



# COVID-19 Follow-up Care

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# Speaker Disclosure

Speakers are required to disclose any commercial relationships before today's presentation.





# Objectives

- Discuss clinical presentations, progression, and evidence for risk factors such as HIV and any evidence leading to COVID-19 complications
- Describe what is known to date about “long-haulers” and follow-up care of COVID-19
- Identify current best practices and discuss potential follow-up care options

# COVID-19: US Data

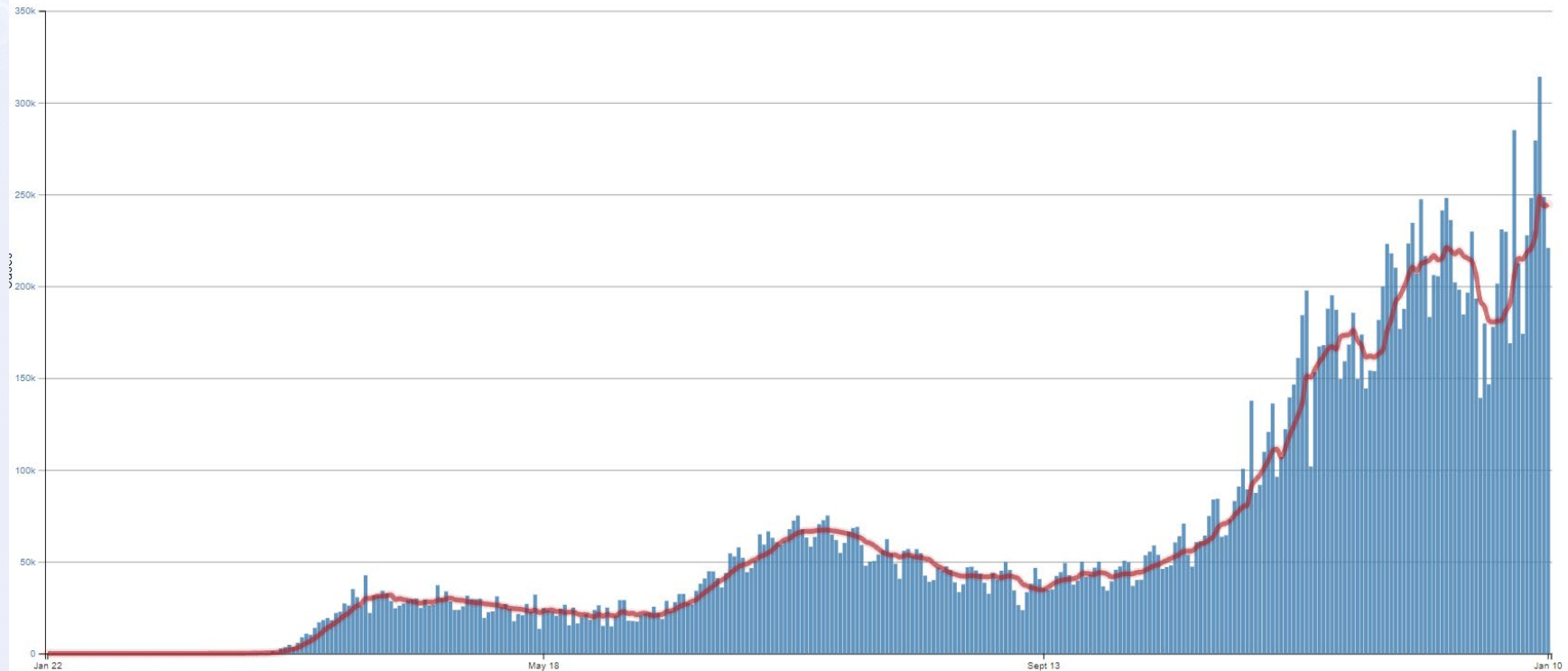
TOTAL CASES  
**22,322,956**  
+220,887 New Cases

AVERAGE DAILY CASES PER 100K IN LAST 7  
DAYS  
**74.1**

TOTAL DEATHS  
**373,167**  
+2,083 New Deaths

CDC | Updated: Jan 11 2021 12:16PM

Daily Trends in Number of COVID-19 Cases in the United States Reported to CDC



[covid.cdc.gov/covid-data-tracker](https://covid.cdc.gov/covid-data-tracker)

