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ORIGINAL RESEARCH

Treat-to-target in rheumatoid arthritis: a real-world study of the application and impact of treat-to-target within the wider context of patient management, patient centricity and advanced therapy use in Europe

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ABSTRACT

Background While treat-to-target (T2T) is endorsed for the management of rheumatoid arthritis (RA), data on the degree of implementation in clinical practice are limited. This study investigated the use of T2T for RA in a real-world setting across Europe.

Methods The Adelphi RA Disease-Specific Programme was a point-in-time survey of rheumatologists and their consulting patients with RA conducted between January and October 2020 in Belgium, France, Germany, Italy, Spain and the UK. Rheumatologists completed an attitudinal survey, and a record form for their next 10–12 consulting patients, who were invited to voluntarily complete a patient-reported questionnaire. Data collected included clinical characteristics, treatment patterns and attitudes towards T2T.

Results Overall, 316 rheumatologists provided data for 3120 patients, of whom 1108 completed the questionnaire. While 86.1% of rheumatologists estimated using T2T principles in clinical practice, only 66.6% of patients were reported by their physician to be managed using a T2T approach. Achieving disease remission was the most commonly reported treatment goal identified by rheumatologists (79.7%), followed by symptom control (47.8%) and reducing impact on quality of life (44.5%). 40.8% of rheumatologists and their patients were in agreement that a treatment goal had been set. When there was agreement on treatment goals, we observed better patient satisfaction, engagement and treatment success.

Conclusions Despite recommendations, the T2T approach in RA appears to be suboptimally implemented in clinical practice. This highlights the importance of patient-centricity in the decision-making process to define meaningful targets and select appropriate treatments to improve disease outcomes.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ While treat-to-target (T2T) principles are endorsed for the management of rheumatoid arthritis (RA), there are limited data on the degree of implementation in clinical practice.

WHAT THIS STUDY ADDS

⇒ The results of this study indicate that while a majority of rheumatologists (86%) support T2T principles, only two-thirds of their patients with RA were managed using a T2T approach.

⇒ A minority of rheumatologists and their patients (41%) were in agreement that a T2T goal had been set.

⇒ Where there was agreement on a T2T goal between rheumatologist and patient, higher rates of patient satisfaction, engagement and treatment success result.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ There is a need to expand adoption of T2T strategies in the management of people living with RA in order to further optimise achievable quality of life goals.

⇒ These findings highlight the importance of shared decision-making that involves patients in defining meaningful targets and in selection of appropriate treatments to achieve them.

INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune disease characterised by chronic inflammation and is associated with progressive cartilage damage and joint destruction.[1 2] RA remains without a cure and if left untreated, results in loss of physical function, reduced overall quality of life (QoL), disability and increased mortality. The main treatment goal is to achieve disease remission, or at least maintain a low level of disease activity as an

alternative target, therefore, it is important to diagnose early and initiate treatment as early as possible.[1 3 4]

Due to the heterogeneity of RA, both in terms of disease course and patient variability, management requires careful treatment consideration, with treatment choices driven by regular disease activity evaluation and consistent patient clinical assessment. In 2019, the EULAR published updated recommendations for the management of RA with respect to positioning of targeted-synthetic and biological disease-modifying antirheumatic drugs (DMARDs), including tumour necrosis factor inhibitors (TNFis), interleukin-6 receptor inhibitors (IL-6Ris), anti-CD20 inhibitors (CD20is), selective co-stimulation modulators and Janus kinase inhibitors (JAKis).[2]

A treat-to-target (T2T) approach, based around the principles of shared decision-making between the patient and their rheumatologist, improves the prognosis of patients with RA,[2 3 5–7] and forms part of the treatment recommendations of EULAR and the American College of Rheumatology (ACR) guidelines.[2 7 8] There is evidence that a T2T management strategy yields superior medium-term and long-term outcomes (eg, prevention of damage, maintenance of physical function and reduction of comorbidity risks) compared with standard care, both in early and late RA.[6 9] However, T2T principles are not applied universally. Individual preferences, clinical characteristics and the patient–provider relationships play important roles, as do barriers in healthcare structure and socioeconomic factors.[10] Evidence of a failure, in line with treatment guidelines, to change therapies and modify treatment approaches in patients despite the indication of moderate or high disease activity has been identified, as well as issues with regular disease activity assessments and access to care.[11]

Although T2T has been widely endorsed as the strategy of choice for the management of RA and there is a recognised need to commit to T2T strategies and individualised treatment decision-making, there are limited data on the degree of implementation in the real-world clinical setting. There are indications that T2T has not been extensively adopted, and therefore, there are opportunities to increase application of a T2T strategy in daily clinical practice.[9 12 13] Hence, the objective of this study was to explore the implementation of T2T and stated treatment goals among physicians and their patients, as well as to explore the impact of physician and patient aligned T2T decision-making on patient outcomes within the wider context of advanced therapy use in real-world clinical practice in six European countries.

METHODS

Study design

Data were derived from the Adelphi RA Disease-Specific Programme (DSP), conducted in Belgium, France, Germany, Italy, Spain and the UK from January to October 2020. DSPs are large, multinational point-in-time studies of physicians and their patients presenting in a real-world clinical setting that describe current disease management, disease-burden impact and associated treatment effects. A complete description of the study methodology has been previously published and validated.[14–16]

A geographically diverse sample of rheumatologists were recruited by local fieldwork agents, and were invited to participate following the completion of a short screening questionnaire. Rheumatologists were eligible to participate in the survey if they were personally responsible for treatment decisions and management of patients with RA; were seeing six or more patients with RA per month; and agreed to adhere to all study rules and regulations. Physician participation was financially incentivised, with reimbursement on survey completion according to fair market research rates.

Patients were eligible for inclusion if they were aged ≥18 years at the time of data collection, had a physician-confirmed diagnosis of RA and visited the rheumatologist for consultation. They could not be participating in a clinical trial at the time of data collection. Patients were not compensated for participation.

Physician reported data

All rheumatologists completed a physician survey regarding their current caseload and attitudes towards RA treatment and management, including T2T use. Rheumatologists were then instructed to complete patient record forms for their next 10–12 consecutively consulting patients who visited them for routine care, to mitigate against selection bias. This patient record form contained detailed questions on patient demographics and clinical characteristics, including age, sex, body mass index (BMI), disease activity as defined by the Disease Activity Score-28 (DAS28),[17] pain, number of tender joints, number of swollen joints and time since diagnosis. Physician-reported T2T use and barriers to T2T implementation were also collected, including physician-reported treatment goals, advanced therapy use and barriers to advanced therapy initiation, reasons for advanced therapy choice and satisfaction with treatment outcomes. These comprised a predefined list of themes and answers depending on the question asked, with an option to state ‘do not know’, ‘not known’ or ‘other’ (with a free text option where appropriate for completeness).

