

COVID At Almost 3 Years

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COVID: It's Been 3 Years of
This; Yes, I'm Sick of It Too,
But Here We Are....

Seems Like A Lifetime Ago...



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Subject: PRO/AH/EDR> Undiagnosed pneumonia - China (HU): RFI

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UNDIAGNOSED PNEUMONIA - CHINA (HUBEI): REQUEST FOR INFORMATION

A ProMED-mail post

<http://www.promedmail.org>

ProMED-mail is a program of the
International Society for Infectious Diseases

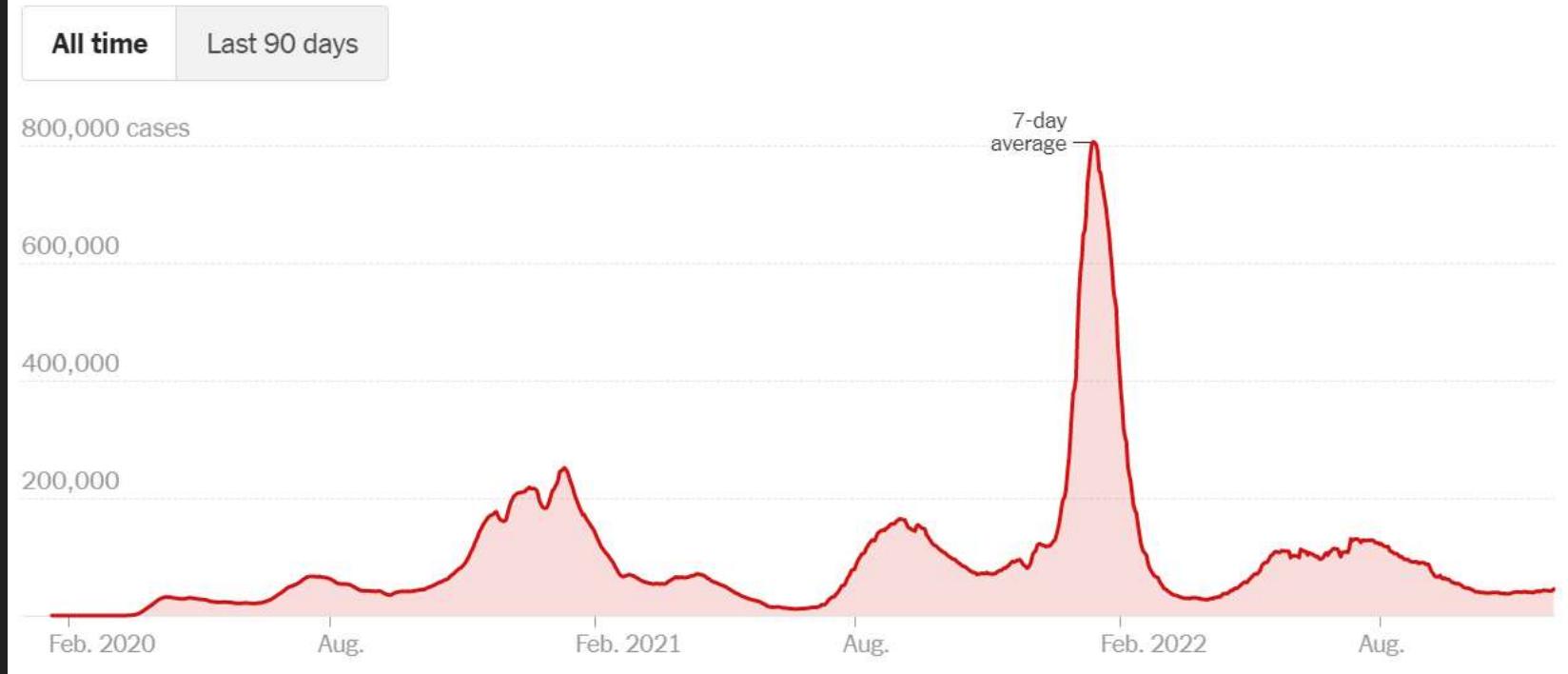
<http://www.isid.org>

Much Has Changed

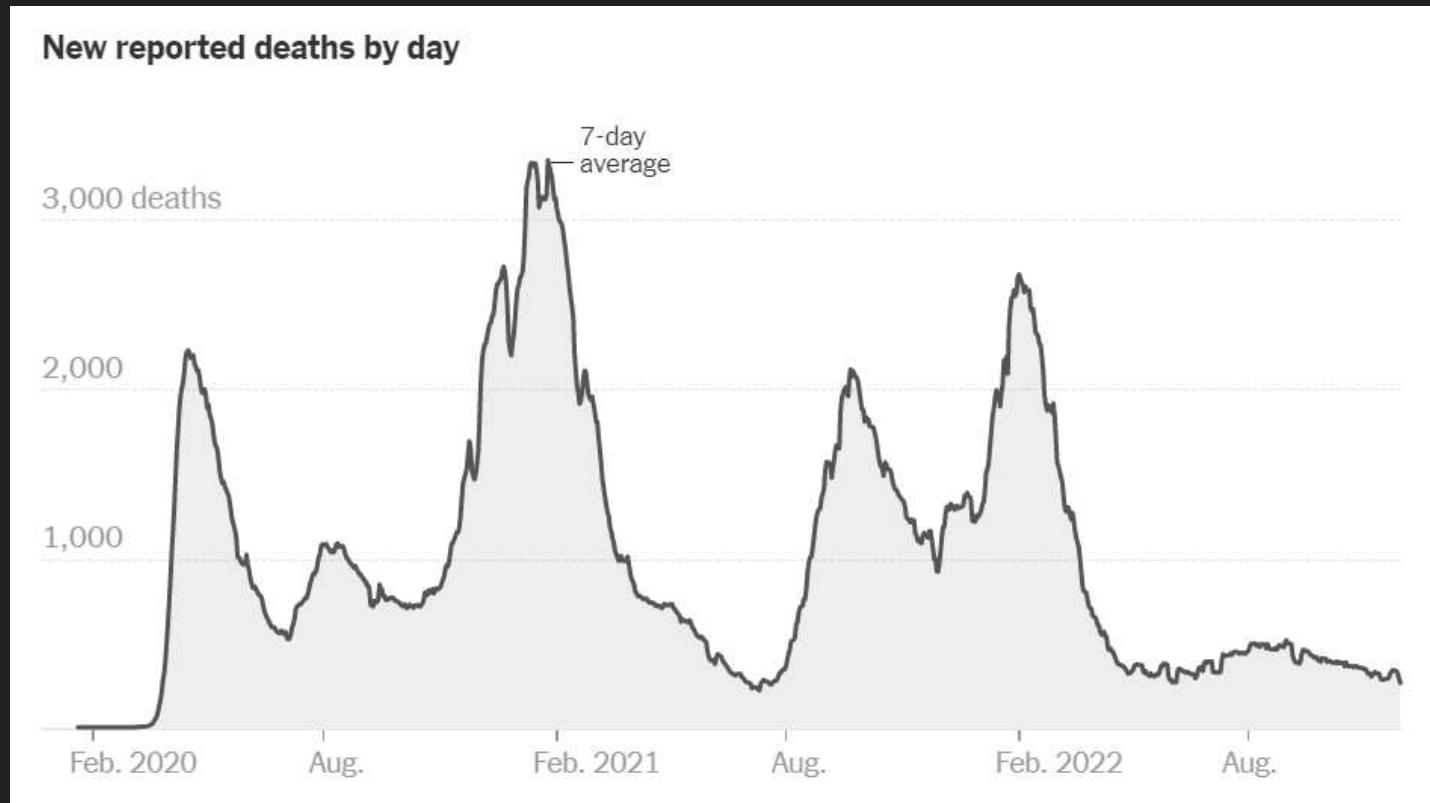
- Remdesivir
- Dexamethasone
- Baricitinib
- Tocilizumab/Sarilumab
- Anticoagulation
- Monoclonals
 - Treatment
 - Pre-exposure prophylaxis (PrEP)
- Vaccines
- Paxlovid

