

The influence of the SARS-CoV-2 lockdown on patients with inflammatory rheumatic diseases on their adherence to immunomodulatory medication

- a cross sectional study over 3 months in Germany -

Hasseli R^{1§}, Müller-Ladner U¹, Keil F², Broll M³, Dormann A⁸, Fräbel C⁴, Hermann W¹, Heinmüller C-J⁵, Hoyer BF⁶, Löffler, F¹, Özden F⁷, Pfeiffer U⁸, Saech J⁹, Schneidereit T⁸, Schlesinger A¹⁰, Schwarting A¹¹, Specker C¹², Stapfer G¹, Steinmüller M¹³, Storck-Müller K¹⁴, Strunk J¹⁵, Thiele A⁸, Triantafyllias K¹¹, Vagedes D¹⁶, Wassenberg S¹⁷, Wilden E¹⁸, Zeglam S¹⁰, Schmeiser T⁸

- 1) Department of Rheumatology and Immunology, Campus Kerckhoff, Justus-Liebig-University Giessen, Germany
- 2) Department of Electrical Engineering and Information Technology, Technical University Darmstadt, Germany
- 3) Private Practice, Wetzlar, Germany
- 4) Department of Cardiology, University Hospital Giessen, Justus-Liebig-University Giessen, Germany
- 5) Private Practice, Wuppertal, Germany
- 6) Department of Rheumatology and Clinical Immunology, Clinic for Internal Medicine I, University Hospital Schleswig-Holstein, Campus Kiel, Germany
- 7) Private Practice, Nienburg, Germany
- 8) Department of Rheumatology and Immunology, Saint Josef Hospital, Wuppertal
- 9) Private Practice "Rheumatologie-Centrum", Leverkusen, Germany
- 10) Department of Internal Medicine, Pulmonology and Rheumatology, Marienhospital, Cologne, Germany
- 11) Acura Rheumatology Center Rhineland Palatinate, Bad Kreuznach, Germany
- 12) Department of Rheumatology and Clinical Immunology, Kliniken Essen-Mitte, Essen, Germany
- 13) Private Practice, Ehringshausen, Germany
- 14) Rheumazentrum Mittelhessen, Bad Endbach, Germany
- 15) Hospital Porz am Rhein, Department of Rheumatology Cologne, Germany
- 16) Medical care centre Barmherzige Brüder, Straubing, Germany
- 17) Private Practice "Rheumazentrum Ratingen", Ratingen, Germany
- 18) Private Practice, Cologne, Germany

§Corresponding author

Dr. Rebecca Hasseli
Department of Rheumatology and Clinical Immunology
Campus Kerckhoff, Justus-Liebig-University Giessen
Benkestrasse 2-8
D-61231 Bad Nauheim, Germany
Email: r.hasseli@kerckhoff-klinik.de

Abstract

Objectives

To evaluate the influence of the SARS-CoV-2 pandemic on the adherence of patients with inflammatory rheumatic diseases (IRD) to their immunomodulatory medication during the three-months lockdown in Germany.

Methods

From March 16th until June 15th 2020, IRD patients from private practices and rheumatology departments were asked to answer a questionnaire addressing their behaviour with respect to their immunomodulating therapy. Eight private practices and nine rheumatology departments which included rheumatology primary care centres and university hospitals participated. 4252 questionnaires were collected and evaluated.

Results

The majority of patients (54%) were diagnosed with rheumatoid arthritis, followed by psoriatic arthritis (14%), ankylosing spondylitis (10%), connective tissue diseases (12%) and vasculitides (6%). The majority of patients (84%) reported to continue their immunomodulatory therapy. Termination of therapy was reported by only 3% of the patients. The results were independent from the type of IRD, the respective immunomodulatory therapy and by whom the patients were treated (private practices vs rheumatology departments). Younger patients (<60 years) reported just as often as older patients to discontinue their therapy.

Conclusion

The data show that most of the patients continued their therapy in spite of the pandemic. A significant change in behavior with regard to their immunomodulatory therapy was not observed during the three months of observation. The results support the idea that the immediate release of recommendation of the German Society of Rheumatology were well received, supporting the well-established physician-patient-relationship in times of a crisis.

Keywords

SARS-CoV-2 pandemic, adherence, immunomodulatory drugs, influence, patient's behaviour, doctor patient relationship

Key messages

- The majority of IRD patients continued their immunomodulatory therapy during the SARS-CoV-2 pandemic lockdown
- The results were independent of age, type of therapy and IRD
- This could reflect a trustful physician-patient-relationship in times of crisis and that patients followed the recommendations during the pandemic

