

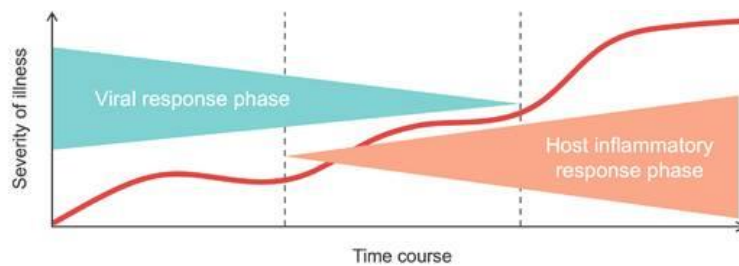
# COVID-19 Pathway v10.0: Table of Contents

**Stop and Review**

## Inclusion Criteria

- Suspected COVID-19 acute infection
- OR
- Fever AND critically ill
- OR
- Persistent fever  $\geq 3$ d AND ill-appearing AND concern for MIS-C
- OR
- Persistent unexplained fever  $\geq 5$  days

## COVID-19 (Acute COVID and MIS-C) Care



The features of acute COVID infection complicated by hyperinflammation and MIS-C may overlap; consider time course and clinical scenario and refer to both MIS-C and acute COVID algorithm as needed (Adapted from Siddiqi, HK, and Mehra, MR. 2020).

Vaccination

Acute COVID Care and Treatment

MIS-C Care and Treatment

Monoclonal Antibody Products for Mild-Moderate COVID-19

Anticoagulation in COVID-19 and MIS-C

Differential Diagnoses & Labs to Consider with Consultants

Definitions of Organ System Involvement

Resources

## Appendix

Version Changes

Approval & Citation

Evidence Ratings

Bibliography

# COVID-19 Pathway v10.0: Vaccination

- All patients and family members should receive a 2-3 dose series of COVID-19 vaccination; contraindications are age ineligible, current COVID infection or current MIS-C, severe allergy to vaccine component, received monoclonal antibody within 90 days. EUA for Pfizer vaccine if applicable by age can be found here: <https://www.cvdvaccine-us.com/>
- State-wide resource: <https://vaccinelocator.doh.wa.gov/>
- Outpatients or family members may schedule now through the [Seattle Children's public portal](#)
- Inpatient care teams may email [PatientCOVIDVaccine@seattlechildrens.org](mailto:PatientCOVIDVaccine@seattlechildrens.org) with the subject line: Inpatient Vaccination Request.
- Vaccine post-MIS-C: CDC and AAP recommend patients with a history of MIS-C should consider delaying vaccination until after they have recovered from illness (including return to normal cardiac function) and for at least 90 days following their diagnosis of MIS-C. Currently, there are limited data about the safety and efficacy of COVID-19 vaccine in patients with a history of MIS-C. Pediatricians and patients/families should participate in shared decision making in weighing risks and benefits of COVID-19 vaccination for each individual patient.

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[Acute COVID Care and Treatment](#)

[MIS-C Care and Treatment](#)

# COVID-19 Pathway v10.0: Acute COVID

**Stop and Review**

## Inclusion Criteria

- Suspected COVID-19 acute infection

## Illness Severity Definitions

### Mild

- Symptoms of viral illness or upper respiratory tract infection (such as fever, cough, diarrhea, myalgias, rhinorrhea, sore throat, etc.)

### Moderate

- Signs or symptoms of pneumonia (such as tachypnea, retractions, abnormal chest xray, etc.) AND
- No sustained hypoxia

### Severe

- Signs or symptoms of pneumonia AND
- New or increased oxygen requirement

### Critical

- Pneumonia AND one of the following:
- Requiring positive pressure ventilation OR
- Signs of sepsis or multi-organ failure

PCR+ or high clinical suspicion for COVID

Review illness severity and consider **MIS-C**

## Labs

### Tier 1 Labs

- COVID PCR if no recent positive, CBC/d, CRP, ESR, BMP, ALT, albumin
- Consider UA and RVP
- Testing guidance documents
  - Antibody Testing Indications
  - Guidance on Who to Test

### Tier 2 Labs

- BNP, troponin, D-dimer, ferritin, fibrinogen, INR/PT/PTT, specimen storage (red, freeze), COVID IgG, blood culture if indicated

Consider [Sepsis Pathway](#) labs

## Asymptomatic, Mild, or Moderate Illness

No hypoxia

- No labs indicated
- Review admission criteria
- Inpatient or outpatient supportive care and monitoring for increasing severity
- Home Quarantine
- [Monoclonal antibodies and early antiviral therapy](#)

