

Management of Canadian Pediatric Patients With Glomerular Diseases During the COVID-19 Pandemic: Recommendations From the Canadian Association of Pediatric Nephrologists COVID-19 Rapid Response Team

Canadian Journal of Kidney Health and Disease
Volume 7: 1–17
© The Author(s) 2020
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/2054358120970713
journals.sagepub.com/home/cjk



Cal Robinson^{1*}, Michelle Ruhl^{2*}, Amrit Kirpalani³,
Abdullah Alabbas⁴, Damien Noone¹, Chia Wei Teoh¹,
Valerie Langlois¹, Veronique Phan⁵, Mathieu Lemaire^{1†},
and Rahul Chanchlani^{6†}

Abstract

Purpose: The goal of these recommendations is to provide guidance on the optimal care of children with glomerular diseases during the COVID-19 pandemic. Patients with glomerular diseases are known to be more susceptible to infection. Risk factors include decreased vaccine uptake, urinary loss of immunoglobulins, and treatment with immunosuppressive medications. The Canadian Society of Nephrology (CSN) recently published guidelines on the care of adult glomerulonephritis patients. This guideline aims to expand and adapt those recommendations for programs caring for children with glomerular diseases.

Sources of information: We used the CSN COVID-19 Rapid Response Team adult glomerulonephritis recommendations, published in the *Canadian Journal of Kidney Health and Disease*, as the foundation for our guidelines. We reviewed documents published by nephrology and non-nephrology societies and health care agencies focused on kidney disease and immunocompromised populations. Finally, we conducted a formal literature review of publications relevant to pediatric and adult glomerular disease, chronic kidney disease, hypertension, and immunosuppression in the context of the COVID-19 pandemic.

Methods: The leadership of the Canadian Association of Pediatric Nephrologists (CAPN), which is affiliated with the CSN, identified a team of clinicians and researchers with expertise in pediatric glomerular diseases. The aim was to adapt Canadian adult glomerulonephritis guidelines to make them applicable to children and discuss pediatric-specific considerations. The updated guidelines were peer-reviewed by senior clinicians with expertise in the care of childhood glomerular diseases.

Key findings: We identified a number of key areas of glomerular disease care likely to be affected by the COVID-19 pandemic, including (1) clinic visit scheduling, (2) visit types, (3) provision of multidisciplinary care, (4) blood work and imaging, (5) home monitoring, (6) immunosuppression, (7) other medications, (8) immunizations, (9) management of children with suspected COVID-19, (10) renal biopsy, (11) patient education and support, and (12) school and child care.

Limitations: There are minimal data regarding the characteristics and outcomes of COVID-19 in adult or pediatric glomerular disease patients, as well as the efficacy of strategies to prevent infection transmission within these populations. Therefore, the majority of these recommendations are based on expert opinion and consensus guidance. To expedite the publication of these guidelines, an internal peer-review process was conducted, which may not have been as rigorous as formal journal peer-review.

Implications: These guidelines are intended to promote optimal care delivery for children with existing or newly diagnosed glomerular diseases during the COVID-19 pandemic. The implications of modified care delivery, altered immunosuppression strategies, and limited access to existing resources remain uncertain.

Keywords

infectious diseases, pediatric nephrology, glomerular diseases, health services delivery

Received September 28, 2020. Accepted for publication October 9, 2020.



Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (<https://us.sagepub.com/en-us/nam/open-access-at-sage>).

Purpose

On March 11, 2020, the World Health Organization declared COVID-19 to be a global pandemic. The COVID-19 pandemic is likely to have a prolonged course, with enormous consequences around the world. The pandemic has already dramatically impacted the delivery of care to children with chronic kidney and glomerular diseases. A joint statement from national and international nephrology societies has called for urgent collaborative research, the production of guidelines, and the widespread dissemination of information regarding kidney diseases during the COVID-19 pandemic.¹

To date, few recommendations exist that address care for pediatric patients with renal disease during the COVID-19 pandemic. In response, pediatric nephrology programs across Canada are developing policies to ensure that the delivery of optimal care is maintained. The Canadian Association of Pediatric Nephrologists (CAPN) is working to consolidate local and provincial guidelines into national guidance documents on the care of children with glomerular diseases. Children and adolescents with glomerular diseases are particularly vulnerable populations, due to their immunocompromised status, preexisting medical comorbidities and the disruptions to their usual health care visits, and disease surveillance methods.²⁻⁴ These guidelines provide a framework to address these challenges while prioritizing the safety of patients, family members, and members of the health care team.

These guidelines were adapted from the Canadian Society of Nephrology (CSN) adult glomerulonephritis (GN) recommendations.⁵ The overarching aim is to optimize care delivery for children with glomerular diseases, with an emphasis on infection prevention, rationalization of health care system exposures, optimization of immunosuppression regimen, and contingency planning for care disruption. The recommendations in this document are most pertinent to pediatric glomerular disease care in a Canadian setting. Importantly, separate rapid guidelines will be published by the CAPN to address the care of patients with other kidney diseases (eg, renal replacement therapy and kidney transplantation).

Introduction

As of the end of August, 25 million cases of COVID-19 have been reported globally and 129 000 Canadians have been infected.⁶ Children appear to be less commonly and severely affected than adults, accounting for 1% to 4% of all COVID-19 cases and 0% to 1% of fatalities.^{2,7-12} In Canada, children ≤ 19 years of age account for 7% of COVID-19 cases and 1% of hospitalizations.¹³ Children with a confirmed diagnosis of COVID-19 are more frequently asymptomatic (13%-21%)^{10,11,14} or mildly symptomatic (43%-58%),^{10,14} and the majority of cases self-resolve within 1 to 2 weeks. Less than 10% of children with symptomatic COVID-19 require respiratory support, and $< 5\%$ require intensive care unit admission.^{9-11,14,15} It remains unclear why children are less susceptible to SARS-CoV-2 than adults. Possible protective factors include induction of a less vigorous immune response, reduced viral loads, and lower expression of the SARS-CoV-2 receptor on lung epithelial cells (angiotensin-converting enzyme-2 [ACE-2] receptors).^{16,17}

Systemic and Renal Complications of Pediatric COVID-19

Despite excellent overall pediatric outcomes, severe and fatal cases do occur.¹⁶ Children with severe COVID-19 are more likely to have preexisting medical conditions (eg, cardiac, respiratory, neurodevelopmental, malignancy, or immunosuppression).^{2,3,9,14,15} Multiple recent reports describe clusters of children presenting with “multisystem inflammatory syndrome in children (MIS-C),” which has features strikingly similar to that of Kawasaki disease shock syndrome.^{18,19} This rare complication of childhood COVID-19 is likely due to an antibody- or immune complex-mediated post-infectious inflammatory syndrome. Adult COVID-19 is associated with high rates of proteinuria (44%) and hematuria (27%),²⁰ and may also be responsible for a form of COVID-associated nephritis.²¹ COVID-19 has also been reported to trigger relapses among children with steroid-dependent nephrotic syndrome.²² Together, these findings raise concerns that SARS-CoV-2 infection can trigger

¹Department of Paediatrics, Division of Nephrology, The Hospital for Sick Children, Toronto, ON, Canada

²Department of Paediatrics, Division of Nephrology, University of Saskatchewan, Saskatoon, Canada

³Department of Paediatrics, Division of Nephrology, Western University, London, ON, Canada

⁴Department of Paediatrics, Division of Nephrology, University of Alberta, Edmonton, Canada

⁵Department of Paediatrics, Division of Nephrology, Université de Montréal, QC, Canada

⁶Department of Paediatrics, Division of Nephrology, McMaster University, Hamilton, ON, Canada

*The first two authors are co-first authors.

†The last two authors are co-senior authors.

Corresponding Authors:

Mathieu Lemaire, Department of Paediatrics, Division of Nephrology, The Hospital for Sick Children, 555 University Avenue, Toronto, ON, Canada M5G 1X8.
Email: mathieu.lemaire@sickkids.ca

Rahul Chanchlani, Division of Pediatric Nephrology, Department of Pediatrics, McMaster Children's Hospital, Hamilton, Canada.
Email: chanchlr@mcmaster.ca

relapses among patients with glomerular or autoimmune disorders.

