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American College of Rheumatology Guidance for the Management of Pediatric Rheumatic Disease During the COVID-19 Pandemic: Version 1

Dawn M. Wahezi,[1] Mindy S. Lo,[2] Tamar B. Rubinstein,[1] Sarah Ringold,[3] Stacy P. Ardoin,[4] Kevin J. Downes,[5] Karla B. Jones,[4] Ronald M. Laxer,[6] Rebecca Pellet Madan,[7] Amy S. Mudano,[8] Amy S. Turner,[9] David R. Karp,[10] and Jay J. Mehta[5]

Due to the rapidly expanding information and evolving evidence related to COVID-19, which may lead to modification of some guidance statements over time, it is anticipated that updated versions of this article will be published, with the version number included in the title. Readers should ensure that they are consulting the most current version.

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Objective. To provide clinical guidance to rheumatology providers who treat children with pediatric rheumatic disease (PRD) in the context of the coronavirus disease 2019 (COVID-19) pandemic.

Methods. The task force, consisting of 7 pediatric rheumatologists, 2 pediatric infectious disease physicians, 1 adult rheumatologist, and 1 pediatric nurse practitioner, was convened on May 21, 2020. Clinical questions and subsequent guidance statements were drafted based on a review of the queries posed by the patients as well as the families and healthcare providers of children with PRD. An evidence report was generated and disseminated to task force members to assist with 3 rounds of asynchronous, anonymous voting by email using a modified Delphi approach. Voting was completed using a 9-point numeric scoring system with predefined levels of agreement (categorized as disagreement, uncertainty, or agreement, with median scores of 1–3, 4–6, and 7–9, respectively) and consensus (categorized as low, moderate, or high). To be approved as a guidance statement, median vote ratings were required to fall into the highest tertile for agreement, with either moderate or high levels of consensus.

Results. The task force drafted 33 guidance statements, which were voted upon during the second and third rounds of voting. Of these 33 statements, all received median vote ratings within the highest tertile of agreement and were associated with either moderate consensus (n = 6) or high consensus (n = 27). Statements with similar recommendations were combined, resulting in 27 final guidance statements.

Conclusion. These guidance statements have been generated based on review of the available literature, indicating that children with PRD do not appear to be at increased risk for susceptibility to SARS–CoV-2 infection. This guidance is presented as a "living document," recognizing that the literature on COVID-19 is rapidly evolving, with future updates anticipated.

INTRODUCTION

The rapid global spread of coronavirus disease 2019 (COVID-19) has resulted in an urgent need to evaluate and address the impact of severe acute respiratory syndrome coronavirus 2 (SARS–CoV-2) infection in children with pediatric rheumatic disease (PRD) and the implications of immunomodulatory medications on their risk for severe disease. The medical community and the Centers for Disease Control and Prevention (CDC) have urged caution related to SARS–CoV-2 infection for individuals with a compromised immune system, including those with rheumatic disease who are being treated with immunosuppressive drugs (1). However, to date, there are very few data to suggest that adults or children with rheumatic disease are at increased risk of infection with SARS–CoV-2 or at increased risk of experiencing more severe outcomes due to COVID-19.

The American College of Rheumatology (ACR) COVID-19 Clinical Guidance for Pediatric Rheumatology Task Force convened on May 21, 2020, charged by ACR leadership to provide clinical guidance to rheumatology providers who treat children with PRD in the context of the COVID-19 pandemic. These recommendations have been generated to supplement clinical judgment, guide disease management, and support shared decision-making among providers, patients, and families. They have been developed to provide guidance for children up to age 18 years. Guidance for adults with rheumatic diseases has been recently published (2). Multiple factors must be taken into consideration when interpreting these guidance statements, including individual patient characteristics such as underlying rheumatic disease, current disease activity and treatment, and the prevalence of SARS–CoV-2 transmission in the patient's community. The approach to patients who are exposed to SARS–CoV-2 should consider the duration and proximity of exposure. The approach to infected patients should consider the severity of COVID-19 symptoms and the presence of additional risk factors for poorer outcomes (3–5). This guidance is presented as a "living document," recognizing that the literature on COVID-19 is rapidly evolving. The ACR anticipates that these statements will be updated as scientific evidence accumulates. Clinical guidance regarding the evaluation and management of multisystem inflammatory syndrome in children (MIS-C) is the focus of a separate ACR task force and thus will not be addressed herein.

