

# Rapid Review of Medication Taking (Adherence) Among Patients With Rheumatic Diseases During the COVID-19 Pandemic

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**Objective.** We aimed to identify, appraise, synthesize, and contextualize rapidly emerging reports on medication taking (adherence) among patients with rheumatic diseases during the COVID-19 pandemic.

**Methods.** We searched MEDLINE, EMBASE, and CINAHL for peer-reviewed communications, letters, and articles published during the COVID-19 pandemic evaluating medication taking among individuals with rheumatic diseases. We appraised assessment and reporting of medication adherence according to established definitions of 3 distinct problems of medication taking (i.e., noninitiation, poor implementation, and discontinuation) and pooled findings using random-effects models.

**Results.** We included 31 peer-reviewed studies in our synthesis from various jurisdictions, of which 25 described medication taking among rheumatology patients and 6 described medication prescribing among rheumatology providers. The pooled prevalence of overall medication nonadherence was 14.8% (95% confidence interval [95% CI] 12.3–17.2) and that of medication discontinuation (i.e., stopping of prescriptions) and poor implementation (i.e., not taking medication at the dose/frequency prescribed) as 9.5% (95% CI 5.1–14.0) and 9.6% (95% CI 6.2–13.0), respectively. Noninitiation (i.e., not starting/not filling new prescriptions) was not addressed.

**Conclusion.** Medication taking among individuals with rheumatic diseases during the COVID-19 pandemic varies globally. Unclear reporting and extensive variation in research methods between studies create barriers to research replication, comparison, and generalization to specific patient populations. Future research in this area should use consistent and transparent approaches to defining and measuring medication taking problems to ensure that findings appropriately describe the epidemiology of medication adherence and have the potential to identify modifiable targets for improving patient care.

## INTRODUCTION

In response to the COVID-19 pandemic, international recommendations for rheumatic disease management were rapidly released, including those from the American College of Rheumatology (1), and the European Alliance of Associations for Rheumatology (2), all of which consistently call for adherence to medication therapies, including conventional synthetic, biologic, and targeted synthetic disease-modifying antirheumatic drugs (csDMARDs, bDMARDs, tsDMARDs) as well as

other therapies such as nonsteroidal antiinflammatory drugs (NSAIDs) (1,2). Indeed, taking medications as prescribed is important to the management of rheumatic diseases across both routine and exceptional circumstances, such as the COVID-19 pandemic, as patients rely on medications to relieve symptoms, perform daily life activities, and prevent irreversible joint and organ damage. However, as a result of the COVID-19 pandemic, adherence with therapies among patients with rheumatic diseases has become increasingly complex due to health care system factors, such as the occurrence of medication

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Ms. Rebić is a recipient of a Canadian Institutes of Health Research Canada Graduate Scholarship Doctoral Award. Dr. De Vera holds a Tier 2 Canada Research Chair and is a recipient of a Scholar Award from the Michael Smith Foundation for Health Research.

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Author disclosures are available at <https://onlinelibrary.wiley.com/action/downloadSupplement?doi=10.1002%2Facr.24744&file=acr24744-sup-0001-Disclosureform.pdf>.

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Submitted for publication March 16, 2021; accepted in revised form July 1, 2021.

### SIGNIFICANCE & INNOVATIONS

- We synthesized rapidly emerging reports during the COVID-19 pandemic, including 25 on medication taking (adherence) among rheumatology patients and 6 on medication prescribing among providers.
- We calculated pooled prevalence estimates of 9.5% for poor implementation, 9.6% for discontinuation, and 14.8% for medication nonadherence overall, suggesting that most patients with rheumatic disease are taking medications as prescribed during the COVID-19 pandemic.
- We identified a number of serious and persistent barriers (e.g., challenges obtaining medications, personal beliefs, and fears) to accessing medications and care identified by patient and providers.
- Our findings reveal the necessity for researchers to use standardizing methods for assessing and measuring medication adherence to ensure that research findings have the potential to inform interventions and support patient care.

shortages and limitations on nonessential health care visits. For example, hydroxychloroquine (HCQ), a csDMARD used to treat systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), was initially speculated to be a viable treatment for COVID-19, leading to concerns regarding access for patients with rheumatic diseases. Early reports of successful treatment with HCQ (3) and emergency authorization by the US Food and Drug Administration led to critical shortages in medication availability (4). The therapeutic efficacy of interleukin-6 inhibitor against COVID-19 has also been discussed in a recent systematic review and meta-analysis (5). Condition- and patient-related factors may also place barriers to optimal rheumatic disease management and patients' medication taking as prescribed. Indeed, patients with rheumatic disease are known to be at higher risk of infection secondary to immune-modulating treatments, immune-dysfunction, and the presence of comorbidities (6). Therefore, concerns regarding immunosuppressive effects secondary to antirheumatic therapy may contribute to nonadherence to medications.

