COVID-19 Follow-up Care

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Speaker Disclosure

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

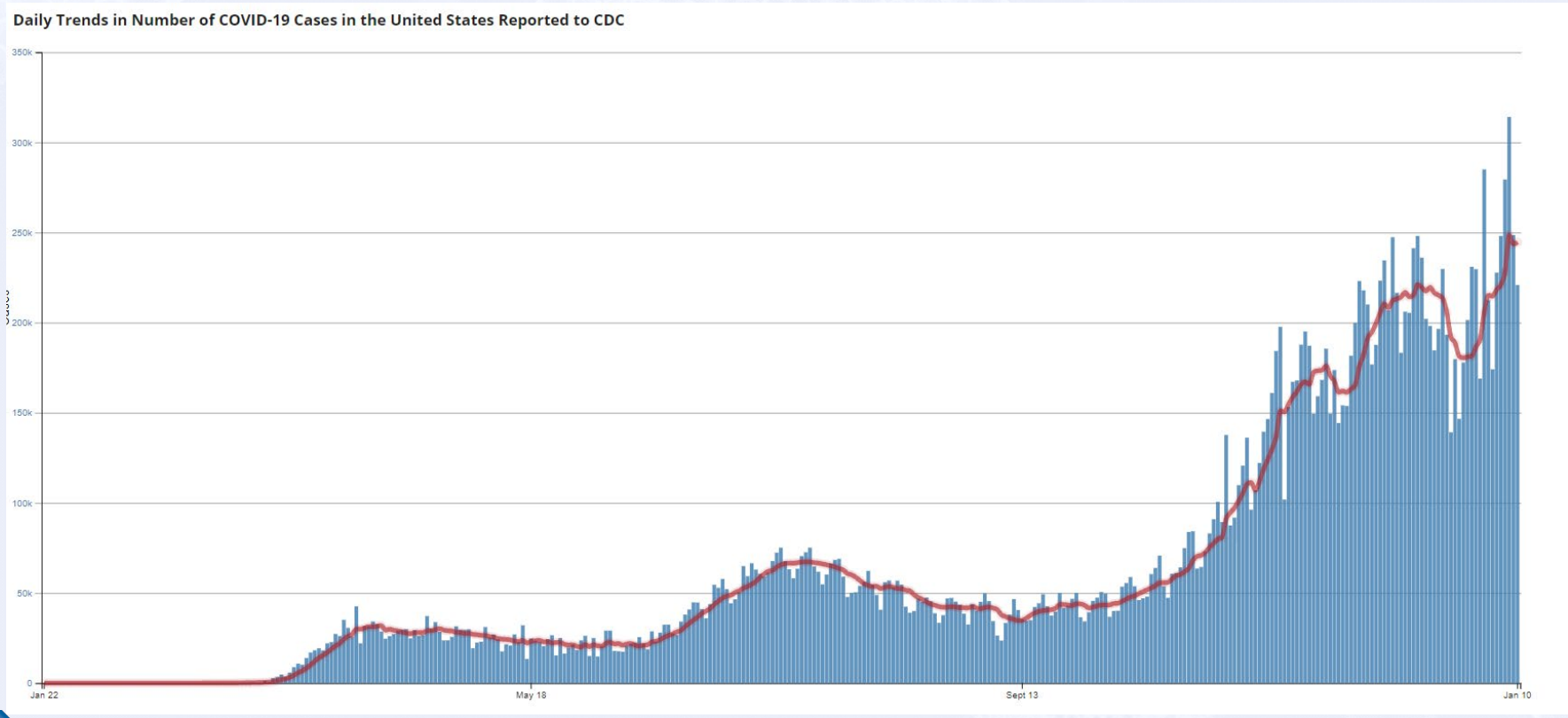
Objectives

- 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	AVERAGE DAILY CASES PER 100K IN LAST 7 DAYS	TOTAL DEATHS
22,322,956	74.1	373,167
+220,887 New Cases		+2,083 New Deaths

