Improving treatment adherence in patients with rheumatoid arthritis: what are the options?

Low adherence to therapeutic regimens is a prevalent and persistent healthcare problem, particularly for patients with chronic disorders. Many patients with rheumatoid arthritis (RA) show inadequate therapeutic adherence resulting in poor health outcomes. Reasons for nonadherence can be unintentional or intentional. The characteristics of patient–doctor interactions are also likely to play a role although they have not been well studied for patients with RA. While many educational and cognitive behavioral interventions have been proposed to improve adherence, the few studies that have examined the efficacy of these programs in RA have had disappointing results. Future studies involving the use of mobile technologies have shown promise in other chronic diseases and could prove useful for patients with RA.

Keywords: • adherence • educational interventions • patient education • rheumatoid arthritis

Medical prescribing is the most common intervention in daily clinical practice. The treatment of chronic illnesses commonly includes the long-term use of pharmacotherapy. Although drug therapy can be effective in chronic disease, full benefits are often not realized because many patients do not take their medications as prescribed [1,2]. Poor adherence contributes to poor clinical outcomes and increased healthcare utilization and costs [3].

Rheumatoid arthritis (RA) is a chronic, inflammatory, destructive joint disease, characterized by painful, tender and swollen joints. It is associated with major consequences for affected individuals, causing loss of function, poor quality of life, work disability and important societal economic consequences. Treatment with disease-modifying antirheumatic drugs (DMARDs) typically begins shortly after RA diagnosis. Different agents are currently available, including conventional or targeted synthetic DMARDs, and biologic DMARDs. Patients often also use NSAIDs and steroids to alleviate pain and swelling [4]. Currently, rec-

ommendations for treatment endorse 'treatto-target' strategies, including increasing drug dosages, adding therapeutic agents or switching drugs to achieve remission or at least low-disease activity. 'Treat-to-target' disease management can reduce symptoms, structural and radiological progression and improve long-term outcomes in patients with RA [5]. In order to achieve therapeutic goals, this strategy requires adequate patient adherence to physician recommendations. Low adherence in patients with RA may result in substantial costs, disease progression, increased disability and additional medical therapy, and sometimes surgery, later on [6]. Enhancing adherence can therefore improve the effectiveness of medical recommendations and reduce health and financial costs associated with RA. The objective of this review is to summarize the recent literature on determinants of adherence, and related interventions, that can improve therapeutic adherence in patients with RA.

Compliance, concordance & adherence: evolution of terminology

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over time

Medical terminology regarding medicine-taking behaviors has evolved following our understanding of issues related to individual attitudes and factors related to following healthcare recommendations [7].

Compliance was initially used to define 'the extent to which the patient's actual history of drug administration corresponds to the prescribed regimen' [8]. However, this concept reflects to some degree a paternalistic approach to the patient-physician relationship: the physician selects what the most appropriate treatment is and decides for the patient. A broader definition was proposed later on: 'the extent to which a person's behavior in terms of taking medication, following diets or executing lifestyle changes coincides with medical or health advice' [9]. Over time, the concept of compliance has become more patient centered. The term concordance has been used to refer to 'the extent to which patients are successfully supported both in decision-making partnerships about medicines and in their medicine taking' [10]. It implies a consensual agreement about treatment established between patient and practitioner [11]. Currently, the term adherence is more often defined as 'the extent to which patients follow through decisions about medicine taking' [12]. This term incorporates the broader notions of concordance, cooperation and partnership, in the adoption of medical advice [13]. Treatment adherence has three components: initiation (when the patient takes the first dose of a prescribed medication), implementation (defined as the extent to which a patient's actual dosing corresponds to the prescribed dosing regimen, from initiation until the last dose is taken) and discontinuation (when the next dose to be taken is omitted and no more doses are taken thereafter) [14].