Completion of the physician-reported patient record forms was undertaken through consultation of existing patient clinical records, as well as the judgement and diagnostic skills of the respondent physician, consistent with decisions made in routine clinical practice. The study was designed to facilitate understanding of real-world clinical practice, and thus rheumatologists could only report on data they had to hand at the point of consultation, representing the evidence they had when making any clinical treatment and other management decisions at that time. No additional tests, treatments or investigations were

required as part of this survey beyond those conducted at recruitment.

Patient reported data

Each patient for whom the rheumatologist completed a record form was then invited to voluntarily complete a patient-reported questionnaire, and on agreement provided their informed consent to participate. Patient-reported questionnaires were completed by the patient independently from their treating rheumatologist and were returned in a sealed envelope, ensuring the patient's responses were kept confidential from their physician.

The patient-reported questionnaire contained detailed questions on current symptomatic burden, perceptions of T2T and treatment goals, levels of engagement and satisfaction with their treatment, with questions and predefined possible answers aligned with those asked of their treating rheumatologist (as appropriate), along with other validated patient reported outcomes.

Data collection was undertaken in line with European Pharmaceutical Market Research Association guidelines,[18] and as such did not require ethics committee approval, with the survey materials reviewed and given exemption by the Western Institutional Review Board (reference number: 1-1253914-1). No identifiable protected health information was extracted during the course of the study. Data were collected in such a way that rheumatologists and their consulting patients could not be identified directly; all data were aggregated and de-identified before receipt. As data were collected according to market research guidelines, no source validation was possible or required.

In addition, the survey was performed in full accordance with relevant legislation at the time of data collection, including the US Health Insurance Portability and Accountability Act 1996,[19] and Health Information Technology for Economic and Clinical Health Act legislation.[20]

Data analysis

Aggregated data for all countries combined were analysed using descriptive statistics, with results interpreted at the overall European level. Mean, SD and range were calculated for quantitative, continuous variables and frequency counts and percentages for qualitative, categorical variables.

Results were derived from matched pairs of physician-reported patient record forms and patient-reported questionnaires. Any patient with missing data for a particular variable was removed from all analyses involving that variable. However, patients who were removed from one set of analysis were still eligible for inclusion in other analyses. Missing data were not imputed; therefore, the base of patients for analysis could vary from variable to variable and was reported separately for each analysis. All analyses were conducted in Stata V.15.1.[21]

RESULTS

Study cohort

Overall, 316 rheumatologists (Belgium: 13; France: 73; Germany: 60; Italy: 60; Spain: 60; UK: 50) completed the physician survey, providing details of their attitudes towards RA treatment and management, including T2T use. The majority of rheumatologists practised in a public hospital setting (59%), with 23.4% practising in a public office, 13.6% in a private office and 4% in a private hospital setting. On average, rheumatologists surveyed had a mean (SD) caseload of 93.4 (76.65) patients with RA in a typical month.

These same rheumatologists completed physician-reported patient record forms for a total of 3120 patients (Belgium: 79; France: 662; Germany: 600; Italy: 599; Spain: 600; UK: 580). In addition, a total of 1108 voluntary patient-reported questionnaires were received (35.5% completion rate) (Belgium: 32; France: 152; Germany: 399; Italy: 153; Spain: 245; UK: 127). Of the 1108 patient-reported questionnaires, a total of 1050 were matched to a corresponding physician-reported patient record form.

Patient demographics and clinical characteristics

Patient demographics and clinical characteristics at the time of data collection are summarised in table 1. The mean (SD) patient age was 53.1 (14.0) years, 66.8% of patients were female, the mean (SD) BMI was 25.5 (4.1) and the mean (SD) time since diagnosis was 7.3 (7.2) years. Overall, 42.5% of patients were in remission (classified as a DAS28 score <2.6), 34.1% of patients had low disease activity (DAS28 2.6–3.2), 19.6% had moderate disease activity (DAS28 3.2–5.1) and 3.8% had severe disease activity (DAS28 >5.1). Demographics and clinical characteristics in patients who completed the voluntary patient-reported questionnaire compared with those who did not complete the questionnaire are shown in online supplemental file 1.

Physician-reported perceptions of treat to target principles

Rheumatologists were surveyed regarding their attitudes towards RA treatment and management, including T2T use, in an overall setting (n=316). Based on their perceived patient caseload, the majority of rheumatologists (86.1%) estimated that they followed T2T principles in at least some of their patients with RA. Rheumatologist-estimated levels of T2T implementation were highest in Spain (100.0%) and the UK (96.0%), and the lowest in Germany (56.7%) (figure 1A). Rheumatologists who reported following T2T principles in at least some of their patients (n=272) were then asked to estimate the proportion of their overall patient caseload that had a T2T management approach currently implemented. On average, rheumatologists estimated that 89.9% of their current overall caseload had a T2T management approach implemented at the time of data collection, with 66.4% of patients implemented on a T2T management approach when first diagnosed with RA, and 23.5% implemented later in the patients' management

Table 1 Patient demographics and clinical characteristics

	n=3120
Age (years), mean (SD) (n=3117*)	53.1 (14.0)
Sex, n (%)	
Male	1037 (33.2)
Female	2083 (66.8)
BMI, mean (SD)	25.5 (4.1)
Physician-perceived disease activity, n (%)	
Remission (DAS28 <2.6)	1327 (42.5)
Low (DAS28 2.6–3.2)	1063 (34.1)
Moderate (DAS28 3.2–5.1)	613 (19.6)
High (DAS28 >5.1)	117 (3.8)
Physician-perceived pain, n (%)	
None	770 (24.7)
Mild	1517 (48.6)
Moderate	690 (22.1)
Severe	125 (4.0)
Don't know	18 (0.6)
No of tender joints, mean (SD) (n=1451)	7.2 (6.4)
No of swollen joints, mean (SD) (n=810)	5.6 (5.1)
Time since diagnosis (years), mean (SD) (n=2643)	7.3 (7.2)
Currently receiving glucocorticoid, n (%)	754 (24.2)
Currently receiving low dose glucocorticoid, n (%)	687 (22.0)
Currently receiving high dose glucocorticoid, n (%)	67 (2.1)
Currently receiving csDMARD, n (%)	1884 (60.4)
Currently receiving methotrexate, n (%)	1611 (51.6)
Currently receiving advanced therapy, n (%)	2142 (68.7)

*n=3 patients classified as >90 years old, excluded from mean patient age.
BMI, body mass index; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DAS28, Disease Activity Score-28; SD, standard deviation.