Preexisting Renal Disease Versus Risk of Pediatric COVID-19

Another major concern is that adult COVID-19 disproportionately affects patients with preexisting hypertension, chronic kidney disease (CKD), and/or end-stage renal disease (ESRD).²³⁻²⁵ On that basis, it is reasonable to consider children with glomerular diseases at high-risk for symptomatic or severe COVID-19 since hypertension and CKD are prevalent in this patient population. It is important to note that there are currently limited data supporting this assertion.²⁶ The association between adverse outcomes in COVID-19 patients and use of renin-angiotensin-aldosterone system (RAAS) inhibitors or ACE-2 receptor expression levels have raised concerns about the use of RAAS inhibitors among hypertensive patients.^{23,25}

Immunosuppression Versus Risk of Pediatric COVID-19

Normally, nearly all children with a glomerular disease would be considered at high-risk for COVID-19 infection because most standard treatments include potent immunosuppressants, and glomerular proteinuria leads to urinary wasting of immunoglobulins. However, current data suggest that coronavirus infections are not more frequent or severe in immunocompromised hosts (unlike many other viral pathogens).²⁷ In addition, transplant recipients and other immunocompromised individuals were found to have outcomes similar to that of the general population following SARS-CoV or MERS-CoV infection.^{27,28} Early reports describe a similar pattern of SARS-CoV-2 infection among adult transplant recipients (from Italy or the United States), patients with immune-mediated inflammatory disorders, and immunosuppressed children (from New York City).^{27,29-33} Preliminary data from the RECOVERY (Randomized Evaluation of COVid-19 tHERApY) trial has also suggested that low-dose dexamethasone may reduce the risk of mortality among adults with COVID-19 requiring ventilation or supplemental oxygen.³⁴

Recent Data on the Risk of COVID-19 for Pediatric GN Patients

Of particular relevance for these guidelines, 2 recent reports have described reassuring outcomes of symptomatic COVID-19 infections among children with glomerular diseases. Marlais et al³⁵ reported preliminary survey data collected from 18 immunosuppressed children with COVID-19 infections from 11 different countries. A third of these patients had a glomerular disease, including nephrotic syndrome (3), ANCA-associated vasculitis (2), and atypical hemolytic-uremic

syndrome (1). Although the majority were admitted to hospital, only ~20% were treated with supplemental oxygen, and none required intensive care unit admission or died. Melgosa et al²² published data on 16 Spanish children with chronic kidney conditions (including 5 with nephrotic syndrome, 1 with vasculitis, and 1 with IgA nephropathy). Nine of the 16 children were on chronic immunosuppression, which was modified in 4 children during infection. They found that the incidence and outcomes of symptomatic COVID-19 were similar among children with chronic kidney conditions, compared with healthy Spanish children. Eight children were hospitalized but none required supplemental oxygen, intensive care or died. All children recovered within 1 month, although COVID-19 infection triggered relapse in 2 patients with steroid-dependent nephrotic syndrome. Among CKD and transplant patients admitted with symptomatic COVID-19 in Brescia, Italy, there were no children with a GN diagnosis.³⁶⁻³⁸ Overall, the risk of a clinically significant COVID-19 infection for immunosuppressed children with glomerular diseases appears to be lower than predicted.

Adapting Pediatric GN Management During COVID-19

Currently, there is a paucity of data on COVID-19 disease characteristics, outcomes, and risk factors for children with glomerular diseases. Prior to the COVID-19 pandemic, children with glomerular diseases typically had frequent health care contacts. Optimal care for these children requires close surveillance, with early detection of relapse, disease progression, and/or complications of immunosuppression. Decisions regarding initiation, escalation, or reduction of immunosuppression are informed by our knowledge of the significant risks of untreated disease. The COVID-19 pandemic has disrupted this fine balance by forcing clinicians to manage these patients based on limited data potentially increasing the risks of unchecked immunosuppression or delayed diagnosis. Since patient safety remains a top priority during pandemic times, medical teams must rapidly adapt their protocols/policies for pediatric glomerular diseases. Key principles to the delivery of safe care to children with glomerular diseases during the COVID-19 pandemic include prevention of infection transmission, reduction of excess burden on the health care system, mitigation of diagnostic and therapeutic delays, and optimization of immunosuppression.

Methods

The CSN recently created the COVID-19 Rapid Response Team by recruiting volunteers from the CSN board to identify relevant experts within the nephrology community. A survey of Canadian GN programs was conducted between April 9 and April 15, 2020, to evaluate GN care provision during the COVID-19 pandemic. They identified a number

of current challenges, including communication barriers during virtual care, safe laboratory testing and renal biopsy protocols, and decision-making regarding immunosuppression. Their group recently published guidelines for adult GN care in the *Canadian Journal of Kidney Health and Disease*.⁵

Following this, the CAPN decided to adapt their recommendations to address the management of Canadian children with glomerular diseases. The CAPN selected a team of experts recognized in the field of glomerular diseases to produce these guidelines, supported by pediatric nephrology trainees. A formal literature review was conducted to identify published and pre-print articles related to glomerular and other kidney diseases, hypertension, autoimmune disorders, and immunocompromised populations during the COVID-19 pandemic. Relevant guidance and webinars from various national and international societies were also reviewed. The updated pediatric guidelines were then peer-reviewed by senior clinicians with significant expertise in the field of childhood glomerular diseases.

Narrative Summary of Pediatric GN Management Across Canada During the COVID-19 Pandemic

In preparing this document, we were able to draw on the experiences of pediatric nephrologists from across Canada in caring for children with glomerulonephritis during the COVID-19 pandemic. There were many similar elements in the response between programs, although at some sites these recommendations were more formalized than others. The following areas were identified.

Detection of Acute Glomerulonephritis

At the beginning of the COVID-19 pandemic, there was concern that patients may stay at home with progressive disease rather than come to the hospital where the risk of contracting COVID-19 was perceived to be higher. (All) programs reported new cases of glomerulonephritis diagnosed during the COVID-19 pandemic, with a range of severity of presentation similar to a non-pandemic baseline.

Diagnosis of Acute Glomerulonephritis

Renal biopsy is frequently required in the diagnosis of acute glomerulonephritis and is used for staging the severity and chronicity of disease. Biopsies are very resource-intensive, requiring the use of an operating or procedure room with general anesthetic or sedation provided by an anesthesiologist. At all sites, non-urgent renal biopsies were canceled or postponed. Urgent renal biopsies for hospitalized patients were generally performed. At some centers, outpatient laboratory testing was limited to a restricted menu of tests to free up resources for testing COVID-19 samples. This restricted menu did not include some of the complement or antibody testing

required to diagnose acute glomerulonephritis, requiring extra steps to secure approval before this testing could be done.

Induction Immunosuppression

The use and choice of immunosuppressive agents has been carefully considered by pediatric nephrologists during the COVID-19 pandemic. With no specific evidence to guide practice, most programs continued to follow the best disease-specific evidence in determining an immunosuppressive regimen. Programs modified their practice to include testing for COVID-19 prior to administering immunosuppressive agents such as high-dose pulse corticosteroids and rituximab.

Maintenance Immunosuppression

All programs balanced the risk of developing severe COVID-19 infection while on immunosuppression against the increased risk of relapse caused by reducing stable immunosuppression for each patient. These discussions were individualized and resulted in collaborative decisions with patients and families.

Outpatient Clinic Activity

Programs generally continued planned follow-up for glomerulonephritis patients to monitor for symptoms of relapse. Clinic visits have been delivered virtually via telephone, video, or videoconference software, unless there were urgent concerns requiring an in-person visit. Barriers to virtual consultations have included lack of Internet bandwidth to effectively use videoconference programs and the added complexity of using translation services by phone or video. All in-person clinic visits required pre-screening for symptoms of COVID-19 and enhanced infection-control practices.

Disease Monitoring

Where possible, programs across the country moved to home monitoring of disease activity with urine dipstick or Albustix to limit the number of visits required for laboratory testing. Home weight and blood pressure measurements were also used, where possible. Home monitoring was supplemented as needed with in-person blood draws and urine studies. The decisions regarding this testing were individualized based on patient-reported symptoms, risk of relapse, and requirements for monitoring of immunosuppression levels.

Patient and Family Education and Reassurance

Many families contacted their care team with concerns about being on immunosuppressive medication during the COVID-19 pandemic. Some centers were able to proactively reach out to families by phone, e-mail, or mail to inform them of recommended self-isolation practices, as well as the methods of access testing or care in case of

COVID-19 symptoms. During clinic visits, counseling has been provided for specific scenarios as provincial re-opening plans are unveiled.

Multidisciplinary Care

All programs continued multidisciplinary care, usually within the clinic format whether this was delivered virtually or in-person. Allied health professionals often contacted patients and families outside of clinic visits to provide extended counseling on stressors related to COVID-19. Several programs reported that patients were very responsive to conversations and counseling in this format and were more open to sharing mental health concerns by phone rather than in-person.

Challenges Identified

1. Resource reallocation during COVID-19 resulting in new procedures to access diagnostic testing and renal biopsy.
2. Challenges with virtual care: lack of technology/infrastructure to support virtual visits, inability to perform physical examination, and communication challenges during virtual visits.
3. Lack of evidence to guide recommendations on modifying immunosuppression during COVID-19.
4. Limitations of home monitoring; difficulty providing patient access to weighing scales and home blood pressure equipment.
5. Patient and family anxiety about contracting COVID-19 during contact with the health care system, resulting in late presentation with symptoms of flare and/or missed laboratory investigations.
6. Challenges with re-organizing outpatient clinics to reduce the risk of COVID-19 transmission.

Successes Identified

1. Virtual visits offered improved convenience and access for patients living in rural and remote areas.
2. Home monitoring gives patients and families a sense of agency in identifying and managing glomerulonephritis.
3. Clinics were able to communicate with patients quickly and effectively regarding recommendations for self-isolation.
4. To date, children with glomerular diseases and/or are immunosuppressed have not been shown to be at increased risk of symptomatic or severe COVID-19.
5. Clinics continued to offer multidisciplinary patient care with specific attention to the mental health challenges that developed during the COVID-19 pandemic.

Recommendations for Patients at Low-Risk for COVID-19

“Low-risk” individuals are those that do not have suspected or confirmed COVID-19, do not have symptoms suggestive of COVID-19, and have not been in close contact with a case of COVID-19 or traveled to an area of high community SARS-CoV-2 transmission in the previous 14 days.

Clinic Visit Scheduling

1. We suggest adhering to clinic visit schedules (virtual or in-person), where resources permit.^{4,39-41}
2. We suggest an individualized approach regarding clinic visits if blood work is deemed routine or is unavailable.
3. We suggest that families of children with glomerular diseases are kept informed of the center’s plans for ongoing care, including telehealth and in-person visit procedures and measures implemented to prevent infection transmission.^{4,42}
4. We suggest that centers consider increasing intervals between routine follow-up visits if deemed clinically safe based on an individual’s overall situation.
5. We suggest that standardized protocols be established for triaging new referrals and follow-up visits, based on clinical priority.
6. Access to telephone interpretation services during telehealth visits should be made available to families, where needed.
7. We suggest that all relevant contact details are documented within the child’s medical record, including all potential caregivers, pharmacies and laboratories used.

