Title

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Journal

Arthritis Care & Research, 73(9)

ISSN

2151-464X

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Publication Date

2021-09-01

DOI

10.1002/acr.24611

Peer reviewed

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Article type : Original Article

DMARD Changes for Patients with Rheumatoid Arthritis in the US During the COVID-19 Pandemic: A 3-Month Observational Study

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keywords: COVID-19, Rheumatoid Arthritis, DMARDs, Access to Care, Drug Persistence
Word count: 3800

This analysis was funded by Pfizer Inc. EA is an employee of Pfizer, Inc. There are no other sources of financial support to report.

ABSTRACT

Objective: To understand medication, lifestyle, and clinical care changes by persons with RA during the first months (March through May 2020) of the COVID-19 pandemic in the US.

Methods: Data were provided by adults with RA participating in FORWARD, The National Databank for Rheumatic Diseases, observational registry who answered COVID-19 web-based surveys in May 2020 and previously provided baseline (pre-COVID) characteristics and medication use. We compared medication changes by DMARD exposure in logistic models adjusting for age, sex, comorbidities including pulmonary and cardiovascular diseases, education, health insurance, RA activity, fatigue, and polysymptomatic distress.

Results: Of 734 respondents, 221 (30%) reported medication changes. Changers more commonly used glucocorticoids (GCs) (33% vs 18%) and less commonly used non-hydroxychloroquine conventional DMARDs (49% vs 62%) pre-COVID and reported more economic hardship during COVID (23% vs 15%). While JAK inhibitor use was associated (OR 1.9 [95%CI 1.0, 3.4]) with change, only pre-COVID GCs remained a strong predictor (OR 3.0 [1.9, 4.9]) in multivariable models. Change in care was significantly associated with pulmonary disease (OR 2.9 [1.3, 6.5]), worse RA activity (OR 1.1 [1.0, 1.1]), and GC use (OR 1.6 [1.0, 2.5]). While the incidence of medication change before and after ACR guidelines were published was the same, self-imposed changes were approximately twice as likely before, and physician guided changes were more likely after.

Conclusion: Persons with RA in the US made substantial medication changes during the first three months of the COVID-19 pandemic. Changes after publication of ACR recommendations were made with increased physician guidance.

SIGNIFICANCE AND INNOVATION

- This is the first study to track DMARD changes in people with rheumatoid arthritis during the pandemic.
- Respondents made substantial medication changes during the first three months of the COVID-19 pandemic, both with and without physician guidance.
- Changes made after publication of the ACR guidelines were more likely to be made with physician guidance, though this was not statistically significant.

INTRODUCTION

In December 2019, the novel coronavirus called Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) was identified in Wuhan, China. It was determined to be responsible for the outbreak of the coronavirus disease (COVID-19) which was declared a pandemic by the World Health Organization (WHO) in March 2020. People with rheumatic and musculoskeletal diseases (RMDs) have been impacted during this pandemic through their greater risk of infection due to immune dysregulation, comorbidities, and immune-modulating treatments (1-3), while simultaneously many of these immune-modulating treatments (e.g., HCQ, GCS, IL1i, IL6i, JAKi) are being tested to prevent or treat COVID-19 (4-6), creating some confusion and concerns on actual risks (7). Additionally, changes in access to treatment and care have made it difficult for patients to understand how best to take care of their health with their conditions. From our recent survey during the first two weeks of the pandemic, almost half of RMD patients described significant disruptions to their rheumatology care, including disrupted or postponed appointments and self-imposed or physician-directed changes to medications (8).

The pandemic has also presented particular challenges to rheumatologists in caring for and managing their patients. On April 13, 2020 the American College of Rheumatology (ACR) provided the first clinical guidance on treatment for RMDs including rheumatoid arthritis (RA), highlighting the need to stay on disease-modifying antirheumatic drugs (DMARDs), control disease activity, and discontinue or reduce prednisone / glucocorticoid steroid (GCs) use. For those with documented or presumptive COVID-19 infection, only hydroxychloroquine (HCQ) and IL-6 biologics were recommended for continued use (9).

Despite the multitude of new literature on COVID-19 (10), there is still little known about treatment patterns at the individual level in the midst of this pandemic. For example, are individuals with RA and prescribers following ACR recommendations? Are persons with RA practicing social distancing? Are patients prescribed certain medications pre-COVID more likely to discontinue therapy than others? The aims of this study therefore were to fill important knowledge gaps concerning changes in treatment and to understand prescriber and patient behaviors around management of medications and disease condition during the

pandemic. We set out to characterize lifestyle and clinical care changes, to understand the rationale for changes in medication, and to identify associations between those changes and baseline characteristics in persons with RA.

PATIENTS AND METHODS

The study population consisted of participants with RA age ≥18 years in FORWARD, The National Databank for Rheumatic Diseases, an observational, multi-disease patient registry (11). In addition to regular comprehensive semiannual questionnaires, participants were invited by email every two weeks between March 25 and June 2, 2020 to complete up to five supplemental COVID-19 questionnaires. The results of the first March 25, 2020 survey were published previously (8).