CDC | Updated: Jan 11 2021 12:16PM



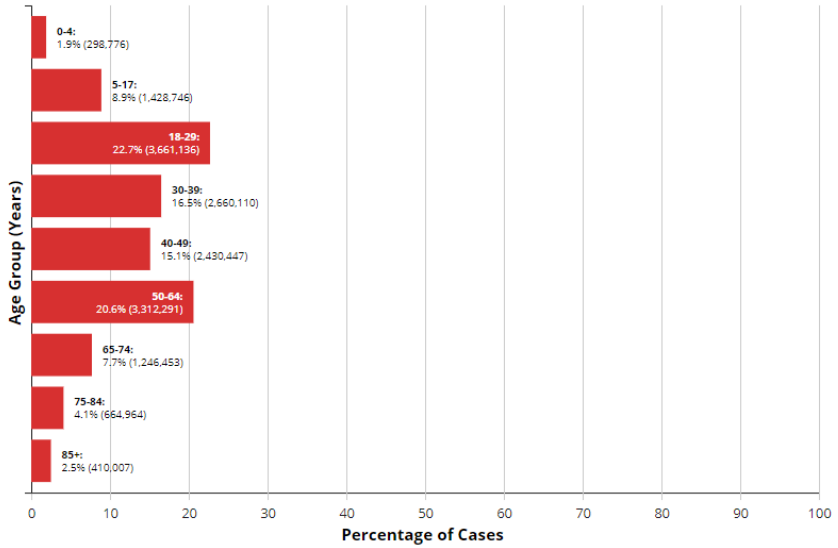
covid.cdc.gov/covid-data-tracker

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:

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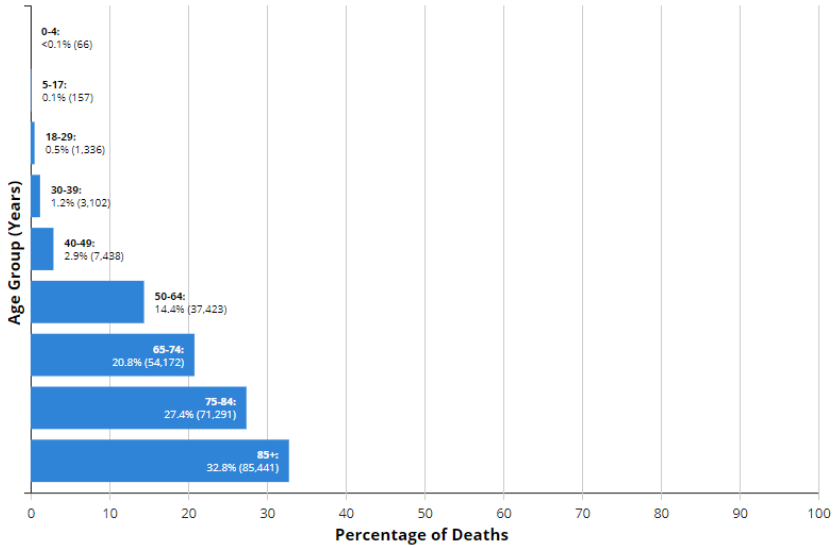
Data from 260,456 deaths. Age group was available for 260,426 (99%) deaths.



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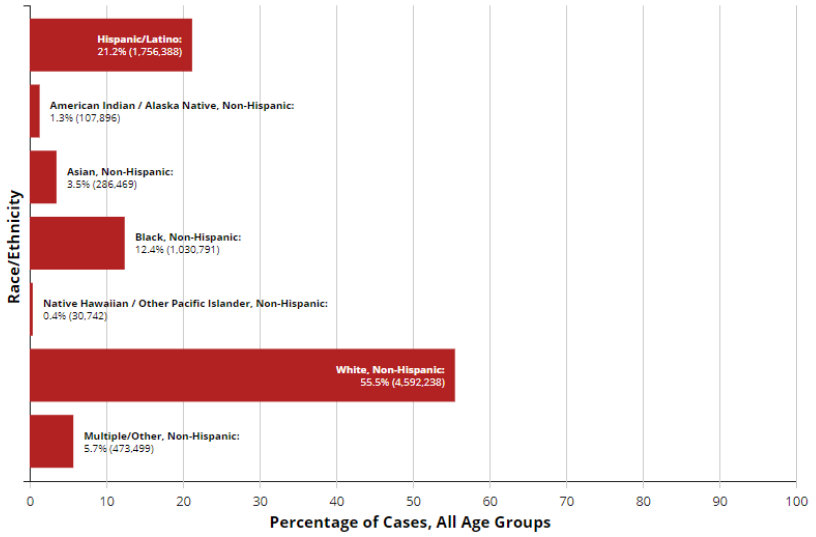
COVID-19: US Demographic Race/Ethnicity Data

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:

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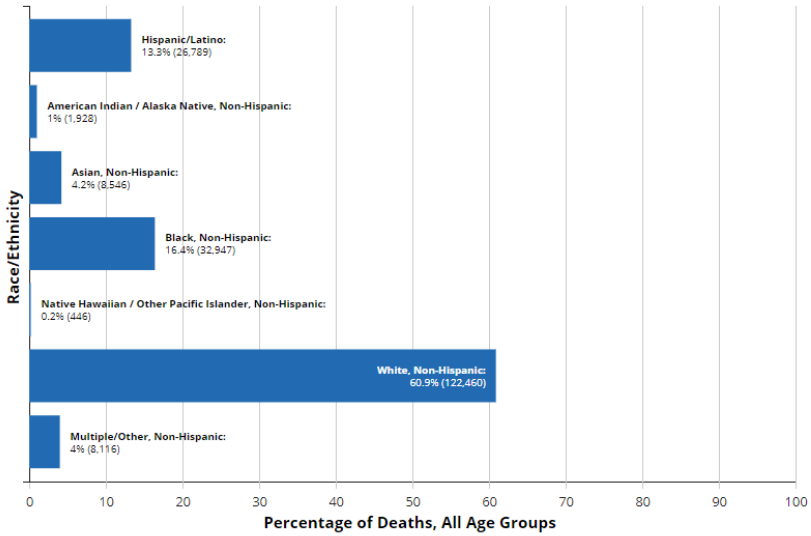
Data from 260,456 deaths. Race/Ethnicity was available for 201,232 (77%) deaths.

