ORIGINAL ARTICLE

Deep dive into achieving the therapeutic target: results from a prospective, 6-month, observational study nested in routine rheumatoid arthritis care

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KEY WORDS

glucocorticoids, low-disease activity, remission, rheumatoid arthritis, treat-to-target

EDITORIAL

by Głuszko P

ABSTRACT

INTRODUCTION Achieving remission or low disease activity (LDA) is an integral principle of treat-to-target (T2T) strategy in rheumatoid arthritis (RA). Prior studies have reported that achieving T2T therapeutic goals may be realistic only for a fraction of patients. Prospective, real-world data on achieving target disease control in ambulatory care populations are limited for Central and Eastern European countries.

OBJECTIVES The aim of the study was to analyze the efficacy of treatment and determine simple predictors of achieving T2T therapy goals in daily RA practice.

PATIENTS AND METHODS This multicenter, 6-month study evaluated therapy outcomes and clinical characteristics of 791 consecutive RA outpatients, meeting the preset criteria of inadequate disease control.

RESULTS Only 9% of RA patients achieved remission or LAD after 3 months and 35% after 6 months. Achieving treatment targets after 6 months was associated with lower rates of pain, disability, presenteeism and absenteeism, which reflected improved quality of life. Provider views on adherence appeared discordant with patient claims, and did not predict target achievement. Never smoking, lower body mass index, and lower prednisone dose (<7.5 mg daily) were independently associated with a higher likelihood of achieving T2T therapeutic goals after 6 months.

CONCLUSIONS A combination of clinical characteristics and provider treatment decisions shapes the "profile" of a patient failing to achieve T2T goals. Low-dose steroid equivalent, never smoking, and lower body mass index appear as individual characteristics independently associated with achieving LDA/remission at 3 and 6 months.

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Received: February 22, 2022.
Revision accepted: April 14, 2022.
Published online: April 14, 2022.
Pol Arch Intern Med. 2022; 132 (9): 16244
doi:10.20452/pamw.16244

INTRODUCTION Rheumatoid arthritis (RA) is an autoimmune disease with a chronic and progressive course characterized by systemic inflammation and multiorgan involvement. Pathogenesis of the disease is complex and seems to combine genetic susceptibility and environmental factors that contribute to polyarthritis through mechanisms involving post-transcriptional gene regulation, protein citrullination, and loss of immune tolerance.[1] Early recognition of RA is crucial to capture the "window of opportunity" (variably defined across studies from the first 12 weeks

WHAT'S NEW?

While novel therapeutic agents for rheumatoid arthritis are emerging with considerable success in clinical trials, it is still widely recognized that an evidence-practice gap exists, in that the real-life effectiveness is not synonymous with the trial efficacy. Prior studies adopting stringent protocol criteria of patient management showed success in achieving more optimal outcomes by following a more strict control of the disease activity, intensifying therapy, and more frequent, regular monitoring. This is a prospective, observational study that evaluates the achievement of therapeutic goals in routine rheumatoid arthritis care. Moreover, clinical characteristics are analyzed as potential predictors of achieving the optimal target. Suprisingly, the rate of remission and adequate disease control is very low, despite several years having passed since the introduction of this therapeutic paradigm. These data indicate an urgent need for an educational intervention or structured approaches to implement treat-to-target strategy in daily care.

up to 2 years) and promptly initiate antirheumatic disease-modifying drug (DMARD) therapy.[2,3] Maintaining remission or at least low disease activity (LDA) through stringent monitoring and therapy escalation (if indicated and tolerated) prevents structural damage and functional disability.[4-6] It should be kept in mind that following a treat-to-target (T2T) strategy improves remission rates,[7] quality of life (QoL) and cost-efficiency over usual care.[8-10]