## Severe Illness

New or increased oxygen requirement

- Tier 1 labs
- EKG, CXR
- Trend labs and add Tier 2 if symptoms worsen to monitor for complications such as hyperinflammation or MIS-C

## Critical Illness

Requires positive pressure ventilation, sepsis, or multi-organ failure

- Tier 1 and 2 labs
- Consider [Sepsis Pathway](#)
- ED Guidance: Resuscitation for High-Risk COVID Patient
- EKG, CXR, consider ECHO
- Consult PICU and Infectious Disease
- Consult Rheumatology for hyperinflammation
- Imaging for thrombi as indicated by clinical evaluation as D-dimer expected to be elevated in inflammation

**Consider MIS-C if cardiac involvement or labs indicative of severe inflammation and/or multi-organ involvement**

## Lab Evidence of Hyperinflammation

No lab criteria is diagnostic; consider if multiple markers of inflammation

### Common values:

- CRP >3 mg/dL
- ESR >40 mm/h
- ferritin >500 ng/mL
- ANC >7700
- ALC <1500
- platelet <150k
- D-dimer >2 ug/mL
- fibrinogen >400 mg/dL
- albumin <3 g/dL
- anemia for age
- ALT >40 U/L
- INR >1.1

Clinically worse OR lab evidence of hyperinflammation?

Yes

## Phase Change

Go to [Acute COVID Treatment](#)

## Inpatient Admit Criteria

Admit to Special Isolation Unit (SIU)

- Hypoxia
- Inability to tolerate PO
- Increased work of breathing (grunting, retracting, tachypnea)

## PICU Admit Criteria

- Concern for respiratory failure, sepsis
- Need for positive pressure ventilation
- Hypotension requiring inotropic support

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# COVID-19 Pathway v10.0: Acute COVID Treatment

## Acute COVID Treatment for Patients with Severe or Critical Illness

- Review [MIS-C algorithm](#) if indicated
- Plan for daily multi-disciplinary consultant and primary team discussion, and more often if escalation of care
- Consider if clinical trials are applicable
- For patient  $\geq 18$ , please refer to [NIH COVID-19 Treatment Guidelines](#)

### Antiviral Therapy:

- Remdesivir:
  - Note:** international guidelines do not have consensus on use in adults and benefit is unknown in children
  - Consider for patients with COVID pneumonia age  $\geq 12$  at higher risk of poor outcome OR  $\geq 16$  regardless of risk factors; AND both of the following
    - with severe illness and increasing need for O<sub>2</sub>
    - within first 10 days of illness
  - FDA approved for  $\geq 12$ , but may be prescribed for patients age  $< 12$  with verbal consent. See “Fact Sheet for Caregivers” in English or Spanish here <https://www.gilead.com/remdesivir>
  - Check BUN, Cr, and AST/ALT prior to initiation
  - A 5- day course of treatment is recommended for most patients; stop therapy when meeting discharge criteria

### Immunomodulatory:

- Dexamethasone: Consider for patients, especially adolescents, with critical illness or rapidly progressive severe illness
  - 0.15 mg/kg/dose (6 mg max) once daily for up to 10 days or until discharge
- Other corticosteroids: Consider for ARDS or in consultation with Rheumatology for hyperinflammation
- Biologic immunomodulatory medications
  - In consultation with Rheumatology for hyperinflammation

### Adjunctive:

- Mechanical thromboprophylaxis with SCDs if possible
- Prophylactic anticoagulation with heparin or enoxaparin if severely or critically ill with risk factors (see [anticoagulation page](#))
- Stress dose hydrocortisone: For patients on chronic glucocorticoids if febrile, requiring O<sub>2</sub>, hypotensive, or unexplained vomiting

## Discharge Instructions

### Isolation:

- Determine length of isolation and need for repeat testing based on severity of illness, first positive PCR or onset of illness, and immunosuppression (patients receiving steroids are considered immunosuppressed by IP) using Infection Prevention Guidance document (*for SCH only*)
- Advise family, PCP, and followup providers of end date of isolation and, if immunosuppressed, that repeat PCR x2 after 20 days of isolation is needed to end healthcare facility-based isolation (it should not be needed to end home isolation)
- Please obtain repeat PCR if result may clear patient from healthcare facility-based isolation (ex: if immunosuppressed and 20 days have passed since first positive PCR)

### Return to sports or exercise:

- **Children with asymptomatic/mild illness:** PCP evaluation after isolation period.
- **Children with moderate/severe illness (prolonged fever or hospitalized):** PCP evaluation and an ECG after symptom resolution and after isolation.
- **Children with critical illness/MIS-C:** No strenuous exercise for least three to six months and obtain cardiology clearance prior to resuming training or competition (refer prior to discharge).