Measurement of adherence

Adherence can be assessed using direct or indirect methods. Direct methods include performing biologic assays (metabolites or markers) and direct observation. Biologic assays may seem as the most precise method but they are not readily available for many drugs, they are expensive and impractical for patients and their interpretation can be hindered by individual pharmacokinetics [15]. Direct observation is performed by administering the medication or observing the patient ingesting or autoadministrating it. This is only practical for single-dose therapies, spaced intermittent administration or for patients attending infusion centers or in hospital [13]. Direct measures are difficult to implement because of their invasiveness and high cost. Indirect methods include review of pharmacy prescription filling data, patient diaries, pill counts and patient interviews. Indirect methods are more frequently used

than direct ones [13,16]. Self-report methods are less costly and easier to use but can result in overestimation of adherence [17]. Advances in technology have enabled the development of a modern indirect method based on electronic monitoring of medication taking. An example is the medication events monitoring system, which has an electronic chip in the cap of a medicine bottle. Each time the bottle is opened, the chip records the time and date of the opening. The system uses special software to download the chip information and to estimate a variety of adherence measures. It is considered the best indirect method to measure adherence. While it is assumed that a dose is taken every time the bottle is opened, it cannot be proven that the dose has indeed been taken. However, it is unlikely that patients would elect to open the bottle at the required times during the period of observation and then would not take the medication [17].

Unfortunately, despite the clinical importance of suboptimal medication adherence, adherence behaviors are not systematically considered in clinical practice. While several methods have been used for research, there is no validated simple measure proposed to measure adherence in clinical settings. Patients may have a social desire to please their providers and report high adherence when asked as part of the medical interaction. Moreover, patient attitudes and behaviors toward their treatments may vary over time, from visit to visit. Failure to ascertain and discuss adherence regularly can result in inaccurate assessment of therapeutic effectiveness.

Nonadherence: a complex process

Seeking, evaluating and following medical advice involves many steps, which can be influenced by individual clinical aspects, psychosocial constructs, elements of the medical interaction, specifics of the treatments recommended, and external environmental and societal factors. Examples of nonadherence include not filling a prescription, taking an incorrect dose or taking the medication at wrong times (underuse and overuse), stopping the treatment too soon without a physician's or healthcare provider's advice (secondary noncompliance) and failing to make or attend recommended healthcare appointments [13].

Nonadherence behavior can conceptually be categorized into unintentional or intentional. Unintentional nonadherence is generally due to forgetfulness, lack of understanding of recommendations or intercurrent illnesses or events. Intentional nonadherence is based on the patient's decision to stop treatment or modify prescribed regimen, for example, lower dosages than those prescribed. Intentional nonadherence is influenced by the patients' beliefs about the effectiveness of the

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Study (year)	Medication	RA patients (n)	Study type	Adherence method	Adherence	Ref.
Deyo <i>et al.</i> (1981)	NSAIDs Penicillamine	171	6 months longitudinal	Refill rates	NSAIDs: 58–73% Penicillamine: 84%	[54]
Owen <i>et al.</i> (1985)	NSAIDs Traditional DMARDs	178	Cross-sectional	Interview	64%	[55]
Pullar e <i>t al.</i> (1988)	Penicillamine	26	Cross-sectional	Patient interview	96%	[56]
				Pill count	77%	
				Pharmacokinetic marker	58%	
				Estimation physician	42%	
Doyle <i>et al.</i> (1993)	Penicillamine	59	Cross-sectional	Pharmacokinetic marker	39%	[57]
Taal e <i>t al.</i> (1993)	Global treatment	96	Cross-sectional	Interview	93%	[58]
Brus e <i>t al.</i> (1999)	Traditional DMARDs	55	6 months randomized clinical trial	Pill count	Intervention group: 82%	[59]
					Control group: 91%	
Viller <i>et al.</i> (1999)	Global treatment	592	Longitudinal (36 months)	Interview	Baseline adherence: 59– 65%	[60]
					Consistent adherent: 36%	
					Consistent nonadherent: 24%	
Park <i>et al.</i> (1999)	Global treatment	121	Longitudinal (1 months)	MEMS	Perfect adherence: 38%	[20]
De Klerk <i>et al.</i> (2003)	Traditional DMARDs	127	Longitudinal (6 months)	MEMS	NSAIDs: 76-82%	[17]
					Methotrexate: 107%	
					Sulfasalazine: 72%	
Tuncay e <i>t al.</i> (2007)	Global treatment	100	Longitudinal (6 months)	Interview	Baseline adherence: 52%	[61]
					Consistent adherent: 30%	
					Consistent nonadherent: 12%	
Curkendall <i>et al.</i> (2008)	Etanercept	2285	Longitudinal (12 months)	Refill data	22–56% (depending copayment)	[62]
	Adalimumab					
Garcia- Gonzalez <i>et al.</i> (2008)	Global treatment	70	Cross-sectional	Interview	50%	[63]