(figure 1B). When rheumatologist-reported reasons for implementing T2T were investigated, the most commonly stated patient groups in which rheumatologists would implement a T2T management approach were patients with moderate or severe disease activity (61.4%), followed by the most uncontrolled patients (36.4%), those who are proactive/motivated with their treatment (34.2%), and those who do not respond well to initial therapy (33.8%) (figure 1C).

Physician-reported use of treat to target in real-world clinical practice

Rheumatologist-reported use of T2T in a real-world clinical setting was then investigated, with data analysed at an individual patient level using data derived from the patient record forms (n=3120 patients). Overall, rheumatologists stated that 66.6% of their consulting patients with RA were being managed using a T2T approach. Implementation of T2T was highest in Belgium (89.9%), Spain (80.2%) and the UK (79.0%), with the lowest level of implementation in Germany (30.7%) (figure 2a).

Rheumatologist-reported T2T use varied across disease activity groups, with 78.7% of patients in remission (DAS28 <2.6), 57.6% of patients with low disease activity (DAS28 2.6–3.2), 56.4% of patients with moderate disease activity (DAS28 3.2–5.1) and 65.0% of patients with high disease activity (DAS28 >5.1) were reported to be managed using T2T principles (figure 2b). The most frequent rheumatologist-reported reasons for not implementing T2T at an individual patient level were physician preference not to adjust current treatment (34.5%), patient preference not to adjust current treatment (23.2%) and 'there are no achievable targets for this patient' (16.1%) (figure 2c).

Rheumatologist and patient-reported alignment on implementation of T2T

When data from the patient-reported questionnaires were analysed (n=1050), patients reported a lower degree of T2T implementation than was reported by rheumatologists. Overall, 56.7% (n=595) of patients stated that they had a treatment goal or target set for their RA, with 31.4% of patients (n=330) reporting that they were involved in setting their T2T goals, while 25.2% (n=265) stated that their T2T goals were set by their physicians only (figure 3a). When evaluating the patients with a matching physician-completed patient record form and patient self-reported questionnaire for alignment on whether a T2T goal had been set, there was agreement between physicians and patients that a goal had been set for 40.8% of patients, agreement for 26.0% of patients that a goal had not been set, and a disconnect (physician 'yes'/patient 'no' or patient 'yes'/physician 'no') for 33.2% of patients (figure 3b). Among patients for whom their physician state they are following a T2T approach (n=620), only 28.3% of patients report they are following a T2T approach.

Impact and outcomes associated with alignment on implementation of T2T approach approach

In patients who were aligned with their physician that a treatment goal had been set (n=420), 32.1% of patients reported that they were 'very satisfied' with the control the current treatment approach provided for their RA, in comparison to 16.5% of patients who were either misaligned with their physician that a T2T goal had been set or aligned that a T2T goal had not been set (n=607) (figure 4a).

When asked how confident they felt when managing their condition, 27.0% of patients aligned with their physician that a T2T goal had been set reported that they were 'very confident', compared with 14.2% of patients

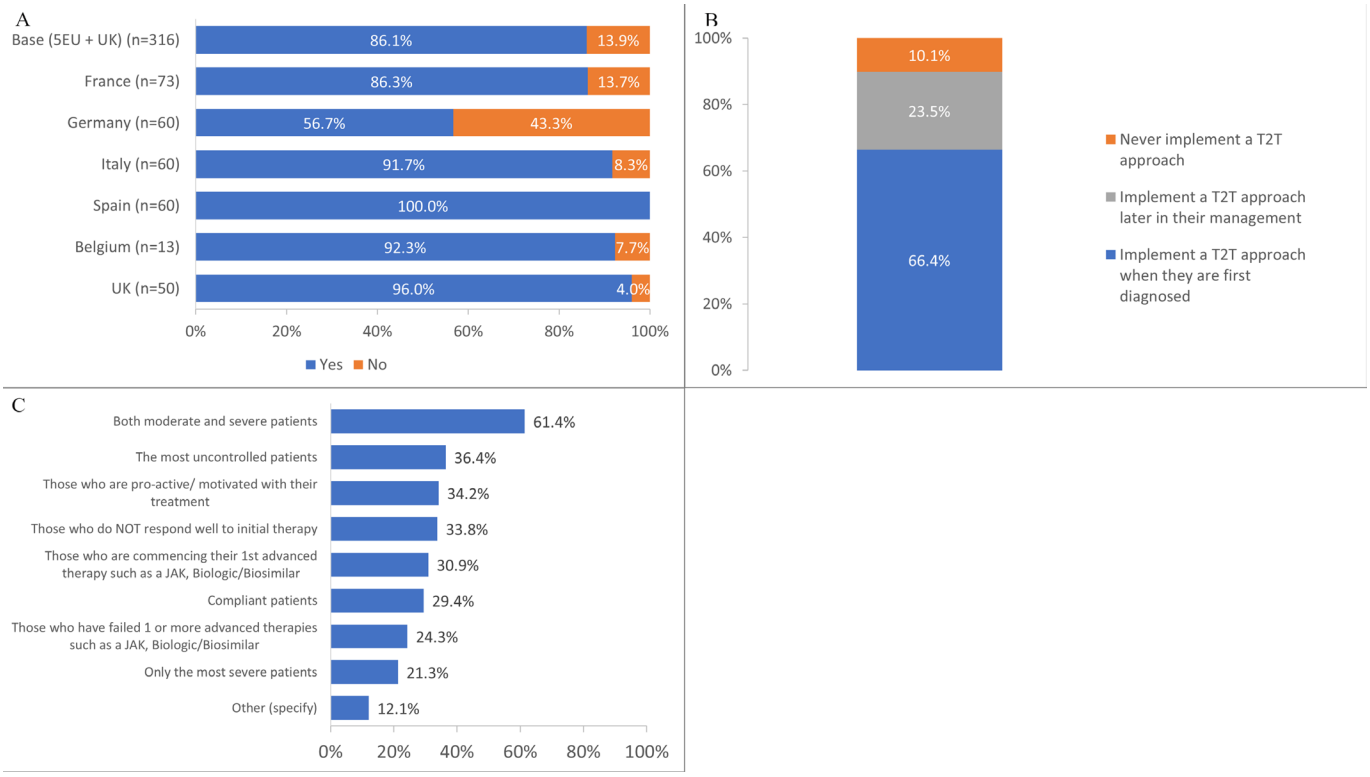

Figure 1 Physician perceptions of treat to target use. Data derived from the physician attitudinal survey (n=316 rheumatologists). (A) Do you follow the principles of T2T management in at least some of your patients with RA in clinical practice? (Stratified by country.) (B) Physician perception of timing of T2T use. (C) In which patient types would you follow a T2T approach in? (Physician could select more than one option.) RA, rheumatoid arthritis; JAK, Janus kinase; T2T, treat-to-target.