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# COVID-19 Pathway v10.0: MIS-C

**Stop and Review**

!

**Consider differential diagnosis including acute COVID**

## Inclusion Criteria

- Fever AND critically ill
- OR
- Persistent fever  $\geq 3$ d AND ill-appearing AND concern for MIS-C
- OR
- Persistent unexplained fever  $\geq 5$  days

## MIS-C Case Definitions

- [CDC](#)
- [WHO](#)

## Clinical Features/Evidence of MIS-C

- Most patients have  $\geq 4$  organ system involvement;  $\geq 2$  required for diagnosis
- Involvement of following systems (percent of patients in case series):
  - Gastrointestinal (92%)
  - Cardiovascular (80%)
  - Hematologic (76%)
  - Mucocutaneous (74%, 59% had rash)
  - Respiratory (70%)
  - Musculoskeletal (23%)
  - Renal (8%)
  - Neurologic (6%)
  - See [definitions](#) of organ system involvement
- Recent COVID illness OR exposure (note: not necessary to suspect MIS-C)

## Lab Evidence of MIS-C

- No lab criteria is diagnostic; most patients have 4 or more markers of inflammation*
- **Evidence of inflammation, common values:** CRP  $>3$  mg/dL, ESR  $>40$  mm/h, ferritin  $>500$  ng/mL, ANC  $>7700$ , ALC  $<1500$ , platelet  $<150k$ , D-dimer  $>2$  ug/mL, fibrinogen  $>400$  mg/dL, albumin  $<3$  g/dL, anemia, ALT  $>40$  U/L, INR  $>1.1$
  - **Other:** AKI, hyponatremia, high LDH, high troponin, BNP  $>400$  pg/mL, prolonged PT or PTT; If ESR low but high ferritin and CRP, consider MAS

*Percentages and values adapted from Feldstein et al, NEJM June 2020*

- **Initial Labs:** CBCd, CRP, ESR, BMP, ALT, albumin, UA, COVID PCR, COVID IgG, RVP
- **Additional Labs:** BNP, troponin, ferritin, D-dimer, coags, fibrinogen, LDH, blood culture if indicated, red top to hold prior to IVIG (freeze), further labs on consultant advice

## Signs of Shock?

Yes

No

- Obtain **Initial Labs**
- If high clinical suspicion, add **Additional Labs***
- CXR (if resp sx)

- Obtain **Initial and Additional Labs**, EKG, CXR
- ECHO (early if signs of cardiac dysfunction)
- Consider [Sepsis Pathway](#)
- Caution with boluses; monitor for cardiac dysfunction*

## Lab Evidence of MIS-C?

Yes

No

- Consider alternate diagnoses
- Consider discharge with close follow-up

- Obtain **Additional Labs**
- EKG
- Contact Cardiology to discuss necessity/timing of Echo

## Complete or Incomplete Kawasaki?

Yes

No

- Follow [Kawasaki Disease Pathway](#) if COVID testing negative or while pending
- Monitor closely for signs of shock

## Evidence of MIS-C without alternate diagnosis?

Yes

**Phase Change**  
Go to [MIS-C Treatment](#)

**PCR or IgG+ with recent exposure/ infection OR cardiac dysfunction**

**Patients with MIS-C have significant risk for developing shock**

## Inpatient Admit Criteria

- Admit to Special Isolation Unit (SIU)
- Suspected MIS-C (review case definition "clinically severe illness")

## PICU Admit Criteria

- Altered mental status
- Concern for respiratory failure, sepsis
- Need for positive pressure ventilation
- Hypotension or shock

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# COVID-19 Pathway v10.0: MIS-C Treatment

**Review case definition:** age <21, >24h fever, lab evidence of inflammation (most patients have 4 or more markers), multi-system involvement, and clinically seriously ill, without alternative diagnosis (review [differential diagnosis](#)) plus confirmed recent SARS-CoV-2 or known exposure within 6 weeks. (For age >21 see NIH Guidelines for adults)

- ECHO if not already done; repeat as indicated
- Antibiotics per Sepsis Pathway only if and while bacterial infection suspected
- Consider supportive care only for patients who have mild\* illness; monitor for increasing severity until clearly improving
- Consult Infectious Disease, Cardiology, and Rheumatology as needed to support primary team diagnostic or therapeutic decision making

