

Asthma and post-COVID sequelae

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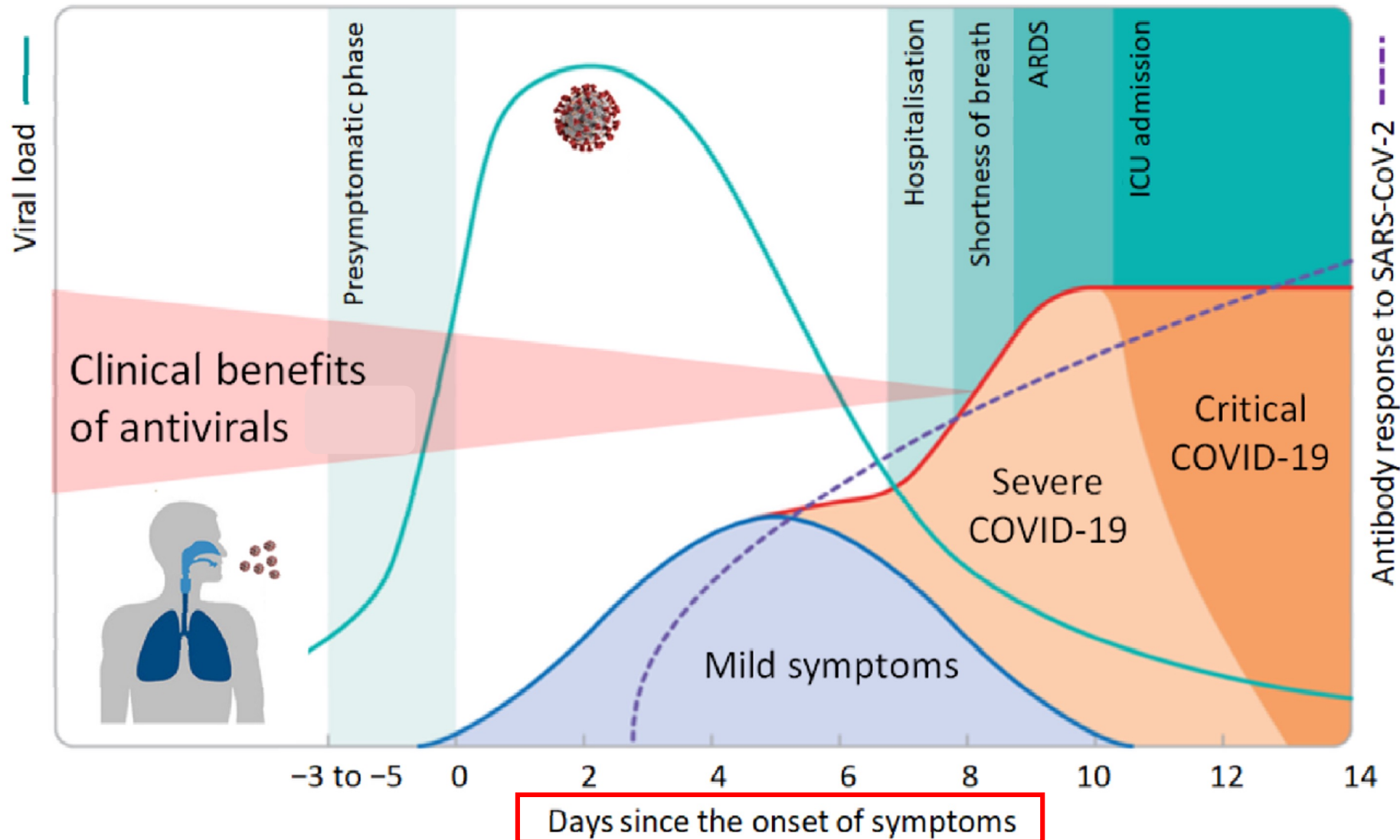
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Direct Organ and Tissue Effects of Infection with SARS-CoV-2

Phases of Illness/Therapies



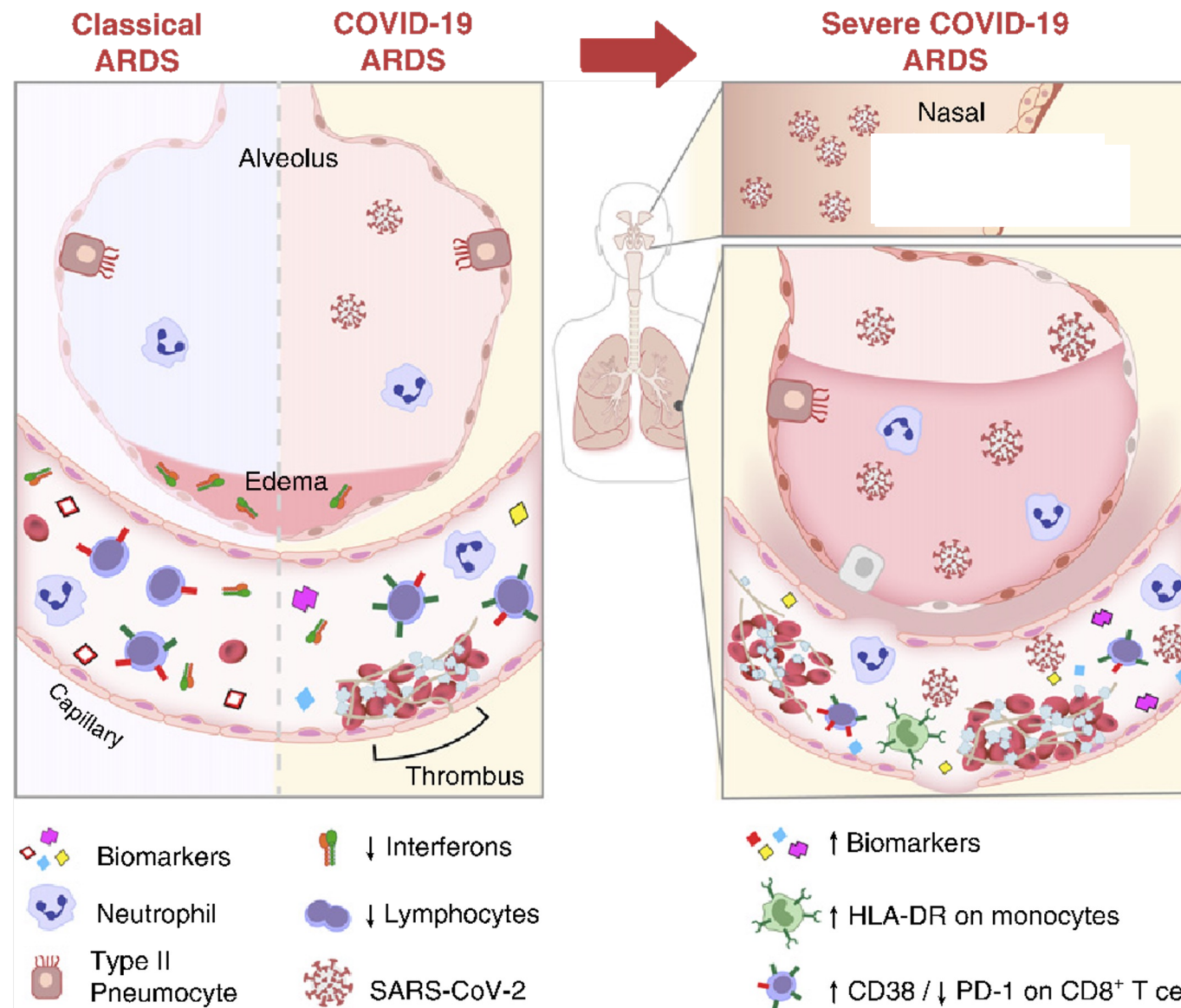
Antivirals:
<5 days

Immune modulators: > 5 days

Must **TEST** to know which
therapy!

