fear for loss of career opportunities in the work environment, could lead to non-disclosure of condition to the employer and colleagues and to non-adherent behaviour.

Rheumatology nurse (63 years, female): *"Yes, people still think: "Rheumatism? Oh, those are dropouts, contract but not renew."*

Barriers to medication adherence

A factor that was mentioned by most HCPs as a social and economic barrier to patients' medication adherence, was travelling, due to difficulties with scheduling medication intake, requirements for certain contraindicated vaccinations and difficulties with medication storage. According to the HCPs, discussing these inconveniences with regard to medication use with the patients can sometimes lead to simple solutions.

Rheumatology nurse (63 years, female): *"In case of travelling and you need to inject during your holidays, we often advise (after agreement among our team): "You know, just leave your injection for a week, because the risk of infection in terms of storage and temperature is higher than skipping one time your medication"."*

Furthermore, the HCPs mentioned that barriers such as the impact of social media, or stories in newspapers or online about negative medication experiences as well as stories about negative experiences from peers about medication, may trigger non-adherent behaviour. For some patient groups, religious reasons can also affect medication use,

such as the Ramadan (not allowing believers to consume food or drinks during daytime, often required in combination with medication).

DISCUSSION

In this study, HCPs involved in rheumatology care reported multiple factors they perceive to influence medication adherence in patients with RA.

Besides therapy-related factors, such as (onset of) medication effectiveness and medication side-effects, the largest variety was found within patient-related factors and reflected patients' beliefs, ways of coping, and (self-management) skills toward medication and their condition. In addition, factors related to the condition (e.g., level of disease activity), healthcare team and system (e.g., trust in HCP), and social and economic context (e.g. social and work-related support) were reported.

Two previous studies reported the insights of rheumatologists into medication adherence in patients with immune-mediated inflammatory conditions [17, 18]. Differences between findings in this study and findings of previous research predominantly reflect cultural and health system/contextual factors. In contrast to the findings of Heidari et al., [18], access to, and availability of medication was not mentioned as a barrier to adherence by the HCPs in our study. In the Netherlands, all patients have medical insurance and costs of (expensive) medications are fully reimbursed. Access to healthcare professionals and pharmacies are firmly embedded in the Dutch healthcare system. Furthermore, in contrast to Ammoury et al., [17] the interviewed HCPs in our study did not report on certain, more or less fixed, patient-related factors such as disease duration, sex, age and smoking as factors for medication adherence. An explanation might be that according to the interviewed HCPs, patients will probably not give their sex as barrier to medication use, since they may not be aware of a possible association between these factors and (non) adherence. Furthermore, in contrast to Heidari et al., [18], HCPs in this study and patients in our previous study [9] mentioned that support, both in a professional and in a social environment, is important with regard to medication use. Besides these differences, most factors identified in this study are in line with the majority of barriers and facilitators reported in previous mentioned studies.

Most barriers and facilitators of medication adherence mentioned by the HCPs in our study were patient-related. However, this conclusion should be interpreted with care: the interview guide used in this study may have influenced the variety in the reported factors, since most questions focussed on patient-related issues, such as e.g. beliefs, emotions, motivation and goals. It is therefore essential to be aware of the fact that the frequency and variety of mentioned factors by the HCPs in this study yields no indication of the impact of these factors for medication adherence. This requires a different study design, such as a maximum difference scaling exercise [28]. Furthermore, for the interpretation of barriers and facilitators that influence patients' adherence reported by the HCPs, it is important to take contextual factors (e.g. socioeconomic situation of countries, healthcare system) into account when optimizing medication adherence strategies involving patients and HCPs.

Notably, the majority of barriers and facilitators to DMARD use reported by the HCPs in this study are consistent with those reported by patients in previous studies [9, 29–31], and with the results of a recent systematic review that summarizes factors for medication adherence across several patient populations, showing that most factors contributing to medication adherence were patient-related [32]. This suggests that Dutch HCPs seem to be well aware of barriers and facilitators that may hinder or help patients with regard to their DMARD use resulting in (non) adherent behaviour.

Clinical relevance

As HCPs seem to be well aware of the potential barriers interfering with the use of medication by patients, the question arises why these potential barriers to medication use are often not the topic in consultations, and even described as "conspiracy of silence" [33]. Especially given the fact that most modifiable barriers can be addressed in patient education and self-management interventions, such as having trouble to understand instruction inserts, not believing in (the need for lifelong) prescribed medication, not believing medication will always be available, or believing that the condition can be cured [34]. Furthermore, effective (e-health) interventions that are relatively easy to use, can help to address patients' health literacy, patients' self-efficacy to manage their condition and may help to overcome the limited consultation time of physicians by offering other supportive ways for patients to discuss their barriers for medication adherence [35]. As for interpersonal factors, a trusting bond between HCP and patient, to be able to discuss adherence barriers and facilitators

and providing tailored information in all phases of the treatment process (e.g. before treatment initiation, in the treatment initiation phase and in the treatment persistence phase) were mentioned as facilitating medication adherence. Several studies report that the relationship between healthcare professional and patient is key to enhance adherence and health outcomes [8, 36]. In a recent study of Roodenrijs et al., the presence of adverse events was prioritized as the most important adherence barrier and a good relationship with the HCP was prioritized as the most important adherence facilitator [37]. Although in this study, we have explored, but not prioritized, which barriers and facilitators are important for medication adherence according to HCPs, findings can be interpreted as comparable since the experience of side effects and creating a bond/empathy/trust with the patient, were factors that were mentioned by most HCPs. A good relationship with the HCP, described in the study of Nota et al., involves themes such as mutual respect between HCP and patient, trust and an open style of communication [38].

HCPs endorsed the view that they should create the conditions for shared decision-making (SDM) during their encounters with the patient to create a common playing field with the patient while discussing the pros and cons of medication and medication adherence in different stages of the condition. Although most RA patients prefer SDM, their preference may vary according to the situation they are in (type of treatment and severity of complaints) and the extent to which they experience barriers in getting more actively involved [38]. Unawareness of having a choice is still a major barrier for patient participation. The HCP has an important role as facilitator in enhancing patient participation by raising awareness and offering options, but implementing SDM is a shared responsibility; all parties need to be involved and educated [38].

Future research

In a previous maximum difference scaling exercise, patients identified the most important barriers and facilitators [28]. Reducing symptoms, maintaining independency and shared decision-making were found to be the three most important contributors to medication adherence. Factors identified in the current study are in line with these latter observations, although a difference scaling exercise could add knowledge of the relative importance to the factors identified by the HCPs in this study.

Strength and limitations

The strength of this study is that the qualitative theory-based in-depth interviews were conducted with different health professionals. This provided insight from different healthcare professionals' perspectives into patients' facilitators and barriers to medication use.

As limitations, the use of a predetermined interview guide based on an adjusted TDF model [9, 39, 40], could be considered as a stringent way to identify possible barriers and facilitators for medication use, however, by adding a question if there were factors that HCPs felt important to mention beside the factors already discussed, this potential limitation has been accounted for. No additional factors have been mentioned at the end of each interview.

In addition, the sample size of this study was limited to 15 healthcare professionals. Yet, saturation was reached in the 13th interview. This is in line with the findings of a review study by Guest et al. [27] into saturation and variability. They found that saturation can occur within 12 interviews and elements of key themes can already be presented after six interviews. Data collection and analyses were alternated to ensure that saturation could properly be established.

Furthermore, this study was conducted in one healthcare system of a single European country, which may limit the transferability of the findings, particularly to non-Western countries.

Conclusions

In summary, multiple barriers and facilitators have been identified that influence patients' medication adherence according to their physicians, nurses and pharmacists. Largest variation in barriers and facilitators were patient-related. According to the outcome of this study, Dutch HCPs are aware of the reasons for patient's non-adherence, therefore adherence should be a topic in consultations between HCP and patient. Our findings can be the base for the development of (digital) interventions and/or health services to increase medication adherence among patients using disease-modifying antirheumatic drugs. Most mentioned barriers in this study, such as personal (e.g. patients' beliefs and knowledge) and interpersonal factors (e.g. the quality of the patient-provider interaction) are potential modifiable and can be addressed to enhance medication adherence.

Abbreviations

DMARDs: Disease-Modifying Anti-Rheumatic Drugs; TDF: Theoretical Domains Framework; RA: Rheumatoid Arthritis; HCPs: Healthcare Professionals; WHO: World Health Organisation; COREQ: Consolidated Criteria for Reporting Qualitative Research; SDM: Shared Decision Making.

Acknowledgements

We thank the interviewees for their time and effort by consenting to an interview.

SUPPLEMENTARY INFORMATION

Additional file 1

COREQ (COnsolidated criteria for REporting Qualitative research) Checklist

Topic	Item No.	Guide Questions/Description
Domain 1: Research team and reflexivity		
Personal characteristics		
Interviewer/facilitator	1	Which author/s conducted the interview or focus group?
Credentials	2	What were the researcher's credentials? E.g. PhD, MD
Occupation	3	What was their occupation at the time of the study?
Gender	4	Was the researcher male or female?
Experience and training	5	What experience or training did the researcher have?
Relationship with participants		
Relationship established	6	Was a relationship established prior to study commencement?
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research
Interviewer characteristics	8	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic
Domain 2: Study design		
Theoretical framework		
Methodological orientation and Theory	9	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis
Participant selection		
Sampling	10	How were participants selected? e.g. purposive, convenience, consecutive, snowball
Method of approach	11	How were participants approached? e.g. face-to-face, telephone, mail, email
Sample size	12	How many participants were in the study?

Topic	Item No.	Guide Questions/Description
Non-participation	13	How many people refused to participate or dropped out? Reasons?
Setting		
Setting of data collection	14	Where was the data collected? e.g. home, clinic, workplace
Presence of non-participants	15	Was anyone else present besides the participants and researchers?
Description of sample	16	What are the important characteristics of the sample? e.g. demographic data, date
Data collection		
Interview guide	17	Were questions, prompts, guides provided by the authors? Was it pilot tested?
Repeat interviews	18	Were repeat inter views carried out? If yes, how many?
Audio/visual recording	19	Did the research use audio or visual recording to collect the data?
Field notes	20	Were field notes made during and/or after the inter view or focus group?
Duration	21	What was the duration of the inter views or focus group?
Data saturation	22	Was data saturation discussed?
Transcripts returned	23	Were transcripts returned to participants for comment and/or correction?
Domain 3: Analysis and findings		
Data analysis		
Number of data coders	24	How many data coders coded the data?
Description of the coding tree	25	Did authors provide a description of the coding tree?
Derivation of themes	26	Were themes identified in advance or derived from the data?
Software	27	What software, if applicable, was used to manage the data?
Participant checking	28	Did participants provide feedback on the findings?
Reporting		
Quotations presented	29	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number

Topic	Item No.	Guide Questions/Description
Data and findings consistent	30	Was there consistency between the data presented and the findings?
Clarity of major themes	31	Were major themes clearly presented in the findings?
Clarity of minor themes	32	Is there a description of diverse cases or discussion of minor themes?

Developed from: Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

REFERENCES

1. Smolen JS, Breedveld FC, Burmester GR, Bykerk V, Dougados M, Emery P, et al. Treating rheumatoid arthritis to target: 2014 update of the recommendations of an international task force. Ann Rheum Dis. 2016;75(1):3–15.
2. Nell VP, Machold KP, Eberl G, Stamm TA, Uffmann M, Smolen JS. Benefit of very early referral and very early therapy with disease-modifying antirheumatic drugs in patients with early rheumatoid arthritis. Rheumatology (Oxford, England). 2004;43(7):906–14.
3. Souto A, Maneiro JR, Gómez-Reino JJ. Rate of discontinuation and drug survival of biologic therapies in rheumatoid arthritis: a systematic review and meta-analysis of drug registries and health care databases. Rheumatology (Oxford, England). 2016;55(3):523–34.
4. Pascual-Ramos V, Contreras-Yáñez I, Villa AR, Cabiedes J, Rull-Gabayet M. Medication persistence over 2 years of follow-up in a cohort of early rheumatoid arthritis patients: associated factors and relationship with disease activity and with disability. Arthritis Res Ther. 2009;11(1):R26.
5. Contreras-Yáñez I, Cabiedes J, Villa AR, Rull-Gabayet M, Pascual-Ramos V. Persistence on therapy is a major determinant of patient-, physician- and laboratory- reported outcomes in recent-onset rheumatoid arthritis patients. Clin Exp Rheumatol. 2010;28(5):748–51.
6. Contreras-Yanez I, Ponce De Leon S, Cabiedes J, Rull-Gabayet M, Pascual- Ramos V. Inadequate therapy behavior is associated to disease flares in patients with rheumatoid arthritis who have achieved remission with disease- modifying antirheumatic drugs. Am J Med Sci. 2010;340(4):282–90.
7. Harrold LR, Andrade SE. Medication adherence of patients with selected rheumatic conditions: a systematic review of the literature. Semin Arthritis Rheum. 2009;38(5):396–402.
8. Pasma A, van't Spijker A, Hazes JM, Busschbach JJ, Luime JJ. Factors associated with adherence to pharmaceutical treatment for rheumatoid arthritis patients: a systematic review. Semin Arthritis Rheum. 2013;43(1):18–28.
9. Voshaar MJH, Vriezekolk J, van Dulmen S, van den Bemt B, van de Laar M. Barriers and facilitators to disease-modifying antirheumatic drug use in patients with inflammatory rheumatic diseases: a qualitative theory based study. BMC Musculoskelet Disord. 2016;17(1):442.
10. van Bruinessen IR, van Weel-Baumgarten EM, Gouw H, Zijlstra JM, Albada A, van Dulmen S. Barriers and facilitators to effective communication experienced by patients with malignant lymphoma at all stages after diagnosis. Psychooncology. 2013;22(12):2807–14.
11. Harrington J, Noble LM, Newman SP. Improving patients' communication with doctors: a systematic review of intervention studies. Patient Educ Couns. 2004;52(1):7–16.
12. Nota I, Drossaert CH, Taal E, van de Laar MA. Arthritis patients' motives for (not) wanting to be involved in medical decision-making and the factors that hinder or promote patient involvement. Clin Rheumatol. 2016;35(5):1225–35.

13. Mathijssen EGE, van den Bemt BJF, Wielsma S, van den Hoogen FHJ, Vriezekolk JE. Exploring healthcare professionals' knowledge, attitudes and experiences of shared decision making in rheumatology. RMD Open. 2020;6(1):e001121.
14. Menckeberg TT, Bouvy ML, Bracke M, Kaptein AA, Leufkens HG, Raaijmakers JA, et al. Beliefs about medicines predict refill adherence to inhaled corticosteroids. J Psychosom Res. 2008;64(1):47–54.
15. Horne R, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. J Psychosom Res. 1999;47(6):555–67.
16. Van Steenis M, Driesenaar J, Bensing J, Van Hulten R, Souverein P, Van Dijk L, et al. Relationship between medication beliefs, self-reported and refill adherence, and symptoms in patients with asthma using inhaled corticosteroids. Patient PreferAdher. 2014;8:83–91.
17. Ammoury A, Okais J, Hobeika M, Sayegh RB, Shayto RH, Sharara AI. Adherence to systemic therapies for immune-mediated inflammatory diseases in Lebanon: a physicians' survey from three medical specialties. Patient Prefer Adher. 2017;11:939–45.
18. Heidari P, Cross W, Weller C, Team V, Nazarinia M, Crawford K. Rheumatologists' insight into medication adherence in patients with rheumatoid arthritis: a qualitative study. Int J Rheum Dis. 2019;22(9):1695–705.
19. Zwikker HE, Lesuis N, den Broeder AA, Van den Ende CH, Horne R, Van Dulmen A, et al. Rheumatologists' beliefs about medication barely differ from patients' medication beliefs. Eur J Pers Cent Healthc. 2017;5(3):308–14.
20. Paskins Z, Crawford-Manning F, Cottrell E, Corp N, Wright J, Jinks C, et al. Acceptability of bisphosphonates among patients, clinicians and managers: a systematic review and framework synthesis. BMJ Open. 2020;10(11):e040634.
21. Conn VS, Ruppar TM, Enriquez M, Cooper PS, Chan KC. Healthcare provider targeted interventions to improve medication adherence: systematic review and meta-analysis. Int J Clin Pract. 2015;69(8):889–99.
22. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. Int J Qual Health Care. 2007;19(6):349–57.
23. Michie S, Johnston M, Abraham C, Lawton R, Parker D, Walker A. Making psychological theory useful for implementing evidence based practice: a consensus approach. Qual Saf Health Care. 2005;14(1):26–33.
24. Boeije H. Analysis in qualitative research: sage publications; 2009.
25. Strauss A, Corbin JM. Basics of qualitative research: grounded theory procedures and techniques. Newbury Park, Cal: SAGE publications; 1990.
26. Glaser B, Strauss A. Grounded theory: the discovery of grounded theory. Sociol J Br Sociol Assoc. 1967;12:27–49.
27. Guest G, Namey E, Chen M. A simple method to assess and report thematic saturation in qualitative research. Plos One. 2020;15(5):e0232076

28. Voshaar MJH, Vriezekolk JE, van Dulmen AM, van den Bemt BJF, van de Laar M. Ranking facilitators and barriers of medication adherence by patients with inflammatory arthritis: a maximum difference scaling exercise. BMC Musculoskelet Disord. 2021;22(1):21.
29. Murage MJ, Tongbram V, Feldman SR, Malatestinic WN, Larmore CJ, Muram TM, et al. Medication adherence and persistence in patients with rheumatoid arthritis, psoriasis, and psoriatic arthritis: a systematic literature review. Patient Prefer Adher. 2018;12:1483–503.
30. Palominos PE, Gasparin AA, de Andrade NPB, Xavier RM, da Silva Chakr RM, Igansi F, et al. Fears and beliefs of people living with rheumatoid arthritis: a systematic literature review. Adv Rheumatol (London, England). 2018;58(1):1.
31. Vangeli E, Bakhshi S, Baker A, Fisher A, Bucknor D, Mrowietz U, et al. A systematic review of factors associated with non-adherence to treatment for immune-mediated inflammatory diseases. Adv Ther. 2015;32(11):983–1028.
32. Peh KQE, Kwan YH, Goh H, Ramchandani H, Phang JK, Lim ZY, et al. An adaptable framework for factors contributing to medication adherence: results from a systematic review of 102 conceptual frameworks. J Gen Intern Med. 2021;36(9):2784–95.
33. van Bussel E, Reurich L, Pols J, Richard E, Moll van Charante E, Ligthart S. Hypertension management: experiences, wishes and concerns among older people-a qualitative study. BMJ Open. 2019;9(8):e030742.
34. Zangi HA, Ndosi M, Adams J, Andersen L, Bode C, Bostrom C, et al. EULAR recommendations for patient education for people with inflammatory arthritis. Ann Rheum Dis. 2015;74(6):954–62.
35. Pouls BPH, Vriezekolk JE, Bekker CL, Linn AJ, van Onzenoort HAW, Vervloet M, et al. Effect of interactive eHealth interventions on improving medication adherence in adults with long-term medication: systematic review. J Med Internet Res. 2021;23(1):e18901.
36. Salt E, Frazier S. Adherence to disease modifying anti-rheumatic drugs in rheumatoid arthritis patients: a narrative review of the literature. Orthop Nurs. 2010;29(4):260–75.
37. Roodenrijs NMT, van der Goes MC, Welsing PMJ, van Oorschot EPC, Nikiphorou E, Nijhof NC, et al. Non-adherence in difficult-to-treat rheumatoid arthritis from the perspectives of patients and rheumatologists: a concept mapping study. Rheumatology (Oxford). 2021;60(11):5105–16.
38. Nota I, Drossaert CH, Taal E, van de Laar MA. Arthritis patients' motives for (not) wanting to be involved in medical decision-making and the factors that hinder or promote patient involvement. Clin Rheumatol. 2016;35(5):1225–35.
39. Michie S, van Stralen MM, West R. The behaviour change wheel: a new method for characterising and designing behaviour change interventions. Implement Sci. 2011;6(1):42–53.
40. Easthall C. Developing the identification of medication adherence barriers (IMAB) instrument; a novel application of behaviour change theoretical frameworks; 2012.


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Chapter 6

Talking about barriers to disease-modifying anti-rheumatic drugs: content analysis of audio-recorded routine clinical visits of patients with rheumatoid arthritis

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Abstract

Purpose: Effective healthcare professional-patient communication is essential for medication adherence. Conversations about patient's barriers to medication use, for example, could help to enhance adherence and consequently improve treatment outcomes. However, it is unclear whether and how barriers to medication use are discussed during routine rheumatology consultations. The aims of this study were to examine 1) the barriers and facilitators to medication use raised by patients during real-life rheumatology outpatient consultations, and whether the issue of medication (non)adherence was discussed (communication content); and 2) how rheumatologists responded to the barriers (communication process).

Methods: A total of 134 audio-recordings of real-life outpatient rheumatology consultations were analysed. Barriers and facilitators for the current use of disease-modifying anti-rheumatic drugs were identified and categorized using a previously adapted Theoretical Domains Framework. The way rheumatologists responded to the barriers brought up by the patients was analysed using relevant parts of the Roter Interaction Analysis System.

Results: In 58 of the 134 consultations, at least one barrier or facilitator to current medication use was brought up by the patient; in 31 out of 134 consultations, medication (non)adherence was addressed. Most facilitators were related to the quality of the needles, the use of an injection pen instead of a syringe, dose reduction because of low disease activity and timing of the medication. The majority of barriers were related to experiencing side effects and doubts about efficacy and resistance of (long-term use of) medication. Rheumatologists' responses to barriers related to disease-modifying anti-rheumatic drugs were mostly a combination of instrumental (counselling) and affective (agreement) communication.

Conclusion: Barriers to current disease-modifying anti-rheumatic drugs' use raised by patients and discussed during routine rheumatology consultations were primarily related to side effects and concerns about the efficacy and long-term use. Continuous attention of these barriers and tailored responses to patients' concerns are key to promote better adherence to treatment.

INTRODUCTION

The cornerstone of the treatment of rheumatoid arthritis (RA) is the use of disease-modifying anti-rheumatic drugs (DMARDs) which decrease symptoms and radiographic progression of joint destruction and improve patient functioning.[1,2] Numerous efficacious synthetic and biologic DMARDs are available to achieve and maintain this goal.[3,4] However, the desired effects can only be achieved when patient's medication-intake behaviour corresponds with the medication regimen agreed upon with the healthcare professional (HCP), called medication adherence.[5] In RA, patients' adherence to DMARDs is often suboptimal, ranging from 25% (underdosing) to 107% (overdosing), depending on the measurement method and population, potentially compromising treatment outcomes.[6-8]

Effective HCP-patient communication has been found to be related to medication adherence.[9] Previous studies among primary care and specialty practices found that better adherence was related to greater information provided by the HCP, while poor physician communication increased the risk of non-adherence by 19%.[10,11] For HCP-patient communication to be effective, HCPs should pay as much attention to instrumental or cognitive needs of patients (their need to understand) by providing information and advice as to affective or socio-emotional needs of patients (their need to be understood) by providing reassurance or empathy.[12-18] Both types of communication (instrumental and affective communication) are equally important for enhancing patients' medication adherence (Figure 1).[11]

In order to enhance patients' medication adherence, it is essential to know which barriers to medication use patients have. Consequently, barriers to medication use should be identified and discussed during consultations. However, limited research has explored whether and which barriers to medication use are discussed between patients and HCPs. The current study aims to observe and describe 1) the barriers and facilitators to current DMARD use raised by patients with RA during real-life outpatient consultations, and whether the issue of medication (non) adherence was addressed; and 2) how rheumatologists responded to the barriers mentioned by patients.

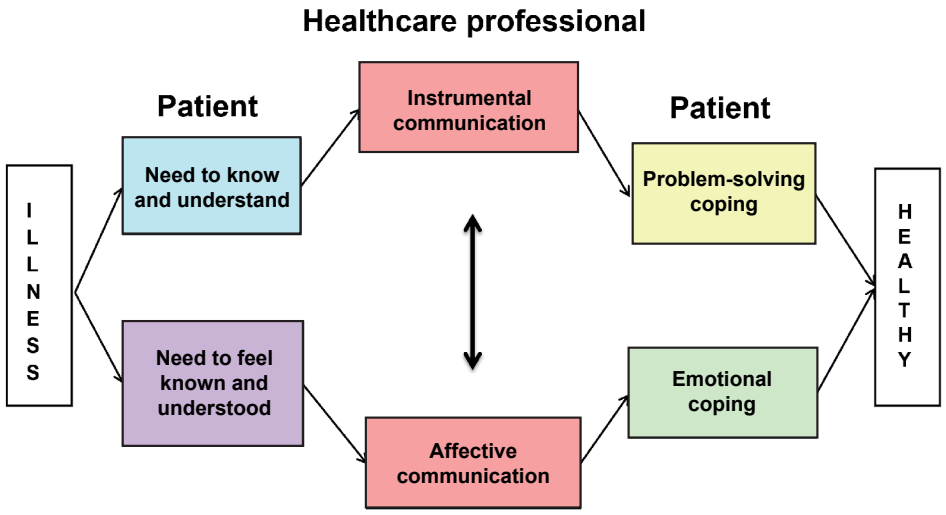


Figure 1. Dual needs of the patient.

MATERIALS AND METHODS

Study Design

Data were used from a previous multicentre cohort study.[19] In this study, consultations between HCPs and patients with RA in two Dutch hospitals, were audio-recorded. Audio recordings (n = 176) from this cohort study were used in the current cross-sectional study. Since HCP-patient communication may vary, depending on the discipline of the healthcare professional (e.g., a medical specialist or a (rheumatology) nurse), only audio recordings of interactions between rheumatologists and patients were selected for this study (n = 142).[20]

Participants

HCPs, working at two rheumatology centres in the Netherlands (Sint Maartenskliniek in Nijmegen and Reade in Amsterdam), were asked to participate, and informed consent (IC) was signed.[19] Consecutive patients, eligible for participation, were invited by the HCPs between July 2016 and July 2017. Patients were eligible for participation if they were aged 18 years or older, had a confirmed diagnosis of RA according to the American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) 2010 RA classification criteria, and were treated in one of the rheumatology centres for at least one year with one or more synthetic DMARD(s), whether or not combined with (a) biologic DMARD(s). In

case patients agreed to participate, an informed consent was signed. The informed consent of HCPs and patients included permission to use all data, including publication of anonymized quotes.

Data Collection and Data Analysis

Characteristics of HCP and Patient

HCPs completed a questionnaire on sociodemographic characteristics: rheumatology centre, sex, age, profession and work experience. Patients also completed a questionnaire on sociodemographic characteristics: sex, age and educational level. Medication-taking behaviour was measured by self-report, and patients filled out a validated Compliance Questionnaire on Rheumatology (CQR). Clinical characteristics (disease duration, presence of comorbidities, current DMARDs use), were extracted from patients' medical records. For patients' and HCPs' characteristics, descriptive statistics were conducted. To ensure the patients' privacy, all identifying information was anonymized.

Characteristics of the Consultations

Real-life outpatient rheumatology consultations were audio-recorded. Per patient, one audio recording was made of a single consultation. Audio recordings were checked for sound quality and completeness. Audio recordings of poor sound quality and the ones not containing the full consultation were removed (n = 8).

Content Analysis of the Audio-Recorded Consultations

A total of 134 audio-recorded consultations were used for the analyses. MAXQDA (version 24.0.0), a qualitative analysis software package, was used to facilitate the content analysis.

