

Facilitators and Barriers to Adherence in the Initiation Phase of Disease-modifying Antirheumatic Drug (DMARD) Use in Patients with Arthritis Who Recently Started Their First DMARD Treatment

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ABSTRACT. Objective. To explore themes associated with adherence in the initiation phase for first-time use of disease-modifying antirheumatic drugs (DMARD) in patients with inflammatory arthritis using focus groups and individual interviews.

Methods. Thirty-three patients were interviewed in focus groups and individual interviews. Interviews were transcribed verbatim and imported into ATLAS.ti software (Scientific Software Development GmbH). Responses that included reasons for adherence or nonadherence in the initiation phase were extracted and coded by 2 coders separately. The 2 coders conferred until consensus on the codes was achieved. Codes were classified into overarching themes.

Results. Five themes emerged: (1) symptom severity, (2) experiences with medication, (3) perceptions about medication and the illness, (4) information about medication, and (5) communication style and trust in the rheumatologist.

Conclusion. Perceptions about medication and the communication style with, and trust in, the rheumatologist were mentioned the most in relation to starting DMARD. The rheumatologist plays a crucial role in influencing adherence behavior by addressing perceptions about medication, providing information, and establishing trust in the treatment plan. (First Release Dec 15 2014; J Rheumatol 2015;42:379–85; doi:10.3899/jrheum.140693)

Key Indexing Terms:

MEDICATION ADHERENCE RHEUMATOID ARTHRITIS PSORIATIC ARTHRITIS
QUALITATIVE RESEARCH DISEASE-MODIFYING ANTIRHEUMATIC DRUGS

The prognosis of early arthritis is significantly improved by an early, intensive, and tightly controlled treatment with disease-modifying antirheumatic drugs (DMARD) within 3 months of diagnosis^{1,2,3,4}. This, however, requires the patients to adhere to the prescribed medication as soon as possible, which is for some patients too big of a hurdle. Prevalence data on adherence in this early stage are lacking, but there is a significant number of patients not adhering to their medication in the later phase of the disease (1.5%–50.5%, depending on methodology and definition of

adherence)⁵. We may assume that many patients with arthritis also have difficulty initiating medication, because this has been shown for other diseases⁶. It would be helpful to get insight into the reasons for nonadherence in the initiation phase, so that we could intervene at an early stage to prevent the disease from becoming worse⁷.

Adherence to medication is a continuous process that can be divided into 3 parts: (1) initiation (or acceptance), (2) implementation, and (3) discontinuation⁸. In the initiation phase, the patient learns to accept the need for the medication and learns to fit the medication schedule into daily life⁹. The length of the initiation phase differs between diseases. For inflammatory arthritis, we set this stage at 3 months of DMARD use because it takes generally 3 months before the full effectiveness of the DMARD can be felt and tested. The initiation phase is followed by the implementation phase, in which the patient should maintain adherence to the therapy. This phase can last a lifetime because inflammatory arthritis is a chronic disease.

Most studies of adherence focus on the implementation phase, ignoring the part that precedes it: the initiation of medication. For this reason, little is known about determi-

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nants of therapy initiation. For determinants of adherence in the implementation phase, on the other hand, there is a small body of evidence^{10,11,12,13,14}. Garcia Popa-Lisseanu, *et al*¹⁰ reported 4 barriers to medication adherence in patients with rheumatoid arthritis (RA) in the implementation phase: (1) fear of side effects, (2) perceived lack of efficacy of therapies, (3) cost of medication, and (4) difficulty in obtaining treatment in a publicly funded healthcare environment. Other factors found to influence medicine intake in patients with RA in the implementation phase were ignorance and confusion about the medication regimen and interruptions to the daily routine¹¹. For other chronic diseases, beliefs about the necessity of medication and concerns about medication as well as illness perceptions seemed to play an important role in adherence behavior^{15,16}. The necessity-concerns framework is a framework used to improve our understanding of the relationship between patients' beliefs and adherence¹⁷.