All Age Groups



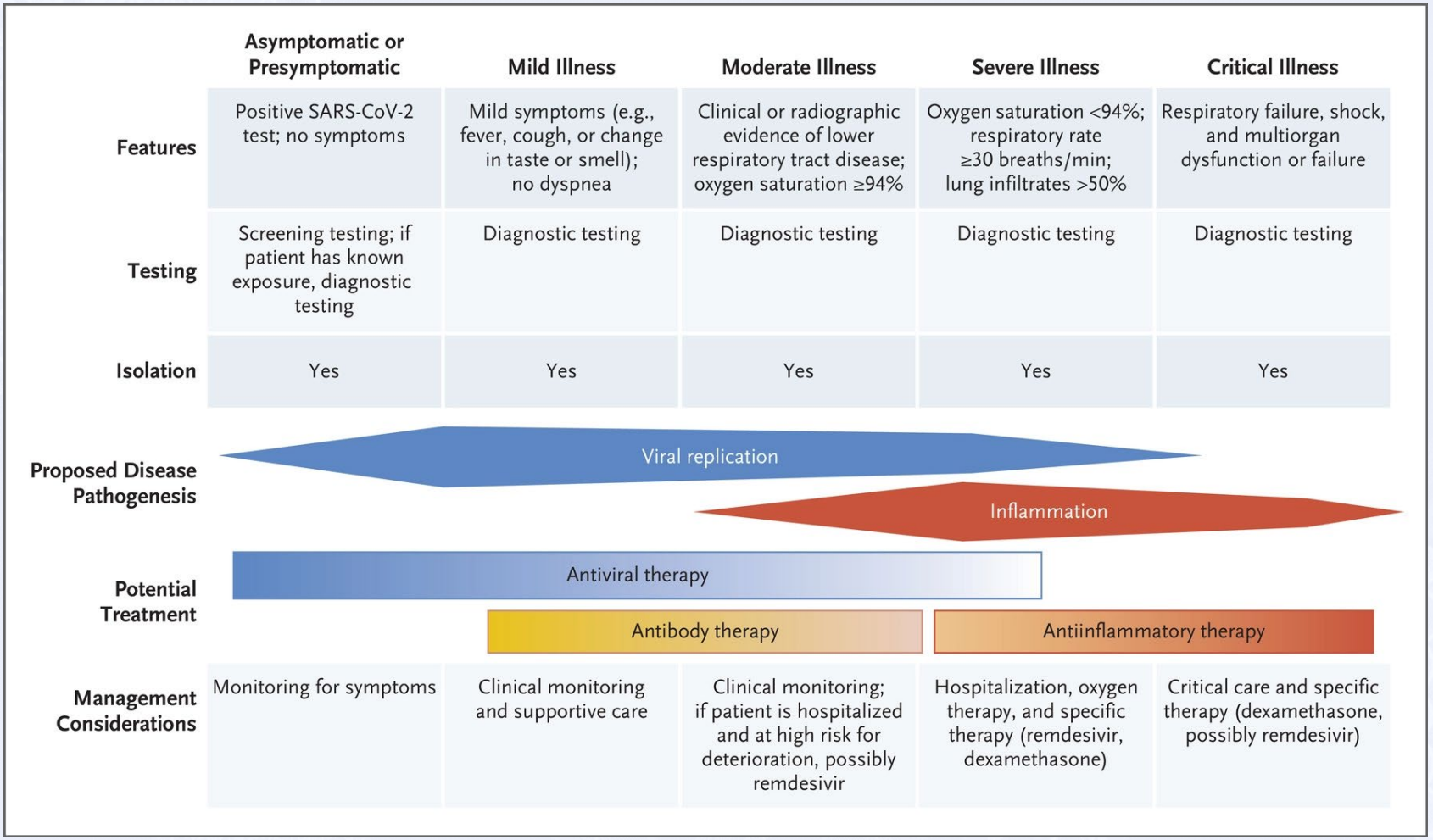
covid.cdc.gov/covid-data-tracker

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



Ghandi et al, *N Eng J Med,* October 2020

COVID-19 Clinical Presentations (2)

