

# **Post-COVID 19 Sequelae and Complications Management in Outpatient Setting**

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# Poll Questions

1. A 33 y/o M with hx of obesity and HTN is evaluated in the ED and diagnosed with Covid 19. He is febrile, anxious and dyspneic. D dimer is 7290. CTPE is neg for PE and O2 sat is 94%. The ED staff discharges him to home with instructions to quarantine and follow up with his PCP. As his PCP, would you:

- Start him on broad spectrum antibiotics?
- Start him on VTE prophylaxis?
- Repeat the CTPE
- Get an echocardiogram
- Insist on hospitalization for more thorough evaluation and monitoring

# Poll Questions

2. What proportion of Covid-19 patients with Covid pneumonia have persistent dyspnea after hospital discharge?

- < 2 %
- 5%
- 15 %
- 30%
- 50%

# Poll Questions

3. Secondary infection is common after viral infection. You suspect that your patient who was diagnosed with Covid-19 infection 2 weeks ago, then seemed to improve, but now presents to your office with recurrent fever and productive cough may have a secondary infection. Which is the most common secondary infection noted after Covid-19 diagnosis?

Acinetobacter baumannii

Candida Species

Aspergillus

Streptococcus pneumoniae

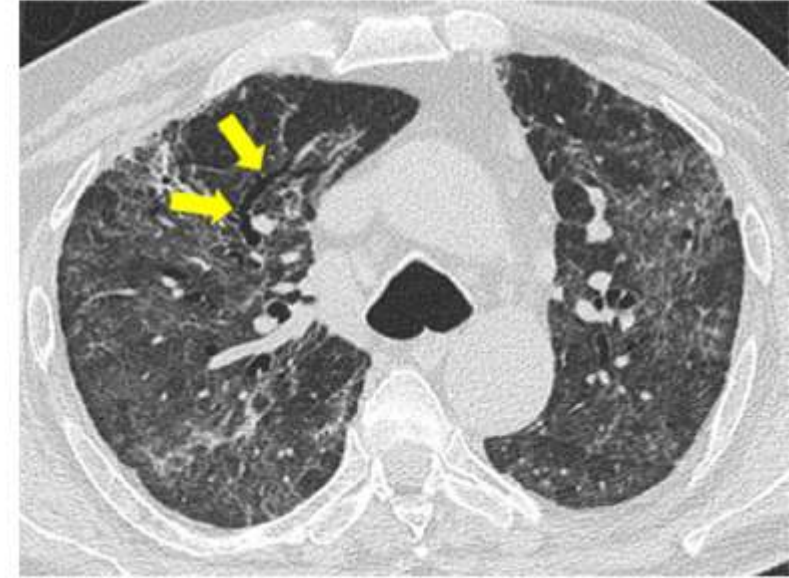
Klebsiella pneumoniae

# Case

- 33 y/o M with hx of obesity and HTN dx Covid 19 on 3/24/20
- Progressive cough, N/V/D, anosmia, decreased taste seen in ED –sent home to quarantine
- Progressive dyspnea, anxiety, and inability to tolerate PO-- Hospitalization 3/27-3/29 –CXR with multifocal pneumonia but nml O2 sats. No abx given. Treated with Zofran, Ativan. D dimer =940.
- Returned to ED 4/9 with recurrent fever/dry cough/SOB ---abnormal ECG, neg troponin. Elevated d dimer (7,290), neg CTPE. O2 sats stable at 94 -Slightly improved multifocal pneumonia. Follow up with ID



In typical cases of COVID-19 pneumonia, the chest X-ray shows multiple bilateral peripheral opacities



**Figure 2** CT in COVID-19 extubated survivor: a study performed during recovery (26 days after onset of COVID-19 pneumonia). Image section at the level of the carina demonstrating widespread ground-glass opacification and considerable architectural distortion. There is definite CT evidence of fibrosis—note the varicose dilatation ('traction bronchiectasis') of the anterior segmental bronchus in the right upper lobe (arrows).

No pulmonary embolism.

