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ORIGINAL ARTICLE

Standardizing and personalizing the treat to target (T2T) approach for rheumatoid arthritis using the Patient-Reported Outcomes Measurement Information System (PROMIS): baseline findings on patient-centered treatment priorities

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Abstract A treat to target (T2T) approach to management has become the standard of care for patients with rheumatoid arthritis (RA). While consensus T2T recommendations call for patient involvement in the treatment process, the targets commonly used to drive therapeutic decisions involve limited patient input. A pilot study was developed to explore whether the Patient-Reported Outcomes Measurement Information System (PROMIS) could add value to the T2T approach by providing a way to bring patient goals into the process. We report here the baseline data from this study. RA patients from an academic rheumatology practice were recruited to participate in this 1-year study. Patients were asked to complete PROMIS computer-assisted testing at quarterly visits during the year. At baseline, they were asked to identify the PROMIS domain (Pain Interference, Fatigue, Depression, Physical Function, and Social Function) that felt most important to their quality of life. They were then asked to select five representative items from this domain, to be followed through the year. Complete baseline data was available for 119 patients. Most selected Physical Function (39%) or Pain Interference (37%) as their highest priority PROMIS domain. Sixty percent ranked Depression as their lowest priority domain. Younger patients more frequently prioritized Social Function, while older patients more frequently prioritized Fatigue. The incorporation of PROMIS questionnaires into routine clinic visits is a feasible mechanism for incorporating patient preferences into a T2T approach to managing RA.

Keywords PROMIS · Rheumatoid arthritis · Treat to target

Key message PROMIS questionnaires provide a feasible mechanism for incorporating patient preferences into the management of RA.

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Introduction

The treat to target (T2T) recommendations for the management of rheumatoid arthritis (RA) were first developed by an international task force in 2010 and reported in a publication that laid out four overarching principles and 10 specific recommendations for treating RA [1]. These recommendations included setting the primary target for treatment of RA as clinical remission, adjusting drug therapy at least every 3 months until the desired treatment target is reached, and measuring and documenting disease activity more frequently for patients with high/moderate disease activity and less frequently for patients with sustained low disease activity or remission. At the time of publication, these recommendations were based on expert opinion and a small body of published evidence [2–5]. Subsequently, a number of published studies have demonstrated the effectiveness of the T2T approach in RA [6–8]. In one such study, the Dutch DREAM registry examined both the feasibility and outcomes of employing a T2T strategy in routine clinical practice. Investigators looked at remission rates and predictors of remission in newly diagnosed RA patients treated with a T2T strategy and concluded that this strategy was both more effective and more cost effective than usual care [7, 8]. As this registry enrolled patients

with a new diagnosis of RA, it is unclear whether or not these findings can be generalized to RA patients in long-term management.

In their initial T2T recommendations, the task force identified the importance of patient involvement in the treatment process, and published a patient version of these recommendations [9]. Patient involvement is important for a number of reasons. It can help patients prepare for a visit and improves communication between patient and physician [10]; it can also ensure that the target for treatment is appropriate for the patient. Open communication and increased patient involvement have been shown to increase treatment adherence and increase patient satisfaction [11]. Despite the guidance to include patient involvement, the success of the T2T strategy in clinical trials has primarily been assessed using clinical disease activity outcomes, such as remission, and not patient-centered outcomes [12]. In many ways, this method of evaluation runs counter to both the T2T recommendations and recent literature highlighting the importance of patient-centered care and the integration of patient priorities into treatment decision-making. Patient concerns regarding the value and costs of their therapy, and patient-centered outcomes, such as work productivity, have not typically been considered when implementing and assessing T2T strategies in clinical care [13, 14]. Additionally, patients and physicians tend to consider different aspects of disease when making treatment decisions [20,21]. Unfortunately, there is no existing tool that enables RA clinicians to include, in an objective manner, patients' perspectives when setting goals and monitoring their response to therapy.