Introduction

More than 48 million cases of infection with severe acute respiratory syndrome coronavirus (SARS-CoV-2) were reported globally and more than 1.2 million fatal courses from resulting coronavirus disease 2019 (COVID-19) have been registered as of November 5th, 2020 [1]. Regardless of these high numbers it has not been fully elucidated whether patients with inflammatory rheumatic diseases (IRD) or specific immunomodulatory treatments have a higher risk to develop a severe course of COVID-19, although data suggest that patients with IRD are at higher risk for bacterial, viral and opportunistic infections compared to the general population [2, 3]. At the beginning of the pandemic, no clear recommendations for patients with IRD were available in Germany. On March 16th, 2020 hospitals were ordered by the respective authorities to reduce and postpone elective procedures substantially and to prioritize the remaining operative and personnel resources to facilitate treating patients with severe COVID-19. It was recommended that patients should reduce their visits to hospitals and private practices, if not essential for disease management. This caused a dramatic reduction of in- and outpatient visits. In some cases, patients did not even receive their immunomodulatory treatment, intravenous application of immunomodulatory drugs were prolonged, necessary adaptations of treatment strategies in case of disease relapse were postponed and personal appointments were nearly completely cancelled to reduce the overall risk of a SARS-CoV-2 infection in Germany [4]. In addition, on March 22th, 2020 the German government restricted personal contacts outside of family circles to not more than two people, resulting in social isolation. One can quite easily imagine how these measures left some patients completely on their own. Already in April, the German Society for Rheumatology (DGRh), similar to other societies, such as EULAR, BSR and ACR published preliminary recommendations for management of patients with IRD in the context of the current pandemic [5–7]. All of them

suggested the maintenance of immunomodulating therapies during the SARS-CoV-2 pandemic to avoid disease relapses.

In order to be able to estimate the patients' behavior with respect to their immunomodulatory therapy, a Germany-wide survey was established during the SARS-CoV-2 pandemic, with a distinct focus on the patients' view on their immunomodulatory therapy. This was based upon the hypothesis that influenced by public media, personal restrictions in the lock-down situation and possibly also by recommendations released from the national rheumatological societies patients may have changed their behavior regarding immunomodulatory therapy [8, 9].

Indeed, this hypothesis was challenged by data of pulmonologists, who showed that pneumological appointments at the beginning of 2020 resulted in an increased adherence to therapy in COPD patients by 15%. However, it could not conclusively be clarified whether improved compliance was due to the context of the impending pandemic [10].

Methods

From March 16th until June 15th, 2020 IRD patients from private practices and rheumatology departments were anonymously asked for adherence to their immunomodulating therapy. Nine private practices and eight rheumatology departments from 6 federal states across Germany participated. A one-page questionnaire was developed which included the range of age, type of IRD and immunomodulatory treatment (suppl. 1). Patients had to choose one out of seven options to answer this question (suppl. 1). The inclusion criteria were: a) age \geq 18 years, b) presence of an IRD. There were no inclusion/exclusion criteria for the participating general and private practices and departments. Participation was voluntary and without reimbursement. The time period from March 16th until March 20th 2020 was defined as "before lockdown" and the time period from March 21st until June 15th 2020 was defined as "during and after lockdown".

Google Trends analysis

To investigate further potential reasons, why patients could have discontinued their immunomodulatory therapy, we performed an analysis on "Google Trends" which is a free accessible online portal of Google Inc. [11]. Google Trends allows users to interact with Internet search data, which can provide deep insights into behaviours of the population and health-related phenomena [11]. Google Trends answers queries and keeps a record of such searches. The data is compiled to display trends automatically. The weekly trends can be accessed from Google Trends, a special open-access domain of Google

(<https://trends.google.com/trends/>) [12]. We therefore systematically searched for following queries:

- "corona cortisone" (German: „Corona Kortison“)
- „corona rheuma“
- „corona mtx“
- „corona adalimumab“
- „corona Humira“
- „covid-19 cortisone“
- covid-19 rheuma“
- „covid-19 mtx“
- covid-19 adalimumab
- „covid-19 Humira“

After approval of the study by the ethics committee of the Justus-Liebig-University Giessen (#32-20) and registration (EuDRACt 2020-004064-25), the survey started on March 16th. The survey was announced to German rheumatologists on a nationwide basis which resulted in increasing number of participating private practices and rheumatology departments.

Statistical analysis

First, the proportion of patients' characteristics (age, type of IRD, IRD therapy) and opinion were calculated to evaluate relevant changes. Second, exact binomial tests were used to assess significant differences between patients' characteristics and the opinion. Python version 3.8.2 in conjunction with several libraries was used for statistical analyses and for the graphs. P values were 2-sided, and statistical significance was set at $P \leq 0.05$.

Results

Most of the participating centres were located in North Rhine-Westphalia (8), followed by centres in Hesse (5), Lower Saxony (1), Schleswig-Holstein (1), Bavaria (1), Rhineland-Palatinate (1; suppl. 2). 4252 questionnaires were collected and evaluated, 279 questionnaires before lockdown and 3973 questionnaires during and after lockdown. Most patients (29%) were aged between 51-60 years, followed by 22% of patients, which were between 61-70 or 31-50 years old, and 15% were 71-80 years (fig.1A). Patients reported to suffer from rheumatoid arthritis (54%), psoriatic arthritis (14%), ankylosing spondylitis (10%), systemic lupus erythematosus (6%), polymyalgia/giant cell arteritis (5%), systemic sclerosis (3%) and

Sjögren's syndrome (2%). Approximately 1% of patients had a granulomatosis with polyangiitis, eosinophilic granulomatosis with polyangiitis or polymyositis/dermatomyositis. Gout, fever syndromes and other rare diseases were grouped together under "other diseases".