- Estimated 40-45% of infections remain asymptomatic[1]
- Of those who develop clinical disease (ie symptoms)[2,3]
  - 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

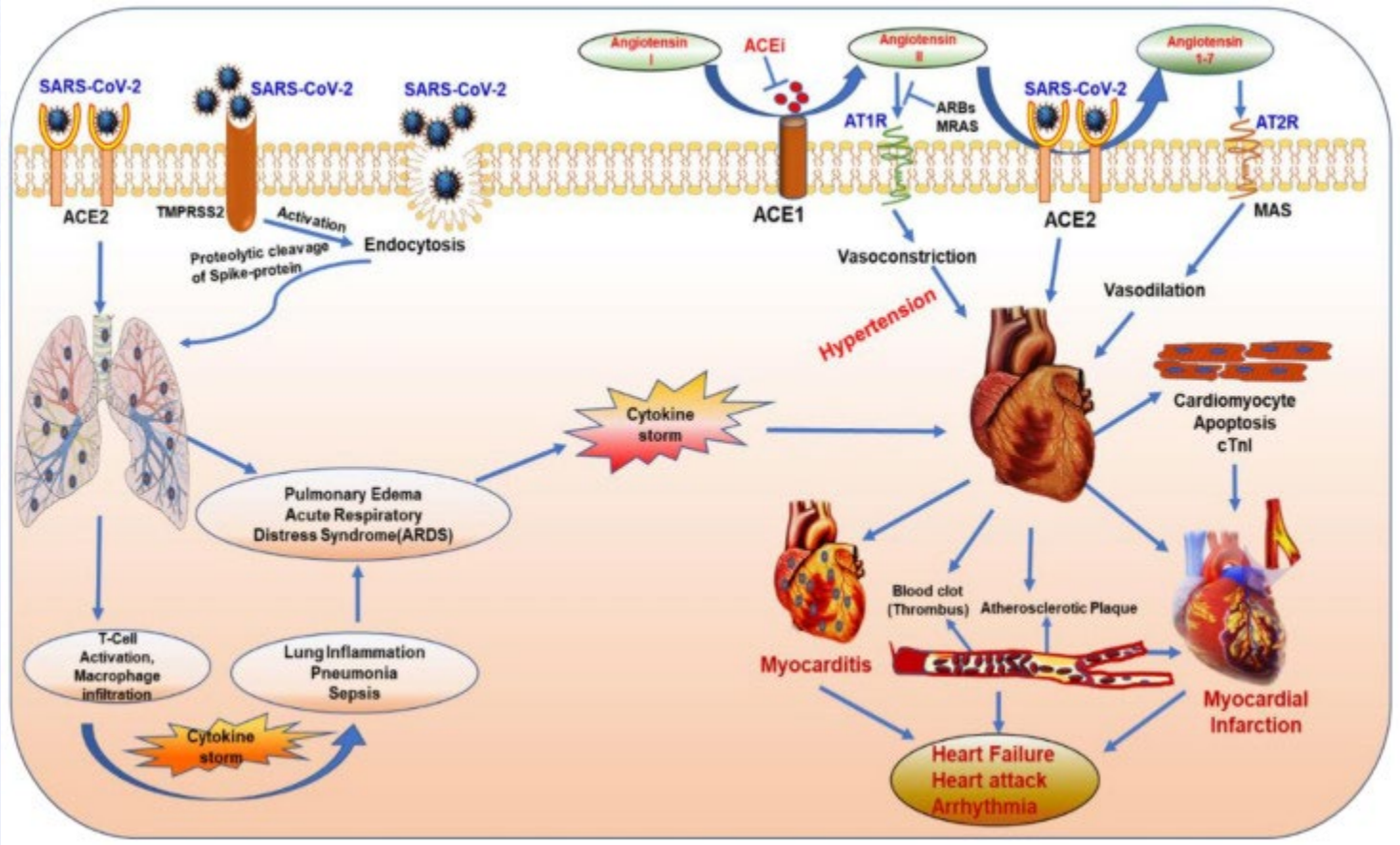
Tzotzos et al, *Crit Care,* Aug 2020

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%[1]
- Median time to ARDS: 8 to 12 days from symptom onset[2]
- Identified risk factors:[2]
  - older age
  - co-morbidities: chronic lung disease, HTN, diabetes
  - *US: ethnicities at higher risk: American Indian, African American and Hispanic[3]