## First-line treatment for all seriously\* ill patients with MIS-C:

- IVIG 2 g/kg (use ideal body weight, max dose 100g) over 12 hours
- Anti-platelet: ASA 3-5 mg/kg (max of 81 mg) due to risk of developing coronary aneurysms, hold ASA if Plt <50 k
- Mechanical thromboprophylaxis with SCDs if possible
- Anticoagulation prophylaxis is usually indicated: see [anticoagulation page](#)
- Steroids are indicated for most seriously ill patients with MIS-C; consider short course (3-5 days) for patients who are not critically ill and improve rapidly, or wean over 2-3 weeks
  - Methylprednisolone 1-2 mg/kg/day divided BID (max dose 30mg BID for low/mod dose), PO route when tolerating diet
  - Consider higher dose steroids (methylprednisolone 10mg/kg/day) for patients who are worsening despite treatment, or with moderately or severely depressed cardiac function, in consultation with Heart Failure team and Rheumatology
  - Start H2 blocker for GI ulcer prophylaxis while on both steroids and ASA

**Second-line:** Anakinra if not improving post steroid initiation or if labs suggestive of MAS

- 4 mg/kg/dose q6 hours (or frequency per Rheumatology), max dose 100 mg/dose

Trend CBCd, CRP, LDH, ALT, Albumin, Ferritin, Creatinine, Lytes, D-Dimer, Fibrinogen and BNP (frequency dependent on clinical status and medication weaning; post-discharge labs per consultants)

*Classification of illness severity is not well defined. Consider:*

*\*Mild: Normal vital signs apart from fever, does not meet inpatient criteria other than poor PO, mild dehydration, or monitoring for worsening.*

*\*Serious: Definitively meets case definition and any of: ill-appearing, evidence of organ dysfunction/injury, require for respiratory or cardiovascular support.*

## Discharge Instructions

### Isolation

- Determine length of isolation and need for repeat testing based on severity of illness, first positive PCR or onset of illness, and immunosuppression (patients receiving steroids are considered immunosuppressed by IP) using Infection Prevention Guidance document (*for SCH only*)
- Advise family, PCP, and followup providers of end date of isolation and, if immunosuppressed, that repeat PCR x2 after 20 days of isolation is needed to end healthcare facility-based isolation (it should not be needed to end home isolation)
- Please obtain repeat PCR if result may clear patient from healthcare facility-based isolation (ex: if immunosuppressed and 20 days have passed since first positive PCR)
- Avoid NSAIDs while on aspirin

### Return to sports or exercise

- **Children with asymptomatic/mild illness:** PCP evaluation after isolation period.
- **Children with moderate/severe illness (prolonged fever or hospitalized):** PCP evaluation and an ECG after symptom resolution and after isolation.
- **Children with critical illness/MIS-C:** No strenuous exercise for least three to six months and obtain cardiology clearance prior to resuming training or competition (refer prior to discharge).

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# Monoclonal Antibodies and Antiviral Medications for Mild-Moderate COVID-19

**Background:** FDA Emergency Use Authorizations (EUAs) allow for the use of monoclonal antibody products and oral antivirals for early treatment of mild-moderate COVID-19 in high-risk patients. Efficacy of specific drugs varies with current circulating SARS-CoV-2 variants. Supplies of all of these products remain limited.

**Guidance statement:** Based on current evidence available, we suggest *against* routine administration of these treatments for COVID-19 in most children or adolescents. Rather, the Seattle Children's Hospital COVID-19 Therapeutics Committee will consider the use of monoclonal antibodies and other therapies on a case-by-case basis for outpatients at high risk of progression to severe disease.

**Rationale:** There are limited safety or efficacy data for these products in pediatric patients. Based on our experience both internally and around the globe, pediatric patients in general have lower risk of progression to severe disease and poor outcomes. In addition, clear risk factor stratification data is limited. Finally, supplies of these products are very limited at this time and based on allotments from the public health department.

## Eligibility criteria:

1. Severe immunocompromise, Severe obesity (BMI  $\geq$  35 or 95%ile), Medical complexity WITH respiratory technology dependence OR
2. MULTIPLE moderate risk factors (diabetes, other immunocompromise, sickle cell disease, obesity (BMI  $\geq$  25 or 85%ile), other medical complexity, chronic cardiac, respiratory or kidney disease)
3. Most products require children to be at least 12 years of age and 40 kg

In times of limited availability, monoclonal antibody therapy will be prioritized for those who are incompletely vaccinated or unlikely to respond to vaccination.