Around 22% of patients were on monotherapy with conventional synthetic disease-modifying antirheumatic drugs (csDMARD). A combination of csDMARDs and biological (b)DMARDs was reported in 11% of the patients. Only, less than 1% received GC as monotherapy, in 31% of the cases a combination with GC was reported. One fifth of the patients (20%) received a therapy with non-steroidal anti-inflammatory drugs (NSAIDs), of which 16% reported combination therapy with other immunomodulating drugs. Biologics were used in 34% of the patients (TNF-inhibitors 20%, interleukin (IL)-6-inhibitors 5%, IL-17-inhibitors 3%, abatacept 2%, rituximab 2%, IL-12/23-inhibitor 1%, IL-1-inhibitor 1%, belimumab 1%) and Janus kinase inhibitors (JAK-i) in 6% of the patients (fig. 1B). From March till June 84% of the patients reported to continue their immunomodulatory therapy. In fig. 2 the influence of the pandemic before, during and after the lockdown on the patient's behaviour regarding their therapies is displayed. Before the national lockdown, only 4% of the patients reported to discontinue their medication on their own or in consultation with their rheumatologists (fig. 2A). During and after the national lockdown the number of reported discontinuations even decreased (fig. 2B). There was no relevant difference in the behaviour before, during and after the lockdown. Younger patients (18-30 years old, 2.8%) and patients between 71-80 of age (2.2%) reported to discontinue their medication less often compared to patients between 31-50 years old (4,4%) which were the largest group (fig. 3). The difference was not found to be significant as more younger patients (<60 years) participated in the survey (fig. 1A). There was no relevant difference in patients' opinion with regard to the type of IRD (data not shown).

There were no obvious differences in patient's adherence regarding specific immunomodulatory therapies (data not shown). In fig. 4A the development of patients' opinion over time is displayed. No significant difference could be detected over time. At the beginning of the pandemic more patients reported to discontinue their medication, than the number of patients who reported to discontinue their immunomodulatory therapy by their own decreased slightly (fig. 4B). With decreasing number of infected patients in the general population, less patients with IRD reported to discontinue their therapy. When SARS-CoV-2 infections spread again the number of patients reporting to discontinue their medication increased as well (fig. 4B).

In the Google Trends analysis, only for the items „corona steroids”, “corona humira”, “corona rheuma” sufficient results could be detected. Humira® (adalimumab, manufacturer AbbVie) has been the best-selling bDMARD in Germany for years. We correlated the weekly results of Google Trends for the selected queries with the number of patients who reported to discontinue

their immunomodulatory therapy. The weekly course of the number of queries were similar to the course of the number of patients who reported to discontinue their medication (fig. 5).

Discussion

To our knowledge, this study is the largest investigation to light up patients' opinions on immunomodulating therapy in IRD during the SARS-CoV-2 pandemic. The study reflects behavior of IRD patients over a period of 3 months in a lockdown setting with very limited or even no access to rheumatologists nationwide in Germany. In view of these circumstances, rheumatologic societies did not recommend discontinuing the immunomodulatory therapy to avoid disease relapse necessitating new or higher dosage of glucocorticoids putting patients on substantial risk for infections. Our study shows that patients followed these recommendations of rheumatologists. In view of the fact, that the management of patients with IRD was highly impacted by the pandemic, this can be interpreted as a hint for a trustful physician-patient relationship. Other studies could also observe a high number of patients who reported to continue their immunomodulatory therapy [13, 14]. In comparison to these results, medication adherence in patients with arterial hypertension in Germany is estimated to be around 66% in a non-pandemic setting [15].

Of note, no relevant difference in discontinuation rate could be observed with respect to age, type of IRD, type of immunomodulatory drug and the time elapsed since start of the pandemic. As the distribution of age in the study population is comparable to IRD patients in general, the results can be probably transferred to the entirety of IRD patients in Germany.

The results in the Google Trends analysis, which show a time-dependent interest for the topics "corona & rheuma", "corona & cortisone" and "corona & humira", could reflect an influence on patients' decision to discontinue their immunomodulatory therapy. A possible reason could be the fear to develop a severe course of SARS-CoV-2 infection due to the immunomodulatory drug.