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

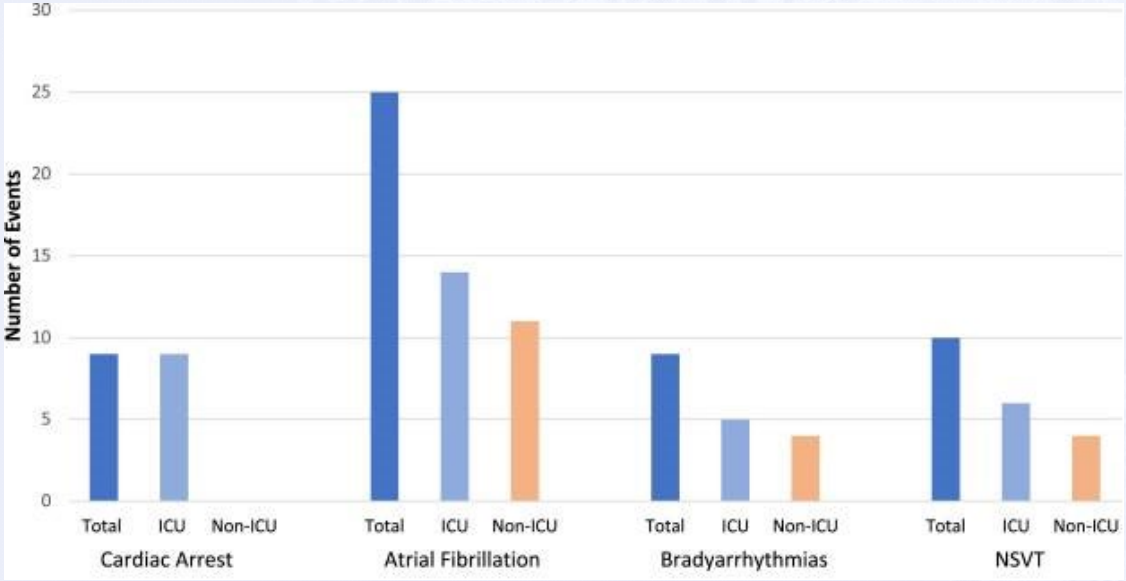
COVID-19 Complications



Samidurai and Das, *Int J Mol Sci,* Sep 2020

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[1]
  - Washington ICU series: 33% developed cardiomyopathy[2]
  - 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[1]
- Dutch study: 184 ICU patients, 27% cumulative incidence of VTE despite prophylaxis[2]
- NY ICU study: 829 patients, VTE in 13.6% (6.2% PE, 9.4% DVT)[3]
- Non-ICU study in NY: 2,505 hospitalized cases, 11.5% had thrombotic event (VTE 3.6%, arterial 8.4%)[3]

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[1]
- Severe infection: 6 weeks or longer[1]
- 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[2]
    - Symptoms: dyspnea on exertion (24%), shortness of breath (17%), cough (15%), loss of taste/smell (13%)[2]
  - 100 patients surveyed following UK hospitalization[3]
    - 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[4]
    - 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