Since the start of the COVID-19 pandemic, numerous reports have assessed experiences with medication taking among patients with rheumatic diseases. Accordingly, we conducted a rapid review to systematically identify studies, synthesize findings, and describe the data to date examining the medication taking experiences among this patient population as well as the prescribing experiences of rheumatology providers.

## MATERIALS AND METHODS

**Search strategy.** We conducted a rapid review informed by guidelines from the Cochrane Rapid Reviews Methods Group (7). A search strategy was developed collaboratively with all

authors, including an information scientist (UE), to identify peer-reviewed studies on medication taking (adherence) among patients with rheumatic diseases during the COVID-19 pandemic. Searches were performed by UE of the databases Ovid MEDLINE, Ovid EMBASE, and CINAHL (all from March 2020), using subject headings and keywords of unindexed terms related to "medication adherence," "rheumatic diseases," and "COVID-19." Additional resources were searched, including the Cochrane COVID-19 Study Register, Epistemonikos COVID-19 Living Overview of Evidence, and Prospero. The searches were conducted on January 13, 2021 (see Supplementary Tables 1, 2, and 3, available on the *Arthritis Care & Research* website at <http://onlinelibrary.wiley.com/doi/10.1002/acr.24744>, for the complete search strategy).

**Study selection.** Two authors (NR and RG) screened titles and abstracts for peer-reviewed concise communications, letters, and articles that fulfilled inclusion criteria: 1) observational design, 2) study sample including individuals with rheumatic disease (e.g., ankylosing spondylitis, psoriatic arthritis, RA, SLE) and/or health care providers, 3) evaluation of medication taking (adherence) among individuals with rheumatic disease, and 4) during the COVID-19 pandemic. Any conflicts were resolved via consensus and/or consultation with the corresponding author (MADV). The Covidence platform was used to support the screening process.

**Data extraction and appraisal.** Two study authors (NR and JYP) extracted information on the type of publication (e.g., article, letter), country, study period, and study sample characteristics, including information on types of rheumatic disease, age, and sex. In extracting information on medication taking problems among rheumatology patients, we applied definitions by the International Society of Medication Adherence (8) that describe distinct problems of medication taking, corresponding to 3 types of medication nonadherence: 1) noninitiation, that is, not filling a prescription or starting a dosing regimen; 2) poor implementation of the dosing regimen, where scheduled doses are delayed or omitted; and 3) discontinuation or stopping of drug therapy. Instances when authors reported a cumulative measure not defined as any of the aforementioned types of medication taking problems were assigned as overall medication nonadherence. In addition to extracting and classifying medication taking according to each type of medication nonadherence, we also extracted corresponding information on the extent of the problem (e.g., percentage of patients), as well as potential reasons, when available. If a newer publication for the same study previously identified was found, only the newer results were extracted, unless the earlier publication reported information that was not reported in the more recent publication. With respect to articles describing prescribing by rheumatology providers, we extracted information on reported practice patterns (e.g., continuing,

switching, delaying, discontinuing medications) and experiences (e.g., drug shortages) during the COVID-19 pandemic.

We appraised the quality of medication adherence measurement and reporting using the International Society of Pharmacoeconomics and Outcomes Research Medication Compliance and Persistence Special Interest Group (9), as we have done in prior systematic reviews on medication adherence in rheumatic diseases (10,11). We adapted and condensed this checklist, which aims to establish standards for reporting of medication adherence studies, to 10 priority items (e.g., clarity of study objectives, description of data collection methods/data source, and explicit definition of medication taking problem), awarding a single point for each criterion for a maximum score of 10.

**Statistical analysis.** We conducted a narrative synthesis of included studies. Where possible, we also pooled and reported the prevalence of medication nonadherence according to each type of medication taking problem (noninitiation, poor implementation, or discontinuation) as well as overall nonadherence using random-effects models. We used the proportion (of patients) and corresponding 95% confidence intervals (95% CIs) as estimates. All data analysis was performed using Stata, version 15.