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Study (year)	Medication	RA patients (n)	Study type	Adherence method	Adherence	Ref.
Borah <i>et al.</i> (2009)	,	3829	Longitudinal (12 months)	Refill data	Adalimumab: 63% (naive users) 70% (existing users)	[64]
					Etanercept: 65% (naive users) 73% (existing users)	
Van der Bernt <i>et al.</i> (2009)	Traditional DMARDs	228	Cross-sectional	Interview	99%	[65]
				Questionnaires (CQR-MARS)	66–67%	
Contreras- Yañez <i>et al.</i> (2010)	Traditional DMARDs	93	Longitudinal (6 months)	Interview	51%	[66]
Grijalva <i>et al.</i> (2010)	Traditional and biological DMARDs	14,586	Longitudinal	Refill data	Methotrexate: 59%	[67]
					Leflunomide: 69%	
					Hydroxychloroquine: 49%	
					Sulfasalazine: 33%	
					Etanercept: 73%	
Waimann e <i>t al.</i> (2013)	Traditional DMARDs and steroids	107	Longitudinal (24 months)	MEMS	DMARDs: 64%40%	[19]
					Methotrexate: 63%	
					Leflunomide: 71%	
					Hydroxychloroquine: 63%	
					Sulfasalazine: 58%	
					Prednisone: 70%	
Rauscher <i>et al.</i> (2015)	Traditional DMARDs	78	Longitudinal (3 months)	CQR (results expressed using overall weighted CQR)	Adherent based on taking compliance: 14%	[22]
					Adherent based on correct dosing: 4%	
Chu <i>et al.</i> (2015)	Etanercept (n = 1587)	2151	Retrospective (24 months)	Refill data	Proportion of days covered for etanercept: 67%	[68]
	Adalimumab (n = 564)				Proportion of days covered for adalimumab: 63%	
					Attrition rate for etanercept: 32%	
					Attrition rate for adalimumab: 43%	

Study (year)	Medication	RA patients (n)	Study type	Adherence method	Adherence	Ref
Bliddal <i>et al.</i> (2015)	Methotrexate	18,703	Retrospective	Refill data	Mean adherence time in private practice: 1925 (IQR: 467–3056) days	[69]
					Mean adherence time in patients treated in hospital : 1892 (IQR: 452– 3316) days	

healthcare recommendation, their knowledge about the disease and their self-efficacy to achieve proposed health goals. Conceivably, nonadherence is most often multifactorial and therefore, interventions tailored to meet each patient's needs may be more successful in improving adherence [13,18].

Prevalence & consequences of nonadherence in rheumatoid arthritis

Reports of patients' adherence to their medications range from 14 to 80% [18-22]. Table 1 shows a summary of studies reporting treatment adherence in RA. Adherence to biologic agents appears to be higher than adherence to conventional synthetic DMARDs. Studies using Medication Events Monitoring System devices and refill data generally show lower adherence than those using self-report measures. The variation in adherence rates in RA can be related to the patient population under study, the method used to measure adherence and the drug class. Adherence to biologic agents seems to be higher.

Low adherence has been shown to negatively impact RA outcomes, with increased disease activity and radiological progression rates in patients who do not adhere to recommended therapeutic regimens [19].

Determinants of adherence in patients with rheumatoid arthritis

Nonadherence is most often multifactorial, and can fluctuate over the course of the disease. Prompt recognition of factors leading to nonadherence can assist healthcare providers in identifying patients at risk of poor adherence.

The WHO has identified several factors as determinants of adherence to healthcare recommendations including: healthcare systems, patient-provider relationship, disease characteristics, recommended treatment and socioeconomic factors [1]. In addition, a number of psychosocial factors related to patients' attitudes toward their disease and treatment, their selfefficacy to manage their disease, and their social support and environment also play a major role in adherence behaviors.

