Evidence-Based Medicine InfoSheet: Clinical Presentation
Updated [03/08/2021]
Review completed by: [Anisha Guda, Kavina Patel, Aleena Vargas, Tracey Vuong, Caroline Zhu, Taylor McCracken, Salma Yazji, Anusha Sherwani, Noah Hodson, Cindy Jiang, Vish Rajesh, Keerthana Nimmagadda, Ashley Andrew]
Peer Review by: [Dr. Philip Ponce, Dr. Kelly Echevarria]

Key topic areas / questions identified:

What is the "typical" clinical presentation of COVID-19?
https://www.covid19treatmentguidelines.nih.gov/overview/
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7229949/
(Duration of illness link above)

- https://www.theijoem.com/ijoem/index.php/ijoem/article/view/1921/1195
    - CT/X-ray = shows bilateral lung involvement
    - Procalcitonin normal
    - Incubation period = 3-6 days
    - Fever, cough, dyspnea, myalgia/fatigue
- Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis
    - Fever more likely in adults than children
    - Mean age = 51.97
    - 36.8% of cases with comorbidities
    - Common lab findings:
        - Decreased albumin
        - High CRP, LDH, ESR
        - Lymphopenia
- Clinical Characteristics of Coronavirus Disease 2019 in China
    - Median age = 47
    - Ground glass opacity on radiography
    - Lymphocytopenia
- https://www.ncbi.nlm.nih.gov/pubmed?term=32091533
    - Mild (no or mild pneumonia) = 81%
    - Severe disease (dypsnea, hypoxia) = 14%
    - Critical disease (resp failure, shock, multiorgan failure) = 5%
- https://www.ncbi.nlm.nih.gov/pubmed?term=32031570
    - Fever (99%), Fatigue (70%), Dry cough (59%), Anorexia (40%), Myalgias (35%), Dyspnea (31%), Sputum production (27%)

- https://www.ncbi.nlm.nih.gov/pubmed?term=32215618
    - Possible anosmia and dysgeusia
- https://www.ncbi.nlm.nih.gov/pubmed?term=32251668
    - GI symptoms in 17.6%
        - Diarrhea in 13%
        - N/V in 10%
        - Abdominal pain in 9%
- https://medium.com/@nigam/higher-co-infection-rates-in-covid19-b24965088333.
    - Prelim data describes co-infection with other resp pathogens up to 24.5%.

- https://pubmed.ncbi.nlm.nih.gov/31986264/?dopt=Abstract -
    - Common symptoms at onset of illness were fever (40 [98%] of 41 patients), cough (31 [76%]), and myalgia or fatigue (18 [44%]); less common symptoms were **sputum production** (11 [28%] of 39), **headache (**three [8%] of 38), **haemoptysis** (two [5%] of 39), and diarrhoea (one [3%] of 38). Dyspnoea developed in 22 (55%) of 40 patients (median time from illness onset to dyspnoea 8·0 days [IQR 5·0-13·0]). 26 (63%) of 41 patients had lymphopenia. All 41 patients had pneumonia with abnormal findings on chest CT. Complications included acute respiratory distress syndrome (12 [29%]), ***RNAaemia*** (six [15%]), acute cardiac injury (five [12%]) and secondary infection (four [10%]). 13 (32%) patients were admitted to an ICU and six (15%) died. ***Compared with non-ICU patients, ICU patients had higher plasma levels of IL2, IL7, IL10, GSCF, IP10, MCP1, MIP1A, and TNFα.***
- https://pubmed.ncbi.nlm.nih.gov/32305287/?from_term=covid19+AND+clot&from_pos=6
- https://pubmed.ncbi.nlm.nih.gov/32394237/
    - Uncommon - acute pulmonary embolism:
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7179995/
    - Immune thrombocytic purpura - single case report
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7273820/
    - Subacute thyroiditis - case report, published as a letter to the editor
- https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19-cutaneous-manifestations-and-issues-related-to-dermatologic-care#H378059545.
    - Exanthematous (morbiliform) rash, pernio (chilblain)like acral lesions (aka COVID toes), livedo-like/retiform purpura/necrotic vascular lesions, urticaria, vesicular (varicella-like) eruptions, multisystem inflammatory syndrome in children (MIS-C)
- https://pubmed.ncbi.nlm.nih.gov/32179659/
    - Children from whom coronaviruses are detected from the respiratory tract can have viral co-infections in up to two-thirds of cases.