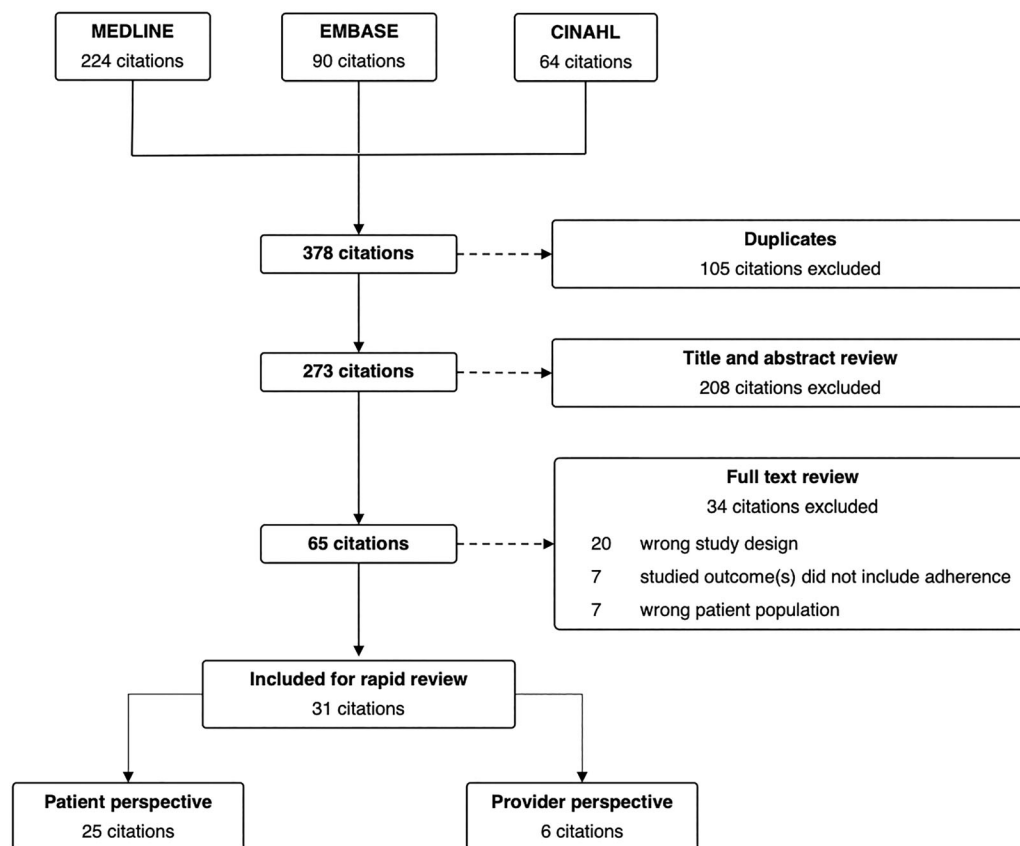
## RESULTS

Our search identified 273 articles after the exclusion of duplicates (Figure 1). Of these, we identified 35 studies that met our inclusion criteria, including 25 assessing medication taking among rheumatology patients and 6 assessing medication prescribing among rheumatology providers.

### Medication taking among rheumatology patients.

We describe the characteristics of 25 included studies assessing medication taking in Table 1. Altogether, studies spanned several countries predominantly located across the Asian, European, North African, and North American continents. All of the studies were based on self-report, with the majority based on surveys and 4 based on interviews.

The quality appraisal score of included studies is reported in Supplementary Table 4, available on the *Arthritis Care & Research* website at <http://onlinelibrary.wiley.com/doi/10.1002/acr.24744>. The majority of studies clearly described their aims, their study sample, the timeframe for data collection, and methods for determining medication taking problems. All studies described their methods for data collection and appropriately presented findings on medication taking; however, the majority of studies did not define medication taking problems (nonadherence) and none