However, this study has some limitations: i) In order to rule out that patients were repeatedly asked for their opinion, the examination interval was limited to three months. Due to the anonymous survey, it is not possible to exclude that patients have participated in the survey more than once. However, as the majority of the patients do not have more than one outpatient visit within three months, a repetition of the survey is most likely only the case for a negligible number of patients. ii) as the questionnaire was completely anonymous, gender was not recorded, and iii) since it would not be clear at the beginning of the survey that disease activity and the dose of GC could have an influence on the course of a COVID-19, these aspects were not included in the questionnaire; iv) the pandemic is peaking in different regions at different

times which might have an influence on the opinion. Although general practitioner and private practices and departments from 6 federal states were involved in the recruitment of the patients, data from other federal states are missing, which could have an impact on the results. In most of the represented federal states, the prevalence of SARS-CoV-2-infections were higher compared to the missing federal states [16]; v) the study population consists of patients with diseases that are associated with higher risk of severe organ involvement, e.g. vasculitides and connective tissue disease. The prevalence of these diseases in the study population is higher compared to the prevalence among IRD patients in general (suppl. 3). It is possible that these patients attended their medical visits despite lockdown, so the distribution of patients could have been different without a lockdown scenario. These might have an impact on the decision of the patients. Unfortunately, there are no data available about the distribution of the diseases treated in general practitioner and private practices and rheumatology departments in general.

Taken together, the results of the study not only illustrate and reflect the patient's relation to their immunomodulatory therapy on a large-scale basis but specifically the essential value of the patient-physician partnership in the crisis.

Acknowledgements

The authors would like to thank all patients who participated at the survey.

Contributors:

RH, TS and UML contributed equally and performed the study design. RH and TS performed the research and the interpretation of the data. FK analysed and performed the statistical analysis. RH wrote the manuscript. All authors performed physician recruitment, contributed to preparation of the project, and read and approved the final manuscript.

Funding:

RH was supported by the Justus-Liebig-University Giessen Clinician Scientist Program in Biomedical Research (JLU-CAREER) to work on this project.

Competing interests:

The authors declare that there is no conflict of interest regarding the publication of this article.

Data Availability Statement:

All datasets generated for this study are included in the article/supplementary material.

References

1. John Hopkins University & Medicine. Coronavirus Resource Center. <https://coronavirus.jhu.edu/map.html>.
2. Zen M, Fuzzi E, Astorri D, Saccon F, Padoan R, Ienna L, et al. SARS-CoV-2 infection in patients with autoimmune rheumatic diseases in northeast Italy: A cross-sectional study on 916 patients; 2020.
3. Sfriso P, Ghirardello A, Botsios C, Tonon M, Zen M, Bassi N, et al. Infections and autoimmunity: the multifaceted relationship. *J Leukoc Biol.* 2010;87:385–95. doi:10.1189/jlb.0709517.
4. Freudenberg S, Vossen D. Auswirkungen von COVID-19 auf die rheumatologische Versorgung : Eine nationale Umfrage im April 2020. *Z Rheumatol.* 2020;79:584–9. doi:10.1007/s00393-020-00833-z.
5. Schulze-Koops H, Specker C, Iking-Konert C, Holle J, Moosig F, Krueger K. Preliminary recommendations of the German Society of Rheumatology (DGRh eV) for the management of patients with inflammatory rheumatic diseases during the SARS-CoV-2/Covid-19 pandemic. *Ann Rheum Dis* 2020. doi:10.1136/annrheumdis-2020-217628.
6. Landewé RB, Machado PM, Kroon F, Bijlsma HW, Burmester GR, Carmona L, et al. EULAR provisional recommendations for the management of rheumatic and musculoskeletal diseases in the context of SARS-CoV-2. *Ann Rheum Dis.* 2020;79:851–8. doi:10.1136/annrheumdis-2020-217877.
7. Mikuls TR, Johnson SR, Fraenkel L, Arasaratnam RJ, Baden LR, Bermas BL, et al. American College of Rheumatology Guidance for the Management of Adult Patients with Rheumatic Disease During the COVID-19 Pandemic. *Arthritis & rheumatology (Hoboken, N.J.)* 2020. doi:10.1002/art.41301.
8. Hassen LM, Almaghlouth IA, Hassen IM, Daghestani MH, Almohisen AA, Alqurtas EM, et al. Impact of COVID-19 outbreak on rheumatic patients' perceptions and behaviors: A cross-sectional study. *Int J Rheum Dis* 2020. doi:10.1111/1756-185X.13959.
9. Pulvirenti F, Cinetto F, Milito C, Bonanni L, Pesce AM, Leodori G, et al. Health-Related Quality of Life in Common Variable Immunodeficiency Italian Patients Switched to Remote Assistance During the COVID-19 Pandemic. *The Journal of Allergy and Clinical Immunology: In Practice.* 2020;8:1894-1899.e2. doi:10.1016/j.jaip.2020.04.003.
10. Kaye L, Theye B, Smeenk I, Gondalia R, Barrett MA, Stempel DA. Changes in medication adherence among patients with asthma and COPD during the COVID-19 pandemic. *The Journal of Allergy and Clinical Immunology: In Practice.* 2020;8:2384–5. doi:10.1016/j.jaip.2020.04.053.
11. Nuti SV, Wayda B, Ranasinghe I, Wang S, Dreyer RP, Chen SI, Murugiah K. The use of google trends in health care research: a systematic review. *PLoS One.* 2014;9:e109583. doi:10.1371/journal.pone.0109583.
12. Verma M, Kishore K, Kumar M, Sondh AR, Aggarwal G, Kathirvel S. Google Search Trends Predicting Disease Outbreaks: An Analysis from India. *Healthc Inform Res.* 2018;24:300–8. doi:10.4258/hir.2018.24.4.300.
13. Ziade N, El Kibbi L, Hmamouchi, I, Abdulateef, N, Halabi H, Hamdi W, Abutiban F, et al. The Impact of the COVID-19 Pandemic on Patients with Chronic Rheumatic Diseases: A Study in 15 Arab Countries [abstract]. <https://acrabstracts.org/abstract/the-impact-of-the-covid-19-pandemic-on-patients-with-chronic-rheumatic-diseases-a-study-in-15-arab-countries/>.
14. Murray K, Quinn S, Turk M, O'Rourke A, Molloy E, O'Neill L, et al. Covid-19 and Rheumatic and Musculoskeletal Disease Patients: Infection Rates, Attitudes and Medication Adherence [abstract]. <https://acrabstracts.org/abstract/covid-19-and-rheumatic-and-musculoskeletal-disease-patients-infection-rates-attitudes-and-medication-adherence/>.