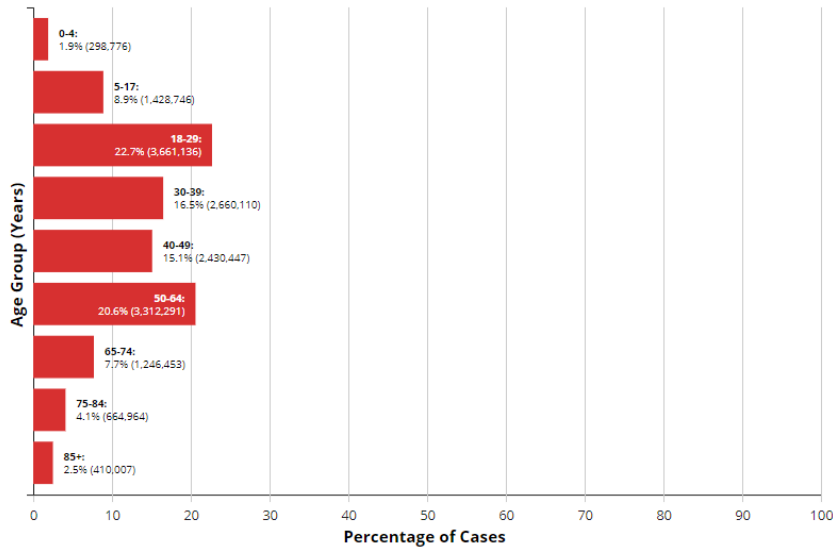


# COVID-19: US Demographic Age Data

## Cases by Age Group:

Download

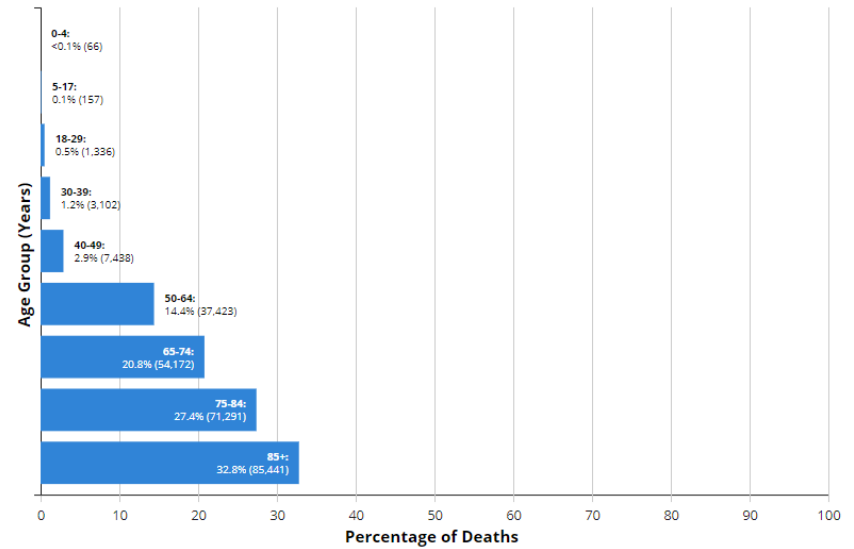
Data from 16,212,877 cases. Age group was available for 16,112,930 (99%) cases.



## Deaths by Age Group:

Download

Data from 260,456 deaths. Age group was available for 260,426 (99%) deaths.



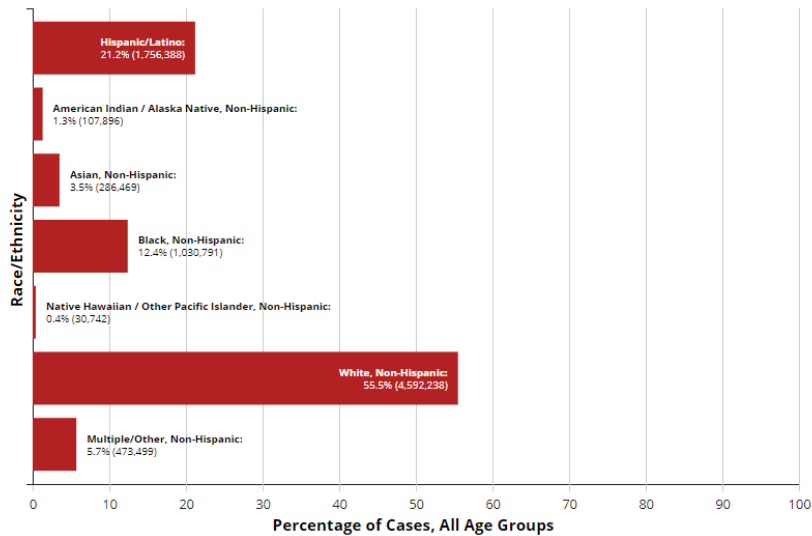
# COVID-19: US Demographic Race/Ethnicity Data

## Cases by Race/Ethnicity:

Download

Data from 16,212,877 cases. Race/Ethnicity was available for 8,278,023 (51%) cases.

All Age Groups

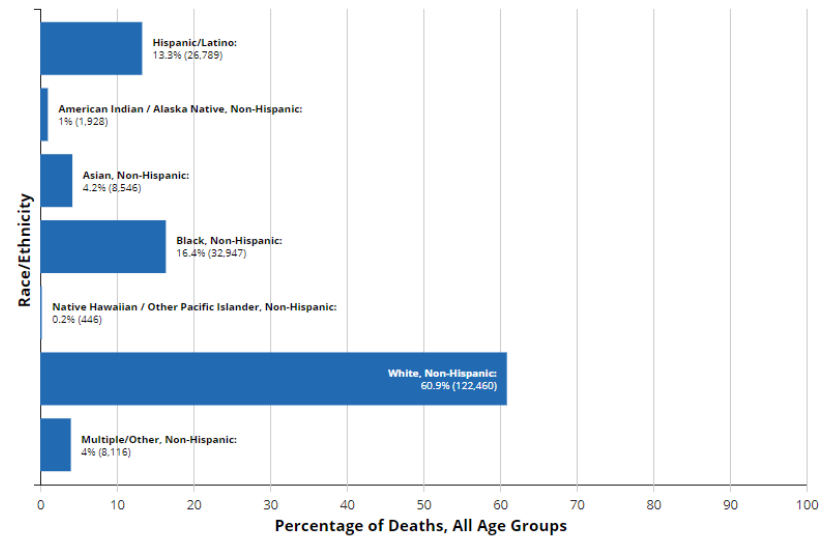


## Deaths by Race/Ethnicity:

Download

Data from 260,456 deaths. Race/Ethnicity was available for 201,232 (77%) deaths.