To explore barriers, facilitators, and adherence issues to current DMARD use, only recordings in which barriers and/or facilitators of current DMARD use were raised by patients, were selected. Subsequently, in these recordings, issues related to medication adherence were explored. An extraction sheet facilitated this process and field notes were made during listening to the audio-recordings. To facilitate the content analysis, these audio recordings were transcribed verbatim.

The content analysis was conducted by two researchers independently (MV & JV).[21] They read all transcripts and extracted excerpts that pertained to discussion about DMARD-related barriers and facilitators. A third researcher (SvD) read 10 transcripts and studied the excerpts, to ensure the trustworthiness of the analysis. The barriers and facilitators identified from the excerpts were coded and categorized using the Identification of Medication Adherence Barriers (IMAB) model, an adjusted model of the Theoretical Domains Framework.[22,23] This model comprises several domains that facilitate the mapping of factors important for medication adherence, such as skills, environmental context and resources and knowledge and was previously used to identify relevant factors with regard to medication use in patients with RA. In addition, the IMAB domains were grouped according to the higher order components: Capability, Opportunity and Motivation of the Behaviour Change Wheel: (COM-B).[24] The coding process was discussed until consensus was reached among the two researchers (MV & JV). In case no consensus could be reached, another researcher (BvdB) made the final decision.

Next, the verbal responses of rheumatologists were analysed from the selected audio-recordings, which only contained excerpts of barriers to current use of DMARDs. Therefore, the audio recordings in which only facilitators were discussed were excluded. One researcher (MV) coded the verbal responses. Relevant parts of the Roter Interaction Analysis System (RIAS), a widely used international observation system with proven validity and reliability, were used for the analysis of the conversations between rheumatologist and patient.[25–27] RIAS distinguishes two communication categories: affective or socio-emotional communication and instrumental communication. These categories can be further subdivided into various verbal responses. For affective communication, these include agreement, verbal attentiveness, making jokes, personal remarks, and reassurance. For instrumental communication, these verbal responses include a question (open-ended or closed-ended question), providing information, or an advice for the patient to change behaviour (counselling).

RESULTS

Sample Characteristics

In Table 1, the characteristics of rheumatologists and patients are displayed.

Table 1. Characteristics of the Rheumatologists and Patients with Rheumatoid Arthritis

Rheumatologists (n=20)	
Rheumatology centre, n (%)	
Amsterdam	7 (35)
Nijmegen	13 (65)
Male sex, n (%)	15 (75)
Age in years, mean (SD)	49 (8.6)
Work experience in years, mean (SD)	16 (9.4)
Patients (n=134)	
Rheumatology centre, n (%)	
Amsterdam	47 (35)
Nijmegen	87 (65)
Male sex, n (%)	44 (33)
Age in years, mean (SD)	60.9 (11.7)
Educational level#*, n (%)	
Low	32 (23.9)
Moderate	55 (41)
High	43 (32.1)
Disease duration in years, median (IQR)	8.5 (3 - 15)
Comorbidities, n (%)	
No	33 (24.6)
Yes	101 (75.4)
Number of synthetic DMARDs in use, n (%)	
1	108 (80.6)
2	20 (14.9)
3	6 (4.5)
Use of biologics, n (%)	
No	92 (68.7)
Yes	42 (31.3)
Medication beliefs, necessity subscale, mean (SD)	19.8 (3.5)

Table 1. Continued

Medication beliefs, concerns subscale, mean (SD)	13.8 (3.9)
CQR correct dosing, adherent, n (%)	82 (61.2)

Notes: #Educational level: low = up to and including lower technical and vocational training, moderate = up to and including secondary technical and vocational training, high = up to and including higher vocational training and university.

*Missing values ≤ 3%.

Abbreviation: DMARDs, Disease-modifying anti-rheumatic drugs.

One hundred and thirty-four eligible routine consultations with unique patients were available (Figure 2). In 43% (n = 58) of the consultations, barriers and/or facilitators to DMARD use were raised by patients.

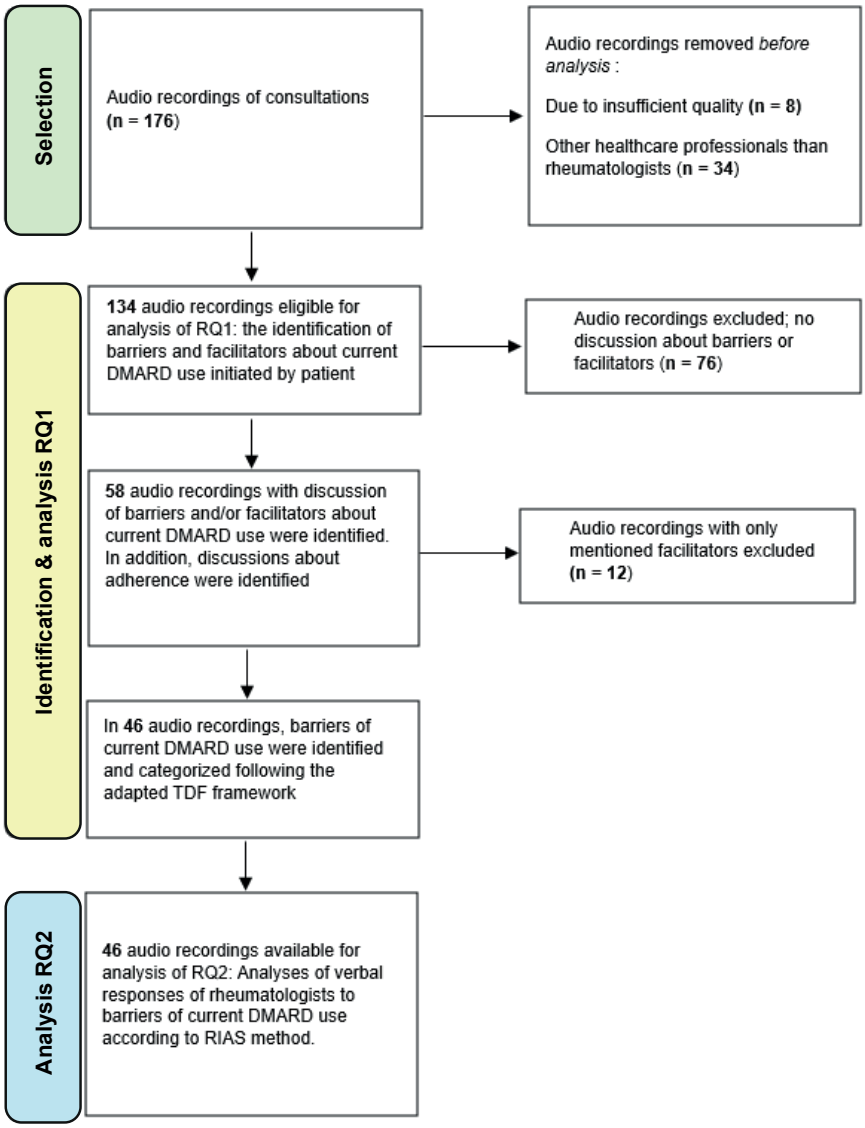


Figure 2. Flowchart of selection and analysis of audio recordings.

Barriers, Facilitators, and (Non)adherence Issues for Current DMARD Use

In Tables 2 and 3, facilitators and barriers for current DMARD use are displayed, as well as patients' quotes illustrating these barriers and facilitators.

Table 2. Facilitators About Current DMARD Use Categorized According to the COM-B Model and IMAB Domains

COM-B	IMAB Domain	Facilitators	Quote
CAPABILITY	Memory and Attention	Treatment effect Aids (to remember) Embedded in daily routine/timing medication use	"Yes, look, I'll take them just before going to bed, then [the nausea] vanishes by itself.."
	Decision-making process	Self-management (patient proposes/ decides)	"My question is; just an option: that we go back from 25 gr MTX to 20? ...Is that a nice idea?" [proposing a different dose]
OPPORTUNITY	Environmental context and resources	Good quality of needles/pens instead of injections	"..With the other syringe, I needed the help of my husband...But, this one, I can administer myself"
	Social influences	Health professionals (rheumatologist, pharmacist, nurse, general practitioner): capabilities, trust, and empathy	"It was a really good advice from the pharmacist taking my medication in the evening...I used to take them in the morning and then I got nauseous..."
MOTIVATION	Beliefs about capabilities	Self-efficacy (adjusting dose/using GCs/ timing medication use)	"I have adjusted my dose by raising it with one pill"
	Beliefs about consequences	Belief of treatment effect/need for medication	"I have not taken my medication for two weeks....and since then I started again, because the disadvantages do not outweigh the advantages.."

Abbreviations: COM-B model, Capability, Opportunity and Motivation-Behaviour model; IMAB domains, Domains according to the Identification of Medication Adherence Barriers model.

Table 3. Barriers About Current DMARD Use Categorized According to the COM-B Model and IMAB Domains

COM-B	IMAB Domain	Barriers	Quote
CAPABILITY	Memory and Attention	Forgetting to take medication Lack of treatment effect/Resistance	"Yes, difficult to do so. To remind oneself that it must… and then to actually do [take medication] …"
OPPORTUNITY	Environmental context and resources	Quality of product (needle) Logistics (medication storage temperature, pharmacy has no stock) Change of name/appearance of medication/ change pharmaceutical (biosimilar)	"All the issues with the different pharmaceutical prescribers, I do not like it. In the future, the physician can better prescribe a blank recipe…."
	Social influences	Lack of support from colleagues (incomprehension, negative reactions/ advise from third parties)	"…My alternative therapist said: "That is not allowed. When you are with me, you can't increase or change your medication."
MOTIVATION	Beliefs about capabilities	Difficulty in adherence because of procrastination Lack of daily routine	"..[instead of daily use]..to taking the medication every other day, yes….for me, that is more complex to remember"
	Beliefs about consequences	Belief/Fear of experiencing (long- and short-term) side effects/comorbidity because of long life use of medication Belief that medication will be harmful: higher disease activity Lack of belief/Doubts in/about efficacy Dependency on medication Less acceptance of (long-term and many) medications Non-acceptance of diagnosis	"..doubts about the efficacy of the [medication], yes, I have the feeling that it does not….Yes, not sufficient, it is not working. The symptoms have not improved.."
	Emotions	Anxiety/Fear Anger Dependency on medication Insecurity/Loss of trust in medication	"Well, I have two [pills] left…so I could stop [taking the medication], Or do I have the chance that [symptoms] it will flare up? Because, that would frighten me…"

Table 3. Continued

COM-B	IMAB Domain	Barriers	Quote
	Motivation and Goals	Worse health status/wellbeing Side effects Long time before effectiveness shows Comorbidity Negative effect lower dose	"Because, I have accidently been taken 17,5 mg, and I experienced some [negative] effect. So, this [25 mg] appears to be the right dose!"
	Goal conflict	Experiencing side effects Restrictions due to using medication (i.e., no alcohol) Not able to participate (social, work)	"And now, I always feel nauseous the following Sunday, and then I think: Well, I really can't have that, while on a trip…"

Abbreviations: COM-B model: Capability, Opportunity and Motivation-Behaviour model, IMAB domains: Domains according to the Identification of Medication Adherence Barriers model.

Facilitators for Current DMARD Use

In a small number of consultations (n = 12), only facilitators were brought up by patients. Facilitators mentioned were for instance related to the (good) quality of the needles, the use of an injection pen instead of a syringe, dose reduction because of low disease activity, timing of the medication, a medication box in which the pills are organized per day, and the helpful advice of the pharmacist about the timing of medication use.

Barriers for Current DMARD Use

In one-third of the consultations (n = 46), various barriers were raised by patients with regard to the use of their DMARDs. Sporadically, barriers were mentioned by a family member who accompanied the patient to the hospital. Most barriers were related to side effects (predominantly nausea and not feeling – physically and/or mentally – well, but also headaches, stomach complaints and infections), timing of medication use, alcohol consumption, doubts about efficacy of medication, and resistance of medication use and dependency. Most barriers were categorized into the IMAB domains: "Beliefs about consequences" and "Motivation and goals". These domains were subsequently categorized under the higher order component "Motivation", of the COM-B model, indicating that "Motivation" was the most mentioned component in experiencing barriers to medication use.

Some barriers were categorized into two IMAB domains, because the barrier was accompanied with a strong emotion. For example, one barrier was about an injection, of which the patient expressed anger (emotions/motivation) and explained that the needle was painful to use (quality of needle, environmental context and resources/Opportunity): "Well, it is horrible nasty injection. That I can tell you!!"

Adherence

In the conversations about barriers and facilitators to medication use (n = 58), (non)adherent behaviour was discussed in 19 consultations. These conversations were mostly initiated by the rheumatologists by using (closed-ended) questions, such as:

It is going well, the intake of medication?

The medication that you use, do you forget this sometimes?

How are you doing, taking the methotrexate?

Are you able to take your medications every day?

You stopped taking the methotrexate because you felt that it wasn't really helping you very much, right?

You skipped it [taking medication] twice during the vacation, right?

Non-adherent behaviour was mainly related to forgetfulness, experiencing side effects and lack of routine (such as holidays).

Rheumatologists' Verbal Responses to Barriers for Current DMARD Use

In Table 4 and Table 5, the rheumatologists' responses to the barriers raised by patients are displayed. Table 4 shows that the verbal responses of rheumatologists on the various barriers were mainly a combination of instrumental and affective communication. Rheumatologists provided in many cases several instrumental responses combined with a single affective response per barrier.

Specifically, the responses were often combinations of counselling, a closed-ended question with agreement, and confirmation (Table 5). An example of such a combined rheumatologist's response to a raised barrier was:

Patient: *No, but it is a...it is really a complex daily routine (barrier) HCP: Yes, I think so too. (affective response, agree)*

Patient: *You need to take something when you get up [medication] and [medication] with meals and...*

HCP: *I have to say that the time of intake of [medication x and y] is less relevant and it won't hurt when those times vary a little... (instrumental response, information)*

Table 4. Barriers to DMARD Use Mentioned in 46 Consultations by Patients and Rheumatologists' Responses Categorized in Main Communication Categories: Instrumental, Affective, Combination or No Response

			Response			
Com-b	**Imab domains**	**Barriers**	**Instrumental**	**Affective**	**Combination Instrumental and Affective**	**No response**
C	Memory and attention	Forgetting to take medication		x		
		Mistake in dosing medication		x		
C	Skills	Insufficient cognitive, communicative, or physical skills to understand and/or administer medication			x	
O	Social Influences	Lack of support from others (wrong advice)				x
O	Environmental context and resources	Quality of product (needle) 2* *(also scored under emotions anger)*			xx	
		Change of name or appearance 3*	x		x	x
		Logistics 2*	x	x		
M	Goal Conflict	Restrictions due to using medication (no alcohol) 2*			xx	
		Not able to participate (socially/work) 2*	x	x		
		Worse well-being (limits holidays)			x	
M	Emotions	Fear 3*			xxx	
		Anger			x	
		Despair			x	
		Dependency of medication		x		

Table 4. Continued

Com-b	Imab domains	Barriers	Response			
			Instrumental	Affective	Combination Instrumental and Affective	No response
M	Belief about consequences	Experience of (long- and short term) side effects 5*	xx	xx	x	
		Lack of belief in efficacy 5* *(1 also scored under emotions despair)*	xx	x	x	x
		Less acceptance of (long-term) medication 5*	xxxx		x	
		Belief that medication will be harmful 2*	x		x	
		Lack of belief in necessity (more) medication 2*	x		x	
		Negative expectations for tapering *(also scored under emotions fear 3*)*			x	
M	Motivation and goals	Side effects 36*	13x	7x	14x	2x
		Tapering failure	x			
		Time to treatment effect	x			
		Difficulty administration medication			x	
M	Beliefs about capabilities	Lack of daily routine 2*		x	x	
		Postponement intake due to struggle necessity			x	

Notes: *Number of times mentioned as barrier X Number of times mentioned as response *Italic*: barrier mentioned under several domains. **Abbreviations**: DMARD: Disease-modifying anti-rheumatic drug, COM-B model: Capability, Opportunity and Motivation-Behaviour model, IMAB domains: Domains according to the Identification of Medication Adherence Barriers model.

Table 5. Barriers to DMARD Use Mentioned in 46 Consultations by Patients and Rheumatologists' Instrumental and Affective Responses Specified According to RIAS Coding

			Instrumental response				Affective response			
Com-b	**Imab domains**	**Barriers**	**Open-ended Question**	**Closed-ended Question**	**Information**	**Counselling**	**Agree**	**Reassurance**	**Verbal attentiveness**	**Personal remark**
C	Memory and attention	Forgetting to take medication							x	
		Mistake in dosing medication					x			
C	Skills	Insufficient cognitive, communicative, or physical skills to understand and/or administer medication				x		x		
O	Social Influences	Lack of support from others (wrong advice)								
O	Environmental context and resources	Quality of product (needle) 2* *(also scored under emotions anger)*		x	x	x	x	x		
		Change of name or appearance 3*		x	x	x	x			
		Logistics 2*			x				x	
M	Goal Conflict	Restrictions due to using medication (no alcohol) 2*		xx		x	x		x	x
		Not able to participate (socially/ work) 2*		x		x	x			
		Worse well-being (limits holidays)		x		x	x			

Table 5. Continued

			Instrumental response				Affective response			
Com-b	**Imab domains**	**Barriers**	**Open-ended Question**	**Closed-ended Question**	**Information**	**Counselling**	**Agree**	**Reassurance**	**Verbal attentiveness**	**Personal remark**
M	Emotions	Fear 3*			x	xx	xx	x	x	
		Anger			x			x		
		Despair				x	x			
		Dependency of medication							x	
M	Belief about consequences	Experience of (long- and short term) side effects 5*		xx		xx	xxx			
		Lack of belief in efficacy 5* *(also scored under emotions despair)*			xx	xxx	x		x	
		Less acceptance of (long-term) medication 5*		xx		xxx	x			
		Belief that medication will be harmful 2*			xx	x	x			
		Lack of belief in necessity (more) medication 2*				xx			x	
		Negative expectations for tapering *(also scored under emotions fear)* Concerns about long term use of medication	x		x		x			

Table 5. Continued

			Instrumental response				Affective response			
Com-b	**Imab domains**	**Barriers**	**Open-ended Question**	**Closed-ended Question**	**Information**	**Counselling**	**Agree**	**Reassurance**	**Verbal attentiveness**	**Personal remark**
M	Motivation and goals	Tapering failure Side effects 36* ^ not specified, see footnote				x				
		Time to treatment effect		x						
		Difficulty administration medication			x		x			
M	Beliefs about capabilities	Lack of daily routine 2*				x	xx			
		Postponement intake due to struggle necessity				x		x		

Notes: Number of times mentioned as barrier X Number of times mentioned as response *Italic*: barrier mentioned under several domains ^Side effects: most instrumental responses were "asking closed questions" and "providing counselling"; the affective response was predominantly "verbal attentiveness"; when the HCP offered (in most cases) a combined instrumental and affective response, the HCPs responded with "open questions" and occasionally with a joke. **Abbreviations**: DMARD: Disease-modifying anti-rheumatic drug, RIAS: Roter interaction analysis system COM-B model: Capability, Opportunity and Motivation-Behaviour model, IMAB domains: Domains according to the Identification of Medication Adherence Barriers model.

Table 5 shows that when rheumatologists responded in an instrumental manner, they most often applied counselling, followed by information provision. Most of the questions asked by rheumatologists were closed-ended. An example of a counselling advice was:

> *Some people are scared and some people experience pain, because of injections. However, these injections are easier to use. But if you feel insecure using these injections, you have to discuss this with the pharmacist. You can always go there and inject with the help of the pharmacist. Or, you can inject here, with the help of a nurse. Because, you need to be sure that it goes well. (Counselling)*

Affective responses were typically expressed as agreement followed by verbal attentiveness when patients discussed barriers. A few times, rheumatologists responded with reassurance, a joke, or a personal remark. An example of a rheumatologist's response was:

> *Look, they say sometimes, never change a winning team. So, if it is really acceptable, well, if you say: 'I am a satisfied person', then I would not change anything. But, if you say specifically: 'I have often, while taking the methotrexate, a heavy feeling in my stomach on that day'...well, the dose can be reduced, right? That is possible (instrumental response, counselling). Because I do not have any shares in that stuff, do I? (affective response, laughs, joke)*

In a few cases, the rheumatologists did not provide a response; the patients gave long monologues with various questions and the rheumatologists responded to one of the more urgent topics in those monologues.

DISCUSSION

This is the first study in which communication about barriers to DMARD use is analysed through audio recordings. In the current study, 134 audio recordings of real-life outpatient rheumatology consultations were assessed to gain insight into whether patients with RA and rheumatologists discussed barriers, facilitators, and adherence issues to current DMARD use, and how rheumatologists responded to the issues raised. In about one out of three consultations, barriers to DMARD use were brought up by patients. Most barriers discussed were related to experiencing side effects and doubts about efficacy and resistance of

(long-term use of) medication. Rheumatologists' responses to barriers of DMARD use were mostly a combination of instrumental (counselling) and affective (agreement) communication.

The barriers of DMARD use raised by patients in the current study are in line with preceding papers.[28–32] Although insufficient cognitive, communicative or physical skills to understand and/or administer medication have been reported in a previous study, these were not identified in this recent study.[33] The different study designs may account for these discrepancies. In a focus group discussion with patients, for instance, patients have sufficient time to think of, discuss, and report potential barriers to medication use, for themselves or for patients in general, which may not be the case in real-life outpatient rheumatology consultations. Another possibility is that patients do not want to mention their barriers for medication use to avoid burden for the rheumatologist or when medication-related problems were related to emotional or sensitive topics.[30,31] This reflects a dependable, sensitive and unequal relationship, in which understanding, trust, empathy, respect and time are proven barriers or facilitators in conversations.[34–36]

In line with other studies, we found that rheumatologists do not always explore and discuss problems with regard to medication.[32,37,38] Oton et al (2022) showed that HCPs almost exclusively focus on physical symptoms and pay less or no attention to other issues of relevance to patients.[28] Adherence to DMARD use is critical for disease management and potential barriers to medication use are widely acknowledged, but addressing (non) adherence issues remains suboptimal. Tools to facilitate this process in future consultations would be recommendable.[39]

The current study also shows that the way rheumatologists responded to patients' barriers for DMARD use, was predominantly a combination of an instrumental (i.e., counselling) style and an affective (i.e., agreement) style. This is in line with Bensing et al, reporting that in medical consultations which have often a problem-solving approach, a therapeutic approach in which affective behaviour is necessary to create a warm and trusting atmosphere, is a purpose in itself. Addressing patients' dual needs is shown to be important in medical consultations.[12]

Although the terms instrumental or affective communication are not always applied, it is evident that many descriptions reflect those communication styles in consultations, such as empathic responses

(affective) by the HCP, eliciting the patient's perspective that makes the patient feel understood (affective). The instrumental style is reflected by asking questions by the HCP, providing an appropriate follow-up by providing solutions.[40] Possible solutions to over-come barriers were discussed in the current study, such as to build a daily routine around medication use, to use medication twice a day instead of once a day to avoid side effects, to change dosing, to place medication in sight to avoid forgetfulness, a different way of administering, or the rheumatologist provided more detailed information about the medication. When different communication styles are applied in consultations, it will enhance patients' satisfaction, even if the actual time spent with the patient is short.[41]

Instrumental communication plays a crucial role in ensuring that the need of patients with RA to receive full disclosure of all available treatment options (i.e., changes in medication treatment), and their associated risks and benefits are met, as previous studies have demonstrated.[37,42,43] Moreover, it has been shown that HCPs often underestimate or undervalue patients' information needs.[38] In the current study, patients did not mention that, eg, information on the inserted leaflet in medication boxes was not clear to them, nor that relevant information was omitted. This may suggest that the patients were well informed, which could have influenced the findings in the current study.

A scoping review indicated that affective communication, characterized by emotional engagement from healthcare professionals (HCPs), has the potential to empower, enable, and motivate patients to take an active role in managing their disease.[44] Additionally, recognizing and appreciating the patient's individuality, behaviours, and fears are identified as critical factors in supporting patients. These findings underscore the importance of integrating both instrumental and affective communication approaches to effectively address the barriers reported by patients, with the aim of mitigating non-adherent behaviour.[45]

HCPs most often responded to an affective utterance by the patient with agreement. Since patients' characteristics and needs can differ because of, e.g., personalities, disease duration or disease severity, one might assume that not all patients prefer the same style of communication, and a potential need for additional support to overcome problems with regard to medication use is therefore patient-specific.[31,46,47] Sometimes the emphasis on providing information or discussing practical solutions can

be sufficient to enhance adherence, while in other situations, an affective response can have the same positive effect on adherent behaviour. This asks for patient-centred communication by the HCP which departs from inquiring about patient's momentary informational and emotional needs, to actively engage patients in the conversation, encourage them to express their needs and ask questions, and to involve patients in treatment decision-making.[9,34]

Strengths and Limitations

There are several strengths and limitations of this study worth mentioning. Strengths were the large number of audio-recorded consultations (n = 134) and the use of an observer-based measure (i.e., RIAS) to explore in-depth the discussions about barriers of DMARD use and the way the rheumatologists responded to these. However, several limitations should also be acknowledged. First, audio-recording the consultations may have affected the behaviour of both rheumatologists and patients. Nevertheless, at the time of these consultations neither rheumatologists nor patients were aware that the audio recordings would be used for the current study. Second, only a single consultation per patient was audio-recorded, and the consultations were snapshots of daily practice. The possibility that barriers to DMARD use had already been discussed in a previous consultation or would be discussed in a future one cannot be ruled out. Still, barriers that may have emerged in a previous consultation need attention in each follow-up consultation. A longitudinal study assessing verbal and nonverbal behaviour of patients and rheumatologists during consultations is needed to strengthen the ecological validity of our findings.[48] Third, only barriers and facilitators related to *current* DMARD use by patients were analysed. It should be pointed out that experienced barriers in the past and barriers related to future use of DMARDs may have an impact on (non)adherent behaviour in the future as well and should be acknowledged when discussing medication use, specifically when new medication treatment is prescribed.[32] Fourth, the external validity of the results might be compromised due to the high proportion of adherent participants. The latter might indicate selection bias, since it is well known that predominantly highly motivated patients participate in adherence studies.[49,50] Lastly, due to the qualitative study design, it was not possible to draw conclusions about a relationship between the barriers to DMARD use raised by patients and their potential non-adherent behaviour. Factors such as medication adherence, HCP-patient familiarity, and patient' health literacy may have influenced the conversations and could therefore be of interest in future research.

Implications

These findings present a list of barriers and facilitators of DMARD use raised by patients with RA. Considering that non-adherence to DMARDs is relatively high in patients with RA, having a negative impact on health and societal costs, it would be beneficial that patients and rheumatologists discuss potential reasons for non-adherent behaviour.[51] Therefore, HCPs working in rheumatology (e.g., rheumatologists, nurses, pharmacists) could be educated to ask specifically for barriers to DMARD use in an egalitarian setting and tailor their communication to patient's needs. Patients could be educated as well to initiate a discussion about barriers with their HCPs.

Conclusions

In nearly one-third of the real-life outpatient rheumatology consultations, various barriers to current medication use were discussed. Most mentioned barriers were experiencing side effects and doubts about efficacy and resistance to (long-term use of) medication. Rheumatologists responded in most cases with a combination of instrumental and affective communication style. These findings may support rheumatologists to become aware of the most common barriers patients may perceive regarding their DMARD use and tailor their communication style to meet patients' needs.