It is unknown whether, and to what extent, these determinants of adherence in the implementation phase are also applicable to the initiation phase. Because new patients are not familiar with their disease and medication, and because it takes a while for the medication to have an effect, other factors, such as concerns about having to live with a long-term condition¹⁸, may also play a role. A recent study on preferred outcomes in patients with early RA showed that patients prefer "returning back to normal" and pain relief as outcomes¹⁹. It could well be that these preferred outcomes are also factors influencing adherence behavior. Knowing these factors may help clinicians to identify factors that influence DMARD initiation and thereby optimize treatment effectiveness. In overcoming the gap in literature regarding factors influencing medication initiation, we used qualitative methodologies to study the reasons for DMARD initiation and visualize the data synthesis in a conceptual model.

MATERIALS AND METHODS

Design. We set up focus groups that allowed for an interactive discussion on the topic of adherence, to generate data²⁰. Focus groups were set up until the same topics of adherence kept reoccurring in multiple groups. During the recruitment for these group interviews, it became apparent that patients willing to participate were rather adherent. Because we were interested in barriers to adherence, we also wanted to include less-adherent patients in our sample. Therefore, 10 additional individual interviews were conducted with less-adherent or nonadherent patients. Individual interviews made it possible to adapt the interview setting to specific preferences of these patients and to ensure that they felt safe to open up about nonadherence.

Recruitment. Forty consecutive patients were invited by their rheumatologists from the Erasmus Medical Center (EMC)'s Rheumatology Department to participate in focus groups, of whom 24 were able and willing to participate. Main reasons for nonparticipation were not being able to travel, or no interest. Six focus groups were formed with 3 to 6 patients. One interviewee did not fulfill the inclusion criteria and was excluded from analysis. For the individual interviews, rheumatologists asked patients whether they either had a delayed start with DMARD, altered their medication dose, or

took their medication intermittently. When patients responded with "yes," they were invited to participate. Twelve patients were invited, of whom 10 were willing to participate.

Inclusion criteria were a minimum age of 18 years, and a prescribed treatment with DMARD that started less than 2 years ago for polyarthritis (RA, psoriatic arthritis, and unclassified inflammatory arthritis) to ensure that they could recall starting medication. All patients had symptomatic disease for which they required standard care (Figure 1) and DMARD. Approval was gained by the EMC Medical Ethics Committee, and all subjects gave consent for participation.

Measures. A semistructured interview schedule was developed based on items found during a literature review²¹ and on relevant determinants of the Health Belief Model, a frequently used behavioral model in healthcare in which perceived barriers and benefits of behavior are weighted against each other²². Lead questions were "How was your experience when you started the medication?" and "What were your considerations before starting the medication?" The interview guide is available upon request.

Procedure. A male psychologist (AS) and a female epidemiologist (JL) with experience in conducting interviews each led 3 focus groups that were held at a quiet location in the hospital. During the focus groups, participants were invited to discuss and share experiences with each other. The sessions lasted about 90 min. One female researcher (AP) interviewed 10 participants individually by telephone or face-to-face at the hospital. These interviews lasted 20–90 min. The interviewers introduced themselves as being

