Barriers to achieving controlled rheumatoid arthritis in the United Arab Emirates: a cross-sectional study

Citation: Moufarrej, Mira Noura, Ziyad Mahfoud, and Humeira Badsha. "Barriers to Achieving Controlled Rheumatoid Arthritis in the United Arab Emirates: a Cross-Sectional Study." Rheumatology International 35, no. 4 (October 15, 2014): 759–763.

As Published: http://dx.doi.org/10.1007/s00296-014-3151-7

Publisher: Springer Berlin Heidelberg

Persistent URL: http://hdl.handle.net/1721.1/107693

Version: Author's final manuscript: final author's manuscript post peer review, without publisher's formatting or copy editing

Barriers to achieving controlled Rheumatoid Arthritis in the United Arab Emirates: a cross-sectional study

Mira Noura Moufarrej[1*], Ziyad Mahfoud[2], Humeira Badsha[3]

1 – Department of Biological Engineering – Massachusetts Institute of Technology, Cambridge, MA, USA – 479 Commonwealth Ave. Boston, MA, USA 02215

2 – Department of Public Health – Weill Cornell Medical School, Qatar Foundation Doha, Qatar - Education City, PO Box 24144, Doha, Qatar

3 – Dr. Humeira Badsha Medical Center Dubai, UAE - Beach Park Plaza, PO Box 391203, Dubai, UAE

*Corresponding Author: – Phone: +14019354474 – Fax: +97143856119
miramou@mit.edu

CONFLICT OF INTERESTS:
The authors declare no conflict of interests.

FUNDING:
The authors declare that they received no source of funding.

Barriers to achieving controlled Rheumatoid Arthritis in the United Arab Emirates: a cross-sectional study

ABSTRACT:
Objective:
To better understand the factors that affect low disease activity (DAS28 ≤ 3.2, LDA) in rheumatoid arthritis (RA) and barriers within the UAE.
Methods:
Demographic/treatment data and DAS28 scores were collected through chart reviews of 182 consecutive RA patients seen at a private clinic in Dubai over a 2-month period. Patients were separated into a LDA group and a group comprised of moderate (3.2 < DAS28 < 5.1) or high disease activity (DAS28 ≥ 5.1) (MHDA). We then examined variables that may be associated with LDA and re-examined the MHDA group for barriers.
Results:
While 97 (53%) of the 182 patients had achieved the treatment target of DAS 28 ≤ 3.2, 85 (47%) had MHDA. A significantly larger portion of LDA patients had been previously treated with sulfasalazine (36 in LDA vs 14 in MHDA, P0.002) or was presently on biological treatments (24 vs 9, P0.013). For the 85 MHDA patients, 40 (22%

of 182) exhibited resistant disease with 25 (13.7% of 182) failing their current first tier disease-modifying anti-rheumatic drug (DMARD) treatment or combinations and 15 (8.2% of 182) failing current anti-TNF or biologic treatment. Reasons listed were primarily socioeconomic with 40% of the resistant disease group unable to afford biologicals and 52% of the patient-driven preference group discontinuing DMARDs against professional advice.

Conclusions:

Going forward, emphasis on the agreement between patient and rheumatologist on treatment, specifically to how DMARDs help relieve symptoms and their proper use, could help reduce the percentage of MHDA patients in the UAE.

KEYWORDS:
Rheumatoid Arthritis, Disease Activity Score, Disease Control, Treat to Target

Treating rheumatoid arthritis (RA) to target (T2T) is quickly becoming a standard of care around the globe after the strategy's success with diabetes and hypertension [1]. In clinical trials, T2T has proven more effective in achieving treatment goals than standard care [2-4] Despite the aforementioned trials' promise, the realities of daily clinical care can create obstacles in achieving treatment goals [5, 6]. Due to patient cohort selectivity, which often negatively selects for co-morbidities, co-prescriptions, and long-standing disease, trial results do not directly translate to success in regular care [7]. In addition, the majority of countries' insurance plans only allow for the use of biological agents after traditional disease modifying anti-rheumatic drugs (DMARDs) fail to adequately control a patient's RA [8]. This treatment plan stands in stark contrast to the results of several clinical trials, which found that early RA patients had significantly greater improvement when treated early with biologics [9, 10].