In internal medicine, there seems to be a degree of clinical inertia in daily care, as can be suspected based on reports on the control of hypertension and hyperlipidemia in the general population.[11] Reports from other common, chronic conditions show that in prospective analyses of the effectiveness of maintenance treatment, therapeutic success is not uniform. For example, patient and physician-rated asthma control increases from approximately one-fourth to two-thirds of cases by 6 months.[12] Similarly, uncertainty remains over whether the T2T strategy is feasible for routine care. Even in protocol-based studies, the level of physician adherence to T2T varies.[13,14] Daily practice is a substantially different environment due to multiple physician (eg, lack of confidence in composite indices), patient (eg, illness beliefs, preference), and health care barriers (eg, time constraints, reimbursement).[14-16] Studies have shown that in daily care only a minority of patients achieve or remain in remission.[17] Findings appear to differ by country, welfare, and health care. A considerable geographical variation in assessing quality indicators (eg, the disease activity, function, remission) has been observed in the international METEOR database.[18] It has further been shown that the disease activity and biological DMARD (bDMARD) usage varies worldwide.[19] Geographical differences in national income level affect the access to conventional synthetic DMARD (csDMARD) and bDMARD, which can be particularly striking. Novel targeted synthetic DMARDs (tsDMARDs) are emerging,[20] but their accessibility across lower welfare countries is not fully known. Moreover, financial and administrative barriers are identified among chief restrictions to bDMARD access.[21] We conducted an in-depth examination to assess the real-world situation regarding T2T and RA care in Poland, which is a Central Eastern European country (consequently, limited data are available at present). In our prior nationwide analyses, bDMARD access was estimated at only 3% of the RA patient population.[22] These findings point toward the need for population-specific real-world evidence with regard to T2T strategy implementation, its effectiveness, and potential barriers to widespread uptake. The rationale for the present study was drawn from a prior survey in a nationwide, representative sample of Polish rheumatologists,[23] which suggested disparities between some practice patterns and the European League Against Rheumatism (EULAR) guidelines. For example, nearly two-thirds of patients are estimated to never achieve remission.[23]

We aimed to examine implementation of selected aspects of T2T strategy in a cohort of RA patients without "adequate" disease control (ie, at least moderate disease activity according to the disease activity score using 28-joint count [DAS28]).

PATIENTS AND METHODS

Patient recruitment

At commencement, the study sample was estimated to include between 50 to 100 rheumatologists, with each specialist restricted to recruiting 10 consecutive patients fulfilling the inclusion criteria. This study model was based on prior experience with physician and patient recruitment: the rheumatologists were invited to participate if they were not employed in biologic care centers (in previous research, we observed an overrepresentation of rheumatologists working in this setting), and returned a written questionnaire to the study coordinators. This investigation was nested in ambulatory care (there were 2280 outpatient rheumatology clinics in Poland as of 2010),[24] as inclusion of tertiary care centers may have obscured the unmet needs of daily RA care. Variability between the physicians and centers in practicing T2T was previously demonstrated.[14] A final sample of 82 rheumatologists or specialists in training participated in the present study, and each provider recruited 10 consecutive patients with RA. The patients were required to: (1) have a specialist-confirmed diagnosis of RA based on the American College for Rheumatology criteria from 1997[25] or the EULAR 2010 criteria,[26] (2) express willingness to adhere to the follow-up time frame, and (3) present with at least moderate disease activity (defined as DAS28 >3.2). The last criterion was set as the patients in remission already achieved the primary target of treatment at baseline. Assessing sustained remission was not the objective of the present study. Exclusion criteria included prior lack of efficacy of csDMARDs at recommended maximal or tolerated

dose and contraindications to all csDMARDs, as these patients are likely to require specialized care in tertiary centers (ie, rheumatology clinics with access to novel agents that are not accessible to the vast majority of practitioners).

Data collection was based on separate questionnaires for patients and physicians and was conducted at 3 timepoints: baseline assessment and subsequent visits at 3 and 6 months. The time frame was set to the reflect the recommended goal of improvement at 3 months and achieving disease control by 6 months, which has been upheld by the current recommendations.[3,27]

The primary aim of this study was to assess the rate of LDA or remission achieved at 3 and 6 months in a real-world cohort of RA patients in ambulatory care.