    - Available data suggest that children may have more upper respiratory tract involvement (including nasopharyngeal carriage) rather than lower respiratory tract involvement.
- Imaging
    - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7467801/
        - Chest ultrasounds are showing to be potentially more useful than chest x rays, particularly in early clinical management in clinically suspected covid patients because it is more widely available, less exposure to radiation, and is more rapid. Additionally, it is more efficacious at showing peripheral pathologies and interstitial disease.

Asymptomatic presentation:

- Prevalence of Asymptomatic SARS-CoV-2 Infection: A Narrative Review: Annals of Internal Medicine: Vol 173, No 5
    - Asymptomatic persons seem to account for approximately 40% to 45% of SARS-CoV-2 infections, and they can transmit the virus to others for an extended period, perhaps longer than 14 days. Asymptomatic infection may be associated with subclinical lung abnormalities, as detected by computed tomography.
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7470698/#__ffn_sectitle
    - Cannot distinguish with imaging from presymptomatic individuals as asymptomatic still may have CT abnormalities

Lingering Symptoms

https://pubmed.ncbi.nlm.nih.gov/32513065/ - Persistent Smell Loss Following Undetectable SARS CoV-2

- Preliminary data showing persistence of loss of smell despite clinical resolution and undetectable nasal viral DNA

https://pubmed.ncbi.nlm.nih.gov/32498691/ - neurological defects

- Immediate and long-term consequences of COVID-19 infections for the development of neurological disease

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7529085/- long term pulmonary consequences

- The lingering manifestations of COVID-19 during and after convalescence: update on long-term pulmonary consequences of coronavirus disease 2019 (COVID-19)

What are the key groups for whom clinical presentation might be different?

- **Immunocompromised**

COVID-19 in Immunocompromised Hosts: What We Know So Far

- **Cancer patients**
  - breast and prostate cancers were more common in the United States [11, 17]. Presenting symptoms were similar to the noncancer population, with fever, dry cough, dyspnea, and diarrhea being most frequent, although it is important to note some reports of asymptomatic infection in patients with lung cancer [32, 33]. Healthcare exposure was a significant risk factor for infection in both China and United States [11, 15].
  - Compared with patients without cancer with COVID-19, those with cancer appeared to have an increased risk of severe outcomes including intubation and death after adjusting for other COVID-19 risk factors.
- **Organ transplant patients**
  - In US studies reporting race/ethnicity [41, 42, 47, 53], significant proportions of patients were Hispanic (up to 42%) [41, 42] or African American (up to 39%) [42]. Comorbidities including hypertension, diabetes, cardiovascular disease, chronic kidney disease, and obesity were highly prevalent
  - While there is significant heterogeneity among studies, many suggest increased disease severity and mortality among SOT recipients with COVID-19
- **HIV patients & patients on biologics**
  - Third, patients taking biologics may not be at higher risk of severe disease based on current data; whether they are actually at lower risk of severe COVID-19 is not yet clear. Fourth, the current data in PWH are inconclusive regarding whether HIV imparts a higher risk of severe disease.

COVID-19 in a patient with long-term use of glucocorticoids: A study of a familial cluster

- Longer incubation and viral shedding period in patients on long term glucocorticoids

COVID-19 and liver disease

- Patients with pre-existing liver disease may be more susceptible to liver damage from Covid. Biological drugs like tocilizumab and baricitinib may also cause HBV

reactivation and lead to dec liver function. Still unknown if Covid exacerbates cholestasis in those with underlying cholestatic liver disease

[First cases of COVID-19 in heart transplantation from China]

- 2 heart transplant patients with infection - one presented severely and the other had a mild presentation (n=2)

[Coronavirus Disease 2019 Pneumonia in Immunosuppressed Renal Transplant Recipients: A Summary of 10 Confirmed Cases in Wuhan, China]

- Kidney transplant patients have more severe COVID-19 pneumonia but most of the recovered after prolonged clinical course and virus shedding.

[The Science Underlying COVID-19 | Circulation]

- Troponin, BNP together with presence of underlying cardiovascular disease or CV risk factors are highly prognostic of requirement of ICU admission, ventilation, death.