Healthcare systems

Patients with poor access to healthcare facilities, often from disadvantaged socioeconomic strata, can encounter multiple barriers that interfere with their adherence to healthcare recommendations. They can experience problems navigating the health system, financial difficulties to pay for services or therapies not covered and gaps in coverage. A study of patients with RA and systemic lupus erythematosus with low socioeconomic status reported that patients experienced financial problems and barriers to appointment keeping, which included transportation and difficulties in scheduling, which hindered their ability to adhere to healthcare recommendations [23].

Patient-provider relationship

Several studies have reported that good quality communication between physician and patient increases patient adherence to treatment in the primary care setting [24–26]. Studies that have addressed patient–doctor communication in patients with rheumatic disease have not specifically addressed adherence [27–29]. Nevertheless, these studies have shown that rheumatic patients have difficulties in the interaction with their providers, especially those from ethnic minorities and lower education. This emphasizes the need to focus on patients' preferences and values to deliver individualized patient-centered care that could potentially enhance adherence [27,30–33].

Disease characteristics

Clinical characteristics and disease severity can influence adherence. Patients with RA who had shorter disease duration, better mental health and lower disease activity were shown to have better adherence than patients without opposite characteristics [19].

Recommended treatment

Type of therapy, including administration route, frequency of dosing and incidence of adverse events are all factors that can determine adherence to therapy. In general biologic DMARDs show higher rates of adherence than oral agents. Medication burden, including number of pills, injectables or drugs administered through other routes for various indications also can determine individual adherence; the more complex the regimen, the lower the adherence. The effect of pill burden in RA has not clearly been established, although one study did not show a clear impact [19].

Demographic & socioeconomic factors

While some studies have reported that older patients are more adherent to therapy than younger ones, others have not found this relationship [18]. Being married has also been associated with higher adherence [19]. In general, patients with lower education and socioeconomic status are more likely to have poor adherence than those in higher socioeconomic strata; however, these findings are often difficult to discern because they are closely inter-related to barriers in access to care. While health literacy has been proposed as a determinant of adherence, a study in patients with RA did not find a significant association between these two constructs [34].

Psychosocial factors

Many factors related to patients' knowledge, attitudes and behaviors have been associated with nonadherence, specifically intentional nonadherence. Lack of knowledge about the disease and its treatment, perception of lack of effectiveness and fear of adverse events can result in patients' intentional discontinuation or irregular adherence to prescribed medications [35]. These beliefs can result in poor self-efficacy and selfmanagement skills, which have been related to the ability of patients to follow and maintain prescribed recommendations.

Interventions to enhance treatment adherence

Interventions targeting adherence must incorporate health behavior changes. Not only is it difficult to change established behavior patterns, maintenance of these behaviors can be even more challenging. Evidence suggests that simply providing patients with information and advice, or using dominant or persuasive communication, do not result in permanent changes in adherence health behaviors.

Historically, adherence interventions have proposed logistic techniques such as simplifying dosage regimens and providing adherence aids or education to address the practical issues of adherence; however, these interventions have only demonstrated marginal effects [36]. While they might be somewhat useful, alone, they are unlikely to change intentional behaviors in the majority of nonadherent patients.

The transtheoretical model [37] proposes that changes in behavior follow consecutive steps: an initial motivational stage, when people become motivated to take action; an action stage, when people engage in active changes in behavior, requiring support and guidance; and a maintenance or disengagement stage, where the efforts are placed in maintaining desired behaviors and preventing relapse into maladaptive or unhealthy behaviors [38]. Through an understanding of the challenges faced in changing behaviors, novel cognitive-based behavioral techniques have emerged. These interventions aim to change a patient's behavior by altering their thoughts, feelings, confidence or motivation to adhere. These interventions can vary widely in content and can include techniques and skill-based instruction to enhance patients' sense of self-efficacy, motivation and problem solving [36].

Educational interventions

Historically, patient education has been an integral part of the clinical care. Traditionally, education was imparted informally by the physician or nurse [39]. It was shown that simply providing patients with information or advice was not sufficient enough to change health behaviors [38]. More recent educational interventions have included other activities beyond providing information on the disease and its treatment [39]. More current patient education programs include activities designed and planned to result in the adoption of skills and behaviors, beyond disease knowledge alone.