Abbreviations

HCP, Healthcare professional; ACR, American College of Rheumatology; DMARDs, Disease-modifying antirheumatic drugs; EULAR, European League Against Rheumatism; IC, Informed consent; MAXQDA, MAXQDA is a qualitative software to analyse qualitative findings; COM-B, Capability, Opportunity and Motivation-Behaviour model; IMAB, Identification of Medication Adherence Barriers model; RIAS, Roter Interaction Analysis System; METC, Medical research ethics committee; in Dutch: medisch-ethische toetsingscommissie; RA. Rheumatoid arthritis; Wbp, Dutch personal data protection act; in Dutch: wet bescherming persoonsgegevens; WMO, Medical research involving human subjects act; in Dutch: wet medisch-wetenschappelijk onderzoek met mensen.

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REFERENCES

1. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. Arthritis Rheumatol. 2016;68(1):1–26. doi:10.1002/art.39480
2. Smolen JS, Landewe R, Bijlsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheumatic Dis. 2017;76(6):960–977. doi:10.1136/annrheumdis-2016-210715
3. Aletaha D, Smolen JS. Diagnosis and management of rheumatoid arthritis: a review. JAMA. 2018;320(13):1360–1372. doi:10.1001/jama.2018.13103
4. Kahlenberg JM, Fox DA. Advances in the medical treatment of rheumatoid arthritis. Hand clin. 2011;27(1):11–20. doi:10.1016/j.hcl.2010.09.002
5. Sabaté E, World Health O. Adherence to long-term therapies: evidence for action. World Health Organization. 2003. https://iris.who.int/handle/10665/42682
6. de Klerk E, van der Heijde D, Landewe R, van der Tempel H, Urquhart J, van der Linden S. Patient compliance in rheumatoid arthritis, polymyalgia rheumatica, and gout. J Rheumatol. 2003;30(1):44–54.
7. Waimann CA, Marengo MF, de Achaval S, et al. Electronic monitoring of oral therapies in ethnically diverse and economically disadvantaged patients with rheumatoid arthritis: consequences of low adherence. Arthritis Rheum. 2013;65(6):1421–1429. doi:10.1002/art.37917
8. Salt E, Frazier S. Adherence to disease modifying anti-rheumatic drugs in rheumatoid arthritis patients: a narrative review of the literature. Orthop Nurs. 2010;29(4):260–275. doi:10.1097/NOR.0b013e3181e5c2c9
9. de Haes H, Bensing J. Endpoints in medical communication research, proposing a framework of functions and outcomes. Patient edu counseling. 2009;74(3):287–294. doi:10.1016/j.pec.2008.12.006
10. Hall JA, Roter DL, Katz NR. Meta-analysis of correlates of provider behavior in medical encounters. Med Care. 1988;26(7):657–675. doi:10.1097/ 00005650-198807000-00002
11. Zolnierek KB, Dimatteo MR. Physician communication and patient adherence to treatment: a meta-analysis. Med Care. 2009;47(8):826–834. doi:10.1097/MLR.0b013e31819a5acc
12. Bensing JM, Dronkers J. Instrumental and affective aspects of physician behavior. Med Care. 1992;30(4):283–298. doi:10.1097/00005650-199204000-00001
13. Bensing JM, Verhaak PFM. Communication in medical encounters. In: Health Psychology. Blackwell Publishing; 2004:261–287.
14. Willson P, McNamara JR. How perceptions of a simulated physician-patient interaction influence intended satisfaction and compliance. Soc sci med. 1982;16(19):1699–1704. doi:10.1016/0277-9536(82)90095-8
15. Hall JA, Roter DL, Katz N. Task versus socioemotional behaviors in physicians. Med Care. 1987;25:399–412. doi:10.1097/00005650-198705000-00004

16. Roter DL, Hall JA, Katz NR. Relations between physicians' behaviors and analogue patients' satisfaction, recall, and impressions. Med Care. 1987;25(5):437–451. doi:10.1097/00005650-198705000-00007

17. Weiland A, Van de Kraats RE, Blankenstein AH, et al. Encounters between medical specialists and patients with medically unexplained physical symptoms; influences of communication on patient outcomes and use of health care: a literature overview. Perspect Med Educ. 2012;1(4):192–206. doi:10.1007/s40037-012-0025-0

18. DiMatteo MR. A social-psychological analysis of physician-patient rapport: toward a science of the art of medicine. J Curr Soc Issues. 1979;35 (1):12–33. doi:10.1111/j.1540-4560.1979.tb00787.x

19. van Heuckelum M, Linn AJ, Vandeberg L, et al. Implicit and explicit attitudes towards disease-modifying antirheumatic drugs as possible target for improving medication adherence. PLoS One. 2019;14(8):e0221290. doi:10.1371/journal.pone.0221290

20. Henselmans I, Heijmans M, Rademakers J, van Dulmen S. Participation of chronic patients in medical consultations: patients' perceived efficacy, barriers and interest in support. Health Expect. 2015;18(6):2375–2388. doi:10.1111/hex.12206

21. Graneheim UH, Lundman B. Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness. Nurse Educ Today. 2004;24(2):105–112. doi:10.1016/j.nedt.2003.10.001

22. Michie S, Johnston M, Abraham C, Lawton R, Parker D, Walker A. Making psychological theory useful for implementing evidence based practice: a consensus approach. Qual Saf Health Care. 2005;14(1):26–33. doi:10.1136/qshc.2004.011155

23. Easthall C, Taylor N, Bhattacharya D. Barriers to medication adherence in patients prescribed medicines for the prevention of cardiovascular disease: a conceptual framework. Int J Pharm Pract. 2019;27(3):223–31. doi:10.1111/ijpp.12491

24. Michie S, van Stralen MM, West R, et al. The behaviour change wheel: a new method for characterising and designing behaviour change interventions. Article Implement Sci. 2011;6(1):42–53. doi:10.1186/1748-5908-6-42

25. Ong LM, Visser MR, Kruyver IP, et al. The Roter Interaction Analysis System (RIAS) in oncological consultations: psychometric properties. Psycho-Oncology. 1998;7(5):387–401. doi:10.1002/(sici)1099-1611(1998090)7:5<387::aid-pon316>3.0.co;2-g

26. Takekuma Y, Mori A, Kobayashi M, et al. Analysis by using Roter method of interaction process analysis (RIAS) of the ability of pharmacy students to communicate after clinical training for pharmacy. Yakugaku zasshi. 2018;138(12):1579–1586. doi:10.1248/yakushi.18-00032

27. Roter D, Larson S. The roter interaction analysis system (RIAS): utility and flexibility for analysis of medical interactions. Patient Educ Couns. 2002;46(4):243–251. doi:10.1016/s0738-3991(02)00012-5

28. Otón T, Carmona L, Andreu JL. Patient's experiences of the barriers and facilitators to methotrexate. Musculoskeletal Care. 2022;20(1):158–166. doi:10.1002/msc.1577

29. El Masri H, Hollingworth SA, van Driel M, Benham H, McGuire TM. Real-world questions and concerns about disease-modifying antirheumatic drugs (DMARDs): a retrospective analysis of questions to a medicine call center. BMC Rheumatol. 2020;4:27. doi:10.1186/s41927-020-00126-7

30. Wohlfahrt A, Campos A, Iversen MD, et al. Use of rheumatology-specific patient navigators to understand and reduce barriers to medication adherence: analysis of qualitative findings. PLoS One. 2018;13(7):e0200886. doi:10.1371/journal.pone.0200886

31. Haegens LL, Huiskes VJB, Smale EM, Bekker CL, van den Bemt BJF. Drug-related problems reported by patients with rheumatic diseases: an observational study. BMC Rheumatol. 2023;7(1):7. doi:10.1186/s41927-023-00326-x

32. Blalock SJ, DeVellis BM, DeVellis RF, Chewning B, Jonas BL, Sleath BL. Medication risk communication during rheumatology office visits. Arthritis Care Res. 2015;67(2):161–168. doi:10.1002/acr.22424

33. Voshaar MJH, Vriezekolk J, van Dulmen S, van den Bemt B, van de Laar M. Barriers and facilitators to disease-modifying antirheumatic drug use in patients with inflammatory rheumatic diseases: a qualitative theory-based study. BMC Musculoskeletal Disorders. 2016;17(1):442. doi:10.1186/ s12891-016-1289-z

34. Ong LM, de Haes JC, Hoos AM, Lammes FB, de Haes JCJM. Doctor-patient communication: a review of the literature. Soc sci med. 1995;40 (7):903–918. doi:10.1016/0277-9536(94)00155-m

35. Rolfe A, Cash-Gibson L, Car J, Sheikh A, McKinstry B. Interventions for improving patients' trust in doctors and groups of doctors. Cochrane Database Syst Rev. 2014;2014(3). doi:10.1002/14651858.CD004134.pub3

36. McCabe R, Healey PGT, Priebe S, et al. Shared understanding in psychiatrist-patient communication: association with treatment adherence in schizophrenia. Patient Educ Couns. 2013;93(1):73–79. doi:10.1016/j.pec.2013.05.015

37. Mathijssen EGE, Vriezekolk JE, Eijsbouts AMM, van den Hoogen FHJ, van den Bemt BJF. Support needs for medication use and the suitability of eHealth technologies to address these needs: a focus group study of older patients with rheumatoid arthritis. Patient Prefer Adherence. 2018;12:349–58. doi:10.2147/PPA.S152759

38. Kinnersley P, Edwards AGK, Hood K, et al. Interventions before consultations for helping patients address their information needs. Cochrane Database Syst Rev. 2010(3). doi:10.1002/14651858.CD004565.pub2

39. Pouls BPH, Vriezekolk JE, Bekker CL, et al. Effect of interactive eHealth interventions on improving medication adherence in adults with long-term medication: systematic review. J Med Internet Res. 2021;23(1):e18901. doi:10.2196/18901

40. Mauksch LB, Dugdale DC, Dodson S, Epstein R. Relationship, communication, and efficiency in the medical encounter: creating a clinical model from a literature review. Arch Intern Med. 2008;168(13):1387–1395. doi:10.1001/archinte.168.13.1387

41. Voogt SJ, Pratt K, Rollet A. Patient communication: practical strategies for better interactions. Fam Pract Manag. 2022;29(2):12–16.

42. Fraenkel L, Bogardus S, Concato J, Felson D. Preference for disclosure of information among patients with rheumatoid arthritis. Arthritis Care Res. 2001;45(2):136–139. doi:10.1002/1529-0131(200104)45:2136

43. Neame R, Hammond A, Deighton C. Need for information and for involvement in decision making among patients with rheumatoid arthritis: a questionnaire survey. Arthritis Care Res. 2005;53(2):249–255. doi:10.1002/art.21071

44. Gillespie H, Kelly M, Duggan S, Dornan T. How do patients experience caring? Scoping review. Patient Educ Counseling. 2017;100 (9):1622–1633. doi:10.1016/j.pec.2017.03.029

45. Soundy A, Stubbs B, Freeman P, Coffee P, Roskell C. Factors influencing patient's hope in stroke and spinal cord injury: a narrative review. Int J Ther Rehabil. 2014;21:210–218. doi:10.12968/ijtr.2014.21.5.210

46. Hope HF, Hyrich KL, Anderson J, et al. The predictors of and reasons for non-adherence in an observational cohort of patients with rheumatoid arthritis commencing methotrexate. Rheumatology. 2020;59(1):213–223. doi:10.1093/rheumatology/kez274

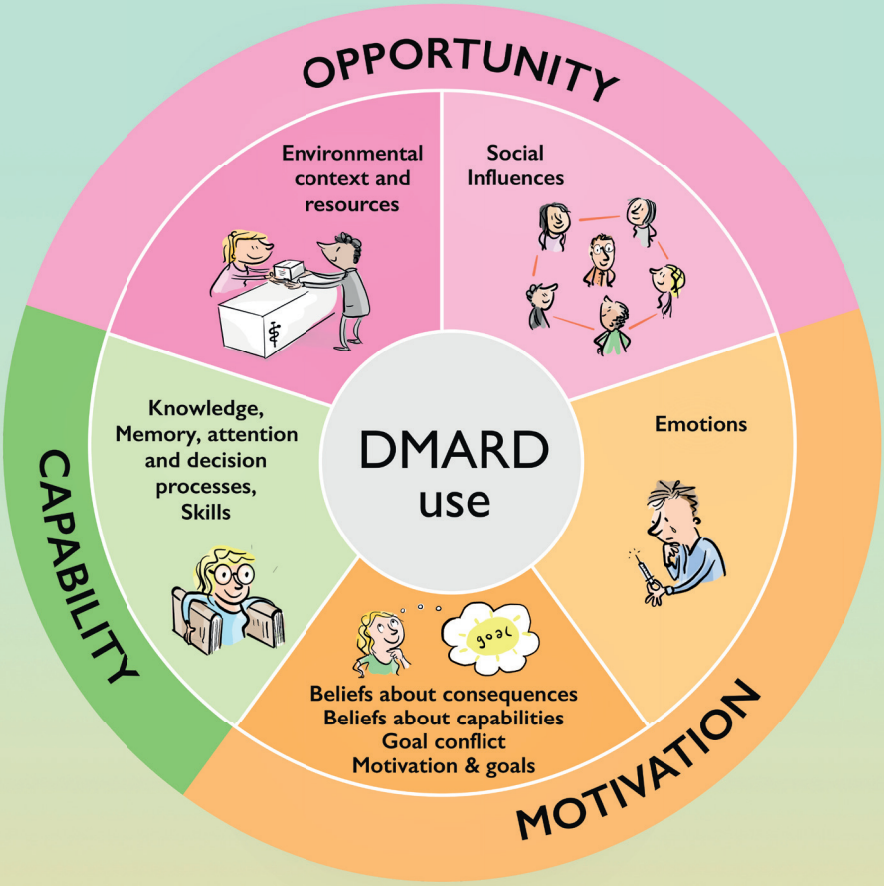
47. Shea B, Swinden MV, Tanjong Ghogomu E, et al. Folic acid and folinic acid for reducing side effects in patients receiving methotrexate for rheumatoid arthritis. Cochrane Database Syst Rev. 2014(5). doi:10.1002/14651858.CD000951.pub2

48. Gionfriddo MR, Branda ME, Fernandez C, et al. Comparison of audio vs. audio + video for the rating of shared decision making in oncology using the observer OPTION5 instrument: an exploratory analysis. BMC Health Serv Res. 2018;18(1):1–6. doi:10.1186/s12913-018-3329-x

49. Bender B, Milgrom H, Apter A. Adherence intervention research: What have we learned and what do we do next? J Allergy Clin Immunol. 2003;112(3):489–494. doi:10.1016/S0091-6749(03)01718-4

50. Huiskes VJB, CHMvd E, Dijk L, Burger DM, BJFvd B. Association between healthcare practitioners' beliefs about statins and patients' beliefs and adherence. Br J Clin Pharmacol. 2021;87:1082–1088. doi:10.1111/bcp.14467

51. van den Bemt BJ, Zwikker HE, van den Ende CH. Medication adherence in patients with rheumatoid arthritis: a critical appraisal of the existing literature. Expert Rev Clin Immunol. 2012;8(4):337–351. doi:10.1586/eci.12.23


OPPORTUNITY
Environmental context and resources
Social Influences
CAPABILITY
Knowledge, Memory, attention and decision processes, Skills
DMARD use
Emotions
goal
Beliefs about consequences
Beliefs about capabilities
Goal conflict
Motivation & goals
MOTIVATION

Chapter 7

General discussion

PERSONAL MOTIVATION

Living with rheumatoid arthritis since the age of 20 has deeply shaped both my personal and professional journey. My own experiences navigating life with a chronic condition have been the driving force behind my research. Each study I conducted reflects a personal struggle, learning moment, or realization, motivated by a desire to improve the experience for others facing similar challenges.

My first study (Chapter 2) was inspired by the importance of patient centred care, and more specifically, patient education, empowerment and involvement. In the early years after my diagnosis, I learned how crucial it is to understand your condition to actively participate in your own care. Good communication with healthcare professionals (HCPs), shared decision-making, and the involvement of family and friends gave me a foundation of support. This sense of safety and understanding helped me carry the emotional and physical burden of my condition. I wanted to explore how these patient experiences and activities can help others feel similarly equipped in managing their condition.

Main findings first study: This narrative review illustrates that incorporating patient-centred care (PCC) in rheumatoid arthritis, by addressing individual needs, concerns, and preferences, positively influences treatment outcomes, including safety, effectiveness, and cost-efficiency. PCC fosters patient empowerment and shared responsibility, and its integration into routine care may enhance health outcomes and quality of life in individuals with established RA.

The second study (chapter 3) was born from personal barriers I experienced in accepting and adhering to medication. I initially declined gold injections, which led to tension in my relationship with my HCP. Later, when methotrexate was prescribed, I didn't disclose that I had chosen not to take it, something I only confessed a year later. My hope was to function well on a biological monotherapy. The experience revealed how complex medication use can be: from accepting the chronic nature of the illness to confronting beliefs about side effects and navigating communication imbalances with HCPs. These insights shaped my motivation to research these barriers more deeply.

Main findings second study: In this mixed methods study exploring patients' barriers and facilitators of optimal DMARD use, we found that

barriers and facilitators of DMARD use in patients with inflammatory arthritis are highly heterogeneous, reflecting diverse and individually varying experiences across multiple behavioural domains. Furthermore, we found that the theoretical model applied (TDF/COM-B) was useful for assessing and developing tailored/targeted strategies to improve medication adherence.

In my third study (chapter 4) I was curious how patients themselves rank the importance of various barriers and facilitators to medication use. Personally, I always assumed side effects would be the biggest issue, but I wanted to hear directly from patients. My goal was to give their voices weight in clinical practice, highlighting that what matters most to patients should be acknowledged and addressed.

Main findings third study: This maximum difference scaling study revealed that symptom relief, autonomy, and shared decision-making are the three most important drivers for DMARD adherence in patients with established inflammatory arthritis.

I often wondered whether HCPs truly understand what patients are up against. If they did, could this awareness improve how they communicate, empathize, and support medication adherence? Bridging that gap seemed essential. My fourth study (chapter 5) - an interview study - shifted the focus to healthcare professionals' awareness of patients' barriers and facilitators to medication use.

Main findings fourth study: The semi-structured in-depth interviews, guided by an interview protocol based on the adapted version of the Theoretical Domains Framework (TDF), revealed that Dutch healthcare professionals appear to be aware of the barriers and facilitators influencing DMARD use among patients with rheumatoid arthritis.

Finally, from personal experience, I know that the quality of communication during consultations is pivotal. It can make or break a patient's motivation to follow through on decisions about medication. When communication is open, respectful, and mutual, it can transform a patient's outlook. That belief, rooted in both hardship and growth, has been at the heart of all my research. The fifth study was therefore particularly meaningful for me.

Main findings fifth study: Based on the analysis of audio recordings of consultations between healthcare professionals and patients with RA in

two Dutch hospitals, we found that barriers to current DMARD use raised by patients and discussed during routine rheumatology consultations were primarily related to side effects and concerns about efficacy and long-term use. Continuous attention for these barriers and tailored responses to patients' concerns are key to promote better adherence to treatment.

GENERAL DISCUSSION

DMARDs are essential for controlling inflammatory arthritis, but obviously their effectiveness is mediated by adherence. Not surprisingly, studies reveal a wide range of observed adherence rates, depending on patient population and methodology.[1-4] To improve adherence rates, it is essential to understand the drivers that underlie patient's decisions about DMARD use. The aim of this thesis was therefore to add knowledge about which barriers and facilitators influence DMARD use in patients suffering from inflammatory arthritis. This general discussion seeks to combine the findings of this thesis and to put these in a broader perspective, aiming to offer directions for optimizing medication adherence. The following topics will be addressed:

I. The central role of (lack of) motivation when exploring barriers to medication adherence
II. Patient-HCP communication about barriers and facilitators to the use of disease-modifying antirheumatic drugs
III. The use of theoretical models to assess medication use

I. THE CENTRAL ROLE OF (LACK OF) MOTIVATION IN BARRIERS TO MEDICATION ADHERENCE

A consistent finding across our studies is the central role of motivation in achieving medication adherence in patients with inflammatory arthritis (IA). When mapped onto the COM-B model,[5] most patient-reported barriers fall within the "Motivation" domain. These include both reflective (conscious) processes, such as beliefs about medication necessity, ambivalence, fear of dependency or concerns about long-term use, and on the other hand automatic processes (nonconscious), such as emotional resistance.

Reflective motivational barriers, such as doubts about necessity or long-term dependency, were salient across patient responses in our earlier qualitative TDF-based study (Chapter 3). Among the highest ranked barriers and facilitators in our maximum difference scaling study (Chapter 4), were also reflective motivational facilitators, demonstrated by statements like "Arthritis medications help to reduce my symptoms" and "I can decide, together with my physician, about my arthritis medication". These high scores indicate strong patient prioritisation of motivation-related facilitators.

This strong emphasis on motivation is not always taken into account in conventional adherence interventions, which often target capability (e.g., education) or opportunity (e.g., access to care) while overlooking the complex and deeply personal nature of motivational processes. As noted in the patient-centred care framework (Chapter 2), interventions that fail to address internal motivations are unlikely to achieve sustainable adherence.

Importantly, many of these motivational barriers are modifiable. For example, beliefs about medication necessity and concerns about side effects can be addressed through behaviour change techniques (such as advice to seek, arrange or deliver social support, (agreed upon) instruction on how to perform a behaviour, etc.) and communication strategies. Techniques such as Motivational Interviewing (MI) have been shown to effectively reduce ambivalence and enhance intrinsic motivation in chronic illness populations, including RA.[6,7] Likewise, approaches grounded in Self-Determination Theory (SDT) suggest that enhancing patients' sense of autonomy, competence, and relatedness supports more self-determined, sustained medication use.[8,9] This can be achieved through autonomy-supportive communication (e.g., offering meaningful choices and avoiding controlling language), competence-building strategies (e.g., providing tailored education and helping patients develop concrete action plans for medication use), and fostering relatedness (e.g., creating a trusting clinical relationship and encouraging peer support). These strategies not only improve patient engagement but also contribute to better adherence by aligning treatment with patients' values, preferences, and life context.

This is supported by our findings (Chapter 2), which reflect that interventions grounded in patient-centred care, particularly those that foster shared decision-making, empowerment, and emotional support,

are better suited to target modifiable motivational constructs, such as self-efficacy and perceived treatment value.

However, not all barriers are equally modifiable. Some structural or contextual barriers, like polypharmacy, complex regimens, limited health literacy or healthcare system limitations, may be more difficult to change at the individual level or may require a different healthcare approach than currently being offered.[10-12] Others, such as deeply rooted cultural beliefs or chronic emotional distress, may require longer-term and multi-faceted strategies. The theoretical domains framework used in our studies (Chapter 3, 5 and 6) helps to distinguish potentially modifiable psychological and behavioural determinants from more stable or external constraints.

Thus, a nuanced approach is essential, one that recognises motivation as the final common pathway through which other factors (relating to capability or opportunity) exert their influence but also considers the modifiability and nature of each barrier. This underscores the need for adherence interventions that are not only multidimensional, targeting capability, opportunity, and motivation, but also personalised, addressing modifiable factors specific to each patient's context and experience, i.e., a more person-centred approach.

II. PATIENT-HCP COMMUNICATION ABOUT BARRIERS AND FACILITATORS TO THE USE OF DISEASE-MODIFYING ANTIRHEUMATIC DRUGS

Effective communication between healthcare professionals (HCPs) and patients is essential to optimize adherence to disease-modifying antirheumatic drugs (DMARDs) in rheumatoid arthritis (RA). However, as demonstrated in our study examining how barriers to DMARD use are addressed in clinical consultations (Chapter 6), barriers to DMARD use and adherence-related behaviours remain insufficiently addressed in routine clinical encounters. In our analysis of 134 outpatient consultations, barriers or facilitators to DMARD use were raised by patients in only 43% of consultations, and medication (non)adherence was discussed in just 23%. This finding is remarkable when considering that adherence to DMARDs in patients with inflammatory arthritis ranges from 22% to 107%.[13] And when barriers are discussed, often the emphasis is on (fear of) side effects, in contrast to the findings in our study (Chapter 4)

that side effects were ranked by patients as number 7 in a top 10 scale of importance to DMARD use.[13-15] How can this "conspiracy of silence" be explained and more importantly, how can it be overcome? Despite the well-established link between effective communication and better adherence,[16] such conversations are often overlooked in practice.

Responsibility for initiating these discussions largely rests with HCPs. The structure and tone of the consultation are typically guided by the HCP, who should create an open, empathetic space where patients feel safe to express concerns.[17,18] Moreover, as mentioned in our study (Chapter 6), many patients may hesitate to disclose non-adherence or barriers unprompted, due to relational dynamics, perceived time constraints, or fear of being judged or stigmatized.[19] Proactively asking about potential barriers is thus a core professional responsibility.

At the same time, patients also bear responsibility in fostering effective communication about their medication use. Transparency about experienced barriers, whether related to side effects, medication beliefs, daily routines, or emotional factors, is essential for enabling HCPs to tailor treatment and support appropriately.[20] Fostering patient activation, which includes self-efficacy, communication skills, and confidence to voice concerns, has been shown to correlate positively with adherence and shared decision-making outcomes.[21,22]

Involving other professionals, such as rheumatology nurses and clinical pharmacists, can strengthen effective communication to enhance adherence. Rheumatology nurses often have more time to engage in personalized counselling, reinforce adherence messages, and explore barriers in a supportive environment.[23,24] Pharmacists can contribute valuable expertise on medication management, address technical or logistical barriers, have more insight in patient's adherence due to patient's refill history and offer adherence-enhancing interventions such as medication reviews, adherence monitoring, or tailored counselling.[25,26] Multidisciplinary collaboration has been shown to enhance adherence-related behaviour, especially self-efficacy and coping, which are essential for sustained adherence to DMARD therapy in RA patients.[27]

Several additional interventions can enhance communication. Training HCPs in both instrumental (informational) and affective (empathic) communication enhances patient satisfaction and adherence.[17,28] Structured tools, such as the Identification of Medication Adherence

Barriers (IMAB) model[29] and COM-B-informed approaches,[5] can systematically identify barriers. Shared decision-making[30] and pre-consultation interventions, such as question prompt lists or leaflets,[31] can empower patients to voice concerns more openly. Notably, a significant gap in perceived communication quality between patients and rheumatologists has been reported, despite agreement on its relevance for treatment effectiveness and adherence.[32] Such misalignment in communication perceptions may undermine patient engagement and compromise sustained adherence over time.

In response to escalating costs, HCPs-shortages, and system-wide crises, remote consultations, especially accelerated during the COVID 19 pandemic, have increasingly become a mainstream mode of healthcare delivery. Telemedicine visits in the U.S. rose dramatically, from under 1% to nearly one-quarter of all outpatient encounters within a few months.[33,34] While this expansion helps alleviate resource bottlenecks and supports access, it also risks marginalizing nuanced discussions around medication adherence, side-effect management, and emotional well-being.[35,36] To safeguard these relational and informational aspects, HCPs are urged to employ tailored communication strategies during virtual visits, such as structured adherence check-ins and empathy scaffolding, to ensure patient concerns are acknowledged and addressed.[37] Importantly, eHealth interventions, when designed with user needs in mind, can actively enhance patient-HCP communication and support shared decision-making. As Pouls et al. show, digital tools that enable symptom tracking, medication monitoring, and asynchronous messaging can facilitate more personalized and continuous interactions between patients and HCPs.[26] This strengthened communication not only improves patient satisfaction and engagement but may also positively influence medication adherence by fostering trust, improving information exchange, and aligning treatment plans with patients' values and experiences.