[One case of coronavirus disease 2019 (COVID-19) in a patient co-infected by HIV with a low CD4 + T-cell count]

- HIV + patient with low CD4 count case report reports pt presented with fever, dry cough and respiratory difficulty. Testing negative on nasopharyngeal swab 3 times, one swab showed ORF1ab gene positive, but N gene negative, and only testing positive for Covid with serum IgM test at specialty hospital
- Co-infection with HIV and SARS-Cov-2 have a longer course and slower generation of specific antibody. Nucleic acid detection, gene sequencing and antibody detection can confirm diagnosis.

[Computed tomography imaging of an HIV-infected patient with coronavirus disease 2019]

- HIV+ man with non severe COVID infection had a non enhanced CT showed multiple high-density patchy shadows with unclear boundaries in peripheral lung involving interlobar fissures. This is different from typical CT findings of ground glass opacity followed by consolidation and interlobular septal thickening. The resolution of the lung lesions in the HIV + man was around day 7 following initial symptoms and substantially disappeared around day 15, which may be due to ART drug therapy prior to infection due to HIV infection. This is different from typical COVID presentation with peak severity of lung lesions at day 10 after initial symptoms and improvement after day 14.

[The clinical characteristics of pneumonia patients coinfected with 2019 novel coronavirus and influenza virus in Wuhan, China]

- Coinfection of influenza and COVID-19 : Study of 5 patients
    - All had fever, cough, fatigue, headache.
    - 3/5 patients had nasal tampono and pharyngalgia which isn't common in typical COVID-19

- Upon admission all patient's WBC were within normal limits, but lymphocytes were below the reference range. Liver ALT, AST, and CRP may show mild abnormalities.

- **Children** (<=18)

https://www.cdc.gov/mmwr/volumes/69/wr/mm6914e4.htm?s_cid=mm6914e4_w

- Less likely to present with fever, SOB, and cough than adults (18-64)
  - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7090728/
  - Fever (50%), cough (38%)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7574780/

- 15-35% of infected children can be asymptomatic

http://pediatrics.aappublications.org/lookup/doi/10.1542/peds.2020-0702

- Compared to adult patients, children diagnosed with COVID-19 seem to have less severe disease. In 1 epidemiology study of 2143 children, over 90% of the cases were mild or moderate in nature. Young children, especially infants seemed to be more susceptible to severe disease than older children; 10% of patients under 1 year of age had severe or critical disease. The only death in the series was a 14 year-old male

https://www.nejm.org/doi/10.1056/NEJMc2005073

- In a study of 1391 children, fever was present in 41.5% of the children at any time during the illness. Other common signs and symptoms included cough and pharyngeal erythema. A total of 27 patients (15.8%) did not have any symptoms of infection or radiologic features of pneumonia. A total of 12 patients had radiologic features of pneumonia but did not have any symptoms of infection. During the course of hospitalization, 3 patients required intensive care support and invasive mechanical ventilation; all had coexisting conditions (hydronephrosis, leukemia [for which the patient was receiving maintenance chemotherapy], and intussusception). The most common radiologic finding was bilateral groundglass opacity (32.7%).

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7363381/

- Incubation period varied between 2 and 25 days. Mean 7 days.
- Virus isolated from nasopharygneal secretions for up to 22 days and from stool for >30 days
- Co-infections reported in up to 79% children (mainly mycoplasma and influenza). Up to 35% asymptomatic. Most common symptoms were cough (48%), fever (42%), pharyngitis (30%). Further symptoms nasal congestion, rhinorrhea, tachypnea, wheezing, diarrhea, vomiting, headache and fatigue
- Radiology: unilateral or BIL infiltrates with ground glass opacities or consolidation with a surrounding halo sign

- Lab findings: both increased and decreased lymphocyte, less commonly neutrophil counts, mildly elevated ESR, CRP or procalcitonin, liver enzymes, creatine kinase, LDH or D-dimers
- Neonatal complications: respiratory distress or pneumonia (18%), DIC (3%), asphyxia (2%), 2 perinatal deaths

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7200209/

- Eight (16%) patients had lymphopenia, seven (14%) with thrombocytopenia, four (8%) with lymphocytosis, two (4%) with thrombocytosis, ten (20%) with elevated C-reactive protein, four (8%) with hemoglobin above, and six (12%) with below standard reference values.