The secondary aim was based on prior evidence of suboptimal T2T implementation in Poland. We aimed to identify predictors of T2T achievement and to construct a simple regression model based on clinical parameters available to the average provider. These data will also serve as a basis for a 2-way education programme for providers and patients alike.

Data set included socio-demographic characteristics (eg, sex, age, place of residence, education, professional activity), medical history (eg, criteria used in the diagnosis of RA, the duration of symptoms), clinical parameters (eg, disease activity score using DAS28, C-reactive protein, erythrocyte sedimentation rate, initiation of disease-modifying therapy (with doses), current treatment with DMARDs, nonsteroid anti-inflammatory drugs [NSAIDs], glucocorticoids [GCs]), and patient-reported outcomes (eg, health assessment questionnaire [HAQ], global assessment of pain, and health on the 100 mm visual analogue scale).

The patient data were colleted anonymously, and the study coordinators did not process any personal data. The study was performed in accordance with the Helsinki Declaration and Good Clinical Practice guidelines, and approved by the Bioethics Committee in Lodz (L.dz. OIL/KBL/3/2016).

Data analysis The assessment of RA activity was based on DAS28-ESR or DAS28-CRP criteria (at individual centers' discretion). DAS28 below 3.2 was scored as a remission or LDA, that is, achieved the T2T goal, while DAS28 of 3.2 and higher was treated as moderate or high disease activity and the lack of achieving the T2T goal.

Statistical analysis Statistical analysis was conducted with STATISTICA 11.0 PL software (Tibco Software Inc., Palo Alto, California, United States). No data imputation was performed. Forty patients were excluded from the analysis, including 32 patients without data for DAS28 calculation, and 8 patients with LDA at enrolment. Therefore, the finally analyzed cohort included 791 RA patients.

Nominal and ordinal data were expressed as percentages, while interval data with nonparametric distribution were expressed as medians with interquartile ranges (IQR). Distribution of variables was evaluated by the Shapiro–Wilk test. The Mann–Whitney test was used to calculate statistical significance. Categorical variables were compared using the χ^2 test. Logistic regression was used to assess the relationship between achievement of remission or LDA after 3 or 6 months, and a set of potential predictors. A multivariable model was built based on a step-wise backward selection procedure including significant predictors selected based on univariable models. Statistical significance was set at a P value below 0.05.

RESULTS In the present cohort of RA patients treated in routine care, only 9% achieved LDA or remission by 3 months, and 35% achieved the target at 6 months. The patients were stratified by their status of achieving the target at 3 and 6 months. We examined clinical characteristics across the groups to identify the factors associated with worse disease control at a given timepoint (**TABLES 1** and **2**). The achievement of treatment targets is reflected in both clinical and objective (ie, levels of acute phase reactants) measures of inflammation and inflammatory activity. At both timepoints, younger age and a higher degree of education were demographic factors positively associated with achieving LDA and/or remission. A higher body mass index (BMI) was negatively linked with achieving T2T goals, and its effect was stronger at 6 months. The patients failing to achieve the target at both the 3- and 6-month mark had a higher median duration of sick leave than the individuals meeting T2T goals, but the difference was insignificant for both timepoints.

Self-reported impairment at work was substantially less frequent in the treatment goal-achieving groups at both 3 and 6 months. This finding is reflected in the observation that the patients achieving RA treatment targets were more often employed full-time. Although the proportion of part-time workers was similar initially, the patients achieving the treatment targets were less frequently working part-time in the long-term. Combined with a greater proportion of participants working full-time, this suggest that their work capacity may have improved. By 6 months, RA duration alone had a negative impact on the target goals. However, our study may be insufficiently powered to identify this relationship, as the majority of patients had an established disease.

At both timepoints, pain and physical disability were significantly higher among the patients failing to achieve the target. Interestingly, although smoking status was negatively associated with the disease control at 3 months, this was not reflected in the analysis for 6 months, which could be due to other confounding factors.