**Figure 1.** Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart.

**Table 1.** Characteristics of included studies assessing medication taking among rheumatology patients\*

Author (ref.)	Publication type	Data collection	Study period	Country	Rheumatic disease	No.	Age	Female, %	Medication taking		
									No initiation	Poor implementation	Discontinuation Reasons
Abuafadi et al, 2021 (39)	Article	Survey	06/-/20 to 08/-/20	Egypt	RA	1,037	Mean ± SD 44.2 ± 12.3	82.4	o	o	o
Ciurea et al, 2021 (18)	Article	Structured interview and survey	01/01/20 to 06/30/20	Switzerland	Axial SpA, RA, PsA	666	Mean ± SD: axial SpA: 47.1 ± 11.8; RA: 55.3 ± 13.2; PsA: 52.6 ± 10.7	Axial SpA: 82.4; RA: 71.8; PsA: 49.6	o	•	o
Costantino et al, 2021 (12)	Article	Survey	04/18/20 to 05/21/20	France	SpA, RA, PsA	655	Mean ± SD 51.0 ± 13.4	61.8	o	•	•
Fragoulis et al, 2021 (19)	Letter	Structured interview	04/14/20 to 04/22/20	Greece	IA, MCTD, SLE, SSC, vasculitis, APS, SS, PMR, other	500	Mean ± SD 53.7 ± 15.3	73.2	o	o	•
George et al, 2021 (20)	Article	Survey	03/29/20 to 05/26/20	US	RA, PsA, AS, SLE	1,517	Mean ± SD 55.1 ± 11.7	88.3	o	o	•
Glintborg et al, 2021 (15)	Article	Survey	03/-/20 to 06/-/20	Denmark	RA, PsA, axial SpA, other	12,789	≤39: 8%; 40-59: 35%; 60-79: 53%; ≥80: 4%	65	o	•	•
Hassen et al, 2020 (22)	Letter, article	Survey	03/-/20 to 04/-/20	Saudi Arabia	RA, SLE, BD, SpA, SS, other	637	Mean ± SD 35.7 ± 9.6	87.3	o	•	•
Kavadichanda et al, 2021 (32)	Article	Structured interview	04/15/20 to 04/30/20	India	SLE, IIM, MCTD, SSC, other CTDs	373	35 (IQR 25-44)	88.7	o	o	•
Khabbazi et al, 2020 (29)	Letter	Interview	07/10/20 to 07/24/20	Iran	RA, SpA, SLE, APS, BD, vasculitis, IJA, IIM, SSC, SS, other	858	Mean ± SD 48.8 ± 13.4	68.9	o	•	•
Koker et al, 2020 (26)	Article	Survey	05/01/20 to 05/20/20	Turkey	JIA, autoinflammatory diseases, CTDs, vasculitis	414	Mean ± SD 12.5 ± 4.7	54.1	o	o	•
López-Medina et al, 2021 (31)	Letter	Survey	04/25/20 to 05/05/20	Spain	SpA, PsA, RA, systemic autoimmune diseases, fibromyalgia, OA	644	Missing data	Missing data	o	•	•
Maldonado et al, 2021 (24)	Article	Survey	05/08/20 to 06/01/20	US	SLE, RA, JIA, DM, PM, sarcoidosis, other	361	42 (IQR 23-58)	88	o	•	•
Michaud et al, 2020 (28)	Article	Survey	03/25/20 to 04/01/20	US	RA, OA, SLE, other	530	Mean ± SD 65.0 ± 10.9	84.4	o	•	•
Murray et al, 2021 (30)	Article	Survey	04/28/20 to 05/05/20	Ireland	RA, SpA, CTD, vasculitis, other	1,381	<40: 24.1%; 41-60: 59.2%; >60: 16.7%	87.8	o	•	•
O'leary et al, 2020 (40)	Letter	Missing data	Missing data	Ireland	Missing data	398	Missing data	Missing data	o	o	o