15. Carvalho AS, Santos P. Medication Adherence In Patients With Arterial Hypertension: The Relationship With Healthcare Systems' Organizational Factors. *Patient Prefer Adherence*. 2019;13:1761–74. doi:10.2147/PPA.S216091.
16. Robert-Koch-Institute. Coronavirus Disease 2019. https://www.rki.de/DE/Content/InfAZ/N/Neuartiges_Coronavirus/Situationsberichte/2020-06-08-en.pdf?__blob=publicationFile.

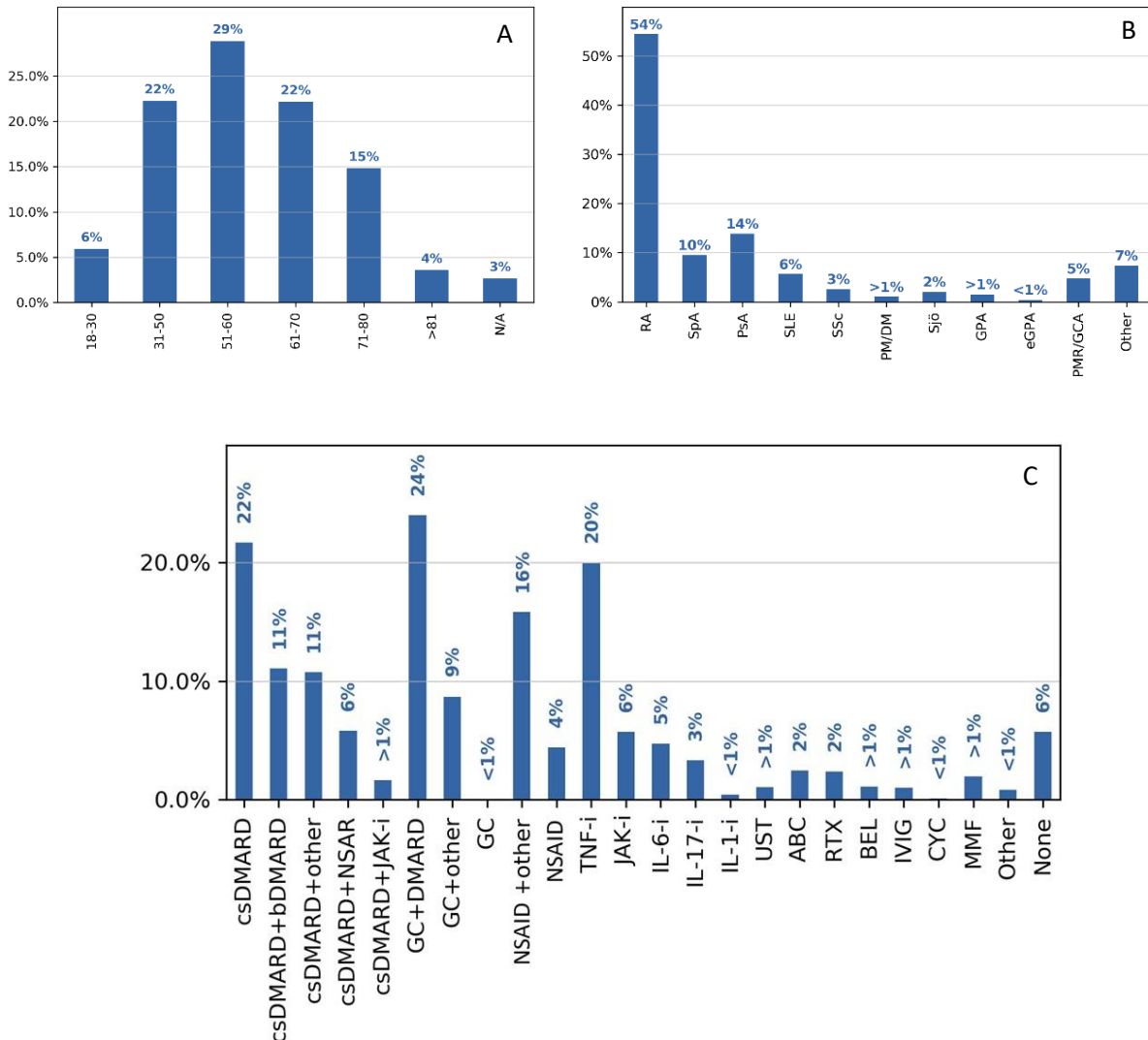


Figure 1: Basic characteristics of IRD patients

Figure 1A: Age of the patients (in %): Most of the patients (29%) were between 51-60 years old followed by 22% of the patients which were between 61-70 years old and 15% of the patients which were 71-80 years old (fig.1). The minority of the patients were 18-30 years (6%) old or more than 81 years (4%) old. In 3% of the cases no age was reported.

Figure 1B: Distribution of the reported inflammatory rheumatic diseases (in %): 54% of the reported patients suffered from RA; 14% from PsA; 10% from AS; 6% from SLE, 3% from SSc, more than 1% from PM/DM & GPA, 2% from Sjö, 5% from PMR/GCA and 7% from other IRD.

Figure 1C: Distribution of immunomodulatory drugs reported in the survey (in %): 22% were on monotherapy with csDMARD, 11% on combination therapy with csDMARD and bDMARD, 11% with csDMARD & other immunomodulatory drugs (e.g. GC), 6% on csDMARDs & NSAID, more than 1% were on csDMARD & JAK-i, 24% on GC & DMARD, 9% on GC & other immunomodulatory drugs, less than 1% were only on GC, 16% on NSAID & other immunomodulatory drugs, 4% on monotherapy with NSAR, 20% on TNF-i, 6% on JAK-i, 5% on IL-6-i, 3% on IL-17-i, around 1% each received IL-1-i, ustekinumab (UST), belimumab (BEL), immunoglobulins (IVIG), cyclophosphamide (CYC) and MMF, 6% reported no therapy, and <1% received other immunomodulatory drugs.