TABLE 1 Baseline characteristics of rheumatoid arthritis patients stratified based on achievement of the treatment target at 3- and 6-month follow-up

Parameter	Achieving treatment target at 3 months (n = 69)	Not achieving treatment target at 3 months (n = 722)	*P* value	Achieving treatment target at 6 months (n = 277)	Not achieving treatment target at 6 months (n = 513)	*P* value
Sociodemographic characteristics						
Male sex, n (%)	14 (20.3)	183 (25.3)	0.35	85 (30.7)	112 (21.9)	0.01
Age, y	50 (42–57)	58 (48–65)	<0.001	55 (45–65)	58 (49–64)	0.03
Age <55 y, n (%)	42 (60.9)	297 (41.1)	0.002	137 (49.5)	199 (38.8)	0.004
Basic education, n (%)	3 (4.3)	45 (6.2)	0.01	11 (4.0)	37 (7.2)	0.02
Secondary or professional education, n (%)	31 (44.9)	446 (61.8)		156 (56.3)	318 (62.0)	
Higher education, n (%)	35 (50.7)	231 (32.0)		110 (39.7)	158 (30.8)	
Clinical characteristics						
Disease duration, y	1.5 (0.4–4.1)	1.0 (0.3–3.3)	0.21	1.0 (0.3–2.6)	1.1 (0.4–3.9)	0.01
Smoking at present, n (%)	9 (13.0)	170 (23.5)	0.01	163 (58.8)	255 (49.7)	0.45
Nonsmoker (ever), n (%)	52 (75.4)	369 (51.1)		64 (23.1)	115 (22.4)	
BMI, kg/m^2	24.4 (21.9–27.5)	26.0 (23.9–29.3)	<0.001	25.3 (23.0–29.3)	26.3 (24.0–29.3)	0.001
Overweight, n (%)	20 (29.0)	318 (44.0)	0.02	96 (34.7)	244 (47.6)	<0.001
CVE family history, n (%)	10 (14.5)	45 (6.2)	0.01	18 (6.5)	35 (6.8)	0.86
Seropositive disease, n (%)	67 (97.1)	699 (96.8)	0.90	271 (97.8)	494 (96.3)	0.24
DAS28-ESR, standard unit	4.40 (3.69–4.57)	5.51 (4.96–0.06)	<0.001	4.87 (4.57–5.49)	5.59 (5.16–6.12)	<0.001
DAS28-CRP, standard unit	4.40 (3.68–4.67)	5.48 (4.96–6.07)	<0.001	4.87 (4.59–5.40)	5.62 (5.21–6.13)	<0.001
HAQ, standard unit	0.21 (0.04–0.64)	1.00 (0.54–1.31)	<0.001	0.69 (0.21–1.21)	1.00 (0.62–1.34)	<0.001
Treatment-related characteristics						
NSAID, n (%)	54 (78.3)	567 (78.5)	0.96	239 (86.3)	381 (74.3)	<0.001
GC, n (%)	12 (17.4)	493 (68.3)	<0.001	121 (43.7)	381 (74.3)	<0.001
Prednisone equivalent, mg/d	5.0 (5.0–5.0)	5.0 (5.0–7.5)	<0.01	5.0 (5.0–7.5)	5.0 (5.0–8.0)	<0.01
Low dose GC (<7.5 mg/d prednisone equivalent), n (%)	12 (17.4)	338 (46.8)	<0.001	90 (32.5)	258 (50.3)	<0.001
csDMARD, n (%)	30 (43.5)	377 (52.2)	0.17	137 (49.5)	274 (53.4)	0.29
csDMARD ≥2, n (%)	2 (2.9)	146 (20.2)	<0.001	26 (9.4)	122 (23.8)	<0.001

Interval data are shown as medians with interquartile ranges.