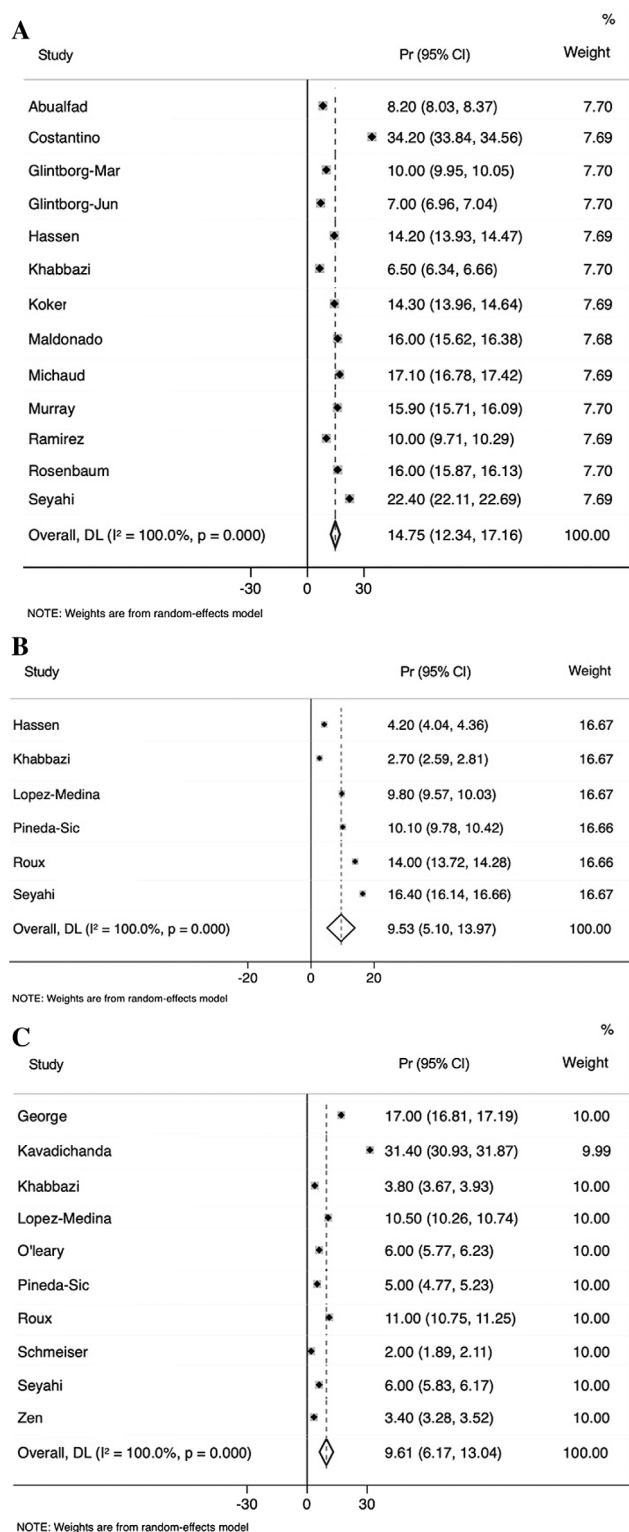
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**Table 1.** (Cont'd)

Author (ref.)	Publication type	Data collection	Study period	Country	Rheumatic disease	No.	Age	Female, %	Medication taking		
									No initiation	Poor implementation	Discontinuation Reasons
Pineda-Sic et al, 2021 (21)	Letter	Survey	05/14/20 to 05/25/20	Mexico	RA, SLE, SS, axial SpA, PsA, IIM, scleroderma, vasculitis, other	345	<30: 13.9%; 30-60: 65.8%; >60: 20.3%	90.2	o	•	•
Ramirez et al, 2020 (17)	Article	Survey	02/-/20 to 04/-/20	Italy	SLE	417	<30: 12%; 31-40: 20%; 41-50: 25% >50: 43%	91	o	•	•
Rathi et al, 2020 (23)	Article	Survey	04/-/20 to 05/-/20	India	SLE	1,040	Mean ± SD 27.5 ± 19.1	9:1 (F:M ratio)	o	•	•
Rosenbaum et al, 2020 (13)	Letter	Survey	04/10/20 to 05/07/20	US, 64 other countries	AS, other	2,992	Median: F: 53; M: 54	61.4	o	•	o
Roux et al, 2020 (16)	Letter	Survey	04/10/20 to 04/21/20	France	SpA	609	Mean ± SD 45 ± 11	76	o	•	o
Schmeiser et al, 2020 (41)	Letter	Survey	03/16/20 to 04/03/20	Germany	RA, SpA, PsA, SLE, SSC, PMR, SS, GPA, PM, EGPA, other	656	<30: 7%; 30-60: 52%; >60: 23%	Missing data	o	o	o
Seyahi et al, 2020 (25)	Article	Survey	Missing data	Turkey	RA, CTD, SpA, BD, FMF, vasculitis	771	42 (range 16-81)	-	o	•	•
Singh and Edwards, 2020 (14)	Article	Survey	04/-/20 to 06/-/20	US	Gout	122	Mean ± SD 54.2 ± 13.8	35	o	•	o
Ziadé et al, 2020 (27)	Article	Survey	05/08/20 to 05/22/20	14 Arab countries†	Missing data	2,163	Mean ± SD 40.0 ± 11.9	72.3	o	o	•
Zen et al, 2020 (42)	Article	Survey	04/09/20 to 04/25/20	Italy	SLE, SSC, RA, AAV, IIM	916	Mean ± SD 53.6 ± 14.3	78.6	o	o	•

