Agreement with the French 2019 Recommendations on Treatment Adherence in Rheumatic Diseases among 357 Health Professionals

Laure Gossec, Anna Moltó, Catherine Beauvais, Eric Senbel, René-Marc Flipo, Sophie Pouplin, Christophe Richez, Alain Saraux, Philippe Gaudin, Daniel Wendling, et al.

Agreement with the French 2019 recommendations on treatment adherence among 357 health professionals

Authors: Laure Gossec 1,2, Anna Molto 3,4, Catherine Beauvais 5, Eric Senbel 6, René-Marc Flipo 7, Sophie Pouplin 8, Christophe Richez 9,10, Alain Saraux 11, 12, Philippe Gaudin 13, 14,Daniel Wendling 15, 16, Maxime Dougados 3, 4

Affiliations
1 : Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique, 47-83 Bd Hopital, 75013 Paris, France
2 : Pitié Salpêtrière hospital, APHP, Rheumatology department, 75013 Paris, France
3 : Rheumatology Department, Cochin Hospital, AP–HP.Centre, 75014 Paris, France
4: Inserm Unit 1153, Université de Paris, PRES Sorbonne Paris-Cité, 75014 Paris, France.
5: Sorbonne Université; Saint-Antoine Hospital, APHP, Rheumatology department, 75012 Paris, France.
6 : Private practice, 24 Place Castellane, 13006 Marseille
7 : Department of Rheumatology, CHRU Lille, Lilly University, 59000 Lille, France
8 : Department of Rheumatology, Rouen Hospital, 76081 Rouen, France.
9 : Department of Rheumatology, Pellegrin Hospital, 33000 Bordeaux, France
10 : Bordeaux University, CNRS 5164, 33000 Bordeaux, France.
11 : Department of Rheumatology, CHU Brest, 29200 Brest, France
12 : INSERM 1227, Université Bretagne Occidentale (UBO), 29200 Brest, France.
13 : Université Grenoble Alpes, GREPI EA7408, 38400 Saint-Martin-d'Hères, France
14 : CHU Grenoble Alpes Hopital Sud, Department of Rheumatology, 38434 Echirolles
15 : Department of Rheumatology, CHRU de Besançon, 25030 Besançon, France
16 : EA 4266, Université de Franche-Comté, 25030 Besançon, France.

Corresponding author:
Prof. Laure Gossec, Service de Rhumatologie, Hôpital Pitié Salpétrière et Sorbonne Université, 47-83 Bd Hôpital, 75013 Paris France laure.gossec@aphp.fr

Emails
laure.gossec@gmail.com; anna.molto@aphp.fr, Catherine Beauvais <catherine.beauvais@aphp.fr>, eric senbel <eric.senbel@wanadoo.fr>, FLIPO Rene-Marc <Rene-Marc.FLIPO@chru-lille.fr>, <sophie.pouplin@chu-rouen.fr>, christophe Richez <christophe.richez@chu-bordeaux.fr>, Alain Saraux <alain.saraux@chu-brest.fr>, Philippe Gaudin <PGaudin@chu-grenoble.fr>, Daniel Wendling <dwendling@chu-besancon.fr>, <**maxime.dougados@u-paris.fr>**

Acknowledgments:
This study was conducted thanks to an unrestricted grant from Abbvie France (Rencontres d'Experts en Rhumatologie program). AbbVie employees were present during the Rencontres d'Experts en Rhumatologie initial meeting and the face-to-face dissemination meetings across France, but did not participate in the scientific discussions. AbbVie did not review the content or have influence on this manuscript.

Disclosures of interest
Maxime DOUGADOS has received honorarium fees from Abbvie for his participation as the convenor of this initiative. All the other coauthors have received honoraria from Abbvie as members of the scientific committee. No other relevant disclosures.

Key words: adherence; compliance; rheumatoid arthritis; spondyloarthritis; recommendations; implementation.