T2T works by pre-establishing a treatment goal and working to achieve that treatment goal through regular assessment of disease activity and subsequent prescription adjustment when disease persists [2]. For RA, the T2T goal is typically remission or low disease activity (LDA) for long-standing disease where remission may be unrealistic [11]. There exist several definitions of LDA, but here, it is defined as a disease activity score in 28 joints (DAS28) ≤3.2. When translated to clinical practice, however, achieving target disease activity can be difficult with some patients remaining on one DMARD despite persistent disease.

In the UAE where this paper's patient cohort was based, the average DAS28 score remains a high 4.3 with an average of 3 swollen joints of 28 [12]. This paper set out to determine factors that affect LDA and possible barriers to disease control in patients with

moderate or high disease activity (MHDA) within the UAE. Barriers were based on prevalent barriers to disease control in a similar study in Australia [7] and included irreversible joint damage, inability to pay for treatment, resistant disease, patient driven preferences, etc. In better understanding the major barriers within the UAE, rheumatologists of the region may be better able to control persistent disease and allow more patients to reach their treatment goal.

PATIENTS AND METHODS:

The cohort consisted of 182 of 182 consecutive patients seen at a private clinic by the same rheumatologist in Dubai, UAE over a 2-month period. Following study approval by the local ethics board, data were collected through chart reviews with the written informed consent of patients during routine follow up appointments permitting a cross sectional look at the clinic's RA patients. Data collected included treatment/demographic and DAS28 data, all of which are collected routinely by the rheumatologist. Following data collection, patients were then separated into two groups: LDA (DAS28≤3.2) and MHDA comprised of patients with either moderate disease activity (3.2< DAS28< 5.1) or high disease activity (DAS28≥5.1). We then examined the data for variables, which may be associated with LDA, and re-examined the MHDA group for barriers as described below.

Clinical Evaluation

The consulting rheumatologist reviewed RA clinical features (classification criteria, comorbidities, etc), noted all previous and current DMARDs and reasons for discontinuation if relevant, and performed a 28-joint count noting the number swollen or tender joints. The charts also included a physician global assessment of disease activity

and laboratory tests noting erythrocyte sedimentation rate (ESR), c-reactive protein (CRP) levels, rheumatoid factor (RF) status, and anti-cyclic citrullinated protein (anti-CCP) status. Demographic data such as sex, age, height, weight, delay to diagnosis/treatment, and ethnicity were also collected.

Patient Self-Report

Patients completed the standard Health Assessment Questionnaire (HAQ) and a visual analog scale (VAS) for patient global status. The HAQ administered did not include an "aids and devices" or "help from other people" section.

Disease Activity Measures

Current disease activity was measured using DAS28 scores. DAS28 scores were calculated using the standard formula according to a 28-joint count of both swollen joints (SJC28) and tender joints (TJC28). Data were then entered into the formula DAS28 = 0.56*sqrt(TJC28) + 0.28*sqrt(SJC28) + 0.70*Ln(ESR) + 0.014*patient global status from 1 to 100. Patients were then separated into LDA and MHDA as described previously.

Statistical Methods

Demographic and clinical characteristics were computed separately for those with LDA and MHDA using the means and standard deviations for numeric variables (e.g age, delay in treatment, etc.) and frequency distributions for categorical variables (e.g race, RF status, etc.). Differences between the two patient groups on such variables were tested using the independent T-test (or Wilcoxon rank sum test for variables that were not normally distributed) for numeric variables and the chi-squared test (or Fisher's exact test when expected cell counts fell below 5) for categorical variables.

RESULTS:

Patients

Current DAS28, calculated with a recent ESR measurement, were available for all 182 patients, consisting of 149 females and 33 males with a corresponding 4.52:1 female to male ratio and an average DAS28 of 3.35 ± 1.29. RF and/or anti-CCP status were not available for 31 patients due to varying insurance plan coverage. Overall, 97 patients (53%) met the criteria for LDA. Age, gender, delay to treatment, HAQ, and other demographic/RA related variables for both groups are summarized below (Table 1).