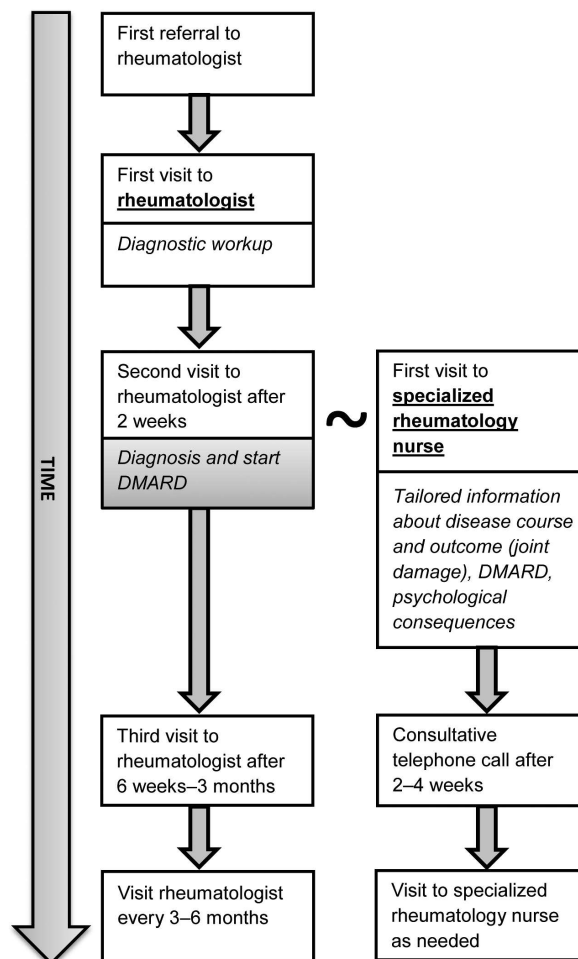


Figure 1. Standard rheumatology care for patients with arthritis in the first 3 months. DMARD: disease-modifying antirheumatic drug.

interested in the topic of adherence and emphasized the confidentiality of the interviews. Focus groups and individual interviews were audiotaped with prior consent of all participants and transcribed verbatim. Field notes were made during the interviews. To ensure anonymity, identifying information was removed from the transcripts.

Data analysis. Transcripts were imported into ATLAS.ti software (Scientific Software Development GmbH), which facilitates qualitative content analyses. Field notes were used to verify discrepancies in the transcripts. The thematic analysis of the transcripts was inductive; the formation of themes was driven solely by the data content²³. The inductive analysis followed guidelines described by Arcury and Quandt²⁴. One coder (AP) read the interview transcripts several times to familiarize herself with the data. Statements by patients that included reasons for the initiation of DMARD were coded with the key word that identified the dominant content of the quote. The codes were then categorized and grouped into overarching themes. A second investigator (MW) read and coded 2 transcripts independently of the first coder. The 2 investigators discussed the themes until consensus was achieved. A comprehensive model was formed based on the themes. The number of quotes was counted as an indication of the importance of the theme.

RESULTS

Demographics of the participants. Table 1 summarizes the participants' demographic characteristics. Although the inclusion criteria stated that patients had to have a prescription for DMARD for less than 2 years, 4 participants received their first DMARD prescription more than 2 years ago with a median of 3 years because they delayed their start with DMARD.

Themes. Below we describe the themes that influenced the initiation of DMARD and illustrate them with typical quotes. Table 2 summarizes the themes and the number of quotes per theme.

Symptom severity. Symptom severity was not only determined by specific arthritis pain, but also by fatigue and feelings of disability caused by arthritis. Patients stated that the more severe their complaints were, the more likely they were to take the medication.

“Well, you do take them if it hurts. That’s the thing. If it

hurts, you take them. [...] It’s that simple.” (P1, Female, 62 years old, RA.)

Experiences with medication. Previous negative experiences with any kind of medication before starting with DMARD could affect perceptions about DMARD and therefore could inhibit initiation.

Some patients received a corticosteroid injection as a bridging therapy and immediately felt the positive effect of this injection. This caused a positive attitude toward taking DMARD.

“I took the tablets for the first time and at night I needed to go to the bathroom [...]. I walked to the door and noticed that I was there right away. I thought ‘wow, this seems like a miracle.’ And then I started using methotrexate. And my first experience was this positive that I believed it only worked in a positive way.” (P2, Female, 69 years old, RA.)

After their first intakes of DMARD therapy, patients started weighing the symptom severity against the perceived experiences with the medication. A reason to stop using DMARD was if the side effects of the medication out-weighed the symptom severity.

“When I started taking the sulfasalazine as well, I felt so miserable. I’d just start crying for no reason at all. [...] I felt sick and ... I think I’d rather have the darn pain than feel like that.” (P3, Female, 47 years old, RA.)

Perceptions and feelings about medication and the illness. Negative perceptions about medication in general or about DMARD in particular were the most frequently mentioned reasons for reluctance to initiate DMARD. Most patients had difficulty explaining why they had these negative feelings about DMARD. Some patients regarded these medicines as “poison,” but when asked to explain further, patients responded with more nuanced expressions such as “it is just not natural” or “I don’t want this in my body.” Participants explained how perceptions about medication were shaped by numerous factors, e.g., previous negative experiences with medication, not accepting the diagnosis, influence from important others, and available information about the medication.

“I often didn’t take them because I was like: ‘No, this is junk, I’m not putting that in my body. Never had to take any pills and now I have to...’ Just reading the leaflet got me saying: ‘No way, this is not for me’.” (P4, Female, 35 years old, RA.)

