Barriers to, Facilitators of, and Interventions to Support Treat-to-Target Implementation in Rheumatoid Arthritis: A Systematic Review

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Barriers to, Facilitators of, and Interventions to Support Treat-to-Target Implementation in Rheumatoid Arthritis: A Systematic Review

(16/20 words)

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Key Indexing Terms: arthritis, rheumatoid; decision making, shared; guideline adherence; patient education; psychosocial intervention; quality improvement

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ABSTRACT

Objective. Treat-to-target (T2T) is recommended in the management of rheumatoid arthritis (RA) but its implementation is suboptimal. We aimed to identify interventional strategies targeted at improving T2T implementation in RA by systematically reviewing published evidence on barriers to, facilitators of, and interventions to support T2T implementation.

Methods. Systematic and scoping literature searches in PubMed/MEDLINE®, BIOSIS Previews®, Derwent Drug File, Embase®, EMCare®, International Pharmaceutical Abstracts, and SciSearch® were conducted to identify barriers/facilitators and interventions relating to T2T implementation in RA. The quality of included studies was assessed using Critical Appraisal Skills Programme (CASP) checklists. Data related to barriers/facilitators and interventions were extracted, grouped, and summarized descriptively, and a narrative synthesis was generated.

Results. In total, 146 articles were analyzed, of which 123 (84%) included ≥50% of the items assessed by CASP checklists. Of the 146 studies, 76 evaluated T2T barriers and facilitators, from which 329 relevant statements were identified and regrouped into 18 target areas, including: healthcare professionals' (HCPs') or patients' knowledge or perceptions; patient–HCP communication or alignment; and time or resources. Overall, 56 interventions were identified from 70 studies across the 18 target areas; 54% addressed disease activity or patient-reported outcome assessments. Of the 56 interventions identified, 36 improved T2T implementation and/or patient outcomes in RA.

Conclusion. Despite long-established T2T recommendations, there remain many barriers to its implementation. Interventions to improve T2T should be developed further and

assessed, with a particular focus on tailoring them to individual countries, regions, and healthcare settings.

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SIGNIFICANCE & INNOVATIONS

- The treat-to-target (T2T) approach, although recommended for the management of rheumatoid arthritis (RA), is still suboptimally implemented in clinical practice.
- Interventions designed to improve T2T implementation in RA are available, but there is limited evidence for their direct impact on T2T implementation and patient outcomes, and their effectiveness and feasibility will likely vary by region and healthcare system.
- Most of the 56 identified interventions were designed to streamline disease activity or patient-reported outcomes (PRO) assessments, improve shared decision-making (SDM), and reduce the burden on time or resources.
- To facilitate implementation of the T2T strategy in RA in practice, future priorities include focusing on eHealth intervention, SDM, and HCP self-reflective learning.

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INTRODUCTION

Remission and low disease activity (LDA) states in rheumatoid arthritis (RA) are associated with better clinical outcomes, quality of life and productivity, and lower medical costs, compared with when these treatment targets are not achieved (1,2). Treat-to-target (T2T) recommendations were introduced in management of RA in 2010 when consensus supported remission as an achievable goal of therapy (3,4). The T2T approach comprises assessing disease activity regularly, adjusting treatment as needed according to these assessments, shared decision-making (SDM) between the healthcare professional (HCP) and patient, and accounting for comorbidities and other patient characteristics or preferences (3). When T2T is used, patients with RA are significantly more likely to achieve remission or LDA compared with when T2T is not applied (5). Despite this, less than 25% of patients with RA achieve remission 24 months after initiating treatment in clinical practice (6). Furthermore, one or more T2T components, including recording a disease target and activity measure, and SDM, are not performed in more than 50% of routine visits (7,8). Patients with high disease activity are not always offered a change of treatment or may decline the offer (9). Moreover, many HCPs believe incorrectly that they are fully adherent to T2T guidelines (10).

Previous reports and narrative reviews have outlined some of the barriers to T2T implementation in RA, including the willingness of HCPs and/or patients to adhere to T2T, time and resource limitations, comorbidities, and communication challenges between HCPs and patients (11–14). However, previous reviews have not examined barriers in detail or, importantly, identified and evaluated implementation strategies. Our objective was to perform a systematic literature review (SLR) and detail the published evidence on barriers to, facilitators of, and interventions that support T2T implementation in RA.

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METHODS

A panel of 6 expert rheumatologists, who authored this manuscript and from here on are referred to as "working group", defined the research objectives and developed the research protocol for this SLR. The Population, Intervention, Comparison, Outcome, Time (PICOT) framework (15) was used to formulate 2 research questions (Table 1):

(1) What are the barriers to and facilitators of T2T implementation in RA?