who were either misaligned with their physician that a T2T goal has been set or aligned that a T2T goal had not been set (figure 4b). Regarding patient-perceived engagement, 51.8% of patients stated that they felt their doctor had kept them 'very well informed' about their condition when they were aligned with their physician that a T2T goal had been set compared with 28.7% of patients who were either misaligned with their physician that a T2T goal had been set or aligned that a T2T goal had not been set (figure 4c).

With respect to treatment goals, 38.1% of patients who were aligned with their physician regarding whether their T2T goal had been achieved felt that their T2T goal had been fully achieved, compared with 21.2% of patients who did not align with their physician or did not have a T2T goal set (figure 4d).

Comparison of rheumatologist and patient-reported treatment goals

Rheumatologist and patient-reported treatment goals were then compared. In patients for whom rheumatologists had stated that T2T had been implemented (n=2079), achieving disease remission was the most commonly reported treatment goal identified by rheumatologists (79.7%), followed by symptom control (47.8%) and reducing impact on quality of life (QoL) (44.5%). In patients who stated that they or their physician had set a treatment goal (n=586), the most common treatment goals reported by the patients themselves were symptom control (64.7%) and achieving remission (57.0%) and reducing impact on QoL (50.3%). Other similarities and differences between rheumatologists and their patients are shown in figure 3C.

Treatment patterns and advanced therapy use

Overall, 68.7% of patients in this study were on advanced therapy (n=2142); of these, 55.7% were receiving a TNFi, 18.5% were receiving a JAKi and 25.7% were receiving a non-TNFi biologic. 44.1% of patients receiving a TNFi were receiving it as monotherapy, 57.4% were receiving a JAKi as monotherapy and 46% were receiving a non-TNFi biologic as monotherapy.

Of 954 patients who had either discontinued advanced therapy or who had never received advanced therapy, physicians reported that 15.3% of patients' current clinical condition warranted the use of advanced therapy. When physician-reported reasons for not initiating advanced therapy in these patients were investigated (n=146), the most frequently selected reasons were 'patient concerns regarding infection' (24.0%), 'csDMARD therapies are safe and tolerable in this patient' (18.0%) and 'patient dislikes injections/infusions' (17.1%) (table 2).

For the 516 patients whose disease activity was deemed moderate or high by their rheumatologist and who were on advanced therapy, the most commonly selected physician-stated reason for any advanced therapy choice

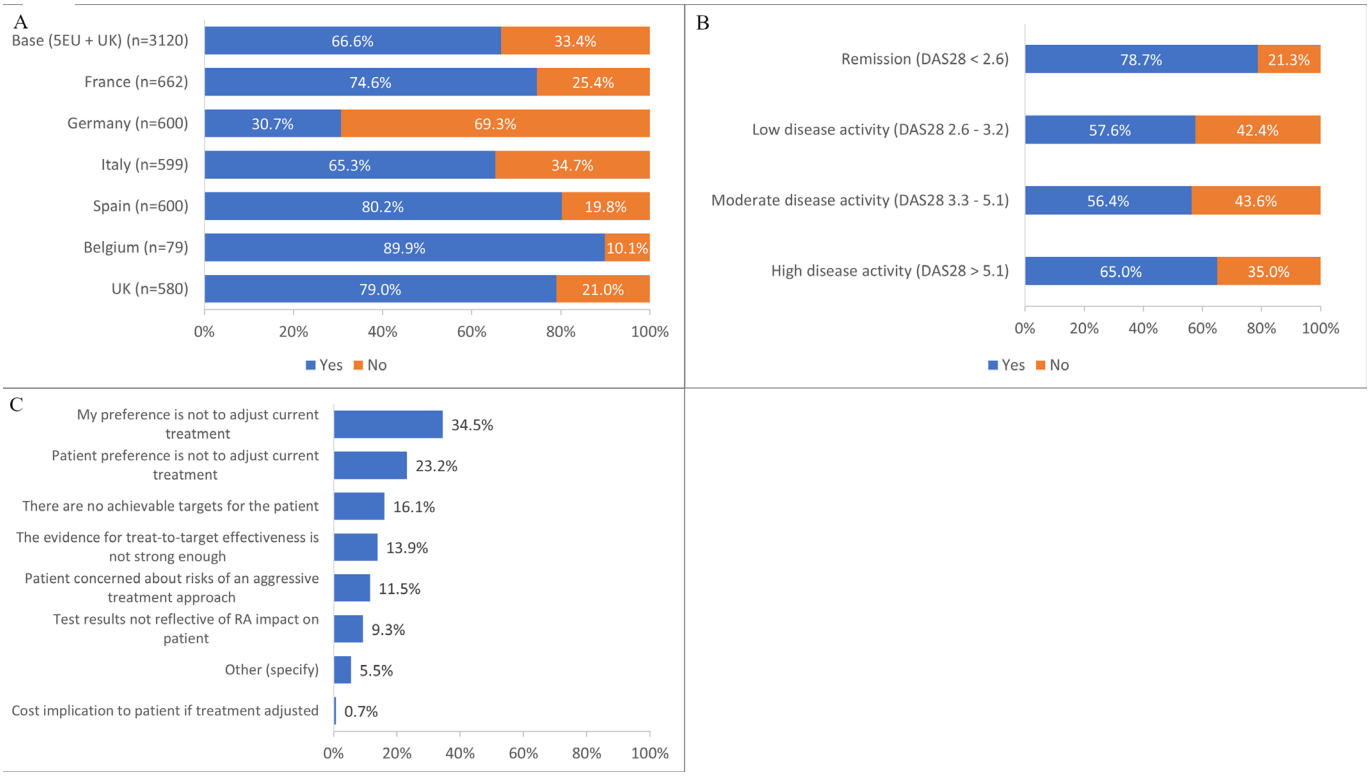

Figure 2 Physician-reported use of treat to target in real-world practice. Data derived from the patient record forms at an individual patient level (n=3120 patients). (A) Are you using a T2T approach in this patient? (Stratified by country.) (B) Are you using a T2T approach in this patient? (Stratified by physician-perceived disease activity (DAS28).) (C) Why has a T2T approach not been implemented in this patient? (Physician could pick one response.) DAS28, Disease Activity Score-28; RA, rheumatoid arthritis; T2T, treat-to-target.