For this analysis, we required completion of at least one semiannual questionnaire between January 2018 and January 2020 and at least one COVID-19 questionnaire administered in May and June of 2020. Additionally, we required participants to be taking at least one of the following medications: hydroxychloroquine (HCQ), another conventional disease-modifying anti-rheumatic drug (csDMARD), tumor necrosis factor inhibitor biologic DMARD (TNF bDMARD), non-TNF (NTNF) bDMARD, Janus kinase inhibitor (JAKi), non-steroidal anti-inflammatory drugs (NSAIDs), and/or glucocorticoids (GCs).

Questionnaires. Semiannual questionnaires are administered every January and July and collect an array of patient-reported outcomes. Information on treatments include doses, pill sizes, months taken, start and stop dates, discontinuation reasons, and side effects. In addition, demographics, socioeconomic status, productivity, comorbidities, important medical events, health-related quality of life, health symptoms, and disease-specific outcomes measures are assessed (11).

The COVID-19 questionnaires used in these analyses were administered between May 6 and June 2, 2020 and focused on patient perspectives and experiences in the two weeks prior to questionnaire completion (See Appendix). Participants were asked about their RA activity, development of new COVID-19-related symptoms, testing for COVID-19, changes in their rheumatology care, and lifestyle and economic changes due to the pandemic.

Outcomes and variables of interest. Participants were characterized by demographics and clinical status including age, sex, ethnicity, marital status, geographical area (urban vs rural), smoking status, body mass index (BMI), Rheumatic Disease

Comorbidity Index (RDCI)(12), function (Health Assessment Questionnaire [HAQ]-II)(13), self-reported disease activity (Patient Activity Scale [PAS]-II)(14), patient global health assessment, ratings of fatigue and pain, number of prior DMARDs, polysymptomatic distress scale (PSD)(15), self-reported disease activity at the time of supplemental questionnaire completion (low/moderate/severe), and economic changes as a result of the pandemic (defined as any loss of employment, reduced household income, and/or loss of health insurance).

DMARD group was categorized in a mutually-exclusive hierarchical manner, assigning each patient to their highest category following this sequence: no DMARDs, csDMARDs, TNF bDMARDs, NTNF bDMARDs, and JAKi. Although a csDMARD, HCQ use was modeled separately as a binary indicator due to the attention it has received in the pandemic and its common concomitant use to treat RA. Additionally, binary indicators for all drug groups including NSAIDs and GCs were used since patients could be taking more than one drug simultaneously.

Patients were classified as "medication changers" if they discontinued a medication, added other drugs, or changed the dose of a DMARD, GCs, or NSAID after March 1, 2020. Non-changers were those who indicated that they did not make any medication changes in the specified time period. The medication changers were sub-classified by type of change. Reasons for medication change, whether the change was self-initiated or directed by a physician or other healthcare provider, and the dates for these drug changes were also collected. Patients were also categorized according to whether they reported any changes in rheumatology care or lifestyle.

Statistical methods. Participants were described at baseline (based on the most recent semiannual observation) according to whether they did or did not report any changes in medications on the COVID-19 questionnaire. T-tests for continuous variables and chi-squared/Fisher's exact tests for categorical variables were used as appropriate. Those who reported changes in medications, healthcare, and lifestyle were described by DMARD group.

Logistic regression models were performed to assess the likelihood of changing medication and of reporting a change in care by DMARD group, adjusting for disease

severity (PAS-II), demographics, and clinical information. We used the following two models: Model 1, DMARD group, HCQ, and GC; Model 2, Model 1 plus age, sex, pulmonary disease, cardiovascular disease, RDCI (excluding pulmonary and cardiovascular disease), educational level, Medicare status, PAS-II, fatigue, history of prior DMARDs, and PSD score.

Sensitivity analyses were performed to ascertain the robustness of results: (1) the logistic models were estimated by entering each DMARD drug variable as an individual binary variable, allowing for overlapping use; and (2) replacing PAS-II with its three components HAQ-II, pain, and patient global. Reasons for medication changes were reported by type of change, drug class, and whether they were physician-directed or self-decided.

Finally, a time-to-event analysis was conducted to determine the time (in days) to a drug change from March 1, 2020. For those with no changes, the time from March 1, 2020 until the COVID-19 questionnaire date was calculated. Kaplan-Meier estimator and log-rank tests were used to compare the different DMARD groups with respect to this outcome. This analysis also assessed how the release of ACR recommendations for RMD treatment in the context of the pandemic were associated with drug changes. Analyses were performed for those who made changes prior to ACR guidelines (March 1 to April 15) and those who made changes after (April 16 to questionnaire completion) by reason for change and physician-directed status.

RESULTS

Patients. Of the 1,411 participants who completed at least one of the COVID-19 questionnaires and a prior semiannual questionnaire, 734 had RA as their primary diagnosis and were on treatment with at least one of the drugs of interest (HCQ, other csDMARDs, TNF bDMARD, NTNF bDMARD, JAKi, NSAID, or GCS). Median (IQR) time between prior FORWARD questionnaire and supplemental questionnaire was 8 (6-9) months, the mean (SD) was 8 (3) months, and 98% of participants were between 4 and 12 months.

Respondents had an average age of 65 years, were mostly female (86%) and Caucasian (93%), with an average of 15 years of education (Table 1). In terms of the drug class distributions (each person could be in more than one category), 21% were on HCQ, 58% on other csDMARDs, 35% on TNF bDMARD, 27% on NTNF bDMARD, and 10% on JAKi.