Ongoing Circulation of Virus With Surges

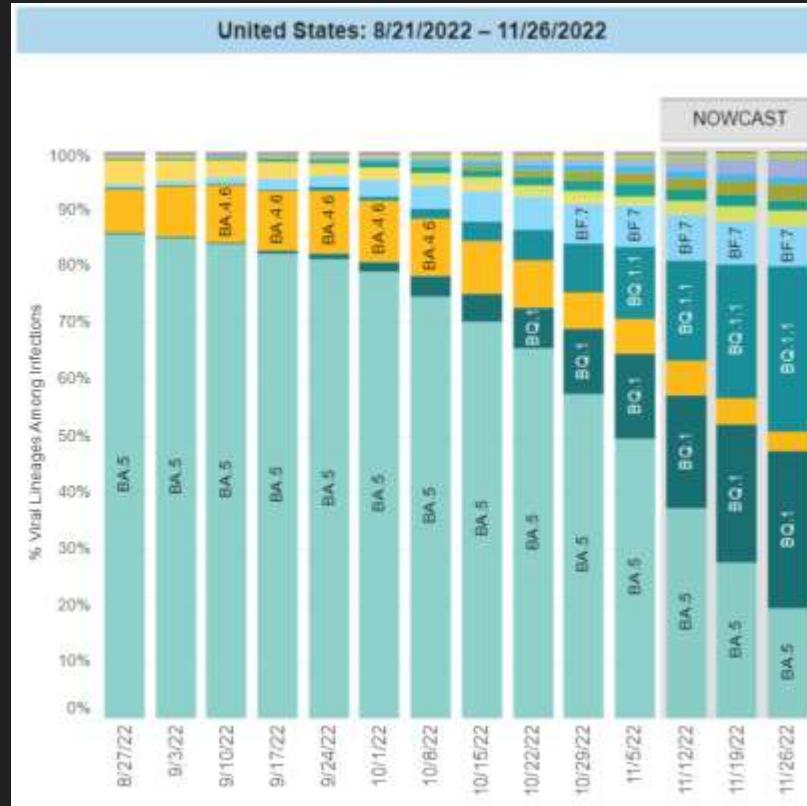
New reported cases



Dramatic Improvement in Mortality



Continued Viral Evolution



BQ 1, BQ 1.1, and Sublineages

- BQ 1
 - 3 significant mutations in spike protein
 - K444X
 - N460X
 - F486X
- BQ 1.1
 - 4 significant mutations in spike protein
 - R346X
 - 3 mutations seen in BQ 1

Immune Evasion

- Antibodies produced with vaccine-induced adaptive immune response do not work as well to neutralize virus
- Gives these variants competitive advantage in transmission

Implications For Prevention

- We will all probably need another booster
- Tixagevimab/Cilgavimab (Evusheld) likely no longer effective
 - Immunocompromised need to be extra diligent about risk-reducing behaviors
 - Still authorized in the absence of alternative options
 - Immunocompromised patients who become ill should be started on pre-emptive therapy as quickly as possible

Implications For Therapeutics

- Monoclonals are also much less effective
 - Bye-bye Bebtelovimab

FDA Announces Bebtelovimab is Not Currently Authorized in Any US Region



[11/30/2022] The U.S. Food and Drug Administration today announced bebtelovimab is not currently authorized for emergency use in the U.S. because it is not expected to neutralize Omicron subvariants BQ.1 and BQ.1.1., according to data included in the [Health Care Provider Fact Sheet](#).

Everything Old Is New Again



bioRxiv posts many COVID19-related papers. A reminder: they have not been formally peer-reviewed and should not guide health-related behavior or be reported in the press as conclusive.

New Results

[Follow this preprint](#)

Plasma after both SARS-CoV-2 boosted vaccination and COVID-19 potently neutralizes BQ.1.1 and XBB.1

David J Sullivan, Massimo Franchini, Jonathon W. Senefeld, Michael J. Joyner, Arturo Casadevall,