was strong overall efficacy (71.3%); this was also the case for the different classes of advanced therapy (table 3). Strong overall efficacy was the most selected reason for choice of TNFi (68.0%), although this was selected less frequently as a choice than for all other classes. Inhibition of disease progression (43.6%) and my familiarity/experience with product (37.8%) are the second and third most selected reasons for choice of TNFi, respectively. Fast onset of action and strong efficacy as monotherapy were identified as additional key drivers of treatment choice for JAKis (39.7% and 35.3% of patients, respectively). For IL-6Ris, drivers of treatment choice included strong efficacy as monotherapy, control of acute episodes and fast onset of action (51.0%, 49.0% and 41.2%, respectively), while overall safety profile was a treatment attribute selected by physicians for 56.9% of patients treated with CD20/28is (table 3).

When patient-centric, rheumatologist-stated, reasons for any advanced therapy choice were investigated, the most commonly selected responses were 'acceptability of method of delivery for the patient' (23%), 'ease of product use for the patient' (16%) and 'low out of pocket cost/affordability for patients' (10%). Similar rates were reported for the different classes of advanced therapy, except JAKis, for which a higher rate of 'acceptability of method of delivery for the patient' (35%) and 'ease of product use for the patient' (24%) were observed (table 3).

DISCUSSION

This study provides real-world insights into the use of T2T principles across Europe and, in particular, a discordance between perceived and actual adoption of T2T in clinical practice. Our data suggest there was broad acceptance of the value of T2T, with 86.1% of rheumatologists surveyed estimating that they followed T2T principles in at least some of their patients with RA. Physicians most commonly estimated implementing a T2T management approach in patients with moderate or severe disease activity, the most uncontrolled patients, those who are proactive/motivated with their treatment, and those who do not respond well to initial therapy. Overall, among rheumatologists who reported ever having treated patients using T2T principles, two-thirds reported that this was implemented at first RA diagnosis, with a further one-quarter opting to implement T2T later in the management pathway.

However, when we investigated T2T at the individual patient level, a T2T strategy was not implemented in around 30% of patients. The most frequent rheumatologist-reported reasons for this were physician preference not to adjust current treatment, patient preference not to adjust current treatment and 'there are no achievable targets for this patient'.

We observed a discordance between patients and physicians on whether a T2T goal had been set, with only 4 in

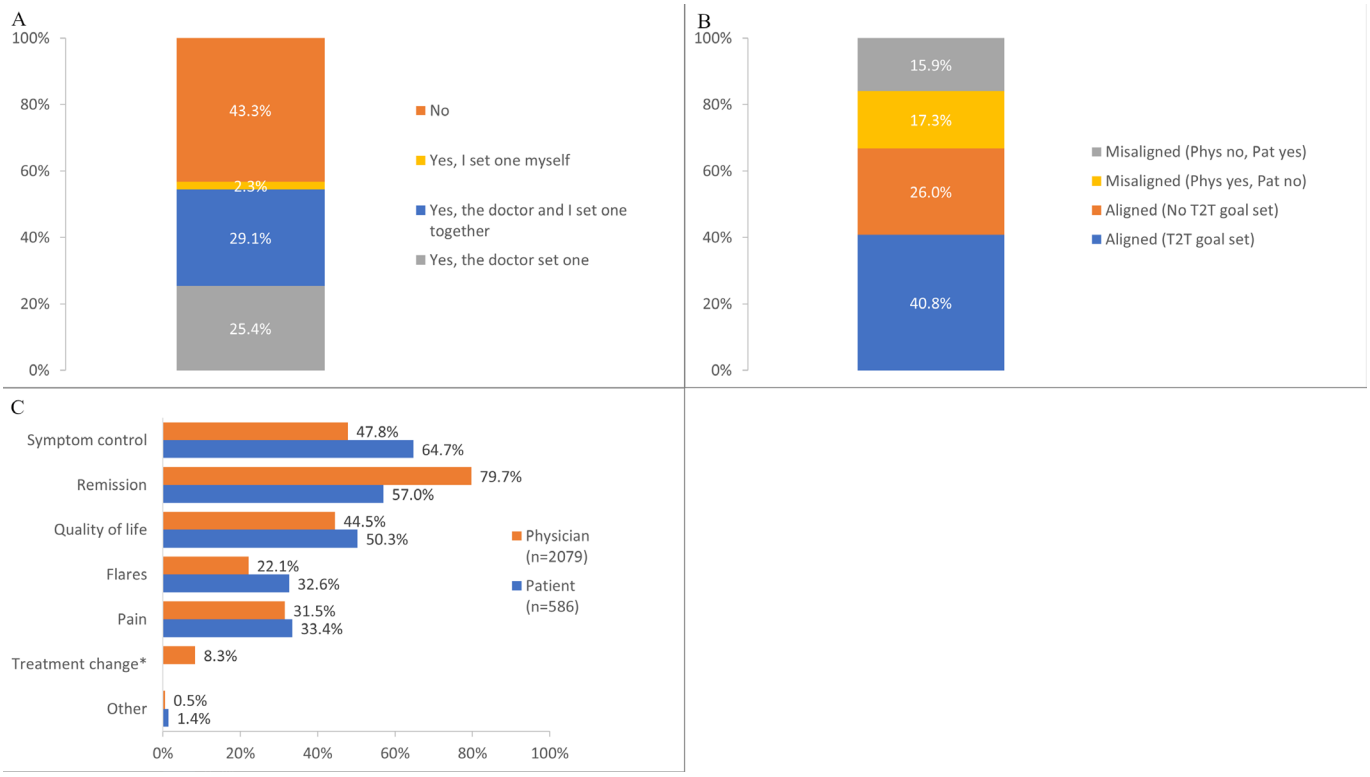

Figure 3 Physician and patient-reported alignment on treat to target implementation and goal setting. (A)Have you and/or your doctor set a treatment goal or target for your RA? **(**B) Has a T2T goal been set: Patient and physician alignment. (C) What are the goal(s) of the T2T approach? (Only asked to physicians and patients who selected that a T2T approach is being followed.) *Treatment change not available as a response option within the patient self-reported questionnaire. Pat, patient; Phys, physician; RA, rheumatoid arthritis, T2T, treat-to-target.