Treatment

Overall the majority of both LDA and MHDA patients had either previously or were currently taking methotrexate, typically the primary standard of RA care [13, 14]. Other notable differences in treatment patterns between the two groups were the significantly larger portion of LDA patients currently on biological treatment (24 vs 9) and who had previously taken sulfasalazine (SSA, 36 vs 14).

Barriers to Disease Control

Figure 1a summarizes the barriers listed by the consulting rheumatologist. Of the 17 patients who fell under patient-driven preference, 10 stopped or refused treatment against professional advice and 7 stopped treatment due to pregnancy-related reasons. In addition, the rheumatologist noted that the 3 listed under other all had high ESR scores due to infection despite LDA indications otherwise. Safety concerns included active Hepatitis C infection and concurrent cancer treatment. Non-inflammatory musculoskeletal pain was primarily due to fibromyalgia or other chronic illnesses. There

also remained 40 patients who should have - following T2T theory - changed treatment plans due to persistent disease, yet according to our data had failed to do so. Upon further examination of the 25 patients who were failing current DMARD treatment and 15 failing current biologic treatment, we found several prevalent, primarily socioeconomic reasons, which had prevented the rheumatologist from successfully implementing T2T (Figure 1b and 1c).

DISCUSSION:

Barriers to disease control can be divided into two categories – modifiable and fixed. Barriers such as irreversible joint damage, comorbidities, etc., we considered fixed, as the treating rheumatologist could do little differently to achieve the target. On the other hand, barriers such as patient-driven preference and inability to afford biologics, we felt could possibly be modified through educational efforts and increased insurance coverage. Given 9 of 17 patients under patient driven preference stopped treatment on their own against professional advice citing that they felt the treatment was no longer necessary at the time, we highlight the need for an agreement between patient and rheumatologist on treatment [1] with emphasis on the effects of DMARD treatment and the responsibilities of the patient during the course of treatment. In addition, while we recognize that the ability to afford biologics does not directly correlate with LDA, the number of patients who could not access all treatment options presently available is alarming. It should be noted that when a patient was unable to access all treatment options, another solution was provided as per Smolen's 2010 recommendations [1]. Nonetheless, we feel that a study looking at the result of treating those MHDA patients unable to afford biologicals with the latter and could be of interest in the future. In addition, we feel that a study, which

examines the possibility of barriers to disease control in the LDA patient group would yield further insight into the application of T2T clinically in the UAE.

When comparing past and present treatment plans of LDA vs MHDA, there was a significantly higher percentage of LDA patients who had either previously been treated with SSA or were currently on biologicals. While our second finding correlates with findings in the literature regarding biological treatment [14], the first provides an interesting point of investigation. Although literature does exist on the benefits of SSA treatment [15], no literature mentions the benefits of previous SSA treatment on controlling RA. After further examination of the LDA group previously treated with SSA, we found no other notable commonalities amongst the group. The result therefore may be due to our cohort choice, further elaborated on below, or a finding worthy of future investigation.

Although this study represents a unique and novel opportunity to examine controlled RA barriers within the UAE, several limitations are recognized. Due to the short data collection period, several patients fell into the MHDA group due to insufficient time to assess present treatment effects. Hence we cannot be sure if the aforementioned patients' treatment plans were later effective. In addition, we recognize that patient data for this study was collected at one private clinic within the UAE; however, given the small number of practicing rheumatologists within major UAE cities, we felt we captured a relatively accurate picture of the general RA cohort within the nation. We also recognize that the cohort size may have been relatively small, however because one month of data collection fell during the holy Islamic month of Ramadan, there was a significantly smaller number of patients who visited the clinic during that time. It is

possible that the high percentage of LDA patients previously treated with SSA may also be due to cohort size. In addition, we recognize that patient visit frequency is variable and dependent on the degree of disease activity; however, because data was collected over 2 months and routine follow up appointments are regularly scheduled for all patients, we feel we were able to capture an accurate cross-section of the patient cohort.