- **Pregnant women**

https://onlinelibrary.wiley.com/doi/full/10.1002/jmv.25789
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7156118/
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30360-3/fulltext
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7144599/

- Severity is 86% mild, 9.3% severe, and 4.7% critical according to NYP-Colombia study (similar to nonpregnant adults)
- Many pregnant patients initially present asymptomatically - 14 of 43 patients (32.6%) initially presented without COVID-19–associated symptoms (NYP-Colombia)
- Lung consolidation is more common
- Pure ground glass opacity (GGO) and GGO with reticulation are less common
- Initial normal body temperature more common
- Leukocytosis more common
- Elevated neutrophil ratio more common
- Lymphopenia more common
- “Probable” absence of fever prior to delivery
- Low-grade postpartum fever
- Mild respiratory symptoms
- No evidence for intrauterine infection

- **Elderly**

Detection of SARS-CoV-2 Among Residents and Staff Members of an ...

- 3/4 residents tested in senior living homes were asymptomatic at the time of testing + for Covid

Clinical Characteristics of Patients With 2019 Novel Coronavirus (2019-nCoV)–Infected Pneumonia in Wuhan, China

- The median age for pts admitted to ICU is significantly older than the pts who did not require ICU care. The pts requiring ICU care were more likely to have underlying comorbidities.

Clinical Features of 85 Fatal Cases of COVID-19 from Wuhan. A Retrospective Observational Study

- Median age of retrospective study of 85 fatal cases of Covid was 65.8

Coronavirus disease 2019 in elderly patients: Characteristics and prognostic factors based on 4-week follow-up

- In a retrospective study of 339 pts 60 or older, common symptoms included fever (92.0%), cough (53.0%), dyspnea (40.8%) and fatigue (39.9%). Lymphocytopenia was a common laboratory finding (63.2%). Common complications included bacterial infection (42.8%), liver enzyme abnormalities (28.7%) and acute respiratory distress syndrome (21.0%). The median duration of hospital stays for the discharged was 21 days (interquartile range, 15–26). Lymphocytopenia was found in 211 cases (63.2%).

Lessons from Mass-Testing for COVID-19 in Long Term Care Facilities for the Elderly in San Francisco

- COVID-19 can cause significant mortality in the elderly in Long Term Care Facilities (LTCF). We describe four LTCF outbreaks where mass testing identified a **high proportion of asymptomatic infections** (4-41% in health care workers and 20-75% in residents), indicating that **symptom-based screening alone is insufficient for monitoring for COVID-19 transmission**.

National French survey of COVID-19 symptoms in people aged 70 and over

- This national French survey shows that older adults with COVID-19 exhibit a paucisymptomatic clinical picture with less than 3 signs during the first 72h of the infection, generally combining general and respiratory signs (e.g. hyperthermia and cough) with **peculiarities that should alert the clinician (e.g. sudden deterioration of general condition, diarrhea, lymphopenia, and/or geriatric syndromes including falls and delirium)**. Various clinical profiles were highlighted across older adults, especially among the oldest-old ≥80years and those with chronic diseases such as MND.

What are the common complications of COVID-19?

- ARDS (https://www.ncbi.nlm.nih.gov/pubmed/?term=Clinical+Characteristics+of+138+Hospitalized+Patients+With+2019+Novel+Coronavirus–Infected+Pneumonia+in+Wuhan%2C+China)
  - Reported in 15-33% of cases. Children can quickly progress to ARDS

    - Factors that increase risk of ARDS and death include older age, neutrophilia, elevated lactate dehydrogenase, and elevated D-dimer levels
    - Can develop at a median of 8 days after the onset of symptoms
    - Age >65, diabetes mellitus, and hypertension are each associated risk factors
- Acute respiratory failure (https://www.ncbi.nlm.nih.gov/pubmed/?term=Epidemiological+and+clinical+characteristics+of+99+cases+of+2019+novel+coronavirus+pneumonia+in+Wuhan%2C+China%3A+a+descriptive+study)
    - Reported in 8% of patient cases in Wuhan, China
    - Leading cause of mortality in patients with COVID 19
- Pneumonia
- Cardiovascular (https://www.ncbi.nlm.nih.gov/pubmed/32219363)
    - Vascular inflammation, cardiac arrhythmias, myocarditis, cardiomyopathy, acute onset heart failure, myocardial infarction, cardiac arrest
    - Acute cardiac injury reported in 7% to 20% of cases. Prevalence is high among patients who are severely or critically ill.
    - Less common: myopericarditis, cardiac tamponade and fulminant myocarditis (1 case)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7348211/

    - Pericarditis, effusion and tamponade may occur in the absence of pulmonary findings.