Manuscript length: 479 Words (limit 500), 1 table (limit 2), 10 refs (limit 10)

Sir,

In chronic inflammatory rheumatic diseases, including rheumatoid arthritis, spondyloarthritis, connective tissue diseases and crystal-induced arthritis, long-term adherence to disease-modifying drugs (DMARDs) is only moderate, reported in the range of 30 to 80%.[1-3] Non-adherence may lead to increased disease activity, unnecessary treatment switches and heightened costs [4,5]. In 2017, 105 experts in France developed recommendations to facilitate the evaluation and management of non-adherence to DMARDs in daily practice [1] **(Table 1).** The implementation of recommendations rests on their dissemination and the agreement of health professionals (HPs) with the content and the applicability for usual care.[6] The objective of this study was to evaluate the agreement of French HPs with the recent adherence recommendations, and their perceived feasibility/ease of application in usual care.

In 2018, in 38 face-to-face meetings across France, the recommendations and the key supporting data were presented [1]. Participants then completed a paper form anonymously, with their agreement (from 1 to 5, where 5 is highest) and perceived feasibility (1-5) for each recommendation. Mean agreement and perceived feasibility were calculated for each recommendation, and logistic regression identified the characteristics of the participants who rated feasibility higher than the median.

Overall, 357 participants assessed the recommendations: mean age 46 years [standard deviation, SD 13]; 223 (63%) were female. Among the 247 (69%) rheumatologists, one third were hospital based (N=90, 37%). Other HPs were nurses (N=81, 23%) or pharmacists (N=14, 4%).

Pooled agreement with the overarching principles was very high (mean 4.4 [0.5]): **Table 1**. Agreement with the 10 recommendations was also high: pooled mean 4.3 [0.4]; the recommendation with the lowest agreement (mean 3.9 [0.9]) was recommendation 3 (**Table 1**).

Perceived feasibility was lower (pooled mean 3.4 [0.5]) with lowest perceived feasibility for recommendations 3 and 8 (**Table 1**). The only factor correlated with greater perceived feasibility was being a HP other than a rheumatologist:

odds ratio 2.52 [95% confidence interval 1.23-5.15], while age, gender and type of exercise were not significant (data not shown).

Our results indicate French HPs are in agreement with recently-published recommendations for the evaluation and optimization of adherence to DMARDs [1]. However, feasibility was lower, especially with regard to complex evaluation of non-adherence, and targeted interventions. Adherence may be assessed by simple open-ended questions, or by complex assessments such as questionnaires, health resources use or blood tests.[7] As expected, complex assessments had lower agreement and perceived feasibility. Targeted interventions to improve adherence to medications are often based on patient education, difficult to perform in usual care, which may explain why recommendation 8 rated lower in perceived feasibility [8-10]. Regarding predictive factors, perceived feasibility was higher among non-physician HPs, which may be due to the selection of HPs with a strong interest on patient education.

This initiative has contributed to the dissemination of the recommendations and has allowed a positive assessment of their face validity; however, their implementation will need to be further assessed.

Table 1. Agreement with and perceived feasibility of recommendations regarding drug adherence in inflammatory diseases [1]

	Overarching principles		Agreement
A	Drug adherence covers 2 complementary notions: compliance, i.e., treatment intake as prescribed, and persistence, i.e., maintenance of intake over time.		4.7 (0.6)
B	Non-adherence to disease-modifying anti rheumatic drugs is frequent. It can be detrimental, leading to lower drug efficacy and potential cost increases.		4.3 (0.9)
C	In non-adherence, factors known as "unintentional" (simply forgetting, ...) and "intentional" (linked to the patient's beliefs and fears, ...), are often intertwined.		4.1 (0.8)
D	Knowledge both of the disease and of the treatment, and patients' perceptions of the benefit/risk of the treatment are key elements in drug adherence.		4.5 (0.7)
E	In the context of shared decision-making/therapeutic alliance, caregiver-patient communication about treatment is a key factor in drug adherence.		4.6 (0.6)
	Recommendations	**Agreement**	**Applicability**
1	Adherence should be assessed at each patient visit. It must be systematic if the treatment target is not reached and before any therapeutic change.	4.3 (0.8)	3.2 (0.9)
2	Adherence should be evaluated during outpatient visits by at least one open question.	4.4 (0.7)	3.9 (0.9)
3	The assessment of adherence, particularly in the context of multidisciplinary care, can be carried out by more complete methods than an open question alone (self-reported questionnaires, dispensation data, etc.).	3.9 (0.9)	2.8 (0.9)
4	Adherence to hydroxychloroquine can be verified by a blood test and explaining the results to the patient can improve adherence.	4.0 (1.0)	3.3 (1.1)
5	When assessing adherence, risk factors for nonadherence should be examined, in particular those related to the patient (young subject, fear of side effects, mood disorders,...), treatment (polymedication,...) and environment (caregiver-patient relationship, ...).	4.4 (0.7)	3.4 (0.9)
6	In order to optimize drug adherence, the patient should be an actor in his disease and his care within the framework of a shared decision (therapeutic alliance).	4.6 (0.6)	3.6 (0.8)