(2) What are the practical methods for changing the behaviors and practice of HCPs and patients to improve and maintain T2T implementation in RA that are most feasible and impactful?

To address both questions, a SLR and scoping literature searches were performed to review and detail published evidence on the barriers to, facilitators of, and interventions (i.e., organized activities designed to improve health by changing or promoting specific behavioral patterns) (16) that support T2T implementation in RA.

Identification and selection of relevant publications. *SLR.* The SLR was performed in 2 parts using the following databases: BIOSIS Previews®, Derwent Drug File, Embase®, EMCare®, International Pharmaceutical Abstracts, PubMed/MEDLINE®, and SciSearch®: a Cited Reference Science Database. A search based on the PICOT questions was performed using the time period of January 1, 2015 up to March 1, 2021 for barriers/facilitators and January 1, 2010 up to July 1, 2021 for interventions to support T2T implementation (search strategy available in Supplementary Table S1).

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SLR data selection. Titles and abstracts of publications were screened, followed by full text review by a single reviewer (CC). A second independent reviewer (HW) screened a random 50% sample of publications at the screening stage and a further random 50% sample at the full text review stage. Publications were eligible if they were primary studies or SLRs that met the defined PICOT eligibility criteria (Table 1) and were published in English; narrative reviews were excluded.

Scoping searches. Following the SLR, a manual scoping PubMed literature search was conducted using additional keywords to cover other key aspects of the T2T pathway not included in the SLR search strategy for PICOT question 1 (RA + T2T, RA + treatment switch + perception, RA + patient–physician disconnect, RA + SDM) using the same date ranges. Reference lists of selected papers were scanned for additional relevant references.

Data extraction. Information on sample size and study design was collected. Statements associated with T2T barriers/facilitators were extracted and recorded, including those related to key steps of the T2T pathway. A short description of the intervention, study location (country and healthcare setting), and reported effectiveness of the intervention were recorded for studies describing interventions. Data extraction was conducted by a single reviewer (CC), with the second reviewer (HW) screening a random 20% sample independently for accuracy, with disagreements resolved by consensus.

Quality of evidence assessment. The quality of evidence for each of the eligible studies was assessed using the Critical Appraisal Skills Programme (CASP) checklist (17). Each CASP checklist includes 10–13 questions that can be answered either categorically

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("Yes," "No," or "Can't tell") or qualitatively. Studies were categorized as addressing or not ≥50% of the information evaluated in CASP checklists as there are no predefined criteria on interpreting the CASP results.

Grouping of T2T barriers, facilitators, and interventions. Statements related to T2T barriers/facilitators were assigned to target areas and grouped further within these areas into 1–4 subcategories of barriers/facilitators by 2 reviewers (CC and HW), followed by working group discussion. The same process was followed (without the subcategorization) to group interventions into types. Barriers/facilitators' target areas and intervention types were grouped further by stakeholder (patient, HCP, patient–HCP [barriers/facilitators], or system [interventions]).

Assessment of the interventions. The reported effectiveness of interventions was based on the presence of numeric and/or significant improvement in T2T implementation, defined as improvement in ≥1 of the following T2T components (adapted from Yu, et al. 2018 [7]): (1) recording a disease target, (2) recording a disease activity measure, (3) engaging in SDM, or (4) changing treatment if not at disease target; general RA management or care, and/or patient outcomes (DAS, remission or LDA rates, PRO) versus a control (or over time). Non-inferiority was considered as effective if designated as the primary endpoint. The feasibility of each intervention type was evaluated by the working group based on perceived ease of implementation; time, cost, and resource utilization; acceptability by HCPs and/or patients; and generalizability to other contexts.

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Narrative synthesis and expert opinion. Given the expected heterogeneity of study designs and outcomes (18,19), a narrative synthesis was considered more appropriate than a meta-analysis. This was conducted by grouping the extracted data first, followed by discussion of the results by the working group. Here, experts evaluated the evidence separately first, then convened to discuss the evidence and develop their proposals during 2 online meetings. Owing to the nature of narrative syntheses, all statistics presented are descriptive (18).

To develop the final narrative synthesis, the working group discussed the robustness and limitations of the analyses and aligned on recommended intervention strategies during a 3-hour online meeting. The final synthesis included a list of proposed intervention strategies considered by the working group to be most impactful and feasible in improving T2T implementation in RA in practice.