10 physicians and patients agreeing that a goal had been set and a quarter of patient and physicians agreeing that no goal had been set. However, as these were rheumatologist and patient-perceived rates of T2T implementation, and reported independently from each other for the sake of confidentiality and to mitigate against potential bias, we could not verify whether T2T goals were officially documented or informally discussed, which may account for some of this variability. Where there was agreement that a T2T goal had been set, there was also likely to be shared decision-making on treatment options. This is unsurprising, given that patients' preferences and expectations are known to be key determinants of treatment success.[22]

Achieving disease remission, symptom control and reducing impact on QoL were identified by physicians as the main treatment goals in patients for whom they had stated that T2T was implemented, while the main goals selected by patients themselves were symptom control, remission and reducing impact on QoL. These findings highlight the importance of enlisting patients as partners in T2T, whereby the patient is appropriately informed about the treatment target, the planned tactic to achieve this, and the risks and benefits of a T2T approach.[23 24] Interestingly, a T2T approach had been successfully applied in 78.7% of patients currently in remission, suggesting that a proportion of these patients may have attained remission having previously been experiencing higher disease activity. In patients with long-standing disease or more severe or complicated disease, clinical remission is not always achievable. In these patients, adopting T2T principles is perhaps even more relevant, in that the shared decision-making process allows rheumatologists and their patients to identify achievable targets to improve symptomatic burden.

T2T is just one consideration in the wider context of a holistic approach to disease management in RA; it is important to strike a balance between treatment efficacy, safety, tolerance, formulation and patient preference, which are all key determinants of treatment success.[5 9] In clinical trials, T2T has been shown to give good efficacy outcomes at a group level, however, there may need to be greater considerations given to T2T approaches with respect to benefit:risk and also with regard to the major aspect(s) of life impacted by RA when considering optimum management at the individual level. Evidence on patient-centred care in RA demonstrates that involving the patient as an individual with unique needs, concerns and preferences, has a relevant impact on treatment outcomes such as safety, effectiveness, adherence and costs. It is important, therefore, that patients feel more confident and empowered when it comes to decisions surrounding their care, with patient education and engagement key to this process.[25] It is vital to treat the individual needs of a person living with RA and to ascertain whether these can be addressed, or might be

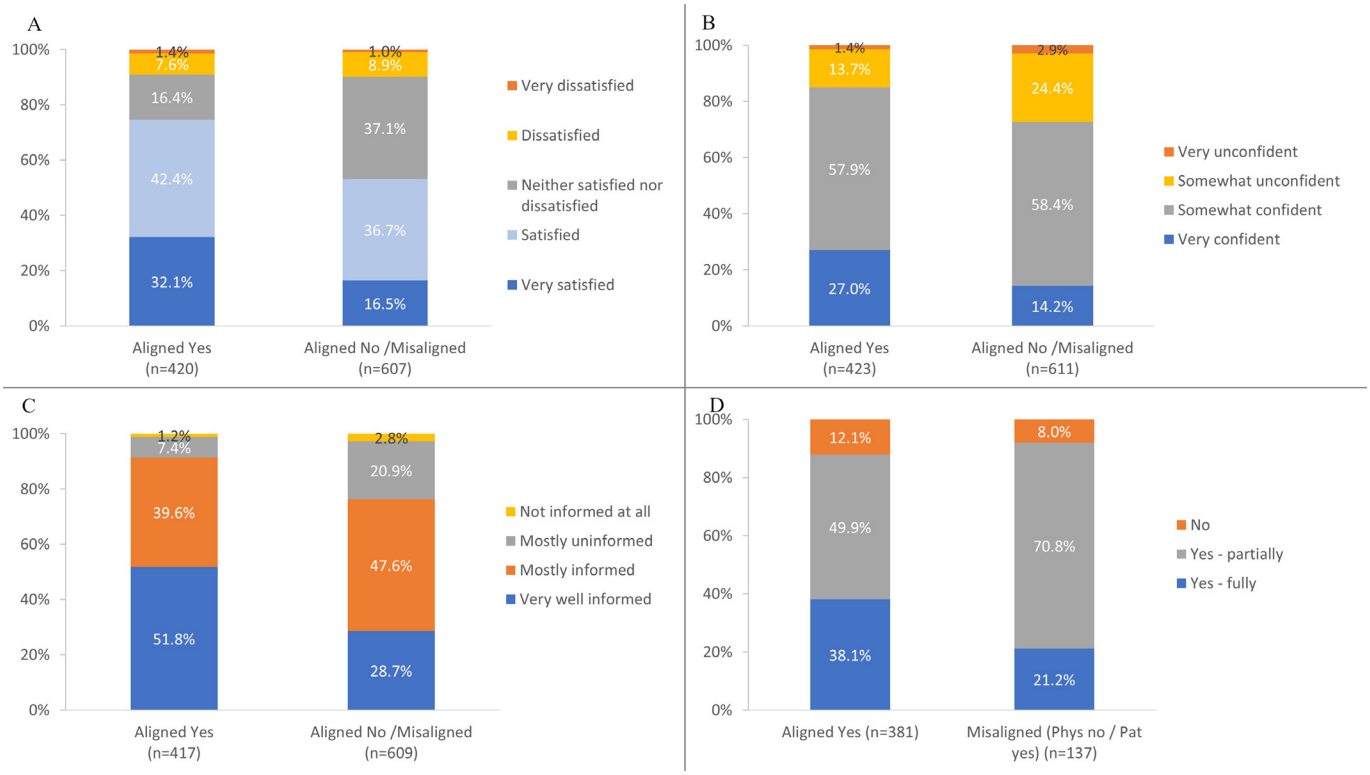

Figure 4 Patient-reported outcomes and impact of physician and patient alignment (A) Patient satisfaction: Which option best describes your satisfaction with the control the current treatment approach is providing? (B) Patient engagement: To what degree do you feel confident in managing your condition? (C) Patient engagement: How well informed has your doctor kept you about your condition? (D) Do you feel the treatment goal(s) have been achieved? (Note: Only patients to have stated they follow a T2T approach are asked this question, therefore only misaligned (Phys no/pat yes) are included.) Pat, patient; Phys, physician; T2T, treat-to-target.

overlooked, by focusing solely on composite scores of disease activity. While there are many different definitions of remission based on composite scores of disease activity, this study used DAS28 <2.6 to determine therapeutic response. This was due to DAS28 being the most familiar and widely used measure in the geographical regions this survey was conducted, and the fact this was collected for all patients based on physician perceptions of the score.