2. Mild multifocal groundglass opacities, most prominent in the right lower lobe. Findings are nonspecific but compatible with multifocal pneumonia in the context of this COVID-19 positive patient

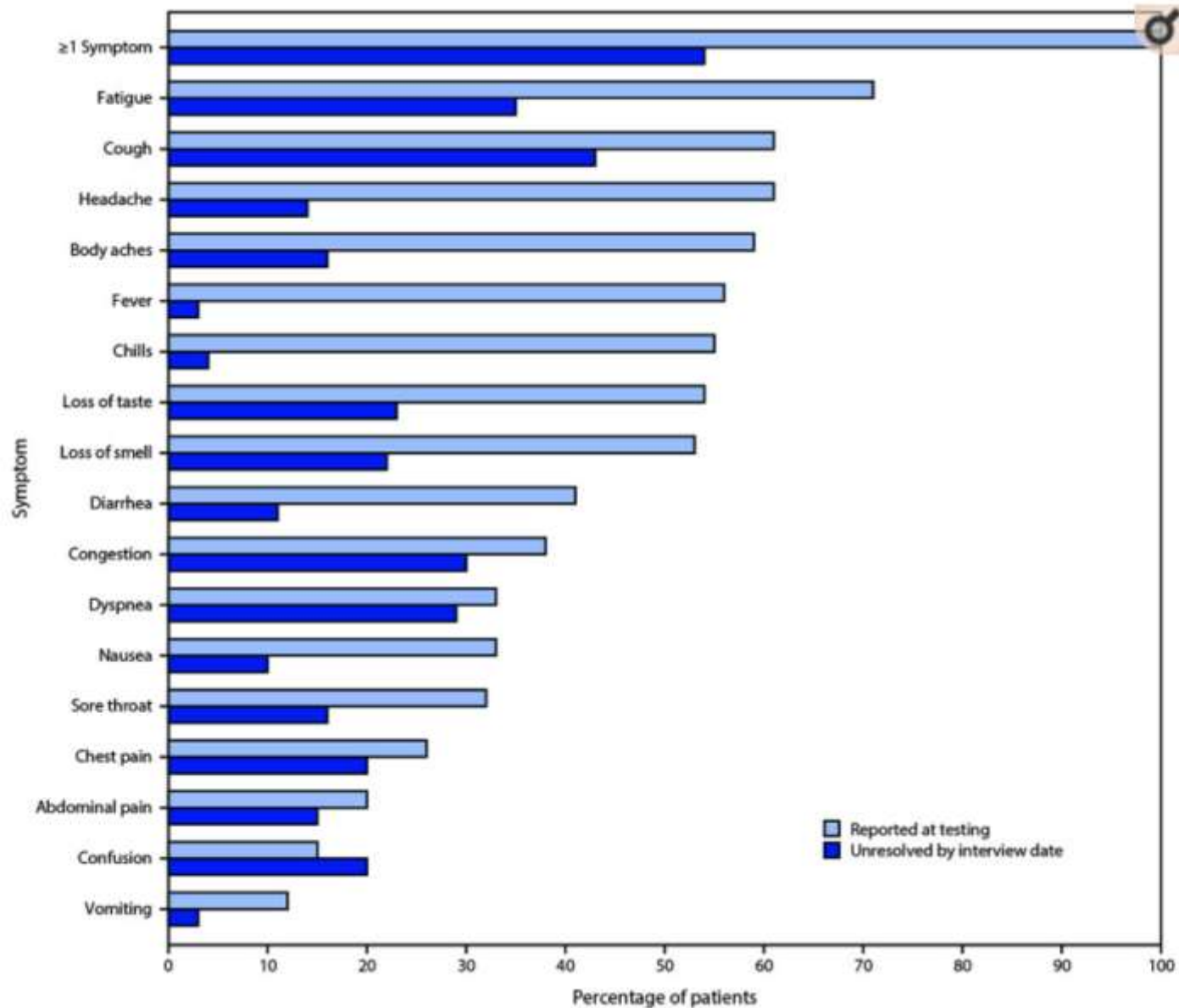
# Case Questions

How long do respiratory symptoms persist after diagnosis of Covid-19?

What are the recommendations for ID follow up of Covid pneumonia?

What are the recommendations for ID follow up of elevated D Dimer?

Could the patient have a secondary infection?