RESULTS

Identification and selection of relevant publications. Of the 254 publications identified through the first part of the SLR (PICOT question 1; T2T barriers/facilitators in RA), scoping searches and review of reference lists, 76 fulfilled the eligibility criteria for PICOT question 1 and were included (Figure 1; Supplementary Table S2). For PICOT question 2 on interventions to support T2T implementation in RA, 489 publications were identified from both parts of the SLR and review of reference lists and 70 were included (Figure 1; Supplementary Table S3).

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Quality of evidence assessments. Of the 76 studies reporting T2T barriers/facilitators, 96% addressed ≥50% of the information evaluated in the CASP checklists, and 50 (71%) of the 70 studies reporting interventions addressed ≥50% of the information evaluated in the CASP checklists (Supplementary Table S4).

Data extraction. From the 76 publications in the barriers/facilitators analysis, 329 statements relating to T2T barriers/facilitators were extracted (Supplementary Table S5). Most publications were primary observational (n = 50; 66%) or qualitative (n = 22; 29%) studies (Supplementary Table S4).

In total, 56 interventions were identified from the 70 studies included. Observational cohort or cross-sectional studies were the most common (53% of studies), followed by randomized controlled trials (RCTs) (31%; Supplementary Table S4). Most (80%) of these interventions were designed and evaluated in North America and Europe, with <30% conducted at multiple centers (Supplementary Table S6).

Grouping of barriers to/facilitators of T2T implementation. Statements related to T2T barriers/facilitators were assigned to 18 target areas related to patients (n = 7), HCPs (n = 6), and both patients and HCPs (n = 5; Figure 2). These broadly covered knowledge/experience in RA and T2T; perception of RA management strategies and treatment options; perceived and assessed disease activity; time and resources; patients' clinical conditions and social determinants of health; and patient–HCP relationship, communication, and alignment (Figure 3). Across target areas, statements were grouped into a further 46 subcategories, each reflecting a specific T2T barrier/facilitator in RA (Supplementary Table S5).

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Grouping of interventions to support T2T implementation. The 56 identified interventions were classified into 18 types: 6 targeting the patient, 5 targeting the HCP, and 7 targeting healthcare systems (Figures 2 and 4). Many interventions targeted more than 1 aspect of T2T and were included more than once. Over half of interventions (n = 30; 54%) were designed to streamline disease activity or PRO assessments, including: electronic disease assessment recording; integrated PRO assessment; ultrasound assessment; disease assessment processes/quality improvement (QI) initiatives; telehealth monitoring; and patient PRO dashboard/visual feedback tools. Improvement of SDM was the focus of 41% (n = 23) of interventions (HCP training, learning collaboratives, decision-making tools, and T2T/SDM prompts; and patient educational tools, decision aids, telehealth education, and nurse-led patient education), while 39% (n = 22) of interventions aimed to reduce the burden on time/resources (HCP decision-making tools, patient decision aids, patient telehealth education, nurse-led patient education, allied HCP-supported T2T strategies, and multidisciplinary team programs).

Relationships between data reporting T2T barriers, facilitators, and interventions. The most frequent target areas associated with interventions were patient assessment of disease activity or PROs (n = 10 intervention types), HCP time and resource constraints (n = 9), patient perceptions of treatment efficacy (n = 8), HCP disease assessment (n = 8), SDM (n = 8), and patient–HCP alignment on disease activity (n = 8) (Figure 3). Only 1 intervention type was targeted at other aspects of patient–HCP alignment, and 1 at patients' time, resources, and social determinants of health.

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Reported effectiveness of T2T interventions. An assessment of effectiveness versus a control was reported for 42 (75%) of the 56 interventions identified. Across these 42 studies, patient cohort sizes ranged from 18 to 68,247, depending on the type of study (Supplementary Table S6). Most studies reported a majority of female patients (61–90%), although a small number of studies included mostly male patients (87–88%). Mean disease duration was reported in only a small subset of studies, ranging from ≤1 year to 15.7 years, and most included patients with established disease (Supplementary Table S6).

Overall, 36 (64%) of the 56 interventions were reported as effective in improving RA management or care and none were associated with worse T2T implementation or patient outcomes (Supplementary Table S6). Fourteen of the 56 interventions (25%) reported a numeric or significant improvement in T2T implementation. These included disease assessment tools or processes (including QI initiatives) that improved documentation of composite disease activity measures (20–22) and HCP training and/or feedback, which led to more global improvements in T2T application including SDM (23−25). Improvement in patient outcomes was reported for only 8 (14%) of the 56 interventions, with higher percentages of patients achieving treatment targets with electronic disease assessment recording and QI initiatives (20,24,26), allied HCP or multidisciplinary support (27,28), and a text message telehealth monitoring tool (29). While interventions such as patient educational materials (30-32), patient decision aids (33-35), and discussion of ultrasound assessment results (36,37) did not directly improve T2T implementation or patient outcomes, they improved patient knowledge and treatment adherence, and/or reduced decisional conflict.