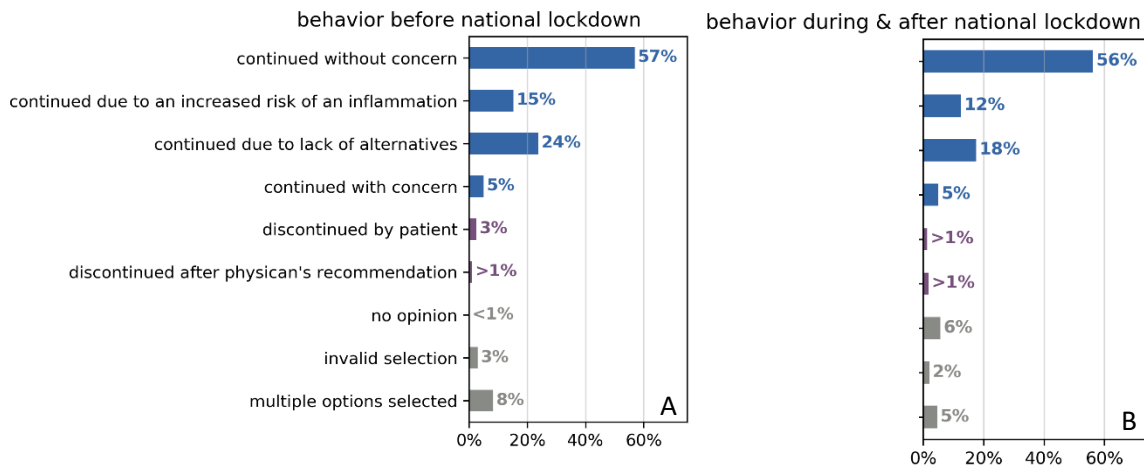


Figure 2: Patients' behaviour before, during and after the national lockdown in Germany: Patients had the opportunity to choose between seven answers to describe their adherence to their immunomodulatory medication. Some of the patients chose more than on answer (before: 8%, during and after lockdown 5%).

Figure 2A: Patients' behaviour before the national lockdown in Germany: Patients had the opportunity to choose between seven answers to describe their adherence to their immunomodulatory medication. Some of the patients chose more than on answer. Before the national lockdown 57% of the patients reported to continue their immunomodulatory treatment without concern, 15% to continue due to an increased risk of a disease flare, 24% due to lack of alternatives and 5% continued their immunomodulatory drug with concern. Only 3% of the patients reported to discontinue their medication by their own and around 1% in consultation with their rheumatologists. Less than 1% of the patients reported to have no opinion of their treatment and 2% did not choose any option.

Figure 2B: Patients' behaviour during and after the national lockdown in Germany: During and after the national lockdown 56% of the patients reported to continue their immunomodulatory treatment without concern, 12% to continue due to an increased risk of a disease flare, 18% due to lack of alternatives and 5% continued their immunomodulatory drug with concern. Around 1% of the patients reported to discontinue their medication by their own and around 1% in consultation with their rheumatologists. 6% of the patients reported to have no opinion of their treatment and less than 1% did not choose any option.

