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SQUEEZE

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Prevalence and Correlates of Adherence to Disease Modifying Antirheumatic Drugs (DMARDs) in Adults With Rheumatoid Arthritis and Its Consequences – A Scoping Review

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INTRODUCTION

Adherence to conventional (cDMARDs) or biological/target synthetic DMARDs (b/tsDMARDs) appears to be suboptimal, with reported rates of **adherence varying widely**, ranging from 20–80%. This variation might be attributed to the distinct operational **definitions of medication adherence (MA)** and diverse (measurement) methods used. In this review, the **ABC-defintions of adherence**[1] are applied (Figure 1).

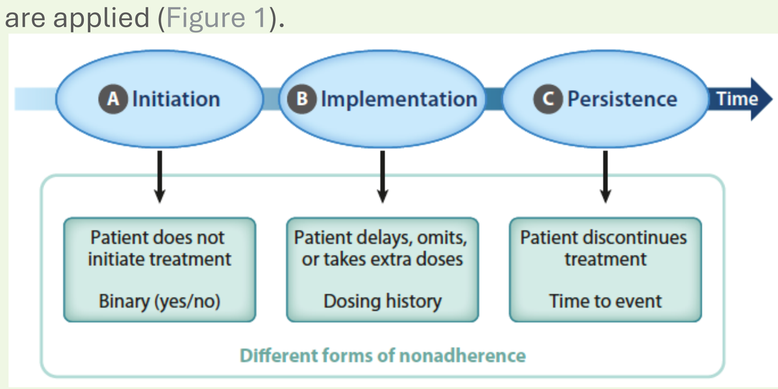


Figure 1. *Definitions of adherence according to the ABC-taxonomy (1)*

AIM

To synthesize the evidence on MA – considering the **phases (A) initiation, (B) implementation, and (C) persistence** [1] – among adult patients with Rheumatoid Arthritis (RA) treated with DMARDs:

- **(I) Prevalence** of adherence to DMARDs
- **(II) Clinical and economic consequences** of adherence to DMARDs
- **(III) Correlates** of adherence to DMARDs
- **(IV) Methodological aspects** of the studies (study design, study populations, measurements used)

METHODS

- Joanna Briggs Institute **(JBI) methodology** was used.
- **Protocol registered at OSF** registries[2].
- Literature searched in PubMed via Medline, CINAHL, Embase, and PsycINFO from 1998-2023.
- Peer-reviewed research articles that assessed **patient-initiated MA** to (a combination of) cDMARDs, bDMARDs or tsDMARDs in adults with RA in real-world settings were included.
- **Risk of Bias** tool for Observational Adherence Studies (RoBOAS) was applied.

RESULTS

Eligible articles

Screening 8904 titles/abstracts and 526 full-text articles resulted in **121 eligible articles** (Table 1), including 193,465 patients (Table 2).

Study characteristics (Table 1)

MA measurement methods:

- Medication event monitoring system (MEMS, n=5)
- Questionnaires (n=68)
- Refill-/claim data (n=43)
- Drug levels (n=1)
- Self-report/interviews (n=18)

Follow-up duration: 3 months to 10 years.

Table 1. *Summary of study characteristics (n=121)*

Study characteristics	Valid n (studies)	%
Year of publication	**121**	
2002–2009 (8 years)	11	9.1
2010–2016 (7 years)	40	33.1
2017–2023 (7 years)	70	57.9
Study design	**121**	
Cross-sectional	54	44.6
Cohort, retrospective	35	28.9
Cohort, prospective	32	26.4
DMARD groups assessed		
csDMARD(s)	52	42.9
tsDMARD(s)	25	20.7
bDMARD(s)	44	36.4
Medication adherence phase		
Initiation	0	0
Implementation	102	84.3
Persistence	19	15.7

Table 2. *Summary of participants analysed (n=193,465)*

Patient characteristics	Valid n (patients)	%	Median	Mean	SD	Min.	Max.
Total participants (analysed)	**193465**	100					
Number of participants per study			261	1598.9	4798.9	14	40024
Total participants of studies reporting gender	136481						
Total female participants	91643	67.1					
Female participants per study			213	825.6	7.3	37	14498
Age (years)	96191		55.70	55.16	5.90	39.10	69.90
Disease duration (years)	20616		10.50	10.44	4.30	1.50	22.62

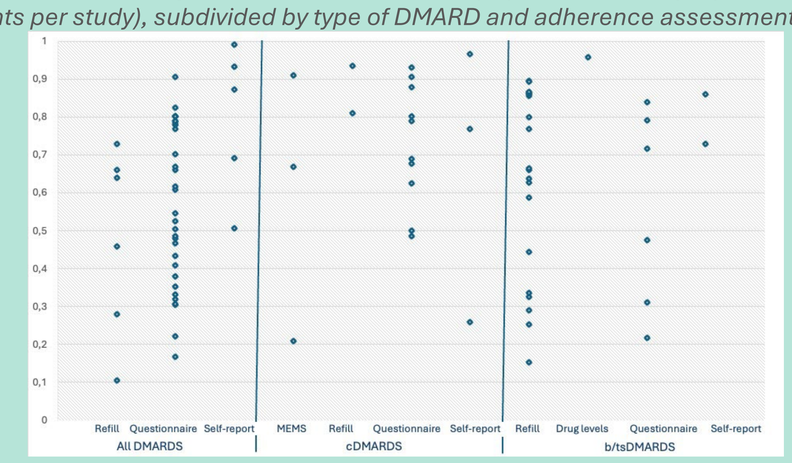
Prevalence of implementation adherence: The proportion of adherent patients, assessed in 89 studies, **varied between 10.5%-99.2%** for all DMARDs (Figure 2).

The variety remained when cDMARDs (21.0%-96.7%) and b/tDMARDs were analysed separately (15.3%-95.9%) and when different measurements tools were compared.

Impact of implementation non-adherence: In 16 studies, the impact of nonadherence on disease activity/inflammation was assessed; in **12 (75%) non-adherence was associated with more disease activity/inflammation**.

Only one study evaluated the financial consequences of non-adherence to DMARDs; **non-adherent patients seemed to have higher hospital costs**.

Figure 2. *Overview* ***implementation adherence*** *(expressed as the proportion of adherent patients per study), subdivided by type of DMARD and adherence assessment instrument*



Prevalence of medication persistence ranged between 32%-98%.

Determinants: 479 correlates of adherence to DMARDs were studied. However, synthesis of these determinants to identify predictors/intervention targets is complicated due to heterogenicity in the measurement tools applied for either assessing the determinants and/or the extent of adherence.

CONCLUSIONS

Synthesizing the results of 121 DMARD adherence studies highlighted that **medication non-adherence is prevalent** and impacts patient's disease activity.

Our work also revealed a **wide variety of operational MA definitions**, methods to calculate non-adherence, measurement tools used, determinents assessed, study designs and study populations.

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