METHODS

Clinical questions and first webinar. The North American COVID-19 Clinical Guidance for Pediatric Rheumatology Task Force was selected by task force leadership (DMW and JJM) based on their clinical expertise in rheumatology and infectious diseases, and included 7 pediatric rheumatologists, 2 pediatric infectious disease physicians, 1 adult rheumatologist, and 1 pediatric nurse practitioner. The task force was composed of academic clinicians from the United States and Canada. All individuals who were approached to develop this guidance agreed to participate. Prior to the first meeting, task force members were subdivided into 3 workgroups to address the following topics: 1) general guidelines, risk assessment, and consideration of SARS–CoV-2 exposure in children with PRD; 2) ongoing treatment of children with PRD in the absence of SARS–CoV-2 exposure or infection; and 3) ongoing treatment of children with PRD in patients with probable or confirmed SARS–CoV-2 infection. During the first webinar on May 21, 2020, participants agreed with the task force leadership about the importance of addressing these 3 overarching topics as well as the structure of the workgroups. The first webinar was used to confirm that the target audience for the guidance would be pediatric rheumatology providers, and that the guidance would focus on the management of PRD in the context of the COVID-19 pandemic. All panelists agreed to develop consensus through a modified Delphi process that included 3 rounds of asynchronous, anonymous voting and 3 webinars to discuss voting results (Table 1).

Evidence review. From May 22, 2020 to May 28, 2020, the workgroups developed preliminary recommendation statements within their assigned topic, based on expert opinion and a nonsystematic evidence review, including PubMed searches using key words from the clinical questions, as well as supplemental postings from the ACR, CDC, American Academy of Pediatrics (AAP), and other online media sources. Evidence

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[1]Dawn M. Wahezi, MD, MS, Tamar B. Rubinstein, MD, MS: Children's Hospital at Montefiore and Albert Einstein College of Medicine, New York, New York; [2]Mindy S. Lo, MD, PhD: Boston Children's Hospital and Harvard Medical School, Boston, Massachusetts; [3]Sarah Ringold, MD, MS: Seattle Children's Hospital, Seattle, Washington; [4]Stacy P. Ardoin, MD, MS, Karla B. Jones, CPNP, MS: Nationwide Children's Hospital and Ohio State University, Columbus, Ohio; [5]Kevin J. Downes, MD, Jay J. Mehta, MD: Children's Hospital of Philadelphia and University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania; [6]Ronald M. Laxer, MDCM, FRCPC: University of Toronto and The Hospital for Sick Children, Toronto, Ontario, Canada; [7]Rebecca Pellet Madan, MD, MSc: New York University Grossman School of Medicine and Hassenfeld Children's Hospital, New York, New York; [8]Amy S. Mudano, MPH: University of Alabama at Birmingham; [9]Amy S. Turner: American College of Rheumatology, Atlanta, Georgia; [10]David R. Karp, MD, PhD: University of Texas Southwestern Medical Center, Dallas.

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Address correspondence to Dawn M. Wahezi, MD, MS, Children's Hospital at Montefiore, 3415 Bainbridge Avenue, Bronx, NY 10467. Email: dwahezi@montefiore.org.

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was not formally assessed, but was generally determined to be of low quality, and was limited to case series, retrospective cohort studies, and very few controlled trials. A detailed evidence report was generated by each subgroup, and then collated and distributed to the entire task force to inform the first round of voting.

Voting. *Round 1.* The task force voted virtually and anonymously using the RAND/University of California at Los Angeles (UCLA) Appropriateness Method (6). This method has been shown to be highly reproducible (7) and was successfully applied by the ACR COVID-19 Clinical Guidance Task Force in the development of guidance statements for adult patients with rheumatic disease (2). A 9-point scale was used by task force members to rate the appropriateness of each of the statements. A score of 9 was considered to be the highest level of appropriateness, while a score of 1 indicated that the statement was entirely inappropriate. Prior to voting, median scores of 1–3 were defined as inappropriate, 4–6 as uncertain, and 7–9 as appropriate. Consensus was prespecified as high if all 11 votes coalesced within the same tertile, while low consensus was recognized when voting was dispersed widely along the 9-point scale (with ≥3 votes in the 1–3 score range and ≥3 votes in the 7–9 score range). Moderate consensus encompassed all other scenarios.

The votes of each task force member were counted equally and tallied. The results of the initial voting were distributed to the task force and reviewed during a 90-minute webinar on June 3, 2020. Statements that were rated as uncertain (median score 4–6) and/or characterized by moderate or low consensus were addressed first. The panelists were then encouraged to discuss the remaining statements.

Rounds 2 and 3. Input from the initial voting and discussion was incorporated into the draft guidance statements by task force leadership (DMW and JJM), and the document was redistributed to the entire task force for a second round of voting. Voting in this phase was conducted in the same manner as described above, and results were reviewed at a third webinar on June 11, 2020. Guidance statements that earned a median score of 7–9 with moderate or high levels of consensus during the second round of voting were approved by the panel.