Rationale. Continuing clinical care via in-person or virtual clinics as previously scheduled will ensure patients continue to receive appropriate care, personalized advice regarding their immunosuppression, and the support of the clinical program in case of COVID-19 infection. Blood work monitoring is typically required in this population for assessment of disease activity, complications of therapy, and drug-level monitoring. Ongoing communication between care providers and patients is essential to avoid patient-initiated clinic visit cancellation with the associated risk of becoming “lost to follow-up.” A local or provincially developed letter to all glomerular disease patients may be helpful.

Clinic Visit Type

1. We suggest that patients receive telehealth visits as permitted by local and provincial guidance unless an in-person visit is deemed required by the care team.^{4,39-41} Telehealth visits may be supplemented by photographs of relevant physical findings or urine

samples, and home-based monitoring of vital signs (including blood pressure).

2. We suggest that telehealth visits can serve as a screening tool to identify children that require in-person visits.⁴²
3. We suggest that in advance of the telehealth visit, families are telephoned with instructions regarding necessary blood work, asked to prepare a current medication list and to measure the child's weight, height, and blood pressure, where resources permit.
4. For children that are deemed to require an urgent in-person visit, we suggest that they and their accompanying caregiver undergo risk screening for COVID-19 by telephone and/or at hospital entry using local Infection Prevention and Control questions.
5. We suggest that patients who screen positive should be directed to the most appropriate facility, as per local Infection Prevention and Control guidelines.
6. We suggest that policies should be implemented within clinic spaces to minimize the risk of COVID-19 transmission, as per local Infection Prevention and Control guidelines. These may include restriction to 1 caregiver accompanying the child; universal masking for families, children (age 2 and over), and staff; physical distancing measures in waiting and clinic rooms; minimizing wait times within the clinic; effective hand hygiene; and the disinfection of surfaces and equipment following each visit.^{4,39,40,42,43}

Rationale. In this document, we adhere to the World Health Organization's description of telehealth, which includes the use of various information and communication technologies to deliver health care services where providers and patients are separated by distance.⁴⁴ Telehealth can provide patients with ongoing access to care while maintaining physical distancing, reducing the risk of COVID-19 transmission to patients and clinical staff. Evidence for provision of glomerular disease care via telehealth is generalized from available literature including CKD clinic, general nephrology (of which 5.7% had chronic glomerulonephritis), and pediatric nephrology (of which 16% had nephrotic syndrome).⁴⁴⁻⁴⁷

Communication with patients prior to telehealth visits with reminders to have blood work completed, medication list prepared, and blood pressure and weights documented should improve both clinic efficiency and effectiveness. Recommended actions in case of COVID-19 infection may be disseminated to patients via a formal letter or communicated verbally at the time of telehealth visit. We suggest that glomerular disease clinic contact information should include both contact phone number and out-of-hours contact information and/or instructions. In-person visits should be reserved for patients requiring urgent assessment to minimize exposure risk for both health care providers and patients.

Provision of Multidisciplinary Care

1. We suggest that multidisciplinary care continue to be provided, where resources permit.
2. We suggest that health care providers within the multidisciplinary team remain physically distanced during both in-person and telehealth encounters.
3. We suggest providers continue to communicate with 1 another via telephone and secure e-mail to remain informed of each child's status.
4. We suggest that prescriptions, bloodwork and other requisitions generated during clinic visits be created and transmitted electronically, where possible. Necessary documentation should be handled by the fewest number of individuals possible.
5. We suggest that clinic documentation be continued as per usual standards of care, and information continue to be conveyed to the primary care and other health care providers. Processes for identifying patients and obtaining consent to participate in telehealth visits should be implemented. Details of this consent process should be included in clinic documentation (Appendix).

Rationale. The use of telehealth to deliver chronic kidney disease multidisciplinary care has previously been demonstrated to be non-inferior to standard in-person care with composite outcome of death, hospitalization, emergency department visits, and admission to skilled nursing facilities.⁴⁷ Utilization of telehealth will allow for continued multidisciplinary care of this complex population.

Blood Work and Imaging

1. We suggest that blood work frequency should be individualized. As long as it does not compromise usual care, it would be acceptable to reduce the frequency of blood work for children with stable disease and no signs of medication toxicity, particularly in areas with active community SARS-CoV-2 transmission.
2. We suggest that blood work should be consolidated, wherever possible, with other specialty requests and coordinated with any scheduled in-person health care visits.
3. We suggest that all blood work should be performed in testing facilities with established safety procedures to mitigate the risk of SARS-CoV-2 transmission and with adequate experience in pediatric phlebotomy (in-hospital and/or community laboratories).
4. We suggest that therapeutic drug-level monitoring (tacrolimus, cyclosporine, mycophenolate) should continue as required on an individual basis.
5. If a clinic visit is deferred, we suggest establishing procedures to follow-up on laboratory testing in a time-sensitive manner.

6. We suggest that renal imaging studies that are not critical to the immediate management of a patient should be delayed, following the confines of local guidelines regarding imaging restrictions.

Rationale. Laboratory management forms the cornerstone of monitoring for disease activity, treatment toxicity, and efficacy. Although adult guidelines favor the use of community laboratories for GN patients, there are a number of additional considerations relevant to the pediatric population. Compared with adult hospitals and community laboratories, the risk of SARS-CoV-2 transmission during visits to pediatric hospitals may be relatively lower. Pediatric hospital laboratories may also have shorter wait times and more robust infection prevention strategies than community laboratories. Access to appointments and experience in pediatric phlebotomy should also be considered when selecting a laboratory, to ensure timely and reliable collection of blood work in advance of telehealth visits. Although renal imaging studies in children with glomerular diseases are important to document appropriate renal growth, these studies can often be safely deferred until the local risk of COVID-19 infection is low. However, more urgent renal imaging may be required in certain situations (eg, suspected renal artery/vein thrombosis, renal artery stenosis, urinary tract obstruction, and unexplained hematuria or deterioration in renal function).

Renal Biopsy

1. We suggest that a renal biopsy should be performed if it is reasonably likely to impact clinical decision-making (eg, suspected rapidly progressive GN, small vessel vasculitis, acute interstitial nephritis or steroid-resistant nephrotic syndrome).⁴³
2. If a renal biopsy is unlikely to modify patient outcomes and/or a high pretest probability exists for a particular diagnosis without a biopsy, these children should be managed empirically. Such nonurgent biopsies should be subsequently performed once the local risk of COVID-19 infection is low, or after failure of empiric treatment.⁴³ However, if it is reasonably likely that a renal biopsy result may preclude the need to introduce or escalate immunosuppression, biopsy should be considered.

Rationale. Renal biopsies for children are generally done in an operating or procedure room with general anesthetic or sedation provided by an anesthesiologist. This makes these procedures very resource-intensive and also, in the case of intubation, makes them aerosol-generating procedures. For the safety of patients and hospital staff, patients should be carefully screened and, if necessary, tested for COVID-19 prior to biopsy.

Home-based Monitoring

1. Where resources and family circumstances permit, we suggest that blood pressure measurements are performed at home with a calibrated device and an appropriately sized pediatric cuff. If this is not feasible, blood pressure measurements should be performed opportunistically, at every in-person primary or specialty care visit.
2. Patients should receive prescriptions for home blood pressure monitoring equipment, with an appropriately sized pediatric cuff. Available funding options should be explored with families to minimize the expense and make this equipment available to all patients.
3. We suggest that equipment is prescribed or provided for home urine testing (eg, dipstick or Albustix) and that these home measurements are correlated with laboratory values, when possible.
4. We suggest that families measure their child's weight and height at home. Measurement frequency should be individualized, but should occur prior to all telehealth visits.
5. Parents should receive training in the appropriate use of equipment for home blood pressure monitoring and urine testing. They should also be instructed on how to accurately measure their child's weight and height at home. This training may occur during scheduled telehealth visits.
6. We do not recommend testing asymptomatic pediatric glomerular disease patients for COVID-19, unless they have been directed to do so by their local Public Health agency, or as required prior to elective admissions, procedures, or administration of long-acting induction immunosuppression.

Rationale. Having tools to monitor blood pressure, weight, and height at home are essential to facilitate telehealth visits and promote each family's self-management skills. Real-time information about changes in disease activity allows for appropriate disease-modifying therapy and symptom management. Patients with glomerular diseases should be supplied with these tools regardless of socioeconomic status. However, education on the proper use of this equipment is necessary to ensure that accurate information is supplied to the clinic in a timely manner.