Modified from Dolken
et al., Viruses, 2021

Mechanisms of COVID-19 Respiratory Failure



Matthay, AJRCCM, 2020

Practical Approach to Dealing With So Many New Therapies

- Have trusted sources
- Know how to access the key information quickly
- Apply principles of treatment
 - Test early for symptoms
 - Antivirals early, Immunomodulators later
 - Therapeutic choices also vary by illness severity
 - Support organ systems and optimize comorbid diseases
 - Low threshold to treat elderly, immunocompromised and other high-risk groups

WHO Provides Up-to-date Guidance



*No one group always right, but reasonable to stick with credible source or your institutional guidelines



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Therapeutics and COVID-19: living guideline

3 March 2022 | COVID-19: Clinical care



Overview

The WHO *Therapeutics and COVID-19: living guideline* contains the Organization's most up-to-date recommendations for the use of therapeutics in the treatment of COVID-19. The **latest version** of this living guideline is available in [pdf](#) format (via the 'Download' button) and via an [online platform](#), and is updated regularly as new evidence emerges.

This ninth version of the WHO living guideline now contains 15 recommendations, including

WHO TEAM

WHO Headquarters (HQ)

EDITORS

World Health Organization

NUMBER OF PAGES

109

<https://www.who.int/publications/i/item/WHO-2019-nCoV->

FDA Fact Sheets Are Very Helpful for Prescribing Unfamiliar Drugs

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use **HEPARIN SODIUM IN 0.45% SODIUM CHLORIDE INJECTION** or **HEPARIN SODIUM IN 5% DEXTROSE INJECTION** safely and effectively. See full prescribing information for **HEPARIN SODIUM IN 0.45% SODIUM CHLORIDE INJECTION** or **HEPARIN SODIUM IN 5% DEXTROSE INJECTION**.

HEPARIN SODIUM, for intravenous use
Initial U.S. Approval: 1939

INDICATIONS AND USAGE

Heparin sodium is an anticoagulant indicated for: (1)

- Prophylaxis and treatment of venous thromboembolism and pulmonary embolism
- Atrial fibrillation with embolization
- Treatment of acute and chronic consumptive coagulopathies (disseminated intravascular coagulation)
- Prevention of clotting in arterial and cardiac surgery
- Prophylaxis and treatment of peripheral arterial embolism
- Anticoagulant use in blood transfusions, extracorporeal circulation, and dialysis procedures.

DOSAGE AND ADMINISTRATION

Recommended Adult Dosages:

- **Therapeutic Anticoagulant Effect with Full-Dose Heparin*** (2.3)

Intermittent Intravenous Injection	Initial Dose	10,000 units
	Every 4 to 6 hours	5,000 to 10,000 units
Continuous Intravenous Infusion	Initial Dose	5,000 units by intravenous injection
	Continuous	20,000 to 40,000 units/24 hours
- **Surgery of the Heart and Blood Vessels** (2.5)

Intravascular via Total Body Perfusion	Initial Dose	≥ 150 units/kg; adjust for longer procedures
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- **Extracorporeal Dialysis** (2.8)

Intravascular via Extracorporeal Dialysis	Follow equipment manufacturer's operating directions carefully.
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- See full prescribing information for recommended pediatric dosage. (2.4)

DOSAGE FORMS AND STRENGTHS

Heparin sodium is available as: (3)

Heparin Sodium in 0.45% Sodium Chloride Injection:

- Injection: 50 USP units per mL in 0.45% Sodium Chloride clear solution (25,000 USP units per 500 mL) in single-dose **freeflex**[®] bag
- Injection: 100 USP units per mL in 0.45% Sodium Chloride clear solution (25,000 USP units per 250 mL) in single-dose **freeflex**[®] bag

Heparin Sodium in 5% Dextrose Injection:

- Injection: 40 USP units per mL in 5% Dextrose clear solution (20,000 USP Units per 500 mL) in single-dose **freeflex**[®] bag
- Injection: 50 USP units per mL in 5% Dextrose clear solution (25,000 USP Units per 500 mL) in single-dose **freeflex**[®] bag
- Injection: 100 USP units per mL in 5% Dextrose clear solution (25,000 USP Units per 250 mL) in single-dose **freeflex**[®] bag

CONTRAINDICATIONS

- History of Heparin-Induced Thrombocytopenia (HIT) and Heparin-Induced Thrombocytopenia and Thrombosis (HITT) (4)
- Known hypersensitivity to heparin or pork products (4)
- In whom suitable blood coagulation tests cannot be performed at appropriate intervals (4)

WARNINGS AND PRECAUTIONS

- **Fatal Medication Errors:** Confirm choice of correct strength prior to administration. (5.1)
- **Hemorrhage:** Fatal cases have occurred. Use caution in conditions with increased risk of hemorrhage. (5.2)
- **HIT and HITT:** Monitor for signs and symptoms and discontinue if indicative of HIT and HITT. (5.3)
- **Monitoring:** Blood coagulation tests guide therapy for full-dose heparin. Monitor platelet count and hematocrit in all patients receiving heparin. (5.5)

ADVERSE REACTIONS

Most common adverse reactions are hemorrhage, thrombocytopenia, HIT and HITT, hypersensitivity reactions, and elevations of aminotransferase levels. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Kabi USA, LLC at 1-800-551-7176 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Drugs that interfere with coagulation, platelet aggregation or drugs that counteract coagulation may induce bleeding. (7)