Abbreviations: BMI, body mass index; CRP, C-reactive protein; csDMARD, conventional synthetic disease-modifying antirheumatic drugs; CVE, cardiovascular event; DAS28, disease activity joint score using 28-joint count; ESR, erythrocyte sedimentation rate; GC, glucocorticoids; HAQ, health assessment questionnaire; NSAID, nonsteroid anti-inflammatory drugs; RA, rheumatoid arthritis

The variables significantly associated with treatment target achievement at 6 months were somewhat different than their 3-month counterparts (see TABLE 3 and 4). Male sex, younger age, and lower BMI appeared as factors of significance positively associated with LDA and / or remission in the long-term. Meanwhile, smoking status and lower prednisone dosage remained significant predictors of T2T status at both 3 and 6 months.

DISCUSSION Achieving the treatment target is of high importance for optimizing patient outcomes in RA. Multinational studies have indicated that a sustained T2T strategy (which encompasses a wide range of treatment and management-related decisions) leads to improved outcomes and a higher likelihood of remission.[7] On the other hand, while achieving sustained remission is possible, it is viewed as a realistic target only for a proportion of patients.[28] Studies have shown that the disease control rates vary substantially across Europe.[29] In the present cohort of RA patients treated in routine care, only 9% achieved LDA or remission by 3 months, and 35% of patients achieved the target at 6 months. In comparison, in a Dutch cohort of very early RA, 47% achieved DAS28 remission by 6 months.[30] In randomized trials prior to the era of T2T, achieving remission in usual care was estimated at 16%, while 31% remission rate was achieved in centers with stringent monitoring by 6 months.[31] More recently, real-life cohorts with established RA have shown that LDA is achievable by half of the patients after 1 year.[32] Our data may fall into the lower-bound estimates for achieving T2T goals, however, it should be noted that our study was nested in routine care, rather than specialized, tertiary centers.

TABLE 2 Productivity and clinical status at 3- and 6-month follow-up of daily rheumatoid arthritis care

Parameter	Achieving treatment target at 3 months (n = 69)	Not achieving treatment target at 3 months (n = 722)	*P* value	Achieving treatment target at 6 months (n = 277)	Not achieving treatment target at 6 months (n = 513)	*P* value
Work ability						
Sick leave days, n	3 (2–60)	21 (12–30)	0.82	12 (3–26)	18 (5–30)	0.08
Presenteeism[a], points	25 (15–40)	40 (30–50)	<0.001	40 (30–48)	40 (35–50)	<0.001
Full-time work, n (%)	41 (59.4)	314 (43.5)	0.01	139 (50.2)	215 (41.9)	0.03
Half-time work, n (%)	5 (7.2)	63 (8.7)	0.68	12 (4.3)	56 (10.9)	0.002
Clinical characteristics						
HAQ, standard units	0.29 (0.19–0.38)	0.65 (0.31–1.00)	<0.001	0.15 (0.00–0.30)	0.56 (0.21–1.00)	<0.001
Patient global assessment, points	20.0 (15.0–35.0)	45.0 (35.0–50.0)	<0.001	20.0 (10.0–30.0)	35.0 (30.0–50.0)	<0.001
Pain[b], points	30.0 (16.3–35.0)	40.0 (35.0–50.0)	<0.001	20.0 (10.0–30.0)	35.0 (30.0–47.0)	<0.001
Tender joint count, n	2.0 (2.0–2.0)	6.0 (4.0–8.0)	<0.001	1.0 (1.0–2.0)	5.0 (3.0–6.0)	<0.001
Swollen joint count, n	1.0 (1.0–2.0)	3.0 (2.0–4.0)	<0.001	1.0 (1.0–2.0)	2.0 (1.0–4.0)	<0.001
CRP, mg/l	0.42 (0.20–1.18)	10.00 (6.0–16.0)	<0.001	2.60 (0.26–4.06)	8.00 (5.93–10.05)	<0.001
ESR, mm/h	12.0 (10.0–18.3)	24.0 (18.0–32.0)	<0.001	10.0 (9.00–12.0)	20.0 (16.0–28.0)	<0.001
DAS28-ESR, standard units	2.90 (2.45–3.12)	4.60 (3.99–5.11)	<0.001	2.67 (2.45–2.92)	4.09 (3.56–4.65)	<0.001
DAS28-CRP, standard units	2.88 (2.44–3.14)	4.65 (3.99–5.13)	<0.001	2.66 (2.45–2.96)	4.15 (3.56–4.70)	<0.001
Treatment characteristics						
NSAID use at present, n (%)	54 (78.3)	567 (78.5)	0.96	190 (68.6)	364 (71.0)	0.49
GC use at present, n (%)	12 (17.4)	493 (68.3)	<0.001	55 (19.9)	381 (74.3)	<0.001
Prednisone equivalent, mg/d	5.0 (3.8–7.5)	5.0 (5.0–7.5)	0.98	2.5 (2.5–2.5)	5.0 (2.5–5.0)	<0.001
Low dose GC (<7.5 mg/d prednisone equivalent), n (%)	5 (7.2)	166 (23.0)	0.002	34 (12.3)	154 (30.0)	<0.001
Adherence reported by patients, n (%)	69 (100)	691(95.7)	0.54	277 (100)	503 (98.1)	0.16
Adherence reported by physicians[c], n (%)	69 (100)	695 (96.3)	0.57	260 (93.9)	503 (98.1)	0.002