Looking forward, the integration of artificial intelligence (AI) in rheumatology care offers new opportunities but also potential risks. AI-driven adherence monitoring or decision aids must be designed to complement, not replace, patient-centred communication.[38,39] Healthcare professionals will need to balance digital tools with human empathy, ensuring that AI enhances transparency, trust, and shared understanding.[40,41] Moreover, fostering patients' digital health literacy

and supporting their ability to engage with AI-assisted care will become increasingly important.[42-44]

At the same time, emerging evidence indicates that eHealth interventions are primarily effective for low-complexity consultations, while patients with more complex health needs, limited digital literacy, or a preference for in-person care may be disproportionately disadvantaged within increasingly digital care models.[44,45]

In conclusion, improving communication about DMARD adherence in RA requires systemic, educational, and technological efforts. Both HCPs and patients share responsibility: HCPs must actively inquire about barriers, while patients should be supported to transparently express their experiences and concerns. Involving nurses, pharmacists, and other team members provides additional opportunities to reinforce adherence dialogue and patient support. Preparing for future healthcare contexts, including telemedicine and AI-driven care, demands continuous focus on preserving the human relationship at the core of treatment adherence.

III. THE USE OF THEORETICAL MODELS TO ASSESS MEDICATION INTAKE BEHAVIOUR

In this thesis, we have focussed on understanding which barriers and facilitators in the context of long-term DMARD use are salient in patients with inflammatory arthritis, through a detailed descriptive and interpretative analysis of patients' experiences and perspectives. To systematically explore the barriers and facilitators of DMARD use in patients with inflammatory arthritis, a framework from Michie and coworkers was used.[46] This Theoretical Domains Framework (TDF) comprises 12 theoretical domains derived from 33 health behaviour theories. While numerous behavioural models have been employed to understand medication adherence, no single framework has proven sufficiently comprehensive in identifying the full range of barriers contributing to non-adherence.[47-51] One potential explanation is that widely used models, such as the Health Belief Model,[52] Theory of Reasoned Action,[53] Theory of Planned Behaviour,[54] and Social Cognitive Theory,[55] were originally developed to describe, explain, or predict behaviour rather than to inform the design of behaviour change interventions. As a result, critical determinants of behaviour, such as environmental influences or individual skills, may be underrepresented in these frameworks.[56]

To address this limitation, the TDF, developed to integrate constructs from multiple behavioural theories, encompassing both individual and organisational determinants of behaviour, was used for the studies in this thesis.[46] This integrative approach reduces the likelihood of overlooking key factors relevant to the target behaviour, such as adherence to disease-modifying antirheumatic drugs (DMARDs). Although the TDF has not yet been widely applied in the context of DMARD adherence, it has been utilised in research on medication adherence in other diseases like cardiovascular diseases and organ transplantation. In that context, the framework was adapted to create the Identification of Medication Adherence Barriers (IMAB) model, which includes 10 of the original 12 TDF domains.[29]

To support the implementation of behaviour change strategies, the IMAB domains were subsequently mapped onto the components of the Behaviour Change Wheel: Capability, Opportunity, and Motivation (COM), which collectively influence behaviour.[5] Within the current research, this COM-B framework provides a structured approach for identifying and categorizing the key barriers and facilitators to DMARD use (see Figure 1). In conclusion, the use of integrative theoretical models such as the Theoretical Domains Framework (TDF) and the COM-B model offers a comprehensive and structured approach to understanding medication adherence in patients with inflammatory arthritis. By applying the TDF and COM-B in this thesis, key barriers and facilitators of long-term DMARD use could be systematically identified, supporting the development of targeted, theory-informed strategies to improve adherence.

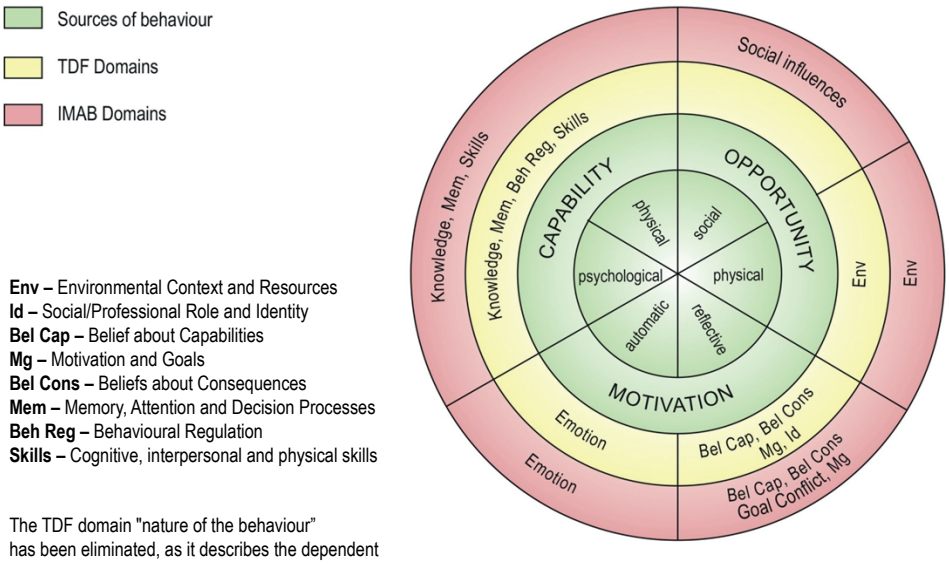


Figure 1. COM-B, derived from the Behaviour Change Wheel,[5] TDF,[46] and IMAB.[29]

TOWARDS BETTER ADHERENCE INTO PRACTICE

Adherence interventions should not focus solely on practical or technical barriers (such as e.g. reminders) but rather aim to strengthen patients' perceived benefit from treatment, their sense of autonomy, and their involvement in decision-making. This statement is related to our findings in Chapter 4 about the ranking of facilitators and barriers to medication adherence by patients and aligns with broader evidence, showing that when patients feel empowered and perceive their medication as effective and aligned with personal goals, they are more likely to adhere.[57] Moreover, assessing non-adherence should begin with exploring whether these motivational needs are unmet, whether patients experience insufficient symptom relief, feel their independence is compromised, or lack a voice in treatment planning. Such an approach allows for more tailored, meaningful clinical conversations and targeted interventions that resonate with patients' lived experiences.

Importantly, prevailing adherence models often assume the clinical appropriateness and uniform benefit of prescribed medications. However, many treatment regimens use "one size fits all" dosing strategies that fail

to accommodate individual variations in efficacy, tolerability, or subtle adverse effects. Consequently, non adherence can represent a rational response, rooted in patients' objective experiences and values, rather than mere ignorance or forgetfulness. This perspective is supported by Laba et al., who found that medication-taking decisions are "subject to rational choices, influenced by the attributes of treatments" (e.g., side effects, benefits, costs, dosing).[58]

To meaningfully improve medication adherence, it is not enough to address patient motivation alone; healthcare professionals (HCPs) must also recognize and understand the barriers their patients face. Such insight is crucial for fostering open dialogue about medication use and tailoring support to individual needs. In line with this, we explored which barriers and facilitators HCPs believe patients encounter when using DMARDs (Chapter 5). Our findings indicate that, in the Netherlands, HCPs are generally aware of the key factors influencing patients' medication use. However, awareness at the individual level does not always translate into practice. As shown by Friesen-Storms et al. and Gossec et al., systemic constraints, such as limited consultation time, clinical uncertainty, and inflexible treatment protocols, continue to hinder shared decision-making and the implementation of personalized care.[59,60] These findings highlight that optimizing adherence requires not only patient engagement but also institutional support and adaptable care structures to enable HCPs to act on their insights effectively.

Future Research

The findings of this thesis underscore several important avenues for future research. While there is considerable variability in how healthcare professionals currently address adherence to DMARDs in clinical practice, there remains significant potential to strengthen this aspect of care. Future studies should focus on the development, evaluation and implementation of tools that can support healthcare professionals and patients in delivering personalized, adherence-sensitive care. In particular, there is a clear need to develop, evaluate and implement strategies to systematically integrate structured adherence communication into routine rheumatology care. Long-term, prospective effectiveness and implementation studies are warranted to determine the sustained effects of such interventions on DMARD adherence and associated clinical outcomes. Furthermore, the role of multidisciplinary care teams - including rheumatology nurses, clinical pharmacists and patients - should be further explored to determine how their

contributions can be optimized to support adherence-related dialogue and enhance shared decision-making between patients and healthcare professionals.

Furthermore, the growing availability of digital health innovations, such as telemedicine platforms and artificial intelligence (AI)-supported decision aids, presents both opportunities and challenges. Future studies should investigate how these technologies can be leveraged to facilitate, rather than impede, patient-centred communication about medication use, with specific attention to maintaining trust and engagement during remote interactions.

Another priority for future research is the empowerment of individual patients to actively participate in adherence-related discussions throughout their care journey. Rather than categorizing patients into broad demographic or cultural groups, future approaches should focus on developing dynamic, personalized patient profiles that integrate clinical, behavioural, cultural, and contextual factors. Given the significant influence of health literacy, digital literacy, and sociocultural context on communication and treatment engagement, studies should explore how communication strategies can be tailored to these evolving individual needs. While the current study population consisted predominantly of Caucasian patients from the Netherlands, limiting the generalizability of findings, future research should aim to include more heterogeneous populations and examine how personal beliefs, cultural practices (e.g., fasting during Ramadan), and differing healthcare system experiences influence medication adherence and communication preferences.

In terms of theoretical framework, this thesis employed the Theoretical Domains Framework (TDF) to comprehensively map barriers and facilitators to DMARD adherence. While the TDF enabled a broad and inclusive categorization of behavioural determinants, it does not specify causal or hierarchical relationships between domains. Future research should aim to examine interrelationships and relative weights of TDF domains in shaping adherence behaviours. Such insights may enhance the specificity and utility of behavioural models in this context.

Additionally, analysing differences across patient groups could provide further insights into variations in the perceived importance of adherence barriers and facilitators. Future studies should assess whether these perceptions differ among patients with other rheumatic conditions, those

using different classes of DMARDs (e.g., targeted synthetic DMARDs), individuals with varying disease durations and disease activity levels (e.g., relating to symptom severity and flare frequency), and across different healthcare systems, as disease activity has been shown to both influence and be influenced by medication adherence.

It is also important to note that the consultation data analysed in this thesis were limited to single recorded encounters per patient, representing isolated snapshots of clinical practice. As such, prior or subsequent discussions regarding medication use could not be captured. Longitudinal research involving repeated recordings and analysis of both verbal and non-verbal communication over time would provide a more comprehensive understanding of how adherence is addressed throughout the therapeutic relationship.

Moreover, this study focused primarily on current DMARD use. However, it is plausible that previous experiences with medication, as well as anticipatory concerns about future treatments, influence current adherence behaviours. Future investigations should incorporate these temporal aspects to more fully capture the dynamic nature of medication adherence.

Lastly, due to the qualitative nature of this research, it was not possible to establish direct associations between the barriers identified and actual non-adherent behaviour. Future studies employing mixed-methods or quantitative designs may help elucidate these relationships and explore how factors such as patient–provider rapport, health literacy, and prior adherence patterns influence treatment adherence over time.

How can my personal experiences and the findings of these studies shape the development of more empathic and effective care by providing authentic, patient-centred insights that bridge clinical practice with lived realities?

Acknowledge emotional complexity in adherence

My initial refusal of gold injections and undisclosed non-adherence to methotrexate reveal how emotional resistance, fear of dependency, and relational dynamics with HCPs can drive decisions. It reveals the emotional complexity behind adherence. This exposes limitations in purely clinical approaches and highlights the need for tailored communication (addressing fears, autonomy and trust), and patient

empowerment (strategies that normalize ambivalence rather than stigmatize non-disclosure).

Redesigning patient-HCP dynamics

My -occasional- tension with HCPs underscores how power imbalances and communication gaps fuel non-disclosure. This informs proactive barrier-screening tools (e.g. IMAB model) to systematically uncover unspoken concerns and shared decision-making frameworks that co-create treatment plans with patient priorities like autonomy and symptom relief leading to goal-setting, moving beyond clinical metrics.

Validating motivational drivers

My prioritization of autonomy and collaborative relationships (e.g., valuing "deciding with my physician") can directly shape research findings by implementing motivation-centred interventions (e.g. motivational interviewing) to target beliefs and emotions, not just education, and by implementing multidisciplinary support, involving nurses and pharmacists to address needs beyond prescriptions.

Advocating for systemic change

My journey exposes systemic flaws such as time-constrained consultations that skip adherence discussions and rigid protocols ignoring individual contexts. This fuels recommendations for structured communication training emphasizing empathy and flexible care models integrating telehealth/AI without sacrificing relational depth, such as implementing hybrid models to combine AI-driven adherence alerts (e.g. dose reminders) with scheduled video check-ins for empathic dialogue. At the same time, digital literacy support should be provided, for example by simplifying eHealth tools for older patients, to maintain their engagement.

Transforming research priorities

My lived experience, not only in the rheumatology landscape, but also in oncology, has shifted my research focus from clinical efficacy to patient-valued outcomes (e.g. autonomy over side-effect reduction) and from theoretical models to actionable tools (e.g. COM-B/TDF mapping for real-world barriers).

My journey in experience and evidence, can hopefully add transformation to care by:

- Grounding interventions in emotional context not just clinical data. Shift from capability-focused education (e.g., "how to take pills") to motivational interviewing (MI) that explores patients' values.
- Democratizing expertise by elevating the patient voice equally to HCP knowledge.
- Championing holistic care where motivation, communication and systemic support are inseparable from treatment success.

"The most profound insights into adherence come not only from observing patients, but from being one. Lived experience is the compass that reorients care from disease management to human healing."

REFERENCES

1. Bluett J, Morgan C, Thurston L, Plant D, Hyrich KL, Morgan AW, et al. Impact of inadequate adherence on response to subcutaneously administered anti-tumour necrosis factor drugs: results from the Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate cohort. Rheumatology. 2015;54(3):494–499.
2. Li L, Cui Y, Yin R, Chen S, Zhao Q, Chen H, Shen B. Medication adherence has an impact on disease activity in rheumatoid arthritis: a systematic review and meta-analysis. Patient Prefer Adherence. 2017;11:1343–1356. doi:10.2147/PPA.S140457
3. Harrold LR, Andrade SE. Medication Adherence of Patients with Selected Rheumatic Conditions: A Systematic Review of the Literature. Semin Arthritis Rheum. 2009;38(5):396–402. doi:10.1016/j.semarthrit.2008.01.011
4. Waimann CA, Marengo MF, De Achaval S, Cox VL, Garcia-Gonzalez A, Reveille JD, et al. Electronic monitoring of oral therapies in ethnically diverse and economically disadvantaged patients with rheumatoid arthritis: Consequences of low adherence. Arthritis Rheum. 2013;65(6):1421–1429. doi:10.1002/art.37917
5. Michie S, Van Stralen MM, West R. The behaviour change wheel: A new method for characterising and designing behaviour change interventions. Implement Sci. 2011;6(1). doi:10.1186/1748-5908-6-42
6. Palacio A, Garay D, Langer B, Taylor J, Wood BA, Tamariz L. Motivational Interviewing Improves Medication Adherence: a Systematic Review and Meta-analysis. J Gen Intern Med. 2016;31(8):929–940. doi:10.1007/s11606-016-3685-3
7. Beauvais C. Motivational interviewing to improve treatment adherence. Joint Bone Spine. 2019;86(5):535–537. doi:10.1016/j.jbspin.2019.02.005
8. Ng JYY, Ntoumanis N, Thøgersen-Ntoumani C, Deci EL, Ryan RM, Duda JL, Williams GC. Self-Determination Theory applied to health contexts: A Meta-Analysis. Perspect Psychol Sci. 2012;7(4):325–340. doi:10.1177/1745691612447309
9. Williams GC, Patrick H, Niemiec CP, Williams LK, Divine G, Lafata JE, et al. Reducing the health risks of diabetes. Diabetes Educ. 2009;35(3):484–492. doi:10.1177/0145721709333856
10. Voshaar MJH, Vriezekolk J, van Dulmen S, van den Bemt B, van de Laar M. Barriers and facilitators to disease-modifying antirheumatic drug use in patients with inflammatory rheumatic diseases: A qualitative theory-based study. BMC Musculoskelet Disord. 2016;17(1):442. doi:10.1186/s12891-016-1289-z
11. Chen Y, Gao J, Lu M. Medication adherence trajectory of patients with chronic diseases and its influencing factors: A systematic review. J Adv Nurs. 2023;80(1):11–41. doi:10.1111/jan.15776
12. Koutsogianni K. SP0164 Barriers and facilitators to adherence to medication in patients with inflammatory arthritis. Ann Rheum Dis. 2017;40.1–40. doi:10.1136/annrheumdis-2017-eular.7133
13. Van den Bemt BJ, Zwikker HE, Van den Ende CH. Medication adherence in patients with rheumatoid arthritis: a critical appraisal of the existing literature. Expert Rev Clin Immunol. 2012;8(4):337–351. doi:10.1586/eci.12.23

14. Wohlfahrt A, Campos A, Iversen MD, Gagne JJ, Massarotti E, Solomon DH, Feldman CH. Use of rheumatology-specific patient navigators to understand and reduce barriers to medication adherence: Analysis of qualitative findings. PLoS One. 2018;13(7):e0200886. doi:10.1371/journal.pone.0200886

15. Andersen KM, Kelly A, Lyddiatt A, Bingham CO, Bykerk VP, Batterman A, et al. Patient Perspectives on DMARD Safety Concerns in Rheumatology Trials: Results from Inflammatory Arthritis Patient Focus Groups and OMERACT Attendees Discussion. J Rheumatol. 2019;46(9):1168–1172. doi:10.3899/jrheum.181185

16. Zolnierek KBH, DiMatteo MR. Physician communication and patient adherence to treatment. Med Care. 2009;47(8):826–834. doi:10.1097/MLR.0b013e31819a5acc

17. Bensing JM, Dronkers J. Instrumental and affective aspects of physician behavior. Med Care. 1992;30(4):283–298. doi:10.1097/00005650-199204000-00001

18. Ong L, De Haes J, Hoos A, Lammes F. Doctor-patient communication: A review of the literature. Soc Sci Med. 1995;40(7):903–918. doi:10.1016/0277-9536(94)00155-M

19. McCabe R, Healey PG, Priebe S, Lavelle M, Dodwell D, Laugharne R, et al. Shared understanding in psychiatrist–patient communication: Association with treatment adherence in schizophrenia. Patient Educ Couns. 2013;93(1):73–79. doi:10.1016/j.pec.2013.05.015

20. Henselmans I, Heijmans M, Rademakers J, Van Dulmen S. Participation of chronic patients in medical consultations: patients' perceived efficacy, barriers and interest in support. Health Expect. 2015;18(6):2375–2388. doi:10.1111/hex.12206

21. Poon BY, Shortell SM, Rodriguez HP. Patient Activation as a Pathway to Shared Decision-making for Adults with Diabetes or Cardiovascular Disease. J Gen Intern Med. 2019;35(3):732–742. doi:10.1007/s11606-019-05351-6

22. Salt E, Frazier SK. Adherence to Disease-Modifying antirheumatic drugs in patients with rheumatoid arthritis. Orthop Nurs. 2010;29(4):260–275. doi:10.1097/NOR.0b013e3181e5c2c9

23. Zangi HA, Ndosi M, Adams J, Andersen L, Bode C, Boström C, et al. EULAR recommendations for patient education for people with inflammatory arthritis. Ann Rheum Dis. 2015;74(6):954–962. doi:10.1136/annrheumdis-2014-206807

24. Mathijssen EG, Vriezekolk JE, Eijsbouts AM, Van Den Hoogen FH, Van Den Bemt BJ. Support needs for medication use and the suitability of eHealth technologies to address these needs: a focus group study of older patients with rheumatoid arthritis. Patient Prefer Adherence. 2018;12:349–358. doi:10.2147/PPA.S152759

25. Peter ME, Zuckerman AD, DeClercq J, Choi L, James C, Cooper K, et al. Adherence and persistence in patients with rheumatoid arthritis at an integrated health system specialty pharmacy. J Manag Care Spec Pharm. 2021;27(7):882–890. doi:10.18553/jmcp.2021.27.7.882

26. Pouls BPH, Vriezekolk JE, Bekker CL, Linn AJ, Van Onzenoort HAW, Vervloet M, et al. Effect of Interactive eHealth Interventions on Improving Medication Adherence in Adults with Long-Term Medication: Systematic Review. J Med Internet Res. 2021;23(1):e18901. doi:10.2196/18901

27. Lahiri M, Cheung PPM, Dhanasekaran P, Wong S, Yap A, Tan DSH, et al. Evaluation of a multidisciplinary care model to improve quality of life in rheumatoid arthritis: a randomised controlled trial. Qual Life Res. 2022;31(6):1749–1759. doi:10.1007/s11136-021-03029-3

28. Bhattacharya D, Easthall C, Willoughby KA, Small M, Watson S. Capecitabine non-adherence: Exploration of magnitude, nature and contributing factors. J Oncol Pharm Pract. 2012;18(3):333–342. doi:10.1177/1078155211436022

29. Easthall C, Taylor N, Wright DJ, Bhattacharya D. Developing the 'Identification of Medication Adherence Barriers (IMAB) Instrument: A Novel Application of Behaviour Change Theoretical Frameworks. [Conference Paper]. UK Society of Behavioural Medicine (UKSBM) 8th Annual Scientific Meeting; 2012; Manchester, UK.

30. Elwyn G, Frosch DL, Kobrin S. Implementing shared decision-making: consider all the consequences. Implement Sci. 2016;11:114. doi:10.1186/s13012-016-0480-9

31. Kinnersley P, Edwards AGK, Hood K, Cadbury N, Ryan R, Prout H, et al. Interventions before consultations for helping patients address their information needs. Cochrane Database Syst Rev. 2007;(3):CD004565. doi:10.1002/14651858.CD004565.pub2

32. Yfantopoulos J, Protopapa M, Mantalias K, Chantzaras A, Koutsogianni K, Yfantopoulos P, Vassilopoulos D. Patients' and Doctors' Beliefs about Treatment and Long-Term Adherence in Rheumatic Diseases. Mediterr J Rheumatol. 2020;31(Suppl 1):152. doi:10.31138/mjr.31.1.152

33. Koonin LM, Hoots B, Tsang CA, Leroy Z, Farris K, Jolly BT, et al. Trends in the use of telehealth during the emergence of the COVID-19 pandemic — United States, January–March 2020. MMWR Morb Mortal Wkly Rep. 2020;69(43):1595–1599. doi:10.15585/mmwr.mm6943a3

34. Bashshur R, Doarn CR, Frenk JM, Kvedar JC, Woolliscroft JO. Telemedicine and the COVID-19 Pandemic, lessons for the future. Telemed J E Health. 2020;26(5):571–573. doi:10.1089/tmj.2020.29040.rb

35. Barlas N, Barlas SB, Basnyat S, Adalier E. Telemedicine in Rheumatoid Arthritis: A Review of the PubMed Literature. Mediterr J Rheumatol. 2023;34(1):16. doi:10.31138/mjr.34.1.16

36. Poitras M, Poirier M, Couturier Y, Vaillancourt VT, Cormier C, Gauthier G, et al. Chronic conditions patient's perception of post-COVID-19 pandemic teleconsulting continuation in primary care clinics: a qualitative descriptive study. BMJ Open. 2022;12(12):e066871. doi:10.1136/bmjopen-2022-066871

37. de Thurah A, Bosch P, Marques A, Meissner Y, Mukhtyar CB, Knitza J, et al. 2022 EULAR points to consider for remote care in rheumatic and musculoskeletal diseases. Ann Rheum Dis. 2022;81(8):1065–1071. doi:10.1136/annrheumdis-2022-222341

38. Sequí-Sabater JM, Benavent D. Artificial intelligence in rheumatology research: what is it good for? RMD Open. 2025;11(1):e004309. doi:10.1136/rmdopen-2024-004309

39. Venerito V, Gupta L, Mileto S, Iannone F, Bilgin E. Ethical challenges and regulatory pathways for artificial intelligence in rheumatology. Rheumatol Adv Pract. 2025;9(2):rkaf035. doi:10.1093/rap/rkaf035

40. Sivaraman V, Bukowski LA, Levin J, Kahn JM, Perer A. Ignore, trust, or negotiate: Understanding clinician acceptance of AI-based treatment recommendations in health care. Proc CHI Conf Hum Factors Comput Syst (CHI '23). 2023;Article 754.

41. Benavent D, Carmona L, Garcia Llorente JF, Montoro M, Ramirez S, Otón T, et al. Empowering rheumatology through digital health technologies: contributions and barriers. Explor Musculoskelet Dis. 2024;2:92–105. doi:10.37349/emd.2024.00038

42. Fitzpatrick PJ. Improving health literacy using the power of digital communications to achieve better health outcomes for patients and practitioners. Front Digit Health. 2023;5:1264780. doi:10.3389/fdgth.2023.1264780

43. Hadjileontiadis LJ, Charisis V, Hadjidimitriou S, Dias SB, Apostolidis G, Dimaridis G, et al. European advances in digital rheumatology: explainable insights and personalized digital health tools for psoriatic arthritis. EClinicalMedicine. 2025;84:103243. doi:10.1016/j.eclinm.2025.103243

44. Knudsen LR, Lomborg K, Hauge E-M, De Thurah A. Facilitators and challenges of implementing a digital patient education programme for rheumatoid arthritis into clinical practice. BMC Health Serv Res. 2024;24(1):1104. doi:10.1186/s12913-024-11597-6

45. Shaw SE, Seuren LM, Wherton J, Cameron D, A'Court C, Vijayaraghavan S, et al. Video consultations between patients and clinicians in diabetes, cancer, and heart failure services: Linguistic Ethnographic Study of Video-Mediated Interaction. J Med Internet Res. 2020;22(5):e18378. doi:10.2196/18378

46. Michie S, Johnston M, Abraham C, Lawton R, Parker D, Walker A. Making psychological theory useful for implementing evidence based practice: A consensus approach. BMJ Qual Saf. 2005;14(1):26–33. doi:10.1136/qshc.2004.011155

47. Treharne G, Lyons A, Kitas G. Medication adherence in rheumatoid arthritis: effects of psychosocial factors. Psychol Health Med. 2004;9(3):337–349. doi:10.1080/13548500410001721909

48. Chaleshgar-Kordasiabi M, Enjezab B, Akhlaghi M, Sabzmakan I. Barriers and reinforcing factors to self-management behaviour in rheumatoid arthritis patients: A qualitative study. Musculoskelet Care. 2018;16(2):241–250. doi:10.1002/msc.1221

49. Neame R, Hammond A. Beliefs about medications: a questionnaire survey of people with rheumatoid arthritis. Rheumatology. 2005;44(6):762–767. doi:10.1093/rheumatology/keh587

50. Park DC, Hertzog C, Leventhal H, Morrell RW, Leventhal E, Birchmore D, et al. Medication adherence in rheumatoid arthritis patients: Older is wiser. J Am Geriatr Soc. 1999;47(2):172–183. doi:10.1111/j.1532-5415.1999.tb04575.x

51. Viller F, Guillemin F, Briançon S, Moum T, Suurmeijer T, Van Den Heuvel W. Compliance to drug treatment of patients with rheumatoid arthritis: a 3-year longitudinal study. J Rheumatol. 1999;26(10):2114–2122.

52. Rosenstock IM. Why people use health services. Milbank Mem Fund Q. 1966;44(3 Pt 2):94–127. doi:10.2307/3348967

53. Fishbein M, Ajzen I. Belief, attitude, intention, and behavior: An Introduction to Theory and Research. Addison Wesley Publishing Company; 1975.