In summary, the factors associated with LDA were current biological use or previous SSA use.

ACKNOWLEDGMENTS:
The authors would like to thank Nurse Joyce Raymond Daoud for her generous help with data collection.

REFERENCES:

1. Smolen JS, Aletaha D, Bijlsma JW, Breedveld FC, Boumpas D, Burmester G, et al. Treating rheumatoid arthritis to target recommendations of an international task force. Ann Rheum Dis 2010;69:631-37.

2. Schoels M, Knevel R, Aletaha D, Bijlsma JW, Breedveld FC, Boumpas DT, et al. Evidence for treating rheumatoid arthritis to target: results of a systematic literature search. Ann Rheum Dis 2010;69:638-43.

3. Knevel R, Schoels M, Huizinga TW, Aletaha D, Burmester GR, Combe B, et al. Current evidence for a strategic approach to the management of rheumatoid arthritis with disease-modifying antirheumatic drugs: a systematic literature review informing the EULAR recommendations for the management of rheumatoid arthritis. Ann Rheum Dis 2010;69:987-94.

4. Goekoop-Ruiterman YP, de Vries-Bouwstra JK, Kerstens PJ, Nielen MM, Vos K, van Schaardenburg D, et al. DAS-driven therapy versus routine care in patients with recent-onset active rheumatoid arthritis. Ann Rheum Dis 2010;69:65-9.

5. Emery P, Breedveld FC, Hall S, Durez P, Chang DJ, Robertson D, et al. Comparison of methotrexate monotherapy with a combination of methotrexate and etanercept in active, early, moderate to severe rheumatoid arthritis (COMET): a randomised, double-blind, parallel treatment trial. Lancet 2008;372:375-82.

6. Breedveld FC, Weisman MH, Kavanaugh AF, Cohen SB, Pavelka K, van Vollenhoven R, et al. The PREMIER study: a multicenter, randomized, double-blind clinical trial of combination therapy with adalimumab plus methotrexate versus methotrexate alone or adalimumab alone in patients with early aggressive rheumatoid arthritis who had not had previous methotrexate treatment. Arthritis Rheum 2006;54:26-37.

7. Tymms, K, Zochling, J, Scott, J, Bird, P, Burnet, S, de Jager, J, et al. Barriers to Optimal Disease Control for Rheumatoid Arthritis Patients With Moderate and High Disease Activity. Arthritis Care Res 2014;66:190-6.

8. Sokka T, Envalds M, Pincus T. Treatment of rheumatoid arthritis: a global perspective on the use of antirheumatic drugs. Mod Rheumatol 2008;18:228-39.

9. Emery P, Durez P, Dougados M, Legerton CW, Becker JC, Vratsanos G, et al. Impact of T-cell costimulation modulation in patients with undifferentiated inflammatory arthritis or very early rheumatoid arthritis: a clinical and imaging study of abatacept (the ADJUST trial). Ann Rheum Dis 2010;69:510-16.

10. Goekoop-Ruiterman YP, de Vries-Bouwstra JK, Allaart CF, van Zeben D, Kerstens PJ, Hazes JM, et al. Clinical and radiographic outcomes of four different treatment

strategies in patients with early rheumatoid arthritis (the BeSt study): a randomized, controlled trial. Arthritis Rheum Suppl 2008;58 Suppl 2:126-35.

11. Felson DT, Smolen JS, Wells G, Zhang B, van Tuyl LH, Funovits J, et al. American College of Rheumatology; European League Against Rheumatism American College of Rheumatology/European League Against Rheumatism provisional definition of remission in rheumatoid arthritis for clinical trials. Arthritis Rheum 2011;63:573-86.

12. Sokka T, Toloza S, Cutolo M, Kautiainen H, Makinen H, Gogus F, et al. Women, men, and rheumatoid arthritis: analyses of disease activity, disease characteristics, and treatments in the QUEST-RA study. Arthritis Res Ther 2009;11: R7.