All Age Groups







# Clinical Presentations

# COVID-19 Clinical Presentations (1)

- **Asymptomatic:** remain symptom free even after diagnosis
- **Presymptomatic:** no symptoms at diagnosis, but eventually develop them
- **Mild:** symptomatic without SOB, dyspnea on exertion, or abnormal CXR
- **Moderate:** SOB/dyspnea with abnormal lung exam and/or lung imaging (but not hypoxic,  $>94\%$  on RA)
- **Severe:** hypoxic  $<94\%$  on RA, or  $RR > 30$  bpm, lung infiltrates  $>50\%$ , or  $P/F < 300$ 
  - **Critical:** ARDS, shock, end organ damage
- **Ongoing symptomatic COVID-19:** symptoms 4 weeks to 12 weeks from onset
- **Post-COVID:** symptoms persisting beyond 12 weeks, not explained by other diagnosis

NIH, COVID19 Treatment Guidelines





	<b>Asymptomatic or Presymptomatic</b>	<b>Mild Illness</b>	<b>Moderate Illness</b>	<b>Severe Illness</b>	<b>Critical Illness</b>
<b>Features</b>	Positive SARS-CoV-2 test; no symptoms	Mild symptoms (e.g., fever, cough, or change in taste or smell); no dyspnea	Clinical or radiographic evidence of lower respiratory tract disease; oxygen saturation $\geq 94\%$	Oxygen saturation $< 94\%$ ; respiratory rate $\geq 30$ breaths/min; lung infiltrates $> 50\%$	Respiratory failure, shock, and multiorgan dysfunction or failure
<b>Testing</b>	Screening testing; if patient has known exposure, diagnostic testing	Diagnostic testing	Diagnostic testing	Diagnostic testing	Diagnostic testing
<b>Isolation</b>	Yes	Yes	Yes	Yes	Yes
<b>Proposed Disease Pathogenesis</b>	<p>Viral replication (blue arrow) spans from Asymptomatic/Presymptomatic to Severe Illness. Inflammation (red arrow) spans from Mild Illness to Critical Illness.</p>				
<b>Potential Treatment</b>	<p>Antiviral therapy (blue bar) spans from Asymptomatic/Presymptomatic to Moderate Illness. Antibody therapy (yellow bar) spans from Mild Illness to Severe Illness. Anti-inflammatory therapy (orange bar) spans from Severe Illness to Critical Illness.</p>				
<b>Management Considerations</b>	Monitoring for symptoms	Clinical monitoring and supportive care	Clinical monitoring; if patient is hospitalized and at high risk for deterioration, possibly remdesivir	Hospitalization, oxygen therapy, and specific therapy (remdesivir, dexamethasone)	Critical care and specific therapy (dexamethasone, possibly remdesivir)

# COVID-19 Clinical Presentations (2)

- Estimated 40-45% of infections remain asymptomatic<sup>1</sup>
- Of those who develop clinical disease (ie symptoms)<sup>2,3</sup>
  - Mild to Moderate: ~ 80%
  - Severe: ~14%
  - Critical: ~2-5%
- Mortality: 1-3%

1. Oran and Topol, *Annals*, September 2020
2. Wu and McGoogan, *JAMA*, February 2020
3. Stokes et al, *MMWR*, June 2020



# Risk Factors for Progression to Severe Disease

Strong Evidence	Mixed/Limited Evidence
Cancer	Asthma
Chronic Kidney Disease	Cerebrovascular Disease
COPD	Hypertension
CAD/CHF/cardiomyopathy	Use of steroids or immunosuppressant medications
Obesity (BMI 30+)	Bone Marrow Transplant
Pregnancy	HIV
Smoking	Immune Deficiencies
Sickle Cell Disease	Inherited metabolic disorders
Solid Organ Transplant	Liver Disease
Type 2 DM	Neurologic disorders
	Other chronic lung disease
	Overweight (BMI 24 - <30)
	Thalassemia
	Type 1 DM

<https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/evidence-table.html>







# COVID-19 Complications

# Complications from COVID-19 (1)

- 1. Pulmonary: Acute Respiratory Distress Syndrome
- 2. Cardiovascular: Myocarditis, arrhythmias, acute cardiac injury
- 3. Thromboembolic: acute stroke, pulmonary embolus, DVT
- 4. Inflammatory complications: “cytokine release storm” but also multisystem inflammatory syndrome (MIS-C), Guillain-Barre syndrome
- 5. Secondary coinfections: bacterial infections most common (10% or higher); reports of invasive aspergillus in some case series





# COVID-19: ARDS and Pulmonary Disease - Incidence

- Incidence of ARDS development varies by patient population
- Among all hospitalized patients: ~25% were admitted to ICU
- Among all hospitalized patients: ~33% developed ARDS
- Among all ICU patients: ~75% developed ARDS
- Among all patients (outpatient and inpatient): 3 – 17% developed ARDS