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Opinions on the feasibility of T2T interventions and intervention strategies. Of the 18 intervention types, the working group felt that HCP training, patient education (tools and telehealth education), HCP and/or patient decision-making tools, and electronic disease assessment recording were the most feasible across diverse settings. The panel emphasized that local systems and resources would determine feasibility of staff- or resource-intensive interventions such as multidisciplinary team programs, allied HCP-supported T2T strategy, nurse-led patient education, and ultrasound assessments.

DISCUSSION

This SLR provides important information on T2T in RA. Of 146 studies identified, 76 evaluated T2T barriers and facilitators, from which 329 relevant statements were identified and regrouped into 18 target areas, including: HCPs or patients' knowledge or perceptions; patient–HCP communication or alignment; and time or resources. Furthermore, 56 interventions to improve T2T implementation were identified from 70 studies and grouped into 18 types, of which 54% (n = 30) addressed disease activity or PRO assessments. However, the effectiveness of the interventions was variable and only 25% (n = 14) of interventions improved T2T implementation in RA, indicating that more work is needed on how to improve T2T implementation.

Target areas associated with T2T barriers/facilitators were not only related to regular disease activity assessment and treatment adjustment, but also captured T2T elements that are often overlooked, such as SDM and accounting for patient factors (e.g., comorbidities and social determinants of health) and preferences (3,38-40). The barriers/facilitators identified were generally consistent with previous narrative reviews, which similarly cited physician adherence, patient willingness to adhere to or adjust treatments, comorbidities,

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patient–HCP communication, and healthcare system factors (11−13). While previous reviews have explored patient and physician barriers independently, our analysis found many parallels between target areas for patients and HCPs, including knowledge and perceptions around RA management or treatments, challenges in disease assessment, and time and resources; and emphasized the need to consider barriers/facilitators affecting the interpersonal relationships and communication between patients and their treating HCPs, as well as social determinants of health (i.e., patient demographics and availability of social support).

Most of the interventions identified related to disease activity/PRO assessment, SDM, and reduction of time and resource burden. Interventions included: electronic health records to incorporate more reliable, consistent, and instructive disease activity/PRO assessments (20,22,41); telehealth monitoring tools or processes (29); delivery of patient education via telehealth or online (42); and online tools to support decision-making (26,34,35,43). Few interventions addressed HCP–patient relationships and alignment, and patient social determinants of health, highlighting these as potential areas for novel interventions or alternative solutions. Although issues relating to time constraints were originally thought to be difficult to modify, there were several interventions aimed at saving time during visits, such as decision aids (33,35,44-48), integrated eHealth disease activity and PRO assessments (20,41,49−53), and allied HCP support (27,28,54−59). The latter is further supported by T2T recommendations, which reinforce the role of the multidisciplinary team, particularly rheumatology nurse specialists (3,60). While only one-third of interventions were associated with a direct improvement in T2T implementation or patient outcomes, an additional one-third will likely have a positive impact on the use and impact of T2T through improving other aspects of RA care (e.g., treatment adherence and

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decisional conflict) (31,33,35,42,61). Overall, the evidence suggests that eHealth interventions can improve T2T implementation, patient outcomes, and/or RA management.

Further education for patients around treatment goals and options is required to support and encourage patient involvement in SDM and self-management. This in turn may address barriers associated with patient–HCP communication and alignment (e.g., by reducing decisional conflict regarding treatment change [62]), save time during visits, and motivate HCPs to involve patients in treatment decisions. The most practical, time-efficient, and generalizable solutions involve sharing educational materials (e.g., videos, infographics, information booklets [30−32,63,64]) for patients to review outside of visits in the waiting room or at home and increase the use of validated patient decision aids during visits (33,35,45,65). Patient education may also be delivered by nurses or allied HCPs, if possible, to save time (32,66). When selecting tools or aids, key considerations include the quality of the materials, individual needs and preferences, and the suitability for the culture or context (67,68). To maximize the uptake and effectiveness of patient materials, patients and clinicians should be involved in their design and adaptation, alongside specialist educators, patient advocates, and allied HCPs, as available (47,69,70).