Knowledge-based informational interventions primarily provide educational materials designed to improve patients' knowledge about their disease and treatment, and the importance of adherence. The information can be delivered as lectures, or using educational tools – booklets, workbooks, audiotapes videos or computer-based lessons. These interventions may include reinforcement or support from healthcare professionals. Information is the primary emphasis.

Psychoeducational interventions can encompass a broad range of activities such as counseling and supportive interventions [40]. These interventions can be delivered individually or in groups and can include peer support and family participation. Psychoeducational interventions in addition to providing patients with information about their disease and therapy, also provide resources and services and training on skillbuilding and problem-solving strategies for coping with the disease. They can include booklets, videos, audiotapes or computer interactive programs and can also provide direct interaction with professionals and peers [39,41]. Studies using these interventions are heterogeneous, varying in specific content, format, frequency and timing of interventions.

Cognitive behavior programs based on the social learning theory propose that humans observe the behaviors of people around them, encode their behavior and later on imitate the behavior they have observed [42]. Programs based on this theory encompass three phases: information (simple explanation of the disease and the inter-relationships between its emotional, cognitive, physical and behavioral components), learning new skills (e.g., relaxation, diversion, cognitive restructuring) and maintenance (transferring new skills to everyday life). These programs need to be led by psychologists or specially trained professionals.

Self-management programs are based on the selfefficacy theory. Self-efficacy is the belief that one has the power to produce a desired effect by completing a given task or activity related to that competency [43]. Self-efficacy programs provide a combination of disease-related information and assistance in learning and adopting new activities and skills. The emphasis is in changing behaviors by presenting disease-related information, learning skills activities (e.g., exercise, relaxation, energy saving techniques) and using group interaction and mutual support. This program emphasizes improving self-efficacy and may be led by trained laypersons or peers.

Motivational interviewing is based on cognitive behavior change techniques. It aims to change behaviors by attaining the motivation necessary to achieve change. It attempts to change thoughts, feelings, confidence or motivation through a personalized patientcentered approach [27]. Through brief interactions, counselors can assist patients in exploring and resolving their ambivalence regarding a specific behavior and ultimately to consider what might be gained through change. Motivational interviewing elicits information from the patient, supporting his/her autonomy and attempts to activate his/her own internal motivation for change [28].

Motivational interviewing has been gaining increased interest in healthcare settings, as it appears to result in better health outcomes than traditional advice giving. It has been used to enhance medication adherence in pharmacy and healthcare settings [29,30]. Alternatives to the more traditional face-to-face interviewing include telephone-based interventions, self-help printed workbooks and computer-based programs [30]. While motivational interviewing primarily addresses intentional nonadherence, it can also aid patients in identifying unrecognized unintentional barriers to adherence and in seeking out patient-centered solutions [36].

A recent systematic review evaluated the effect of telephone-based motivational interview to improve medication adherence in chronic diseases (not RA), showing a beneficial effect of this intervention in increasing adherence in long-term treatments [44].

Peer support programs, in-person or virtual, are increasingly being proposed as a means to enhance positive health behaviors. However, while these groups can improve disease knowledge and sense of support, there is little information as to whether, on their own, they can foster improved health behaviors or adherence.

Mobile technology programs are increasingly being used to improve adherence with medication reminders, and to enhance self-efficacy through the use of informational and supportive messaging. A recent metaanalysis showed that the use of mobile phone messaging applications (short message service) may provide benefit in supporting the self-management of longterm illnesses in patients with diabetes, asthma and hypertension [45]. Multimedia message services can be developed for delivering tailored health strategies [13]. The appeal of these strategies is their market penetration and relative low cost compared with interventions requiring direct human interactions.

Patient-physician communication

Since the 1990s, the medical literature has emphasized the importance of changing the traditional paternalistic approach to patient-doctor interactions that assumes the need for medical control over patient behavior, to a more patient-centered approach. The patient-centered, shared-decision approach to the medical interaction proposes in addition to physician's provision of information, a more holistic sensibility to patient concerns, reassurance and support and participatory decision making. This model requires understanding the perspective of patients about their disease and the care process. Meaningful and empathetic understanding of each patient's experiences and health beliefs and perspectives is needed to empower the patient into becoming a more active participant in health decision making [13,36]. Good patient-physician interactions can enhance patients' self-efficacy, increasing their trust in physicians and improving treatment adherence [36,46]. Limited patient contact time in clinical daily practice is the main limitation in this shared partnership model. Participation of other health providers (nurses, physical therapists, etc.) can also aid in establishing effective communication with respect to recommendations and patients' needs.