- Acute liver injury (https://www.ncbi.nlm.nih.gov/pubmed/?term=Liver+injury+during+highly+pathogenic+human+coronavirus+infections)
    - Higher prevalence of abnormal aminotransferase levels in patients with severe illness (AST and ALT >40 U/L)
    - Reported in 14% to 53% of patients
    - Clinically significant liver injury is uncommon
- Sepsis and septic shock (https://www.ncbi.nlm.nih.gov/pubmed/31986264)
    - Reported in 4% to 8% of patients
- DIC (https://www.ncbi.nlm.nih.gov/pubmed/32234718)
    - Some patients with severe COVID 19 have an inflammatory response similar to cytokine release syndrome, with persistent fevers, elevated inflammatory markers (D dimer ferritin), and elevated proinflammatory cytokines
- Thrombotic complications

(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7146714/)

- 31% incidence of thrombotic complications in COVID patients in one study of 184 ICU patients
- Predisposes to venous and arterial thromboembolic events due to excessive inflammation, hypoxia, immobilization, and DIC
- PE was the most frequent thrombotic complication in the study
- Age and coagulopathy (spontaneous prolongation of the prothrombin time >3 seconds or activated partial thromboplastin time >5 seconds were independent predictors of thrombotic complications

- Secondary infection

(https://www.ncbi.nlm.nih.gov/pubmed/?term=Clinical%2C+laboratory+and+imaging+features+of+COVID-19%3A+A+systematic+review+and+meta-analysis)

- Reported in 6% to 10% of patients
- Bacterial infections with Staphylococcus and Streptococcus species are common

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7228239/?fbclid=IwAR29UkmV1J5kmCXG70MHksaT9SiLnQgNh7SOSgZ9101J7ThLUcjCb46EaRk

- Conjunctivitis seen in 1 case

- Acute kidney injury

(https://www.ncbi.nlm.nih.gov/pubmed/?term=Epidemiological+and+clinical+characteristics+of+99+cases+of+2019+novel+coronavirus+pneumonia+in+Wuhan%2C+China%3A+a+descriptive+study)

- Prevalence is low but is a marker of multiple organ dysfunction and severe disease
- 40% of patients in Wuhan had proteinuria on admission and 26% had hematuria. 5% of patients developed an AKI and had increased risk of in hospital mortality.
- Stage 3 AKI occurred in almost ½ of the patients with kidney injury. Rhabdomyolysis (late complication), metabolic acidosis, and hyperkalemia can also occur.
- Older age, greater severity of illness, diabetes mellitus, and positive fluid balance were independently associated with AKI development

- Neurologic

(https://www.ncbi.nlm.nih.gov/pubmed/?term=Neurologic+manifestations+of+hospitalized+patients+with+coronavirus+disease+2019+in+Wuhan%2C+China.+JAMA+Neurol)

- Viral invasion of the CNS can occur in patients with severe illness
- Observed in 36% of 214 patients and common in patients with severe illness
- Complications include acute cerebrovascular disease, impairment of consciousness, ataxia, seizures, and encephalopathy. Prognosis for these patients is poor.

https://www.cureus.com/articles/33149-atypical-neurological-manifestations-of-covid-19#table-anchor-116338

- Guillain-Barre syndrome seen in 4 cases.
- Neurosensory hearing loss seen in 1 case.

- Pregnancy (https://www.ncbi.nlm.nih.gov/pubmed/?term=Dashraath+P%2C+Jing+Lin+Jeslyn+W%2C+Mei+Xian+Karen+L%2C+et+al.+Coronavirus+disease+2019+(COVID-19)+pandemic+and+pregnancy)
  - Fetal distress, premature labor, newborn thrombocytopenia, elevated liver enzymes, and respiratory distress
  - Miscarriage, intrauterine growth restriction, and preterm birth
  - 1 case of a still birth

What are the risk factors for severe disease/morbidity/mortality?