Induction Immunosuppression

1. Children with progressive disorders and those at risk of significant complications (eg, nephrotic syndrome, acute GN, lupus nephritis, ANCA-associated vasculitis, IgA vasculitis and rapidly progressive GN) should continue to receive standard of care induction immunosuppression without significant delays.^{41,43}

2. For children requiring corticosteroid induction for new or relapsed nephrotic syndrome, decisions around modifications of the rate of steroid tapering and/or total duration of treatment should be tailored for each patient based on individual characteristics and local community context. We suggest that clinicians should review the established measures known to reduce infection risk before each corticosteroid induction phase (eg, social distancing, consistent mask-wearing, and regular hand washing). For most patients, no treatment plan changes are advised since the likelihood of a nephrotic relapse is much higher than the risk of a COVID-19 infection in children, particularly when COVID-19 prevalence in the community is deemed “low” by the local public health experts. The risks and benefits of minimizing steroid exposure should be carefully weighed by the treating team if COVID-19 community prevalence is “high,” especially for patients who have other known risk factors for COVID-19 infections.⁴¹ This process should ideally include a discussion with a local infectious disease and/or immunology expert. It is important to note that while corticosteroids are helpful to treat COVID-19 patients with progressive pulmonary disease,³⁴ there are no data showing benefits when used in uninfected individuals.
3. Consider delaying the initiation of immunosuppression for slowly progressive disorders with stable renal function (eg, IgA nephropathy) or those where immunosuppression has an unclear benefit (eg, immune complex or complement-mediated membranoproliferative GN) until the local risk of COVID-19 infection is low.⁴³
4. We suggest that the risks of long-acting, irreversible induction agents (ie, rituximab and cyclophosphamide) should be balanced against the benefits of these medications over alternative immunosuppressive agents, as well as the risks of inadequately treated glomerular disease, which may be intrinsically immunocompromising.
5. Children should be tested for COVID-19, in addition to screening for fever and other COVID-19 symptoms, prior to administering induction immunosuppression with intravenous cyclophosphamide or rituximab.⁴¹
6. Intravenous induction regimens should be administered in facilities with established safety procedures to mitigate the risk of SARS-CoV-2 transmission and with adequate pediatric experience. Local Infection Prevention and Control policies should be adhered to. Medical day units or infusion centers should be made aware of the immunocompromised status of these children.⁴⁸
7. Consider alternative oral induction agents (eg, cyclophosphamide, corticosteroids, or mycophenolate

mofetil) for conditions where these agents have been shown to be non-inferior and safe.^{41,43,49}

Maintenance Immunosuppression

1. We suggest that reductions to and discontinuation of maintenance immunosuppression should continue as per established standard of care practices. An individualized approach is required for children that are deemed to be at elevated risk of disease relapse or flare following immunosuppression reduction. For these children, the benefits of reducing immunosuppression should be carefully weighed against the potential risk of relapse and the need for immunosuppression re-escalation during the COVID-19 pandemic. As per routine practice, corticosteroids should not be abruptly discontinued.^{40,41,43}
2. We suggest that immunosuppression reduction should be avoided in children with a history of frequently relapsing disease if they remain stable on low-dose immunosuppression and are not experiencing any treatment-related toxicities.⁴¹
3. For children in prolonged remission and/or felt to be at elevated risk of severe COVID-19 infection, immunosuppression reduction may be considered on an individual basis. If immunosuppression is modified, the aim should be to maintain the child on the lowest dose of immunosuppression possible while maintaining remission and avoiding relapse, as per routine care.⁴¹
4. For children on maintenance rituximab regimens, consider increasing the interval between treatments if the risk of disease relapse is assessed to be low and/or they have comorbidities that increase their risk of severe COVID-19 infection.^{40,41,43,49}
5. If immunosuppression is modified, clinics must have procedures in place to maintain close disease surveillance for early detection of relapse or progression, to minimize associated complications. This may include more frequent telehealth assessments, additional home or laboratory monitoring, auto-antibody and/or lymphocyte subset testing.
6. We suggest that all prescriptions be provided in usual quantities (dependent on provincial regulations) to ensure that children have a minimum of 1-month supply of medications available at home. We suggest that health care providers consider providing additional prescription refills, to ensure timely dispensing and avoid unnecessary health care visits.^{4,42}

Rationale. There is little information available about the risk of developing COVID-19 in patients with glomerular diseases. However, some useful information can be gleaned from other recent outbreaks caused by coronaviruses—SARS and MERS. In those 2 outbreaks, there were no fatal

cases in any patient undergoing transplantation, chemotherapy, or immunosuppression of any kind.²⁷ Unlike other viral respiratory pathogens, coronaviruses do not typically have a more severe course in immunosuppressed patients.²⁷ Children with glomerular diseases may also have chronic kidney disease and hypertension. Large studies in adults have identified both of these groups of patients as being at higher risk of severe disease.^{24,50} It is not clear whether the increased risk of severe infection is also true for children with these comorbidities.

Induction therapy decisions will include consideration of underlying diagnosis, kidney biopsy findings, degree of renal dysfunction, level of proteinuria, and underlying comorbidities. Choice of immunosuppressive agents may be more robustly supported by evidence for some forms of glomerulonephritis than others. There is little evidence to guide adjustment of existing best practices for induction and maintenance of immunosuppression in this rapidly evolving clinical setting. The use of long-acting, irreversible induction agents (ie, rituximab and cyclophosphamide) requires special consideration. Children receiving rituximab may not develop antibodies following SARS-CoV-2 infection or future vaccination, increasing their risk of subsequent COVID-19 infection.⁴¹ Maintenance immunosuppression remains important to prevent acute relapse and subsequent escalation of immunosuppression. It is reasonable to continue routine care by maintaining patients on the lowest dose of immunosuppression that is expected to maintain remission.

Other Medications

1. We suggest that ACEi and ARBs should not be discontinued as a result of the COVID-19 pandemic.^{26,51}
2. We suggest that these agents be held in accordance with usual sick day guidance.
3. We suggest that the initiation of ACEi or ARBs is at the discretion of the individual physician, accounting for the clinical context, the additional recommended monitoring, and potential side-effects. These risks may be outweighed in individual circumstances.
4. We suggest that acetaminophen is used as the first-line analgesic or antipyretic, instead of non-steroidal anti-inflammatory drugs (NSAIDs), as per routine care.

Rationale. The interactions between the RAAS system and SARS-CoV-2 by virtue of the binding of the virus to ACE-2 have generated theories of both potential harm and benefit of RAAS inhibitor use during the pandemic. Evidence supporting or refuting these theories are lacking and we agree with statements issued by Hypertension Canada and multiple other relevant societies; that ACEi and ARBs should not be discontinued as a result of the COVID-19 pandemic.⁵¹

There are plausible mechanisms for harm with the use of NSAID medications in patients with COVID-19.⁵² The risk of acute kidney injury with NSAIDs is well known, particularly in patients with fever and dehydration. The NSAIDs have been associated with higher rates of complications after other respiratory tract infections in both adult and pediatric patients,^{52,53} and have been shown to prolong the duration of symptoms in patients self-managing respiratory tract infections at home.⁵⁴ Based on available information, the WHO does not recommend against the use of ibuprofen in patients with COVID-19, except where known side-effects limit its use in certain patient populations.⁵⁵

Immunizations

1. We suggest that children should continue to receive routine immunizations based on existing guidelines for immunocompromised populations.^{39,56,57}
2. Routine immunizations should be coordinated with or performed opportunistically at other in-person health care visits, where possible.

Rationale. Immunization is important to reduce the risk of serious infections in patients with glomerular diseases. Immunizations may be less effective in patients who are on immunosuppression. However, patients with nephrotic syndrome have still been shown to develop positive antibody titers, even when immunizations are given during active flare or while on immunosuppressive medication.⁵⁸ Care providers often provide advice to give immunizations either before immunosuppressive treatment or when patients are on a lower dose of immunosuppressive treatment.⁵⁷ These available windows for immunization should still be utilized if possible during the COVID-19 pandemic.

Patient Education and Support

1. *Sick day advice*—We suggest reinforcing existing sick day advice to families of children with glomerular diseases during telehealth visits, including explicit advice on specific medications that should be held for a child that is unwell.
2. We suggest that families should keep an up-to-date list of their child's medications and medical conditions to provide to health care providers if their child requires treatment for COVID-19.⁴
3. We suggest that caregivers make contingency plans for situations that may prevent usual care delivery to their child, including them or other family members becoming symptomatic and requiring isolation. This may require additional support from their glomerular disease clinic.⁴
4. We suggest that families continue to receive education about their child's diagnosis, clinical status, and treatment plan. This patient education can be

delivered virtually, but should be supported with additional electronic or physical education materials. If a family has limited access to the Internet and/or electronic devices, we suggest mailing educational materials or conveying the information via telephone.

5. We suggest that vetted lists of informational Web Sites maintained by professional organizations with high-quality information and patient-driven online forums (see section below for a list of relevant sources) should be compiled and shared with families, where appropriate.
6. We suggest that families of children with glomerular diseases be given clear guidance on whom they should contact if any concerns arise. Patients should be advised to contact the clinic team, as per usual practice, for changes in clinical status. Numbers that are accessible during weekdays may be different than weekend numbers, and all patients should be made aware of them. We suggest a dedicated contact phone number that is routinely answered/monitored be made available and be easily accessible on the hospital Web Site or provided in an information letter to families.⁴²

Rationale. Guidance on sick day management is designed to reduce the risk of medication-induced acute kidney injury. Programs that have implemented this type of patient education have highlighted the importance of follow-up with the care team to clarify misunderstandings and give patients confidence in this kind of self-management.⁵⁹ In children with nephrotic syndrome, a clear understanding of the risk of relapse with illness should prompt close monitoring during these episodes. Early diagnosis of relapse may prevent the development of severe edema and associated complications. Providing children and families with accurate, up-to-date information about their clinical status and treatment reinforces compliance and disease self-management. A clear point of contact with the health care team allows patients with mild symptoms of COVID-19 or another illness to be managed at home, protecting both patients and hospitals from unnecessary contact. It is important that families have access to high-quality, up-to-date information about their local risk of community SARS-CoV-2 transmission and the impact of the COVID-19 pandemic on their health and access to care.