Table 2. Intervention studies for improving adherence to treatment in patients with rheumatoid arthritis. IN THIS
TABLE ORAL DRUGS IS NOT LINED UP WITH THE PREVIOUR SENTENCE

RA recent onset Oral drugs [†] RA with active	Pill counts	Educational group program Four meetings during the first month Reinforcement: 4 and 8 months (n =	Brochure (n = 30)	3, 6 and 12 months	No effect at 12 months	[47]
		during the first month Reinforcement: 4 and 8 months (n =				
2 A with active		and 8 months (n =				
A with active		32)				
disease	Pharmacological marker in the blood	Psychoeducational program (n = 51)	Leaflet (n = 49)		Increased adherence favoring experimental group	[48]
Oral drugs						
RA and other chronic diseases.	Self-reported adherence	Telephone interview (n = 261)	Usual care (n = 239)	1 month	Increased adherence favoring experimental group	[49]
Oral drugs						
RA starting	Pill counts, self- report diaries, prescription dispensation	Group counseling (n = 30)	Individual counseling (n = 32)	12 months	No effect	[50]
RA	Self-reported adherence			1 month	No effect	[51]
RA nonadherent	Self-reported adherence	Motivational interviewing (n = 63)	Brochure (n = 60)	12 months	No effect	[52]
Oral drugs						
	Dral drugs A and other chronic liseases. Dral drugs A starting Dral drugs A A conadherent Dral drugs d joint protection als	blood Dral drugs A and Self-reported adherence adherence Self-reported adherence Pill counts, self- report diaries, prescription dispensation Dral drugs A Self-reported adherence Self-reported adherence adherence adherence Self-reported adherence	blood Dral drugs AA and Self-reported adherence (n = 261) Telephone interview (n = 261) Charl drugs Charl drugs Char	bloodOral drugsAA and other chronic liseases.Self-reported adherenceTelephone interview (n = 261)Usual care (n = 239)Oral drugsAA startingPill counts, self- report diaries, prescription dispensationGroup counseling (n = 30)Individual counseling (n = 32)Oral drugsChal drugsAA startingSelf-reported adherence15 min multimedia educational program (n = 54)Education literature (n = 54)Chal drugsSelf-reported adherence15 min multimedia educational program (n = 54)Education literature (n = 60)Chal drugsSelf-reported adherenceMotivational interviewing (n = 63)Brochure (n = 60)Oral drugsSelf-reported adherenceMotivational interviewing (n = 63)Brochure (n = 60)	bloodOral drugsA and other chronic liseases.Self-reported adherenceTelephone interview (n = 261)Usual care (n = 239)1 month (n = 239)Oral drugsA startingPill counts, self- report diaries, prescription dispensationGroup counseling (n = 30)Individual counseling (n = 32)12 monthsOral drugsSelf-reported adherence15 min multimedia educational program (n = 54)Education literature (n = 54)1 monthCA toonadherentSelf-reported adherenceMotivational interviewing (n = 63)Brochure (n = 60)12 monthsCA tonal drugsSelf-reported adherenceMotivational interviewing (n = 63)Brochure (n = 60)12 months	bloodexperimental groupOral drugsSelf-reported adherenceTelephone interview (n = 261)Usual care (n = 239)1 month Increased adherence favoring experimental groupOral drugsPill counts, self- report diaries, prescription dispensationGroup counseling (n = 30)Individual counseling (n = 32)12 monthsNo effectOral drugsSelf-reported adherence15 min multimedia educational program (n = 54)Education literature (n = 54)1 monthNo effectCA honadherentSelf-reported adherence15 min multimedia educational program (n = 54)Education literature (n = 60)1 monthNo effectCA honadherentSelf-reported adherenceMotivational interviewing (n = 63)Brochure (n = 60)12 monthsNo effectCA honadherentSelf-reported adherenceMotivational interviewing (n = 63)Brochure (n = 60)12 monthsNo effect

DMARD: Disease-modifying antirheumatic drug; RA: Rheumatoid arthritis

Educational interventions in rheumatoid arthritis

Several studies have evaluated the role of educational, psychosocial and self-management programs in patients with rheumatic diseases. However, the majority have focused on the effects of these interventions on specific symptoms such as pain, psychological well-being and self-efficacy [39]. Few have addressed adherence as their primary outcome. Table 2 shows the characteristics and results of intervention studies for improving adherence in patients with RA.