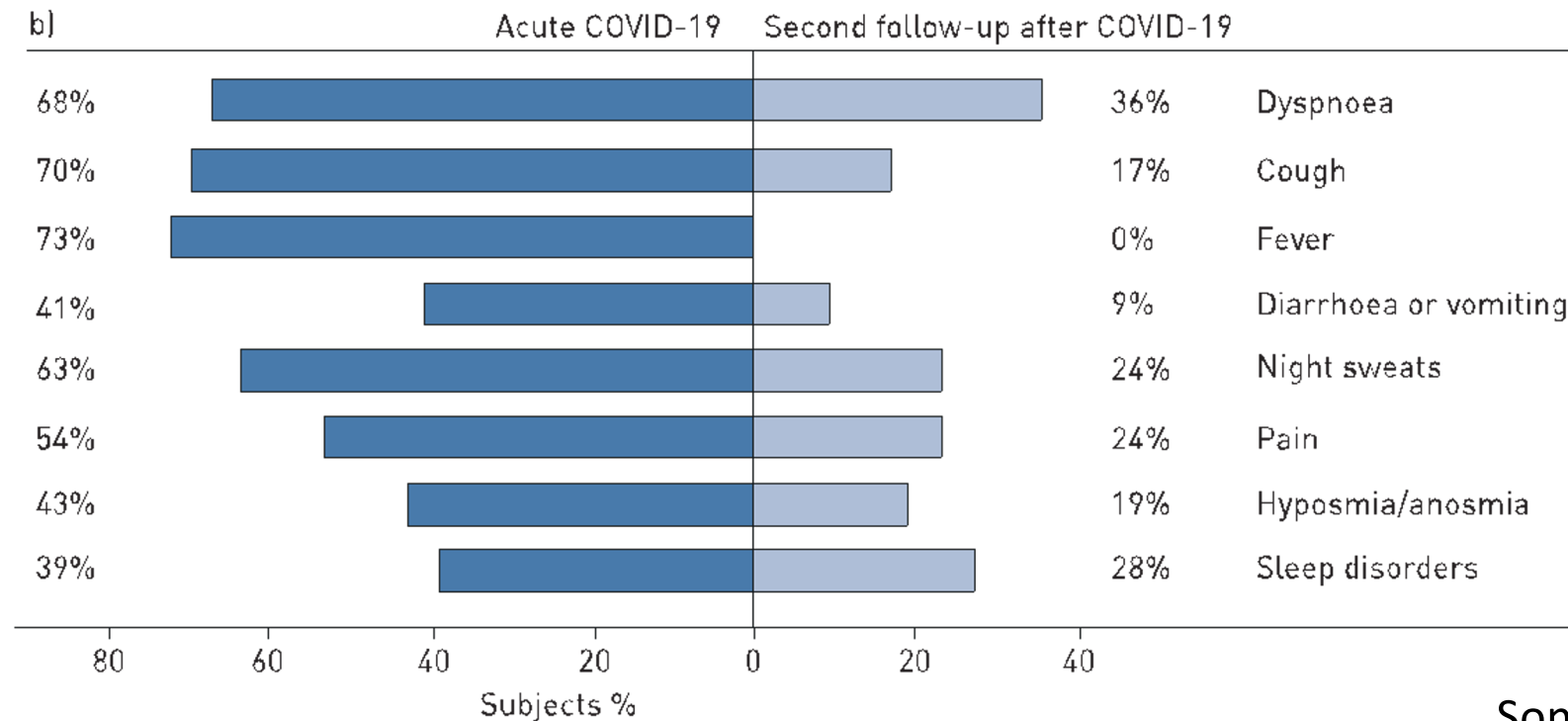
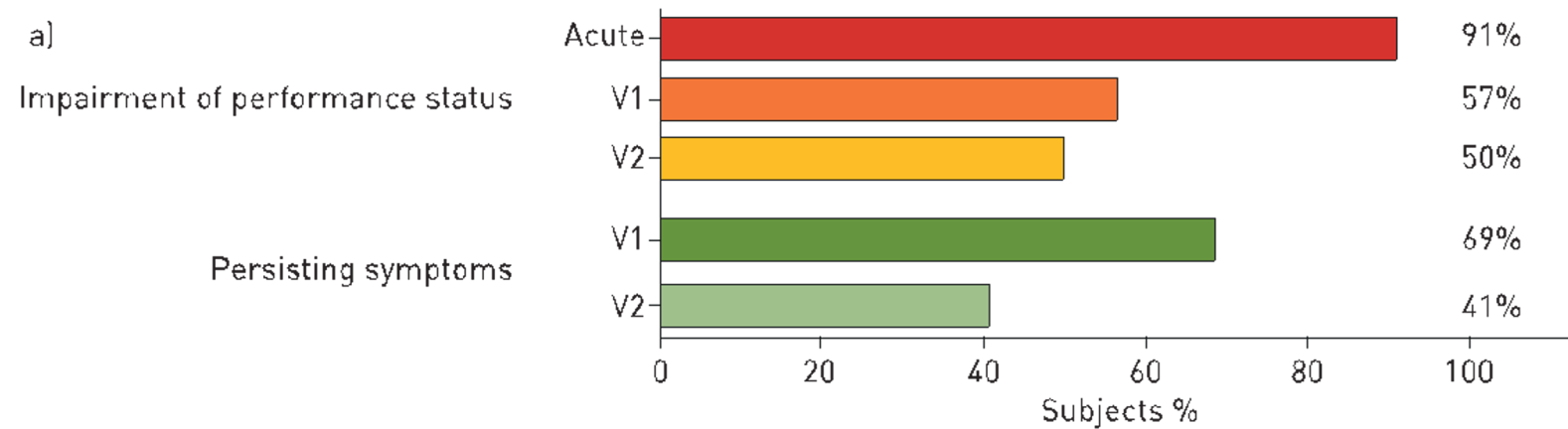
See 17 for PATIENT COUNSELING INFORMATION.

Revised: 08/2017

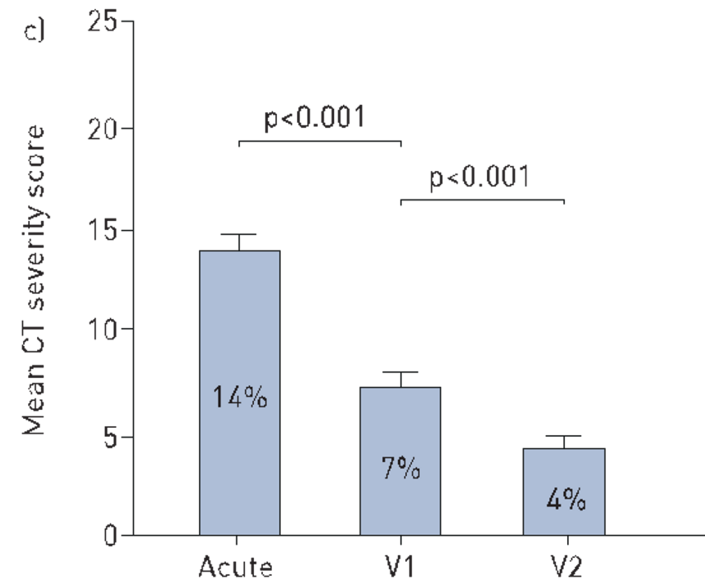
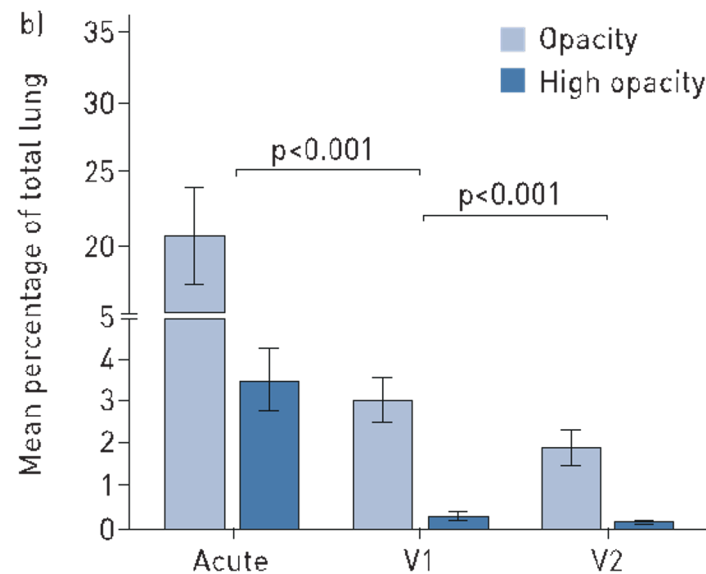
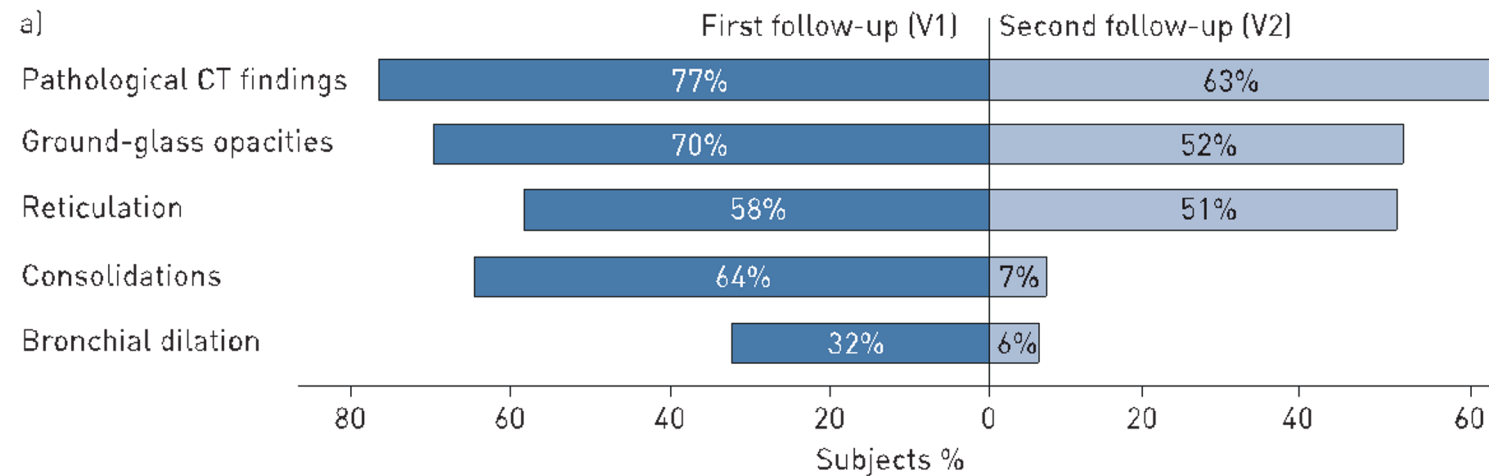
Symptoms, Lung Function, and Structural Lung Abnormalities Following COVID-19