School, Employment, and Other Activities

1. We recommend that children with glomerular diseases should take additional precautions to minimize potential exposures to SARS-CoV-2.
2. We recommend that questions regarding return to school, childcare facilities, employment, or other activities should be considered on an individual basis.

Decisions should be made with particular consideration of the current local risk of community SARS-CoV-2 transmission, the burden of immunosuppression, the presence of other comorbidities that may increase their risk of severe COVID-19 (eg, cardiovascular, respiratory or neurodevelopmental conditions), the characteristics of that particular environment or activity (including implemented safety procedures), psychosocial concerns, learning needs, and alternative options for education (for school participation).

Rationale. Many countries have implemented closures of schools and other public spaces in an attempt to prevent community SARS-CoV-2 transmission. Children were predicted to be “super spreaders” of COVID-19 based on experience from seasonal influenza transmission, but this has not borne out during the COVID-19 pandemic.⁶⁰ Community screening in Iceland and in Italy found no infected children under the age of 10 years and children in other areas of the world have been found to be significantly less likely to become infected than adults.⁶¹ Children are also rarely the index case for transmission within their families.⁶² A number of recent articles in popular media have focused on the risk of COVID-19 transmission due to “super spreader” events.^{59,63-65} Only 1 of these events was outdoors (0.3% of cases); the rest were indoor gatherings, often with increased respiratory droplet production from singing, cheering, or talking loudly in a noisy environment. The key risk factor identified for COVID-19 transmission was virus exposure over an extended period of time in an enclosed space. As well as the specific medical advice they receive during clinic visits, patients can be directed to articles that discuss in plain language the exposure risks of various activities.⁶⁶ Children with glomerular diseases should take additional precautions to avoid exposures within high-risk settings for SARS-CoV-2 transmission (eg, crowded indoor spaces such as schools, places of worship, community centers, movie theaters, and indoor sports; public transportation, pools, and bathrooms; and birthday parties or other large gatherings).

Psychosocial Considerations

1. Marginalized Canadian populations, including Indigenous, immigrant, racialized, and poor families, are at risk of worsening social inequalities during the COVID-19 pandemic. Health care providers caring for these individuals should continue to provide culturally safe and trauma-informed care. Children and families should be screened for poverty, food insecurity, vulnerable housing, and access to the technology needed for telehealth visits. Where needed, health care providers should assist families in accessing appropriate childcare and social services and completing applications for social assistance and Canadian emergency benefits.

2. We suggest that mental health and psychosocial concerns continue to be routinely assessed by the multidisciplinary team during clinic visits and separate communications with patients and families.

Rationale. COVID-19 amplifies existing social inequalities among marginalized and vulnerable groups in Canada, including Indigenous, immigrant, racialized, and poor families. Previous pandemics have disproportionately affected these populations.⁶⁷⁻⁶⁹ Specific risks faced by these populations during the COVID-19 pandemic include a lack of access to health care services (including computer or telephone access for telehealth), limited capacity to physically distance in overcrowded housing, increased food insecurity due to supply chain disruptions, increased caregiver burden from decreased access to childcare and school programs, and financial hardships related to unemployment or loss of income.^{69,70} During the COVID-19 pandemic, health care providers can support these populations by providing culturally safe and trauma-informed care, by screening these families for poverty and food insecurity, by helping families access childcare and school programs, and by assisting with applications for social assistance and COVID-19 emergency benefits.

Depression and anxiety are known to be common in children with chronic kidney disease.^{61,71,72} Mental health concerns can be exacerbated by isolation from peers and the loss of purposeful routine that children with chronic health conditions have experienced during the COVID-19 pandemic.^{73,74} The status of each child and family's mental health and coping should continue to be monitored during clinic visits, recognizing that discussion of these concerns during group telehealth visits may be suboptimal. When potential concerns are identified, individual follow-up should be offered with the most appropriate member(s) of the multidisciplinary team. Mental health status should also be considered when counseling patients on the timing of return to school.

Recommendations for Patients With Suspected or Confirmed COVID-19

General Principles

1. Most of the recommendations listed in the section above on the management of patients at low-risk for COVID-19 apply for those with suspected or confirmed COVID-19, unless otherwise specified.
2. We suggest that families should be informed about how to seek medical care in case their child develops symptoms of COVID-19. This may include 911 for life-threatening symptoms, the emergency department, their primary care provider, or glomerular disease clinic. We suggest patients contact their glomerular disease clinic if their child develops symptoms suggestive of COVID-19 for advice regarding medications.
3. We recommend that health care professionals managing patients with suspected or confirmed COVID-19 use appropriate personal protective equipment (PPE) according to local, provincial, and national guidelines.
4. We recommend appropriate isolation of patients with suspected or confirmed COVID-19 in all clinical settings (outpatient, emergency department, medical day units, inpatient, operating rooms, intensive care unit).
5. We recommend that patients with symptoms suggestive of COVID-19 should be tested according to local hospital and Public Health guidelines.
6. Health care providers caring for children with glomerular diseases should be aware that immunosuppressed patients may present with atypical symptoms of COVID-19 infection, including isolated gastrointestinal symptoms.³⁵ Pediatric patients with mild systemic symptoms may also have prominent dermatological manifestations such as chilblains-like lesions on the hands and feet,⁷⁵ urticarial or vasculitic rashes.⁷⁶ Recognizing these unusual presentations may allow for earlier COVID-19 diagnosis, avoiding misdiagnosis as a disease flare.
7. Patients with SARS-CoV-2 infection that are asymptomatic or have mild symptoms may not require hospital admission. We suggest close monitoring and follow-up of outpatients with suspected or confirmed COVID-19 using telehealth to monitor for development or worsening of symptoms that may warrant hospital admission, such as tachypnea, respiratory distress, or dehydration.

Immunosuppression

1. In patients with symptomatic COVID-19, the decision to continue or modify immunosuppression should be made on an individual basis. Clinicians should consider the severity of the underlying disease, the risks of reducing immunosuppression, whether COVID-19 infection is suspected or confirmed, the stage and severity of COVID-19 infection, and other patient comorbidities.⁴
2. If a decision is made to modify immunosuppression, we suggest initial reduction/discontinuation of antiproliferative agents (mycophenolate mofetil, azathioprine).
3. In patients with severe or progressive COVID-19 infections, we suggest consideration of reduction/discontinuation of calcineurin inhibitors (tacrolimus, cyclosporine) and consideration of high-dose corticosteroids,³⁴ in consultation with the intensive care team.

4. If the child has been on long-term corticosteroids, we suggest consideration of the need for stress dosing during symptomatic COVID-19 illness. Based on studies of corticosteroids in SARS-CoV and MERS-CoV, the WHO does not currently advise starting corticosteroids in COVID-19 unless there is another indication.⁷⁷
5. We suggest that existing sick day rules for immunosuppression adjustment (eg, corticosteroid dosing in nephrotic syndrome) should continue to be applied and these should be reinforced to the families of children with glomerular diseases at telehealth visits.

COVID-19-Specific Therapies

1. Currently, there is insufficient evidence to recommend the use of any specific antiviral or other agents for the treatment of COVID-19, outside of clinical trials.
2. We suggest that decisions regarding the use of these agents should be made in consideration of local guidelines and appraisal of emerging clinical trial data. Health care providers should also consider the phase of COVID-19 illness (ie, viral replication or hyperinflammatory phase) when making decisions regarding the use of these agents.
3. Patients already taking hydroxychloroquine to treat their GN should continue using the medication at the same dose. Dose reductions or alternative agents may need to be considered if drug shortages arise.
4. If hydroxychloroquine and/or azithromycin are used for children with nephrotic range proteinuria, we recommend obtaining serum electrolytes (including calcium and magnesium) and a baseline electrocardiogram to exclude QT prolongation prior to initiation.
5. If antiviral agents are used, we suggest close monitoring for potential side-effects and therapeutic drug monitoring due to possible drug-drug interactions.

Rationale. Our current recommendations represent the consensus opinion of a group of professionals in pediatric glomerular disease care, which are extrapolated from experience with immunosuppression modification for other viral infections and theoretical interactions between specific immunosuppressive agents and SARS-CoV-2 infection. These recommendations should be used in conjunction with hospital and provincial guidelines. Decisions regarding immunosuppression modification should be made in consultation with the pediatric glomerular disease care provider(s).

Most children with COVID-19 will have a mild course of illness.¹² There have been very few cases of COVID-19-positive pediatric patients with glomerulonephritis, but 1 report describes 18 immunosuppressed pediatric patients from 11 countries, including 3 with nephrotic syndrome, 2 with ANCA-associated vasculitis, and 1 with atypical hemolytic uremic syndrome (HUS). All of these patients showed

similar symptoms to other children (72% had fever, 61% cough, 28% rhinitis). Although 61% were admitted to hospital, their hospital course was generally mild with 17% requiring supplemental oxygen, and none requiring intensive care unit admission or intubation.³⁵ Among 16 Spanish children with chronic renal diseases, 9 were using immunosuppressive agents at time of infection (7 on corticosteroids, 7 on calcineurin inhibitors, 3 on mycophenolate, and 3 on azathioprine, everolimus, or leflunomide).²² Four children had immunosuppression modified, typically by reduction/discontinuation of the anti-proliferative agent. Six of the 16 children received hydroxychloroquine and 1 child also received lopinavir-ritonavir. In their series, 50% of children were hospitalized, but none required supplemental oxygen, were admitted to the intensive care unit, or died. All patients recovered within 1-month follow-up. In another report, 15 adult renal transplant patients with COVID-19 infections were managed by discontinuation of antimetabolite, continuation of tacrolimus and low-dose prednisone, and addition of hydroxychloroquine (in 13 patients) with or without azithromycin (in 9 patients).³¹ In their study, 4 patients (27%) required intubation and mechanical ventilation, a similar proportion to the total number of COVID-19 cases in New York City requiring mechanical ventilation. Overall, COVID-19-specific therapies remain investigational, and at physician discretion, based on an individual's clinical status. Among glomerular disease and other immunosuppressed populations, there is currently no evidence to support specific strategies of immunosuppression modification for patients with suspected or confirmed COVID-19.