Self-reported symptoms at the time of positive SARS-CoV-2 reverse transcription–polymerase chain reaction (RT-PCR) testing results and unresolved symptoms 14–21 days later among outpatients (N = 274)\* — 14 academic health care systems,<sup>†</sup> United States, March–June 2020 Tenforde M et al. [MMWR Morb Mortal Wkly Rep. 2020 Jul 31; 69\(30\): 993–998.](https://doi.org/10.15585/mmwr.mm6903a1)



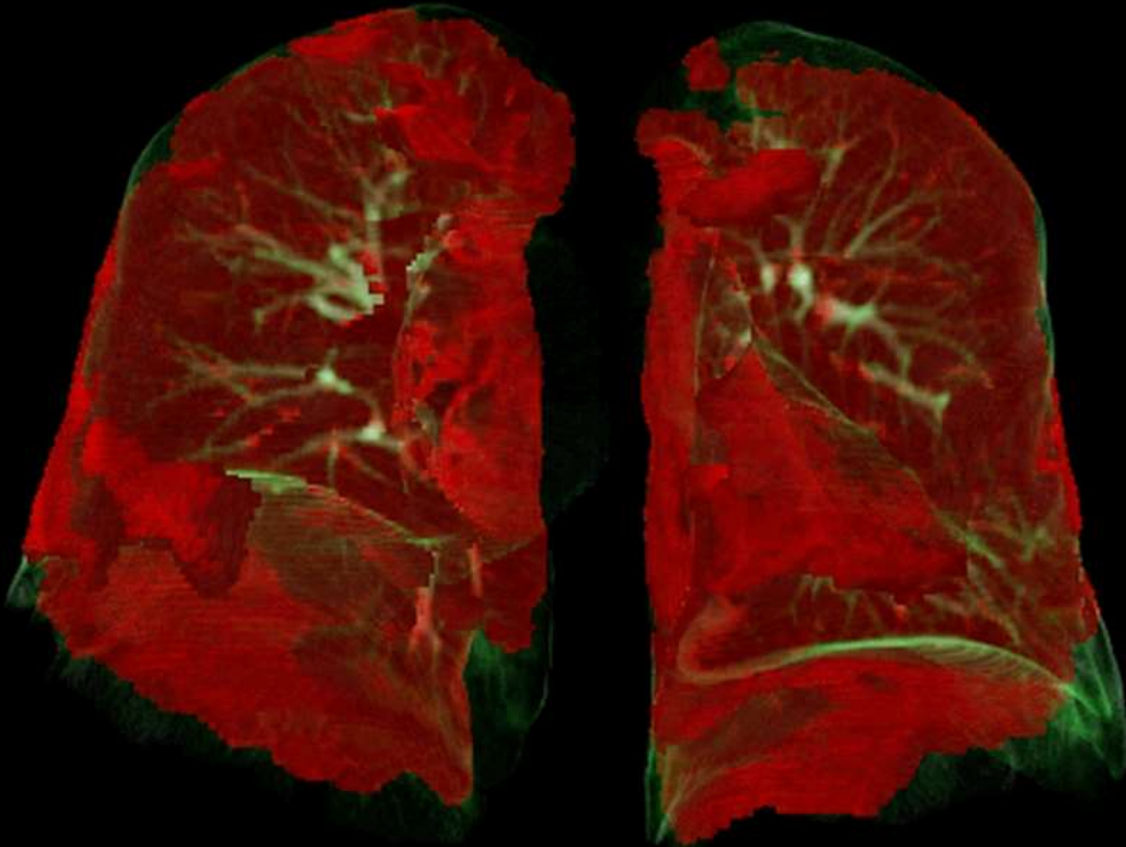
# Persistent Respiratory Sx after Coronavirus

- A study from the United Kingdom
  - 100 hospitalized patients (32 in ICU and 68 on the floor)
  - 72% of the ICU patients and 60% of the ward patients experienced fatigue and breathlessness at 4 to 8 weeks post hospital discharge
  
- 36% of MERS survivors, at a median follow-up point of 6 weeks had residual CXR changes, majority due to pulmonary fibrosis

# Lung Damage After Covid-19

- A USC team analyzed lung CT images of 919 patients from published studies
  - lower lobes of the lungs are the most frequently damaged
  - scans were riddled with opaque patches that indicate inflammation
  - visible damage normally reduced after two weeks
- An Austrian study also found that lung damage lessened with time:
  - 88% of participants had visible damage 6 weeks post discharge
  - by 12 weeks, this number had fallen to 56%