## Exclusion criteria:

Hospitalization for COVID-19, O<sub>2</sub> requirements for COVID-19, SARS-CoV-2 antibody positive, infection >10 days

SCH Providers should email intake form to [COVIDmab@seattlechildrens.org](mailto:COVIDmab@seattlechildrens.org)

Local referring providers should call SCH Infectious Disease On Call or email [COVIDmab@seattlechildrens.org](mailto:COVIDmab@seattlechildrens.org)

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# Monoclonal Antibody Products for Mild-Moderate COVID-19 References

FDA EUA for sotrovimab (22 Dec 2021): [GSK Sotrovimab Fact Sheet for HCP \(fda.gov\)](#)

NIH COVID-19 Treatment guidelines (1 Feb 2022): [Anti-SARS-CoV-2 Monoclonal Antibodies | COVID-19 Treatment Guidelines \(nih.gov\)](#)

NIH prioritization statement (23 Dec 2021): [Statement on Prioritization of Anti-SARS-CoV-2 Monoclonal Antibodies | COVID-19 Treatment Guidelines \(nih.gov\)](#)

King County prioritization (28 Dec 2021): [Interim-DOH Guidance on Prioritization for Use of Anti-SARS-CoV-2 Monoclonal Antibodies \(wa.gov\)](#)

NIH Pediatric specific guidance (Apr 2021): [Children | COVID-19 Treatment Guidelines \(nih.gov\)](#)

Wolf, J., Abzug, M., Anosike, B., Vora, S., et al. J Pediatric Infect Dis Soc. 2022 February 2, piab124: [Updated Guidance on Use of Monoclonal Antibody Therapy for Treatment of COVID-19 Adolescents](#)

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# Anticoagulation in COVID-19 and MIS-C

Patients with severe or critical acute COVID infection or MIS-C are likely at higher risk for thrombosis and therefore should be considered for anticoagulation; review criteria to determine if they require low dose or therapeutic dosing. Also use mechanical thromboprophylaxis with SCDs if possible.

- Relative contraindications to anticoagulation include active major bleeding, platelet level <50,000, and fibrinogen <100mg/dL.
- Discontinue prophylactic anticoagulation at discharge or earlier if patients are improved and risk factors resolved; consider continuation post-discharge for ongoing severe inflammation with other risk factors.
- Consult Hematology for documented thrombosis or as indicated for recommendations in unusual circumstances.
- Asymptomatic, mild, or moderate COVID is not an indication for anticoagulation, use standard indications.

## Indications for low dose anticoagulation (LMWH goal=0.2-0.4units/mL or UFH goal=0.1-0.3units/mL):

Hospitalized with MIS-C or severe/critical COVID-19

AND one or more of the following risk factors:

- D-dimer >2.5 mcg/mL
- Age >12 years or post-pubertal
- Obesity (>95th %ile)
- Concomitant estrogen-containing oral contraceptive use
- First degree family history of unprovoked VTE
- History of thrombosis or acquired or inherited thrombophilia
- Central venous catheter
- Any rhythm abnormalities: heart block, etc.
- Inotropic infusion requirement
- Sedated and muscle-relaxed or complete immobility
- Active malignancy, nephrotic syndrome, flare of underlying inflammatory disease state, sickle cell VOC
- Congenital or acquired heart disease with venous stasis or impaired venous return

## Indications for therapeutic anticoagulation (LMWH goal=0.5-1units/mL or UFH goal=0.3-0.6units/mL):

Hospitalized with MIS-C or severe/critical COVID-19

AND One or more of the following:

- Documented thrombosis (also consult Hematology)
- Moderate to severe ventricular dysfunction per Cardiology
- Coronary aneurysm Z score >10
- **Consider therapeutic anticoagulation for active malignancy, nephrotic syndrome, flare of underlying inflammatory disease state, heart disease with venous stasis or impaired venous return, personal history of thrombosis, or multiple risk factors – discuss indications with specialist managing underlying condition and/or hematology**

Continue therapeutic dosing while indicated and formulate outpatient plan with consultants

Adapted from Goldenberg et al, 2020

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# Differential Diagnoses

## **Kawasaki Disease**

- More common in younger children, if COVID testing negative, and without shock/cardiac dysfunction
- SARS-CoV-2 antibody can remain positive for months after infection and does not necessarily indicate recent infection

## **Bacterial Infections/Sepsis**

- Obtain cultures and evaluate for source
- Consider meningitis

## **Staph/Strep Toxin-Mediated or Post-Infectious**

- Consider Toxic Shock or Acute Rheumatic Fever
- Obtain cultures and evaluate for source including gynecologic or scarlet fever

## **Staph Scalded Skin Syndrome (SSSS)**

- Increasing erythema and bullae
- Younger children
- Obtain cultures

## **Tick-Borne Illnesses**

- With epidemiologic risk factors
- Rocky Mountain Spotted Fever or Leptospirosis

## **Viral Infections**

- Measles, adenovirus, enterovirus, active COVID infection

## **Myocarditis**

- May overlap with MIS-C or have alternate cause

## **Drug Hypersensitivity Reactions**

- Consider SJS, DRESS, or serum sickness like reaction
- History of recent or semi-recent exposure to drug; consider with arthralgias and diffuse mucositis