36% have persistent Dyspnea at 100 days

- 145 patients
- Followed prospectively
- V1 = 60 days
- V2 = 100 days

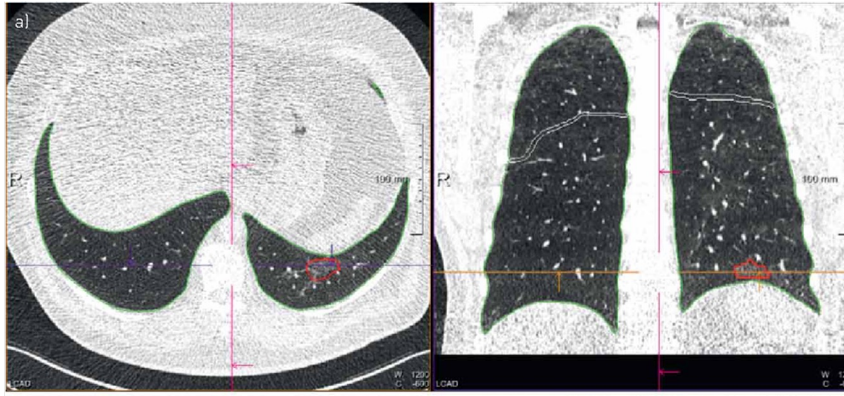


Ground glass and reticulations are most common persistent CT findings

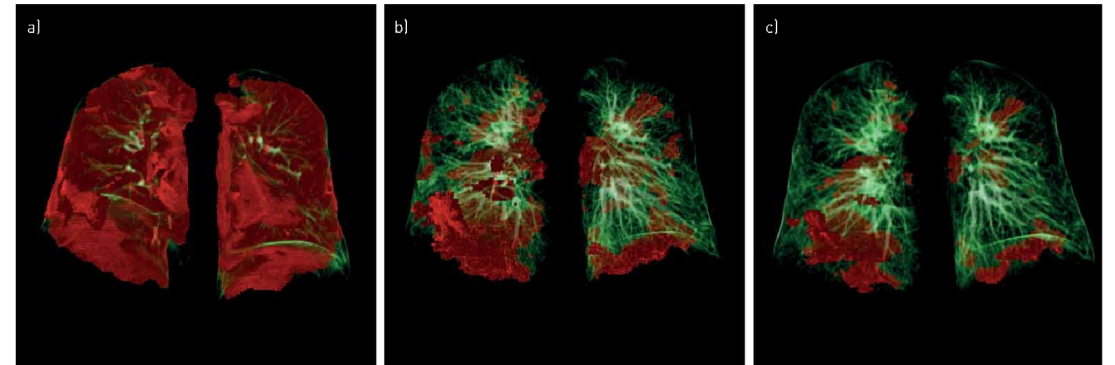


Radiographic abnormalities can vary in severity and time to resolution