Following on from this narrative synthesis, we put forward three strategies that would seem to be the most impactful and feasible in improving T2T implementation in RA focusing on *(1)* eHealth intervention, *(2)* SDM, and *(3)* HCP self-reflective learning (Figure 5). eHealth interventions are expected to play an increasingly important role in RA management (71,72), although future research, validation, and infrastructural changes are required before they become commonplace in clinical practice. For a more straightforward and generalizable approach, we suggest supporting T2T application during eHealth consultations by providing guidance to HCPs and patients on how to prepare for these visits,

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including training on online or self-directed joint assessments (69). Indeed, high-quality patient education and HCP training are integral to T2T implementation, especially to support SDM, but should ideally be individually tailored and needs-based (3,25,67). Structured HCP training delivered as a group-based learning collaborative program integrating QI principles and improvement feedback has also been successful in improving both HCP skills and T2T implementation (25,43,73). We therefore propose that these are incorporated into existing medical education and scientific meetings to encourage self-directed improvement. It should be noted, however, that large-scale validation and uptake of evidence-based interventions to support T2T through SDM (e.g., patient decision aids) has not yet been observed (65).

This literature review has some limitations. We were unable to perform a meta-analysis since the data were highly heterogeneous. A narrative synthesis is inherently a more subjective process based on expert evaluation and discussion (18,19). However, we grouped the barriers and facilitators to allow for a comprehensive overview. The target areas were defined by the topics that emerged from the studies, although alternative methods of synthesizing these data could have been considered. It was challenging to assess whether the interventions increased T2T. Indeed, fewer than one-third of interventions were evaluated through RCTs, a quarter of studies lacked comparative assessment of effectiveness, and there were few reports on feasibility or long-term adherence to T2T interventions in the clinic. Furthermore, the generalizability of the findings across healthcare systems or settings may be imperfect due to a regional bias in the included studies. Expert opinion was able to fill in some of these publication gaps, albeit subjectively, representing a strength of this analysis. However, this highlighted the need for future research (especially RCTs) to allow for comparison using standardized outcomes (e.g., T2T scores) (24) over a

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longer time frame and across broader healthcare settings. The working group did not include patient research partners or non-rheumatologist healthcare professionals however, it would have been interesting to know if their expertise would have produced additional interpretations to our findings. The time interval between the literature search cut-off date of 2021 and this publication is a limitation of our work. However, we are not aware of any other major publications in the field and believe our study and conclusions remain valid in 2024. Additionally, although T2T is widely accepted, alternatives have been proposed, such as the dual T2T strategy approach, where separate targets are defined for control of inflammation (biological remission) and control of disease impact (symptom remission) (74). Stricter implementation of T2T may not lead to further improvements in treatment outcomes over less strict implementation of T2T. In patients with RA, a study involving two cohorts of patients with RA with varied T2T implementations demonstrated that stricter implementation of T2T led to improved outcomes (75) whilst the longitudinal analysis of the RA-BIODAM cohort showed strict implementation did not result in less radiographic progression (76). Similarly, in patients with undifferentiated arthritis already in low disease activity, further treatment intensification did not result in meaningful functional improvements (77) This could be due to the fact that the intention to apply T2T by itself is sufficient, and a more rigorous approach does not further improve outcomes.

Moreover, strict implementation of T2T can be hindered by a lack of adherence to T2T in a substantial proportion of patients, as demonstrated in the RA-BIODAM cohort. This is due mainly to physician decision that treatment was acceptable and could be predicted by patients' clinical features (78

Such alternatives need further confirmatory data.

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Overall, although T2T has been widely recommended in the management of RA, there remain many barriers to its implementation. Interventions to improve T2T should be developed further and assessed, with a particular focus on tailoring interventions to specific countries, regions, and healthcare settings.

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FIGURE LEGENDS

Figure 1. Identification of publications in the systematic literature review and scoping searches. PICOT = Population, Intervention, Comparison, Outcome, Time; RA = rheumatoid arthritis; SLR = systematic literature review; T2T = treat-to-target.

Figure 2. Data extraction and grouping of T2T barriers/facilitators and interventions to support T2T implementation. * The full list of target areas is shown in Figure 3. †The full list of intervention types is shown in Figure 4. ‡Statements related to T2T barriers/facilitators were grouped into 1–4 subcategories of barriers/facilitators within each target area (Supplementary Table S5). HCP = healthcare professional; RA = rheumatoid arthritis; T2T = treat-to-target.

Figure 3. Target areas of T2T barriers/facilitators and the number of intervention types addressing each target area. Details and examples of barriers/facilitators for each target area are shown in Supplementary Table S5. *Based on the 18 target areas; each intervention type (full list shown in Figure 4) may address ≥1 barrier. HCP = healthcare professional; PRO = patient-reported outcome; SDM = shared decision-making; T2T = treat-to-target.