Of the 734 RA respondents, 30.1% reported at least one medication change. Those who had changes were more likely to be younger and to have worse (higher) patient-reported outcome measure values, including HAQ-II (0.9 vs 0.7) and PAS-II (3.1 vs 2.7). Changers also were more frequently using GCs (33% vs 18%) and less likely to be taking non-HCQ csDMARDs (49% vs 62%) pre-COVID. No differences in comorbidities were found. Changers were more likely to have experienced a negative economic impact during this period (23% vs 15%) and to report non-rheumatic disease medication changes (15% vs 10%) (Table 1).

Medication, care, and lifestyle changes. Table 2 presents the percentage of respondents who reported medication changes, care changes, and lifestyle changes by type of change within each DMARD class. Participants could have experienced more than one change for the same DMARD group and could be allocated to more than one DMARD group.

The percentage of respondents who had medication changes by DMARD group varied between 12% for HCQ and 23% for TNF bDMARDs. By type, bDMARD (irrespective of mechanism of action) and JAKi users reported stopping or delaying the intake of that DMARD more often than csDMARDs or HCQ (16-18% vs 4-8%). Further inspection of the

JAKi group showed that this difference was driven primarily by use of upadacitinib and baricitinib, which had 71% (5 out of 7) stop or delay, while tofacitinib had 11% (7 of 64) stop or delay. Five percent reported adding HCQ to their treatment regimen. All other medication changes related to adding drugs or changing dose were reported by fewer than 4% of the patients for any DMARD group. The percentage of patients who did not report a change varied between 77% and 88%.

Regarding care changes, the percentage of respondents who canceled or postponed appointments was relatively uniform by DMARD group, varying between 28% and 35%. Persons on NTNF bDMARD or JAKi reported switching to telehealth appointments more frequently (42% for NTNF, 47% for JAKi) than the HCQ and other csDMARD groups (34-36%) and TNF bDMARD group, which reported the lowest percentage (31%). Between 3% to 6% could not reach their rheumatology office, and 4% to 7% could not obtain their medication, except for HCQ users, who reported a higher frequency (10%).

Some types of lifestyle changes were adopted by almost all of the cohort regardless of DMARD treatment, including washing hands more often and wearing a mask (≥94% in all drug groups). Self-quarantining was reported for more than half of the sample for all DMARD categories (53-56%), except for JAKi (39%), but higher rates of hand sanitizer use and canceled travel were observed in the latter group.

Association between changers and baseline characteristics. Results from the logistic models are presented in Table 3 with models for both medication changers and care changers. In Model 1, medication changers seemed more likely to be JAKi users (odds ratio [95% confidence interval]: OR 1.9 [1.0, 3.4]), but this result was not significant and was attenuated in the multivariable Model 2. GC use was the only strong factor influencing the association between medication changes and baseline characteristics (OR 3.0 [1.9, 5.2]).

When analyzing care changes, no association was found with any particular DMARD group in either model. Care changers were more likely to have pulmonary disease (OR 2.9 [1.3, 6.5]), with a tendency for worse disease activity (OR 1.1 [1.0, 1.1]), and GC use (OR 1.6 [1.0, 2.5]).

Reasons for medication change. Participants were asked to report reasons why they stopped/delayed a drug or changed the dose. This question was not prompted when the change type was "added other drugs." Reasons by change type and physician approval are presented in Table 4. Adding a new medication and changing the dose of a medication were significantly more likely to be directed by a physician (90% and 66%, respectively) compared to stopping/delaying a medication (physician-directed 53% of the time; $p<0.001$).

Of six participants who reported a COVID-19 diagnosis (four presumed by physician, one PCR, and one antibody test), three had medication changes (two of the presumed positive and the one who was PCR positive) and three did not. Of those with changes, two had physician approval and one did not.

The most reported reason for stopping or delaying a drug was concern about COVID-19 (39%) followed by concern about other illness or infections (16%), canceled/postponed appointments (13%), and side effects (12%). All other reasons were reported by less than 10% of patients. For those who reported a change of dose, having a flare was the most frequent reason (41%), followed by concern about COVID-19 (17%) and other unspecified reasons (13%). Among individuals that stopped, delayed, or changed the dose of a medication, those who did so due to concern about COVID-19 reported higher fatigue scores (4.8 [2.7] vs 3.7 [2.8], $p=0.02$) but had no other significant differences in patient-reported outcomes, comorbid conditions, or demographics (Supplementary Table 1). When looking at reasons by type of change and physician approval, efficacy, side effects, and no longer needing a medication were more likely to be directed by the physician as a reason for stopping/delaying a medication, as opposed to worry about COVID-19, availability of the drug, or canceled/postponed appointments. For respondents who reported changing the dose, no significant differences were found between reasons, regardless of whether the change was physician-directed or not.

Reasons for change were further inspected by change type within each drug class (Supplementary Table 2). Worry about COVID-19 was a constant and, in most of the cases, the most common reason for any change, irrespective of drug class. For HCQ users, the lack of availability was the main reason for stopping/delaying the drug or changing dose. For

other csDMARDs, having a flare was the main reason for adding other drugs. Worry about infections or other illness was also a frequent reason for stopping in TNF and NTNF users, and in the latter, cancellation of appointments was also considered a significant reason for stopping or delaying the medication. Lastly, for those on JAKi, canceled appointments and worry about COVID-19 were the main reasons for stopping or delaying medication.