Interval data are shown as medians with interquartile ranges.

a At least 51 points on a 100-point numeric scale, impaired at work

b At least moderate intensity of pain, based on at least 21 points on a 100-point numeric visual analogue scale

c Defined as "always" and "very frequent" treatment compliance

Abbreviations: see **TABLE 1**

For early RA, 3 months are an important timepoint of clinical significance, which is tied to future likelihood of achieving the remission.[33] Considering that the majority of the patients recruited in this study had an established disease, by the time they had come into contact with a rheumatologist, they may have missed the window of opportunity. Earlier studies have suggested that achieving treatment targets for RA is suboptimal in Poland; 64% of patients are estimated to never achieve remission, while only 21% of bDMARD-naïve (of note, bDMARD accessibility is estimated at 3% in Poland) patients are reported with "adequate" RA control.[23] Similarly, only 26% of patients in a cross-sectional sample from a national Polish RA study were reported with the disease remission.[22] Our study extended these earlier findings and provided a prospective overview on the real-world achievement of treatment targets. It should also be noted that DAS28 is considered a less stringent measure for remission due to high weight of acute phase reactants, which may reflect an even lower rate of "true" remissions than currently observed.[34] Our data suggest that in routine RA care, achieving LDA or remission is not common. Whether T2T is feasible for routine care is debatable[35,36]; it is a set of principles for best practice that clinicians should strive to adhere to but nonmedical factors are likely to hamper the actual practice.[37,38] It is difficult to identify the main culprit for low rates of treatment success. Studies have shown a discrepancy between provider-reported adherence to guidelines and the actual practice.[39] This may account, to some extent, for the unsatisfactory rates of adequate disease control observed at present.

TABLE 3 Predictors of achieving the treatment target in daily rheumatoid arthritis care at 3 months (n = 791)