“But, in the past, I didn’t want to use any pills. When I had a headache, I thought, oh, it will pass. And then you find yourself standing with a box [of medicines] in your hands.” (P3, Female, 47 years old, RA.)

“Because I think, they are means from the outside, and why can’t my body heal itself? Why am I just not healthy from nature?” (P5, Female, 41 years old, RA.)

Mostly, taking medication symbolized for patients that they had become a chronic patient with a serious illness. Nonadherence was a way of resisting this new position.

Table 1. Demographics of the participants.

Characteristics	Total, n = 33
Female, n	29
Median age, yrs (IQR)	51 (39–59)
Time since diagnosis	
≤ 1 yr	12
> 1 to ≤ 2 yrs	12
> 2 to 5 yrs	9
Median time since medication, mos (IQR)	13 (6–19)
Diagnosis	
RA	23
PsA	10
No. DMARD	
1	12
> 1	21

IQR: interquartile range; RA: rheumatoid arthritis; PsA: psoriatic arthritis; DMARD: disease-modifying antirheumatic drug.

Table 2. Overview of the 5 themes into which the respondents' reasons were grouped.

Themes	Examples of Reasons Mentioned	No. Quotes
Symptom severity	Pain, fatigue, disability.	46
Experiences with medication	Previous experience with medication for other diseases or current experience with DMARD, side effects.	61
Perceptions about medication and the illness	Expectations about medication, confrontation with having a chronic illness by the use of medication.	89
Information about medication/ knowledge acquisition	In the early phase, patients started gathering information. Information obtained from the rheumatologist, the medication information leaflet, or by searching the Internet.	15
Communication style and trust in the rheumatologist	The rheumatologist should build toward a trustful relationship, for instance by acknowledging fears about medication and explaining the treatment plan in detail.	54

DMARD: disease-modifying antirheumatic drug.

Some patients felt their health depended too much on the medication. Other patients were angry because they felt betrayed by their own body. The patients seemed to be in a state of denial and were reluctant to start with medication.

“No. Because then you feel like you really are sick, as it were. That you actually have something. And I didn't want to start, and I ... I keep repeating to myself: ‘I don't have arthritis, I don't have arthritis. I'm too young.’” (P5 Female, 41 years old, RA.)

Fears and doubts about the longterm effects of DMARD were also mentioned as a reason for nonadherence. Some interviewees said they felt that if they took the DMARD, it would shorten their lives because the medication could have serious side effects on their liver and kidneys. They accepted that nonadherence would result in higher levels of pain.

Some patients had the feeling that they had no choice whether to start with the medication. The quote below explains this feeling:

“Honestly, I am fed up with it. But I have no choice [but to take the medication]. You will not get away without it. Because, how else would I go on?” (P1, Female, 62 years old, RA.)

Information about the medication. Information about medication shaped perceptions about medication, which in turn influenced adherence. The 3 main information sources were the rheumatologist, the medication leaflet, and the Internet.

“And then you start looking and searching on the Web. And when I read what a hassle it [the medication] can give, I thought to myself: ‘My God, what if I get all those things!’ Because I think, then I don't want it [the medication] any longer.” (P1, Female, 62 years old, RA.)

Patients used these information sources differently. The medication leaflet mostly focused on medication effects and side effects, whereas rheumatologists gave tailored information and could also address the patient's emotions. Most

patients gained information from the Internet from Websites with an unclear source.

Communication style and trust in the rheumatologist. The rheumatologist's communication style and patient trust in the rheumatologist were mentioned frequently as reasons to initiate DMARD. Patients talked about the need to trust their rheumatologist to feel able to adhere to the medication. To build this trust, the patients said that the rheumatologist needed to acknowledge the patient's fear of medication. Being interested in the patient's needs, doubts, and fears, and a thoughtful response to these items were mentioned as important, as was the way of providing information about the medication and its side effects by the rheumatologist. Indeed, an open and trustworthy communication with the rheumatologist was regarded as the most effective way to modify the patient's knowledge and perceptions about medication. Miscommunication about medication types and dosages were reported as serious events that could easily break the trust in the rheumatologist.