The addition of a standardized and validated patient-reported outcome assessment to the existing core set of treatment targets already available may be one approach to addressing the gap in patient involvement in RA treatment. The Patient Reported Outcomes Measurement Information System (PROMIS) is an NIH Common Fund initiative that developed patient-reported outcome measures for use across chronic conditions. PROMIS instruments were developed utilizing a rigorous, mixed methodology (qualitative and quantitative) [22] and have been validated in RA [23]. These measures assess outcomes relevant to patients with RA, including pain interference, physical function, social function, fatigue, and depression. While recent research provides further support for the reliability and validity of the PROMIS measures in patients with RA, [16] there is limited data on the feasibility of incorporating PROMIS instruments into a clinical setting. We instituted a pilot project to evaluate the added value of linking PROMIS instruments to an existing T2T RA treatment approach. We now report baseline data on the feasibility of adding PROMIS assessments to the existing electronic health record (EHR) for RA patients in a way that enables individualized patient goal-setting. We also report patient-identified treatment targets using PROMIS domains (pain, fatigue, depression, physical function, and social function), including specific priority items within a specified domain that are most important to patients, demographic differences in patients' treatment targets, and baseline differences in PROMIS domains based on number of comorbid conditions.

Materials and methods

Participant recruitment

The patient population for this study is drawn from a single academic rheumatology clinic. Participants were recruited over a 16-month period from May 2014 to September 2015. Our goal was to recruit a sample of 120, a number we believed to be feasible within the clinic during the time framed planned for the study; as this was a pilot study, we did not perform a formal power calculation. Potential participants were approached by a study coordinator during routine visits to the clinic, with an attempt to recruit a cohort that was evenly divided between remission or low disease activity (clinical disease activity index [CDAI] <10) and moderate to high disease activity (CDAI ≥10).

Inclusion criteria (a) Physician-confirmed diagnosis of RA, (b) 18 years of age or older, (c) English speaking, (d) current CDAI score available at the time of study enrollment, (e) if CDAI ≥10, patient is an appropriate candidate for treatment acceleration in the opinion of the investigator and would be willing to escalate therapy if indicated, and (f) ability to understand and willingness to provide written informed consent

Exclusion criteria (a) Cognitive impairment that would interfere with completing a face-to-face interview, (b) primary rheumatologic diagnosis other than RA, (c) current and uncontrolled thyroid disease, diabetes, depression, cardiac, pulmonary, renal, gastrointestinal, hepatic, or metabolic disease, (d) documented diagnosis of fibromyalgia or other pain conditions, other than RA, that are likely to interfere with assessments of RA disease activity, (e) women who are pregnant, breastfeeding or planning to become pregnant during the study period, and (f) functional class IV (bedridden) as defined by the ACR classification of functional status

Procedures

All consenting patients received a modified T2T disease management approach, which included PROMIS computer adaptive tests (CATs) of pain, fatigue, depression, physical function, and social function, in addition to standard clinical

assessments that included the CDAI and the Routine Assessment of Patient Index Data 3 (RAPID3). Patients were assessed at baseline and approximately every 3 months during the 12-month follow-up period, for a total of five scheduled assessments. Visits were intended to coincide with routine clinic visits; missed visits were not rescheduled. The baseline assessment consisted of sociodemographic questions, PROMIS CATs, and the Functional Assessment of Chronic Illness Therapy-Treatment Satisfaction-Patient Satisfaction (FACIT-TS-PS) [15]. Participants were instructed to rank PROMIS domains of Pain, Fatigue, Depression, Physical Function, and Social Function based on which domain they felt was most important to their quality of life. After selecting their most important domain, participants then selected five questions within the domain that addressed their treatment goals.