Parameter	Level (n)	Achieving treatment target at 3 months, n (%)	Univariable regression		Multivariable regression	
			OR (95% CI)	*P* value	OR (95% CI)	*P* value
Sex	Men (n = 197)	14 (7.1)	0.75 (0.41–1.38)	0.35	–	–
	Women (n = 594)	55 (9.3)	–			
Age	<55 y (n = 339)	42 (12.4)	2.23 (1.34–3.69)	0.002	–	–
	≥55 y (n = 452)	27 (6.0)	–			
Education	Higher (n = 266)	35 (13.2)	2.19 (1.33–3.60)	0.002	1.65 (0.96–2.81)	0.07
	Other (n = 525)	34 (6.5)	–			
Disease duration	<3 m (n = 138)	13 (9.4)	0.91 (0.47–1.75)	0.77	–	–
	3–12 m (n = 255)	15 (5.9)	0.54 (0.295–1.01)	0.05	–	–
	>12 m (n = 398)	41 (10.3)	–			
Smoking	Past smoking (n = 191)	8 (4.2)	0.31 (0.14–0.67)	0.003	0.40 (0.19–0.89)	0.02
	Smoking (n = 179)	9 (5.0)	0.38 (0.18–0.78)	0.01	0.45 (0.21–0.96)	0.04
	Never smoking (n = 421)	52 (12.4)	–			
Seropositive disease	Yes (n = 766)	67 (8.7)	1.10 (0.25–4.78)	0.90	–	–
	No (n = 25)	2 (8.0)	–			
BMI, kg/m^2	≥25 (n = 483)	29 (6.0)	0.43 (0.26–0.71)	0.001	0.59 (0.34–1.00)	0.05
	<25 (n = 308)	40 (13.0)	–			
CVE family history	Yes (n = 55)	10 (18.2)	2.59 (1.24–5.40)	0.01	3.37 (1.49–7.62)	0.003
	No (n = 746)	59 (8.0)	–			
Prednisone	≥7.5 mg/d (n = 155)	0	0.01 (0–0.21)	0.002	–	–
	<7.5 mg/d (n = 350)	12 (3.4)	0.14 (0.08–0.27)	<0.001	0.27 (0.14–0.52)	<0.001
	None (n = 286)	57 (19.9)	–			

Abbreviations: see **TABLE 1**

TABLE 4 Achieving treatment target in daily rheumatoid arthritis care at 6 months (n = 791)

Parameter	Level (n)	Achieving treatment target at 6 months, n (%)	Univariable regression		Multivariable regression	
			OR (95% CI)	*P* value	OR (95% CI)	*P* value
Sex	Men (n = 197)	85 (43.1)	1.59 (1.14–2.21)	0.01	2.34 (1.62–3.39)	<0.001
	Women (n = 593)	192 (32.4)	–			
Age	<55 y (n = 336)	137 (40.8)	1.54 (1.15–2.07)	0.004	1.48 (1.07–2.06)	0.02
	≥55 y (n = 454)	140 (30.8)	–			
Education	Higher (n = 268)	110 (41.0)	1.48 (1.09–2.01)	0.01	–	–
	Other (n = 522)	167 (32.0)	–			
Disease duration	<3 m (n = 135)	54 (40.0)	1.30 (0.87–1.95)	0.20	–	–
	3–12 m (n = 253)	87 (34.4)	1.03 (0.74–1.43)	0.88	–	–
	>12 m (n = 402)	136 (33.8)	–			
Smoking	Past smoking (n = 193)	50 (25.9)	0.55 (0.38–0.80)	0.002	0.52 (0.36–0.78)	0.001
	Smoking (n = 179)	64 (35.8)	0.87 (0.61–1.25)	0.46	–	–
	Never smoking (n = 418)	163 (39.0)	–			
Seropositive disease	Yes (n = 765)	271 (35.4)	1.74 (0.69–4.40)	0.24	–	–
	No (n = 25)	6 (24.0)	–			
BMI, kg/m^2	≥25 (n = 487)	144 (29.6)	0.54 (0.40–0.72)	<0.001	0.51 (0.37–0.72)	<0.001
	<25 (n = 303)	133 (43.9)	–			
MI in parents	Yes (n = 53)	18 (34.0)	0.95 (0.53–1.71)	0.86	–	–
	No (n = 737)	259 (35.1)	–			
Prednisone	≥7.5 mg/d (n = 154)	31 (20.1)	0.21 (0.14–0.34)	<0.001	0.16 (0.10–0.26)	<0.001
	<7.5 mg/d (n = 348)	90 (25.9)	0.30 (0.21–0.41)	<0.001	0.29 (0.20–0.41)	<0.001
	None (n = 288)	156 (54.2)	–			