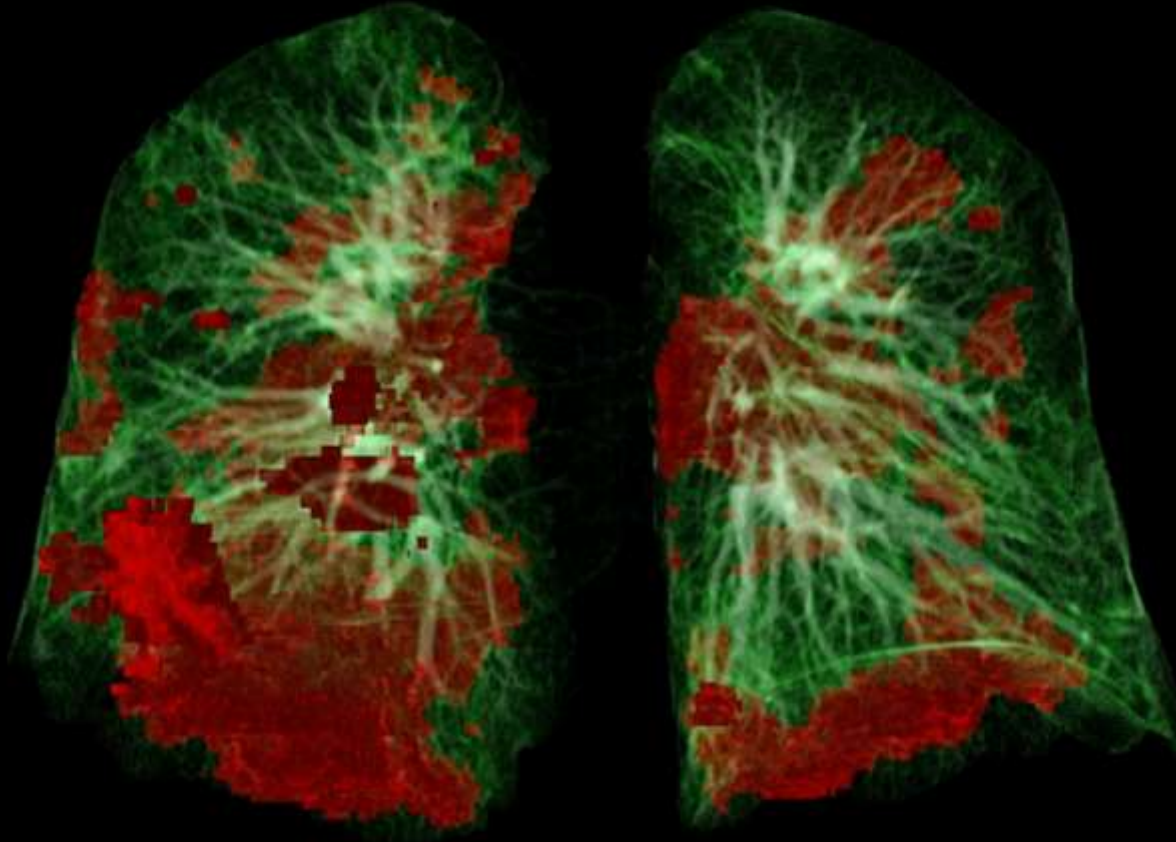
# Onset of COVID-19



Lung scans from a 50-year-old show that damage from COVID-19 (red) can improve with time — but many patients have lasting symptoms. Credit: Prof. Gerlig Widmann, Dr. Christoph Schwabl, Dr. Anna Luger - Dpt. of Radiology, Innsbruck Medical University

Marshall M. The lasting misery of coronavirus long-haulers. *Nature*. 2020;585(7825):339-341