\* o = not reported; • = reported. AAV = ANCA-associated vasculitis; APS = antiphospholipid syndrome; AS = ankylosing spondylitis; BD = Behçet's disease; CTD = connective tissue disease (e.g., systemic lupus erythematosus [SLE], SSC [systemic sclerosis], SS [Sjögren's syndrome]); DM = dermatomyositis; EGPA = eosinophilic granulomatosis with polyangiitis; FMF = familial Mediterranean fever; GPA = granulomatosis with polyangiitis; IA = inflammatory arthritis; IIM = idiopathic inflammatory myopathies; IOR = interquartile range; JIA = juvenile idiopathic arthritis; MCTD = mixed connective tissue diseases; OA = osteoarthritis; PM = polymyositis; PMR = polymyalgia rheumatica; PsA = psoriatic arthritis; RA = rheumatoid arthritis; ref. = reference; SpA = spondyloarthritis; UJA = undifferentiated inflammatory arthritis.

† Iraq, Saudi Arabia, Egypt, Morocco, Algeria, Kuwait, Lebanon, Jordan, Tunisia, United Arab Emirates, Syria, Libya, Palestine, Oman, Qatar, other.



**Figure 2.** Forest plots: **A**, overall medication nonadherence, **B**, poor implementation, and **C**, discontinuation among rheumatology patients during the COVID-19 pandemic. 95% CI = 95% confidence interval; Pr = prevalence.

used accepted definitions. Overall, definitions of medication nonadherence varied between reports, so that meaningfully synthesizing findings was challenging.

Twelve studies ( $n = 22,842$ ) reported the overall prevalence of nonadherence to therapy, which ranged from 6.5% to 34.2% of patients. Pooling the crude estimates of overall nonadherence resulted in a prevalence of 14.8% (95% CI 12.3–17.2) (Figure 2A). No studies reported on noninitiation (i.e., not starting/not filling new prescriptions). Six studies ( $n = 3,884$ ) reported the overall prevalence of poor implementation (i.e., not taking medication at the dose/frequency prescribed), which ranged from 2.7% to 16.4%. Pooling the crude estimates of poor implementation resulted in a prevalence of 9.5% (95% CI 5.1–14.0) (Figure 2B). Ten studies ( $n = 7,087$ ) reported the overall prevalence of medication discontinuation (i.e., stopping prescription), which ranged from 2% to 31.4%. Pooling the crude estimates of discontinuation resulted in a prevalence of 9.6% (95% CI 6.2–13.0) (Figure 2C). Six studies (12–17) additionally reported on specific counts based on medication type (i.e., csDMARDs, bDMARDs, tsDMARDs, corticosteroids, NSAIDs, etc.), with 1 reporting on HCQ specifically (17). Three of these studies (12,14,16) provided specific counts for the type of medication change (i.e., dose increase/decrease, frequency changes). Two studies (15,18) collected repeated measures of medication taking (i.e., >1 timepoint) within their sample.

The majority of studies reported some findings related to reasons for medication taking changes. Glintborg et al (15) performed multivariable logistical regression analyses and found that male sex (odds ratio [OR] 1.51 [95% CI 1.21–1.89],  $P < 0.001$ ), age  $\geq 80$  years compared to  $\leq 39$  years (OR 0.11 [95% CI 0.006–0.52],  $P = 0.03$ ), lower education (OR 0.56 [95% CI 0.45–0.69],  $P < 0.001$ ), working (OR 1.52 [95% CI 1.16–1.99],  $P = 0.003$ ), and use of bDMARDs (OR 1.86 [95% CI 1.02–3.81],  $P = 0.05$ ) were associated with patients changing at least 1 medication due to fear of COVID-19. Fragoulis et al (19) performed univariable logistical regression analyses and found that therapy discontinuation due to fear of immunosuppression was associated with unemployment (OR 9.19 [95% CI 1.30–64.7],  $P = 0.03$ ) and chronic obstructive pulmonary disease (OR 27.53 [95% CI 3.17–239.1],  $P = 0.003$ ). George et al (20) performed univariable logistical regression analyses and found that participants who stopped a DMARD were more likely to avoid office visits (OR 1.46 [95% CI 1.04–2.04],  $P = 0.03$ ) and to report that telehealth options were not available to them (OR 2.26 [95% CI 1.25–4.08],  $P < 0.01$ ). Additionally, some studies examined issues related to medication taking, which included lack of medication availability (15,19,21–23), medication shortages (12,17,20,24–27), difficulty obtaining medication (20,23,25,27,28) or an infusion (20,23,24), fear of medication-related immunosuppression (15,19,20,24,29,30), fear of contracting COVID-19