Figure 4. Interventions to support T2T implementation in RA by type. *Structured learning sessions and performance feedback. †Interventions may be assigned to ≥1 type. HCP = healthcare professional; PRO = patient-reported outcome; RA = rheumatoid arthritis; SDM = shared decision-making; T2T = treat-to-target.

Figure 5. Overall strategies and recommended interventions to improve T2T implementation in RA

Table 1. Research questions defined using the PICOT methodology (15)

Research question	P Population	I Intervention	C Comparison	O Outcome	T Time
Barriers to and facilitators of T2T implementation in RA	Patients with RA and their treating HCPs	Overarching principles and individual recommendations of T2T in RA (3)	N/A	Patients' and HCPs' perceived barriers to and facilitators of T2T implementation	Based on studies conducted in the past 6 years (2015–2021)
Research question 1	What are the barriers to and facilitators of T2T implementation in RA?				
Interventions to support T2T implementation in RA	Patients with RA and their treating HCPs	Practical interventions for improving T2T implementation	Standard of care/no intervention	Improved T2T implementation in a sustainable way in RA	Based on studies conducted since the introduction of T2T in RA (2010–2021); any duration of intervention
Research question 2	What are the practical methods for changing the practice and behaviors of HCPs and patients to improve and maintain T2T implementation in RA that are most feasible and impactful?				

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HCP = healthcare professional; N/A = not applicable; PICOT = Population, Intervention, Comparison, Outcome, Time; RA = rheumatoid arthritis; T2T = treat-to-target.

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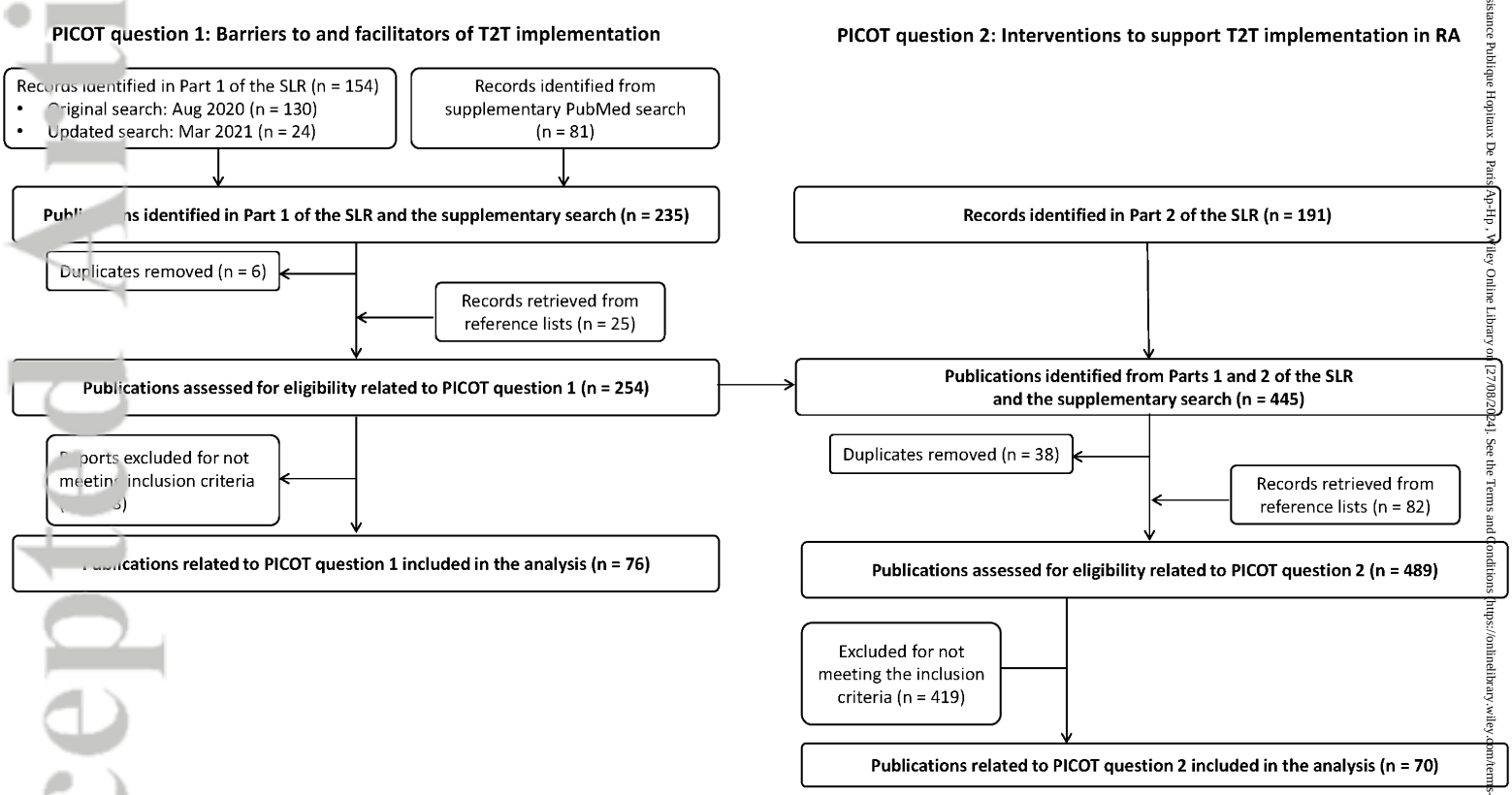