- Down Syndrome was recently found to show possibly a 4 fold increase in COVID hospitalization and 10 fold increase in COVID related death.
  - https://www.acpjournals.org/doi/10.7326/M20-4986
  -
- Severe disease

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7099829/pdf/12931_2020_Article_1338.pdf
https://www.aging-us.com/article/103000/text
https://www.jacionline.org/article/S0091-6749(20)30495-4/pdf
https://poseidon01.ssrn.com/delivery.php?ID=970088027008066097095123099077112004086087058042010063026060110031025025063014052027058091076042081077050047002035007056069029011068097072084006113005127117120010092075094093088100022021066105087121121081064026105070089064095092122004080095011116&EXT=pdf
https://www.degruyter.com/view/journals/cclm/58/7/article-p1021.xml
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7094472/
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7083240/
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7213702/
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7102663/
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7194601/

  - Older age
  - Black, Hispanic, or South Asian ethnicity

        - https://pubmed.ncbi.nlm.nih.gov/32640463/ "Compared with people of white ethnicity, Black and South Asian people were at higher risk, even after adjustment for other factors (HR 1.48 (1.29-1.69) and 1.45 (1.32-1.58), respectively)."
    - Hypertension
    - High cytokine levels (IL-2R, IL-6, IL-10, and TNF-a)
    - High LDH level
    - Diabetes
    - COPD
    - Cardiovascular disease
    - Cerebrovascular disease
    - Obesity (BMI ≥ 28 kg/m2)
    - Mildly elevated WBC count (WMD: 0.41×10^9/L)
    - Elevated biomarkers of cardiac and muscle injury
    - significant elevations in liver enzymes (alanine aminotransferase and aspartate aminotransferase), renal biomarkers (blood urea nitrogen, creatinine), and coagulation measures
    - significantly greater increases were observed for IL-6 and serum ferritin in non-survivors vs. survivors (WMD: 4.6 pg/mL and 760.2 ng/mL, respectively) as compared to severe vs. non-severe form (WMD: 1.7 pg/mL and 408.3 ng/mL, respectively).
    - elevated C-reactive protein (CRP)
    - Elevated procalcitonin associated with a nearly 5-fold higher risk of severe disease
    - Smoking (current > former)
    - tumour necrosis factor alpha (TNF-α), interferon-γ-induced protein 10 (IP-10), monocyte chemoattractant protein 1 (MCP-1), chemokine (C-C motif), ligand 3 (CCL-3), and distinct interleukins (IL) (IL-2, IL-6, IL-7, IL-10) were significantly associated with disease severity and particularly observed among cases admitted to ICUs. IL-1 and IL-8 were not associated with severity
    - https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(20)30309-0/fulltext - risk factors in cancer patients - advanced tumour stage, elevated TNF-α and NT-proBNP, and decreased CD4+ T cells and albumin–globulin ratio
    - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7245300/ - overweight also a risk factor
    - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7309210/ - chills, body temperature > 37.5 °C, findings of pneumonia on chest X-ray associated w/progression to severe disease

- Morbidity

https://www.journalofinfection.com/article/S0163-4453(20)30153-5/pdf
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7087935/pdf/392_2020_Article_1626.pdf
https://www.journalacs.org/article/S1072-7515(20)30400-2/pdf
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7083240/
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7213702/

  - Increased neutrophil count
  - Increased BUN and LDH related to renal failure, heart failure, or multi-organ failure (MOF)
  - Acute cardiac injury 13 times more common in ICU COVID patients than in non-ICU COVID patients
  - Fibrinolysis shutdown (elevated D-Dimer and complete failure of clot lysis at 30 minutes on TEG) predicts thromboembolic events and need for hemodialysis
  - Smoking (current > former)
  - Thrombocytopenia

- Mortality

Case Fatality Rate of Cancer Patients with COVID-19 in a New York Hospital System

  - COVID-19 in patients with cancer is associated with a significantly increased risk of case fatality, suggesting the need for proactive strategies to reduce likelihood of infection and improve early identification in this vulnerable patient population.
  - Highest susceptibility appears to be in hematologic and lung malignancies

https://www.thelancet.com/action/showPdf?pii=S0140-6736%2820%2930566-3
https://www.bmj.com/content/bmj/368/bmj.m1091.full.pdf
https://www.journalofinfection.com/article/S0163-4453(20)30208-5/pdf
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7110296/
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7144257/pdf/ERJ-00524-2020.pdf
https://jamanetwork.com/journals/jama/fullarticle/2762130
https://www.ncbi.nlm.nih.gov/pubmed/32240670

https://onlinelibrary.wiley.com/doi/full/10.1111/jth.14768

https://www.degruyter.com/view/journals/cclm/58/7/article-p1021.xml

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7083240/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7213702/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7102663/