54. Ajzen I. The theory of planned behavior. Organ Behav Hum Decis Process. 1991;50(2):179–211. doi:10.1016/0749-5978(91)90020-T

55. Bandura A. Social foundations of thought and action: A Social Cognitive Theory. Prentice Hall; 1986.

56. Prochaska JO, DiClemente CC, Norcross JC. In search of how people change. Applications to addictive behaviors. Am Psychol. 1992;47(9):1102–1114. doi:10.1037/0003-066X.47.9.1102

57. Brown MT, Bussell JK. Medication adherence: WHO cares? Mayo Clin Proc. 2011;86(4):304–314. doi:10.4065/mcp.2010.0575

58. Laba T, Brien J, Jan S. Understanding rational non-adherence to medications. A discrete choice experiment in a community sample in Australia. BMC Fam Pract. 2012;13:61. doi:10.1186/1471-2296-13-61

59. Friesen-Storms JH, Bours GJ, Van Der Weijden T, Beurskens AJ. Shared decision making in chronic care in the context of evidence based practice in nursing. Int J Nurs Stud. 2014;52(1):393–402. doi:10.1016/j.ijnurstu.2014.06.012

60. Gossec L, Bessette L, Xavier RM, Favalli EG, Östör A, Buch MH. Barriers to, facilitators of, and interventions to support treat-to-target implementation in rheumatoid arthritis: A systematic review. Arthritis Care Res. 2024. doi:10.1002/acr.25408

Chapter 8

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ENGLISH SUMMARY

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Rheumatoid arthritis (RA) is a chronic condition for which long-term treatment with disease-modifying antirheumatic drugs (DMARDs) is essential to slow or even stop disease progression and preserve functioning. Although DMARDs are effective, their full clinical potential is often not realised in daily practice due to among others suboptimal medication adherence. To date, effective and sustainable interventions to structurally improve adherence in RA are lacking.

Traditional adherence research has primarily focused on demographic and disease-related factors, which have proven insufficient to distinguish patients at increased risk of non-adherence. Where HCPs are well educated and skilled to make the diagnosis and advice on (curative) treatment options, especially administration of medication is almost exclusively executed by the patient herself. This underscores that medication use in RA is a complex behavioural process, influenced by cognitive, emotional, social, and contextual factors.

Over the past decades, healthcare research and HCPs shifted towards acknowledgement of the importance of the interaction between patients and HCPs. Improving outcomes that matter to patients are the only reason to spend billions in healthcare. Healthcare is shifting towards patient-centred care (PCC), in which active patient involvement, shared decision-making, and self-management are central toward the best possible outcomes, that matter for her (him).

Nevertheless, knowledge remained limited and fragmented regarding which barriers and facilitators patients experience in relation to DMARD use, which of these factors are most relevant from the patient perspective, how healthcare professionals perceive these factors, and to what extent such barriers are actually discussed in routine clinical practice. These knowledge gaps hinder the development of targeted, patient-centred strategies to improve medication adherence.

The five studies included in this thesis were conducted to systematically address these gaps. By identifying barriers and facilitators from the patient perspective, exploring their relative importance, examining healthcare professionals' perspectives, and analysing communication during routine consultations, this thesis aims to provide a coherent

foundation for the development of more effective, patient-centred approaches to improving DMARD adherence in RA.

Chapter 2: Patient-Centred Care in Established Rheumatoid Arthritis

Patient-centred care (PCC) is highlighted in this review as a key approach to improving outcomes in established rheumatoid arthritis (RA). Medication adherence used as a key example illustrates how patients' experiences, preferences, and everyday realities shape care outcomes. This narrative review showed that recognising patients as individuals with unique needs and preferences positively affects treatment safety, effectiveness, and costs, while strengthening collaboration between patients and healthcare professionals (HCPs).

Because RA requires ongoing management beyond limited clinical encounters, active patient involvement is essential. Effective PCC extends beyond information provision and requires support for patients to develop the knowledge, confidence, and skills needed for shared decision-making and self-management. Educational resources and decision aids can facilitate engagement, particularly when complementing meaningful patient–HCP interactions.

The implementation of PCC is a gradual process that depends on high-quality communication, appropriate professional competencies, interdisciplinary collaboration, and adequate access to care. When these conditions are embedded in routine practice, PCC supports improved health outcomes and quality of life for people with established RA through shared responsibility between patients and HCPs.

Chapter 3: Barriers and Facilitators to DMARD Use in Inflammatory Rheumatic Diseases

In this study, barriers and facilitators to disease-modifying antirheumatic drug (DMARD) use in patients with inflammatory rheumatic diseases (IRDs) were explored. Despite the proven effectiveness of DMARDs, suboptimal adherence remains common, indicating a need to better understand patients' perspectives on medication use.

Using questionnaires (120 patients) and 2 focus group discussions (21 patients), patients' experiences with DMARDs were examined and analysed using the Theoretical Domains Framework (TDF), with findings mapped onto the COM-B model. This approach enabled systematic

identification of psychological, social, and contextual factors influencing adherence behaviour.

The results demonstrated substantial individual variation in barriers and facilitators, with factors spanning patients' capability, opportunity, and motivation. Motivational influences—such as beliefs about treatment necessity, concerns about side effects, and preferences for autonomy—were particularly prominent, alongside practical and communication-related challenges.

These findings highlight the limitations of uniform adherence interventions and support the need for personalised, theory-informed strategies that address patients' individual contexts and lived experiences.

Chapter 4: Ranking Facilitators and Barriers of Medication Adherence in Inflammatory Arthritis

In this study, patients with inflammatory arthritis prioritised facilitators and barriers to adherence to disease-modifying antirheumatic drugs (DMARDs). While many influencing factors have been identified in prior research, insight into their relative importance from the patient perspective has been limited.

Using a maximum difference scaling (MaxDiff) approach, 128 patients ranked 35 previously identified adherence-related factors. The analysis showed that perceived symptom relief was the most important facilitator of adherence, followed by maintaining independence and involvement in shared decision-making with healthcare professionals.

These priorities were consistent across patient subgroups and were not influenced by age, sex, or educational level. Together, the findings highlight a set of core values that underpin adherence behaviour across the inflammatory arthritis population.

The results emphasise the importance of adherence strategies that focus on tangible treatment benefits, support patients' autonomy, and promote shared decision-making. Addressing these patient-prioritised factors may enhance the effectiveness of adherence interventions and strengthen patient-HCP communication in routine clinical care.

Chapter 5: Healthcare Professionals' Perceptions of Barriers and Facilitators to DMARD Use in Rheumatoid Arthritis

In this study healthcare professionals' (HCPs) perspectives on barriers and facilitators influencing adherence to disease-modifying antirheumatic drugs (DMARDs) in patients with rheumatoid arthritis (RA) were explored. While adherence challenges are well documented from the patient perspective, less is known about how HCPs understand and interpret these influences.

In-depth interviews were conducted with rheumatologists, specialised nurses, and pharmacists. Participants described a broad range of factors affecting adherence, including treatment-related issues such as side effects, delayed treatment effects, and regimen complexity. However, the most prominent influences were patient-related, particularly beliefs about medication necessity and harm, coping strategies, and self-management skills.

HCPs also identified disease-related factors, healthcare system characteristics (including trust and continuity of care), and broader social and economic contexts as important determinants of adherence behaviour. Many of the identified factors were considered modifiable through improved communication and tailored support.

Overall, the findings underscore the central role of HCPs in addressing adherence through personalised, trust-based interactions that respond to patients' beliefs, capabilities, and circumstances, thereby supporting more effective long-term management of RA.

Chapter 6: Talking About Barriers to DMARD Use in Routine Rheumatology Care

In this study, it was investigated if and how barriers and facilitators to disease-modifying antirheumatic drug (DMARD) use were discussed during routine consultations between patients with rheumatoid arthritis (RA) and their rheumatologists. Although effective communication is known to support adherence, little is understood about how medication-related issues are addressed in everyday clinical practice.

Analysis of 134 audio-recorded consultations showed that patients raised medication-related barriers or facilitators in fewer than half of visits, and explicit discussion of adherence or non-adherence occurred in less than

a quarter of visits. When facilitators were mentioned, they were mainly practical in nature, such as treatment convenience and integration into daily routines. Barriers more often reflected concerns about side effects, effectiveness, and long-term use.

Rheumatologists typically responded using a combination of informational and empathic communication, addressing both practical questions and emotional concerns. However, many opportunities to proactively explore adherence were missed, with adherence mostly addressed through closed-ended questions by rheumatologists.

Overall, the findings highlight the need for more systematic and patient-centred communication about medication use. Proactively eliciting patients' experiences and concerns may help normalise discussions about adherence, strengthen the therapeutic relationship, and better support sustained DMARD use in routine care.

Chapter 7: General Discussion

Medication adherence to disease-modifying antirheumatic drugs (DMARDs) in patients with inflammatory arthritis from a patient-centred and behavioural perspective, was the focus of this thesis. Across five complementary studies, the research aimed to deepen the understanding of the barriers and facilitators that shape patients' medication use and to identify opportunities for improving medication adherence in clinical practice.

A central finding throughout the thesis was the pivotal role of **motivation** in DMARD adherence. When barriers and facilitators were mapped onto the COM-B framework, most patient-reported factors clustered within the motivation domain, encompassing both reflective processes (such as beliefs about medication necessity, perceived benefits, concerns about long-term use, and autonomy) and automatic processes (including emotional resistance and ambivalence). While traditional medication adherence interventions often focus on education or practical support, the findings of this thesis indicate that such approaches are unlikely to result in sustained adherence if patients' motivational needs are not adequately addressed. Importantly, many motivational barriers are modifiable through patient-centred communication strategies, shared decision-making, and behaviour change techniques such as motivational interviewing and autonomy-supportive care.

Effective **patient–healthcare professional (HCP) communication** emerged as a second key theme. Despite evidence linking communication quality to medication adherence, the observational study in Chapter 6 demonstrated that barriers to DMARD use are discussed in only a minority of routine rheumatology consultations. When barriers are addressed, discussions tend to focus on side effects, even though patients rank other factors, such as symptom relief, independence, and shared decision-making, as more important. These findings point to a persistent gap between what patients find meaningful and what is addressed in clinical encounters. The thesis highlights that responsibility for initiating adherence-related conversations primarily lies with HCPs, who must proactively create a safe, empathetic environment in which patients feel able to disclose concerns. At the same time, empowering patients to actively participate and voice barriers is essential. Multidisciplinary collaboration, involving nurses and pharmacists, as well as structured communication tools, may help bridge this gap.

Finally, the thesis underscores the value of **theoretical frameworks** in understanding and improving medication adherence. By applying the Theoretical Domains Framework (TDF) and linking it to the COM-B model, this research provided a comprehensive and structured approach to identifying behavioural determinants of DMARD use. These frameworks enabled differentiation between modifiable and less modifiable barriers and offer practical guidance for the development of theory-informed, personalised adherence interventions. Together, the findings support a shift away from one-size-fits-all approaches toward patient-centred, motivation-focused strategies that integrate behavioural theory, effective communication, and supportive healthcare systems to improve long-term adherence in inflammatory arthritis.

NEDERLANDSE SAMENVATTING

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Reumatoïde artritis (RA) is een chronische aandoening waarvoor langdurige behandeling met ziekte modificerende antireumatische geneesmiddelen (DMARD's) essentieel is om ziekteprogressie te vertragen of zelfs te stoppen en het functioneren te behouden. Hoewel DMARD's effectief zijn, wordt hun volledige klinische potentieel in de dagelijkse praktijk vaak niet gerealiseerd, onder andere door suboptimale therapietrouw. Tot op heden ontbreken effectieve en duurzame interventies om therapietrouw bij RA structureel te verbeteren.

Traditioneel therapietrouw onderzoek heeft zich voornamelijk gericht op demografische en ziekte gerelateerde factoren. Deze blijken echter onvoldoende onderscheidend om patiënten met een verhoogd risico op therapieontrouw tijdig te identificeren. Waar zorgprofessionals (healthcare professionals; HCP's) goed zijn opgeleid en toegerust om de diagnose te stellen en behandelopties te adviseren, wordt de daadwerkelijke toediening van medicatie in de praktijk vrijwel volledig door de patiënt zelf uitgevoerd. Dit onderstreept dat medicatiegebruik bij RA een complex gedragsmatig proces is, dat wordt beïnvloed door cognitieve, emotionele, sociale en contextuele factoren.

In de afgelopen decennia is binnen het gezondheidszorgonderzoek en onder zorgprofessionals een verschuiving zichtbaar naar erkenning van het belang van de interactie tussen patiënt en zorgverlener. Het verbeteren van uitkomsten die voor patiënten daadwerkelijk van betekenis zijn, vormt de kern van doelmatige zorg en rechtvaardigt de aanzienlijke investeringen in de gezondheidszorg. De zorg ontwikkelt zich daarom steeds meer richting patiëntgerichte zorg (patient-centred care, PCC), waarin actieve betrokkenheid van de patiënt, gezamenlijke besluitvorming (shared decision-making) en zelfmanagement centraal staan om optimale, voor de individuele patiënt relevante uitkomsten te bereiken.

Desondanks bleef de kennis beperkt en gefragmenteerd ten aanzien van de barrières en bevorderende factoren die patiënten ervaren bij het gebruik van DMARD's, welke van deze factoren vanuit patiëntperspectief het meest relevant zijn, hoe zorgprofessionals deze factoren percipiëren, en in welke mate dergelijke barrières daadwerkelijk worden besproken tijdens reguliere consulten. Deze kennishiaten belemmeren de

ontwikkeling van gerichte, patiëntgerichte strategieën ter verbetering van therapietrouw.

De vijf studies die in dit proefschrift zijn opgenomen, zijn uitgevoerd om deze kennislacunes systematisch te adresseren. Door barrières en bevorderende factoren vanuit patiëntperspectief te identificeren, hun relatieve belang te onderzoeken, de perspectieven van zorgprofessionals te verkennen en communicatie tijdens reguliere consulten te analyseren, beoogt dit proefschrift een samenhangende basis te bieden voor de ontwikkeling van effectievere, patiëntgerichte benaderingen ter bevordering van therapietrouw aan DMARD's bij RA.

Hoofdstuk 2: Patiëntgerichte zorg bij gevestigde reumatoïde artritis

Dit hoofdstuk beschrijft patiëntgerichte zorg als een essentieel uitgangspunt voor het verbeteren van behandeluitkomsten bij patiënten met gevestigde reumatoïde artritis (RA). Medicatietrouw wordt gebruikt als een belangrijk voorbeeld om te laten zien hoe ervaringen, voorkeuren en het dagelijks leven van patiënten de zorguitkomsten beïnvloeden.

Het narratief literatuuroverzicht laat zien dat erkenning van patiënten als individuen met unieke behoeften, zorgen en voorkeuren bijdraagt aan verbeterde veiligheid, effectiviteit en kosteneffectiviteit van de behandeling en aan een meer gelijkwaardige patiënt-zorgverlener relatie. Gezien het chronische karakter van reumatoïde artritis vereist patiëntgerichte zorg actieve patiëntbetrokkenheid en ondersteuning bij het ontwikkelen van kennis en vaardigheden voor gezamenlijke besluitvorming en zelfmanagement, waarbij ondersteunende middelen een aanvullende rol hebben naast persoonlijke interacties met zorgverleners.

Hoofdstuk 3: Barrières en bevorderende factoren bij DMARD-gebruik bij inflammatoire reumatische aandoeningen

In dit hoofdstuk worden barrières en bevorderende factoren onderzocht die het gebruik van DMARDs beïnvloeden bij patiënten met inflammatoire reumatische aandoeningen. Ondanks de bewezen effectiviteit van DMARDs blijft suboptimale therapietrouw een veelvoorkomend probleem, wat wijst op de noodzaak om het perspectief van patiënten beter te begrijpen.

Aan de hand van vragenlijsten (ingevuld door 120 patiënten) en 2 focusgroep interviews (in totaal 21 patiënten) werd inzicht verkregen in zowel praktische als emotionele aspecten van DMARD-gebruik.

De resultaten laten zien dat therapietrouw wordt bepaald door een complexe en sterk geïndividualiseerde samenhang van factoren, verspreid over de domeinen capaciteit, gelegenheid en motivatie. Met name motivationele factoren, zoals overtuigingen over de noodzaak van medicatie, zorgen over bijwerkingen en de wens om autonomie te behouden, bleken van groot belang, naast praktische en communicatieve belemmeringen.

Hoofdstuk 4: Het rangschikken van bevorderende factoren en barrières voor therapietrouw bij inflammatoire artritis

Dit hoofdstuk richt zich op de vraag welke barrières en bevorderende factoren voor DMARD-therapietrouw door patiënten met inflammatoire artritis als het meest belangrijk worden beschouwd. Hoewel eerdere studies beïnvloedende factoren hebben geïdentificeerd, bestond er beperkt inzicht in hun relatieve belang vanuit het perspectief van de patiënt.

Met behulp van een *maximum difference scaling* (MaxDiff)-methode rangschikten 128 patiënten met inflammatoire artritis 35 vooraf geïdentificeerde factoren. De resultaten toonden aan dat ervaren symptoomverlichting de belangrijkste bevorderende factor voor therapietrouw was, gevolgd door het behoud van zelfstandigheid en betrokkenheid bij gezamenlijke besluitvorming met zorgverleners. Deze prioriteiten bleken consistent over verschillende subgroepen van patiënten en waren niet afhankelijk van leeftijd, geslacht of opleidingsniveau.

Hoofdstuk 5: Percepties van zorgverleners over barrières en bevorderende factoren bij DMARD-gebruik bij reumatoïde artritis

In dit hoofdstuk wordt onderzocht hoe zorgverleners barrières en bevorderende factoren voor DMARD-therapietrouw bij patiënten met RA waarnemen en interpreteren. Hoewel therapietrouw op verschillende manieren is onderzocht vanuit het perspectief van de patiënt, is minder bekend over de opvattingen van zorgverleners.

Op basis van diepte-interviews met reumatologen, gespecialiseerde verpleegkundigen en apothekers (in totaal 15 zorgprofessionals) werd een breed scala aan beïnvloedende factoren voor medicatie-

therapietrouw geïdentificeerd. Naast behandel-gerelateerde aspecten, zoals bijwerkingen, vertraagde werking en complexiteit van het medicatieregime, legden zorgverleners vooral de nadruk op patiënt-gerelateerde factoren. Hierbij werden overtuigingen over medicatie, coping-strategieën en zelfmanagementvaardigheden als cruciaal beschouwd.

Daarnaast werden ziektekenmerken, kenmerken van het zorgsysteem (zoals vertrouwen en continuïteit van zorg) en sociaaleconomische omstandigheden genoemd als belangrijke factoren van therapietrouw. Veel van deze factoren werden als beïnvloedbaar gezien, met name door verbeterde communicatie en gepersonaliseerde ondersteuning.

Hoofdstuk 6: Het bespreken van barrières voor DMARD-gebruik in de dagelijkse reumatologische zorg

In dit hoofdstuk wordt onderzocht of, en op welke wijze, barrières en bevorderende factoren voor DMARD-gebruik aan bod komen tijdens routinematige consulten tussen patiënten met RA en hun reumatologen. Hoewel effectieve communicatie essentieel is voor therapietrouw, bestaat er beperkt inzicht in hoe vaak en op welke manier medicatie-gerelateerde onderwerpen in de dagelijkse klinische praktijk worden besproken.

Analyse van 134 audio-geregistreerde consulten liet zien dat patiënten in minder dan de helft van de gesprekken medicatie-gerelateerde barrières of bevorderende factoren benoemden. Therapietrouw of therapieontrouw werd in minder dan een kwart van de consulten expliciet besproken, meestal op initiatief van de reumatoloog met gesloten vragen. Bevorderende factoren waren meestal praktisch van aard, terwijl barrières vaker betrekking hadden op zorgen over bijwerkingen, effectiviteit en langdurig gebruik.

Reumatologen reageerden doorgaans met een combinatie van informatieve en empathische communicatiestrategieën. Desondanks bleven veel kansen onbenut om therapietrouw proactief te verkennen. De bevindingen benadrukken de noodzaak van meer systematische en patiëntgerichte communicatie over medicatiegebruik, waarbij zorgverleners actief ruimte creëren voor het bespreken van ervaringen, zorgen en twijfels van patiënten.

Hoofdstuk 7: Algemene discussie

Dit proefschrift onderzoekt therapietrouw aan DMARDs bij inflammatoire artritis vanuit zowel patiënt- als zorgverlenersperspectief, met als doel inzicht te verkrijgen in de onderliggende factoren van medicatiegebruik. Aan de hand van vijf complementaire studies worden barrières en bevorderende factoren geïntegreerd om richting te geven aan verbetering van therapietrouw in de klinische praktijk.

De bevindingen positioneren Motivatie als een kernmechanisme van therapietrouw. Door toepassing van het COM-B-model blijkt dat de meeste factoren van DMARD-gebruik zich bevinden binnen het motivationele domein, waaronder zowel reflectieve processen (zoals overtuigingen, afwegingen en autonomie) als automatische processen (zoals emoties en ambivalentie). Hiermee laat dit proefschrift zien dat benaderingen die primair focussen op kennisoverdracht of praktische ondersteuning tekortschieten wanneer motivationele processen niet expliciet worden geadresseerd.

Communicatie fungeert daarbij als een cruciale schakel tussen motivationele factoren en klinische besluitvorming. Hoewel de kwaliteit van de communicatie samenhangt met therapietrouw, worden relevante barrières in de praktijk beperkt besproken en sluit de focus van consulten onvoldoende aan bij wat patiënten als betekenisvol ervaren. Deze discrepantie onderstreept de noodzaak van proactieve, empathische en patiëntgerichte communicatie, waarin zorgverleners verantwoordelijkheid nemen voor het expliciteren van therapietrouw en patiënten worden ondersteund in actieve participatie.

Tot slot toont dit proefschrift de meerwaarde van theoretisch onderbouwde benaderingen voor het begrijpen en verbeteren van therapietrouw. De integratie van het Theoretical Domains Framework met het COM-B-model maakt het mogelijk om de beïnvloedbare factoren systematisch te identificeren en te vertalen naar gepersonaliseerde interventies. Gezamenlijk ondersteunen de bevindingen een verschuiving van uniforme therapietrouw-interventies naar motivatie-gedreven, patiëntgerichte strategieën die gedragswetenschap, communicatie en zorgsystemen samenbrengen.

DANKWOORD

DANKWOORD

En dan is het 2026: het einde van een lang promotietraject.

En wat heb ik ervan genoten! Ik ben trots op het resultaat, maar misschien heb ik nog wel het meest genoten van de weg ernaartoe. Het was een leerschool op ieder vlak en, juist in medisch moeilijke tijden, een belangrijke rode draad die mij hielp om door te gaan. Daarom wil ik allereerst iedereen oprecht bedanken die dat heeft begrepen en die mij niet voortdurend heeft gevraagd wanneer het einde nu eindelijk eens in zicht kwam of hoe lang het heeft mogen duren😉!

Mijn belangstelling voor de wetenschap is mij niet met de paplepel ingegoten. Sterker nog: van nature ben ik misschien eerder een spiritueel en intuïtief mens. Maar toen ik op mijn twintigste de diagnose reumatoïde artritis kreeg, groeide er een diep verlangen om deze aandoening beter te begrijpen, en haar misschien zelfs te verslaan, met zoveel mogelijk kennis.

Internet stond in die tijd nog in de kinderschoenen. Ik verzamelde daarom stapels folders en brochures, alsof ik mijn eigen bibliotheek aan het opbouwen was. Ook de behandelmogelijkheden waren toen nog beperkt. Mijn agressieve vorm van artritis leidde er al vrij snel toe dat verschillende gewrichten moesten worden vervangen. Ik heb dit altijd proberen te zien als een leerproces: leren omgaan met tegenslag en met het besef dat je nu eenmaal niet alles in de hand hebt. Mijn grootste uitdaging daarbij was — en is nog steeds — dat mijn ambitie vaak groter is dan wat mijn lichaam aankan. Meestal wint die ambitie gelukkig, al kost dat soms bloed, zweet en tranen en vooral (te 😊) veel tijd.

Twee beslissende gesprekken hebben mij uiteindelijk in de richting van de wetenschap geleid.

Het eerste was met **prof. Hans Rasker**. Toen ik in de dertig was, introduceerde hij mij bij OMERACT, een tweejaarlijkse internationale bijeenkomst waar sinds 2002 ook patiënten hun perspectief inbrengen in wetenschappelijk reumaonderzoek. Vanaf dat moment raakte ik bij tal van wetenschappelijke projecten betrokken en werd mijn liefde voor onderzoek geboren. Hans, dank voor de kans die je mij hebt gegeven. En bovendien: je was ook nog eens een van de fijnste reumatologen die ik in mijn patiënten carrière heb mogen hebben!

Het tweede gesprek vond plaats in de achtertuin van mijn ouders, met **prof. Anne van der Meijden** (†), een goede vriend van hen. Hij zei: 'Als je lichaam wat minder kan, stop dan je energie in je geest. Ondanks fysieke beperkingen kun je altijd een beroep doen op je hersenen.' Tijdens datzelfde gesprek kwam een mogelijk promotietraject ter sprake. Het zaadje was geplant. Ik ben hem nog altijd dankbaar voor die inspirerende woorden.

En toen was daar mijn promotieteam: mijn **dreamteam.**



Bart, jij bent niet alleen een van de meest vooraanstaande hoogleraren op het gebied van therapietrouw, maar ook een soort menselijke marathon: altijd in beweging, altijd bezig en schijnbaar onvermoeibaar. Ik geef eerlijk toe dat ik in het begin dacht: hoe moet ik dit tempo ooit bijhouden? Maar je hebt mij vooral laten zien hoe inspirerend het is om duizend dingen tegelijk te doen — én dat het blijkbaar mogelijk is om daarnaast ook nog marathons te lopen. Respect.

Mart, jouw feilloze wetenschappelijke blik en opbouwend-kritische begeleiding hebben mij iedere keer weer een stap verder gebracht. Soms

dacht ik dat ik een eindversie had ingeleverd, totdat jij liet zien dat er nóg een betere versie in zat. En je had altijd gelijk. Door jou heb ik geleerd dat perfectioneren niet hetzelfde is als vasthouden, maar juist vraagt om steeds opnieuw te durven kijken en uiteindelijk ook te durven loslaten. Dank daarvoor.

Sandra, jij was mijn rots in de branding, met een heerlijke combinatie van humor, rust en wijsheid. Je was er niet alleen met scherpe feedback, maar ook met lieve appjes en een luisterend oor op momenten waarop ik het even niet meer zag zitten. Jij hebt mij laten zien dat tegenslagen je sterker kunnen maken. En eerlijk is eerlijk: ooit wil ik jouw baan. Mag ik alvast solliciteren?

Joke, jij was de onmisbare schakel die altijd bereikbaar was, zelfs tussen alle overvolle agenda's door. Jouw feedback kwam sneller terug dan sommige pakketjes van Bol.com — en was minstens zo waardevol. Met jouw stofkam wist je álles te vinden wat nog beter kon. En onze telefoongesprekken waren vaak precies het extra zetje dat ik nodig had om weer verder te gaan.

Samen vormden jullie een geweldig team. Ik prijs mij bijzonder gelukkig dat ik dit traject met jullie heb mogen afleggen. Jullie vulden elkaar perfect aan en hebben mij ieder op jullie eigen manier de tijd, ruimte en energie gegeven om te groeien. Ik ga jullie missen, maar hoop van harte dat dit geen afscheid is en dat onze paden elkaar nog vaak zullen kruisen.