For glomerular disease patients with symptomatic COVID-19 disease, discontinuation of the antimetabolite (mycophenolate mofetil, azathioprine) agent has been recommended.⁴³ This strategy is consistent with clinical experience in pediatric renal transplant, where antimetabolite reduction/discontinuation is recommended for clearance of other viral infections. There is *in vitro* evidence that calcineurin inhibitors (tacrolimus, cyclosporine) may inhibit coronavirus replication.^{43,78,79} Continuation of these agents should be considered in cases of mild-moderate COVID-19. The use of high-dose steroids may be associated with prolonged viral shedding and have not been recommended for cases of nonsevere COVID-19 disease.^{77,80,81}

The implications that illness phase have on potential COVID-19-specific treatments were highlighted in a study of Italian COVID-19 patients.³⁶ This study identified 2 distinct phases to COVID-19 disease: 7 to 10 days of active viral replication, followed by the development of progressive lung injury due to cytokine release and hyperinflammatory syndrome. They hypothesized that there may be specific benefits to using antiviral agents during the first (viral replication) phase and to using immunosuppressive agents in the event of a second (hyperinflammatory) phase. There are several antiviral agents currently under investigation for COVID-19, including remdesivir; lopinavir-ritonavir ± ribavirin; hydroxychloroquine/chloroquine ± azithromycin;

convalescent plasma; interferon beta; IL-1 inhibitors (anakinra); and IL-6 pathway inhibitors (tocilizumab). Preliminary data on remdesivir suggest that it may be effective in shortening time to recovery among hospitalized adults.⁸² A randomized controlled trial of hydroxychloroquine as post-exposure prophylaxis found that it did not prevent COVID-19.⁸³ Anakinra and tocilizumab have both been suggested as potential treatments for the hyperinflammatory syndrome observed in certain patients with severe COVID-19, based on experience with their use in hemophagocytic lymphohistiocytosis and cytokine release syndrome following CAR-T cell therapy.⁸⁴⁻⁸⁸ At the time of publication, there is currently insufficient data to recommend the use of any specific antiviral agent in the treatment of COVID-19 among children with glomerular diseases. Decisions regarding the use of antiviral agents should be made on a case-by-case basis, in consultation with relevant pediatric specialists and in conjunction with hospital, provincial, and national guidelines. Wherever possible, the use of these agents should be performed within the setting of a clinical trial. If these agents are used, health care providers caring for these children should closely monitor them for potential toxicities and drug-drug interactions, which may require additional laboratory and therapeutic drug-level monitoring.

Future Directions

The following are evolving areas of relevance to the management of childhood glomerular diseases during the COVID-19 pandemic:

1. Observational data on disease-specific risks of morbidity and mortality due to COVID-19 infection in patients with glomerular diseases and other immunosuppressed populations are urgently needed to guide treatment recommendations and provide families with estimates of the risks of immunosuppression during the COVID-19 pandemic.
2. The impact of SARS-CoV-2 serological testing on future decisions regarding immunosuppression and health care delivery.
3. Approaches to COVID-19 immunization among immunosuppressed children.

Limitations

A full systematic review of available literature was not attempted for the sake of expediency in developing this guideline. In addition, suggestions outlined here have not been formally proven in clinical environments and the local context may impede their implementation.

Implications

These recommendations are meant to serve as a guide for providing the best patient care we can in a limited resource

environment while protecting patients and health care providers wherever possible by limiting exposure to COVID-19. We recognize that these suggested practices may not be delivered to all patients given time constraints, resource constraints, and local health authority priorities.

Appendix

Scripts for initiation of telehealth visits and documentation of consent

This script is reproduced with permission from the Hospital for Sick Children Glomerular Disease Clinic. It is based on Ontario Medical Association and Canadian Medical Protective Association Guidance for the provision of virtual care using products that do not meet the requirements of provincial personal health information/privacy laws.

Disclosure script

Just like online shopping or email, Virtual Care has some inherent privacy and security risks that your health information may be intercepted or unintentionally disclosed. We want to make sure you understand this before we proceed. In order to improve privacy and confidentiality, you should also take steps to participate in this virtual care encounter in a private setting and should not use an employer's or someone else's computer/device as they may be able to access your information.

If you want more information, please check the link on our [website/confirmation email/etc.]. If it is determined you require a physical exam you may still need to be assessed in person. You should also understand that virtual care is not a substitute for attending the Emergency Department if urgent care is needed. Are you ok to continue?

Documentation script

Informed verbal consent was obtained from this patient to communicate and provide care using virtual and other telecommunications tools. This parent/patient has been explained the risks related to unauthorized disclosure or interception of personal health information and steps they can take to help protect their information. We have discussed that care provided through video or audio communication cannot replace the need for physical examination or an in person visit for some disorders or urgent problems and the patient understands the need to seek urgent care in an Emergency Department as necessary.

Relevant Educational Resources

1. Glomerular diseases in general:
<https://www.cansolveckd.ca/gnregistry/about-gn>
<https://www.ontariorenalnetwork.ca/en/kidney-care-resources/living-with-chronic-kidney-disease/about-glomerulonephritis>

<https://nephcure.org>
<https://www.kidney.org/atoz/content/understanding-glomerular-diseases>
<https://www.aboutkidshealth.ca/article?contentid=3846&language=english>

2. COVID-19-Specific:

<https://www.ontario.ca/page/2019-novel-coronavirus>
<https://www.canada.ca/en/public-health/services/diseases/coronavirus-disease-covid-19>
<https://www.csnsn.ca/covid-19-emergency-preparedness-for-patients-and-caregivers>
[http://www.bcrenalagency.ca/health-info/prevention-public-health/novel-coronavirus-\(covid-19\)](http://www.bcrenalagency.ca/health-info/prevention-public-health/novel-coronavirus-(covid-19))
<https://www.aboutkidshealth.ca/Article?contentid=3863&language=English>
<https://www.asn-online.org/covid-19/>
<https://www.era-edta.org/en/covid-19-news-and-information/#toggle-id-4>
<https://www.espn-online.org/covid-19/>
<https://www.kidneycareuk.org/news-and-campaigns/coronavirus-advice/>

Information Sources

On Behalf of the CAPN COVID-19 Rapid Response Team:
<https://www.lifelabs.com/covid-19-updates/>
<https://www.dynacare.ca/important-notice/covid-19-important-information.aspx>

Authors' Note

Canadian Association of Paediatric Nephrologists COVID-19 Rapid Response Team includes M.L., R.C., C.R., M.R., A.K., A.A., D.N., C.W.T., V.L., and V.P. Steering Committee includes M.L., R.C.

Acknowledgments

The authors acknowledge the following individuals for providing feedback on these guidelines during the CSN COVID-19 Rapid Response Team Webinar: Steven Arora, Abdulaziz Bamhraz, Paul Goodyer, Derrick Soong, Keefe Davis, Abdelhamed Hamdy, Anke Banks, Aicha Merouani, and Swapnil Hiremath.

Author Contributions

C.R., M.R., M.L. and R.C. planned the manuscript. C.R. and M.R. co-wrote the draft, with the help of M.L. and R.C.. A.K., A.A., D.N., C.W.T., V.L. all contributed suggestions, comments and ideas that significantly improved the draft document before the webinar.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iDs

Cal Robinson  <https://orcid.org/0000-0002-2223-0646>

Chia Wei Teoh  <https://orcid.org/0000-0002-5994-0799>

References

1. Nephrology Societies. Nephrology Societies call for ensuring optimal care to patients with kidney diseases during the COVID-19 pandemic. Renal Association. <https://renal.org/wp-content/uploads/2020/05/Nephrology-Societies-COVID-19Joint-Statement.pdf>. Published May 2020. Accessed October 21, 2020.
2. CDC COVID-19 Response Team. Coronavirus disease 2019 in children—United States, February 12–April 2, 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69:422-426.
3. Shekerdemian LS, Mahmood NR, Wolfe KK, et al. Characteristics and outcomes of children with coronavirus disease 2019 (COVID-19) infection admitted to US and Canadian pediatric intensive care units. *JAMA Pediatr.* 2020;174:868-873. doi:10.1001/jamapediatrics.2020.1948.
4. NICE. COVID-19 rapid guideline: children and young people who are immunocompromised. NICE. <https://www.nice.org.uk/guidance/ng174/resources/covid19-rapid-guideline-children-and-young-people-who-are-immunocompromised-pdf-66141961215685>. Published May 2020. Accessed October 21, 2020.
5. CSN COVID-19 Rapid Response Team. Management of patients with glomerulonephritis during the COVID-19 pandemic: recommendations from the Canadian society of nephrology COVID-19 rapid response team. *The Canadian Journal of Kidney Health and Disease.* https://www.csnsn.ca/images/CSN_covid_rapid_review_GN_Final.pdf. Published 2020. Accessed October 21, 2020.
6. Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU). COVID-19 dashboard. Johns Hopkins Coronavirus Resource Center. <https://coronavirus.jhu.edu/map.html>. Published May 21, 2020. Accessed October 21, 2020.
7. American Academy of Pediatrics. Children and COVID-19: state-level data report as of 5/14/20. American Academy of Pediatrics; 2020. <https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/children-and-covid-19-state-level-data-report/>
8. Livingston E, Bucher K. Coronavirus Disease 2019 (COVID-19) in Italy. *JAMA.* 2020;323:1335. doi:10.1001/jama.2020.4344.
9. Tagarro A, Epalza C, Santos M, et al. Screening and severity of coronavirus disease 2019 (COVID-19) in children in Madrid, Spain [published online ahead of print April 8, 2020]. *JAMA Pediatr.* doi:10.1001/jamapediatrics.2020.1346
10. Dong Y, Mo X, Hu Y, et al. Epidemiology of COVID-19 among children in China. *Pediatrics.* 2020;145(6):e20200702. doi:10.1542/peds.2020-0702.
11. Lu X, Zhang L, Du H, et al. SARS-CoV-2 infection in children. *N Engl J Med.* 2020;382:1663-1665.
12. Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. *Acta Paediatr.* 2020;109(6):1088-1095.