Figure 1 300 dpi.tif

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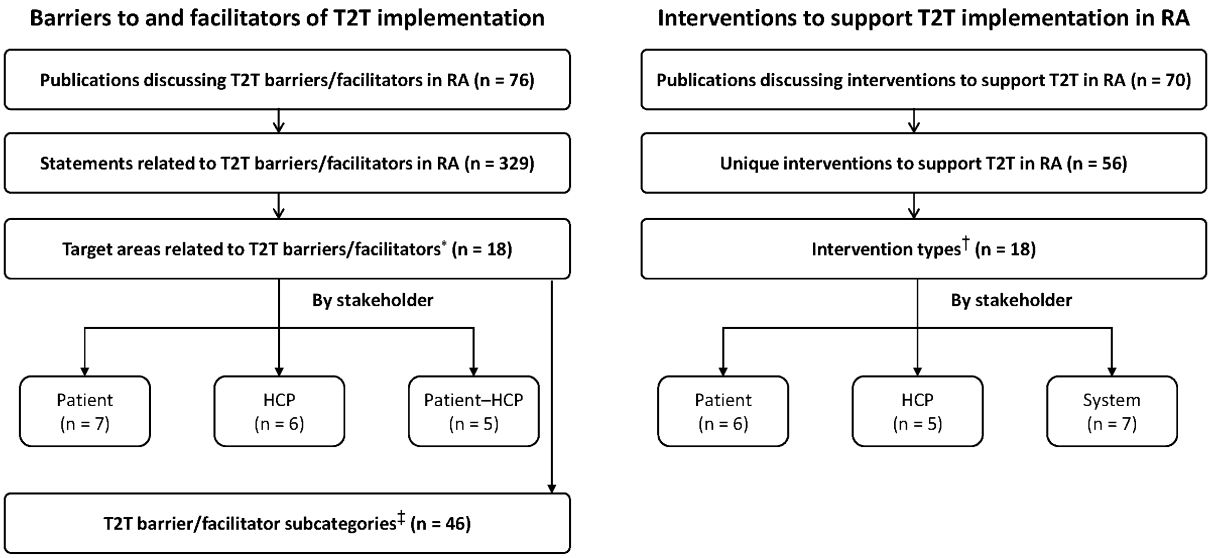