Veel dank ook aan de leden van mijn manuscriptcommissie en aan mijn opponenten.

Prof. dr. Speckens en **Prof. dr. ir. Van Dijk**, heel veel dank voor jullie bereidheid mijn manuscript te lezen en te beoordelen. Wat was ik blij — en opgelucht — met jullie goedkeuring. Dank voor jullie tijd en aandacht.

Prof. dr. Hazes, lieve Mieke, jij bent bijzonder voor mij. Ik ben niet alleen dankbaar dat je mijn manuscript hebt willen beoordelen en tijdens de verdediging wilt opponeren, maar ook voor je jarenlange, fijne begeleiding als mijn reumatoloog. Bovenal koester ik onze vriendschap. Ik vroeg je expliciet of je onbevooroordeeld naar mijn manuscript kon en wilde kijken. Daarvan heb je me overtuigd: jij was de enige die toch nog een constructief-kritische opmerking wist te vinden — die ik uiteraard in de eindversie heb verwerkt 😉. Dank je wel!

Prof. dr. Das, beste Enny, ontzettend leuk dat ik je naam wederom tegenkwam op mijn lijst voor de promotiecommissie! Ik heb je mogen ontmoeten toen ik van 2010-2012 aan de VU in Amsterdam heb gestudeerd. Je hebt daar toen colleges gegeven, mijn scripties beoordeeld en de statistiek enigszins bijgebracht 😉! Nu ontmoeten we elkaar weer, dit keer in Nijmegen waar je als hoogleraar bent terechtgekomen. Een waar voorrecht en hartelijk dank voor je moeite om te willen opponeren.

Prof. dr. Gossec, chère Laure, tu occupes une place toute particulière dans mon cœur. Je t'ai rencontrée il y a des années et le courant est immédiatement passé entre nous. Ta personnalité joyeuse et l'attention que tu portes à chacun, quels que soient son titre ou son rôle, sont pour moi rafraîchissantes dans ce monde médical où, à mon grand étonnement, la hiérarchie joue encore un rôle important. Merci d'avoir accepté de venir aux Pays-Bas pour participer à ma soutenance. Je t'embrasse fort !

Dr. Pascal de Jong, lieve Pascal, wat begon als een grapje tijdens een van onze consulten, is werkelijkheid geworden. Ik zei: 'Ik ben bezig met een promotietraject', waarop jij antwoordde: 'O, dan wil ik wel opponeren.' En nu staan we hier, allebei in een andere rol. Dank je wel voor deze unieke en vooral ontzettend leuke rolwisseling — die ik stiekem misschien nog wel fijner vind dan die van arts en patiënt. Dat neemt niet weg dat ik je medische adviezen zeer ter harte neem, nadat we eerst de richtlijnen, de nieuwste medicatie, de kosten en politiek rond de zorg, internationale ontwikkelingen, congressen, lezingen en vooral onze collega-onderzoekers uitvoerig hebben besproken 😉.

Lieve **Maarten**, jij bent een voorbeeld als voorvechter van patiënten participatie in onderzoek. Mijn hart ligt misschien nog iets sterker bij het bouwen van bruggen tussen zorgprofessionals en patiënten, en juist daarin sluiten onze idealen prachtig op elkaar aan. Samen richtten we Tools2use op, een non-profitstichting die patiënten met uiteenlopende achtergronden en aandoeningen opleidde tot patient research partners: patiënten die op verschillende niveaus meewerken aan wetenschappelijk onderzoek. Ik heb enorm genoten van de talloze OMERACT- en EULAR-congressen die we samen bezochten — waarbij de nodige portjes, biertjes en gezellige collega's daar zeker aan hebben bijgedragen. Dank dat je nu ook als opponent bij mijn verdediging wilt zijn.

En dan: het boekje

Lieve **Suus**, dank je wel voor alle prachtige illustraties die je voor mijn presentaties hebt gemaakt en waarmee je ook dit boekje hebt opgefleurd. Telkens wanneer de inhoud wat taai dreigde te worden, wist jij die met jouw originele tekeningen weer lucht en kleur te geven. Dankzij jou is het bijna een feestje om over therapietrouw te praten. Heel veel dank!

Lieve **Joyce**, jij bracht zo vaak rust wanneer ik weer eens wanhopig probeerde een tabel netjes op een pagina te krijgen, of wanneer de literatuurlijst besloot een geheel eigen leven te gaan leiden. Met jouw hulp heb je mijn digitale onwetendheid uitstekend weten te maskeren. Dank je wel!

Mijn paranimfen

Mijn lieve paranimfen, **Esmeralda** en **Madelon**.

Lieve **Es(meralda)**, we leerden elkaar kennen in de afmeldgroep van een beruchte Groningse studentenvereniging. Mijn reuma speelde tijdens die ontgroening enorm op, iets wat ik met steeds meer moeite probeerde te verbergen. Hoe vaak jij mij hebt gered van extra taken en negatieve aandacht, is nauwelijks te tellen. Onze vriendschap is door de jaren heen alleen maar hechter geworden, zeker sinds we allebei in Amsterdam wonen. We hebben lief en leed gedeeld. Jouw enthousiasme en oprechte belangstelling voor dit traject hebben mij steeds weer gemotiveerd. Dank je wel, met heel veel liefs.

Lieve **Madelon**, onze vriendschap begon al op de middelbare school en sindsdien zijn we elkaar nooit uit het oog verloren. We hebben zo veel samen beleefd, gedeeld en doorstaan: tijden vol gezelligheid en plezier, maar ook met verlies en verdriet. Tijdens mijn operaties, spannende uitslagen en revalidatie was je altijd aan mijn zijde. Nu, in moeilijke tijden voor jou, ben ik er voor je. Het is nog niet zeker bij de druk van dit boekje of je er daadwerkelijk bij kunt zijn, maar je bent mijn lieve paranimf en je komt nooit meer van me af 💞.

Helaas mocht ik maar twee paranimfen kiezen. Maar in het rijtje van vriendschap en liefde horen nog zo veel meer namen: mijn onofficiële paranimfen in het leven. **Mijn zusjes Brigit en Carine, mijn zwagers en hun kinderen, Gijs en Patrice, Marret en Bastiaan, Idel en HP, oom**

Hans en tante Lies, Manon en Herman, mijn jaarclub, mijn wijnclub en iedereen die niet bij naam genoemd is, maar zo intens heeft meegeleefd: jullie zijn de slingers in mijn leven. Wat heerlijk dat jullie deze mijlpaal met mij vieren.

Ook wil ik alle patiënten, reumaverpleegkundigen, apothekers en reumatologen bedanken die aan mijn studies hebben meegewerkt. Dank voor jullie tijd, aandacht, inspanningen en waardevolle inzichten. Ook een woord van dank aan **Roche** en **Pfizer** die enkele studies gefinancierd hebben. Dank voor de prettige contacten, de vrijheid, de onafhankelijkheid en het vertrouwen. Een speciaal woord van dank aan de gezellige dames van het secretariaat Farmacie van de Sint Maartenskliniek: **Sonja, Lisette** en **Jeannette**. Dank voor het inplannen van de talloze vergaderingen — en vooral voor het telkens weer verzetten ervan vanwege al die volle agenda's — en voor de vele uitrijkaartjes 😊. Maar bovenal dank voor de gezellige gesprekjes rondom de overleggen.

Last, but certainly not least

Lieve **mam**, wat ben ik blij en dankbaar dat je hierbij kunt zijn. Je schittert en straalt, zoals altijd. Jouw kracht ligt in je liefde voor anderen en in je vermogen je steeds weer op het positieve te richten. Je bent mijn voorbeeld.

Liefste **pap** (†), jij bent voor een heel groot deel de reden dat deze promotie er is gekomen. Nog voordat ik aan mijn studie begon, kreeg ik reuma. Ik zag hoe je zocht naar een goede oplossing voor mijn toekomst, die er destijds niet rooskleurig uitzag. Je zei: 'Mariek, we zitten allemaal in een roeibootje, alleen jouw spanen zijn korter… Wat ga je doen?' Ik antwoordde: 'Knetterhard roeien.' Dat is wat ik doe. Het heeft mij gevormd tot wie ik ben. I love you.

Lieve **Tim**, je hebt je ongetwijfeld regelmatig vertwijfeld afgevraagd waar ik in hemelsnaam mee bezig was. Dit traject gaf mij een prachtige rode draad, vooral tijdens medisch zware periodes, maar heeft ook voor heel veel stress gezorgd. Jij bent altijd mijn rots in de branding geweest, met eindeloos geduld en liefde. Jouw liefde en respect betekenen alles voor mij. Ditto ❤️.

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ABOUT THE AUTHOR

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Marieke Voshaar was born in Nijverdal, the Netherlands, on 28 January 1968. Her professional journey began in management and communication. After studying Management and International Management, she completed an MSc in Corporate Communication and New Media at Vrije Universiteit Amsterdam. Over time, her interests increasingly shifted towards healthcare, particularly the partnership between patients, researchers and healthcare professionals.

For more than two decades, Marieke has worked to strengthen the patient voice in rheumatology research. Since 2004, she has been closely involved with OMERACT (Outcome Measures in Rheumatology), an international initiative aimed at improving outcome measurement in rheumatology, where she has contributed to numerous working groups. These have addressed topics including remission, flares, joint replacement, shared decision-making, medication adherence, work participation, patient preferences and safety. She also co-founded Tools2use.org, a non-profit organisation dedicated to promoting meaningful patient participation in scientific research.

Marieke has contributed to major national and international research initiatives, including GLORIA (Glucocorticoid low dose in Rheumatoid Arthritis), Treat to Target and RAID (Rheumatoid Arthritis Impact of Disease), and participated in the development of several clinical guidelines for rheumatoid arthritis. She has served on scientific advisory and funding committees for the Dutch Arthritis Foundation and ZonMw, and has lectured and spoken at national and international conferences, including EULAR (European Alliance of Associations for Rheumatology) and PARE (People with Arthritis/Rheumatism across Europe).

She has co-authored more than 100 international scientific publications on patient participation, medication adherence and rheumatology, and wrote the chapter on self-management in the *Oxford Textbook of Rheumatoid Arthritis*. Throughout her work, she has sought to connect

scientific knowledge with patients' lived experiences and to ensure that research addresses the outcomes that genuinely matter to them.

Her PhD research, conducted at the University of Twente and Radboud University Medical Center, explores medication adherence in rheumatoid arthritis. In particular, it examines the barriers and facilitators that influence whether patients take disease-modifying antirheumatic drugs as prescribed. The path towards completing her PhD took longer than anticipated and was interrupted by shoulder surgeries and treatment for breast cancer. These experiences further deepened her understanding of healthcare from the patient's perspective and reinforced her commitment to patient-centred research.

From 2022 to 2026, Marieke worked as a researcher at Nivel on SAFEST, a European project focused on improving patient safety throughout the perioperative journey. In 2026, she joined the board of Stichting 10p5, which works to improve the care, quality of life and life expectancy of people living with rare cancers.

Across the many different roles she has held, as a researcher, author, lecturer, adviser and patient advocate, one guiding principle has remained constant: bringing together patients' lived experience and professional expertise to help make healthcare and research more relevant, humane and effective.

LIST OF PUBLICATIONS

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Included in this thesis:

1. Voshaar, M., Nota, I., Van De Laar, M. a. F. J., & Van Den Bemt, B. J. F. (2015). Patient-centred care in established rheumatoid arthritis. *Best Practice & Research Clinical Rheumatology*, *29*(4–5), 643–663. https://doi.org/10.1016/j.berh.2015.09.007
2. Voshaar, M., Vriezekolk, J. E., Van Dulmen, S., Van Den Bemt, B., & Van De Laar, M. (2016). Barriers and facilitators to disease-modifying antirheumatic drug use in patients with inflammatory rheumatic diseases: a qualitative theory-based study. *BMC Musculoskeletal Disorders*, *17*(1). https://doi.org/10.1186/s12891-016-1289-z
3. Voshaar, M., Vriezekolk, J. E., Van Dulmen, A., Van Den Bemt, B. J. F., & Van De Laar, M. a. F. J. (2021). Ranking facilitators and barriers of medication adherence by patients with inflammatory arthritis: a maximum difference scaling exercise. *BMC Musculoskeletal Disorders*, *22*(1). https://doi.org/10.1186/s12891-020-03874-2
4. Voshaar, M., Van Den Bemt, B. J. F., Van De Laar, M., Van Dulmen, A., & Vriezekolk, J. E. (2022). Healthcare professionals' perceptions on barriers and facilitators to DMARD use in rheumatoid arthritis. *BMC Health Services Research*, *22*(1). https://doi.org/10.1186/s12913-021-07459-0
5. Voshaar, M., Van Den Bemt, B., Van De Laar, M., Van Dulmen, S., & Vriezekolk, J. (2025). Talking About Barriers to Disease-Modifying Anti-Rheumatic Drugs: Content Analysis of Audio-Recorded Routine Clinical Visits of Patients with Rheumatoid Arthritis. *Patient Preference and Adherence*, *Volume 19*, 777–790. https://doi.org/10.2147/ppa.s503083

Other publications:

6. Van Tuyl, L. H. D., & Voshaar, M. (n.d.). Patientenparticipatie in wetenschappelijk onderzoek. In *nvt*. https://www.researchgate.net/publication/254770008_Patientenparticipatie_in_wetenschappelijk_onderzoek
7. Gossec, L., Dougados, M., Rincheval, N., Bălănescu, A., Boumpas, D. T., Canadelo, S., Carmona, L., Jp, D., De Wit, M., Dijkmans, B. a. C., Englbrecht, M., Günendi, Z., Heiberg, T., Kirwan, J. R., Mola, E. M., Matucci-Cerinic, M., Otsa, K., Schett, G., Sokka, T., . . . Kvien, T. K. (2008). Elaboration of the preliminary Rheumatoid Arthritis Impact of Disease (RAID) score: a EULAR initiative. *Annals of the Rheumatic Diseases*, *68*(11), 1680–1685. https://doi.org/10.1136/ard.2008.100271

8. Gaujoux-Viala, C., Smolen, J. S., Landewé, R., Dougados, M., Kvien, T. K., Mola, E. M., Scholte-Voshaar, M., Van Riel, P., & Gossec, L. (2010). Current evidence for the management of rheumatoid arthritis with synthetic disease-modifying antirheumatic drugs: a systematic literature review informing the EULAR recommendations for the management of rheumatoid arthritis. *Annals of the Rheumatic Diseases*, *69*(6), 1004–1009. https://doi.org/10.1136/ard.2009.127225
9. De Wit, M., Berlo, S. E., Aanerud, G. J., Aletaha, D., Bijlsma, J. W. J., Croucher, L., Da Silva, J. a. P., Glüsing, B., Gossec, L., Hewlett, S., Jongkees, M., Magnusson, D., Scholte-Voshaar, M., Richards, P., Ziegler, C., & Abma, T. (2011). European League Against Rheumatism recommendations for the inclusion of patient representatives in scientific projects. *Annals of the Rheumatic Diseases*, *70*(5), 722–726. https://doi.org/10.1136/ard.2010.135129
10. Gossec, L., Paternotte, S., Aanerud, G. J., Bălănescu, A., Boumpas, D. T., Carmona, L., De Wit, M., Dijkmans, B. a. C., Dougados, M., Englbrecht, M., Göğüş, F., Heiberg, T., Hernandez, C., Kirwan, J. R., Mola, E. M., Cerinic, M. M., Otsa, K., Schett, G., Scholte-Voshaar, M., . . . Kvien, T. K. (2011). Finalisation and validation of the rheumatoid arthritis impact of disease score, a patient-derived composite measure of impact of rheumatoid arthritis: a EULAR initiative. *Annals of the Rheumatic Diseases*, *70*(6), 935–942. https://doi.org/10.1136/ard.2010.142901
11. Van Tuyl, L. H. D., & Voshaar, M. (2011a). Participation of patients in medical research. *Nederlands Tijdschrift Voor Geneeskunde*, *155*(30–31), A3501. https://www.researchgate.net/publication/51801239_Participation_of_patients_in_medical_research
12. Van Tuyl, L. H. D., & Voshaar, M. (2011b). Patient participation in scientific research. *Nederlands Tijdschrift Voor Geneeskunde*, *155*(30), 1392–1394. https://www.researchgate.net/publication/282177590_Patient_participation_in_scientific_research
13. Van Tuyl, L. H. D., Smolen, J. S., Wells, G. A., Scholte-Voshaar, M., Hoogland, W., & Boers, M. (2011). Patient Perspective on remission in rheumatoid arthritis. *The Journal of Rheumatology*, *38*(8), 1735–1738. https://doi.org/10.3899/jrheum.110394

14. Van Eijk-Hustings, Y., Van Tubergen, A., Boström, C., Braychenko, E., Buß, B., Félix, J., Firth, J., Hammond, A., Harston, B., Hernandez, C., Huzjak, M., Korandová, J., Kukkurainen, M. L., Landewé, R., Mézières, M., Milincovic, M., Moretti, A., Oliver, S., Primdahl, J., . . . Hill, J. (2011). EULAR recommendations for the role of the nurse in the management of chronic inflammatory arthritis. *Annals of the Rheumatic Diseases*, *71*(1), 13–19. https://doi.org/10.1136/annrheumdis-2011-200185
15. Englbrecht, M., Gossec, L., DeLongis, A., Scholte-Voshaar, M., Sokka, T., Kvien, T. K., & Schett, G. (2012). The Impact of Coping Strategies on Mental and Physical Well-Being in Patients with Rheumatoid Arthritis. *Seminars in Arthritis and Rheumatism*, *41*(4), 545–555. https://doi.org/10.1016/j.semarthrit.2011.07.009
16. Smolen, J. S., Schoels, M., Nishimoto, N., Breedveld, F. C., Burmester, G. R., Dougados, M., Emery, P., Ferraccioli, G., Gabay, C., Gibofsky, A., Gómez-Reino, J. J., Jones, G., Kvien, T. K., Murakami, M., Betteridge, N., Bingham, C. O., Bykerk, V. P., Choy, E., Combe, B., . . . Van Der Heijde, D. (2012). Consensus statement on blocking the effects of interleukin-6 and in particular by interleukin-6 receptor inhibition in rheumatoid arthritis and other inflammatory conditions. *Annals of the Rheumatic Diseases*, *72*(4), 482–492. https://doi.org/10.1136/annrheumdis-2012-202469
17. Rutten, C., Van Eijk Hustings, Y. J., Stadermann, E., Voshaar, M. J. S., Hazes, M., & Boonen, A. (2013). THU0569 Supporting patients in Optimal participation at work in the Rheumatology Clinic: rheumatologists' and rheumatology nurses' opinion. *Annals of the Rheumatic Diseases*, *72*(Suppl 3), A356.3-A357. https://doi.org/10.1136/annrheumdis-2013-eular.1097
18. Van Tuyl, L. H. D., Stamm, T., Boers, M., Davis, B., Flurey, C., Hoogland, W., Kirwan, J. R., Sanderson, T., Sadloňová, M., Van Shaardenburg, A., Scholte-Voshaar, M., Smolen, J., & Hewlett, S. (2013). FRI0553 "back to being normal": the patient perspective on remission in rheumatoid arthritis. *Annals of the Rheumatic Diseases*, *72*(Suppl 3), A562.2-A562. https://doi.org/10.1136/annrheumdis-2013-eular.1680

19. Van Eijk, Y., Logtenberg-Rutten, W., Stadermann, E., Voshaar, M., Hazes, J. M., & Boonen, A. (2013). Health Professionals/Practice and Research Topic area: Health Professionals in Rheumatology (HPR) specific topics Specific topic: Nursing EULAR13-4146 supporting patients in optimal participation at work in the rheumatology clinic: rheumatologists' and rheumatology nurses' opinion C. *Ann Rheum Dis*, *72*(Suppl3), 356. https://doi.org/10.13140/2.1.3992.4000
20. Smolen, J. S., Landewé, R., Breedveld, F. C., Buch, M. H., Burmester, G. R., Dougados, M., Emery, P., Gaujoux-Viala, C., Gossec, L., Nam, J., Ramiro, S., Winthrop, K., De Wit, M., Aletaha, D., Betteridge, N., Bijlsma, J. W. J., Boers, M., Buttgereit, F., Combe, B., . . . Van Der Heijde, D. (2013). EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. *Annals of the Rheumatic Diseases*, *73*(3), 492–509. https://doi.org/10.1136/annrheumdis-2013-204573
21. Smolen, J., Landewé, R., Breedveld, F., Buch, M., Burmester, G., Dougados, M., Emery, P., Gaujoux-Viala, C., Gossec, L., Nam, J., Ramiro, S., Winthrop, K., Wit, M., Aletaha, D., Betteridge, N., Bijlsma, J., Boers, M., Buttgereit, F., Combe, B., & Heijde, D. (2013). *Web table* [Dataset]. https://www.researchgate.net/publication/294993534_Web_table
22. Eijk-Hustings, Y., Buss, B., Fayet, F., Moretti, A., Ndosi, M., Ryan, S., Savel, C., Voshaar, M., De La Torre-Aboki, J., & Tubergen, A. (Eds.). (2013). *Dissemination and evaluation of the EULAR recommendations for the role of the nurse in the management of chronic inflammatory arthritis* [EULAR Congress]
23. Van Tuyl, L. H. D., Hewlett, S., Sadloňová, M., Davis, B., Flurey, C., Hoogland, W., Kirwan, J. R., Sanderson, T., Van Schaardenburg, D., Scholte-Voshaar, M., Smolen, J. S., Stamm, T., & Boers, M. (2014). The patient perspective on remission in rheumatoid arthritis: 'You've got limits, but you're back to being you again.' *Annals of the Rheumatic Diseases*, *74*(6), 1004–1010. https://doi.org/10.1136/annrheumdis-2013-204798
24. Bykerk, V. P., Lie, E., Bartlett, S. J., Alten, R., Boonen, A., Christensen, R., Fürst, D. E., Hewlett, S., Leong, A., Lyddiatt, A., March, L., May, J. E., Montie, P., Orbai, A., Pohl, C., Voshaar, M., Woodworth, T., Bingham, C. O., & Choy, E. (2014). Establishing a core domain set to measure rheumatoid arthritis flares: Report of the OMERACT 11 RA Flare Workshop. *The Journal of Rheumatology*, *41*(4), 799–809. https://doi.org/10.3899/jrheum.131252

25. Kirwan, J. R., Bartlett, S. J., Beaton, D., Boers, M., Bosworth, A., Brooks, P., Choy, E., De Wit, M., Guillemin, F., Hewlett, S., Kvien, T. K., Landewé, R., Leong, A., Lyddiatt, A., March, L., May, J. E., Montie, P., Nikaï, E., Richards, P. S., . . . Gossec, L. (2014). Updating the OMERACT Filter: Implications for patient-reported Outcomes. *The Journal of Rheumatology*, *41*(5), 1011–1015. https://doi.org/10.3899/jrheum.131312
26. Van Eijk-Hustings, Y., Ndosi, M., Buß, B., Fayet, F., Moretti, A., Ryan, S., Savel, C., Scholte-Voshaar, M., De La Torre-Aboki, J., & Van Tubergen, A. (2014). Dissemination and evaluation of the European League Against Rheumatism recommendations for the role of the nurse in the management of chronic inflammatory arthritis: results of a multinational survey among nurses, rheumatologists and patients. *Rheumatology*, *53*(8), 1491–1496. https://doi.org/10.1093/rheumatology/keu134
27. Bartlett, S. J., Bykerk, V. P., Cooksey, R., Choy, E., Alten, R., Christensen, R., Fürst, D. E., Guillemin, F., Halls, S., Hewlett, S., Leong, A. L., Lyddiatt, A., March, L., Montie, P., Orbai, A., Pohl, C., Voshaar, M., Woodworth, T., & Bingham, C. O. (2015). Feasibility and domain validation of Rheumatoid Arthritis (RA) flare Core Domain set: Report of the OMERACT 2014 RA Flare Group Plenary. *The Journal of Rheumatology*, *42*(11), 2185–2189. https://doi.org/10.3899/jrheum.141169
28. Van Tuyl, L. H. D., Sadloňová, M., Davis, B., Flurey, C., Goel, N., Hewlett, S., Hill, C., Hoogland, W., Kirwan, J. R., Van Schaardenburg, D., Scholte-Voshaar, M., Smolen, J. S., Stamm, T., Wells, G. A., & Boers, M. (2015). Remission in Rheumatoid Arthritis: Working toward Incorporation of the Patient Perspective at OMERACT 12. *The Journal of Rheumatology*, *43*(1), 203–207. https://doi.org/10.3899/jrheum.141113
29. Zangi, H. A., Ndosi, M., Adams, J., Andersen, L. P. H., Bode, C., Boström, C., Van Eijk-Hustings, Y., Gossec, L., Korandová, J., Mendes, G. N., Niedermann, K., Primdahl, J., Stoffer, M., Voshaar, M., & Van Tubergen, A. (2015). EULAR recommendations for patient education for people with inflammatory arthritis. *Annals of the Rheumatic Diseases*, *74*(6), 954–962. https://doi.org/10.1136/annrheumdis-2014-206807

30. Castrejón, I., Carmona, L., Agrinier, N., Andrés, M., Briot, K., Caron, M., Christensen, R., Consolaro, A., Curbelo, R., Ferrer, M., Foltz, V., González, C., Guillemin, F., Machado, P., Prodinger, B., Ravelli, A., Scholte-Voshaar, M., Uhlig, T., Van Tuyl, L. H. D., . . . Gossec, L. (2015). The EULAR Outcome Measures Library: development and an example from a systematic review for systemic lupus erythematous instruments. *HAL (Le Centre Pour La Communication Scientifique Directe)*, *33*(6), 910–916. https://hal.univ-lorraine.fr/hal-01816071
31. Cheung, P., De Wit, M., Bingham, C. O., Kirwan, J. R., Leong, A., March, L., Montie, P., Scholte-Voshaar, M., & Gossec, L. (2015a). Recommendations for the Involvement of Patient Research Partners (PRP) in OMERACT Working Groups. A Report from the OMERACT 2014 Working Group on PRP. *The Journal of Rheumatology*, *43*(1), 187–193. https://doi.org/10.3899/jrheum.141011
32. Toupin-April, K., Barton, J. L., Fraenkel, L., Li, L., Grandpierre, V., Guillemin, F., Rader, T., Stacey, D., Jull, J., Petkovic, J., Scholte-Voshaar, M., Welch, V., Lyddiatt, A., Hofstetter, C. R., De Wit, M., March, L., Meade, T., Christensen, R., Gaujoux-Viala, C., . . . Tugwell, P. (2015). Development of a draft core set of domains for measuring shared decision making in osteoarthritis: an OMERACT working group on shared Decision making. *The Journal of Rheumatology*, *42*(12), 2442–2447. https://doi.org/10.3899/jrheum.141205
33. Smolen, J. S., Breedveld, F. C., Burmester, G. R., Bykerk, V. P., Dougados, M., Emery, P., Kvien, T. K., Navarro-Compán, M. V., Oliver, S., Schoels, M., Scholte-Voshaar, M., Stamm, T., Stoffer, M., Takeuchi, T., Aletaha, D., Andreu, J. L., Aringer, M., Bergman, M., Betteridge, N., . . . Van Der Heijde, D. (2015). Treating rheumatoid arthritis to target: 2014 update of the recommendations of an international task force. *Annals of the Rheumatic Diseases*, *75*(1), 3–15. https://doi.org/10.1136/annrheumdis-2015-207524
34. Stoffer, M., Schoels, M., Smolen, J. S., Aletaha, D., Breedveld, F. C., Burmester, G. R., Bykerk, V. P., Dougados, M., Emery, P., Haraoui, B., Gómez-Reino, J. J., Kvien, T. K., Nash, P., Navarro-Compán, V., Scholte-Voshaar, M., Van Vollenhoven, R., Van Der Heijde, D., & Stamm, T. (2015). Evidence for treating rheumatoid arthritis to target: results of a systematic literature search update. *Annals of the Rheumatic Diseases*, *75*(1), 16–22. https://doi.org/10.1136/annrheumdis-2015-207526