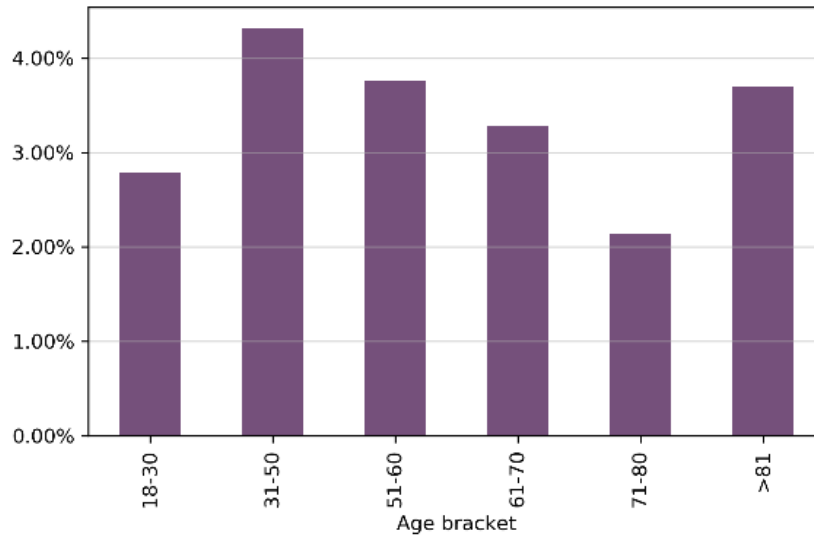


Figure 3: Distribution of discontinue of medication in age: Younger patients (18-30 years old, 2.8%) and patients between 71-80 years old (2.2%) reported less often to discontinue their medication compared to patients between 31-50 years old (4.4%) which were the biggest group followed by 3.7% of the patients between 51-60 years and around 3.6% more than 81 years old and 3.3% of the patients between 61-70 years old

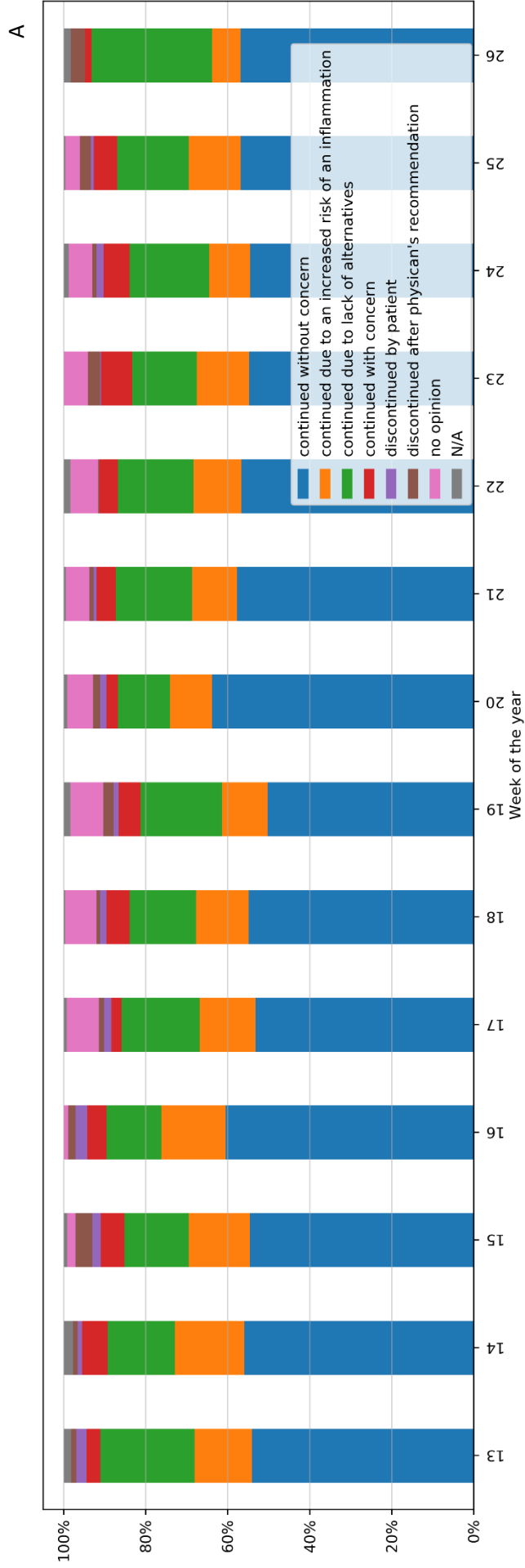


Figure 4: Changes in patients' opinion over the course of the pandemic

Figure 4A: Proportion of patients' opinion over the course of the pandemic: The proportion of patients' opinion did not change relevantly over the course of the pandemic. The different answers are displayed in blue (continued without concern), orange (continued due to an increased risk of a disease flare), green (continued due to lack of alternatives), red (continued with concern), purple (discontinued by patient), brown (discontinued after physician's recommendation), pink (no opinion) and grey (no answer given).