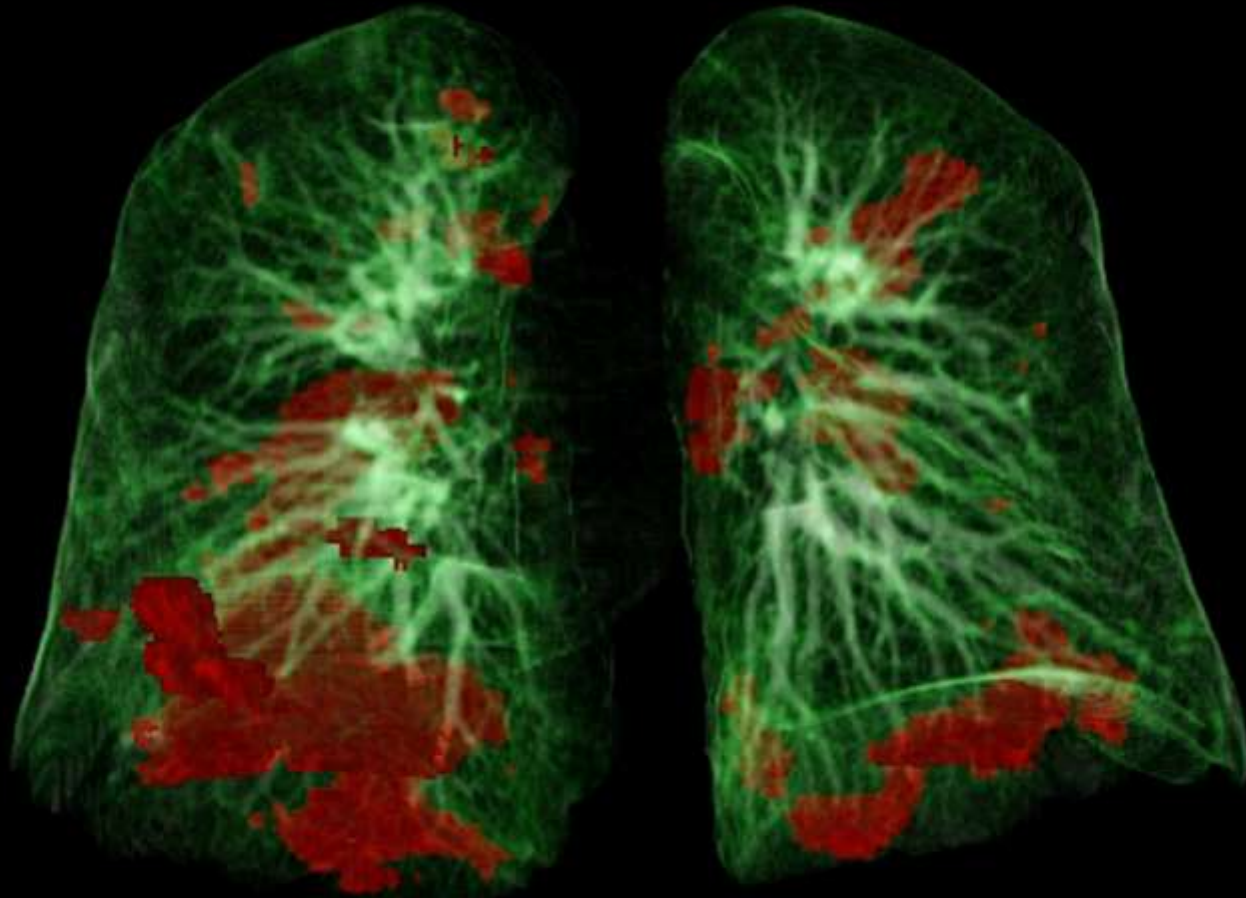
## Six weeks after discharge



Lung scans from a 50-year-old show that damage from COVID-19 (red) can improve with time — but many patients have lasting symptoms. Credit: Prof. Gerlig Widmann, Dr. Christoph Schwabl, Dr. Anna Luger - Dpt. of Radiology, Innsbruck Medical University

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# Twelve weeks after discharge



Lung scans from a 50-year-old show that damage from COVID-19 (red) can improve with time — but many patients have lasting symptoms. Credit: Prof. Gerlig Widmann, Dr. Christoph Schwabl, Dr. Anna Luger - Dpt. of Radiology, Innsbruck Medical University