Tzotzos et al, *Crit Care*, Aug 2020





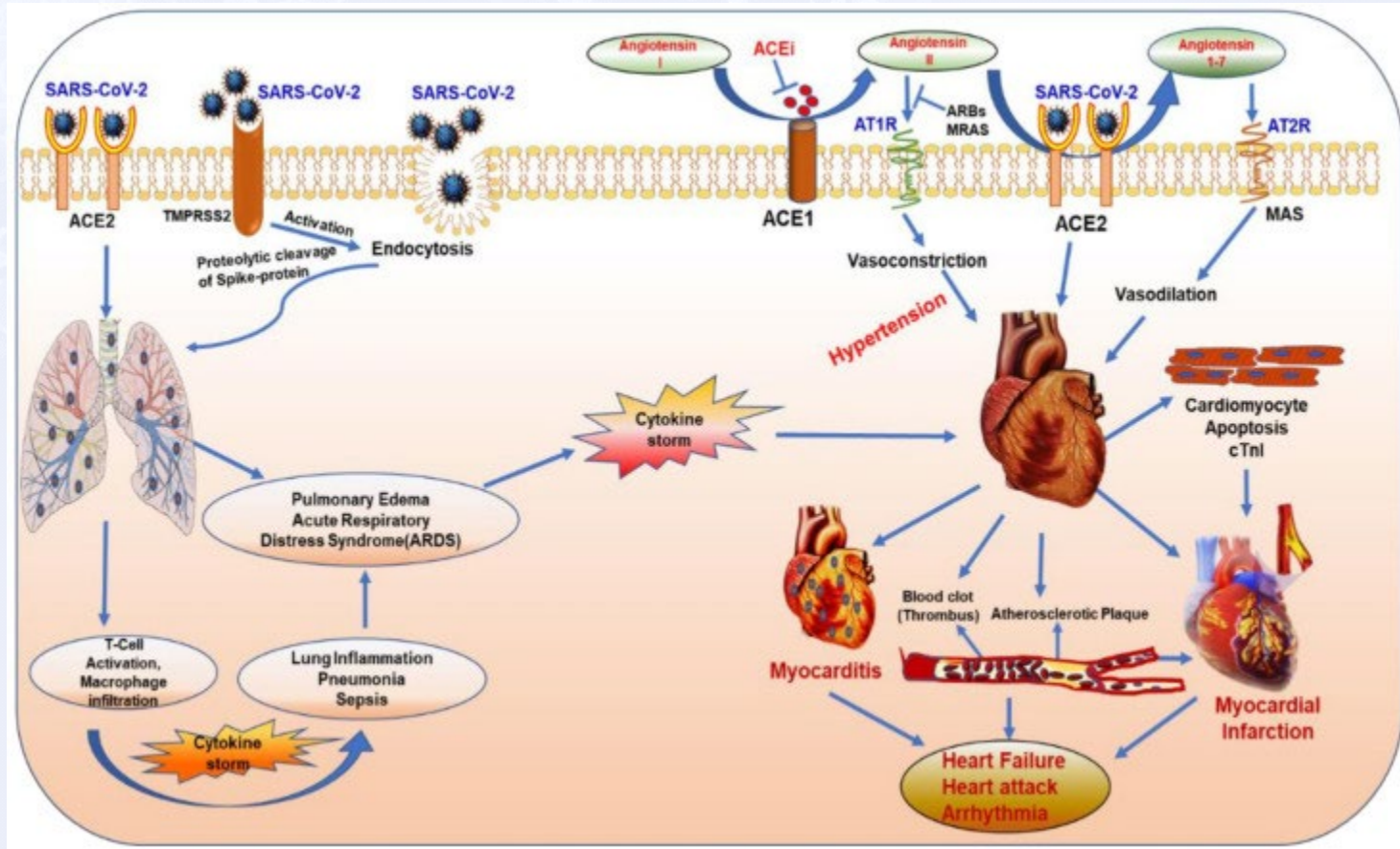
# COVID-19: ARDS and Pulmonary Disease – Additional Data

- Incidence of ARDS development varies by patient population
- Meta-analysis of >50,000 COVID-19 cases reported overall incidence 14.8%<sup>1</sup>
- Median time to ARDS: 8 to 12 days from symptom onset<sup>2</sup>
- Identified risk factors:<sup>2</sup>
  - older age
  - co-morbidities: chronic lung disease, HTN, diabetes
  - \*US: ethnicities at higher risk: American Indian, African American and Hispanic<sup>3</sup>

1. Mesas et al, *Plos One*, Nov 2020
2. Wu and McGoogan, *JAMA*, Feb 2020
3. COVID-NET, Nov 2020



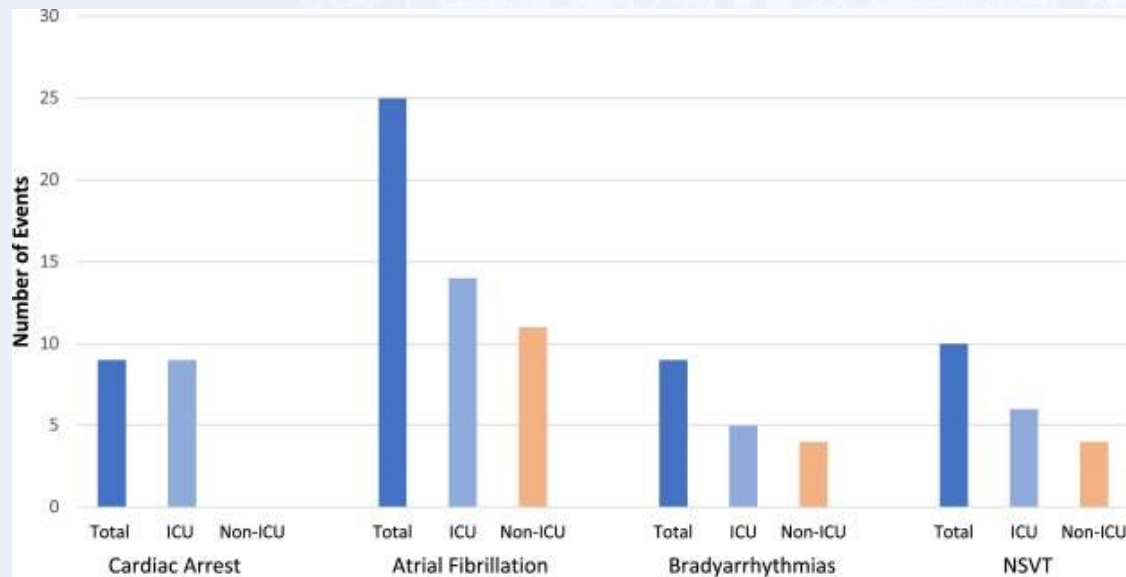
# COVID-19 Complications





# COVID-19: Cardiac complications

- Acute cardiac injury (NSTEMIs), arrhythmias, cardiomyopathy, and cardiogenic shock reported
  - Wuhan, China, 138 hospitalized patients:
    - 17% had arrhythmia, 7% had acute cardiac injury, and 9% had shock<sup>1</sup>
  - Washington ICU series: 33% developed cardiomyopathy<sup>2</sup>
  - University of Pennsylvania: 700 hospitalized patients:



1. Wang et al, *JAMA*, Mar 2020
2. Arentz et al, *JAMA*, Apr 2020
3. Bhatla et al, *Heart Rhythm*, Sep 2020



# COVID-19 and Thromboembolic Events

- Increased incidence known but to what extent depends on severity of illness
- French study: 150 ICU patients, 16.7% developed PE despite prophylactic anticoagulation<sup>1</sup>
- Dutch study: 184 ICU patients, 27% cumulative incidence of VTE despite prophylaxis<sup>2</sup>
- NY ICU study: 829 patients, VTE in 13.6% (6.2% PE, 9.4% DVT)<sup>3</sup>
- Non-ICU study in NY: 2,505 hospitalized cases, 11.5% had thrombotic event (VTE 3.6%, arterial 8.4%)<sup>3</sup>

1. Helms et al, *Intensive Care Med*, May 2020

2. Klok et al, *Thromb Res*, July 2020

3. Bilaloglu et al, *JAMA*, Aug 2020



# COVID-19 and Thromboembolic Events

- Strokes reported less frequently but still possible
- Incidence in hospitalized patients ranges from 0.4 – 2.7%
- Varies again by severity of illness:
  - Mild disease = <1% risk of stroke
  - Severe (ICU) disease = up to 6%





# COVID-19 and MIS-C

- Multisystem inflammatory syndrome in children (MIS-C)
- First identified/reported in April 2020
  - 2 separate cases series (UK and US)
  - Kawasaki-like syndrome
  - Described as hyperinflammation syndrome
    - Rash, conjunctival injection, fever, increased inflammatory markers
    - Older age kids (school age) and increased incidence of shock

Feldstein et al, *N Eng J Med*, July 2020



# COVID-19 and MIS-C: Data

CDC Surveillance Study: 43 PICUs across 26 states

- March 15, 2020 – May 20, 2020
- Total # of cases = 186
- Mean age = 8.3 years
- Days from COVID diagnosis: mean 25 days (range 6-51 days)

Feldstein et al, *N Eng J Med*, July 2020





# COVID-19 and MIS-C: Case Definition

CDC Surveillance Study: 43 PICUs across 26 states

- March 15, 2020 – May 20, 2020
- Case definition:
  1. Illness leading to hospitalization
  2. Age < 21 years
  3. Fever > 24 hours
  4. multisystem organ involvement
  5. lab evidence of inflammation
  6. confirmed COVID-19 illness\* or exposure to confirmed case

Feldstein et al, *N Eng J Med*, July 2020



# COVID-19 and MIS-C: Case Demographics

- 186 cases identified
  - median age 8.3 years
  - 62% male
  - 39% SARS-CoV-2 PCR positive
  - 31% SARS-CoV-2 IgG positive
  - 30% confirmed exposure to COVID-19 case

Feldstein et al, *N Eng J Med*, July 2020





# COVID-19 and MIS-C: Clinical Presentation

- Clinical presentation
  - 90% had fever > 4 days
  - 92% had GI symptoms
  - 80% cardiovascular symptoms
  - 76% hematologic system involvement
  - 70% respiratory system involvement

Feldstein et al, *N Eng J Med*, July 2020



# COVID-19 and MIS-C: Management

- Management
  - 80% received ICU care (4 deaths total)
  - 48% required vasopressor support
  - 20% required mechanical ventilation
  - 77% received IVIG at least once
  - 49% received systemic glucocorticoids
  - 20% received other immunotherapy (tocilizumab or anakinra)

Feldstein et al, *N Eng J Med*, July 2020







# COVID-19 Recovery and Long-term Effects

# Stages of COVID-19 Illness

- Acute COVID-19: symptoms up to 4 weeks from onset
- Ongoing symptomatic COVID-19: symptoms 4-12 weeks from onset
- Post-COVID-19: > 12 weeks from symptom onset

\*\*\* same symptoms as during acute phase



# COVID-19 Recovery

- Mild infection: ~ 2 weeks<sup>1</sup>
- Severe infection: 6 weeks or longer<sup>1</sup>
- Recovery time can be longer, particularly in hospitalized cases:
  - 1600 patients surveyed following hospitalization in US: 33% reported persistent symptoms at day 60 from discharge<sup>2</sup>
    - Symptoms: dyspnea on exertion (24%), shortness of breath (17%), cough (15%), loss of taste/smell (13%)<sup>2</sup>
  - 100 patients surveyed following UK hospitalization<sup>3</sup>
    - 60% non-ICU patients had symptoms day 48 from discharge
    - 72% of ICU patients had symptoms at day 48 from discharge
- Outpatients, even with milder disease, still report prolonged symptoms
  - 292 patients reached by telephone interview 2-3 weeks post diagnosis<sup>4</sup>
    - 35% reported ongoing symptoms
    - Symptoms: cough (43%), fatigue (35%), shortness of breath (29%)

1. World Health Organization, COVID19
2. Chopra et al, *Ann Intern Med*, Nov 2020
3. Halpin et al, *J Med Virol*, Aug 2020
4. Tenforde et al, *MMWR*, Jul 2020



Symptom	% of patients	Time to resolution
Fatigue	15-87%	3 months
Dyspnea	10-71%	2-3 months
Chest pain	12-44%	2-3 months
Cough	17-26%	2-3 months
Anosmia	13%	1 month