35. Cheung, P., De Wit, M., Bingham, C. O., Kirwan, J. R., Leong, A., March, L., Montie, P., Scholte-Voshaar, M., & Gossec, L. (2015b). AB1156 Involvement of patient research partners in clinical research: recommendations developed by Omeract. *Annals of the Rheumatic Diseases*, *74*(Suppl 2), 1289.2-1289. https://doi.org/10.1136/annrheumdis-2015-eular.1702
36. Kirwan, J. R., De Wit, M., Bingham, C. O., Leong, A., Richards, P., Tugwell, P., Voshaar, M., & Gossec, L. (2016). Commentary: Patients as partners: Building on the experience of outcome measures in rheumatology. *Arthritis & Rheumatology*, *68*(6), 1334–1336. https://doi.org/10.1002/art.39678
37. De Wit, M., Kirwan, J. R., Tugwell, P., Beaton, D., Boers, M., Brooks, P., Collins, S., Conaghan, P. G., D'Agostino, M. A., Hofstetter, C. R., Hughes, R., Leong, A., Lyddiatt, A., March, L., May, J. E., Montie, P., Richards, P., Simon, L. S., Singh, J. A., . . . Gossec, L. (2016). Successful stepwise development of patient Research Partnership: 14 years' experience of actions and Consequences in Outcome Measures in Rheumatology (OMERACT). *The Patient: Patient-Centered Outcomes Research*, *10*(2), 141–152. https://doi.org/10.1007/s40271-016-0198-4
38. Van Tuyl, L. H. D., Sadloňová, M., Hewlett, S., Davis, B., Flurey, C., Goel, N., Gossec, L., Brahe, C. H., Hill, C., Hoogland, W., Kirwan, J. R., Hetland, M. L., Van Schaardenburg, D., Smolen, J. S., Stamm, T., Voshaar, M., Wells, G. A., & Boers, M. (2016). The patient perspective on absence of disease activity in rheumatoid arthritis: a survey to identify key domains of patient-perceived remission. *Annals of the Rheumatic Diseases*, *76*(5), 855–861. https://doi.org/10.1136/annrheumdis-2016-209835
39. Buchbinder, R., Page, M. J., Huang, H., Verhagen, A., Beaton, D., Kopkow, C., Lenza, M., Jain, N. B., Richards, B., Richards, P., Voshaar, M., Van Der Windt, D., & Gagnier, J. (2017). A Preliminary Core Domain Set for Clinical Trials of Shoulder Disorders: A Report from the OMERACT 2016 Shoulder Core Outcome Set Special Interest Group. *The Journal of Rheumatology*, *44*(12), 1880–1883. https://doi.org/10.3899/jrheum.161123
40. Singh, J. A., Dowsey, M. M., Dohm, M., Goodman, S. M., Leong, A., Voshaar, M. M., & Choong, P. F. M. (2017). Achieving consensus on total joint replacement trial outcome reporting using the OMERACT filter: Endorsement of the final Core Domain set for total hip and total knee replacement trials for endstage arthritis. *The Journal of Rheumatology*, *44*(11), 1723–1726. https://doi.org/10.3899/jrheum.161113

41. Smolen, J. S., Landewé, R., Breedveld, F. C., Buch, M. H., Burmester, G. R., Dougados, M., Emery, P., Gaujoux-Viala, C., Gossec, L., Nam, J., Smolen, J. S., Winthrop, K., De Wit, M., Aletaha, D., Betteridge, N., Bijlsma, J. W. J., Boers, M., Buttgereit, F., Combe, B., . . . Van Der Heijde, D. (2017). EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Annals of the Rheumatic Diseases*, *76*(6), 960–977. https://doi.org/10.1136/annrheumdis-2016-210715
42. Nam, J., Takase-Minegishi, K., Smolen, J. S., Chatzidionysiou, K., Smolen, J. S., Van Der Heijde, D., Bijlsma, J. W. J., Burmester, G. R., Dougados, M., Scholte-Voshaar, M., Van Vollenhoven, R., & Landewé, R. (2017). Efficacy of biological disease-modifying antirheumatic drugs: a systematic literature review informing the 2016 update of the EULAR recommendations for the management of rheumatoid arthritis. *Annals of the Rheumatic Diseases*, *76*(6), 1113–1136. https://doi.org/10.1136/annrheumdis-2016-210713
43. Smolen, J. S., Sepriano, A., Chatzidionysiou, K., Nam, J., Smolen, J. S., Van Der Heijde, D., Dougados, M., Van Vollenhoven, R., Bijlsma, J. W. J., Burmester, G. R., Scholte-Voshaar, M., Falzon, L., & Landewé, R. (2017). Safety of synthetic and biological DMARDs: a systematic literature review informing the 2016 update of the EULAR recommendations for management of rheumatoid arthritis. *Annals of the Rheumatic Diseases*, *76*(6), 1101–1136. https://doi.org/10.1136/annrheumdis-2016-210708
44. Finger, M., Boonen, A., Woodworth, T., Escorpizo, R., Christensen, R., Nielsen, S. M., Leong, A., Voshaar, M., Flurey, C., Milman, N., Verstappen, S., Alten, R., Guillemin, F., Kloppenburg, M., Beaton, D., Tugwell, P., March, L., Fürst, D. E., & Pohl, C. (2017). An OMERACT Initiative Toward Consensus to Identify and Characterize Candidate Contextual Factors: Report from the Contextual Factors Working Group. *The Journal of Rheumatology*, *44*(11), 1734–1739. https://doi.org/10.3899/jrheum.161200
45. Palmowski, Y., Buttgereit, T., Dejaco, C., Bijlsma, J. W. J., Matteson, E. L., Voshaar, M., Boers, M., & Buttgereit, F. (2017). "Official View" on Glucocorticoids in rheumatoid arthritis: A Systematic review of international guidelines and consensus statements. *Arthritis Care & Research*, *69*(8), 1134–1141. https://doi.org/10.1002/acr.23185

46. Rasch, L., Boers, M., Hill, C., Voshaar, M., Hoogland, W., De Wit, M., Flurey, C., Davis, B., Hetland, M. L., Brahe, C. H., Gossec, L., Wells, G. A., Tugwell, P., Kuriya, B., Goel, N., Singh, J. A., Duarte, C., Da Silva, J. a. P., Van Schaardenburg, D., . . . Van Tuyl, L. H. D. (2017). Validating Rheumatoid Arthritis Remission Using the Patients' Perspective: Results from a Special Interest Group at OMERACT 2016. *The Journal of Rheumatology*, *44*(12), 1889–1893. https://doi.org/10.3899/jrheum.161111
47. Toupin-April, K., Barton, J. L., Fraenkel, L., Li, L., Brooks, P., De Wit, M., Stacey, D., Meara, A., Shea, B., Lyddiatt, A., Hofstetter, C. R., Gossec, L., Christensen, R., Scholte-Voshaar, M., Suarez-Almazor, M. E., Boonen, A., Meade, T., March, L., Pohl, C., . . . Tugwell, P. (2017). Toward the Development of a Core Set of Outcome Domains to Assess Shared Decision-making Interventions in Rheumatology: Results from an OMERACT Delphi Survey and Consensus Meeting. *The Journal of Rheumatology*, *44*(10), 1544–1550. https://doi.org/10.3899/jrheum.161241
48. Bartlett, S. J., Barbic, S., Bykerk, V. P., Choy, E., Alten, R., Christensen, R., Broeder, A. a. D., Fautrel, B., Fürst, D. E., Guillemin, F., Hewlett, S., Leong, A., Lyddiatt, A., March, L., Montie, P., Pohl, C., Voshaar, M., Woodworth, T., & Bingham, C. O. (2017). Content and Construct Validity, Reliability, and responsiveness of the Rheumatoid Arthritis flare questionnaire: OMERACT 2016 Workshop report. *The Journal of Rheumatology*, *44*(10), 1536–1543. https://doi.org/10.3899/jrheum.161145
49. Bech, B., Primdahl, J., Scholte-Voshaar, M., Zangi, H. A., Van Tubergen, A., & Van Eijk-Hustings, Y. (2018). FRI0742-HPR Eular recommendations for the role of the nurse in the management of chronic inflammatory arthritis: 2018 update. *Annals of the Rheumatic Diseases*. https://doi.org/10.1136/annrheumdis-2018-eular.4482
50. Carvalho, P., Goel, N., Voshaar, M., Boers, M., & Silva, J. (2018). SAT0241 Patients' perspective on the efficacy and risks of glucocorticoids in ra – an initiative under the gloria project. *Annals of the Rheumatic Diseases*. https://doi.org/10.1136/annrheumdis-2018-eular.7041

51. Kelly, A., Bartlett, S. J., De Wit, M., Beaton, D., Dawson, T., Evans, V., Gill, M., Hassett, G., March, L., Scholte-Voshaar, M., Singh, J. A., Tong, A., Tugwell, P., Wong, P., & Tymms, K. (2019). Addressing Challenges in Developing a Core Domain Set in Adherence Interventions in Rheumatology: A Report from the OMERACT-Adherence Group. *The Journal of Rheumatology*, *46*(9), 1202–1206. https://doi.org/10.3899/jrheum.181078
52. Nielsen, S. M., Tugwell, P., De Wit, M., Boers, M., Beaton, D., Woodworth, T., Escorpizo, R., Shea, B., April, K. T., Guillemin, F., Strand, V., Singh, J. A., Kloppenburg, M., Fürst, D. E., Wells, G. A., Smolen, J. S., Veselý, R., Boonen, A., Storgaard, H., . . . Christensen, R. (2019). Identifying Provisional Generic Contextual Factor Domains for Clinical Trials in Rheumatology: Results from an OMERACT Initiative. *The Journal of Rheumatology*, *46*(9), 1159–1163. https://doi.org/10.3899/jrheum.181081
53. April, K. T., Barton, J. L., Fraenkel, L., Meara, A., Li, L., Brooks, P., De Wit, M., Stacey, D., Légaré, F., Shea, B., Lyddiatt, A., Hofstetter, C. R., Christensen, R., Voshaar, M., Suarez-Almazor, M. E., Boonen, A., Meade, T., March, L., Jull, J., . . . Tugwell, P. (2019). OMERACT Development of a core domain set of outcomes for shared decision-making interventions. *The Journal of Rheumatology*, *46*(10), 1409–1414. https://doi.org/10.3899/jrheum.181071
54. Smolen, J. S., Page, M. J., Whittle, S. L., Huang, H., Verhagen, A., Beaton, D., Richards, P., Voshaar, M., Shea, B., Van Der Windt, D., Kopkow, C., Lenza, M., Jain, N. B., Richards, B., Hill, C. J., Gill, T. K., Koes, B. W., Foster, N. E., Conaghan, P. G., . . . Buchbinder, R. (2019). The OMERACT Core domain set for clinical trials of shoulder disorders. *The Journal of Rheumatology*, *46*(8), 969–975. https://doi.org/10.3899/jrheum.181070
55. Page, M. J., O'Connor, D., Malek, M., Haas, R., Beaton, D., Huang, H., Ramiro, S., Richards, P., Voshaar, M., Shea, B., Verhagen, A., Whittle, S. L., Van Der Windt, D. A., Gagnier, J., & Buchbinder, R. (2019). Patients' experience of shoulder disorders: a systematic review of qualitative studies for the OMERACT Shoulder Core Domain Set. *Rheumatology*, *58*(8), 1410–1421. https://doi.org/10.1093/rheumatology/kez046

56. De Wit, M., Cooper, C., Tugwell, P., Bere, N., Kirwan, J. R., Conaghan, P. G., Roberts, C., Aujoulat, I., Al-Daghri, N. M., De Carvalho, I. A., Barker, M., Bedlington, N., Brandi, M. L., Bruyère, O., Burlet, N., Halbout, P., Hiligsmann, M., Jiwa, F., Kanis, J. A., . . . Reginster, J. Y. (2019). Practical guidance for engaging patients in health research, treatment guidelines and regulatory processes: results of an expert group meeting organized by the World Health Organization (WHO) and the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO). *Aging Clinical and Experimental Research*, *31*(7), 905–915. https://doi.org/10.1007/s40520-019-01193-8
57. Bech, B., Primdahl, J., Van Tubergen, A., Voshaar, M., Zangi, H. A., Barbosa, L., Boström, C., Boteva, B., Carubbi, F., Fayet, F., Ferreira, R. J. O., Hoeper, K., Kocher, A., Kukkurainen, M. L., Lion, V., Minnock, P., Moretti, A., Ndosi, M., Nikolic, M., . . . Van Eijk-Hustings, Y. (2019). 2018 update of the EULAR recommendations for the role of the nurse in the management of chronic inflammatory arthritis. *Annals of the Rheumatic Diseases*, *79*(1), 61–68. https://doi.org/10.1136/annrheumdis-2019-215458
58. Kelly, A., Crimston-Smith, L., Tong, A., Bartlett, S. J., Bekker, C. L., Christensen, R., De Vera, M. A., De Wit, M., Evans, V., Gill, M., March, L., Manera, K. E., Nieuwlaat, R., Salmasi, S., Scholte-Voshaar, M., Singh, J. A., Sumpton, D., Toupin-April, K., Tugwell, P., . . . Tymms, K. (2019). Scope of outcomes in trials and observational studies of interventions targeting medication adherence in rheumatic conditions: a systematic review. *The Journal of Rheumatology*, *47*(10), 1565–1574. https://doi.org/10.3899/jrheum.190726
59. Smolen, J. S., Landewé, R., Bijlsma, J. W. J., Burmester, G. R., Dougados, M., Kerschbaumer, A., McInnes, I. B., Sepriano, A., Van Vollenhoven, R. F., De Wit, M., Aletaha, D., Aringer, M., Askling, J., Balsa, A., Boers, M., Broeder, A. a. D., Buch, M. H., Buttgereit, F., Caporali, R., . . . Van Der Heijde, D. (2020). EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. *Annals of the Rheumatic Diseases*, *79*(6), 685–699. https://doi.org/10.1136/annrheumdis-2019-216655

60. Hartman, L. M., Paolino, S., Bos, R., Opriș-Belinski, D., Kok, M. R., Griep-Wentink, H., Klaasen, R., Allaart, C. F., Bruyn, G. a. W., Raterman, H. G., Voshaar, M. a. H. O., Gomes, N., Pinto, R. M. A., Klausch, T., Lems, W., & Boers, M. (2020). FRI0581 In elderly patients, caps that record medication bottle openings are unreliable and thus not the gold standard for adherence. *Annals of the Rheumatic Diseases*, *79*(Suppl 1), 894.2-895. https://doi.org/10.1136/annrheumdis-2020-eular.3598
61. Hartman, L. M., Alessandri, E., Van Den Bos, R. R., Opriș-Belinski, D., Kok, M. R., Griep-Wentink, H., Klaasen, R., Allaart, C., De Bruyn, G., Raterman, H. G., Voshaar, M., Gomes, N., Pinto, R. S., Klausch, T., Lems, W., & Boers, M. (2020). AB1165 Medication adherence data in a randomized trial: large challenges to come from raw data to a workable and reliable dataset. *Annals of the Rheumatic Diseases*, *79*(Suppl 1), 1873.2-1873. https://doi.org/10.1136/annrheumdis-2020-eular.3638
62. Ritschl, V., Stamm, T., Aletaha, D., Bijlsma, J. W. J., Böhm, P., Drăgoi, R., Dures, E., Estévez-López, F., Gossec, L., Iagnocco, A., Marques, A., Moholt, E., Nudel, M., Van Den Bemt, B. J. F., Viktil, K. K., Voshaar, M., De Thurah, A., & Carmona, L. (2020). 2020 EULAR points to consider for the prevention, screening, assessment and management of non-adherence to treatment in people with rheumatic and musculoskeletal diseases for use in clinical practice. *Annals of the Rheumatic Diseases*, *80*(6), 707–713. https://doi.org/10.1136/annrheumdis-2020-218986
63. Santiago, T., Voshaar, M., De Wit, M., Carvalho, P., Buttgereit, F., Cutolo, M., Boers, M., & Da Silva, J. a. P. (2020). PARE0004 Patient perspective on the efficacy and risks of glucocorticoids in rheumatoid arthritis – an international survey of 1344 patients. *Annals of the Rheumatic Diseases*, *79*(Suppl 1), 1288.2-1288. https://doi.org/10.1136/annrheumdis-2020-eular.3164
64. Santiago, T., Voshaar, M., De Wit, M., Carvalho, P., Boers, M., Cutolo, M., Buttgereit, F., & Da Silva, J. a. P. (2020). AB1335-HPR Health professionals' perspective on the benefits and risks of low-dose glucocorticoids in rheumatoid arthritis – an international survey of 444 health professionals. *Annals of the Rheumatic Diseases*, *79*(Suppl 1), 1955.1-1956. https://doi.org/10.1136/annrheumdis-2020-eular.3277

65. Nielsen, S. M., Storgaard, H., Ellingsen, T., Shea, B., Wells, G. A., Welch, V., Fürst, D. E., De Wit, M., Voshaar, M., Juhl, C. B., Boers, M., Escorpizo, R., Woodworth, T., Boonen, A., Bliddal, H., March, L., Tugwell, P., & Christensen, R. (2020). Population characteristics as important contextual factors in rheumatological trials: an exploratory meta-epidemiological study from an OMERACT Working Group. *Annals of the Rheumatic Diseases*, *79*(10), 1269–1276. https://doi.org/10.1136/annrheumdis-2020-217237
66. Berthelsen, D. B., Ginnerup-Nielsen, E., Juhl, C. B., Lund, H., Henriksen, M., Hróbjartsson, A., Nielsen, S. M., Voshaar, M., & Christensen, R. (2020). Controversy and Debate on Meta-epidemiology. Paper 1: Treatment effect sizes vary in randomized trials depending on the type of outcome measure. *Journal of Clinical Epidemiology*, *123*, 27–38. https://doi.org/10.1016/j.jclinepi.2019.10.016
67. Kelly, A., Tymms, K., De Wit, M., Bartlett, S. J., Cross, M., Dawson, T., De Vera, M. A., Evans, V., Gill, M., Hassett, G., Lim, I., Manera, K. E., Major, G., March, L., O'Neill, S., Scholte-Voshaar, M., Sinnathurai, P., Sumpton, D., Teixeira-Pinto, A., . . . Tong, A. (2020). Patient and caregiver priorities for medication adherence in gout, osteoporosis, and rheumatoid arthritis: nominal group technique. *Arthritis Care & Research*, *72*(10), 1410–1419. https://doi.org/10.1002/acr.24032
68. Nielsen, S. M., Rasmussen, M. U., Boers, M., Van Der Windt, D., De Wit, M., Woodworth, T., Flurey, C., Beaton, D., Shea, B., Escorpizo, R., Fürst, D. E., Smolen, J. S., Toupin-April, K., Boonen, A., Voshaar, M., Ellingsen, T., Wells, G. A., Reeves, B. C., March, L., . . . Christensen, R. (2020). Towards consensus in defining and handling contextual factors within rheumatology trials: an initial qualitative study from an OMERACT working group. *Annals of the Rheumatic Diseases*, *80*(2), 242–249. https://doi.org/10.1136/annrheumdis-2020-217895
69. Ritschl, V., Stamm, T., Aletaha, D., Bijlsma, J. W. J., Böhm, P., Drăgoi, R., Dures, E., Estévez-López, F., Gossec, L., Iagnocco, A., Negrón, J. B., Nudel, M., Marques, A., Moholt, E., Skrubbeltrang, C., Van Den Bemt, B., Viktil, K. K., Voshaar, M., Carmona, L., & De Thurah, A. (2020). Prevention, screening, assessing and managing of non-adherent behaviour in people with rheumatic and musculoskeletal diseases: systematic reviews informing the 2020 EULAR points to consider. *RMD Open*, *6*(3), e001432. https://doi.org/10.1136/rmdopen-2020-001432

70. Nash, P., Kerschbaumer, A., Dörner, T., Dougados, M., Fleischmann, R., Geißler, K., McInnes, I. B., Pope, J., Van Der Heijde, D., Stoffer-Marx, M., Takeuchi, T., Trauner, M., Winthrop, K., De Wit, M., Aletaha, D., Baraliakos, X., Boehncke, W. H., Emery, P., Isaacs, J. D., . . . Smolen, J. S. (2020). Points to consider for the treatment of immune-mediated inflammatory diseases with Janus kinase inhibitors: a consensus statement. *Annals of the Rheumatic Diseases*, *80*(1), 71–87. https://doi.org/10.1136/annrheumdis-2020-218398
71. Santiago, T., Voshaar, M. a. H. O., De Wit, M., Carvalho, P., Buttgereit, F., Cutolo, M., Paolino, S., Pinheiro, G. R. C., Boers, M., & Da Silva, J. a. P. (2021). Patients' and rheumatologists' perspectives on the efficacy and safety of low-dose glucocorticoids in rheumatoid arthritis—an international survey within the GLORIA study. *Rheumatology*, *60*(7), 3334–3342. https://doi.org/10.1093/rheumatology/keaa785
72. Hartman, L. M., Cutolo, M., Bos, R., Opriș-Belinski, D., Kok, M. R., Griep-Wentink, H., Klaasen, R., Allaart, C. F., Bruyn, G. a. W., Raterman, H. G., Voshaar, M., Gomes, N., Pinto, R. M. A., Klausch, L. T., Lems, W. F., & Boers, M. (2021). Medication adherence in older people with rheumatoid arthritis is lower according to electronic monitoring than according to pill count. *Rheumatology*, *60*(11), 5239–5246. https://doi.org/10.1093/rheumatology/keab207
73. Bekker, C. L., Bossina, S., De Vera, M. A., Bartlett, S. J., De Wit, M., March, L., Shea, B., Evans, V., Richards, D. P., Tong, A., Tugwell, P., Tymms, K., Scholte-Voshaar, M., Kelly, A., & Van Den Bemt, B. J. F. (2021). Patient Perspectives on Outcome Domains of Medication adherence Trials in inflammatory arthritis: an International OMERACT Focus Group study. *The Journal of Rheumatology*, *48*(9), 1480–1487. https://doi.org/10.3899/jrheum.201568
74. Nielsen, S. M., Boers, M., De Wit, M., Shea, B., Van Der Windt, D. A., Reeves, B. C., Beaton, D., Alten, R., April, K. T., Boonen, A., Escorpizo, R., Flurey, C., Fürst, D. E., Guillemin, F., Leong, A., Pohl, C., Rasmussen, M. U., Singh, J. A., Smolen, J. S., . . . Christensen, R. (2021). OMERACT consensus-based operational definition of contextual factors in rheumatology clinical trials: A mixed methods study. *Seminars in Arthritis and Rheumatism*, *51*(3), 601–606. https://doi.org/10.1016/j.semarthrit.2021.03.013

75. Toupin-April, K., Décary, S., De Wit, M., Meara, A., Barton, J. L., Fraenkel, L., Li, L., Brooks, P., Shea, B., Stacey, D., Lydiatt, A., Hofstetter, C. R., Proulx, L., Christensen, R., Voshaar, M., Suarez-Almazor, M. E., Boonen, A., Meade, T., March, L., . . . Tugwell, P. (2021). Endorsement of the OMERACT core domain set for shared decision making interventions in rheumatology trials: Results from a multi-stepped consensus-building approach. *Seminars in Arthritis and Rheumatism*, *51*(3), 593–600. https://doi.org/10.1016/j.semarthrit.2021.03.017
76. Buttgereit, T., Palmowski, A., Forsat, N. D., Boers, M., Witham, M., Rodondi, N., Moutzouri, E., Navidad, A. J. Q., Hof, A. W. V., Van Der Worp, B., Coll-Planas, L., Voshaar, M., De Wit, M., Da Silva, J. a. P., Stegemann, S., Bijlsma, J. W. J., Koeller, M., Mooijaart, S. P., Kearney, P., & Buttgereit, F. (2021). Barriers and potential solutions in the recruitment and retention of older patients in clinical trials—lessons learned from six large multicentre randomized controlled trials. *Age And Ageing*, *50*(6), 1988–1996. https://doi.org/10.1093/ageing/afab147
77. Thomas, M., Fraenkel, L., Boonen, A., Bansback, N., Buchbinder, R., Marshall, D., Proulx, L., Voshaar, M., Richards, P., Richards, D. P., Hiligsmann, M., Guillemin, F., Shea, B., Tugwell, P., & Hazlewood, G. (2021). Patient preferences to value health outcomes in rheumatology clinical trials: Report from the OMERACT special interest group☆. *Seminars in Arthritis and Rheumatism*, *51*(4), 919–924. https://doi.org/10.1016/j.semarthrit.2021.05.008
78. Jones, B., Flurey, C., Proudman, S., Ferreira, R. J. O., Voshaar, M., Hoogland, W., Chaplin, H., Goel, N., Hetland, M. L., Hill, C., Kuriya, B., Mather, K., Rasch, L., Shea, B., Singh, J. A., Smolen, J. S., Da Silva, J. a. P., De Souza, S., Stamm, T., . . . Boers, M. (2021). Considerations and priorities for incorporating the patient perspective on remission in rheumatoid arthritis: An OMERACT 2020 special interest group report. *Seminars in Arthritis and Rheumatism*, *51*(5), 1108–1112. https://doi.org/10.1016/j.semarthrit.2021.07.010
79. Rasch, L., Boers, M., Lems, W. F., Van Schaardenburg, D., Proudman, S., Hill, C., Duarte, C., Kuriya, B., Davis, B., Hoogland, W., Voshaar, M., & Van Tuyl, L. H. D. (2021). Patient perspective on remission in rheumatoid arthritis: Validation of patient reported outcome instruments to measure absence of disease activity. *Seminars in Arthritis and Rheumatism*, *51*(6), 1360–1369. https://doi.org/10.1016/j.semarthrit.2021.07.005