“And she [the rheumatologist] knew how frightened I was, but she just accepted it. And that was really important to me. She didn't say like: ‘Yeah, well, what nonsense. If you don't take this then that's your lookout, your loss.’ No, she accepted it and dealt with it. And that's what persuaded me quite quickly, from that point on really, to just start taking the pills.” (P6 Female, 62 years old, RA.)

Data synthesis. To synthesize the data, relationships between the themes were explored by visualizing them in a model (Figure 1). When a patient experienced symptoms and became a patient, certain perceptions about the disease and the medication started to play a role. The perception that medicines were poisonous could amplify feelings of anxiety about medication. This in turn could delay the patient's medication initiation. This influenced the severity of complaints, and the chain went on as the patient would consult the rheumatologist again. The rheumatologist could address the patient's perception about medication and the

disease, and thereby break the chain. Information about medication and the disease could also change patient perceptions.

DISCUSSION

To our knowledge, ours is the first study that explicitly focuses on the initiation part of the adherence process in patients with inflammatory arthritis, involving perceived barriers and facilitators to initiate DMARD. Five themes emerged: (1) symptom severity, (2) experiences with medication, (3) perceptions and feelings about medication and the disease, (4) information about medication, and (5) the rheumatologist's communication style and the patient's trust in the rheumatologist. As depicted in the conceptual model (Figure 2), the themes influence each other. Perceptions about medication and illness are the most modifiable and can be targeted through the rheumatologists' communication efforts, and through the information received about DMARD and the disease.

No previous studies were available on factors influencing DMARD initiation, but previous qualitative studies on factors influencing adherence in established disease

reported the same 5 themes^{10,12,13,14}. This suggests that we could use similar interventions to promote adherence, although there will be differences. Beliefs about the disease and medication play a role in both the initiation and implementation stages, but they vary. Newly diagnosed patients may have had more general beliefs about the harmfulness and expected effectiveness of medication while patients with established disease may have had more specific cognitions about the necessity of the medication. In the first part of DMARD intake, the rheumatologist has a better opportunity to influence adherence than in a later stage because of the often more frequent visits to the rheumatology clinic, and this interaction can be used to build up trust and change perceptions about the disease and medication.

Known demographic variables influence adherence⁵, but are not modifiable. The patient's perspective, as studied in our paper, gives us more clues for the development of interventions because psychosocial variables such as perceptions are modifiable. Our model (Figure 2) suggests that the theme to target is "perceptions about the medication and the illness." Perceptions are the most modifiable themes in our model²⁵, and can be changed with cognitive behavioral