13. Smolen JS, Landewe R, Breedveld FC, Dougados M, Emergy P, Gaujoux-Viala C, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs. Ann Rheum Dis 2010;69:964-75.

14. Gaujoux-Viala C, Smolen JS, Landewé R, Dougados M, Kvien TK, Mola EM, et al. Current evidence for the management of rheumatoid arthritis with synthetic disease-modifying antirheumatic drugs: systematic literature review informing the EULAR recommendations for the management of rheumatoid arthritis. Ann Rheum Dis 2010;69:1004-9.

15. Plosker GL, Croom KF. Sulfasalazine: a review of its use in the management of rheumatoid arthritis. Drugs 2005;65:2591.

TABLES:

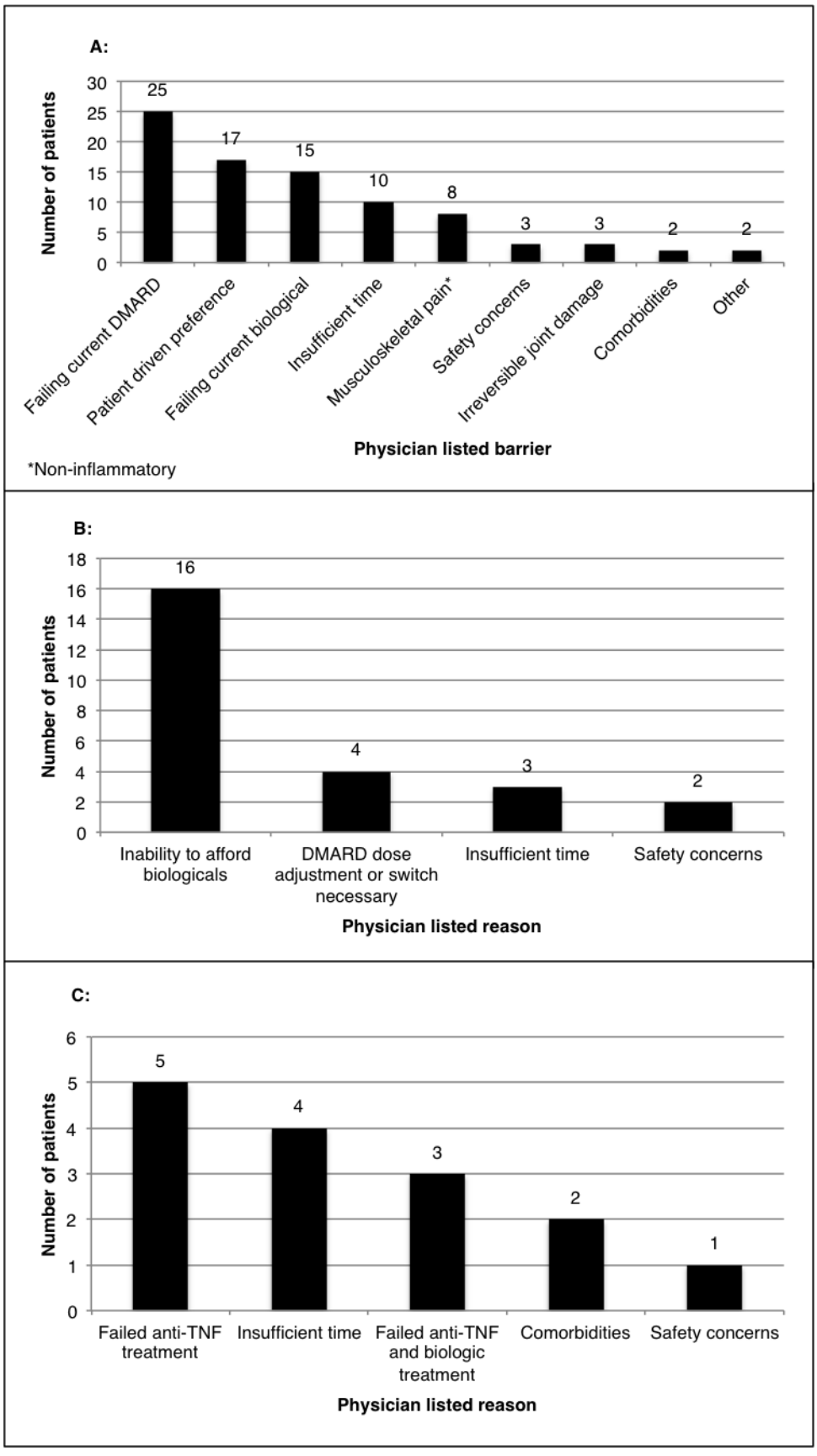
Table 1: Comparing demographics/RA-related variables between LDA and MHDA patients. Notably, patients satisfying the description for LDA were a little over two times as likely to have previously used SSA or currently use biologicals. No significant differences were noted in gender or ethnic distribution, delay to treatment, RF status, or anti-CCP status between categories. On average, patients with MHDA reported higher HAQ scores. In addition, the majority of patients had previously used methotrexate as per standard practice.