80. Jones, B., Bennett, S., Larsson, I., Zangi, H. A., Boström, C., Van Der Elst, K., Fayet, F., Fusama, M., Del Carmen Herrero Manso, M., Hoeper, J. R., Kukkurainen, M. L., Kwok, S. K., Mateus, E. F., Minnock, P., Nava, T., Nikolic, M., Primdahl, J., Rawat, R., Schoenfelder, M., . . . Ndosi, M. (2022). Disseminating and assessing implementation of the EULAR recommendations for patient education in inflammatory arthritis: a mixed-methods study with patients' perspectives. *RMD Open*, *8*(1), e002256. https://doi.org/10.1136/rmdopen-2022-002256
81. Hartman, L., Da Silva, J. a. P., Buttgereit, F., Cutolo, M., Opris-Belinski, D., Szekanecz, Z., Masaryk, P., Voshaar, M., Heijmans, M. W., Lems, W., Van Der Heijde, D., & Boers, M. (2022). POS1410 Development of prediction models for senior patients with rheumatoid arthritis and comorbidities treated with chronic lowdose glucocorticoids in the Gloria Trial. *Annals of the Rheumatic Diseases*, *81*(Suppl 1), 1047. https://doi.org/10.1136/annrheumdis-2022-eular.770
82. Aletaha, D., Kerschbaumer, A., Kastrati, K., Dejaco, C., Dougados, M., McInnes, I. B., Sattar, N., Stamm, T., Takeuchi, T., Trauner, M., Van Der Heijde, D., Voshaar, M., Winthrop, K., Ravelli, A., Betteridge, N., Burmester, G. R., Bijlsma, J. W. J., Bykerk, V. P., Caporali, R., . . . Smolen, J. S. (2022). Consensus statement on blocking interleukin-6 receptor and interleukin-6 in inflammatory conditions: an update. *Annals of the Rheumatic Diseases*, *82*(6), 773–787. https://doi.org/10.1136/ard-2022-222784
83. Kastrati, K., Aletaha, D., Burmester, G. R., Chwala, E., Dejaco, C., Dougados, M., McInnes, I. B., Ravelli, A., Sattar, N., Stamm, T., Takeuchi, T., Trauner, M., Van Der Heijde, D., Voshaar, M., Winthrop, K., Smolen, J. S., & Kerschbaumer, A. (2022). A systematic literature review informing the consensus statement on efficacy and safety of pharmacological treatment with interleukin-6 pathway inhibition with biological DMARDs in immune-mediated inflammatory diseases. *RMD Open*, *8*(2), e002359. https://doi.org/10.1136/rmdopen-2022-002359
84. Hartman, L. M., Da Silva, J. a. P., Buttgereit, F., Cutolo, M., Opriș-Belinski, D., Szekanecz, Z., Masaryk, P., Voshaar, M., Heymans, M. W., Lems, W. F., Van Der Heijde, D., & Boers, M. (2022). Development of prediction models to select older RA patients with comorbidities for treatment with chronic low-dose glucocorticoids. *Rheumatology*, *62*(5), 1824–1833. https://doi.org/10.1093/rheumatology/keac547

85. Berthelsen, D. B., Simon, L. S., Ioannidis, J. P. A., Voshaar, M., Richards, P. S., Goel, N., Strand, V., Nielsen, S. M., Shea, B., Tugwell, P., Bartlett, S. J., Hazlewood, G., March, L., Singh, J. A., Suarez-Almazor, M. E., Boers, M., Stevens, R., Fürst, D. E., Woodworth, T., . . . Group, O. S. W. (2023). Stakeholder Endorsement Advancing the Implementation of a Patient-Reported Domain for Harms in Rheumatology Clinical Trials: Outcome of the Omeract Safety Working Group. *SSRN*. https://doi.org/10.2139/ssrn.4557532
86. Khoo, T., Jones, B., Chin, A., Terrett, A., Voshaar, M., Hoogland, W., March, L., Beaton, D., Gazel, Ü., Shea, B., Tugwell, P., Flurey, C., & Proudman, S. (2023). Defining independence: A scoping review by the OMERACT patient perspective of remission in rheumatoid arthritis group. *Seminars in Arthritis and Rheumatism*, *58*, 152152. https://doi.org/10.1016/j.semarthrit.2022.152152
87. Thomas, M., Marshall, D., Sanchez, A. L., Bartlett, S. J., Boonen, A., Fraenkel, L., Proulx, L., Voshaar, M., Bansback, N., Buchbinder, R., Guillemin, F., Hiligsmann, M., Richards, D. P., Richards, P., Shea, B., Tugwell, P., Falahee, M., & Hazlewood, G. (2023). Exploring perceptions of using preference elicitation methods to inform clinical trial design in rheumatology: A qualitative study and OMERACT collaboration. *Seminars in Arthritis and Rheumatism*, *58*, 152112. https://doi.org/10.1016/j.semarthrit.2022.152112
88. Berthelsen, D. B., Simon, L. S., Ioannidis, J. P. A., Voshaar, M., Richards, P. S., Goel, N., Strand, V., Nielsen, S. M., Shea, B., Tugwell, P., Bartlett, S. J., Hazlewood, G., March, L., Singh, J. A., Suarez-Almazor, M. E., Boers, M., Stevens, R., Fürst, D. E., Woodworth, T., . . . Christensen, R. (2023). Stakeholder endorsement advancing the implementation of a patient-reported domain for harms in rheumatology clinical trials: Outcome of the OMERACT Safety Working Group. *Seminars in Arthritis and Rheumatism*, *63*, 152288. https://doi.org/10.1016/j.semarthrit.2023.152288
89. Décary, S., De Wit, M., Naye, F., Barton, J. L., Fraenkel, L., Li, L., Brooks, P., Stacey, D., Maxwell, L., Campbell, W., Hofstetter, C. R., Voshaar, M., Meara, A., Christensen, R., Boonen, A., Suarez-Almazor, M. E., Meade, T., March, L., Jull, J., . . . April, K. T. (2024). Consensus on the definitions and descriptions of the domains of the OMERACT Core Outcome Set for shared decision-making interventions in rheumatology trials. *Seminars in Arthritis and Rheumatism*, 152381. https://doi.org/10.1016/j.semarthrit.2024.152381

90. Flurey, C. A., Jones, B., Gazel, U., Uzoka, C., Rosser, K., Khoo, T., Voshaar, M., Hoogland, W., Shea, B., March, L., Beaton, D., Tugwell, P., & Proudman, S. (2024). "It means almost forgetting that you've got a disease": An OMERACT study to define independence in the context of rheumatoid arthritis remission from the patient perspective. *Seminars in Arthritis and Rheumatism*, *68*, 152526. https://doi.org/10.1016/j.semarthrit.2024.152526
91. Kordkheili, A. M., Bekker, C. L., Hoens, A. M., Voshaar, M., Campbell, W., Carmona, L., De Wit, M., March, L., Nielsen, S. M., Shea, B., April, K. T., Tugwell, P., Tymms, K., & Kelly, A. (2024). Strategies to promote implementation of core outcomes for medication adherence trials in Rheumatology: A report from the OMERACT-Adherence Group. *Seminars in Arthritis and Rheumatism*, 152411. https://doi.org/10.1016/j.semarthrit.2024.152411
92. Naye, F., Toupin-April, K., De Wit, M., LeBlanc, A., Dubois, O., Boonen, A., Barton, J. L., Fraenkel, L., Li, L., Stacey, D., March, L., Barber, C., Hazlewood, G., Guillemin, F., Bartlett, S. J., Berthelsen, D. B., Mather, K., Arnaud, L., Akpabio, A., . . . Décary, S. (2024). OMERACT Core outcome measurement set for shared decision making in rheumatic and musculoskeletal conditions: a scoping review to identify candidate instruments. *Seminars in Arthritis and Rheumatism*, *65*, 152344. https://doi.org/10.1016/j.semarthrit.2023.152344
93. Weinbrecht-Mischkewitz, M., Kamal, M. M., Asim, F., Guillemin, F., Goel, N., Voshaar, M., Boonen, A., Berthelsen, D. B., April, K. T., López-Olivo, M. A., Sloan, V. S., Boers, M., Jones, C., Van Der Horst-Bruinsma, I., Cashin, A. G., Sharma, S., Leong, A., Alten, R., Shea, B., . . . Nielsen, S. M. (2024). Generating a list of potentially important contextual factors covering Randomized trials, Cohorts, and Measurement property studies: An OMERACT initiative. *Seminars in Arthritis and Rheumatism*, *65*, 152370. https://doi.org/10.1016/j.semarthrit.2024.152370
94. Berthelsen, D. B., Nielsen, S. M., Rasmussen, M. U., Voshaar, M., Richards, P., Bartlett, S. J., Hazlewood, G., Shea, B., Tugwell, P., Ellingsen, T., Jørgensen, T. S., Kristensen, S., Simon, L., Christensen, R., & Flurey, C. (2024). POS0744 "I couldn't carry on taking a drug like that: a qualitative study of patient perspectives on side effects from drug treatment in rheumatology from the omeract safety working group. *Annals of the Rheumatic Diseases*, 593–594. https://doi.org/10.1136/annrheumdis-2024-eular.1455

95. Nash, P., Kerschbaumer, A., Konzett, V., Aletaha, D., Dörner, T., Fleischmann, R., McInnes, I., Primdahl, J., Sattar, N., Tanaka, Y., Trauner, M., Winthrop, K., De Wit, M., Askling, J., Baraliakos, X., Boehncke, W., Emery, P., Gossec, L., Isaacs, J. D., . . . Smolen, J. S. (2025). Expert consensus statement on the treatment of immune-mediated inflammatory diseases with Janus kinase inhibitors: 2024 update. *Annals of the Rheumatic Diseases*. https://doi.org/10.1016/j.ard.2025.01.032
96. Arnal-Velasco, D., Martinez-Nicolas, I., Fabregas, N., Bartakke, A., Calsbeek, H., Emond, Y., Groene, O., León, I., Žaludek, A., Nunes, A. B., Orrego, C., Põlluste, K., Rodriguez, A., Sanduende, Y., Schäfer, W., Silva-García, J., Soria, V., Sousa, P., Valli, C., . . . Romero, E. (2025). Multidisciplinary, evidence-based, patient-centered perioperative patient safety recommendations: a European consensus study. *British Journal of Anaesthesia*. https://doi.org/10.1016/j.bja.2025.04.047
97. Kristensen, K., Wang, S., Velasco, D. A., Põlluste, K., Žaludek, A., Sousa, P., Orrego, C., & Groene, O., on behalf of the SAFEST Consortium. (2025). Sustaining perioperative patient safety improvement: the relevance of patient safety policies and contextual factors in European healthcare systems. International Journal for Quality in Health Care, 37(4). https://doi.org/10.1093/intqhc/mzaf105
98. Gazel, U., Barnes, E., Jones, B., Terrett, A., Voshaar, M., Hoogland, W., March, L., Beaton, D., Khoo, T., Chin, A., Shea, B., Tugwell, P., Proudman, S., & Flurey, C. A. (2026). Towards the development of a definition of independence for individuals diagnosed with rheumatoid arthritis in remission: an 'OMERACT remission in rheumatoid arthritis patient perspective' special interest group report. *Seminars in Arthritis and Rheumatism*, 77, 152948. https://doi.org/10.1016/j.semarthrit.2026.152948
99. Servy, H., Braithwaite, B., Kiltz, U., Van Tubergen, A., Studenic, P., Voshaar, M., Wiek, D., Tropé, S., Burmester, G., Venerito, V., & Gossec, L. (2026b). Artificial intelligence in healthcare faces regulatory challenges: balancing innovation with human oversight. EULAR Rheumatology Open, 2(1), 283–288. https://doi.org/10.1016/j.ero.2026.02.010

100. Berthelsen, D. B., Haugegaard, T., Kamso, M. M., Tugwell, P., Simon, L. S., Ioannidis, J. P., Flurey, C., Boers, M., Voshaar, M., Richards, P., Shea, B., Furst, D. E., Singh, J. A., Stevens, R., Woodworth, T., Bartlett, S. J., Hazlewood, G. S., & Christensen, R. (2026). Validity and utility of a single-item patient-reported measure of treatment-related bother in rheumatoid arthritis: A cross-sectional OMERACT study. Seminars in Arthritis and Rheumatism, 78, 152983. https://doi.org/10.1016/j.semarthrit.2026.152983
101. Berthelsen, D. B., Horgan, B., Simon, L., Ioannidis, J. P., Goel, N., Tugwell, P., Balay-Dustrude, E., Bartlett, S. J., Bingham, C. O., Boers, M., Bouillot, C., Böhm, P., Choy, E., Cowern, M., Dagsvik, K., Djurtoft, C., Furst, D. E., Haugegaard, T., Hazlewood, G. S., . . . Christensen, R. (2026). Development of a single-item patient-reported measure of treatment side-effect burden in clinical trials of rheumatic and musculoskeletal diseases using stakeholder input and large language model refinement. Seminars in Arthritis and Rheumatism, 79, 153026. https://doi.org/10.1016/j.semarthrit.2026.153026
102. Mitter, G., Danisman, E., Konzett, V., Smolen, J., Aletaha, D., Burmester, G.-R., Robinson, B., Rantapää Dahlqvist, S., Voshaar, M., Rönnelid, J., Tanaka, Y., & Reitbrecht, C. (2026). The Role and Significance of Rheumatoid Factor in Rheumatoid Arthritis: A Systematic Literature Review. PROSPERO. CRD420261419000. https://www.crd.york.ac.uk/PROSPERO/view/CRD420261419000

Posters, books, and attachments:

103. Voshaar, M. (2006, July). Patient's perspective on fatique. In *Annals of the Rheumatic Diseases*. Annual European Congress of Rheumatology (EULAR 2006). https://www.researchgate.net/publication/295731101_Patient's_perspective_on_fatique
104. Voshaar, M. S. (2013). SP0152 What risk am I willing to take for what benefit? *Annals of the Rheumatic Diseases*, *71*(Suppl 3), 37.3-37. https://doi.org/10.1136/annrheumdis-2012-eular.1627
105. Voshaar, M. (2014). SP0215 Patients' Perspective of Patient Education-What is in IT for Us? *Annals of the Rheumatic Diseases*, *73*(Suppl 2), 55.3-55. https://doi.org/10.1136/annrheumdis-2014-eular.6232
106. Voshaar, M. M. (2020). Self-management: A patient's perspective. In *Oxford University Press eBooks* (pp. 321–328). https://doi.org/10.1093/med/9780198831433.003.0027
107. Oxford Textbook of Rheumatoid Arthritis. (2020). In *Oxford University Press eBooks*. https://doi.org/10.1093/med/9780198831433.001.0001

108. Ritschl, V., Stamm, T., Aletaha, D., Bijlsma, J., Böhm, P., Dragoi, R., Dures, E., Estévez-López, F., Gossec, L., Iagnocco, A., Negrón, J., Nudel, M., Marques, A., Moholt, E., Skrubbeltrang, C., Bremt, B., Kirsten, V., Voshaar, M., Carmona, L., & De Thurah, A. (2021a). Supplement A – Search Protocol (Guidelines or Systematic Reviews) EULAR Project. In *ResearchGate*. https://rmdopen-2020-November-6-3--inline-supplementary-material-1.pdf
109. Ritschl, V., Stamm, T., Aletaha, D., Bijlsma, J., Böhm, P., Dragoi, R., Dures, E., Estévez-López, F., Gossec, L., Iagnocco, A., Negrón, J., Nudel, M., Marques, A., Moholt, E., Skrubbeltrang, C., Bremt, B., Kirsten, V., Voshaar, M., Carmona, L., & De Thurah, A. (2021b). Supplement_B_PICO_1. In *ResearchGate*. https://rmdopen-2020-November-6-3--inline-supplementary-material-3.pdf
110. Ritschl, V., Stamm, T., Aletaha, D., Bijlsma, J., Böhm, P., Dragoi, R., Dures, E., Estévez-López, F., Gossec, L., Iagnocco, A., Negrón, J., Nudel, M., Marques, A., Moholt, E., Skrubbeltrang, C., Bremt, B., Kirsten, V., Voshaar, M., Carmona, L., & De Thurah, A. (2021c). Supplement_C_PICO_2. In *ResearchGate*. https://rmdopen-2020-November-6-3--inline-supplementary-material-4.pdf
111. Ritschl, V., Stamm, T., Aletaha, D., Bijlsma, J., Böhm, P., Dragoi, R., Dures, E., Estévez-López, F., Gossec, L., Iagnocco, A., Negrón, J., Nudel, M., Marques, A., Moholt, E., Skrubbeltrang, C., Bremt, B., Kirsten, V., Voshaar, M., Carmona, L., & De Thurah, A. (2021d). Supplement_D_PICO_3. In *ResearchGate*. https://rmdopen-2020-November-6-3--inline-supplementary-material-5.pdf
112. Ritschl, V., Stamm, T., Aletaha, D., Bijlsma, J., Böhm, P., Dragoi, R., Dures, E., Estévez-López, F., Gossec, L., Iagnocco, A., Negrón, J., Nudel, M., Marques, A., Moholt, E., Skrubbeltrang, C., Bremt, B., Kirsten, V., Voshaar, M., Carmona, L., & De Thurah, A. (2021e). Supplement_E_PICO_4_Practical things. In *ResearchGate*. https://rmdopen-2020-November-6-3--inline-supplementary-material-6.pdf
113. Ritschl, V., Stamm, T., Aletaha, D., Bijlsma, J., Böhm, P., Dragoi, R., Dures, E., Estévez-López, F., Gossec, L., Iagnocco, A., Negrón, J., Nudel, M., Marques, A., Moholt, E., Skrubbeltrang, C., Bremt, B., Kirsten, V., Voshaar, M., Carmona, L., & De Thurah, A. (2021f). Supplement_F_PICO_4_Non-adherence on outcome. In *ResearchGate*. https://rmdopen-2020-November-6-3--inline-supplementary-material-7.pdf

114. Ritschl, V., Stamm, T., Aletaha, D., Bijlsma, J., Böhm, P., Dragoi, R., Dures, E., Estévez-López, F., Gossec, L., Iagnocco, A., Negrón, J., Nudel, M., Marques, A., Moholt, E., Skrubbeltrang, C., Bremt, B., Kirsten, V., Voshaar, M., Carmona, L., & De Thurah, A. (2021g). Supplement_G_PICO_5_screening of adherence to exercise. In *ResearchGate*. https://www.researchgate.net/publication/353691711_rmdopen-2020-November-6-3--inline-supplementary-material-8pdf
115. Ritschl, V., Stamm, T., Aletaha, D., Bijlsma, J., Böhm, P., Dragoi, R., Dures, E., Estévez-López, F., Gossec, L., Iagnocco, A., Negrón, J., Nudel, M., Marques, A., Moholt, E., Skrubbeltrang, C., Bremt, B., Kirsten, V., Voshaar, M., Carmona, L., & De Thurah, A. (2021h). Supplement_H_PICO_6_what professionals manage adherence. In *ResearchGate*. https://rmdopen-2020-November-6-3--inline-supplementary-material-2.pdf

PHD PORTFOLIO
OF MARIA JOHANNA HELENE VOSHAAR

PHD PORTFOLIO OF MARIA JOHANNA HELENE VOSHAAR

Department:	Apotheek
PhD period:	01/01/2016 - 11/12/2026
PhD Supervisor(s):	Prof. B.J.F. van den Bemt; Prof. A.M. van Dulmen; Prof. M.A.F.J. van de Laar
PhD Co-supervisor(s):	Dr J.E. Vriezekolk

Training activities	
	Hours
Courses	
- Radboudumc - Scientific Integrity (2022)	20
- Radboudumc - eBROK course (2025)	42
Other	
- Co-chair, OMERACT Patient Panel (active throughout PhD period)	75
- Active member, OMERACT Working Group - Patient Definition of Remission	75
- Active member, OMERACT Working Group - Contextual Factors Methods	75
- Active member, OMERACT Working Group - RA Flare Definition	75
- Active member, OMERACT Working Group - Patient Research Partners	75
- Active member, OMERACT Working Group - Total Joint Replacement	75
- Active member, OMERACT Working Group - Shared Decision Making	75
- Active member, OMERACT Working Group - Adherence	75
- Active member, OMERACT Working Group - Worker Productivity	75
- Active member, OMERACT Working Group - Shoulder Pain	75
- Active member, OMERACT Working Group - Patient Preferences	75

– Active member, OMERACT Working Group - Safety	75
– Workshops and advisory activities on Shared Decision Making and medication adherence	60
– Partner, Consortium GLORIA - Horizon 2020 project (2014-2021)	160
– Committee member, ZonMw 'Voor Elkaar' program (2019-2025)	80
– Researcher, NIVEL - SAFEST perioperative patient-safety project (2022-2026)	160
– Board member, Stichting 1op5 (2026)	20
– Author, Oxford Textbook of Rheumatoid Arthritis (2020), Chapter 27, Section 6: Self-management	80
– (Co-)author of 100+ international scientific publications, including 5 publications comprising the PhD research	
Teaching activities	
Lecturing and Conferences	
– Lectures for international healthcare professionals (EULAR HCP) on medication and exercise adherence (2020, 2021, 2024/2025)	40
– Speaker at international congresses, including EULAR and PARE, and at national professional meetings	120
– Courses for patient research partners through Tools2use	120
Total	**1,802**

RESEARCH DATA MANAGEMENT

RESEARCH DATA MANAGEMENT

Ethics and privacy

This thesis is based on the results of research involving human participants, which were conducted in accordance with relevant national and international legislation and regulations, guidelines, codes of conduct, and Radboudumc policy. Statements that Chapter 4 (K17-08), Chapter 5 (2018-4982), and Chapter 6 (2022-13465) were not subject to the Dutch Medical Research Involving Human Subjects Act (WMO), were obtained from the recognized Medical Ethics Review Committee 'METC Oost-Nederland' (Chapter 5 and 6) and Medical Ethics Review Committee Twente (Chapter 4). Chapter 2, a literature-based study, did not require ethical approval as no human data were collected. For Chapter 3, no WMO approval was needed, since participants in this study were not subject to any rules of conduct or burdened with study requirements. In addition, institutional ethical review committees of the Sint Maartenskliniek and Medisch Spectrum Twente have given approval to conduct the studies in Chapter 3 (RR-130-TDF), Chapter 4 (2022-17/73.0), and Chapter 6 (2022-1039).

Funding

The study in Chapter 3, Chapter 5, and Chapter 6 were financially supported by an unrestricted educational grant of respectively Roche (MANL3791R1-G) and Pfizer (WP188931, WP2872684).

Privacy and informed consent

According to Dutch legislation, data collection from electronic patient files was performed by personnel with a treatment relationship with the patient (Chapter 3 and chapter 4), or by the researcher(s) upon consent by the study participant (Chapter 6). The privacy of participants was safeguarded by the use of pseudonymization; the pseudonymization key was stored separately from the research data on secure Sint Maartenskliniek network drives accessible only to authorized researchers. Written informed consent was obtained from all study participants for the collection, analysis, and publication of anonymized data in this thesis. Consent was not obtained for sharing and reuse of the (pseudonymized) data for future research. Due to the sensitivity and confidentiality of the raw qualitative data (Chapters 3, 5-6), which makes sharing the data without compromising confidentiality and privacy impossible, consent for sharing the raw qualitative data was not sought from the participants.

Data collection and storage

Data for Chapter 2 were extracted from published literature using bibliographic databases (e.g., Pubmed). Data for Chapter 3 and 5 were collected through focus group sessions, interviews and questionnaires. Data for Chapter 4 was obtained by using Sawtooth Software (2013) for a secured online maximum difference scaling exercise and converged to SPSS, and data for Chapter 6 was collected through audio-recordings, whereas clinical data was extracted from electronic patient files and converged to Excel. Qualitative data were processed using MAXQDA software.

Raw data from audio-recordings of interviews, focus group sessions, and clinical consultations (Chapters 3, 5-6) are archived in their original form on the institutional server of the Sint Maartenskliniek for 10 years. Processed data and documentation of all studies are archived and securely stored on the institutional server of the Sint Maartenskliniek with automatic backups. These storage practices safeguarded the availability, integrity, and confidentiality of the data.

Data sharing according to the FAIR principles

All studies included in this thesis are published open access. The datasets from Chapter 3-6 are not published with open access. Chapter 2 is based on existing data which was obtained from published literature. The data used for Chapter 3-6 are not owned by Radboudumc. These datasets are archived with closed access for 20 years (Chapter 3-6) by the Sint Maartenskliniek. Questions about the data can be addressed to the research department of the Sint Maartenskliniek.

THESES SINT MAARTENSKLINIEK

THESES SINT MAARTENSKLINIEK

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Radboud University Nijmegen, Nijmegen. The Netherlands.

De Jong, L.A.F. (2023). Effects of lower limb orthotic devices in people with neurological disorders.

Radboud University Nijmegen, Nijmegen. The Netherlands.

Michielsens, C. (2023). Tapering strategies of biologics in inflammatory disorders.

Radboud University Nijmegen, Nijmegen. The Netherlands.

Pouls, B. (2023). Supporting patients'medication management using eHealth. Test cases in rheumatology. Radboud University Nijmegen, Nijmegen. The Netherlands.

Stöcker, J. (2023). Accessible and effective non-pharmacological care for persons with systemic sclerosis. Radboud University Nijmegen, Nijmegen. The Netherlands.

Huiskes, V. (2022). The synergistic role of patients and healthcare providers in reducing drug-related problems. Radboud University Nijmegen, Nijmegen. The Netherlands.

Marsman, D. (2022). Polymyalgia rheumatica. Clinical characteristics and new treatment opportunities. Radboud University Nijmegen, Nijmegen. The Netherlands.

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Van Dijsseldonk, R. (2021). Step into the future: mobility after spinal cord injury.

Radboud University Nijmegen, Nijmegen. The Netherlands.

Pelle, T. (2021). Beating osteoarthritis by e-self management in knee or hip osteoarthritis. Radboud University Nijmegen, Nijmegen. The Netherlands.

Van Heuckelum, M (2020). Novel approaches to improve medication adherence in rheumatoid arthritis. Radboud University Nijmegen, Nijmegen. The Netherlands.

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Bakker, S. (2019). Regional anesthesia and total knee arthroplasty. Anesthetic and pharmacological considerations. Radboud University Nijmegen, Nijmegen. The Netherlands.

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Bekker, C. (2018). Sustainable use of medication. Medication waste and feasibility of redispensing, Utrecht University, Utrecht. The Netherlands.

Bikker, I.(2018). Organizing timely treatment in multi-disciplinary care. University of Twente, The Netherlands.

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Predicting, tapering and transitioning. Radboud University Nijmegen, Nijmegen, The Netherlands.

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Jongerius, P. (2004). Botulinum toxin type-A to treat drooling. A study in children with cerebral palsy. Radboud University, Nijmegen, The Netherlands.

Van de Crommert, H. (2004). Sensory control of gait and its relation to locomotion after a spinal cord injury. Radboud University, Nijmegen, The Netherlands.

Van der Linde, H. (2004). Prosthetic prescription in lower limb amputation. Development of a clinical guideline in the Netherlands. Groningen University, Groningen, The Netherlands.

Hendricks, H. (2003). Motor evoked potentials in predicting motor and functional outcome after stroke. University of Nijmegen, Nijmegen, The Netherlands.

Hosman, A. J. F. (2003). Idiopathic thoracic spinal deformities and compensatory mechanisms. University of Nijmegen, Nijmegen, The Netherlands.

Donker, S. (2002). Flexibility of human walking: a study on interlimb coordination. Groningen University, Groningen, The Netherlands.

Hochstenbach, J. (1999). The cognitive, emotional, and behavioural consequences of stroke. University of Nijmegen, The Netherlands.

De Kleuver, M. (1998). Triple osteotomy of the pelvis. An anatomical, biomechanical and clinical study. University of Nijmegen, Nijmegen, The Netherlands.

Van Balen, H. (1997). A disability-oriented approach to long-term sequelae following traumatic brain injury. Neuropsychological assessment for post-acute rehabilitation. University of Nijmegen, Nijmegen, The Netherlands.

Tromp, E. (1995). Neglect in action: a neuropsychological exploration of some behavioural aspects of neglect. University of Nijmegen, Nijmegen, The Netherlands.

Van Lankveld, W. (1993). Coping with chronic stressors of rheumatoid arthritis. University of Nijmegen, Nijmegen, The Netherlands.

Geurts, A. (1992). Central adaptation of postural organization to peripheral sensorimotor impairments. University of Nijmegen, Nijmegen, The Netherlands.

De Rooij, D. (1988). Clinical and serological studies in the connective tissue diseases. University of Nijmegen, Nijmegen, The Netherlands.

This is not a book to be lightly thrown aside. It should be thrown with great force."

(Naar Bill Miller, To You I Tell It (1929))



Sint Maartenskliniek

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