13. Public Health Agency of Canada. Epidemiological summary of COVID-19 cases in Canada. Government of Canada. <https://health-infobase.canada.ca/covid-19/epidemiological-summary-covid-19-cases.html>. Published 2020. Accessed October 21, 2020.
14. Parri N, Lenge M, Buonsenso D, Coronavirus Infection in Pediatric Emergency Departments (CONFIDENCE) Research Group. Children with COVID-19 in pediatric emergency departments in Italy. *N Engl J Med*. 2020;383:187-190. doi:10.1056/NEJMc2007617.
15. DeBiasi RL, Song X, Delaney M, et al. Severe COVID-19 in children and young adults in the Washington, DC metropolitan region. *J Pediatr*. 2020;223:P199-P203. doi:10.1016/j.jpeds.2020.05.007.
16. Mehta NS, Mytton OT, Mullins EWS, et al. SARS-CoV-2 (COVID-19): what do we know about children? a systematic review. *Clin Infect Dis*. 2020. doi:10.1093/cid/ciaa556.
17. Bunyavanich S, Do A, Vicencio A. Nasal gene expression of angiotensin-converting enzyme 2 in children and adults. *JAMA*. 2020;323:2427-2429. doi:10.1001/jama.2020.8707.
18. Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. *Lancet*. 2020;395:P1607-P1608. doi:10.1016/S0140-6736(20)31094-1.
19. Jones VG, Mills M, Suarez D, et al. COVID-19 and Kawasaki disease: novel virus and novel case. *Hosp Pediatr*. 2020;10:537-540. doi:10.1542/hpeds.2020-0123.
20. Cheng Y, Luo R, Wang K, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. *Kidney Int*. 2020;97(5):829-838.
21. Gross O, Moerer O, Weber M, Huber TB, Scheithauer S. COVID-19-associated nephritis: early warning for disease severity and complications? *Lancet*. 2020;395:e87-e88.
22. Melgosa M, Madrid A, Álvarez O, et al. SARS-CoV-2 infection in Spanish children with chronic kidney pathologies. *Pediatr Nephrol*. 2020;35:1521-1524. doi:10.1007/s00467-020-04597-1.
23. Reynolds HR, Adhikari S, Pulgarin C, et al. Renin-angiotensin-aldosterone system inhibitors and risk of COVID-19. *N Engl J Med*. 2020;382:2441-2448. doi:10.1056/NEJMoa2008975.
24. Henry BM, Lippi G. Chronic kidney disease is associated with severe coronavirus disease 2019 (COVID-19) infection. *Int Urol Nephrol*. 2020;52:1193-1194. doi:10.1007/s11255-020-02451-9.
25. Mancia G, Rea F, Ludergnani M, Apolone G, Corrao G. Renin-angiotensin-aldosterone system blockers and the risk of Covid-19. *N Engl J Med*. 2020;382:2431-2440. doi:10.1056/NEJMoa2006923.
26. South AM, Brady TM, Flynn JT. ACE2, COVID-19, and ACE inhibitor and ARB use during the pandemic: the pediatric perspective. *Hypertension*. 2020;76:16-22. doi:10.1161/HYPERTENSIONAHA.120.15291.
27. D'Antiga L. Coronaviruses and immunosuppressed patients: the facts during the third epidemic. *Liver Transpl*. 2020;26:832-834. doi:10.1002/lt.25756.
28. Hui DS, Azhar EI, Kim Y-J, Memish ZA, Oh M-D, Zumla A. Middle East respiratory syndrome coronavirus: risk factors and determinants of primary, household, and nosocomial transmission. *Lancet Infect Dis*. 2018;18(8):e217-e227.
29. Husain SA, Dube G, Morris H, et al. Early outcomes of outpatient management of kidney transplant recipients with coronavirus disease 2019. *Clin J Am Soc Nephrol*. 2020;15:1174-1178. doi:10.2215/CJN.05170420.
30. Banerjee D, Popoola J, Shah S, Ster IC, Quan V, Phanish M. COVID-19 infection in kidney transplant recipients. *Kidney Int*. 2020;97:P1076-P1082. doi:10.1016/j.kint.2020.03.018.
31. Columbia University Kidney Transplant Program. Early description of coronavirus 2019 disease in kidney transplant recipients in New York. *J Am Soc Nephrol*. 2020;31:1150-1156. doi:10.1681/ASN.2020030375.
32. Haberman R, Axelrad J, Chen A, et al. Covid-19 in immune-mediated inflammatory diseases—case series from New York. *N Engl J Med*. 2020;383:85-88. doi:10.1056/NEJMc2009567.
33. Zachariah P, Johnson CL, Halabi KC, et al. Epidemiology, clinical features, and disease severity in patients with coronavirus disease 2019 (COVID-19) in a Children's Hospital in New York City, New York. *JAMA Pediatr*. 2020; e202430. doi:10.1001/jamapediatrics.2020.2430.
34. RECOVERY Collaborative Group, Horby P, Lim WS, et al. Dexamethasone in hospitalized patients with Covid-19—preliminary report. *N Engl J Med*. 2020. doi:10.1056/NEJMoa2021436.
35. Marlais M, Wlodkowski T, Vivarelli M, et al. The severity of COVID-19 in children on immunosuppressive medication. *Lancet Child Adolesc Health*. 2020;4:E17-E18. doi:10.1016/S2352-4642(20)30145-0.
36. Alberici F, Delbarba E, Manenti C, et al. A single center observational study of the clinical characteristics and short-term outcome of 20 kidney transplant patients admitted for SARS-CoV-2 pneumonia. *Kidney Int*. 2020;97:P1083-P1088. doi:10.1016/j.kint.2020.04.002.
37. Alberici F, Delbarba E, Manenti C, et al. A report from the Brescia Renal COVID Task Force on the clinical characteristics and short-term outcome of hemodialysis patients with SARS-CoV-2 infection. *Kidney Int*. 2020;98:P20-P26. doi:10.1016/j.kint.2020.04.030.
38. Alberici F, Delbarba E, Manenti C, et al. Management of patients on dialysis and with kidney transplant during SARS-CoV-2 (COVID-19) pandemic in Brescia, Italy. *Kidney Int Rep*. 2020;5:P580-P585. doi:10.1016/j.ekir.2020.04.001.
39. Klein JD, Koletzko B, El-Shabrawi MH, Hadjipanayis A, Thacker N, Bhutta Z. Promoting and supporting children's health and healthcare during COVID-19—international paediatric association position statement. *Arch Dis Child*. 2020;105(7). doi:10.1136/archdischild-2020-319370.
40. Vasudevan A, Mantan M, Krishnamurthy S, et al. Managing children with renal diseases during COVID-19 pandemic. *Indian Pediatr*. 2020;57:641-651. doi: 10.1007/s13312-020-1893-8.
41. The Renal Association. Guidance for clinicians with patients receiving immunosuppression treatment for autoimmune conditions of their native kidneys during COVID-19. The Renal Association. <https://renal.org/guidance-clinicians-patients-receiving-immunosuppression-treatment-autoimmune-conditions-native-kidneys-covid-19/>. Published April, 2020. Accessed October 21, 2020.
42. The Renal Association. Checklist for renal services in respect of the COVID-19 pandemic. The Renal Association. <https://renal.org/covid-19/ra-resources-renal-professionals/checklist-renal-services-respect-covid-19-pandemic/>. Published March, 2020. Accessed October 21, 2020.