7	In order to optimize drug adherence, any prescription for antirheumatic treatment must be accompanied by patient information and education.	4.7 (0.6)	3.7 (0.8)
8	The detection of nonadherence to medication must lead to the implementation of a specific intervention (therapeutic education, motivational interview, cognitive behavioural methods, etc.) to improve adherence.	4.2 (0.8)	2.9 (0.9)
9	The patient information and education process, individual or collective, must be carried out repeatedly by one or several health professionals (doctors, pharmacists, specialized nurses...) alone or in a team.	4.3 (0.7)	3.1 (0.9)
10	The patient information and education process can be supplemented by tools such as brochures and multimedia to improve therapeutic adherence.	4.3 (0.8)	3.8 (0.9)

Agreement and applicability were assessed on 1-5 Likert scales where 1= not at all in agreement and 5= fully in agreement. Results are presented as mean (standard deviation).

References

1. Gossec L Molto A, Romand X, Puyraimond-Zemmour D, Lavielle M, Beauvais C, Senbel E, Flipo RM, Pouplin S, Richez C, Saraux A, Mézières M, Gutermann L, Gaudin P, Wendling D, Dougados M. Recommendations for the assessment and optimization of adherence to disease-modifying drugs in chronic inflammatory rheumatic diseases: A process based on literature reviews and expert consensus. Joint Bone Spine. 2019;86(1):13-19.
2. López-Medina C, Moltó A, Gérald F, Dubremetz M, Grange L, Thibaud G, Charles B, Lafarge D, Beauvais C, Gossec L, Dougados M. Assessment of the adherence to disease-modifying drugs in patients with chronic inflammatory rheumatic diseases: Results of a survey of 1594 patients. Joint Bone Spine. 2019 Oct;86(5):610-614.
3. Scheepers LEJM, van Onna M, Stehouwer CDA, Singh JA, Arts ICW, Boonen A. Medication adherence among patients with gout: A systematic review and meta-analysis. Semin Arthritis Rheum. 2018 Apr;47(5):689-702.
4. Contreras-Yáñez I, Ponce De León 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;340:28290.
5. Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. Med Care 2005;43:52130.
6. Weijers JM, Rongen-van Dartel SAA, Hoevenaars DMGMF, Rubens M, Hulscher MEJL, van Riel PLCM. Implementation of the EULAR cardiovascular risk management guideline in patients with rheumatoid arthritis: results of a successful collaboration between primary and secondary care. Ann Rheum Dis. 2018 Apr;77(4):480-483.
7. Puyraimond-Zemmour D, Romand X, Lavielle M, Moltó A, Flipo RM, Richez C, et al. There are 4 main questionnaires to assess adherence in inflammatory arthritis but none of them perform well: a systematic literature review. Ann Rheum Dis 2019: 78 (supplement 2): A1411.
8. Lavielle M, Puyraimond-Zemmour D, Romand X, Gossec L, Senbel E, Pouplin S, et al. Methods to improve medication adherence in patients with chronic inflammatory rheumatic diseases: a systematic literature review. RMD Open. 2018 Jul 27;4(2):e000684. doi: 10.1136/rmdopen-2018-000684. eCollection 2018.
9. van Heuckelum M, Linn AJ, Vandeberg L, Hebing RCF, van Dijk L, Vervloet M, et al. Implicit and explicit attitudes towards disease-modifying antirheumatic drugs as possible target for improving medication adherence. PLoS One. 2019 Aug 30;14(8):e0221290. doi: 10.1371/journal.pone.0221290. eCollection 2019.
10. Latif ZP, Nakafero G, Jenkins W, Doherty M, Abhishek A. Implication of nurse intervention on engagement with urate-lowering drugs: A qualitative study of participants in a RCT of nurse led care. Joint Bone Spine. 2019 May;86(3):357-362.