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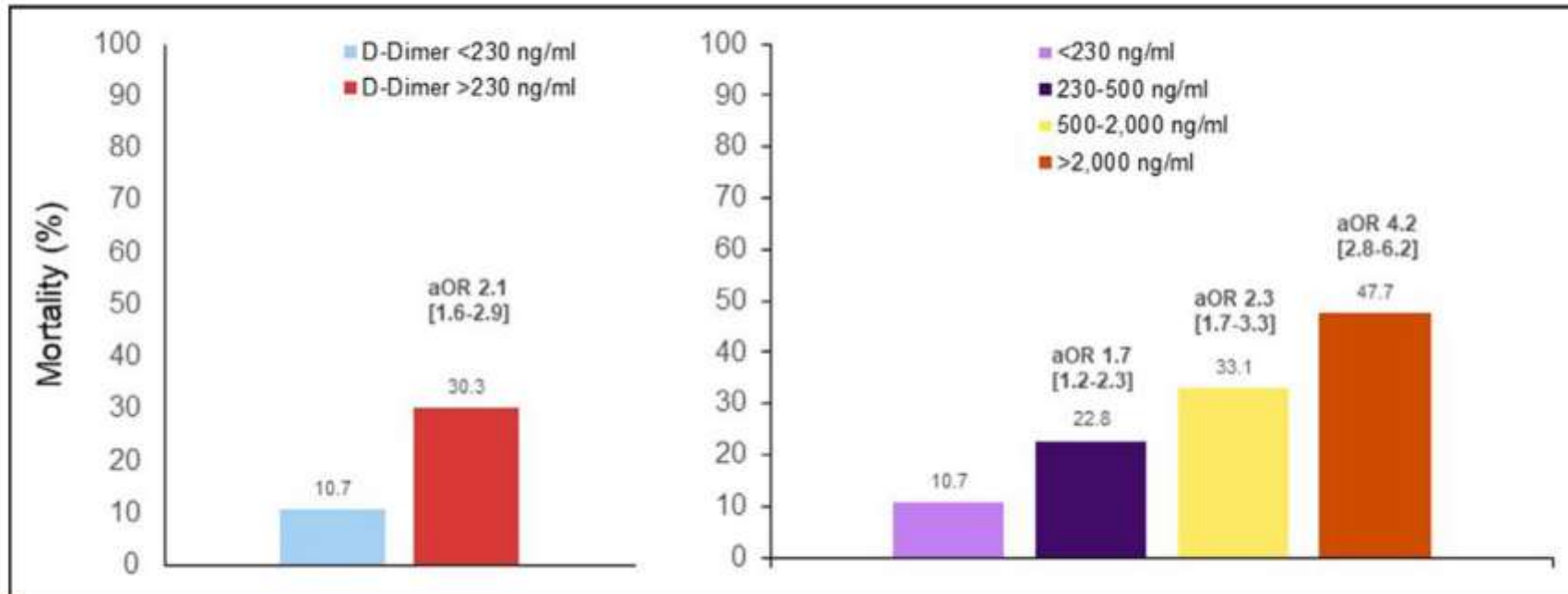
# Covid-19 and VTE

- Unlike the MERS and SARS, acute COVID-19 infection is associated with a high prevalence of VTE disease
- Meta-analysis---Pooled data on 1765 patients overall incidence of VTE was **21.9%**
- a number of patients are diagnosed with acute PE and DVT de novo during the pneumonia recovery

Al-Ani F et al. Thromb Res.2020;192:152–60;Bilaloglu S et al.JAMA. 2020;324:799–801;Lim WS et al.Thorax 2009;64 Suppl 3:iii1;Cui S et al. J Thromb Haemost 2020;18:1421–4;Wichmann D et al. Ann Intern Med 2020.

# Prevalence and Outcomes of D-Dimer Elevation in Hospitalized Patients With COVID-19

- 2377 adults hospitalized with COVID-19 in large hospital system in New York—76% had elevated D-dimer at presentation—they were more likely than those with normal D-dimer to:
- have critical illness (43.9% versus 18.5%; adjusted odds ratio, 2.4 [95% CI, 1.9–3.1];  $P<0.001$ )
- Any thrombotic event (19.4% versus 10.2%; adjusted odds ratio, 1.9 [95% CI, 1.4–2.6];  $P<0.001$ )
- acute kidney injury (42.4% versus 19.0%; adjusted odds ratio, 2.4 [95% CI, 1.9–3.1];  $P<0.001$ )
- death (29.9% versus 10.8%; adjusted odds ratio, 2.1 [95% CI, 1.6–2.9];  $P<0.001$ )
- **Conclusion:** The optimal management of patients with elevated D-dimer in COVID-19 requires further study.



**Figure 3. Baseline D-dimer measurements and all-cause mortality.**

All-cause mortality is defined as death or transfer to inpatient hospice. aOR indicates adjusted odds ratio.



# Secondary Infection

- In this retrospective study, 257 COVID-19 patients in Jiangsu Province were enrolled from January 22 to February 2, 2020
- 242 (94.2 %) patients were co-infected with one or more pathogens
- Streptococcus pneumoniae was the most common, followed by K. pneumoniae and H. influenzae.