PROMIS CATs were administered on computers in the rheumatology clinic using Northwestern's web-based Assessment Center^{SM} data collection platform [16]. PROMIS measures are accessible in Assessment Center^{SM} and the Assessment Center Application Programming Interface (API) that allows local data collection systems to administer self- and proxy-reported measures. The measures, including guidance on scoring and interpretation, also can be downloaded from the HealthMeasures website [17]. The highest priority patient-nominated PROMIS domain and their five selected items were shared with the treating clinician for use in guiding conversations between the patient and provider about whether or not the patient's treatment goals were being met. The electronic health record (EHR) used in the clinic was modified to allow physicians to enter these data into the visit record, so that they could be tracked on subsequent visits. A standardized flow sheet was added to the EHR, which allowed physicians to record to document individual items in the CDAI and RAPID 3 scores as well as PROMIS assessment scores. Direct integration of PROMIS scores from Assessment Center^{SM} into the EHR was not possible with the EHR build that was in use at our site at the time of the study. These flow sheets were cumulative so these scores could be tracked visit to visit. Once physicians were familiar with the flow sheets, they were able to enter scores in less than 30 s. Additional data collected from the medical record included medical history of RA, insurance type, laboratory results, CDAI scores, and current medications. Participants received modest compensation for participation in the study.

PROMIS measures are scored on a *T* score metric, which has a mean of 50 and standard deviation of 10 in the US general population. Higher scores represent a higher level of the measured domain (e.g., more Pain, better Physical Function). This report provides a descriptive summary of the baseline data.

Results

Enrollment and participant demographics

A total of 121 patients were enrolled in the study; we report here on 119 patients who provided complete PROMIS data at their baseline assessment. Most patients were female (91%), and the sample was roughly evenly divided between low and high disease activity (Table 1). The mean age of the participants was 54 years. Based on self-reported date of diagnosis, 18 patients (15%) had been diagnosed within the previous 2 years. Participants reported a range of comorbidities at their baseline assessment: 42% (n = 44) reported concomitant osteoarthritis, 25% (n = 26) reported soft tissue rheumatism, and 24% (n = 25) reported depression. Other prevalent comorbidities reported were hypertension, migraines and anxiety. Patients reported a mean of 1.8 comorbidities (SD = 1.5; median = 2; range = 0 to 6).

PROMIS and FACIT-TS-PS scores

Physical Function and Pain Interference *T* scores in this sample were nearly 8 points worse than the general population mean of 50 (Table 2). Fatigue *T* scores were also substantially worse than the general population with a mean of 56.4 (higher scores indicate more fatigue). Mean Depression and Social

Table 1 Patient characteristics (N = 119)

	Median	Range
Age, years	57	21–77
	N	%
Female	108	91%
Hispanic	14	12%
Race		
White	84	71%
Black	17	14%
Other, multiracial	18	15%
Education		
HS Graduate or less	13	11%
Some college	23	19%
College degree	47	40%
Advanced degree	36	30%
Married or living with partner	78	66%
Employed (including self-employed)	71	60%
Baseline CDAI (n = 3 missing)		
≤10	53	46%
>10	63	54%
	Median	Range
Years since diagnosis	11	0–52
CDAI score (n = 3 missing)	10.5	0–65.5

Table 2 Baseline PROMIS *T* scores and FACIT-TS-PS scores

	Mean (SD)	Range
PROMIS		
Physical function	42.3 (5.9)	30–58
Pain interference	57.6 (7.5)	39–70
Fatigue	56.4 (9.2)	24–76
Social function	47.5 (7.3)	32–68
Depression	51.4 (8.4)	34–73
FACIT-TS-PS		
Physician communication (0–36)	34.0 (3.4)	22–36
Treatment staff communication (0–12)	6.0 (4.6)	0–12
Technical competence (0–9)	8.6 (0.9)	5–9
Nurse communication (0–9)	7.9 (2.3)	0–9
Confidence and trust (0–12)	11.6 (1.0)	6–12

Function *T* scores, however, were not substantially different from those of the general population. FACIT-TS-PS scores suggested that patients had a high level of confidence in the competency and communication skills of the physicians and nurses in the clinic. The communication skills of other clinic staff was ranked somewhat lower (Table 2).

Patient-selected PROMIS domains and items

Most patients selected Physical Function (39%) or Pain (37%) as their PROMIS domain of highest priority (Table 3). Depression was ranked as the lowest priority domain for 60% of patients. A total of 182 unique items were selected within patients' targeted domains. The most commonly selected items for each domain are summarized in Table 4.