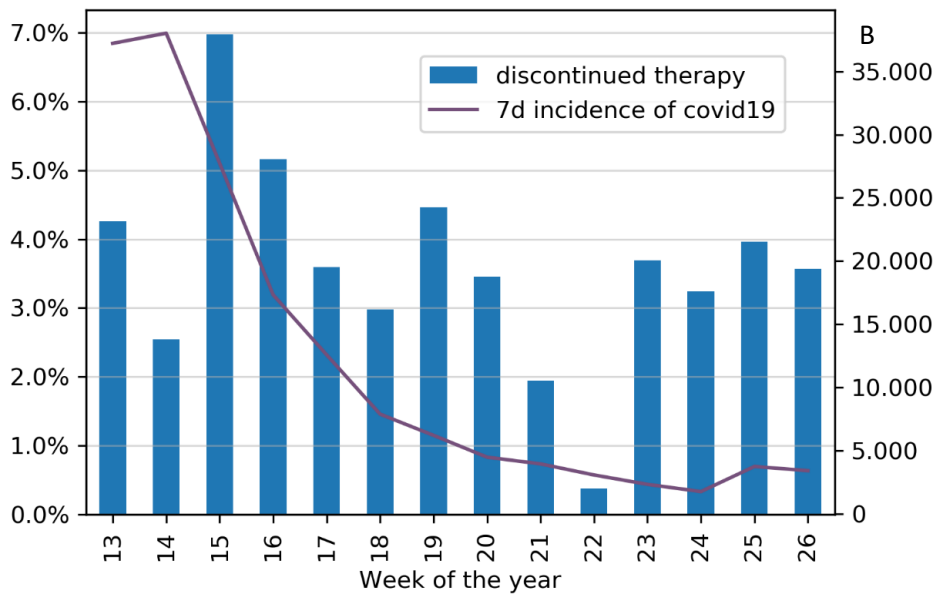


Figure 4: Changes in patients’ opinion over the course of the pandemic

Figure 4B: Number of patients who reported to discontinue their medication over the course of the study: Blue columns display the number of patients who reported to discontinue their medication in % (left scale), purple line displays the 7 days incidence of SARS-CoV-2 infection in the general population (number of patients, right scale).

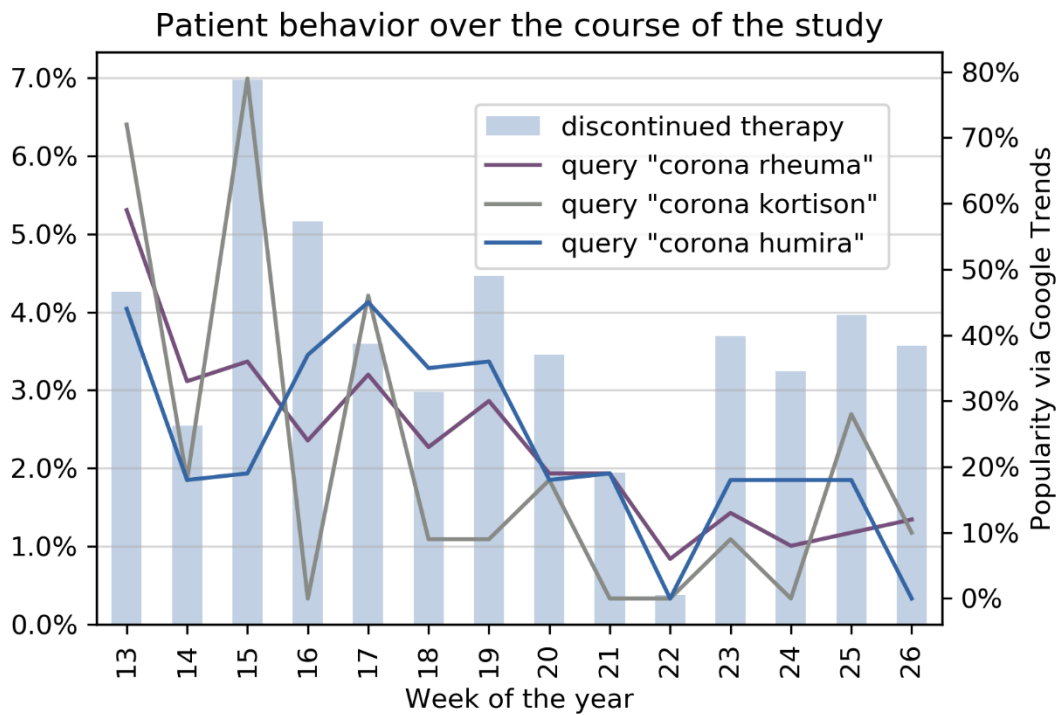


Figure 5: Rate of patients who discontinued their therapy over the pandemic in comparison to the amount of Google Trends queries for selected items: Blue columns display the number of patients who reported to discontinue their medication in % (left scale), purple line displays the query “corona rheuma”, grey line “corona cortisone” (German: Corona Kortison”) and blue line “corona Humira” in % (right scale) over the pandemic (scale below, week of the year)