Guidance statements under the domain of patients with PRD and probable or confirmed SARS–CoV-2 infection were initially dichotomized as either asymptomatic/mild disease or moderate/severe disease. After further discussion, the task force agreed that dichotomizing patients according to categories of either asymptomatic disease or symptomatic disease would be more representative of current clinical practice related to viral illnesses in children with PRD. Seven statements were subsequently redefined and sent back to task force members for a third round of voting using similar methods.

Table 1. Timeline of ACR COVID-19 pediatric rheumatology clinical guidance development*

Date(s)	Milestone
May 18	Invitations to ACR COVID-19 Pediatric Rheumatology Clinical Guidance Task Force
May 18–20	Draft of initial clinical questions
May 21	First webinar: expansion of clinical questions, subgroup assignment
May 22–26	Medical literature review and development of evidence report
May 26–28	Revision of clinical questions and collation of evidence report
May 29–June 1	Evidence report dissemination and first round of voting
June 3	Second webinar: review of first round of voting and generation of guidance statements
June 4–5	Revision and thematic organization of guidance statements
June 6–8	Second round of voting
June 11	Third webinar: review of second round of voting and further refinement of guidance statements
June 12	Revision of 7 statements and third round of voting
June 13–15	Review and task force approval of summary guidance document
June 17	ACR Board of Directors approval of guidance statements
June 18	Draft guidance statements posted on ACR website
June 24	Submission of full manuscript to ACR Board of Directors

* ACR = American College of Rheumatology; COVID-19 = coronavirus disease 2019.

Guidance approval. Following the final webinar, approved statements were refined and, in some instances, combined into 27 final guidance statements to reduce redundancy. A preliminary guidance document was generated, and the entire task force was given an opportunity to review and edit the document. Approval was obtained from each panelist on June 15, 2020 and by the ACR Board of Directors on June 17, 2020 (Table 1).

RESULTS

Of the 119 original clinical questions considered in the first round of voting, the median vote ratings in response to 44 questions indicated uncertainty (median scores 4–6), with the voting on 5 of the questions indicating low consensus based on the predefined thresholds. Clinical questions were reviewed and subsequently excluded if thought to be out of the scope of this task force (e.g., questions related to MIS-C) or if determined to have too much uncertainty and/or lack of sufficient evidence to allow for the drafting of a clinical guidance statement at this time (e.g., questions related to SARS–CoV-2 vaccine). The remaining questions were combined by common themes, and thereafter drafted into 33 guidance statements and voted upon during the second and third rounds of voting (see Supplementary Tables 1–3, available on the *Arthritis & Rheumatology* website at http://onlinelibrary.wiley.com/doi/10.1002/art.41455/abstract).

Of these 33 statements, all received median vote ratings of 7, 8, or 9 and were associated with either moderate consensus (n = 6) or high consensus (n = 27). Statements with similar recommendations were combined, resulting in 27 final guidance statements, which were posted online by the ACR in a clinical guidance summary on June 18, 2020 (https://www.rheumatology.org/Portals/0/Files/COVID-19-Clinical-Guidance-Summary-for-Pediatric-Patients-with-Rheumatic-Disease.pdf).

General guidance regarding patients with PRD. *Approaches to risk reduction.* General guidance statements regarding patients with PRD are presented in Table 2. To date, there is little evidence to suggest a higher risk of severe COVID-19 in children with PRD (8–12) or in children receiving immunomodulatory therapies commonly used for PRD (13–15). Among the published series of hospitalized children with COVID-19, there have been no reports of severe illness in children with PRD (4,16). Similarly, preliminary data from the Global Rheumatology Alliance patient survey reported only 5 cases of COVID-19 in children with PRD, none of whom were hospitalized (17). The Childhood Arthritis and Rheumatology Research Alliance (CARRA) patient registry is currently collecting data on the prevalence of COVID-19 among children with PRD, with results yet to be reported. Based on available evidence, the task force members agreed that children and families of children with PRD should be counseled on utilizing preventative measures similar to those recommended for the general population, including adequate hand washing, social distancing, masking/facial covering (in children >2 years of age), and disinfecting of frequently touched surfaces. In geographic areas with a high incidence of COVID-19, particularly during periods of increased community transmission, children with PRD should adhere to local public health social distancing recommendations and limit close contact with others outside their household.