**Table 2.** Characteristics of included studies assessing medication prescribing among rheumatology providers

Study	Publication type	Data collection	Study period	Location	Provider	No.	Age, no. years (%) or mean $\pm$ SD	Female, %
Akintayo et al, 2021 (33)	Article	Survey	04/28/20 to 05/05/20	20 pan-African countries*	Rheumatologists	554	42.6 $\pm$ 11.2	72
Batu et al, 2020 (34)	Article	Survey	05/-/20	70 countries	Rheumatologists	493	<35 (10.8), 35–44 (34.7), 45–65 (49.9) >65 (4.7)	67
Dejaco et al, 2021 (35)	Article	Survey	05/13/20 to 06/17/20	58 countries†	Rheumatologists	1,286	<30 (4.7), 30–39 (24.9), 40–49 (29.5), 50–59 (26.2), 60–69 (12.8), $\geq$ 70 (2.0)	62.9
Mehta et al, 2020 (38)	Article	Survey	04/08/20 to 05/04/20	US	Rheumatologists	271	25–34 (18.8), 35–44 (33.6), 45–54 (19.6), 55–64 (14.0), >65 (14.0)	57.6
Mehta et al, 2020 (36)	Article	Survey	04/08/20 to 04/27/20	61 countries (US, Europe, other)	Rheumatologists	506	Missing data	51.6
Ziadé et al, 2020 (37)	Article	Survey	05/09/20 to 05/24/20	15 Arab countries‡	Rheumatologists	858	25–34 (24), 35–44 (37), 45–54 (21), 55–64 (15), 65–74 (3)	60

\* Algeria, Egypt, Libya, Morocco, Tunisia, Sudan, Benin, Ghana, Nigeria, Senegal, Mali, Ivory Coast, Cameroon, Kenya, Madagascar, Mauritius, Mozambique, Tanzania, South Africa, Zambia.

† Romania, Italy, Netherlands, Germany, France, Spain, Denmark, Austria, UK, Greece, Switzerland, Portugal, Croatia, Turkey, Sweden, Ireland, Finland, Norway, Hungary, Slovenia, Belgium, Albania, Georgia, Israel, Lebanon, Cyprus, Czech Republic, Latvia, Montenegro, Russian Federation, Bulgaria, Serbia, Belarus, San Marino, North Macedonia.

‡ Levant countries: Iraq, Jordan, Lebanon, Palestine, Syria; Gulf countries: Saudi Arabia, Kuwait, Oman, Qatar, United Arab Emirates; North African countries: Algeria, Egypt, Libya, Morocco, Tunisia.

(12,15,21,26,27,31), experiencing symptoms of respiratory infection/COVID-19 (12,19,20,29,30), financial concerns/challenges paying for medication (20,21,24,32), fear of referral to clinic/hospital (29), challenges accessing public transport (32), a prescriber (24), or a pharmacy (24), and not prioritizing medication taking (24). Three studies (17,30,31) noted whether medication changes were patient or prescriber initiated. However, most studies did not adequately describe how identified medication taking issues related to the specific types of nonadherence, and therefore these results were challenging to synthesize.

**Medication prescribing among rheumatology providers.** We describe the characteristics of 6 included studies assessing medication prescribing in Table 2. Most studies (33–37) reported on medication shortages, specifically HCQ, which ranged from 38.9% (34) to 71% (36), and tocilizumab, which ranged from 8.9% (34) to 14% (35). Several studies (33–35) reported on providers avoiding starting or switching to a new DMARD during the COVID-19 pandemic, ranging from 20% (34) to 74% (35). Two of these studies specifically reported on providers' reluctance to start or switch to a bDMARD or tsDMARD, which ranged from 57.6% (33) to 74% (35), and some reasons for this, including patients' fear to start these medications and decreased patient access to rheumatology care (e.g., screening procedures) (33). Overall, 4 studies (33–35,38) provided specific counts for the type of medication change based on medication type. Of these, 3 (33,34,38) reported on bDMARD medication prescribing, with 50% (38) to 84.2% (34)

remaining unchanged. Additionally, 3 studies (33,35,38) reported providers reducing the dose/frequency of steroids, ranging from 23% (35) to 56% (38), and 3 studies (34,35,38) reported providers reducing the dose/frequency of NSAIDs, ranging from 11% (38) to 15% (35). Overall, measures of prescribing practices varied between reports, so that comparing findings was challenging.