Time to medication change. Table 5 presents descriptive statistics for time to medication change by hierarchical DMARD group. Some respondents were excluded from this analysis because they did not report the date of medication change (17% of changers had missing date of change). The probability of change ranged from 23% to 34%, and there was no significant difference between drug classes when selecting the highest DMARD level of each person. The probability of not experiencing any change in medication within 60 days of March 1 ranged from 76% to 84%, and for 90 days ranged from 63% to 76%.

Finally, Kaplan-Meier analyses estimated the impact of the ACR guidelines on medication use. Figure 1 shows overlaid curves for changers pre- and post-guidelines under a variety of conditions. The overall probability of changing medication was 26.3%, with an annual incidence rate (IR) of 1.39 (95% CI 1.21, 1.61). The number of changers was evenly distributed, with 93 patients making a medication change prior to April 15 (probability of change 13.5%; IR =1.15 (0.93, 1.43) overall; among changers IR 17.67 (14.42, 21.66)) and 90 patients making a medication change after April 15 (probability of change 15.5%; IR =1.74 (1.41, 2.14) overall; among changers IR 21.02 (17.10, 25.84)). However, when restricted to only those who made a medication change in response to COVID-19, most changes occurred prior to April 15 (n=33 vs n=13). While fewer COVID-19-specific changes took place after April 15, the changes that were made occurred more quickly (IR 18.60 [13.22, 26.16] vs 24.60 [14.29, 42.37]). The IRs for both physician-approved and non-approved changes were higher after April 15 than prior, with approximately equal sample sizes.

DISCUSSION

Our results show that persons with RA who had medication changes in the first three months of the COVID-19 pandemic in the US were more likely to have worse disease activity and a higher exposure to prior DMARDs, but no statistical difference was found in terms of comorbidities. Patients on bDMARDs and JAKi reported a higher incidence of discontinuation when compared with csDMARD users (16-18% vs <8%). For changes in care, switching to telehealth appointments was the most commonly reported change for NTNF and JAKi patients (42-46%), followed by cancelling or postponing appointments (28-35%), depending on the DMARD group. Ten percent of HCQ users reported that they did not have access to the drug.

Almost all patients changed their behavior in response to the pandemic by washing their hands more often and wearing a mask or using hand sanitizer more often, independently of DMARD exposure. Other behavior changes (e.g., canceling travel) occurred less frequently but were still relevant. We found that substantially fewer were restricting social contacts than reported by Favalli et al. in Lombardy, Italy where 90% of patients with rheumatic diseases were following social distancing measures(16), although this may have been due to differences in the descriptors (self-quarantine vs. social distancing). Unlike prior US studies of the general population(17, 18), we found no significant differences in education or insurance (Medicare vs. other) in adjusted models.

There were no significant differences in medication change frequency between DMARD groups. However, medication changers were three times more likely to be taking GCs in addition to DMARDs. This may reflect efforts to reduce the perceived risk of infections due to GCs as well as the likely less controlled disease activity associated with GC use(19). The ACR recommendations acknowledged controversies in the available evidence for GC use and COVID-19 risk and stated: “If indicated, glucocorticoids should be used at the lowest dose possible to control rheumatic disease, regardless of exposure or infection status. Glucocorticoids should not be abruptly stopped, regardless of exposure or infection status.”(9) While this recommendation does not differ from the ACR 2015 RA Treatment Guidelines(20), a majority of responding US rheumatologists purposefully

reduced GC use during the early part of the pandemic(21). In addition, the majority of those initiating GCs reported flares (Supplementary Table 2), yet the role of the pandemic in these flares is unclear. Flares may have been the result of stress and lifestyle changes due to the pandemic, which warrants further study. It is beyond the current study's scope to examine treatment for patients with COVID-19, yet some of the best evidence at treating people hospitalized with COVID-19 involved GC use(22).

Since most disruptions in care should affect all during the early weeks due to massive changes in clinical care, we expected those with greater disease activity and medical utilization to be most impacted. Yet pulmonary disease seemed to be the strongest factor associated with changes in care (three-fold increase in risk), followed by GC use. The results were robust regardless of changes in the way the drug variables were categorized, how models were selected, or how disease activity was captured. These findings may be more related to the perceived added risk and/or increased COVID-19 symptoms early in the pandemic (23). Both pulmonary disease and GC use are associated with mortality in RA (24), and recent studies find them similarly associated with COVID-19 case mortality when RA activity was controlled (25).

Fear of COVID-19 was the most commonly reported reason for medication changes, irrespective of drug class. Most changes related to dose or adding new medication were approved by physicians, but only half of changes related to discontinuation were approved. Half of patients worried about COVID-19 stopped medications without physician approval. A snapshot survey of Australian patients with RMDs showed the greatest concern of COVID-19 risk was with taking, in declining order, bDMARDs/tsDMARDs (62%), csDMARDs (methotrexate 55%), and GCs (38%)(7), consistent with our findings albeit their reported concerns with csDMARD were proportionally much higher than ours, since only half of our csDMARD users stopped medications compared to b/tsDMARD users.