Demographic differences in PROMIS domains

The priority domain selected by patients was associated with same-domain PROMIS score severity for Pain, Fatigue, and Depression. For example, patients who assigned higher priority rank to Pain reported worse Pain Interference *T* scores than patients who assigned higher priority to other domains (Table 5). This was not the case for the two PROMIS function domains (Physical Function and Social Function). In addition, among the top two domains selected, priority domain was associated with baseline clinical disease activity: Patients with CDAI >10 prioritized Pain (44%) over Physical Function (37%), while patients with CDAI ≤10 prioritized Physical Function (43%) over Pain (26%).

Within our patient sample, there was a significant difference between domain priority and age. The small number of patients who prioritized Social Function tended to be younger (mean age = 34), whereas those who prioritized Fatigue tended to be older (mean age = 58). Disease duration was not correlated with selection of priority domain. Baseline data showed differences in priority domains based on ethnicity. Fifty-four percent of non-White participants prioritized Pain, whereas White patients were more likely to prioritize Fatigue and Physical Function. We also compared priority domains in patients with up to one comorbidity to patients with two or more comorbidities; 43% of patients with up to one

Table 3 Domain priorities

	1st priority (%)	2nd (%)	3rd (%)	4th (%)	5th priority (%)
Full sample					
Physical function	39	32	17	9	3
Pain	37	23	25	12	4
Fatigue	16	26	32	18	7
Social function	3	14	18	39	25
Depression	5	5	8	22	60
CDAI ≤10 (n = 53)					
Physical function	43	30	15	9	2
Pain	26	23	28	19	6
Fatigue	17	17	26	26	11
Social function	6	23	25	28	19
Depression	8	8	6	17	62
CDAI >10 (n = 63)					
Physical function	37	33	19	8	3
Pain	44	24	24	5	3
Fatigue	16	32	38	11	3
Social function	0	8	11	49	32
Depression	3	3	8	27	59

Table 4 Most frequently selected priority items by domain

Physical function (of 126 total items)	Pain interference (of 45 total items)	Fatigue (of 95 total items)	Social function (of 35 total items)	Depression (of 28 total items)
[14/46] Are you able to exercise for an hour?	[14/44] How much did pain interfere with doing your tasks away from home (e.g., getting groceries, running errands)?	[11/19] How often did you have to push yourself to get things done because of your fatigue?	[3/4] I have trouble doing all of the family activities that I feel I should do	[4/6] I felt emotionally exhausted
[13/46] Does your health now limit you in doing vigorous activities, such as running, lifting heavy objects, participating in strenuous sports?	[14/44] How much did pain interfere with your day to day activities?	[6/19] How often did you have trouble finishing things because of your fatigue?	[2/4] I have trouble doing everything for my family that I feel I should do/[2/4] I have trouble doing all of the work that I feel I should do (include work at home)	[3/6] I found that things in my life were over-whelming
[10/46] Does your health now limit you in doing strenuous activities such as backpacking, skiing, playing tennis, bicycling, or jogging?	[11/44] How much did pain interfere with your ability to work (include work at home)?	[5/19] How often did your fatigue make it difficult to organize your thoughts when doing things at work (include work at home)?	[2/4] I feel limited in the amount of time I have for my family	[6 items tied for 3rd place, rated by 2 patients each]

Number in brackets [*n*/*N*] indicate the number of patients who identified that item in their top 5 (*n*) out of the number of patients who selected that domain as their priority (*N*)

comorbidity listed Pain as their priority versus 32% of patients with more than one. Number of comorbid conditions was associated with worse PROMIS domain scores (Table 6).