By providing patient-centred care through shared decision-making, outcomes considered important by the patients themselves can also be improved.[26] While physicians monitor patients with RA mainly by examining joints and reviewing laboratory findings, and asking patients about disease control, patients have also identified pain, fatigue, sleep disturbance and QoL as important outcomes.[22 26] The ACR/EULAR remission criteria for RA state that four criteria need to be fulfilled: C reactive protein ≤1 mg/dL, swollen joint count ≤1/28, tender joint count ≤1/28 and patient global assessment (PGA) ≤1 cm on a 10 cm Visual Analogue Scale.[27] Studies have indicated that in patients who achieved three of the four criteria, therefore, failing to reach remission, the majority of these were due to patients not fulfilling the PGA criteria, indicating that patient perspectives on what constitutes treatment success in the context of remission and symptom control are more subjective.[28 29] It is important to expand the influence of the patient in the long-term monitoring of both their disease and of treatment response or failure.[30] This is especially important in light of potential risks of overtreatment with advanced therapies if focus of T2T is on remission only, without also considering the patient perspective.[31 32]

Actively involving patients with RA in the management of their condition empowers them to take personal responsibility for their treatment and offers opportunities to increase medication adherence[33] given non-adherence is known to negatively impact T2T goals and disease outcomes.[34] The concept of adherence is complex and multifactorial, with psychological, communicational and logistical themes appearing to influence treatment adherence in RA to a greater extent than sociodemographic or clinical factors.[35] Aligning treatment regimens with patient preferences may increase compliance and adherence,[36] which may ultimately lead to higher real-life effectiveness. Patients' satisfaction with their treatment can also impact on medication adherence and is also closely linked to treatment expectations, with another study demonstrating that suboptimal disease control had a significant impact on patients' treatment satisfaction, working life and healthcare resource utilisation.[37] Adherence to DMARDs has been reported to be relatively low, and not significantly different between patients on biological DMARDs compared with those

Table 2 Physician-reported reasons why patient is not currently receiving advanced therapy if their clinical condition warrants it

Reasons why patient is not currently receiving advanced therapy	(n=146)
Patient concerns regarding infection	24.0%
csDMARD therapies are safe and tolerable in this patient	18.5%
Patient dislikes injections/infusions	17.1%
Other safety/side effects concerns (not infection or malignancy)	16.4%
Very recent diagnosis/too early to prescribe advanced therapy/still receiving their first treatment	16.4%
Patient concerns regarding malignancy/history of cancer	11.0%
My concerns regarding infection	6.8%
Patient does not want to go to an infusion centre	5.5%
Requirement to obtain prior authorisation	4.8%
Formulary restrictions (such as step-edit procedure)	4.1%
Advanced therapies are contraindicated	2.1%
Biologic DMARDs are inconvenient/too troublesome to administer	2.1%
My concerns regarding malignancy/history of cancer	2.1%
Pregnant/lactating	1.4%
Advanced therapy is too expensive for patient (out-of-pocket expense)	–
Other formulary restrictions	–
Unable to secure funding/lack of insurance	–
Other (specify)	16.4%

This question was multichoice, rheumatologists were able to select more than one option, if appropriate.
csDMARD, conventional synthetic disease-modifying antirheumatic drug; DMARD, disease-modifying antirheumatic drug.

on conventional DMARDs, despite different modes of administration.[38]

Both T2T and the choice of therapy are closely connected. Improvements in the ability to make rational treatment choices will facilitate improvements in T2T approaches.[10] Over two-thirds of patients in this study were on advanced therapy at the time of data collection, with rheumatologists more likely to use a T2T approach in patients on advanced therapy. However, there appeared to be a cohort of patients who had a clinical need for advanced therapy but were not receiving it. For these patients, physicians reported that the main reason for not initiating advanced therapy was 'patient concerns about infection', with other safety-related reasons also cited. As a chronic autoimmune inflammatory disease, RA is associated with a higher infection risk,[39] however, this depends on underlying factors such as smoking, concomitant glucocorticoid treatment, age and comorbidities.[40]

While strong overall efficacy was the physician-stated reason for advanced therapy choice for most moderate-severe patients, regardless of class of drug, fast onset of action was selected as one of key drivers for selecting a JAKi, monotherapy for an IL-6Ri, while overall safety profile was selected for more patients on a CD20/28i. Notably, 'acceptability of method of delivery for the patient' was more frequently reported for patients on a JAKi. Moreover, the oral route of administration of JAKis has the potential to minimise drug discontinuation in contrast with parentally administered biological agents.[41] Other studies have reported that for physicians, in addition to efficacy, treatment mode of administration and time to onset of action were decision-making drivers. Interestingly, for patients, efficacy was defined as time with optimal QoL and expectation of this, together with treatment mode of administration were determinants in treatment selection.[24] In Sweden, patients with RA reported either effectiveness, route of administration or severe side effects as the most important treatment attribute. Patients who considered effectiveness as most important were more willing than other patients to accept higher risks of side effects.[42]

Several limitations should be considered in the evaluation of our findings. The DSP study was not based on a true random sample of physicians or patients, as reflected in the particularly high proportion of participants who were receiving advanced therapies. While minimal inclusion criteria governed the selection of the participating physicians, participation was influenced by willingness to complete the survey, which may select for rheumatologists more engaged and proactive with current clinical practice. As this study included only rheumatologists and not primary care physicians, the likelihood was that these physicians were practising in specialist centres. Patients currently consulting with their rheumatologist may have more severe disease or more complicated issues surrounding treatment and management. Physicians were asked to provide data for a consecutive series of patients to avoid selection bias, with data recorded at time of consultation to mitigate against recall bias. However, no formal patient selection verification procedures were in place. Completion of the patient-reported questionnaire was voluntary and not incentivised, which may also mean that patients more engaged in their treatment were more likely to complete these. It is unclear whether patient educational status or economic status may have influenced completion rate of the patient-reported questionnaires or introduced bias into the results. Patient education status was only collected within the voluntary patient-reported questionnaires. However, demographics and clinical characteristics were broadly comparable between those who completed the voluntary questionnaire and those who did not. Despite this potential selection bias towards more proactive rheumatologists and patients, we saw low alignment in terms of T2T

Table 3 Top reasons for treatment choice for each class of advanced therapy among patients with moderate-high Disease Activity Score (DAS28 >3.2).