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# Definitions of Organ System Involvement

## Gastrointestinal 92%

- Nausea/vomiting
- Diarrhea
- Abdominal pain
- Appendicitis
- Pancreatitis
- Hepatitis
- Gallbladder hydrops or edema

## Cardiovascular 80%

- Hypotension or shock
- Cardiac dysrhythmia or arrhythmia
- Ejection fraction <55%
- Pulmonary edema due to left heart failure
- Coronary artery z score  $\geq 2.5$
- Pericarditis or pericardial effusion or valvulitis
- B-type natriuretic peptide (BNP) >400 pg/mL
- Elevated troponin
- Receipt of vasopressor or vasoactive support
- Receipt of cardiopulmonary resuscitation (CPR)

## Hematologic 76%

- Total white blood cell <4k
- Anemia for age
- Platelet count <150,000 / $\mu$ L
- Deep vein thrombosis
- Pulmonary embolism
- Hemolysis
- Bleeding or prolonged PT/PTT
- Ischemia of an extremity

## Mucocutaneous 74%

- Bilateral conjunctival injection
- Oral mucosal changes
- Rash or skin ulcers
- 'COVID' toes
- Swollen red cracked lips
- Erythema of palms or soles
- Edema of hands or feet
- Periungual (nails) desquamation

## Respiratory 70% (more frequent in teens)

- Receipt of mechanical ventilation or any type of supplemental oxygen (or increased support for patients receiving respiratory support at baseline)
- Severe bronchospasm requiring continuous bronchodilators or
- Pulmonary infiltrates on chest radiograph
- Lower respiratory infection
- Pleural effusion
- Pneumothorax or other signs of barotrauma
- Pulmonary hemorrhage
- Chest-tube or drainage required

## Musculoskeletal 23% (more frequent in teens)

- Arthritis or arthralgia
- Myositis or myalgia

## Renal 8%

- Acute kidney injury with or without dialysis

## Neurologic 6%

- Stroke or acute intracranial hemorrhage
- Seizures
- Encephalitis, aseptic meningitis, or demyelinating disorder
- Altered mental status
- Suspected meningitis with negative culture

*Adapted from Feldstein et al, NEJM June 2020*

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## Resources (All Languages)

### Info for parents on child's illness and home care:

[For parents and guardians: what to do when you or your child gets COVID-19 - King County](#)

[How to care for yourself or others with COVID-19 - King County](#)

### Isolation/Quarantine/Testing:

Isolation vs Quarantine: [Isolation and Quarantine for COVID-19: WA Department of Health](#)

Testing: [COVID-19 testing in King County](#)

### Financial assistance:

In King County to stay home from work: [Household Assistance Request program – King County](#)

In other counties in WA: [Care Connect Washington: WA Department of Health](#)

### WA State resources:

List of COVID resources and vaccine locator: [WA State Coronavirus Response \(COVID-19\)](#)

### Vaccine information:

CDC information: [Key things to Know About COVID-19 Vaccines](#)

Vaccine locator above under WA State Resources

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# Summary of Version Changes

- **Version 1.0 (7/9/2020):** Go live.
- **Version 2.0 (8/13/2020):** Removed CK and triglycerides from Labs. Added consult with Cardiology with Echo and added Indications for therapeutic dosing of anticoagulation to Treatment page.
- **Version 3.0 (9/17/2020):** Added Acute COVID algorithm and treatment pages.
- **Version 4.0 (12/21/2020):** Changes include
  - Updated document to the new CSW algorithm template (incl. a Table of Contents)
  - Added illustration of time course highlighting overlap between viral phase and inflammatory phase
  - Acute COVID Tier 1 labs edited to remove D-dimer, LDH, and ferritin; those were moved to Tier 2 due to concern for overuse, guidance added on getting Tier 2 labs for “worsening” cases
  - Added advice on interpreting D-dimer
  - Monoclonal antibody guidance added
  - Updated anticoagulation information: indications for prophylactic and therapeutic dosing as well as contraindications were edited based on Goldenberg et al, 2020.
  - Inpatient and PICU admit criteria added to MIS-C algorithm
  - Steroid wean over “2-3” weeks changed from “minimum 3 weeks” based on ACR guidelines
  - Discharge isolation guidance box added
  - SIU Policies and Guidance page added
  - Bibliography edited to reflect current references
- **Version 5.0 (5/11/2021):** Updated verbiage to reflect appropriate consultation for Acute COVID treatment, updated policy and job aid links, and added appropriate citations to Monoclonal Antibody Products page and Bibliography.
- **Version 6.0 (7/8/2021):** Changed wording to encourage steroid treatment for critically ill patients with MIS-C and added recommendation for post-discharge sports clearance.
- **Version 7.0 (11/4/2021):** Changes include
  - Added Vaccination tab with information and resources
  - Updated language for Acute COVID Treatment Remdesivir guidance
  - Added NSAID recommendation to MIS-C Treatment Discharge Instructions
  - Updated language and added current FDA EUA references to Monoclonal Antibody Products for Mild-Moderate COVID-19 page
  - Updated the COVID-19 mAb Intake Form
  - Updated Resources page (formerly titled SIU Policies and Guidance) to include Patient and Family Handouts and Website COVID Resources
- **Version 8.0 (12/22/2021):** Changes include
  - Updated language on Monoclonal Antibody Products for Mild-Moderate COVID-19 page
  - Updated references on Monoclonal Antibody Products for Mild-Moderate COVID-19 References page
- **Version 9.0 (1/4/2022):** Changes include
  - Updated language on Monoclonal Antibodies and Antiviral Medications for Mild-Moderate COVID-19 page per new guidelines
  - Updated references on Monoclonal Antibody Products for Mild-Moderate COVID-19 References page