The task force additionally discussed issues concerning safe return to schools, camps, daycare, and college. In general, the task force agreed that there may not be unique preventative measures for children with PRD apart from those recommended for all children; however, this was not formulated into a formal recommendation, due to ongoing uncertainties about the evolving pandemic. Families should refer to local school guidance, as well as the most current recommendations from the CDC (18) and AAP (19), to best address the needs of their individual child. The task force also recognized that caregivers of children with PRD may be at risk for occupational exposures that could increase the risk of acquiring COVID-19. Rheumatology providers should counsel families to refer to the CDC guidelines for specific occupations (20) and the Occupational Safety and Health Administration (21) for guidance to protect themselves from occupational exposure to SARS–CoV-2. Caregivers should discuss with employers the need for adequate social distancing, masking/facial covering, and daily health checks as well as the need to consider options for working from home (22). Antibody testing for SARS–CoV-2 was not recommended at this time, due to the variability of the assays and current lack of sufficient evidence to support utility of the antibody tests for informing individuals about their personal risk of reinfection or the safety of returning to school or the workplace (23,24). Providers should also be aware that, as the prevalence of antibodies to SARS–CoV-2 increases in the general population, routine serologic testing may result in false positive antibody findings in patients with PRD receiving intravenous immunoglobulin.

Ongoing clinical management. Shared decision-making should occur between patients, families, and rheumatology providers to discuss additional measures to reduce interruptions in clinical care, particularly during periods of increased community transmission. Such measures may include use of telemedicine for routine, regularly scheduled and nonurgent clinical assessments, and physical therapy. The American Telemedicine Association "Operating Procedures for Pediatric Telehealth" (endorsed by the AAP) serves as an operational reference and educational tool regarding appropriate telehealth care for pediatric patients (25). For ophthalmologic surveillance in children at high risk for chronic

Table 2. General guidance for patients with PRD*

Guidance statement	Level of task force consensus
Children and families of children with PRD should be counseled on general preventative measures, including social distancing, hand washing, and masking/face covering, to limit potential exposure to SAR–CoV-2 infection.	High
Rheumatology providers should be aware that caregivers of children with PRD may be at risk of occupational exposure to SARS–CoV-2 infection and should be counseled on CDC health and safety practices in the workplace.	High
Clinical assessment and treatment via telemedicine should be considered to ensure access to care during periods of increased community transmission of SARS–CoV-2.	High
Routine ophthalmologic surveillance of patients with PRD at high risk for chronic uveitis or with a history of uveitis should continue on schedule via in-person visits with slit lamp examination.	High
Children with PRD should continue routine childhood vaccinations (unless contraindicated due to DMARD therapy), including the annual influenza vaccine.	High
Rheumatology providers should be aware that children and caregivers of children with PRD may be at risk of mental health problems, including anxiety and depression, due to quarantine and other events surrounding COVID-19.	Moderate
At this time, in children with PRD, similar to the general population, SARS–CoV-2 antibody testing is not useful for informing individuals about their history of infection or risk of reinfection.	High

* PRD = pediatric rheumatic disease; SARS–CoV-2 = severe acute respiratory syndrome coronavirus 2; CDC = Centers for Disease Control and Prevention; DMARD = disease-modifying antirheumatic drug.

uveitis or personal history of uveitis, the task force agreed that ongoing in-person ophthalmology evaluation is strongly recommended, due to the risk of asymptomatic uveitis and the long-term sequelae that can result from undetected uveitis in children with PRD (26). The task force also agreed that all patients with PRD should receive routine vaccinations (unless contraindicated), including the annual influenza vaccine, on or as close to schedule as possible. Given concerns about ongoing transmission of COVID-19 during the influenza season, administration of the seasonal influenza vaccine is strongly recommended to limit simultaneous viral outbreaks, possible co-infections, increased hospitalizations, and risks of exceeding hospital capacities.

Other considerations. The task force also recognized the increased prevalence of anxiety and depression in patients with PRD as compared to the general population (27–29) and addressed concerns about additional emotional distress related to the COVID-19 pandemic (30). Rheumatology providers should be aware of the heightened emotional burden posed by the pandemic, including fears of becoming infected, having a family member infected, potential risks from medications, concerns about social isolation, and potential financial hardships. Providers should educate caregivers and patients about strategies for reducing anxiety, including referrals for telehealth or in-person mental health counseling when appropriate (31,32).

Ongoing treatment of patients with PRD in the absence of SARS–CoV-2 exposure or infection. *General treatment recommendations.* The task force unanimously agreed that primary control of underlying rheumatic disease is of utmost importance, recognizing that flares of PRD may increase the need for immunosuppression and lead to increased contact with health care systems. In addition, active inflammatory disease may independently increase infection risk due to immune dysregulation in patients with PRD (9,12,33–35), thus guidance recommendations were targeted for the purpose of limiting medication disruptions. Recognizing that the data are still limited, our task force did not identify current evidence to suggest that nonsteroidal antiinflammatory drugs (NSAIDs), hydroxychloroquine, angiotensin-converting enzyme inhibitors (ACEi)/angiotensin II receptor blockers (ARBs), colchicine, conventional disease-modifying antirheumatic drugs (DMARDs), biologic DMARDs, or targeted synthetic DMARDs contribute to increased susceptibility to SARS–CoV-2 infection (13–15). Despite the dissemination of initial warnings that NSAIDs and ACEi/ARBs might contribute to worse outcomes in COVID-19, we found no clinical data to substantiate these concerns in adults (36,37).