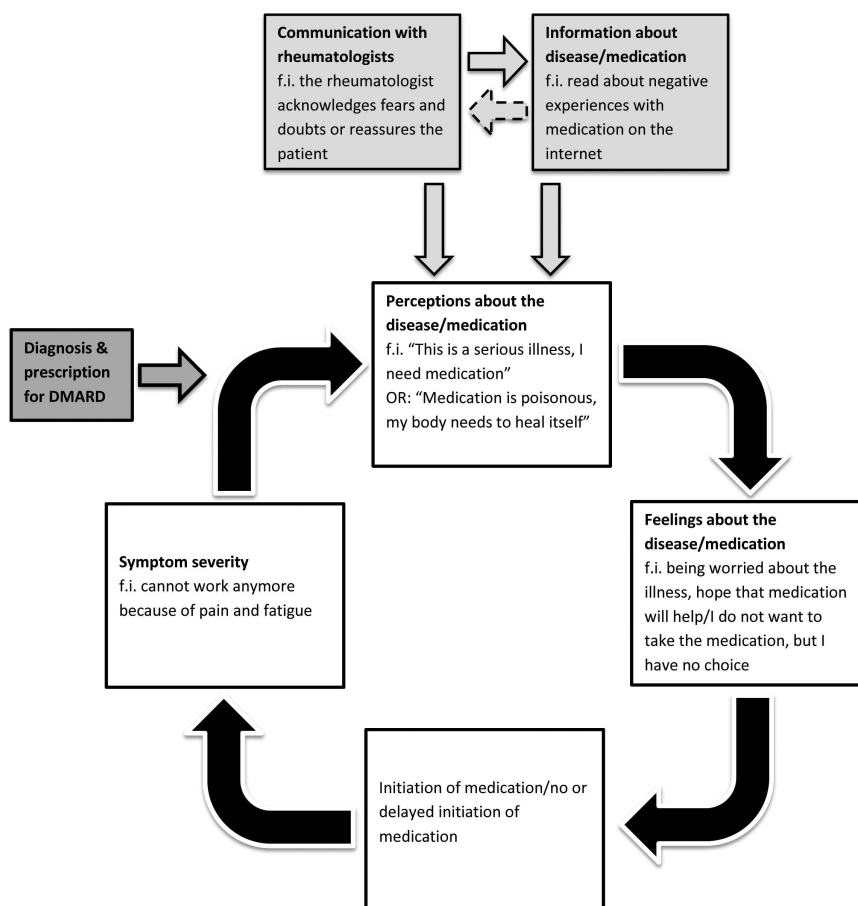


Figure 2. Conceptual model of themes that influence the initiation of medication. DMARD: disease-modifying antirheumatic drug.

techniques, among others. Because trust in the rheumatologist is a key factor, challenging these perceptions in an empathetic way may increase both adherence and the relationship with the rheumatologist.

In patients with established disease, shared decision making is often mentioned as an important topic influencing adherence. In our sample, this was not mentioned. It could be that patients in the months after diagnosis were rather passive and left decisions to their rheumatologist. In a later stage, they became more aware of what they needed and might have been more open to shared decision making.

When elaborating on symptom severity, patients spoke about pain and not about the preventive effects of taking DMARD for potential joint damage. Apparently, patients did not prioritize the preventive effects of DMARD. This low priority was also seen in low adherence rates for other preventive medicines, such as for blood pressure-lowering medication²¹. This might also be an important topic for rheumatologists to address. The speed at which physical improvement takes place might be an important cue for patients that medicines are working and thus influences necessity beliefs.

Although appointments with a specialized rheumatology nurse were firmly embedded in the first months of rheumatology care, interviewees did not mention them in regard to adherence behavior, but they did mention the rheumatologist's role. From our data, it seems that patients viewed the rheumatologist as an authority and this may be why patients only mentioned the role of the rheumatologists.

Our study has several limitations. Interviewees' inclusion in our study depended on the willingness to participate. It could be that we missed patients with particular adherence characteristics that were associated with response to our request to participate. We did not involve patients in the design of our study, which might have been helpful in the study setup. For instance, we missed less-adherent patients in the focus groups and had to conduct additional individual interviews to identify the nonadherent patients' viewpoints. Patients' responses about the start of DMARD intake relied on recall, and could not be verified by other means. Recall bias might have affected feelings about the importance of communication with the rheumatologist, as well as feelings about symptom severity. However, all patients were prescribed DMARD, suggesting that the arthritis symptoms were indeed severe. It might have been more desirable to include patients who received DMARD between 6 and 12 months, but because of difficulties with finding patients in this disease phase, we expanded our inclusion criteria. Most of the interviewees were women, which may mean that the male viewpoint is slightly underrepresented. However, the topics mentioned by the interviewees were not sex-specific and thus were generalizable to both men and women.

Future research should combine quantitative and qualitative methodologies so that the focus lies on both the

patient perspective and the healthcare provider perspective. Our present study gives insight into which themes are involved in nonadherence behavior. The second step would be to perform a quantitative study that shows which themes are most prevalent. That way we gain a proper understanding of the extent of the nonadherence problem, and we will have a clear body of evidence for determinants to target. The third step is to develop a theory-based and evidence-based intervention, as the intervention-mapping protocol describes^{26,27}.

If we bundled these steps into a protocol, we could test whether these suggestions indeed make a difference in adherence to DMARD in patients with early arthritis. Our findings suggest that the rheumatologists' communication efforts may play a decisive role in patients' initiation of DMARD. The rheumatologist should be aware that a newly diagnosed patient may have negative perceptions about medication in general or specific to DMARD, depending on the patient's health literacy. Tailored information gained by the rheumatologist eliciting prior expectations about DMARD can influence these perceptions. Changing the perceptions will, as outlined in our model, improve adherence in the initiation phase of DMARD.

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