*UpToDate*: COVID-19 symptoms





# Psychological or Cognitive Symptoms

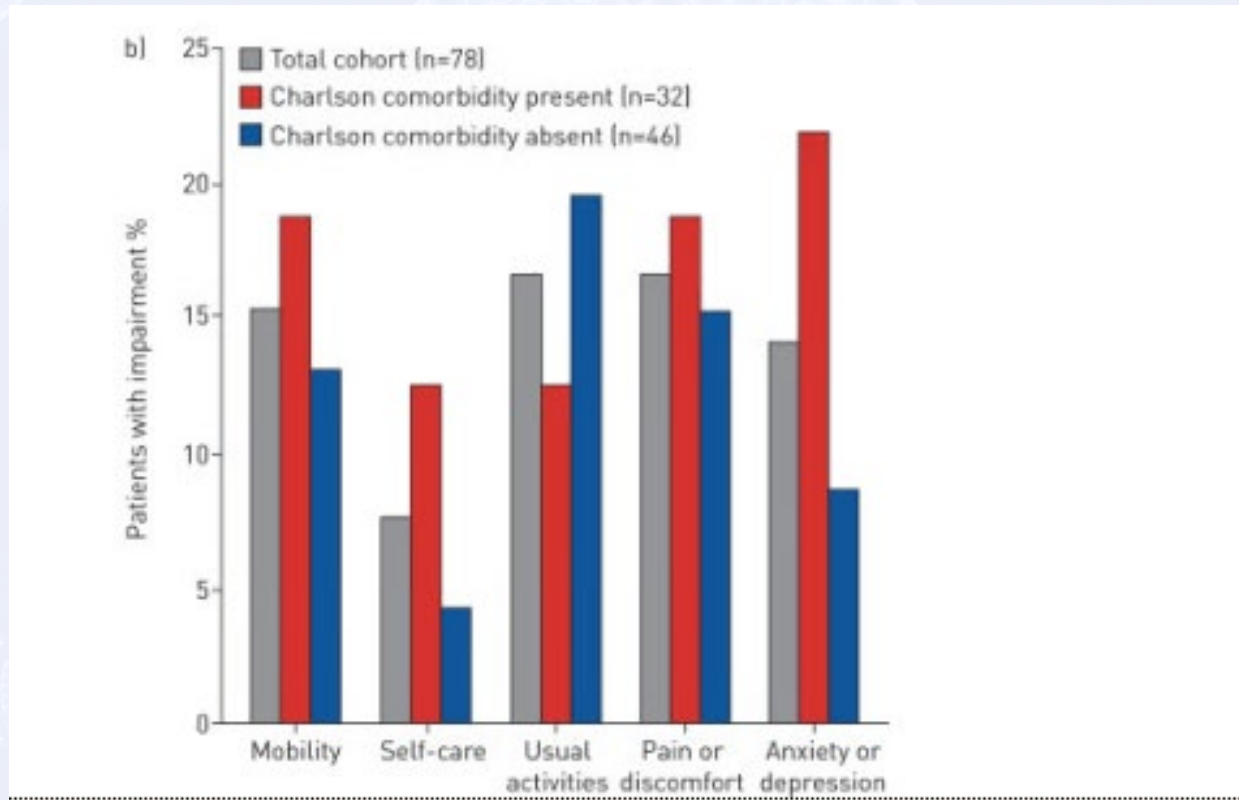
- Reports of PTSD, anxiety, depression, memory impairment, concentration difficulties
- 100 UK hospitalized patients interviewed 1-2 months post discharge<sup>1</sup>
  - 24% PTSD, 18% memory impairment, 16% concentration difficulty
- >400 Italian hospitalized patients interviewed 1 month post discharge<sup>2</sup>
  - 28% PTSD, 31% depression, 42% anxiety

1. Halpin et al, *J Med Virol*, Aug 2020
2. Mazza et al, *Brain Behav Immun*, Oct 2020



# Psychological or Cognitive Symptoms

- 78 Canadian hospitalized patients enrolled in Post-COVID Respiratory Clinic completed PROM survey at 3 months
  - 51% reported reduced QOL



Wong et al, *Eur Respir J*, Nov 2020



# Risks for Persistent Symptoms

- Older age, co-morbidities, and severity of COVID infection
- 150 non-critical COVID patients in France<sup>1</sup>
  - 2 month follow up survey on state of health, persistent symptoms
  - Higher risk for persistent symptoms with:
    - Age 40 – 60, required hospital admission, and severe COVID at diagnosis
- 274 US outpatients (across 13 US states)<sup>2</sup>
  - 2-4 weeks after diagnosis survey administered
  - Primary question: have they returned to their usual state of health
  - Increased risk with following patient factors:
    - Age  $\geq 50$  (aOR 2.29),  $\geq 3$  chronic medical conditions (aOR 2.29), obesity (aOR 2.31), underlying psychiatric condition (aOR 2.32)

1. Carvalho-Schneider et al, *Clin Microbiol Infect* Oct 2020  
2. Tenforde et al, *MMWR* July 2020

# Post-COVID: “Long-Haulers”

- Estimated that 10% of all COVID patients might develop post-COVID or “COVID long-hauler”<sup>1</sup>
- Etiology is still unknown but mimics that of other coronaviruses (and other infections)
  - Chronic fatigue and cognitive impairments reported in survivors from SARS-CoV-1<sup>2</sup>
  - Chronic post-SARS syndrome: chronic pain, sleep disruption, depression, fatigue<sup>3</sup>
- Likely multifactorial in etiology<sup>4</sup>
  - Recovery from organ damage sustained in acute infection
  - Persistent inflammatory state
  - ?viral reservoir
  - Deconditioning
  - Worsening/exacerbation of comorbid conditions

1. Rubin, R. *JAMA* Sep 2020
2. Lam et al, *Arch Intern Med* 2009
3. Moldofsky and Patcai. *BMC Neurol* 2011
4. CDC Late Sequelae, [cdc.gov/coronavirus/2019](https://www.cdc.gov/coronavirus/2019)