Similar to the ACR guidance for the management of rheumatic disease in adults, our task force supported the continued use of immunomodulatory medications in children with PRD who do not have known SARS–CoV-2 exposure or infection (2). Guidance statements for this group are presented in Table 3. Likewise, for patients with newly diagnosed or worsening PRD, initiation of DMARD therapy was recommended in order to adequately control PRD (38,39). The task force also recognized that alternative treatment plans for intravenous medications may need to be considered during periods of increased community transmission of SARS–CoV-2 and when safe access to the hospital may be challenging. In these scenarios, home infusions of medications or transition to oral or subcutaneous maintenance therapies may be considered, when appropriate.

The task force also discussed plans for de-escalation of therapy for patients who remain in clinical remission while on medications. While the task force agreed that patients should not be

Table 3. Guidance for ongoing treatment of patients with PRD in the absence of exposure to or infection with SARS–CoV-2*

Guidance statement	Level of task force consensus
NSAIDs, HCQ, ACEi/ARBs, colchicine, cDMARDs, bDMARDs, and tsDMARDs may be continued or initiated to control underlying disease.	High
Glucocorticoids may be continued or initiated using the lowest dose possible to control underlying disease.	High
For patients with PRD with life- and/or organ-threatening manifestations, high-dose oral or intravenous "pulse" glucocorticoids may be initiated to control underlying disease.†	High
For patients with PRD with life- and/or organ-threatening manifestations, cyclophosphamide may be initiated or continued to control underlying disease.	High
For patients with PRD with active arthritis, intraarticular glucocorticoid injections may be administered.	High
For patients with stable PRD, previously stable laboratory markers, and currently receiving stable doses of cDMARDs, bDMARDs, and/or tsDMARDs, extending the laboratory testing interval for monitoring medication toxicity may be considered, to reduce potential exposure to SARS–CoV-2 during periods of increased community transmission.	High
Laboratory monitoring for disease activity should be continued according to standard practice, to ensure adequate assessment and control of underlying disease.	High
De-escalation of therapy may be continued as planned in patients with PRD after considering the potential risks of disease flare and barriers to follow-up during the pandemic.	High

* PRD = pediatric rheumatic disease; SARS–CoV-2 = severe acute respiratory syndrome coronavirus 2; NSAIDs = nonsteroidal antiinflammatory drugs; HCQ = hydroxychloroquine; ACEi = angiotensin-converting enzyme inhibitors; ARBs = angiotensin II receptor blockers; cDMARDs = conventional disease-modifying antirheumatic drugs; bDMARDs = biologic disease-modifying antirheumatic drugs; tsDMARDs = targeted synthetic disease-modifying antirheumatic drugs.
† High-dose oral glucocorticoids were defined as ≥2 mg/kg/day prednisone equivalent, and high-dose intravenous "pulse" glucocorticoids as ≥10 mg/kg/day methylprednisolone equivalent.

kept on prolonged immunomodulatory therapy unnecessarily, shared decision-making among patients, families, and providers was recommended to discuss potential consequences of withdrawing medications, including risks of disease flare, followed by a need for increased in-person visits, laboratory monitoring, and, potentially, the need for escalation of therapy (including the use of glucocorticoids) (40–42).

Special considerations for cyclophosphamide and rituximab. For patients requiring treatment with cyclophosphamide or rituximab for control of their PRD, the task force recommended continuing current management to adequately control underlying disease and prevent potentially life- and/or organ-threatening manifestations. Children requiring cyclophosphamide therapy may be at significant risk for infection due to an underlying diagnosis, treatment-induced leukopenia/lymphopenia, and concomitant use of glucocorticoids (43–45). Given that cyclophosphamide is reserved for only patients who have life- and/or organ-threatening disease, the task force agreed that the benefits of treatment likely outweigh the risks in this scenario.

Special considerations for glucocorticoids. The task force acknowledged the mixed data regarding the potential immunosuppressive effects of glucocorticoids in adults with infection from SARS–CoV-2. Glucocorticoids may increase the risk of secondary infection and delay viral clearance. Prior studies have shown little benefit from the use of glucocorticoids in the treatment of SARS–CoV-1, Middle East Respiratory Syndrome, influenza, or respiratory syncytial virus (46–48). However, glucocorticoids have also been used to treat the inflammatory sequelae of COVID-19, including acute respiratory distress syndrome, hyperinflammation, and cytokine storm, with reports of improved survival, shorter duration of oxygen supplementation, and shorter intensive care unit stays in adults (49–51). Data regarding the risks and benefits of glucocorticoids in COVID-19 are rapidly evolving.