Limitations of this study may include participation bias as the patients more worried about COVID-19 may have been more willing to participate in the study. In addition, this study required online responses, which excluded almost half of the current participants in the FORWARD registry who either complete mailed paper forms or telephone interviews.

Participants who were unable to respond due to having COVID-19 were left-censored from our study, although this was likely a rare occurrence. While we did not find any association between race and education with access to care or medications, the study participants were largely Caucasian and had higher than US-average education. Also, due to timing of questionnaires, we did not have full medication information from participants after July 2019 because responses from the January 2020 standard questionnaire were not complete, and the 8-month delay may have resulted in patients being mis-allocated to DMARD treatment category if they had switched to another class during that time. Lastly, while the first ACR treatment recommendations during the pandemic are a convenient guidepost, it is possible that the changes observed were due to secular changes such as improved understanding of COVID-19 or improved access to clinical care after the initial lockdowns across the country.

Yet with so many items measured during the early months of the pandemic, this study has provided important evidence of actual patient behavior of changing treatments without physician recommendation due to fear of COVID-19 risk that has only been theorized in editorial(26). While overall risks of contracting COVID-19 in patients with RA are not known and important clinical trials of select RA DMARDs for treating COVID-19 have not concluded(4), there is evidence that GC use is associated with hospitalization for COVID-19(27). These results were published after the current study's surveys but are consistent as we also found statistically important associations between GC use and change in medications and care. Lastly, we also showed the likely importance of providing early recommendations to physicians on how best to treat patients with RA, as physician-guided medication changes increased after the ACR recommendations.

In conclusion, we found persons with RA in the U.S. had relatively high and consistent rates of medication changes through the first three months of the COVID-19 pandemic. Physician approval for medication changes increased after publication of the ACR COVID-19 treatment recommendations, and most medication changes made were due to concerns of COVID-19 risk. We found no significant associations with medication changes and DMARD class. In full models, only GC use was associated with RA medication changes, and GC use and concomitant pulmonary disease were associated with changes in overall

care. Further studies are needed to follow the trends in RA medication use in response to growing knowledge about the pandemic and the impact of medications for both risk and treatment.

ACKNOWLEDGEMENTS

We are grateful for the additional contributions by Rebecca Schumacher, Teresa Simon, and Drs. Yomei Shaw, Jacob Clarke, and Adam Cornish in the creation and implementation of the supplemental survey. As always, we could not have done this study without the many participants in Forward who continue to share their experiences during these challenging times.

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Table 1: Baseline characteristics, % (n), for patients who changed their usual medications compared to those who did not.

	Overall	Non- Changer	Changer	p
% (n)	100.0 (734)	69.9 (513)	30.1 (221)	
Demographics				
Age (years), mean (SD)	64.7 (14.7)	65.9 (10.4)	61.9 (11.7)	<0.001
Male	14.2 (104)	15.8 (81)	10.5 (23)	0.057
White	93.4 (677)	93.7 (474)	92.7 (203)	0.625
Education (years), mean (SD)	15.3 (2.1)	15.3 (2.0)	15.3 (2.2)	0.917
Married	68.1 (487)	68.1 (348)	68.1 (139)	0.993
Rural setting	20.2 (145)	20.1 (101)	20.6 (44)	0.883
Ever smoked	38.3 (281)	38.4 (197)	38.1 (84)	0.920
BMI, mean (SD)	28.5 (7.53)	28.4 (7.54)	28.6 (7.53)	0.865
Medicare health insurance	43.1 (316)	47.2 (242)	33.5 (74)	0.001
Economic change*	17.0 (125)	14.6 (75)	22.6 (50)	0.008
Comorbid conditions				
RDCI, mean (SD)	2.4 (1.81)	2.33 (1.85)	2.38 (1.73)	0.769
Heart disease	7.7 (55)	7.2 (37)	8.8 (18)	0.465
Pulmonary disease	7.5 (55)	7.0 (36)	8.8 (18)	0.408
Type 2 diabetes mellitus	6.3 (45)	6.6 (34)	5.4 (11)	0.538
Medications				
HCQ	20.8 (153)	20.7 (106)	21.3 (47)	0.853
Other csDMARD	58.2 (427)	62.0 (318)	49.3 (109)	0.001
TNFi bDMARD	35.0 (257)	35.3 (181)	34.4 (76)	0.816
non-TNFi bDMARD	27.1 (199)	26.7 (137)	28.1 (62)	0.706
JAKi	9.5 (70)	8.4 (43)	12.2 (27)	0.105
GCs	22.5 (165)	18.1 (93)	32.6 (72)	<0.001
NSAID	37.7 (277)	38.6 (198)	35.8 (79)	0.465
Number of prior DMARDs, mean (SD)	4.0 (2.1)	3.9 (2.1)	4.3 (2.0)	0.029
Other med changes non-RA	11.3 (83)	9.8 (50)	14.9 (33)	0.042
Patient-reported outcomes				
Disease activity**				