## Summary of Version Changes, page 2

- **Version 9.1 (1/25/2022):** Updated link to COVID-19 Monoclonal Antibody and Antiviral Intake Form
- **Version 10.0 (3/15/2022):** Changes include
  - Added information regarding vaccines post-MIS-C
  - Updated MIS-C treatment consultation recommendation
  - Updated MIS-C first line treatment, adding steroids to first line for most seriously ill patients and including greater specificity for steroid use
  - Updated Monoclonal Antibody Products for Mild-Moderate COVID-19 References with current guidance
  - Added information to Differential Diagnoses page under Kawasaki Disease

# Approval & Citation

Approved by the CSW COVID-19 Pathway team for December 21, 2020, go-live

## CSW COVID-19 Pathway Team:

Hospital Medicine, Owner	Katie Kazmier, MD
PICU, Stakeholder	Jesselle Albert, MD, MHA
Immunology, Stakeholder	Maite de la Morena, MD
Medical Unit, SIU, Stakeholder	Chelsea Eckart, MN, RN, CPN
Emergency Medicine, Stakeholder	Sara Fenstermacher, MSN, RN, ACCNS-P
Emergency Medicine, Stakeholder	Emily Hartford, MD, MPH
Rheumatology, Stakeholder	Kristen Hayward, MD, MS
Cardiology, Stakeholder	Mariska Kemna, MD
Hematology, Stakeholder	Dana Matthews, MD
Pharmacy, Stakeholder	Jenna Nickless, PharmD
GME (Resident), Stakeholder	Sarah Nutman, MD
Cardiology, Stakeholder	Michael Portman, MD
Urgent Care, Stakeholder	Denise Shushan, MD
PICU, Stakeholder	Hector Valdivia, MN, ARNP, ACCNS-P, CCRN
Infectious Disease, Stakeholder	Surabhi (Sara) Vora, MD, MPH
Infectious Disease, Stakeholder	Alpana Waghmare, MD

## Clinical Effectiveness Team:

Consultant	Surabhi Vora, MD, MPH
Project Manager	Dawn Hoffer, SAPM
Data Analyst	Wren Haaland, MPH, Clinical Analytics
Librarian	Peggy Cruse, MLIS, Library
Program Coordinator	Ivan Meyer, PMP

## Clinical Effectiveness Leadership:

Medical Director	Darren Migita, MD
Operations Director	Jaleh Shafii, RN, MS

Retrieval Website: <https://www.seattlechildrens.org/pdf/covid-19-pathway.pdf>

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# Evidence Ratings

This pathway was developed through local consensus based on published evidence and expert opinion as part of Clinical Standard Work at Seattle Children's. Pathway teams include representatives from Medical, Subspecialty, and/or Surgical Services, Nursing, Pharmacy, Clinical Effectiveness, and other services as appropriate.

When possible, we used the GRADE method of rating evidence quality. Evidence is first assessed as to whether it is from randomized trial or cohort studies. The rating is then adjusted in the following manner (from: Guyatt G et al. J Clin Epidemiol. 2011;4:383-94, Hultcrantz M et al. J Clin Epidemiol. 2017;87:4-13.):

Quality ratings are *downgraded* if studies:

- Have serious limitations
- Have inconsistent results
- If evidence does not directly address clinical questions
- If estimates are imprecise OR
- If it is felt that there is substantial publication bias

Quality ratings are *upgraded* if it is felt that:

- The effect size is large
- If studies are designed in a way that confounding would likely underreport the magnitude of the effect OR
- If a dose-response gradient is evident

## Certainty of Evidence

★★★★ High: The authors have a lot of confidence that the true effect is similar to the estimated effect