When considering patients with PRD who are receiving long-term treatment with glucocorticoids, there is little evidence to date to suggest that glucocorticoid use increases the risk of acquiring SARS–CoV-2 infection. A preliminary analysis of the first 600 cases in the Global Rheumatology Alliance COVID-19 Registry indicated that hospitalization risk increased among adult patients with rheumatic disease diagnosed as having COVID-19 who were taking prednisone at a daily dose exceeding 10 mg, after accounting for disease activity (52). Thus, the task force recommended that glucocorticoids be continued or initiated when clinically indicated, using the lowest effective dose to control underlying PRD. Given that weight-based dosing strategies (calculated in mg/kg) are most appropriate for pediatric patients, the task force concluded that defining a specific dose (e.g., ≤10 mg prednisone daily) could not be directly applied to the pediatric population.

The task force further acknowledged that higher doses of oral glucocorticoids (≥2 mg/kg/day prednisone equivalent) or intravenous "pulse" glucocorticoids (≥10 mg/kg/day methylprednisolone equivalent) may be indicated in the setting of severe life- and/or organ-threatening clinical manifestations from underlying PRD, and therefore should not be withheld. Additionally, the task force emphasized that patients receiving oral glucocorticoids (>5 mg/day prednisone equivalent) are at risk of developing adrenal suppression (53); therefore, the task force recommends avoidance of abrupt withdrawal of glucocorticoids, keeping in mind the potential need for stress dosing of glucocorticoids in certain clinical scenarios. When considering the need for intraarticular glucocorticoid injections, the task force deemed the risk of systemic immunosuppression minimal and supported proceeding with injections when needed, understanding that access may be limited during times of increased community transmission of SARS–CoV-2.

Ongoing evaluations and clinical care. Routine laboratory monitoring during the pandemic was discussed. While it is recognized that monitoring of medications typically occurs at regularly scheduled intervals (54), these intervals may be modestly extended in patients with PRD who have stable disease, stable medications, and no prior history of laboratory abnormalities associated with medication toxicity. In contrast, the task force concluded that laboratory monitoring for disease activity should continue at the usual intervals, particularly during times of limited access to in-person clinical evaluations.

Ongoing treatment of patients with PRD with exposure to close/household contact with SARS–CoV-2 infection. Recognizing that current data are insufficient to define precisely the duration of time that constitutes a prolonged exposure, the CDC has created an operational definition, reported as an interaction with a person known to have COVID-19 for more than 15 minutes, at a distance of fewer than 6 feet and without both parties wearing masks (55). Shorter interactions may additionally be relevant depending on the symptoms and type of interaction. As previously discussed, recent data both in adults with rheumatic disease and in children with PRD do not suggest an increased risk of susceptibility to COVID-19. Similar to the guidance statements provided in Table 3, our task force agreed that current immunomodulatory medications may be continued after COVID-19 exposure, during which time the patient should be monitored for fever or other symptoms of COVID-19 (Table 4). The task force also agreed that low-to-moderate–dose glucocorticoids could be continued to control underlying PRD after COVID-19 exposure, with an effort to reduce the dose when possible. Given the recommended 14-day monitoring period after exposure, the task force recommended that high-dose oral or intravenous "pulse" glucocorticoids be delayed when feasible, except in the scenario of life- and/or organ-threatening disease.

Ongoing treatment of patients with PRD and SARS–CoV-2 infection. *Cases of asymptomatic SARS–CoV-2 infection*. Although the exact prevalence is unknown, a proportion of children may be asymptomatic despite a polymerase chain

Table 4. Ongoing treatment of patients with PRD with an exposure to close/household contact with SARS–CoV-2 infection*

Guidance statement	Level of task force consensus
For patients with close/household exposure to COVID-19, general preventative measures, such as social distancing, hand washing, and masking/face covering, are of utmost importance to reduce the risk of infection with SARS–CoV-2.	High
NSAIDs, HCQ, colchicine, cDMARDs, bDMARDs, and tsDMARDs may be continued or initiated if necessary to control underlying disease.	Moderate
Glucocorticoids may be continued using the lowest effective dose possible to control underlying disease.	High
For patients with non–life- and/or organ-threatening PRD, initiation of high-dose oral or intravenous glucocorticoids should be delayed for 1–2 weeks, if deemed safe by the treating provider.†	High
For patients with PRD with life- and/or organ-threatening manifestations of PRD, initiation of high-dose oral or intravenous glucocorticoids should not be delayed.†	High