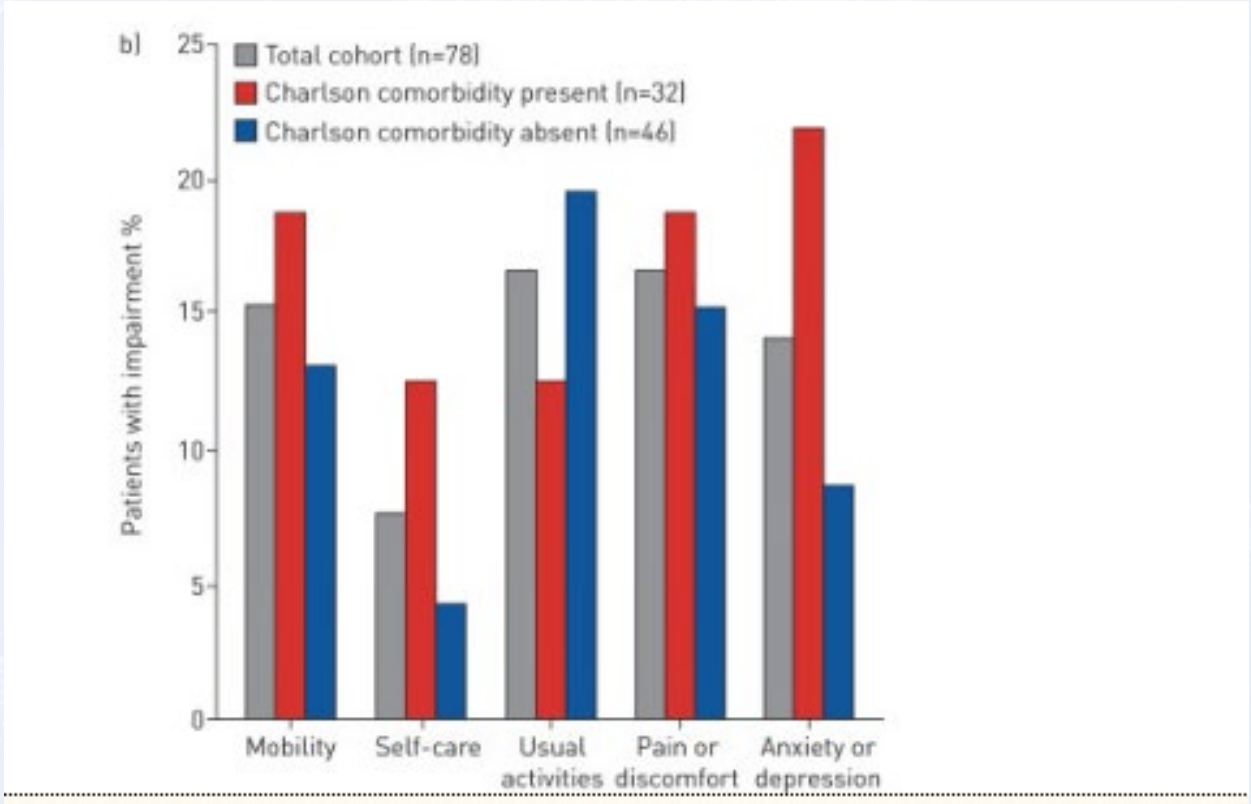
Psychological or Cognitive Symptoms

- Reports of PTSD, anxiety, depression, memory impairment, concentration difficulties
- 100 UK hospitalized patients interviewed 1-2 months post discharge[1]
  - 24% PTSD, 18% memory impairment, 16% concentration difficulty
- >400 Italian hospitalized patients interviewed 1 month post discharge[2]
  - 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[1]
  - 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)[2]
  - 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 ≥50 (aOR 2.29), ≥ 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"[1]
- 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[2]
  - Chronic post-SARS syndrome: chronic pain, sleep disruption, depression, fatigue[3]
- Likely multifactorial in etiology[4]
  - 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/coranvirus/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

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

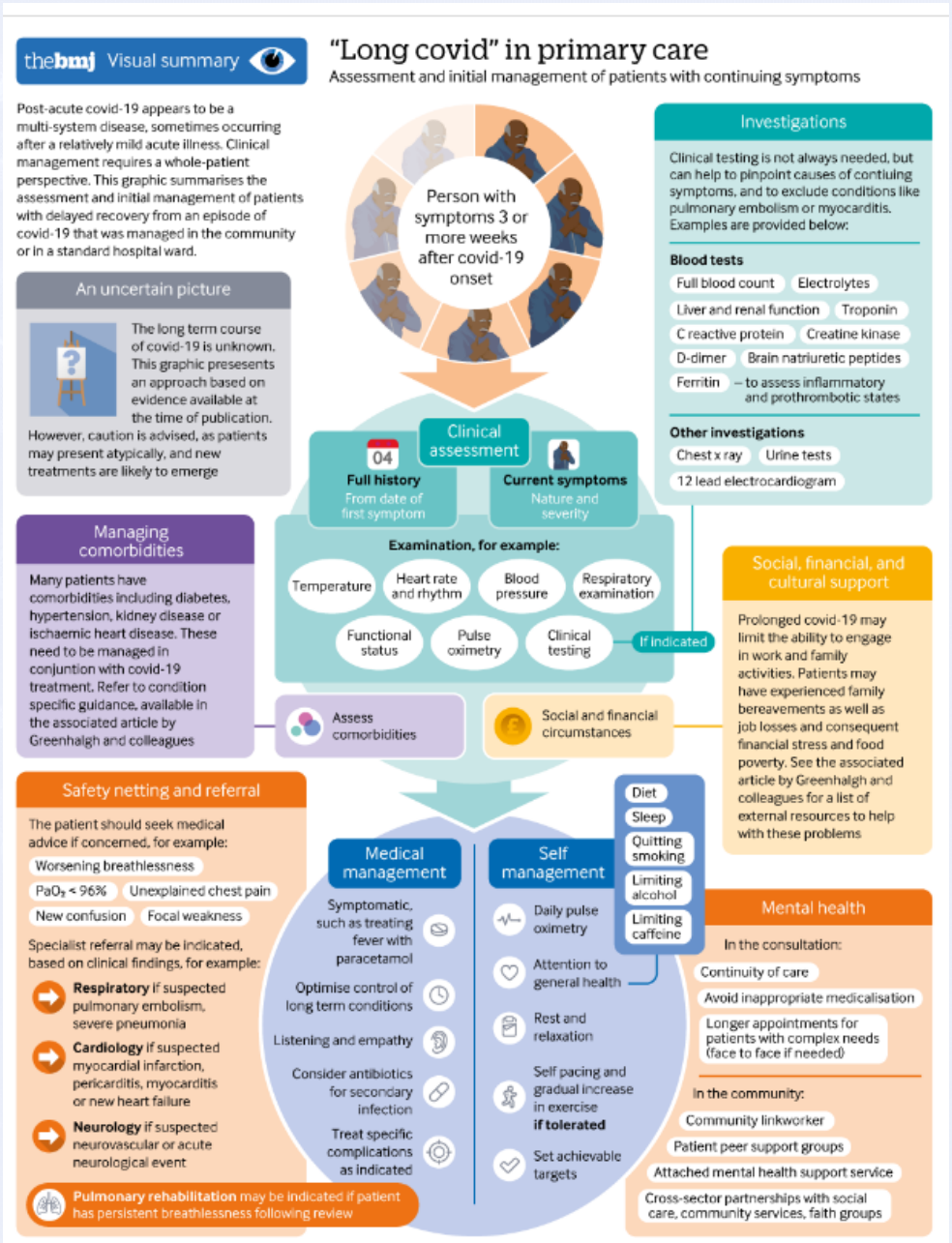
Examples of Post-COVID-19 Clinics (2)