Mild



COVID pneumonia in 56 year old male
Red are areas of consolidation

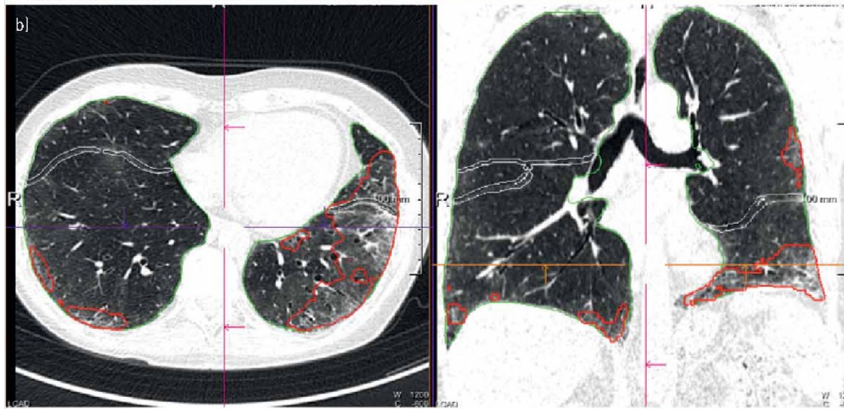


Acute

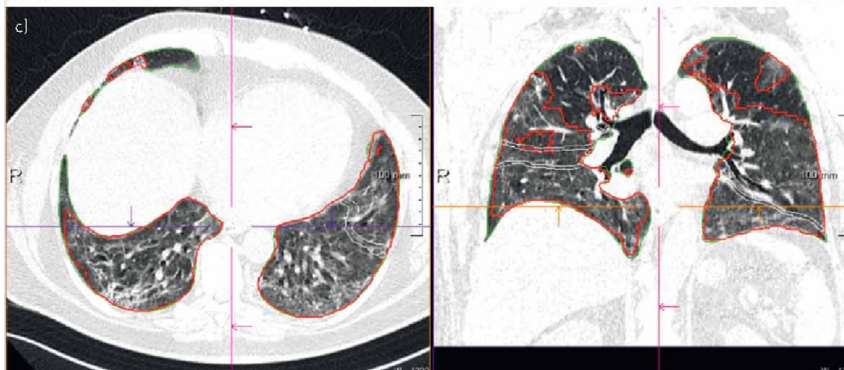
60 days

100 days

Moderate

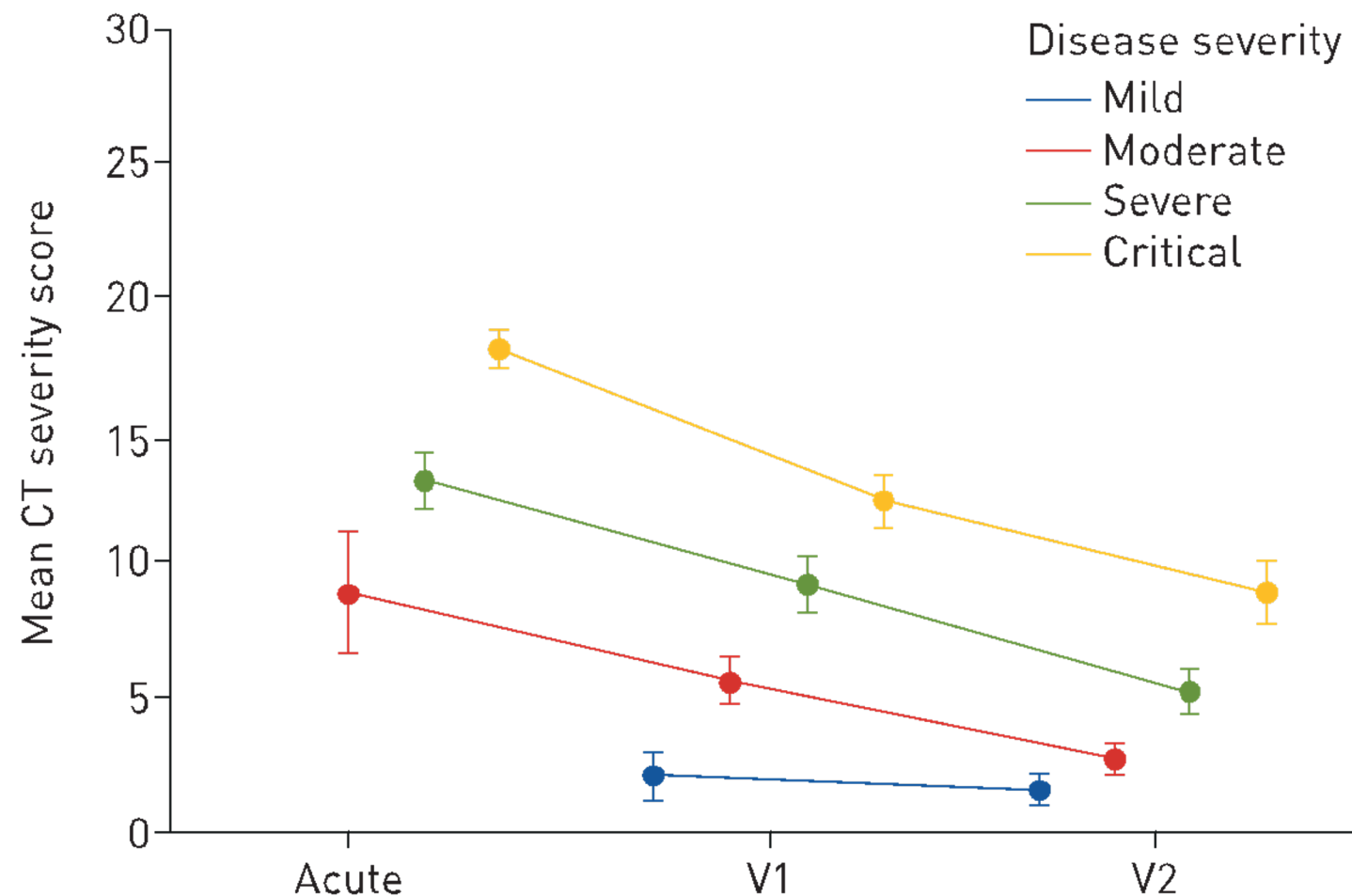


Severe

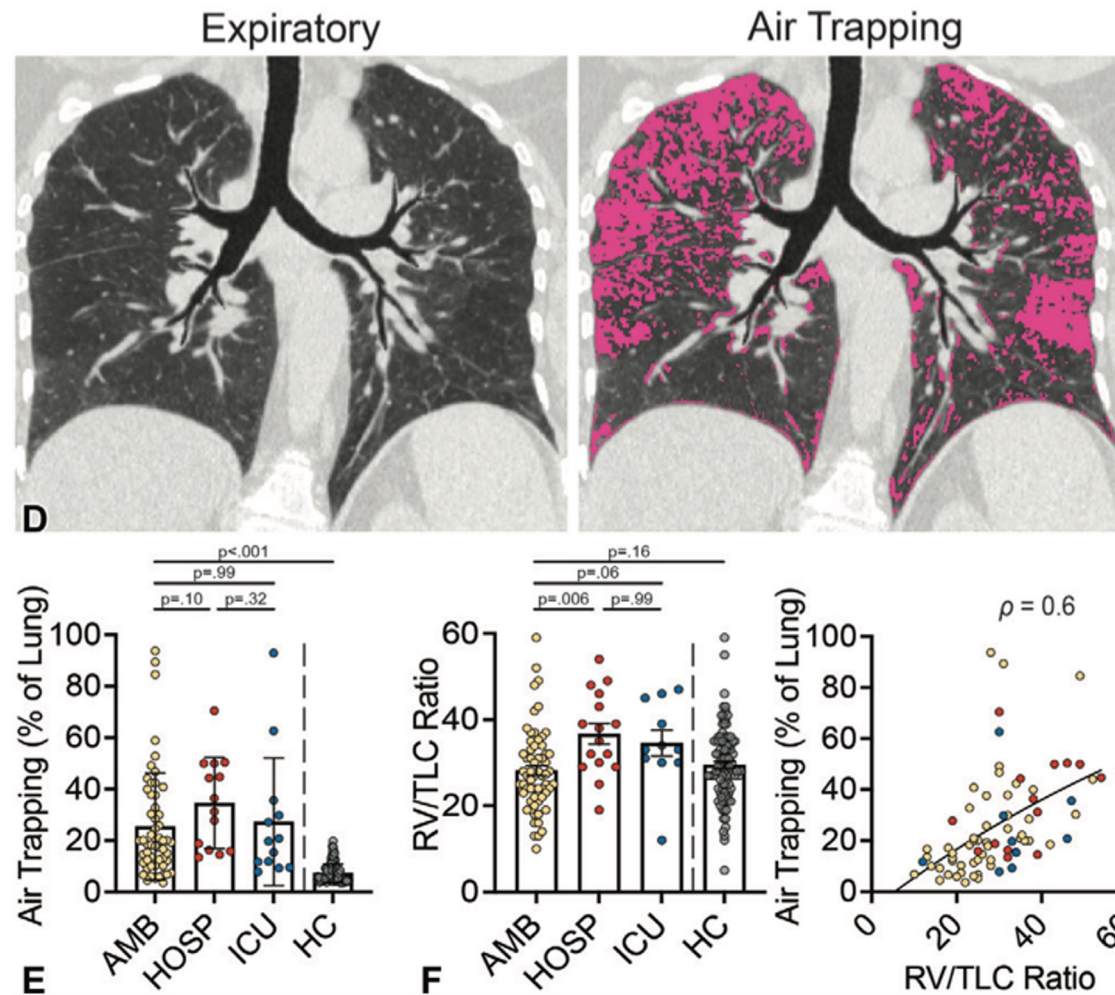


Sonnweber, et al., ERJ, 2021.