★★★○ Moderate: The authors believe that the true effect is probably close to the estimated effect

★★○○ Low: The true effect might be markedly different from the estimated effect

★○○○ Very low: The true effect is probably markedly different from the estimated effect

Guideline: Recommendation is from a published guideline that used methodology deemed acceptable by the team

Expert Opinion: Based on available evidence that does not meet GRADE criteria (for example, case-control studies)

# 2020 Bibliography

## Literature Search Methods

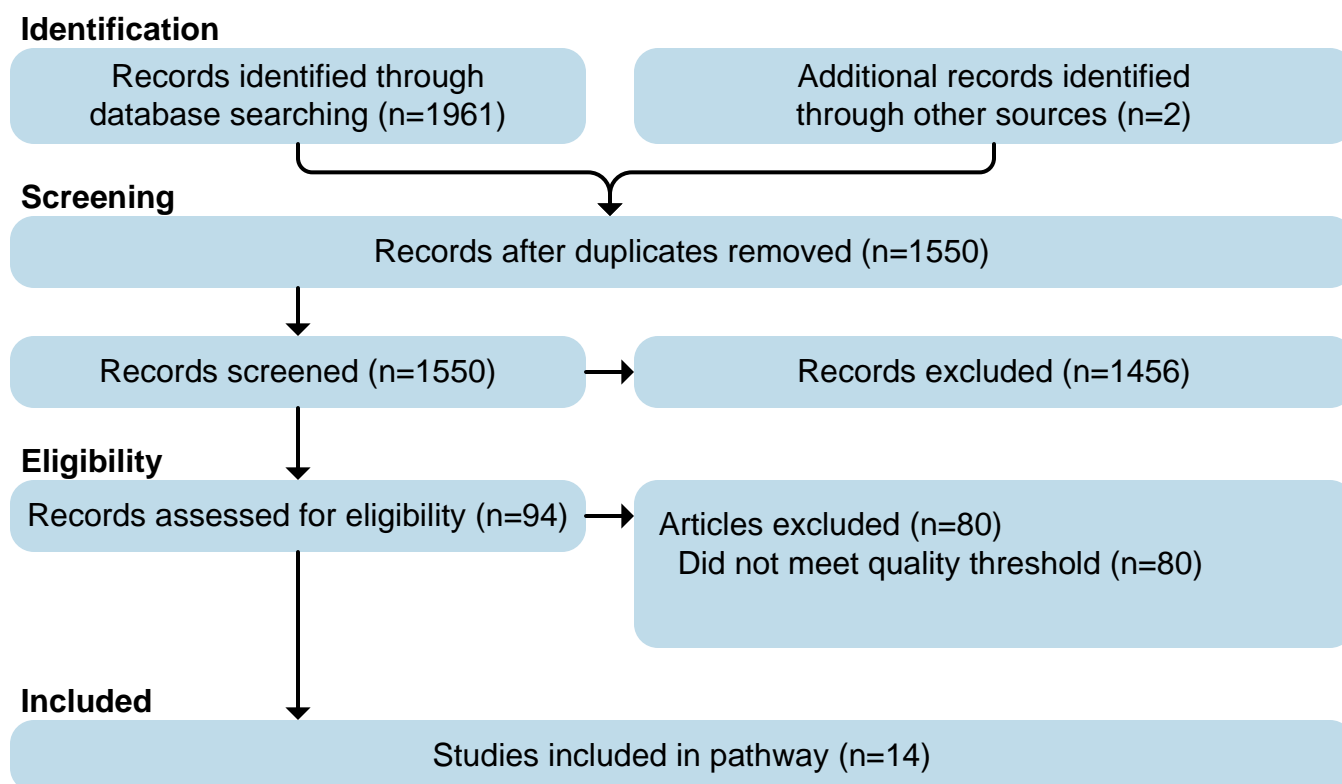
Both CDC and WHO case definitions were utilized in the development of this pathway. The articles cited are a representation of local and international experts' and national societies' resources that were being shared widely, some pre-publication and many that were published by the centers that were diagnosing and treating this new syndrome as the pandemic swept across the globe.

A systematic literature review is in process and may inform future versions of this document. Due to the rapidly evolving literature and the need for urgent guidance, a non-systematic review was used to guide the development of the initial version of this algorithm.

## Literature Search Results

The search retrieved 1961 records. Once duplicates had been removed, we had a total of 1550 records. We excluded 1173 records based on titles and abstracts. We obtained the full text of the remaining 94 records and excluded 80. We included 14 studies. The flow diagram summarizes the study selection process.

December 2020



Flow diagram adapted from Moher D et al. BMJ 2009;339:bmj.b2535

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