- Post-COVID Assessment and Recovery Clinic: Penn Medicine
  - Multidisciplinary with pulmonary and rehab medicine
- 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
- UPMC Post-COVID Recovery Clinic
  - Focus on those with symptoms >12 weeks after onset

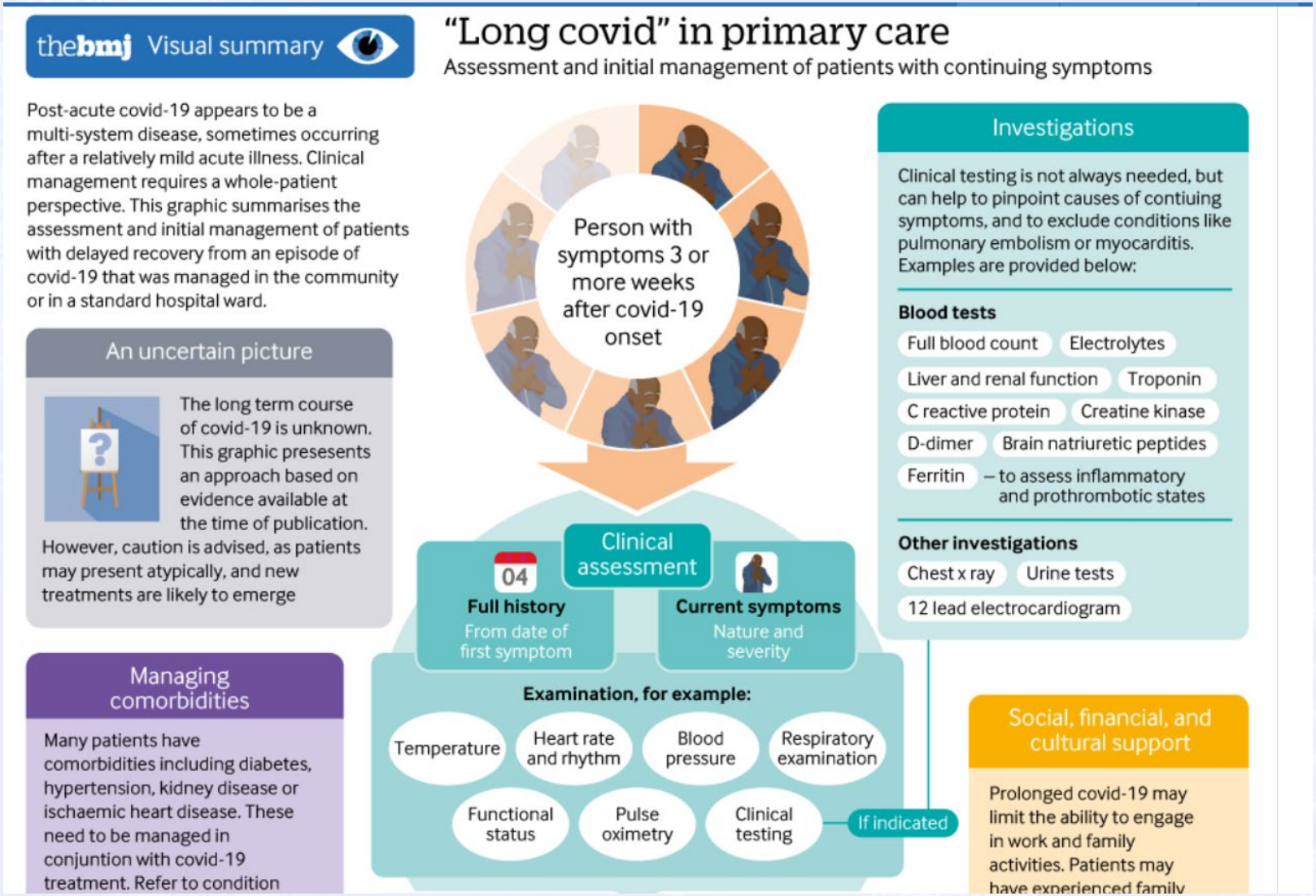
Weiner S. *AAMC Insights* (online) September 25, 2020