* In patients with pediatric rheumatic disease (PRD), close/household contact with severe acute respiratory syndrome coronavirus 2 (SARS–CoV-2) infection was defined as an interaction with a person known to have coronavirus disease 2019 (COVID-19) for more than 15 minutes, at a distance of fewer than 6 feet without masking of both parties. NSAIDs = nonsteroidal antiinflammatory drugs; HCQ = hydroxychloroquine; cDMARDs = conventional disease-modifying antirheumatic drugs; bDMARDs = biologic disease-modifying antirheumatic drugs; tsDMARDs = targeted synthetic disease-modifying antirheumatic drugs.
† High-dose oral glucocorticoids were defined as ≥2 mg/kg/day prednisone equivalent, and high-dose intravenous "pulse" glucocorticoids as ≥10 mg/kg/day methylprednisolone equivalent.

reaction (PCR) test result indicating the presence of SARS–CoV-2 (56–59). With increased availability of testing and recommendations for PCR screening prior to elective surgeries and procedures, cases of children with asymptomatic COVID-19 may be encountered (60). To date, there are no data to suggest that continued use of immunomodulatory medications in infected, asymptomatic children with PRD would alter the clinical course of SARS–CoV-2 infection. Thus, the benefits of continuing immunomodulatory medications in these scenarios appear to outweigh the risks (Table 5). As noted previously, these recommendations have been generated to support shared decision-making between providers and patients and families, and cases need to be considered on an individual basis. Asymptomatic cases should be advised to quarantine, in accordance with the CDC guidelines, and to contact their provider immediately should symptoms of COVID-19 develop (61).

Cases of symptomatic SARS–CoV-2 infection. Most children with COVID-19 experience mild-to-moderate symptoms, with only a small percentage requiring hospitalization (59). Data from 2 major epicenters of disease in the United States (New York and Washington, DC) reported that among children and young adults who were admitted to the hospital with SARS–CoV-2 infection, 28% and 20%, respectively, developed severe disease and required respiratory support (4,16); neither of those reports included patients with PRD nor did they include children receiving baseline DMARD therapy. Similarly, cases of children receiving immunomodulatory therapies that are commonly used in PRD have not shown increased severity of disease (13–15). Despite reassuring data suggesting that patients with rheumatic disease who receive immunomodulatory therapy do not appear to have more severe infection from SARS–CoV-2 (9), the task force did not think there was sufficient literature at this time to support a recommendation to continue medications in the

Table 5. Ongoing treatment of patients with PRD and asymptomatic COVID-19 infection or patients with PRD and probable or confirmed symptomatic COVID-19 infection*

Guidance statement	Level of task force consensus
PRD and *asymptomatic* COVID-19†	
NSAIDs, HCQ, colchicine, cDMARDs, bDMARDs, and tsDMARDs may be continued if necessary to control underlying disease.	High
Cyclophosphamide or rituximab may be continued if necessary to control underlying disease.	Moderate
Glucocorticoids should be continued, using the lowest effective dose possible to control underlying disease and avoid adrenal insufficiency.	Moderate
PRD and probable or confirmed *symptomatic* COVID-19	
NSAIDs, HCQ, and colchicine may be continued if necessary to control underlying disease.	High
cDMARDs, bDMARDs (except IL-1 and IL-6 inhibitors), and tsDMARDs should be temporarily delayed or withheld.	High
IL-1 and IL-6 inhibitors may be continued if necessary to control underlying disease.	High
Glucocorticoids should be continued, with an effort to reduce the dose to the lowest effective dose possible to control underlying disease and avoid adrenal insufficiency.	High

* PRD = pediatric rheumatic disease; NSAIDs = nonsteroidal antiinflammatory drugs; HCQ = hydroxychloroquine; cDMARDs = conventional disease-modifying antirheumatic drugs; bDMARDs = biologic disease-modifying antirheumatic drugs; tsDMARDs = targeted synthetic disease-modifying antirheumatic drugs; IL-1 = interleukin-1.
† Asymptomatic coronavirus disease 2019 (COVID-19) was defined as detection of severe acute respiratory syndrome coronavirus 2 (SARS–CoV-2) RNA by nasopharyngeal polymerase chain reaction, but no evidence of any clinical manifestations of infection.

context of symptomatic COVID-19 infection (Table 5). These recommendations are congruent with conventional clinical practice as they pertain to withholding immunosuppressive therapy in children with PRD and a concurrent infection.