## DISCUSSION

There has been a rapid emergence of peer-reviewed reports describing medication taking among patients with rheumatic diseases during the COVID-19 pandemic, highlighting the importance of medication adherence in rheumatology care. Systematically identifying and synthesizing these reports, our rapid review identified 31 studies of medication taking during the COVID-19 pandemic, including 25 from the perspective of patients with rheumatic disease and 6 from the perspective of health care providers prescribing medication for rheumatic disease treatment. Altogether, with a pooled prevalence of 9.5% for poor implementation, 9.6% for discontinuation, and 14.8% for medication nonadherence overall, the results suggest that most patients with rheumatic disease are taking medications as prescribed during the COVID-19 pandemic. Nevertheless our narrative synthesis identified a number of serious barriers to accessing medications and care from both patient and provider perspectives.

Synthesizing findings across studies to generate pooled estimates on the prevalence of medication nonadherence provides

an indicator of the extent of potential medication taking problems and can help to identify target areas for intervention with respect to different types of medication taking problems. Only 3 studies (15,19,20) in our review conducted regression analyses to identify factors associated with medication nonadherence, with only 1 examining multivariable analyses and reporting that patients who changed the dose of at least 1 of their medications due to fear of COVID-19 were more frequently male, treated with bDMARDs, age  $\leq 39$  years (compared to  $\geq 80$  years), higher educated, and working. Also important is identifying reasons for non-adherence, including systemic barriers (e.g., medication shortages, challenges obtaining medications) as well as individual barriers (e.g., personal beliefs, fears, or capacity to prioritize medication taking), to accessing medications and medical care identified in our review. Moreover, characterizing the impact of the COVID-19 pandemic on how rheumatology providers approach medication prescribing is essential to understanding the context for changes in medication taking among patients, including whether they are patient or provider initiated.

To ensure that emerging research findings can both be replicated and compared across studies, it is critical that researchers use consistent and transparent approaches to defining and measuring medication taking problems. Specifically, we recommend that researchers distinguish between the specific types of medication taking problems (8) (i.e., noninitiation, poor implementation, and discontinuation) to ensure that reporting on this topic appropriately describes the extent of this issue and identifies modifiable targets and areas of intervention that may better support patient care. Moreover, systematically reporting specific counts based on medication type and medication taking change (i.e., dose increase/decrease, frequency changes) as well as collecting repeated measures of medication taking (i.e.,  $>1$  timepoint) within their sample can help provide a more thorough understanding of the phenomenon and add rigor to study findings.

Strengths and limitations of our study warrant discussion. To ensure a thorough literature search, we developed our search strategy in collaboration with an information scientist who executed all database searches. We also took a structured approach to data extraction, particularly in using definitions by the International Society of Medication Adherence (8) as a framework to identify and describe 3 distinct problems of medication taking, corresponding to 3 types of medication nonadherence, that is, noninitiation, poor implementation, and early discontinuation. Nonetheless, our systematic review may be vulnerable to publication bias, given that this limitation is inherent to systematic reviews. With the exception of 1 study that was translated from German (39–42), our included studies were published in English, and relevant publications in other languages may have been missed. In addition, results of our meta-analyses suggested heterogeneity between studies, reflecting the wide variation in approaches to defining and measuring medication taking problems, and we caution the interpretation of pooled estimates.

Moreover, the variation in reported prevalence of nonadherence and the range of issues impacting medication taking during the COVID-19 pandemic demonstrate the relevance of examining adherence by jurisdiction, given regional differences in health care systems and pandemic management.

Altogether, our rapid review shows that medication taking among individuals with rheumatic disease during the COVID-19 pandemic varies globally. As the COVID-19 pandemic progresses, assessing its impact on health care provision, particularly among vulnerable patient populations, is needed. Moreover, researchers in this area must ensure that research findings have the potential to inform patient care through standardizing methods used to assess and measure medication adherence.

## AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. De Vera had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study conception and design.** Rebić, De Vera.

**Acquisition of data.** Rebić, Ellis, De Vera.

**Analysis and interpretation of data.** Rebić, Park, Garg, Ellis, Kelly, Davidson, De Vera.

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