Brus et al. [47] reported that adherence was not improved after 8 months of psychoeducational intervention in patients with RA taking sulfasalazine over a one-year period. However, Hill et al. [48] showed a significantly higher concentration of a pharmacological marker of sulfasalazine in the blood of patients who

received an education program for 6 months compared with control patients. However, the study failed to demonstrate that better adherence impacted positively on clinical outcomes, perhaps, because the sample size of the study was small and lacked sufficient power to detect clinical outcomes. Clifford et al. reported that patients with a recent diagnosis of a chronic condition who were interviewed by trained pharmacists 2 weeks after they had started a new medication, self-reported significantly better adherence at 4 weeks of follow-up than controls [49]. This study also included patients with diseases other than RA.

Homer et al. compared individual and group counseling for patients with RA or psoriatic arthritis initiating treatment with methotrexate, sulfasalazine or leflunomide and found no differences between groups. Both groups had high adherence and there was no control group without intervention [50].

Unk *et al.* [51] reported that a short multimedia educational program was as effective as printed materials to educate patients with RA about their disease and treatment. However, neither multimedia nor literature improved self-reported medication adherence. Finally Zwikker *et al.* [52] found no improvement in adherence to DMARDS in patients undergoing motivational interviewing compared with controls who received a brochure.

The results of these studies are inconclusive and disappointing; however, the literature on adherence in patients with RA is still scarce and any conclusion arising from these findings would be premature. The studies were heterogeneous with respect to disease characteristics, outcomes, type of intervention and measurement of adherence, and they all lacked sufficient power. Yet, the lack of decisive results with a variety of interventions demonstrates the challenges in developing and implementing effective interventions to improve adherence.

Conclusion

Adherence is a complex multifactorial medicationrelated behavior, with intentional and unintentional components. Several studies using different methodologies have demonstrated suboptimal adherence to medications in patients with RA, resulting in deleterious health outcomes. While several interventions have been proposed to increase adherence in patients with chronic disease, few studies have examined patients with RA, and in these, the results have been disappointing.

Future perspective

Evidence over the past three decades has shown that patients with chronic diseases have suboptimal adherence to treatment. Nevertheless, the most frequently proposed interventions including self-management and cognitive behavioral programs have only shown mod-

est results in improving adherence. Additional studies are needed to further establish whether novel interventions involving mobile technology and social support might be effective in enhancing medication-taking behaviors. Furthermore, the role of patient-doctor communication in enhancing adherence has not been well defined since most of the interventions proposed are external to the patient-doctor encounter. Furthermore, it is unclear how often providers discuss adherence with their patients, and if they do, whether these conversations are open and considered nonjudgmental by the patients. Future interventions addressing adherence should combine multiple strategies developed to increase knowledge, motivation and self-efficacy, and to address individual barriers. Finally, innovative, cutting-edge applications, such as those proposed within Health 2.0 may advance the use of technology in this field. These technologies can be used to enable and facilitate peer social networking, participation, apomediation, collaboration and openness between providers and consumers [53]. With increasing use of smart e-technologies, use of reminders and motivational interventions can be easily implemented with an aim to enhance chronic disease self-management and adherence, also reaching underserved communities with more ease, especially through smart phones. While these technologies are the future, additional work will be needed to determine how self-management programs can be implemented and what their ultimate effects are.

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Executive summary

- Adherence is a dynamic complex behavior influenced by unintentional and cognitive intentional determinants.
- Many patients with rheumatoid arthritis (RA) have suboptimal adherence to medications resulting in deleterious health outcomes.
- Interventions for improving treatment adherence in RA have shown modest efficacy.
- The role of the patient–doctor communication on adherence has not been well established in patients with RA, but conceivably could be important as demonstrated for other chronic diseases.
- The role of innovative e-technologies is beginning to be explored and may prove valuable to enhance selfmanagement and adherence in patients with rheumatoid arthritis.

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