# Management of Post-COVID

- To date, no specific guidelines for this patient population in US
  - NIH COVID-19 Treatment Guidelines:
    - discusses long-term symptoms but not management
  - Infectious Disease Society of America (IDSA):
    - provides literature review of reports of persistent symptoms, but not on management
  - Society for Critical Care Medicine (SCCM):
    - Guidelines focused on pulmonary complications and ICU management
- Some countries have developed some guidelines/pathways
  - Royal Australian College of General Practitioners (RACGP)

# RACGP



*Caring for adult patients  
with post-COVID-19  
conditions*

[racgp.org.au/FSDEDEV/media/documents/RACGP/Coronavirus/Post-COVID-19-conditions.pdf](https://racgp.org.au/FSDEDEV/media/documents/RACGP/Coronavirus/Post-COVID-19-conditions.pdf)





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- Some countries have developed some guidelines/pathways
  - Royal Australian College of General Practitioners (RACGP)
- Post-COVID clinics are present at some academic centers with varying formats

# Examples of Post-COVID-19 Clinics (1)

- Post-COVID Assessment and Recovery Clinic: Penn Medicine
  - Multidisciplinary with pulmonary and rehab medicine
- UCHealth (Aurora Colorado) post COVID clinic
  - Focus on respiratory, neurologic, and mental health
- Mount Sinai Health System Center for Post-COVID Care
  - Primary care, infectious disease, pulmonary, cardiology and others
- UCSF OPTIMAL Clinic: Post-COVID 19 care

Weiner S. *AAMC Insights* (online) September 25, 2020





# Examples of Post-COVID-19 Clinics (2)

- Post-COVID Assessment and Recovery Clinic: Penn Medicine
  - Multidisciplinary with pulmonary and rehab medicine
- UCHHealth (Aurora Colorado) post COVID clinic
  - Focus on respiratory, neurologic, and mental health
- Mount Sinai Health System Center for Post-COVID Care
  - Primary care, infectious disease, pulmonary, cardiology and others
- UCSF OPTIMAL Clinic: Post-COVID 19 care
- UPMC Post-COVID Recovery Clinic
  - Focus on those with symptoms >12 weeks after onset

Weiner S. *AAMC Insights* (online) September 25, 2020



# Post-COVID Care

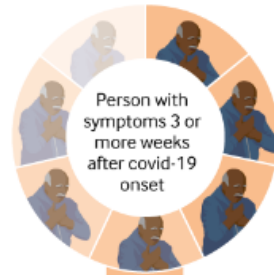
- Most cases patients are seen by PCP or referred to specialist on as needed basis
- Sheer volume of COVID patients makes it very difficult for structured/scheduled follow up for all patients
  - For example: our hospital offered 2 week follow up (in person or virtual) for every patient discharged from COVID unit
  - Majority who kept appointment were recovering as expected and did not request further follow up
  - No longer able to get everyone an appointment within 2 weeks given number of hospitalized patients and clinic availability of our ID section
- Importance of providing PCPs with updates on science (i.e. infectious period) and red flags/conditions that would warrant referral



# "Long covid" in primary care

Assessment and initial management of patients with continuing symptoms

Post-acute covid-19 appears to be a multi-system disease, sometimes occurring after a relatively mild acute illness. Clinical management requires a whole-patient perspective. This graphic summarises the assessment and initial management of patients with delayed recovery from an episode of covid-19 that was managed in the community or in a standard hospital ward.



### An uncertain picture

The long term course of covid-19 is unknown. This graphic presents an approach based on evidence available at the time of publication. However, caution is advised, as patients may present atypically, and new treatments are likely to emerge

### Managing comorbidities

Many patients have comorbidities including diabetes, hypertension, kidney disease or ischaemic heart disease. These need to be managed in conjunction with covid-19 treatment. Refer to condition specific guidance, available in the associated article by Greenhalgh and colleagues

### Safety netting and referral

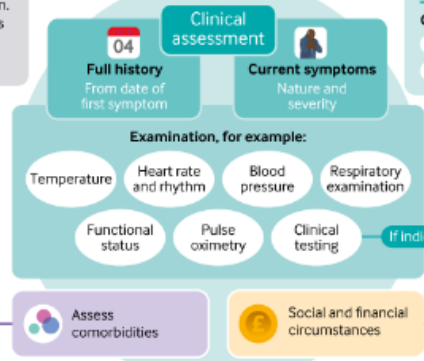
The patient should seek medical advice if concerned, for example:

- Worsening breathlessness
- PaO<sub>2</sub> < 96%
- Unexplained chest pain
- New confusion
- Focal weakness

Specialist referral may be indicated, based on clinical findings, for example:

- Respiratory** if suspected pulmonary embolism, severe pneumonia
- Cardiology** if suspected myocardial infarction, pericarditis, myocarditis or new heart failure
- Neurology** if suspected neurovascular or acute neurological event

Pulmonary rehabilitation may be indicated if patient has persistent breathlessness following review



### Investigations

Clinical testing is not always needed, but can help to pinpoint causes of continuing symptoms, and to exclude conditions like pulmonary embolism or myocarditis. Examples are provided below:

**Blood tests**

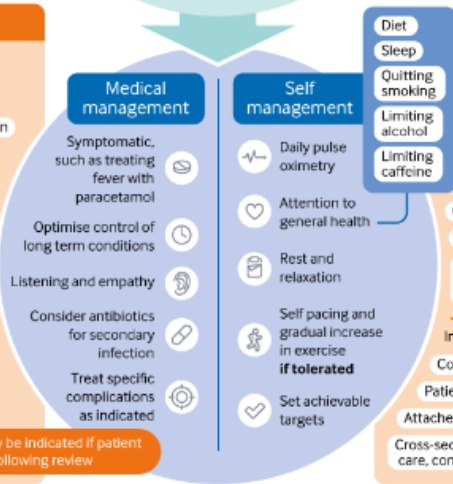
- Full blood count
- Electrolytes
- Liver and renal function
- Troponin
- C reactive protein
- Creatine kinase
- D-dimer
- Brain natriuretic peptides
- Ferritin – to assess inflammatory and prothrombotic states