43. Bomback AS, Canetta PA, Ahn W, Ahmad SB, Radhakrishnan J, Appel GB. How COVID-19 has changed the management of glomerular diseases. *Clin J Am Soc Nephrol*. 2020;15:876-879. doi:10.2215/CJN.04530420.
44. Ryu S. Telemedicine: opportunities and developments in member states: report on the second global survey on eHealth 2009 (global observatory for eHealth series, volume 2). *Healthc Inform Res*. 2012;18:153-155. doi:10.4258/hir.2012.18.2.153.
45. Gómez-Martino JR, Suárez MAS, Gallego SD, et al. [Telemedicine applied to nephrology. another form of consultation]. *Nefrologia*. 2008;28:407-412.
46. Trnka P, White MM, Renton WD, McTaggart SJ, Burke JR, Smith AC. A retrospective review of telehealth services for children referred to a paediatric nephrologist. *BMC Nephrol*. 2015;16:125. doi:10.1186/s12882-015-0127-0.
47. Ishani A, Christopher J, Palmer D, et al. Telehealth by an inter-professional team in patients with CKD: a randomized controlled trial. *Am J Kidney Dis*. 2016;68(1):41-49.
48. American College of Rheumatology. ACR infusion guidance during COVID-19 crisis. American College of Rheumatology. <https://www.rheumatology.org/Portals/0/Files/ACR-Infusion-Guidance-COVID-19.pdf>. Published April, 2020. Accessed October 21, 2020.
49. Kronbichler A, Gauckler P, Windpessl M, et al. COVID-19: implications for immunosuppression in kidney disease and transplantation. *Nat Rev Nephrol*. 2020;16:365-367. doi:10.1038/s41581-020-0305-6.
50. Guan W-J, Liang W-H, Zhao Y, et al. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. *Eur Respir J*. 2020;55:2000547.
51. Khan N. Hypertension, ACE-inhibitors and angiotensin receptor blockers and COVID-19. Hypertension Canada. <https://hypertension.ca/wp-content/uploads/2020/03/2020-30-15-Hypertension-Canada-Statement-on-COVID-19-ACEi-ARB.pdf>. Published March, 2020. Accessed October 21, 2020.
52. Little P. Non-steroidal anti-inflammatory drugs and COVID-19. *BMJ*. 2020;368:m1185.
53. Voiriot G, Philippot Q, Elabbadi A, Elbim C, Chalumeau M, Fartoukh M. Risks related to the use of non-steroidal anti-inflammatory drugs in community-acquired pneumonia in adult and pediatric patients. *J Clin Med Res*. 2019;8:786. doi:10.3390/jcm8060786.
54. Little P, Stuart B, Andreou P, et al. Primary care randomised controlled trial of a tailored interactive website for the self-management of respiratory infections (Internet Doctor). *BMJ Open*. 2016;6:e009769.
55. World Health Organization (WHO) on Twitter. *Twitter*. <https://twitter.com/WHO/status/1240409217997189128>. Accessed October 21, 2020.
56. Moore DL. Immunization of the immunocompromised child: key principles. *Paediatr Child Health*. 2018;23(3):203-205.
57. Rubin LG, Levin MJ, Ljungman P, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. *Clin Infect Dis*. 2014;58:e44-e100.
58. Goonewardene ST, Tang C, Tan Chan KG, et al. Safety and efficacy of pneumococcal vaccination in pediatric nephrotic syndrome. *Front Pediatr*. 2019;7:339.
59. Martindale A-M, Elvey R, Howard SJ, McCorkindale S, Sinha S, Blakeman T. Understanding the implementation of “sick day guidance” to prevent acute kidney injury across a primary care setting in England: a qualitative evaluation. *BMJ Open*. 2017;7:e017241.
60. Viner RM, Mytton OT, Bonell C, et al. Susceptibility to and transmission of COVID-19 amongst children and adolescents compared with adults: a systematic review and meta-analysis. *medRxiv*; 2020.
61. Munro APS, Faust SN. Children are not COVID-19 super spreaders: time to go back to school. *Arch Dis Child*. 2020;105. <https://adc.bmj.com/content/early/2020/05/19/archdischild-2020-319474.abstract>. Published 2020. Accessed October 21, 2020.
62. Danis K, Epaulard O, Bénét T, et al. Cluster of coronavirus disease 2019 (Covid-19) in the French Alps, February 2020. *Clin Infect Dis*. 2020;71:825-832. doi:10.1093/cid/ciaa424.
63. Bromage E, Mohl B, Betancourt S, Jonas M. Coronavirus risks: know them, avoid them. *CommonWealth Magazine*. May 15, 2020. <https://commonwealthmagazine.org/environment/coronavirus-risks-know-them-avoid-them/>. Accessed October 21, 2020.
64. Why do some COVID-19 patients infect many others whereas most don't spread the virus at all?. *Science*. 2020. <https://www.sciencemag.org/news/2020/05/why-do-some-covid-19-patients-infect-many-others-whereas-most-don-t-spread-virus-all>. Accessed October 21, 2020.
65. COVID-19 superspreader events in 28, countries: critical patterns and lessons. *Quillette*. April 23, 2020. <https://quillette.com/2020/04/23/covid-19-superspreader-events-in-28-countries-critical-patterns-and-lessons/>. Accessed October 21, 2020.
66. Aubrey A, Wamsley L, Wroth C. From camping to dining out: here's how experts rate the risks of 14 summer activities. *NPR*. May 23, 2020. <https://www.npr.org/sections/health-shots/2020/05/23/861325631/from-camping-to-dining-out-heres-how-experts-rate-the-risks-of-14-summer-activit>. Accessed October 21, 2020.
67. Fléchéelles O, Fowler R, Juvet P. H1N1 pandemic: clinical and epidemiologic characteristics of the Canadian pediatric outbreak. *Expert Rev Anti Infect Ther*. 2013;11(6):555-563.
68. Boggild AK, Yuan L, Low DE, McGeer AJ. The impact of influenza on the Canadian First Nations. *Can J Public Health*. 2011;102:345-348.
69. Durrani T. COVID-19 disproportionately affects those living in poverty. And this impacts us all. *Healthy Debate*; 2020. <https://healthydebate.ca/2020/03/topic/covid-19-low-income-poverty>. Accessed October 21, 2020.
70. Giroux R, Blackstock C, Jetty R, Bennett S, Gander S. COVID-19 and Indigenous children in Canada: what can paediatricians do? *CPS Blog*. May 27, 2020. <https://www.cps.ca/en/blog-blogue/covid-19-indigenous-children-in-canada-what-can-paediatricians-do>. Accessed October 21, 2020.
71. Kogon AJ, Vander Stoep A, Weiss NS, Smith J, Flynn JT, McCauley E. Depression and its associated factors in pediatric chronic kidney disease. *Pediatr Nephrol*. 2013;28(9):1855-1861.
72. Kiliś-Pstrusińska K, Medyńska A, Adamczak P, et al. Anxiety in children and adolescents with chronic kidney disease—multicenter national study results. *Kidney Blood Press Res*. 2013;37(6):579-587.

73. Golberstein E, Wen H, Miller BF. Coronavirus disease 2019 (COVID-19) and mental health for children and adolescents. *JAMA Pediatr.* 2020;174:819-820. doi:10.1001/jamapediatrics.2020.1456.
74. Liu JJ, Bao Y, Huang X, Shi J, Lu L. Mental health considerations for children quarantined because of COVID-19. *Lancet Child Adolesc Health.* 2020;4(5):347-349.
75. Colonna C, Monzani NA, Rocchi A, Gianotti R, Boggio F, Gelmetti C. Chilblains-like lesions in children following suspected COVID-19 infection. *Pediatr Dermatol.* 2020;37:437-440. doi:10.1111/pde.14210.
76. Castelnovo L, Capelli F, Tamburello A, Maria Faggioli P, Mazzone A. Symmetric cutaneous vasculitis in COVID-19 pneumonia. *J Eur Acad Dermatol Venereol.* 2020;34:e362-e363. doi:10.1111/jdv.16589.
77. Russell CD, Millar JE, Kenneth Baillie J. Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. *Lancet.* 2020;395:473-475. doi:10.1016/s0140-6736(20)30317-2.
78. Willicombe M, Thomas D, McAdoo S. COVID-19 and calcineurin inhibitors: should they get left out in the storm? *J Am Soc Nephrol.* 2020;31:1145-1146. doi:10.1681/ASN.2020030348.
79. Carbajo-Lozoya J, Müller MA, Kallies S, Thiel V, Drosten C, von Brunn A. Replication of human coronaviruses SARS-CoV, HCoV-NL63 and HCoV-229E is inhibited by the drug FK506. *Virus Res.* 2012;165(1):112-117.
80. Ogimi C, Greninger AL, Waghmare AA, et al. Prolonged shedding of human coronavirus in hematopoietic cell transplant recipients: risk factors and viral genome evolution. *J Infect Dis.* 2017;216:203-209.
81. Alhazzani W, Møller MH, Arabi YM, et al. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19). *Intensive Care Med.* 2020;46:854-887.
82. Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the treatment of covid-19—preliminary report. *N Engl J Med.* 2020;383:992-993. doi:10.1056/NEJMoa2007764.
83. Boulware DR, Pullen MF, Bangdiwala AS, et al. A randomized trial of hydroxychloroquine as postexposure prophylaxis for covid-19. *N Engl J Med.* 2020;383:517-525. doi:10.1056/NEJMoa2016638.
84. Allam SR, Dao A, Madhira MM, et al. Interleukin-6 receptor antagonist therapy to treat SARS-CoV-2 driven inflammatory syndrome in a kidney transplant recipient. *Transpl Infect Dis.* 2020;22(4):e13326.
85. Aouba A, Baldolli A, Geffray L, et al. Targeting the inflammatory cascade with anakinra in moderate to severe COVID-19 pneumonia: case series. *Ann Rheum Dis.* 2020;79. doi:10.1136/annrheumdis-2020-217706.
86. Dimopoulos G, de Mast Q, Markou N, et al. Favorable anakinra responses in severe covid-19 patients with secondary hemophagocytic lymphohistiocytosis. *Cell Host Microbe.* 2020;28:P117-P123. <http://dx.doi.org/10.1016/j.chom.2020.05.007>.
87. Capra R, De Rossi N, Mattioli F, et al. Impact of low dose tocilizumab on mortality rate in patients with COVID-19 related pneumonia. *Eur J Intern Med.* 2020;76:31-35.
88. Luo P, Liu Y, Qiu L, Liu X, Liu D, Li J. Tocilizumab treatment in COVID-19: a single center experience. *J Med Virol.* 2020;92(7):814-818.