Clinic flow

Completion of the PROMIS CAT and other questions in a timely fashion immediately prior to the visit proved to be something of a challenge. Patients were able to use the computer in the exam room to access Assessment Center[SM] and complete their assessment while waiting for their provider. On average, patients took 10 min to complete the study questions; the baseline and final assessment took longer, roughly 15 min. Some patients took significantly longer when reading and answering questions, or needed assistance completing the questions. For patients needing assistance, the study coordinator would read individual questions and answers aloud. This assistance made the assessments more time consuming and occasionally slowed down clinic flow. Patients were asked to arrive early for their appointments in order to complete their study questions ahead of time. When the entire assessment could not be completed before the study visit, patients were asked to remain after their visit to complete the assessment. An additional challenge was limited access to computers. When the clinic was full, patients were able to complete their study assessment on laptops in the waiting room before being roomed for their appointment. For subsequent visits, we modified the process to allow patients to complete this information online during the 48 h before coming to clinic. We did not specifically analyze the effect of home versus clinic completion of PROMIS assessment in light of the additional variables involved (visit number, disease activity, and treatment changes). When available, physicians did not find entry of this data into the EHR to be much of a burden, as it was integrated with existing data entry for other clinical outcome measures. Fifty-five percent of patients reported they were very likely to participate in a study like this again. Participating physicians also

Table 5 Mean PROMIS scores and corresponding domain priority rank

Physical function			
Rank	1	2	3–5
N	45	38	33
T score, mean (SD)	43.6 (5.9)	41.5 (6.5)	41.5 (5.2)
Pain interference			
Rank	1	2	3–5
N	43	25	48
T score, mean (SD)	60.9 (6.4)	56.1 (7.9)	55.6 (7.3)
Fatigue			
Rank	1–2	3	4–5
N	48	37	30
T score, mean (SD)	58.7 (7.5)	57.6 (8.4)	51.4 (10.7)
Social function			
Rank	1–3	4	5
N	42	45	29
T score, mean (SD)	49.0 (8.4)	46.7 (6.1)	46.5 (7.2)
Depression			
Rank	1–4	5	
N	46	70	
T score, mean (SD)	55.8 (7.6)	48.6 (7.7)	

Table 6 Mean PROMIS and FACIT-TS-PS by number of patient-reported comorbidities

	Number of comorbidities			
	0–1 (n = 48)	2 (n = 26)	3–6 (n = 29)	ANOVA p value
PROMIS				
Physical function	43.6 (5.5)	42.0 (6.0)	40.4 (4.9)	0.055
Pain interference	56.1 (7.9)	57.4 (6.4)	60.3 (5.8)	0.037
Fatigue	54.9 (9.4)	56.4 (6.9)	59.5 (8.3)	0.076
Social function	48.4 (7.4)	49.0 (6.6)	44.7 (6.3)	0.034
Depression	50.5 (8.1)	52.1 (9.4)	53.6 (6.3)	0.259
FACIT-TS-PS				
Physician communication (0–36)	33.9 (3.3)	34.6 (2.6)	33.6 (3.8)	0.506
Treatment staff communication (0–12)	6.6 (4.3)	6.0 (4.6)	6.0 (4.8)	0.770
Technical competence (0–9)	8.6 (0.9)	8.8 (0.7)	8.6 (0.9)	0.592
Nurse communication (0–9)	8.0 (2.4)	8.1 (2.0)	7.9 (2.2)	0.934
Confidence and trust (0–12)	11.7 (0.9)	11.7 (0.8)	11.3 (1.4)	0.268

indicated a willingness to use this approach in the future, but stressed the importance of integrating the data acquisition into the existing EHR.

Discussion

PROMIS offers an opportunity to provide efficient and flexible patient-centered input into the T2T goal of RA practice. We report our baseline findings with respect to patient domain priorities and patient-identified treatment targets, as well as PROMIS domain preferences and scores associated with disease activity and comorbidity. The results help describe patient-selected treatment targets using the PROMIS domains. The PROMIS CAT assessments were successfully incorporated into clinic flow, reviewed by providers and entered into EMRs.

The high-priority domains most frequently selected by RA patients in this study were Physical Function and Pain. Of note, patient T scores for Physical Function, Pain Interference, and Fatigue in this sample were significantly worse than the general population. They were also worse within the subsamples with more than one comorbid condition. The selected priority domains for clinical attention (Pain, Physical Function, Fatigue) were the same domains that showed patient scores worse than those of the general population (general population mean score = 50). This suggests that patients tend to focus in on seeking help in areas where their lives deviate from their normal expectation. These findings provide further support for the T2T recommendations to evaluate physical function and pain in RA patients, particularly given direct input from the patient perspective.