Post-COVID Care

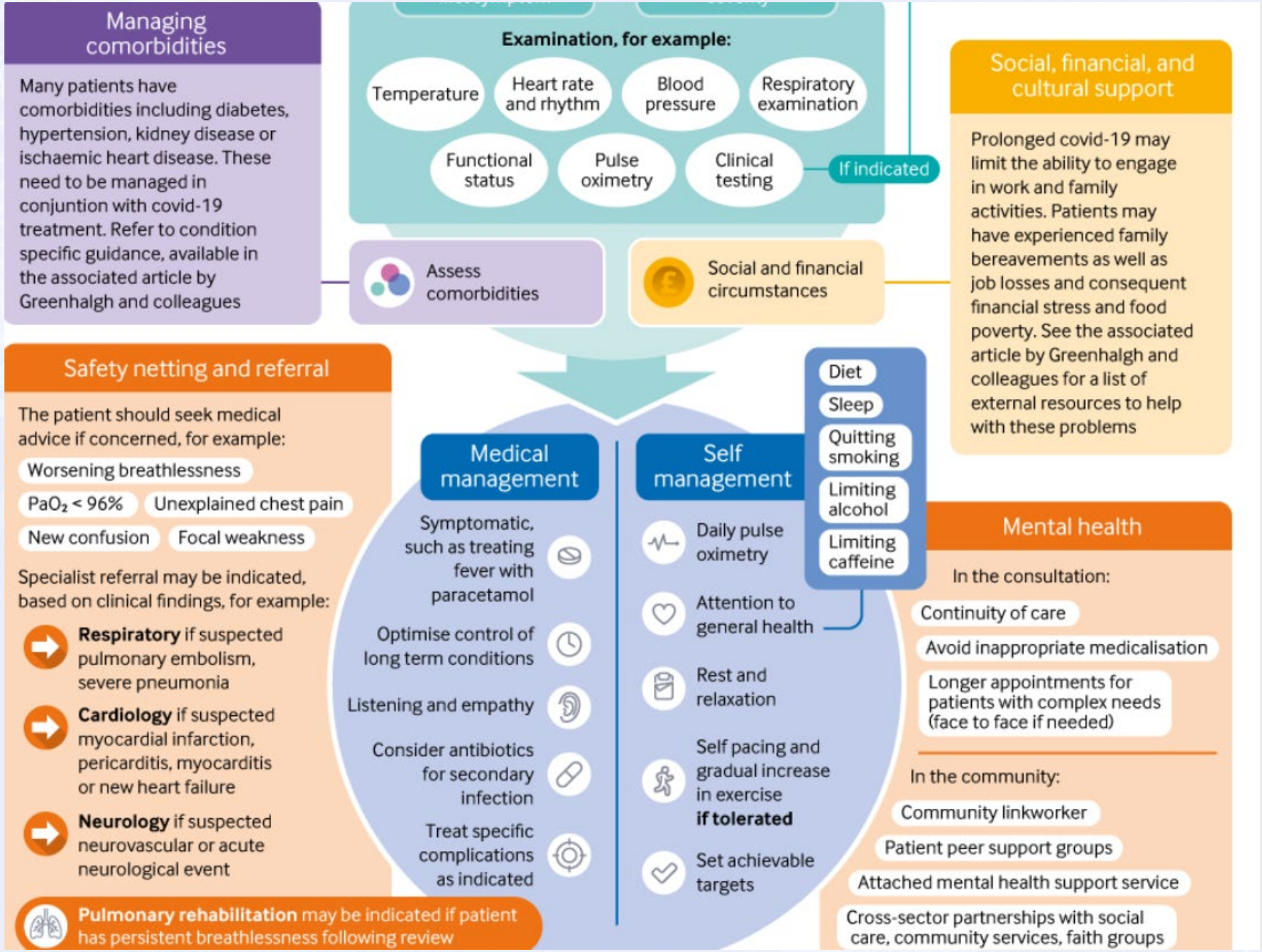
- Most cases patients are seen by PCP or referred to specialist on as needed basis
- Sheer volume of COVID patients makes it very difficult for structured/scheduled follow up for all patients
  - For example: our hospital offered 2 week follow up (in person or virtual) for every patient discharged from 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



Greenhalgh et al, *BMJ,* Aug 2020



Greenhalgh et al, *BMJ,* Aug 2020



Greenhalgh et al, *BMJ,* Aug 2020

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

Greenhalgh et al, *BMJ,* Aug 2020

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

Greenhalgh et al, *BMJ,* Aug 2020

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?

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