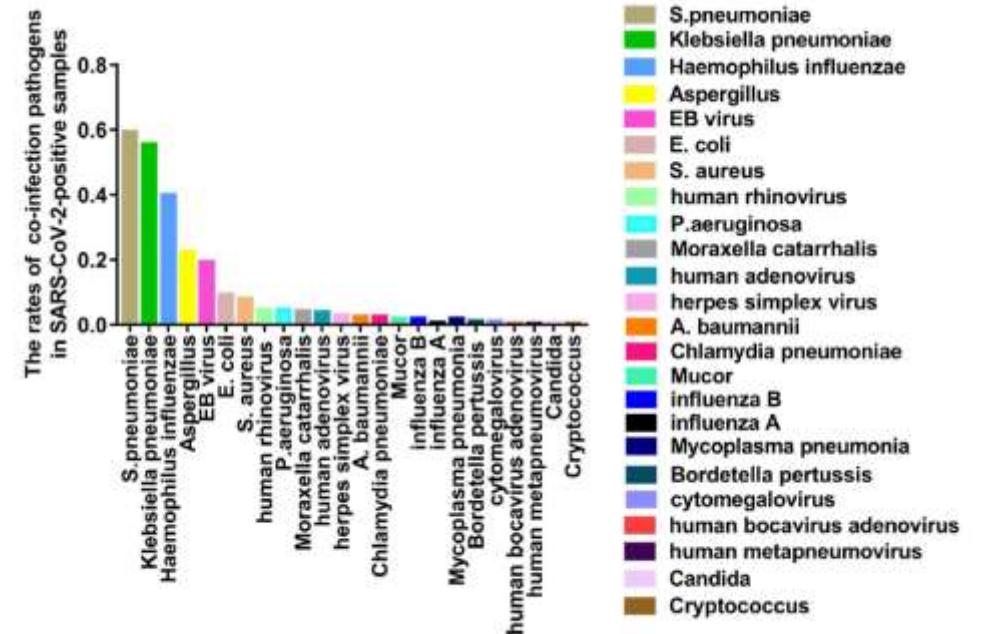
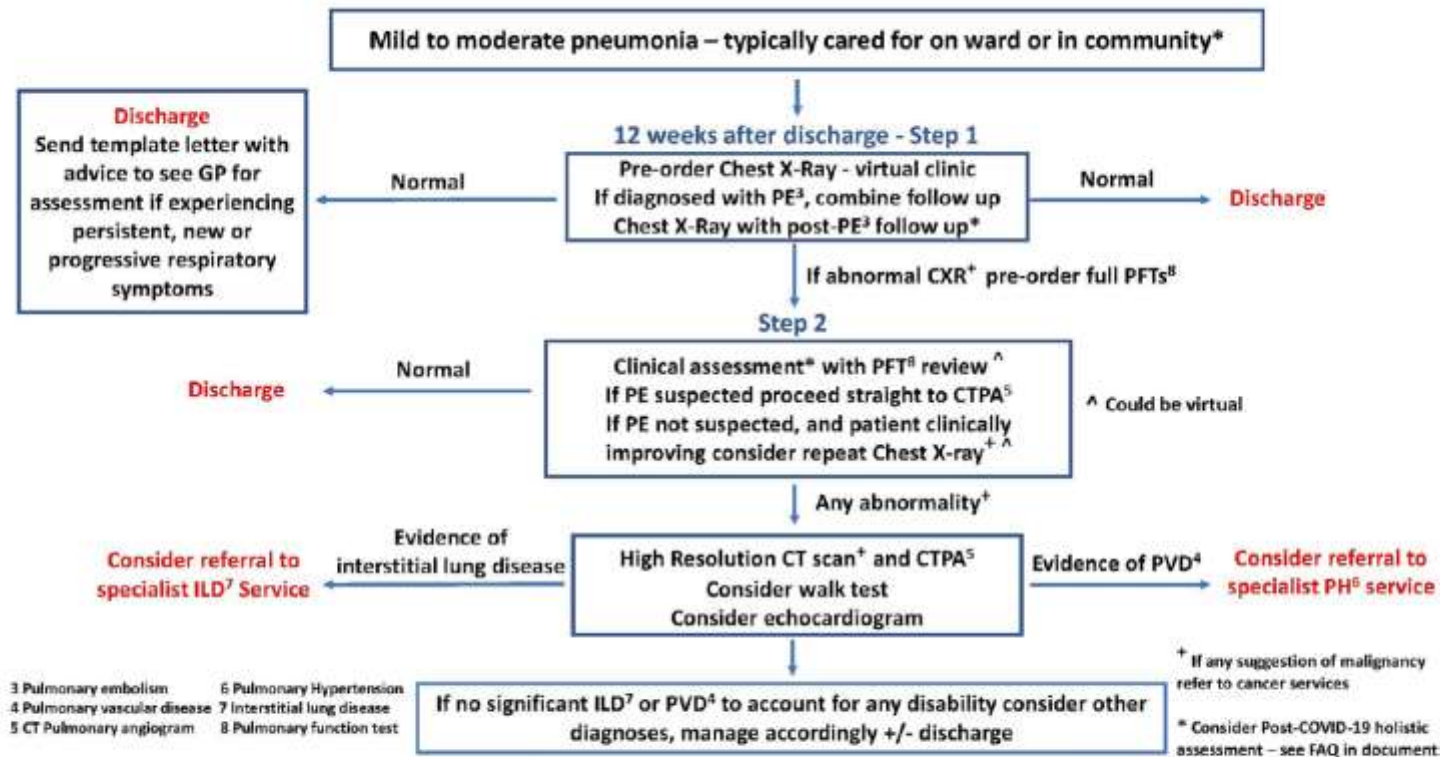