	Class of advanced therapy				
	Base	**TNF inhibitors**	**JAK inhibitors**	**CD20/28 inhibitors**	**IL-6 inhibitors**
Base	**516**	**291**	**116**	**58**	**51**
Strong overall efficacy	71.3%	68.0%	75.0%	74.1%	78.4%
Inhibition of disease progression	44.8%	43.6%	44.0%	50.0%	47.1%
My familiarity/experience with product	37.6%	37.8%	30.2%	43.1%	47.1%
Overall safety profile	34.1%	30.9%	30.2%	56.9%	35.3%
Control of acute episode/flare	32.9%	30.2%	26.7%	43.1%	49.0%
Convincing efficacy data in clinical trials	31.4%	26.7%	34.5%	37.9%	45.1%
Patient centricity combined*	31.4%	25.8%	41.4%	36.2%	35.3%
Reduction in stiffness	30.0%	28.9%	27.6%	27.6%	45.1%
Fast onset of action	28.9%	24.4%	39.7%	19.0%	41.2%
Improvement or maintenance of QoL (work, leisure, outlook, etc.)	27.7%	23.7%	31.0%	25.9%	45.1%
Achievement of clinical remission	27.3%	21.3%	30.2%	34.5%	47.1%
Enabling patient to perform everyday tasks/usual activities	26.9%	22.7%	26.7%	31.0%	47.1%
Achievement of low disease activity	25.4%	20.3%	28.4%	34.5%	37.3%
Maintenance of efficacy over time	25.4%	24.1%	16.4%	36.2%	41.2%
Allows reduction in steroid use	24.8%	20.3%	29.3%	19.0%	47.1%
Product inclusion in local/national formulary	23.8%	24.7%	19.8%	22.4%	29.4%
Acceptability of method of delivery for the patient	22.9%	17.5%	34.5%	24.1%	25.5%
Sustained pain relief	22.9%	17.5%	25.0%	25.9%	45.1%
Strong efficacy as monotherapy	22.3%	14.8%	35.3%	8.6%	51.0%
I believe it will achieve my treat-to-target goal	22.3%	15.8%	30.2%	25.9%	37.3%
Reduction of fatigue	18.8%	14.1%	22.4%	15.5%	41.2%
Ease of product use (for the patient)	15.9%	11.0%	24.1%	19.0%	21.6%
Does not exacerbate comorbidities	12.8%	10.7%	9.5%	31.0%	11.8%
Suitability for patients with C/V risk	11.8%	9.6%	10.3%	20.7%	17.6%
Product provides a reasonable cost benefit ratio	11.0%	13.7%	7.8%	8.6%	5.9%
Does not exacerbate non-autoimmune conditions	10.7%	8.6%	15.5%	17.2%	3.9%
Low out of pocket cost/affordability for patients	9.7%	10.0%	7.8%	10.3%	11.8%
Few administrative controls on product use	9.5%	10.3%	7.8%	10.3%	7.8%
Improving patient's mood/state of mind	9.3%	8.9%	6.0%	10.3%	17.6%
Drug-drug interaction data	8.3%	8.9%	6.9%	8.6%	7.8%

Continued

Table 3 Continued

	Class of advanced therapy				
	Base	TNF inhibitors	JAK inhibitors	CD20/28 inhibitors	IL-6 inhibitors
Contraindication data	7.6%	8.2%	4.3%	13.8%	3.9%
Also improves concomitant autoimmune conditions	7.4%	6.2%	8.6%	12.1%	5.9%

This question was multichoice, rheumatologists were able to select more than one option, if appropriate.
*Patient centricity combined included the proportion of physicians to have selected at least one of the following three patient-centric reasons for choice: 'ease of product use (for the patient)', 'acceptability of method of delivery for the patient' and 'low out-of-pocket cost/affordability for patients'.
C/V, cardiovascular; IL-6, interleukin-6; JAK, Janus kinase ; QoL, quality of life; TNF, tumour necrosis factor.

goal setting, which may mean that this disparity is even greater in real-world practice.

The point-in-time design of this study prevents any conclusions about causal relationships; however, identification of significant associations is possible. We assessed a number of patient and clinical variables, but this was not an exhaustive list of all factors that might influence clinical outcomes in patients with RA. Additional factors associated with suboptimal RA control include older patient age, lower socioeconomic status, language barriers, the failure to recognise symptoms associated with exacerbations, lack of self-management education, poor recognition of triggers and poor disease knowledge. For some of the study period, data collection was undertaken during the first wave of the COVID-19 pandemic, and we cannot rule out the potential impact that this may have had in terms of physician and patient recruitment/enrolment. Our study is also limited by its descriptive nature, but overall, it provides useful insights into perceived and actual T2T use and management decisions for patients with RA in a real-world clinical setting across six European countries.

CONCLUSION

While we observed a high percentage of rheumatologists indicating they used T2T principles, we saw discordance between rheumatologists' overall perception of T2T and what they practice in a real-world clinical setting, indicating that T2T could still be more widely implemented. Importantly, when rheumatologists and their patients were aligned and in agreement on T2T and the patient was aware that a T2T goal had been set, we saw that there were higher rates of satisfaction, patient engagement and more success in terms of achieving a goal. These findings highlight the importance of enlisting patients as partners in T2T, whereby the patient is appropriately informed about the treatment target, the planned tactic to reach this target under physician supervision, the most appropriate treatment regimen to achieve this goal and the risks and benefits of a T2T approach. In line with principles of patient-centred care, the patient should be involved in refining these targets to ensure they are consistent with the patient's values and preferences. Efforts should be made to increase engagement between rheumatologists and their patients with respect to setting of effective and achievable treatment goals and to address potential barriers to treatment introduction in accordance with T2T recommendations.

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Ethics approval This study involves human participants but data collection was undertaken in line with European Pharmaceutical Market Research Association guidelines, and as such did not require ethics committee approval, with the survey materials reviewed and given exemption by the Western Institutional Review Board (reference number: 1-1253914-1). No identifiable protected health information was extracted during the course of the study. Data were collected in such a way that rheumatologists and their consulting patients could not be identified directly; all data were aggregated and deidentified before receipt. Participants gave informed consent to participate in the study before taking part.

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