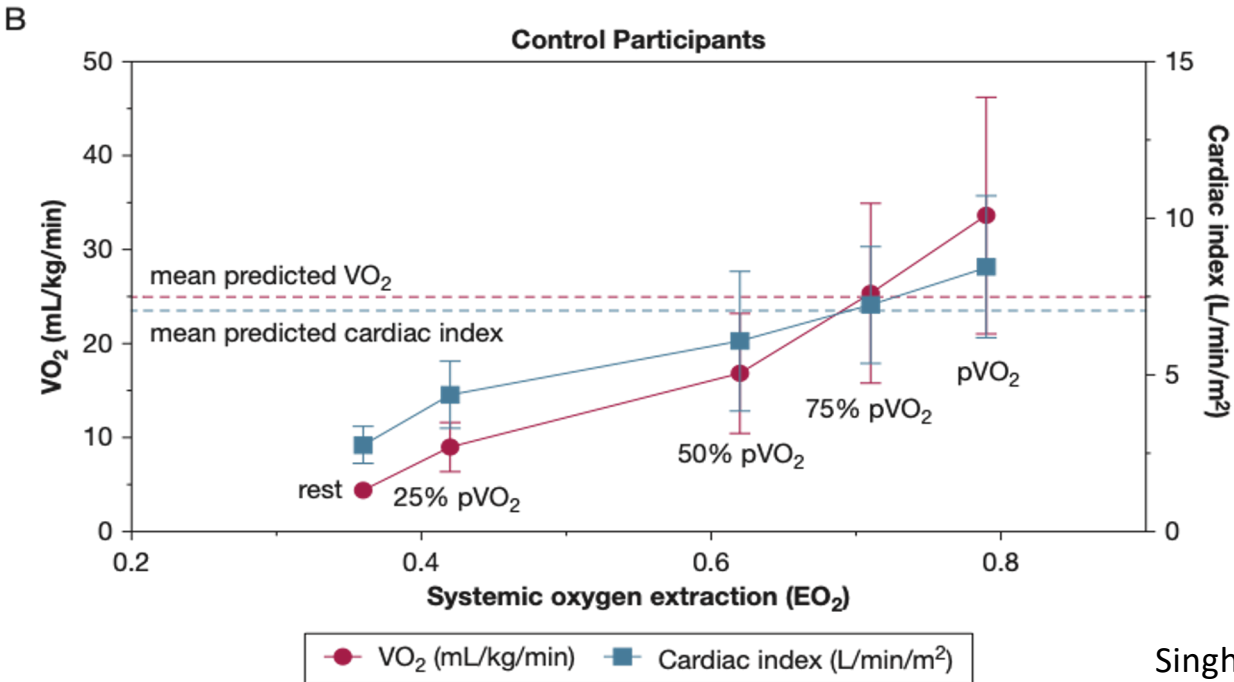
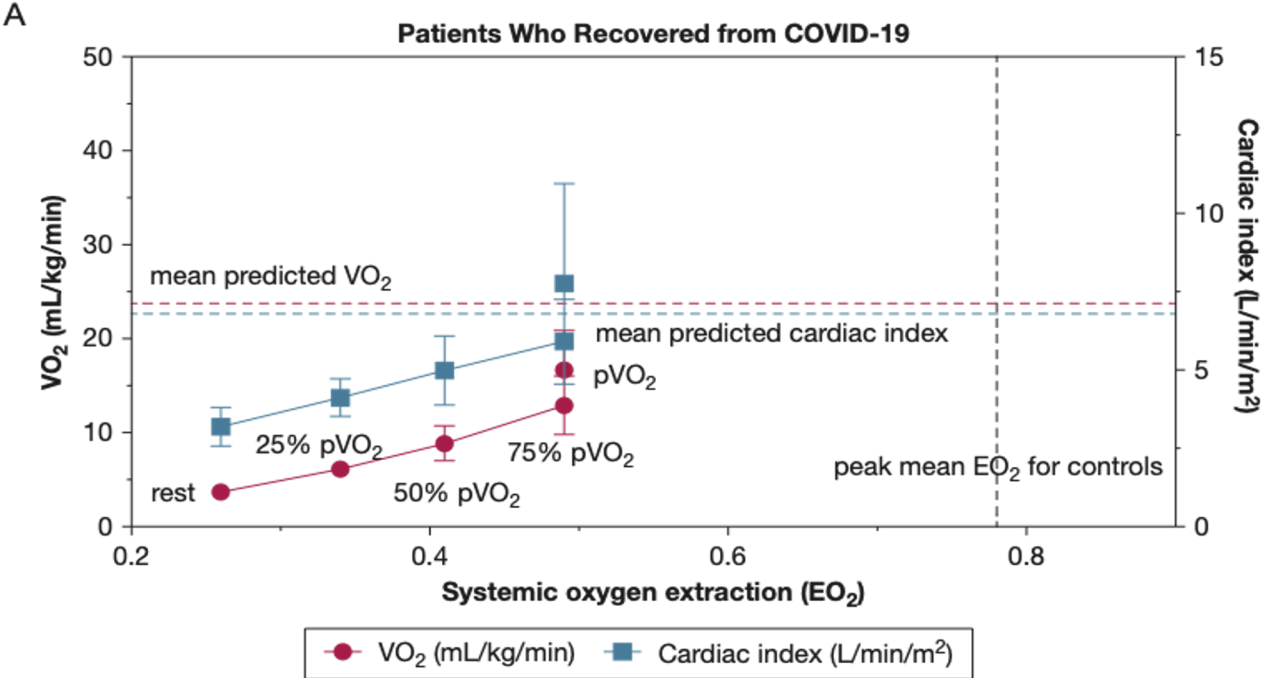
CT abnormalities after COVID-19 depend on severity of acute illness