Fig. 1. Distribution of respiratory pathogens with the SARS-CoV-2 co-infection.

# Follow Up Recommendations



**Figure 4** Respiratory follow-up algorithm for patients with mild to moderate COVID-19 pneumonia—typically cared for on the ward or in the community. GP, general practitioner.

# Venous Thromboembolism Prophylaxis and Screening:

- For non-hospitalized patients with COVID-19, anticoagulants and antiplatelet therapy should not be initiated for prevention of venous thromboembolism (VTE) or arterial thrombosis unless there are other indications **(AIII)**.
- Hospitalized patients with COVID-19 should not routinely be discharged on VTE prophylaxis **(AIII)**. Using Food and Drug Administration-approved regimens, extended VTE prophylaxis can be considered in patients who are at low risk for bleeding and high risk for VTE as per protocols for patients without COVID-19 (see text for details on defining at-risk patients) **(BI)**.
- There are currently insufficient data to recommend for or against routine deep vein thrombosis screening in COVID-19 patients without signs or symptoms of VTE, regardless of the status of their coagulation markers **(BIII)**.



# Patients with COVID-19 Who Are Discharged from the Hospital:

- Routine post-discharge VTE prophylaxis **is not recommended** for patients with COVID-19 (AIII)
- However, the benefits of post-discharge prophylaxis for certain high-risk patients without COVID-19 led to the FDA approval of two regimens:
  - rivaroxaban 10 mg daily for 31 to 39 days
  - betrixaban 160 mg on Day 1, followed by betrixaban 80 mg once daily for 35 to 42 days
- Inclusion criteria for the trials that studied these regimens included:
  - Modified IMPROVE-VTE score  $\geq 4$ ; *or*
  - Modified IMPROVE-VTE score  $\geq 2$  and D-dimer level  $> 2$  times the upper limit of normal; *or*
  - Age  $\geq 75$  years; *or*
  - Age  $> 60$  years and D-dimer level  $> 2$  times the upper limit of normal; *or*
  - Age 40 to 60 years, D-dimer level  $> 2$  times the upper limit of normal, and previous VTE event or cancer

# SUMMARY

- Approximately 30-50% of patients with Covid-19 infection continue to have cough and dyspnea up to 3 weeks post hospital discharge. Some patients may require pulmonary rehabilitation.
- Patients with Covid 19 and an elevated baseline D dimer are at increased risk for critical illness, AKI, any thrombotic event, and death. The optimal management of patients with elevated D-dimer in COVID-19 requires further study.
- Case series have shown an overall incidence of 22% for VTE in patients with Covid-19. Routine post-discharge VTE prophylaxis is not recommended for patients with COVID-19 but may be considered in high risk patients.
- Secondary infections such as *S. pneumoniae*, *K pneumoniae*, and *H. influenzae* have been seen after Covid-19 viral infections