Recognizing that much of the morbidity and mortality related to COVID-19 may be attributed to an individual host immune response and hyperinflammation, several authors have also suggested that maintaining immune regulation in patients with rheumatic disease may provide additional benefit and reduce the risk of severe disease (9,12,34). Selective inhibitors of interleukin-1 (IL-1) and IL-6 have additionally been investigated in the treatment of COVID-19 hyperinflammation (62–67). This observation, coupled with the knowledge that children with autoinflammatory PRDs, such as periodic fever syndromes or systemic-onset juvenile idiopathic arthritis, may be particularly sensitive to medication disruptions, led the task force to recommend that colchicine, IL-1 inhibitors, and IL-6 inhibitors may be continued, even in the context of symptomatic COVID-19 infection. Selective IL-1 inhibitors have been used safely in the setting of other infections and in clinical trials of patients with sepsis (68). In contrast, IL-6 inhibitors may be associated with increased risk of secondary infections, and therefore the appropriateness of this therapy in individual cases should be reviewed. JAK inhibitors have also been investigated as potential therapies in the management of COVID-19 hyperinflammation (35,69). However, inhibition of interferon signaling through the use of JAK inhibitors has been suggested to dampen the innate antiviral response, thereby potentially worsening the host response to viral infection (70). In the absence of robust data regarding the safety of JAK inhibitors in the context of symptomatic SARS–CoV-2 infection, the task force recommended temporarily withholding tsDMARDs in children with PRD and COVID-19 infection.

DISCUSSION

Irrespective of the COVID-19 pandemic, the overall goals of treatment in patients with PRD remain prompt control of active disease, relief of symptoms, prevention of long-term sequelae, and efforts to limit the toxic effects of therapy. These guidance statements have been generated based on review of the available literature, indicating that children with PRD do not appear to be at increased risk for susceptibility to SARS–CoV-2 infection. The purpose of this document is to help guide the management of PRD during the COVID-19 pandemic and to support shared decision-making between providers and individual patients and families. The statements should be used to supplement clinical judgment, recognizing that specific clinical scenarios may vary by individual patient.

There are several strengths to be noted about the effort to create this clinical guidance document. The panel of experts on this task force reflect a multidisciplinary collaboration, with specialists in pediatric rheumatology (both ACR and Association of Rheumatology Professionals members), pediatric infectious disease, and adult rheumatology, with a myriad of clinical expertise and interests. The task force was developed with the intent to include experts from geographic locations across the United States (in which varying degrees of SARS–CoV-2 community transmission have been observed) and to include clinicians who treat patients with diverse demographics and socioeconomic status, to account for the spectrum of clinical disease seen in COVID-19. In addition, in response to the urgent need for clinical guidance during the COVID-19 pandemic, the task force generated statements over a compressed timeline, while maintaining a well-established method of consensus building, to ensure rapid dissemination of clinical recommendations.

There are also limitations in this effort. Although an extensive review of the medical literature was performed to generate a detailed evidence report, it should be reiterated that this was a nonsystematic review of the literature, with limited evidence. Although not formally assessed, evidence was generally of low quality, and not all sources were peer reviewed. The expert opinions and experience of task force members helped inform guidance. Thus, this guidance document does not follow the rigorous guideline methodology routinely used by the ACR when formal clinical practice guidelines are generated. Furthermore, current published evidence primarily reflects pediatric outcomes in the setting of school closures. Ongoing evaluation of outcomes for children with PRD in areas where schools reopen will be critically important in assessing risk.

Finally, there are a few distinctions to be noted between our recommendations and those put forth in the ACR guidance for the management of rheumatic disease in adults during the COVID-19 pandemic (2). Recognizing that children tend to have more mild manifestations of COVID-19, our task force recommended that current ongoing management of PRD be continued (with modifications to glucocorticoid therapy as noted), even in the presence of exposure to SARS–CoV-2 or asymptomatic COVID-19. Our task force had the distinct advantage of having the opportunity to review more recent literature to support the notion that patients with PRD, while receiving or not receiving immunomodulatory therapy, do not appear to be at risk for increased likelihood of contracting COVID-19 or having worse outcomes as compared to the general population. In addition, our task force agreed that selective inhibition of IL-1 is likely to be safe in the setting of infection from SARS–CoV-2 and may provide additional benefit in the management of COVID-19, and therefore treatment with IL-1 inhibitors may be continued, even in symptomatic cases. As our knowledge regarding COVID-19 in children with PRD continues to expand, this document will be reviewed and modified as necessary to provide the most accurate and up to date guidance for rheumatology providers who treat children with PRD.

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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 published. Dr. Wahezi 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.

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Analysis and interpretation of data. Wahezi, Lo, Rubinstein, Ringold, Ardoin, Downes, Jones, Laxer, Madan, Mudano, Karp, Mehta.

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