COVID-19 associated with small airways disease

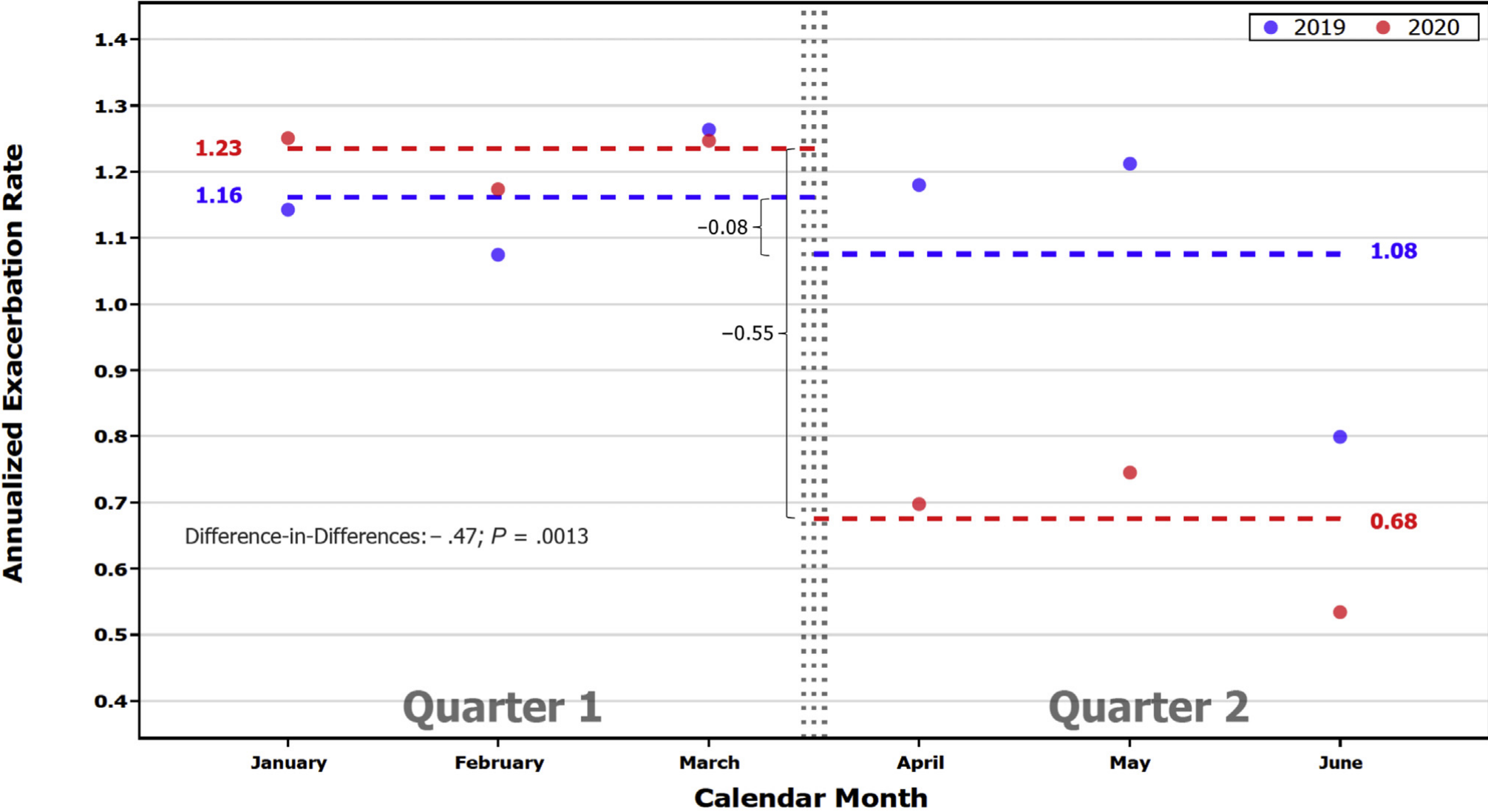


Peak Exercise Capacity Limited At ~1 year



Asthma patients during the pandemic

Asthma exacerbations decreased in 2020



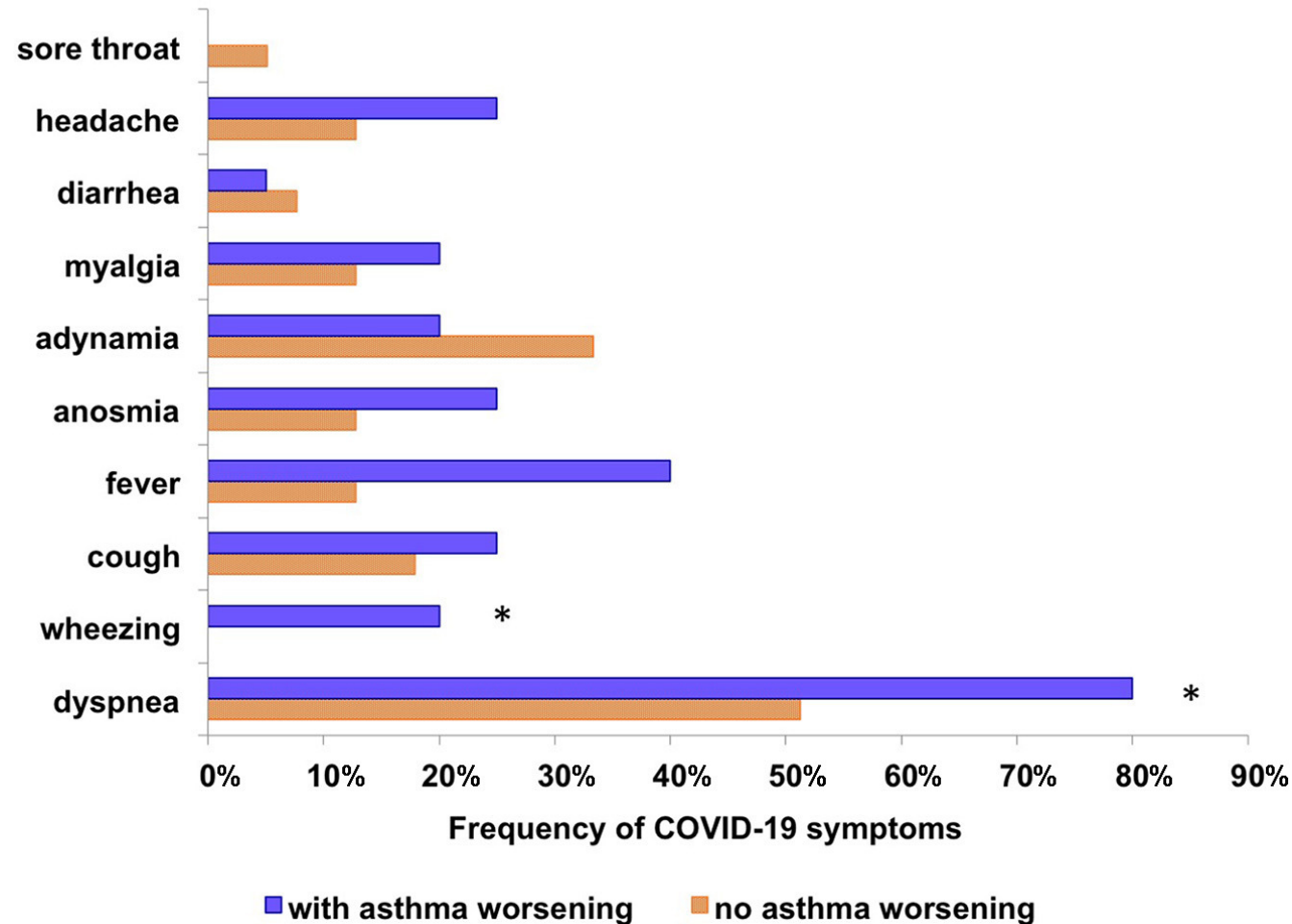
- Exacerbations likely related to viruses
- Many exacerbations are preventable

2019 Rate:	1.14	1.07	1.26	1.18	1.21	0.80
Patient-years:	61.04	59.43	70.08	71.89	75.65	71.60
2020 Rate:	1.25	1.17	1.25	0.70	0.75	0.53
Patient-years:	49.28	42.56	41.18	35.15	31.51	25.28

Asthma patients are not more susceptible

- Lockdown measures may have confounded several studies
 - Varying literature with respect to SARS-CoV-2 susceptibility and disease severity
 - Several studies show worsening asthma control in a subset of patients
 - Asthma effects on COVID severity is still unclear
 - COPD a risk factor for COVID severity, so ACO patients may be at risk of severe disease

Asthmatics requiring step up therapy are more likely to have dyspnea and wheezing




Some observations

- Many people have post-viral reactive airway disease
- Poorly controlled asthma patients exacerbate easily when infected with SARS-CoV-2
- Those who develop multiple long COVID symptoms tend to have longer courses and poorer control
- Deconditioning is important to address in those with prolonged periods of poor control – **utilize pulmonary rehab or PT if possible.**

AAAAI recommendations

- Continue controller medications
- Vaccinate
- Encourage masking/social distancing for severe asthmatics
- Manage according to current guidelines

Some helpful developments in asthma therapy

- Recognition of post-SABA rebound inflammation
 - SMART
 - Reliever-triggered inhaled glucocorticoid
 - Biologics autoinjectors
- 
- Particularly helpful as people improve

SMART

- Single Maintenance and Reliever Therapy (SMART)
- Formoterol – short onset, long-acting, little rebound inflammation
- ICS – budesonide is what is studied.
- Can prescribe budesonide/formoterol as maintenance and step down to PRN
- I use mometasone/formoterol if coverage is an issue

My Asthma Action Plan

For Single Inhaler Maintenance
and Reliever Therapy (SMART)
with budesonide/formoterol

Name: _____ Action plan provided by: _____

Date: _____ Doctor: _____

Usual best PEF: _____ L/min Doctor's phone: _____
(If used)

Normal mode

■ My SMART Asthma Treatment is:

- ☐ budesonide/formoterol 160/4.5 (12 years or over)
- ☐ budesonide/formoterol 80/4.5 (4-11 years)

■ My Regular Treatment Every Day:

(Write in or circle the number of doses prescribed for this patient)

Take [1, 2] inhalation(s) in the morning

and [0, 1, 2] inhalation(s) in the evening, every day

■ Reliever

**Use 1 inhalation of budesonide/formoterol
whenever needed for relief of my asthma symptoms**

I should always carry my budesonide/formoterol inhaler

■ My asthma is stable if:

- I can take part in normal physical activity without asthma symptoms

AND

- I do not wake up at night or in the morning because of asthma

Other Instructions

Asthma Flare-up

■ If over a Period of 2-3 Days:

- My asthma symptoms are getting worse **OR NOT** improving **OR**
- I am using more than 6 budesonide/formoterol reliever inhalations a day (if aged 12 years and older) or more than 4 inhalations a day (if 4-11 years)

I should:

- ☒ Continue to use my regular everyday treatment **PLUS** 1 inhalation budesonide/formoterol whenever needed to relieve symptoms
- ☐ Start a course of prednisolone
- ☐ Contact my doctor

Course of Prednisolone Tablets:

Take _____ mg prednisolone tablets
per day for _____ days **OR**

- If I need more than **12 budesonide/formoterol inhalations (total)** in any day, (or more than 8 inhalations for children 4-11 years)
I **MUST** see my doctor or go to the hospital the same day

Asthma Emergency

■ Signs of an Asthma Emergency:

- Symptoms getting worse quickly
- Extreme difficulty breathing or speaking
- Little or no improvement from my budesonide/formoterol reliever inhalations.

**If I have any of the above danger signs,
I should dial _____ for an ambulance and
say I am having a severe asthma attack.**

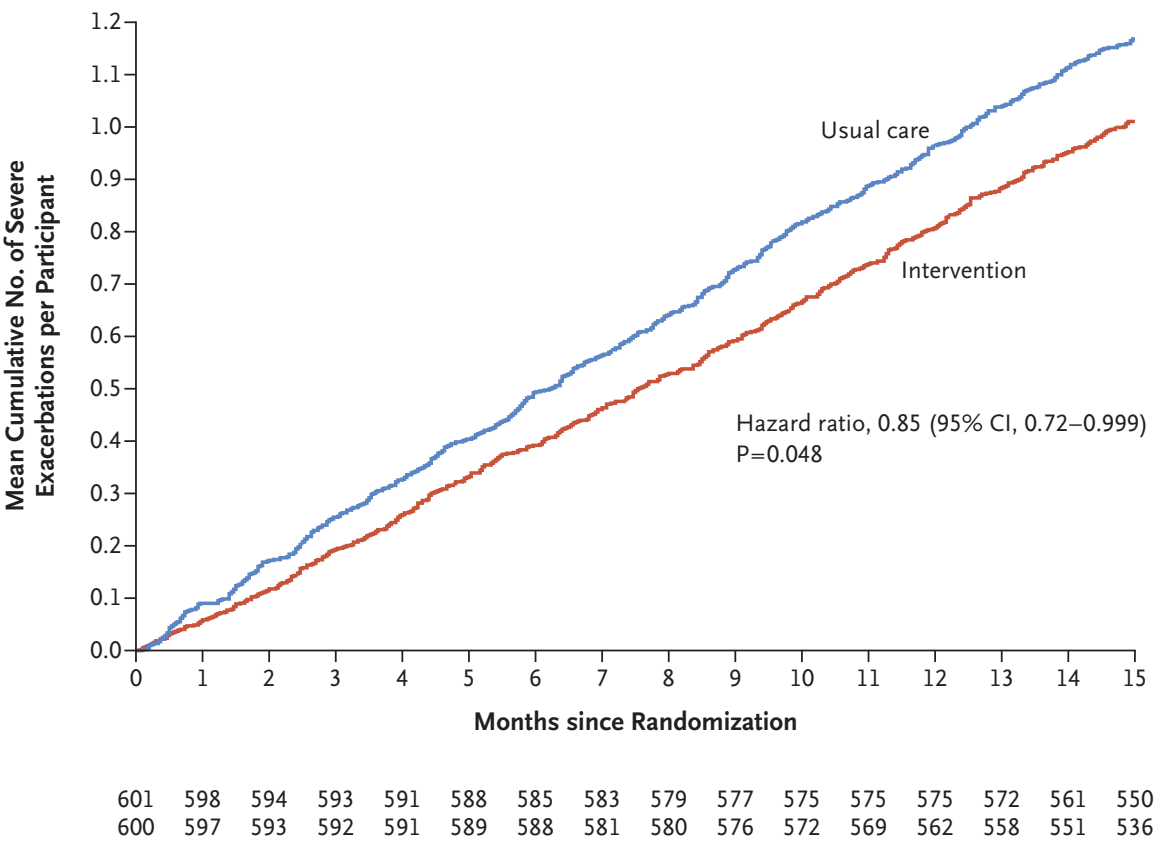
■ While I am waiting for the ambulance start my asthma first aid plan:

- Sit upright and stay calm
- Take 1 inhalation of budesonide/formoterol. Wait 1-3 minutes. If there is no improvement take another inhalation of budesonide/formoterol (up to a maximum of 6 inhalations on a single occasion)
- If only albuterol is available, take 4 puffs as often as needed until help arrives
- Start a course of prednisolone tablets (as directed) while waiting for the ambulance
- Even if my symptoms appear to settle quickly, I should see my doctor immediately after a serious attack

Reliever-Triggered Inhaled Glucocorticoid in Black and Latinx Adults with Asthma

E. Israel, J.-C. Cardet, J.K. Carroll, A.L. Fuhlbrigge, L. She, F.W. Rockhold, N.E. Maher, M. Fagan, V.E. Forth, B.P. Yawn, P. Arias Hernandez, J.M. Kruse, B.K. Manning, J. Rodriguez-Louis, J.B. Shields, B. Ericson, A.D. Colon-Moya, S. Madison, T. Coyne-Beasley, G.M. Hammer, B.M. Kaplan, C.S. Rand, J. Robles, O. Thompson, M.E. Wechsler, J.P. Wisnivesky, M.D. McKee, S.P. Jariwala, E. Jerschow, P.J. Busse, D.C. Kaelber, S. Nazario, M.L. Hernandez, A.J. Apter, K.-L. Chang, V. Pinto-Plata, P.M. Stranges, L.P. Hurley, J. Trevor, T.B. Casale, G. Chupp, I.L. Riley, K. Shenoy, M. Pasarica, R.A. Calderon-Candelario, H. Tapp, A. Baydur, and W.D. Pace

- Moderate-to-severe asthma patients
- SABA + 80 ug beclomethasone (QVAR)
- 1 puff QVAR for each 1 puff SABA
- 5 puffs QVAR for each 1 SABA nebulizer



Biologic auto-injectors

- Home injections easier for *some* patients
- Available for mepolizumab, benralizumab, dupilumab, tezepelumab, omalizumab
- Consider Tezepelumab in those without eosinophilia
- Consider dupilumab particularly in those with eosinophilia and asthma-COPD overlap

Take home points

- COVID-19 can affect the airways and have multiple pulmonary and extra-pulmonary manifestations
- Many asthma exacerbations are probably linked to viral infections
- Standard maintenance therapy and treatment approaches should be applied
- Utilize new approaches which facilitate step down (SMART, SABA + ICS)
- Consider exercise programs/pulmonary rehab for prolonged courses complicated by deconditioning