Low	46.1 (337)	51.1 (375)	35.8 (265)	<0.001
Moderate	44.2 (323)	47.5 (105)	42.8 (218)	
Severe	9.3 (68)	16.7 (37)	6.1 (31)	
Unknown	0.4 (3)	0.5 (1)	0.4 (2)	
Pain VAS, mean (SD)	3.15 (2.49)	3.05 (2.47)	3.41 (2.53)	0.087
Patient global VAS, mean (SD)	3.08 (2.31)	2.92 (2.27)	3.49 (2.38)	0.003
Fatigue VAS, mean (SD)	3.58 (2.81)	3.34 (2.76)	4.20 (2.85)	<0.001
HAQ-II, mean (SD)	0.76 (0.60)	0.72 (0.59)	0.85 (0.62)	0.016
PAS-II, mean (SD)	2.85 (1.94)	2.73 (1.92)	3.14 (1.96)	0.021
Polysymptomatic distress, mean (SD)	7.61 (5.67)	7.21 (5.48)	8.68 (6.05)	0.009

* Reported an economic impact from COVID-19 (loss of employment, reduced household income, and/or loss of health insurance)

** Self-reported disease activity at the time of COVID-19 questionnaire completion

HCQ=hydroxychloroquine; DMARD=Disease Modifying Antirheumatic Drug; csDMARD=conventional synthetic DMARD; bDMARD=biological DMARD; TNFi=Tumor Necrosis Factor inhibitor; JAKi=Janus Kinase inhibitor; GC=Glucocorticoid; NSAID=Nonsteroidal Anti-Inflammatory Drug; PAS-II=Patient Activity Scale-II;

Table 2: Characterization of medication, care, and lifestyle changes by drug class, % (n).

	HCQ	other csDMARD	TNF	NTNF	JAKi	GC
n =	153	427	257	199	70	165
Medication Change						
Stopped /Delayed	3.9 (6)	8.2 (35)	17.6 (46)	15.9 (32)	17.1 (12)	3.6 (6)
Added	5.2 (8)	1.4 (6)	3.5 (9)	3.0 (6)	2.9 (2)	20.0 (33)
Increased dose	2.0 (3)	2.8 (12)	2.3 (6)	1.0 (2)	1.4 (1)	7.9 (13)
Decreased dose	2.0 (3)	3.0 (13)	0.4 (1)	0.5 (1)	2.8 (2)	3.0 (5)
No change	87.6 (134)	85.7 (366)	77.4 (199)	80.4 (160)	77.1 (54)	67.9 (112)
Care Change						
Canceled/postponed appointments	31.0 (48)	32.9 (142)	34.9 (91)	27.9 (56)	30.0 (21)	36.4 (40)
Switched to teleconference	35.5 (55)	33.8 (146)	31.0 (81)	41.8 (84)	47.1 (33)	46.1 (76)
Couldn't reach rheumatology office	4.5 (7)	3.0 (13)	3.1 (8)	3.0 (6)	5.7 (4)	4.9 (8)
Could not obtain medication	10.3 (16)	4.2 (18)	4.2 (11)	5.5 (11)	7.1 (5)	5.5 (9)
Lifestyle Change						
Self-quarantining*	56.8 (88)	53.9 (233)	52.9 (138)	55.7 (112)	39.4 (28)	61.8 (102)
Working/attending school from home	22.6 (35)	20.1 (87)	24.1 (63)	24.4 (49)	25.4 (18)	15.8 (26)
Canceled travel	48.4 (75)	46.3 (200)	48.7 (127)	43.8 (88)	57.8 (41)	38.2 (63)
Washing hands more often	94.8 (147)	95.4 (412)	96.6 (252)	94.0 (189)	98.6 (70)	95.8 (158)
Using hand sanitizer more often	76.8 (119)	74.8 (323)	77.4 (202)	80.6 (162)	93.0 (66)	77.0 (127)
Wearing a mask	96.1 (149)	96.5 (417)	96.2 (251)	93.5 (188)	97.2 (69)	95.8 (158)

Wearing gloves	45.8 (71)	44.9 (194)	48.3 (126)	48.3 (97)	41.4 (29)	41.2 (68)

Results are % (n). Patients can be in more than one drug category.

*Didn't leave home at all in 2 weeks prior to COVID-19 questionnaire completion, or only left for essential services (grocery/pharmacy/healthcare)

Table 3: Regression models examining association between DMARD group and changes in medication/care.

OR (95%CI)	**Medication Change**		**Care Change**	
	Model 1 (N=734)	Model 2 (N=513)	Model 1 (N=734)	Model 2 (N=513)
DMARD Group ref. csDMARDs				
No DMARD	1.59 (0.81 - 3.11)	1.21 (0.49 - 3.01)	0.84 (0.44 - 1.60)	0.72 (0.33 - 1.59)
TNFi bDMARD	1.17 (0.74 - 1.84)	1.05 (0.58 - 1.90)	0.82 (0.54 - 1.23)	0.88 (0.53 - 1.46)
Non-TNFi bDMARD	1.24 (0.77 - 1.99)	1.26 (0.68 - 2.36)	0.95 (0.62 - 1.45)	0.94 (0.55 - 1.62)
JAKi	1.85 (1.01 - 3.38)	1.55 (0.68 - 3.51)	1.21 (0.68 - 2.17)	1.13 (0.53 - 2.40)
Hydroxychloroquine use	1.07 (0.70 - 1.62)	1.06 (0.62 - 1.82)	1.05 (0.72 - 1.55)	1.06 (0.66 - 1.71)
GCs use	2.14 (1.48 - 3.09)	3.02 (1.88 - 4.85)	1.71 (1.18 - 2.48)	1.59 (1.01 - 2.50)
NSAID use		1.07 (0.69 - 1.64)		0.98 (0.67 - 1.42)
Age (yrs)		0.99 (0.96 - 1.01)		0.99 (0.97 - 1.01)
Male sex		0.81 (0.43 - 1.52)		1.24 (0.73 - 2.09)
Rheumatic Disease Comorbidity Index (0-7)*		0.93 (0.81 - 1.08)		0.98 (0.86 - 1.11)
Pulmonary disease		1.60 (0.72 - 3.54)		2.89 (1.28 - 6.54)
Cardiovascular disease		1.07 (0.47 - 2.47)		0.93 (0.44 - 1.94)
Educational level (yrs)		1.06 (0.95 - 1.19)		0.97 (0.88 - 1.07)
Medicare health insurance		0.71 (0.43 - 1.17)		1.03 (0.67 - 1.60)