Figure 2 300 dpi.tif

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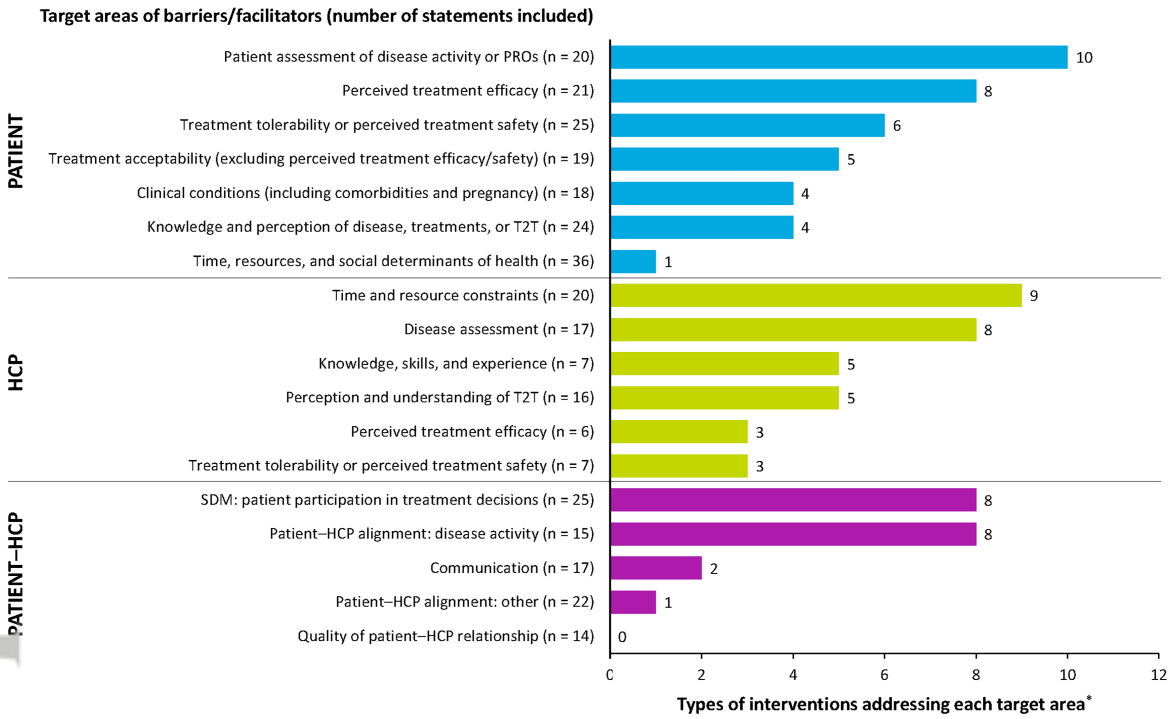

Figure 3 300 dpi.tif

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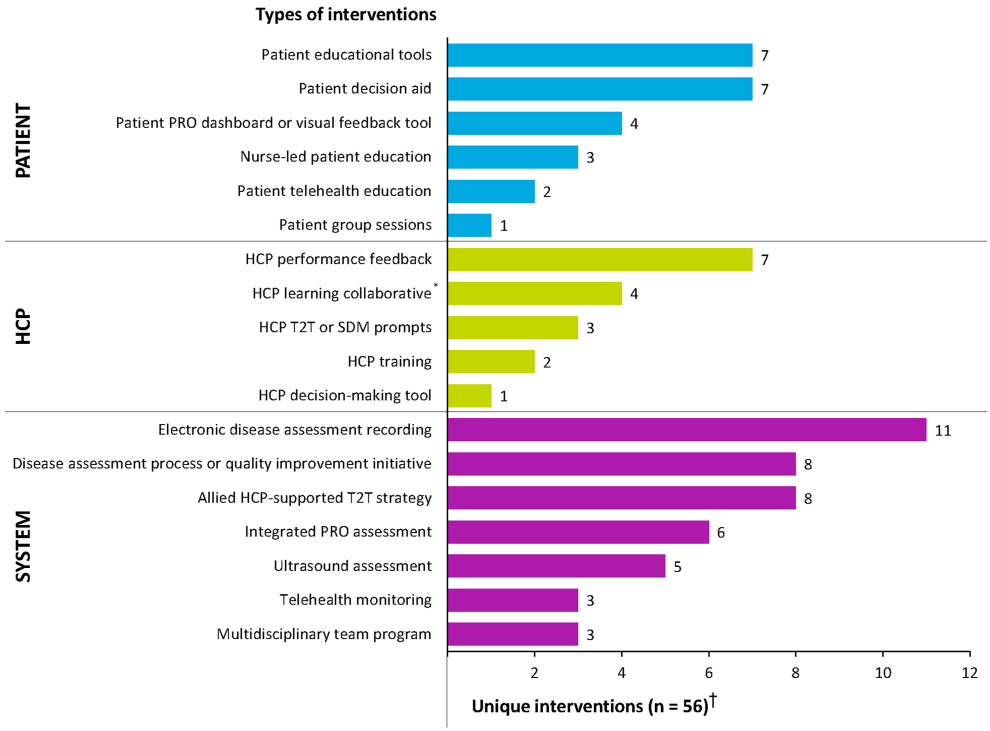

Figure 4 300 dpi.tif

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Strategies	eHealth intervention	Shared decision-making	HCP self-reflective learning
Patient	• Telehealth education	• Decision aids • Educational tools	—
HCP	—	• Decision-making tools • Learning collaboratives • T2T/shared decision-making prompts	• Training • Performance feedback
System	• Electronic disease assessment recording • Telehealth monitoring	—	—

Improve T2T implementation in RA with feasible and impactful strategies derived from the narrative synthesis

Figure 5 300 dpi.tif

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