- Older age (>65 years); specifically -
  - 70-79 y/o had a 8.0% case fatality rate (CFR)
  - 80+ y/o had a 14.8% CFR
- Male sex
- Preexisting comorbidities
  - Cardiovascular disease - 10.5% CFR
  - Diabetes - 7.5% CFR
  - Chronic respiratory disease - 6.3% CFR
  - Hypertension - 6.0% CFR
  - Cancer - 5.6% CFR
- Cerebrovascular disease
- High Sequential Organ Failure Assessment (SOFA) score
- Leukocytosis
- High LDH level
- Cardiac injury
- Hyperglycemia
- High-dose corticosteroid use
- Significantly elevated WBC count (WMD: 4.15×10^9/L)
- CD3+ CD8+ T cells ≤ 75 cell/μL
- Cardiac troponin I ≥ 0.05 ng/mL
- D-dimer > 1 μg/mL
- High FDP
- High neutrophil-to-lymphocyte ratio (especially in males)
- Kidney disease
- AKI during hospitalization
- Smoking (current > former)
- Thrombocytopenia
- Symptoms more commonly seen in deceased than recovered patients:
  - With respect to the severity cohort, non-survivors compared to survivors had more significant increases in WBC count, total bilirubin, creatine kinase, serum ferritin, and interleukin 6 (IL-6), and more significant decreases in lymphocyte count and platelet count.
  - Elevated biomarkers of cardiac and muscle injury
  - significantly greater increases were observed for IL-6 and serum ferritin in non-survivors vs. survivors (WMD: 4.6 pg/mL and 760.2 ng/mL, respectively) as compared to severe vs. non-severe form (WMD: 1.7 pg/mL and 408.3 ng/mL, respectively).

        - Patients who died had significantly elevated cardiac troponin levels at presentation (WMD: 32.7 ng/L)
        - Dyspnea
        - Chest tightness
        - Disorder of consciousness
        - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7184979/ - In pts >60 yo, muscle aches & absence of fever
        -
    - Laboratory value **increases** more commonly seen in deceased than recovered patients:
        - Alanine aminotransferase
        - Aspartate aminotransferase
        - Creatinine
        - Creatine kinase
        - Lactate dehydrogenase
        - Cardiac troponin I
        - N-terminal pro-brain natriuretic peptide
        - D-dimer
    - Complications more commonly seen in deceased than recovered patients:
        - Acute respiratory distress syndrome
        - Type I respiratory failure
        - Sepsis
        - Acute cardiac injury
        - Heart failure
        - Alkalosis
        - Hyperkalaemia
        - Acute kidney injury
        - Hypoxic encephalopathy
    - In a retrospective study of 339 pts 60 or older, common comorbidities were hypertension (40.8%), diabetes (16.0%) and cardiovascular disease (15.7%). Shorter length of stay was found for the dead compared with the survivors (5 (3–8) vs. 28 (26–29), $P < 0.001$). Symptoms of dyspnea (HR 2.35, $P = 0.001$), comorbidities including cardiovascular disease (HR 1.86, $P = 0.031$) and chronic obstructive pulmonary disease (HR 2.24, $P = 0.023$), and acute respiratory distress syndrome (HR 29.33, $P < 0.001$) were strong predictors of death. And a high level of lymphocytes was predictive of better outcome (HR 0.10, $P < 0.001$. Considering the vital signs, significant higher respiration rates were found in the dead group, in comparison to the survived. When compared with the survival group, the count of neutrophils was significantly increased. The counts of CD4+

and CD8+ *T* cells, were all significantly decreased in the dead group. The prothrombin time was significantly prolonged, and the concentration of d-dimer was evidently increased in the dead group. In addition, the markers for myocardial injury, inflammation, and bacterial infections were all increased significantly in the dead group.

- https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2770945?widget=personalizedcontent&previousarticle=0
    - Increased RDW at admission to hospital (>14.5%) and increasing RDW throughout hospitalization was found to be associated with increased mortality for all ages included in the study
    - The association of RDW at admission and mortality risk was independent of D-dimer, absolute lymphocyte count, demographic factors.
    - Patients with increased RDW during hospitalization increased mortality from 6% to 24% for patients with normal RDW at admission, and from 22% to 40% for patients with elevated RDW at admission.