PAS-II (0-10)		0.98	(0.83	- 1.15)		1.10	(0.95	- 1.27)
Number of prior DMARDs		1.07	(0.96	- 1.18)		1.01	(0.92	- 1.11)
Polysymptomatic Distress		1.01	(0.96	- 1.06)		1.01	(0.96	- 1.06)
Fatigue (0-10)		1.11	(0.99	- 1.24)		1.01	(0.91	- 1.11)

*The rheumatic disease comorbidity index was calculated excluding pulmonary and cardiovascular disease, which were controlled individually.

OR=Odds Ratio; CI= Confidence Interval; DMARD=Disease Modifying Antirheumatic Drug; csDMARD=conventional synthetic DMARD; TNFi=Tumor Necrosis Factor inhibitor; JAKi=Janus Kinase inhibitor; GC=Glucocorticoid; NSAID=Nonsteroidal Anti-Inflammatory Drug; PAS-II=Patient Activity Scale-II;

Table 4. Reasons for medication change by type of change and physician approval, % (n).

	Stopped/Delayed Medication				Changed Medication Dose			
		Physician				Physician		
Reason for change	**All**	**Not Approved**	**Approved**	**p-value**	**All**	**Not Approved**	**Approved**	**p-value**
% (n)	100.0 (153)	44.4 (68)	52.9 (81)		100.0 (68)	33.8 (23)	66.2 (45)	
Didn't work	8.5 (13)	1.5 (1)	14.8 (12)	0.004	4.4 (3)	4.3 (1)	4.4 (2)	0.985
Side effects	11.8 (18)	5.9 (4)	17.3 (14)	0.033	8.8 (6)	0.0 (0)	11.1 (5)	0.097
Cost	1.3 (2)	2.9 (2)	0.0 (0)	0.120	0.0 (0)	0.0 (0)	0.0 (0)	-
Canceled/postponed appointments	13.1 (20)	23.5 (16)	4.9 (4)	0.001	0.0 (0)	0.0 (0)	0.0 (0)	-
Wasn't available	3.3 (5)	7.4 (5)	0.0 (0)	0.013	8.8 (6)	8.7 (2)	6.7 (3)	0.762
Worried about COVID-19	39.2 (60)	54.4 (37)	24.7 (20)	0.000	17.6 (12)	26.1 (6)	13.3 (6)	0.192
Other illness/infection	15.7 (24)	13.2 (9)	18.5 (15)	0.382	2.9 (2)	0.0 (0)	4.4 (2)	0.305
Loss of insurance	2.0 (3)	4.4 (3)	0.0 (0)	0.056	1.45 (1)	0.0 (0)	2.2 (1)	0.471
Having a flare	2.6 (4)	0.0 (0)	4.9 (4)	0.063	41.2 (28)	39.1 (9)	42.2 (19)	0.806
Surgery/medical procedure	5.2 (8)	2.9 (2)	7.4 (6)	0.228	0.0 (0)	0.0 (0)	0.0 (0)	-
Doctor recommended, unspecified reason	2.0 (3)	0.0 (0)	3.7 (3)	0.109	2.9 (2)	0.0 (0)	4.4 (2)	0.305
No longer needed (e.g. flare over)	4.6 (7)	0.0 (0)	8.6 (7)	0.013	8.8 (6)	17.4 (4)	4.4 (2)	0.075
Other	9.2 (14)	5.9 (4)	11.1 (9)	0.260	13.2 (9)	8.7 (2)	15.6 (7)	0.430

Results are % (n). Values reflect number of changes and not number of patients. Respondents could select more than one reason. Four did not indicate if their stoppage was physician approved.

Table 5: Survival descriptive statistics for the hierarchical DMARD groups.