Abbreviations: MI, myocardial infarction; others, see **TABLE 1**

Despite achieving the treatment targets, at present, 20% of patients with RA control required steroid use, albeit in small doses. Patient characteristics that are associated with treatment targets are different at 3 and 6 months, which suggests that "early" and "long-term" improvement in RA control is affected by multiple factors to a different extent. However, smoking status and steroids remained significant predictors of achieving treatment targets throughout the timeframe, which points to their importance in therapeutic strategy at any given time. Both these findings confirm data from earlier reports.[40-42] Steroids still remain a mainstay of the combination treatment in ambulatory care, which may be due to their effectiveness, low cost, clinician familiarity with them, and difficulty of initiating a more specialized drug programme referral. Low-dose GCs have been shown to provide favorable clinical and radiological benefits without compromising safety in early RA.[43] However, their long-term use at moderate to high doses is associated with a plethora of toxic side effects and should be applied with great care. Recent reports have shown that switching the target therapy if its goals are not reached by 6 months yields favorable results.[44] In prior analyses examining routine RA care, maintenance of GC use (>6 months) was estimated for 25% of Polish patients. For over one-third of the patients, despite the failure of treatment schemes comprising at least 2 csDMARDs, a second-line therapy (bDMARDs) was not planned in the therapeutic strategy.[23] These findings indicate that a considerable degree of undertreatment or clinical inertia may occur in routine RA care, specifically with regard to second-line treatment options. Even in cohorts that reported favorable T2T results, the provider's discordance with the disease activity measures was noted as a justification for the treatment inertia.[45] A recently published analysis on a cohort of RA patients implies a degree of clinical inertia; observations show a prevalence of low treatment satisfaction and poor disease control, despite claims of adherence.[46] Most patients appear to trust their providers and hold preference for the physicians' treatment goals over their own.[47] Therefore, convincing physicians of the importance of achieving the treatment goals and adequate control of RA activity is of paramount importance.

We found that the provider's opinion of satisfactory adherence was more common regarding patients who failed to reach their treatment goals. This may indicate that the rheumatologists do not always accurately identify and predict the patients' treatment-related behaviors. We remain optimistic that with the advent of biosimilars and greater availability of biological agents, the preferences of clinicians will shift from clinical inertia to implementation of the emerging treatment options such as biosimilars, tsDMARDs, and Janus kinase inhibitors.

Conclusions This is a prospective study on a cohort of RA patients recruited from ambulatory centers, presenting with at least moderate disease activity. By 3 and 6 months, low rates of achieving the treatment goals, specifically LDA or remission, were observed. The patients who achieved the treatment targets were characterized with lower levels of pain, disability, and work impairment, which had a fundamental impact on their QoL. A variety of clinical factors significantly differed between the patients who achieved and failed to achieve the treatment targets by 3 and 6 months. It is likely that a combination of clinical characteristics and provider treatment decisions shapes the "profile" of a patient failing to achieve T2T goals. Low-dose steroid equivalent, smoking, and BMI appear as individual characteristics independently associated with achieving LDA / remission at 3 and 6 months.

ARTICLE INFORMATION

ACKNOWLEDGMENTS None.

FUNDING This research was funded by the Polish Society of Rheumatology.

CONTRIBUTION STATEMENT Conceptualization, BB; methodology, BB, PW; formal analysis, investigation, resources, data curation, writing—original draft preparation, writing—review and editing, project administration, BB, PW, MB, WS, MS, JC. All authors have read and agreed to the published version of the manuscript.

CONFLICT OF INTEREST None declared.

HOW TO CITE Batko B, Jeka S, Wiland P, et al. Deep dive into achieving the therapeutic target: results from a prospective, 6-month, observational study nested in routine rheumatoid arthritis care. Pol Arch Intern Med. 2022; 132: 16244. doi:10.20452/pamw.16244

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