The domain least frequently selected by RA patients in this study was Depression. Only 5% (n = 6) of the study patients listed depression as their highest priority while 60% of patients listed it as their lowest priority. Of the patients that listed depression as a priority, two had low disease activity. This is surprising given that a large body of literature discusses the high prevalence of depression in RA patients. A systematic review and meta-analysis concluded that depression is highly prevalent in patients with RA, is especially associated with higher disease activity and poorer RA outcomes, and concluded that major depression is present in 16.8% of patients with RA [18]. In another study of depression in RA, patients with high disease activity were two times more likely to develop depression [19]. In our study, 24% of patient-reported depression present at the baseline assessment; however, patients tended not to request that depression be the therapeutic target. These findings may be understood by examining current treatment for depression. All but two patients who listed depression as a comorbidity were on medication for their depression or had been on medication. Patients who have depression under control may not prioritize the disease as a treatment goal, particularly in the context of RA therapy. This also could indicate that even patients with depression have other domains that present a greater need for treatment targets. Future research should investigate the rheumatologist's role when treating a patient with RA and depression. Are rheumatologists screening and treating for depression or other mental health concerns? Is this issue being missed because of a patient focus on other priorities?

A number of demographic and disease differences were observed in patient selection of priority domains. Patients with high disease activity (CDAI >10) chose pain as their top priority over the other domains, while patients with lower disease activity (CDAI <10) prioritized physical function over the others. This difference is further reflected in the items patients chose within their domain. In the physical function domain

patients frequently selected items that reflected a loss in and ability to participate in recreational activities such as sports or exercise. However, in the pain domain, patients frequently selected items that reflected a loss in ability to complete activities of daily living such as grocery shopping or laundry (Table 4). Patients with lower disease activity may not experience difficulty or pain with daily activities; however, their disease may impact abilities to participate in recreational activities they were able to do prior to the onset of their disease. Patients with higher disease activities, on the other hand, may experience pain when completing common activities necessary for daily living, shifting their priority to the pain they experience throughout their normal routine.

The difference in priority domain based on age was interesting. Younger adults prioritizing social function while older adults prioritize fatigue may relate to the fact that younger adults are still forming new relationships and maintaining social lives, while older adults rely on established relationships but can experience a natural increase in fatigue, which may be made worse by their rheumatoid arthritis.

Limitations

The results of this research should be considered in light of several limitations. First, this pilot study consisted of a convenience sample of RA patients from a single clinic site. As such, these findings may not be generalizable to different patient populations. Future research could include a more diverse patient sample. It would be interesting to investigate differences in priorities based on ethnicity. Second, given the small sample size, the study may have been underpowered to detect significant differences across participant characteristics with regard to selection of priority PROMIS domains. Future research can compare to these results, using a larger sample.

Despite these limitations, this is the first study to integrate PROMIS measures into a T2T management strategy in RA. We hope that the data from this study will allow us to determine whether the PROMIS physical function and pain interference scores mirror what we can see in standard instruments such as the RAPID3, or whether they bring new insight and value to treatment targets. In future studies, it will be interesting to see how priority domain and PROMIS scores change over time, specifically in high versus low disease activity cases, and whether changes in PROMIS scores correlate with changes in other outcome measures.

Conclusions

This study demonstrates the feasibility of incorporating PROMIS questionnaires into clinic flow and electric medical records. It also affirms the importance of pain, physical function and fatigue in this population of patients. Baseline data indicate that PROMIS instruments are a valid and reliable way to assess patient-reported preferences in clinical practice settings to further advance the T2T approach in RA therapy. By personalizing T2T patient-reported endpoints, clinicians maintain adherence to patient values; by using PROMIS to do so, they enable the use of a common measurement framework and standard score for tracking and reporting.

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Compliance with ethical standards

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