Hierarchical DMARD Drug class	Time at risk (days)	Prob. change	No subjects	Survival time 25%	Survival time 50%	Probability of no change 60 days	Probability of no change 90 days	Log rank p-value
No DMARDs	3635	0.38	55	61	.	0.76	0.59	
csDMARDs	11983	0.23	171	.	.	0.80	0.76	
TNFi	16124	0.25	233	80	.	0.82	0.72	0.11
NTNFi	11855	0.25	171	76	.	0.84	0.72	
JAKi	4380	0.34	66	61	.	0.76	0.63	

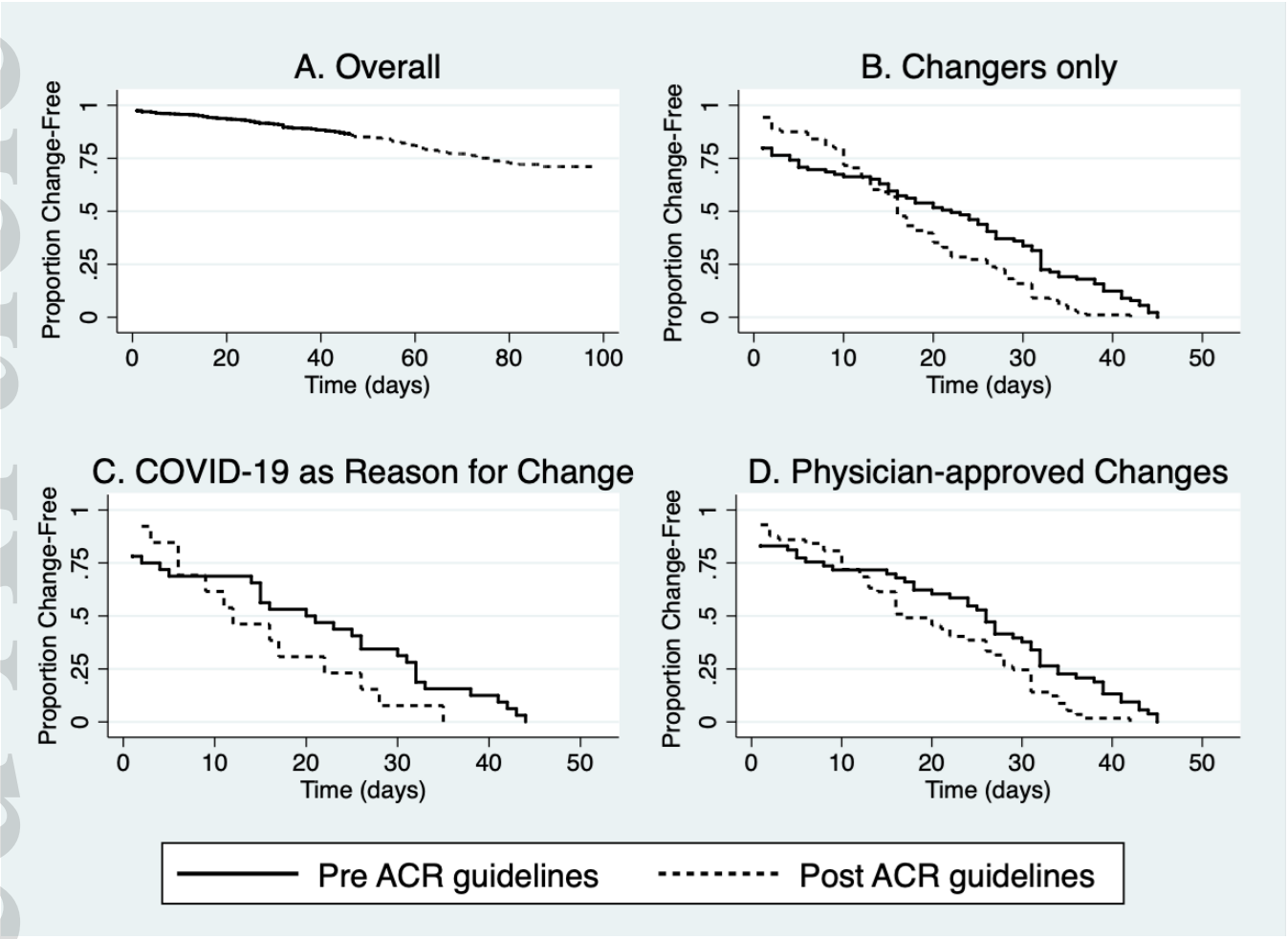

Figure 1: Kaplan-Meier time to medication change by reason for change and physician approval status before and after April 15, 2020, ACR guidelines. All incidence rates are per 100 patients. **(A)** Overall time to change, beginning March 1 and ending at time of questionnaire completion (n=696, annual incidence rate 1.39 [95% CI 1.21, 1.61], and probability of medication change 26.3%). Pre-guidelines (n=696) annual incidence rate 1.16 [0.94, 1.40] and probability of change 13.5%; post-guidelines (n=603) incidence rate 1.74 [1.41, 2.14] and probability of change 14.9%. All subsequent panels are time to change before and after ACR guidelines with curves overlaid. **(B)** Restricted to changers only. Pre-guidelines (n=93) incidence rate 17.67 [14.42, 21.66]; post-guidelines (n=90) 21.02 [17.10, 25.84]. **(C)** Restricted to concern about COVID-19 as reason for medication change. Pre-

guidelines (n=33) incidence rate 18.60 [13.22, 26.16]; post-guidelines (n=13) 24.60 [14.29, 42.37]. **(D)** Restricted to physician approved changes. Pre-guidelines (n=55) incidence rate 15.80 [12.14, 20.59]; post-guidelines (n=59) 19.26 [14.92, 24.86].