**Other investigations**

- Chest x ray
- Urine tests
- 12 lead electrocardiogram

### Social, financial, and cultural support

Prolonged covid-19 may limit the ability to engage in work and family activities. Patients may have experienced family bereavements as well as job losses and consequent financial stress and food poverty. See the associated article by Greenhalgh and colleagues for a list of external resources to help with these problems



### Mental health

**In the consultation:**

- Continuity of care
- Avoid inappropriate medicalisation
- Longer appointments for patients with complex needs (face to face if needed)

**In the community:**

- Community linkworker
- Patient peer support groups
- Attached mental health support service
- Cross-sector partnerships with social care, community services, faith groups

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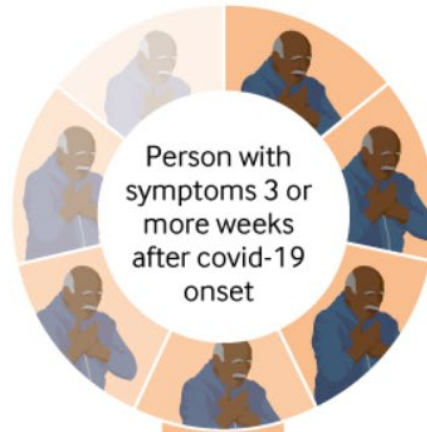


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However, caution is advised, as patients may present atypically, and new treatments are likely to emerge

## Managing comorbidities

Many patients have comorbidities including diabetes, hypertension, kidney disease or ischaemic heart disease. These need to be managed in conjunction with covid-19 treatment. Refer to condition



## Clinical assessment

04

**Full history**  
From date of first symptom

**Current symptoms**  
Nature and severity

### Examination, for example:

- Temperature
- Heart rate and rhythm
- Blood pressure
- Respiratory examination
- Functional status
- Pulse oximetry
- Clinical testing

If indicated

## Investigations

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## Social, financial, and cultural support

Prolonged covid-19 may limit the ability to engage in work and family activities. Patients may have experienced family





## Managing comorbidities

Many patients have comorbidities including diabetes, hypertension, kidney disease or ischaemic heart disease. These need to be managed in conjunction with covid-19 treatment. Refer to condition specific guidance, available in the associated article by Greenhalgh and colleagues

### Examination, for example:

Temperature

Heart rate and rhythm

Blood pressure

Respiratory examination

Functional status

Pulse oximetry

Clinical testing

If indicated



Assess comorbidities



Social and financial circumstances

## Social, financial, and cultural support

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Worsening breathlessness

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Unexplained chest pain

New confusion

Focal weakness

Specialist referral may be indicated, based on clinical findings, for example:

➔ **Respiratory** if suspected pulmonary embolism, severe pneumonia

➔ **Cardiology** if suspected myocardial infarction, pericarditis, myocarditis or new heart failure

➔ **Neurology** if suspected neurovascular or acute neurological event

➔ **Pulmonary rehabilitation** may be indicated if patient has persistent breathlessness following review

## Medical management

Symptomatic, such as treating fever with paracetamol

Optimise control of long term conditions

Listening and empathy

Consider antibiotics for secondary infection

Treat specific complications as indicated

## Self management

Daily pulse oximetry

Attention to general health

Rest and relaxation

Self pacing and gradual increase in exercise **if tolerated**

Set achievable targets

Diet

Sleep

Quitting smoking

Limiting alcohol

Limiting caffeine

## Mental health

In the consultation:

Continuity of care

Avoid inappropriate medicalisation

Longer appointments for patients with complex needs (face to face if needed)

In the community:

Community linkworker

Patient peer support groups

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Cross-sector partnerships with social care, community services, faith groups

# Management of Post-COVID (1)

- Priority is to ensure accurate diagnosis
  - Diagnosis of exclusion (don't have a test to confirm)
  - Rule out COVID complications such as cardiomyopathy or thromboembolism
    - Clinical symptoms and exam findings can guide need for testing
    - Basic lab evaluation: cbc, inflammatory markers, kidney and liver function
    - Chest imaging or cardiac testing if indicated by symptoms/vitals
      - Hypoxia? Abnormal heart rhythm
  - Status of their co-morbid conditions, chronic conditions



# Management of Post-COVID (2)

- Allow longer visit time for initial evaluation and discussion
- Patient may have faced some stigma or disbelief by family, friends, employer
  - Often symptoms are subjective (i.e. exam findings are normal)
  - Need to validate these symptoms and knowledge gap we have with post-COVID
- Symptomatic management where indicated
- Discuss importance of wellness to healing
  - Diet, sleep, activity, stress management, emotional support



# Management of Post-COVID (3)

- Close follow up (can be virtual)
- Set appropriate expectations
  - Timeline of recovery is individual, so cannot make predictions
  - Not enough data to really provide guidance on this
  - Will not be day to day changes, rather larger sections of time
    - *I'll recommend patients keep a calendar/log (doesn't have to be detailed) but rating each day on a scale 1-10, or simply rating as difficulty day, so-so day, okay day, good day*
- As provider, stay updated on new literature, new guidelines as they become available



# Questions?

- Rebecca Reece
  - [rreece@hsc.wvu.edu](mailto:rreece@hsc.wvu.edu)