Variable	DAS28≤3.2 97 (53%)	DAS28>3.2 85 (47%)	P-value
Age (years)	45.6 (10.5)	48.5 (12.1)	0.088
Gender			
Female	78 (52.3%)	71 (47.7%)	0.586
Male	19 (57.6%)	14 (42.4%)	
Race			0.740
South Asian	47 (55.3%)	49 (50.5%)	
Arab	10 (11.8%)	10 (10.3%)	
Caucasian	20 (23.5%)	30 (30.9%)	
Other	8 (9.4%)	8 (8.2%)	
Delay to Treatment (months)	16.5 (31.0)	21.2 (42.0)	0.692
RF Status (+)	55 (66.3%)	65 (70.7%)	0.532
Anti CCP Status (+)	41 (56.2%)	39 (48.8%)	0.359
HAQ	0.26(0.31)	0.68 (0.56)	<0.001*
Past Medication†			
Methotrexate	78 (80.4%)	70 (82.4%)	0.738
Imuran	4 (4.1%)	5 (5.9%)	0.736
SSA	36 (37.1%)	14 (16.5%)	0.002*
ARAVA	16 (16.5%)	23 (27.1%)	0.083
Biological	32 (33.0%)	20 (23.5%)	0.159
Current Medication†			
Methotrexate	54 (55.7%)	49 (57.6%)	0.788
Imuran	4 (4.1%)	5 (5.9%)	0.736
SSA	18 (18.6%)	8 (9.4%)	0.079
ARAVA	5 (5.9%)	8 (9.4%)	0.266
Biological	24 (24.7%)	9 (10.6%)	0.013*
Health insurance (Yes)	74 (76.3%)	57 (67.1%)	0.167

*Significant difference at the 5% level; †percentages don't add to 100% since patient might be taking several drugs or have taken several drugs

FIGURE LEGEND:

Figure 1 – Analyzing MHDA barriers to disease control. **1A** - A quantification of the barriers to disease control listed by the consulting physician. **1B** - An in-depth analysis of the MHDA "Failing current DMARD" group to quantify prevalent reasons for failing DMARD treatment. **1C** - An in-depth analysis of the MHDA "Failing current biological" group to quantify prevalent reasons for failing biological treatment


A:
Number of patients
30
25
20
15
10
5
0
25
17
15
10
8
3
3
2
2
Failing current DMARD
Patient driven preference
Failing current biological
Insufficient time
Musculoskeletal pain*
Safety concerns
Irreversible joint damage
Comorbidities
Other
Physician listed barrier
*Non-inflammatory
B:
Number of patients
18
16
14
12
10
8
6
4
2
0
16
4
3
2
Inability to afford biologicals
DMARD dose adjustment or switch necessary
Insufficient time
Safety concerns
Physician listed reason
C:
Number of patients
6
5
4
3
2
1
0
5
4
3
2
1
Failed anti-TNF treatment
Insufficient time
Failed anti-TNF and biologic treatment
Comorbidities
Safety concerns
Physician listed reason