Daniele Focosi

doi: <https://doi.org/10.1101/2022.11.25.517977>

Ways To Obtain High-Titer Convalescent Plasma For Patients

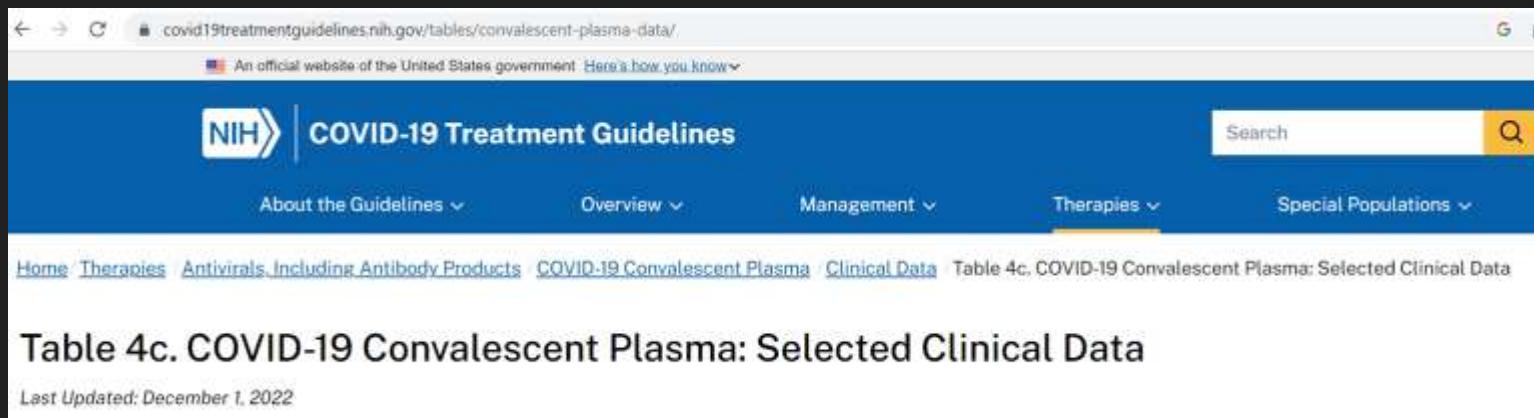
- EUA
 - Limited eligible patient population
 - Not required to report use to FDA
 - Must maintain records of any patients treatment
 - Must investigate any adverse reactions after transfusions
 - Any deaths must be reported to FDA
- Clinical Trials
 - Preferred
- Traditional IND Pathway
 - Not eligible under EUA
 - Not eligible for clinical trials

Criteria For EUA

- Immunosuppressive disease
- Immunosuppressive treatment

Why Not Authorized For Everyone?

- No benefit in immunocompetent hospitalized adults
 - RECOVERY
 - CONCUR-1
 - REMAP-CAP
- Conflicting data in non-hospitalized immunocompetent adults



The image is a screenshot of a web browser displaying the COVID-19 Treatment Guidelines website. The URL in the address bar is covid19treatmentguidelines.nih.gov/tables/convalescent-plasma-data/. The page title is "COVID-19 Treatment Guidelines". The navigation menu includes "About the Guidelines", "Overview", "Management", "Therapies" (which is highlighted in yellow), and "Special Populations". Below the menu, a breadcrumb trail shows "Home / Therapies / Antivirals, Including Antibody Products / COVID-19 Convalescent Plasma / Clinical Data". The main content is titled "Table 4c. COVID-19 Convalescent Plasma: Selected Clinical Data". At the bottom left, a note says "Last Updated: December 1, 2022".

Consider IND Pathway

- Immunocompetent
- Non-hospitalized
- Mild or moderate disease
- Risk factors for progression to severe disease
- Contraindications to use of antiviral drugs

For Most Non-hospitalized Patients

- Paxlovid (nirmatrelvir/ritonavir)
 - Ritonavir: most potent inhibitor of cytochrome P450 (CYP 3A4) in clinical use
 - Check for drug-drug interactions!
 - Extreme caution if using in transplant recipients
 - Tacrolimus (Prograf)

For Those In Whom You Can't Use Paxlovid

- Remdesivir x 3 days
 - Intravenous only
 - Outpatient use is logistically challenging
- Molnupiravir
 - Would only use if no other options
 - Much less benefit than Paxlovid and Remdesivir
 - Viral mutagen

Post-Acute Sequelae COVID (PASC) ie Long COVID

- Most Americans have probably had COVID at this point
- About 30% of people develop protracted symptoms after recovery
- Risk rises with each subsequent infection
- Possible economic impact: US \$3.7 TRILLION
- No clear treatments
- Studies underway

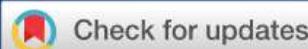
Vaccination Seems To Reduce Risk of PASC

ARTICLES | VOLUME 53, 101624, NOVEMBER 01, 2022

Impact of COVID-19 vaccination on the risk of developing long-COVID and on existing long-COVID symptoms: A systematic review

Kin Israel Notarte • Jesus Alfonso Catahay • Jacqueline Veronica Velasco • Adriel Pastrana • Abbygail Therese Ver •
Flos Carmeli Pangilinan • et al. [Show all authors](#)

Open Access • Published: August 26, 2022 • DOI: <https://doi.org/10.1016/j.eclinm.2022.101624> •



Antiviral Treatment During Acute Phase May Also Reduce Risk of PASC

Nirmatrelvir and the Risk of Post-Acute Sequelae of COVID-19

 Yan Xie,  Taeyoung Choi,  Ziyad Al-Aly

doi: <https://doi.org/10.1101/2022.11.03.22281783>

This article is a preprint and has not been peer-reviewed [what does this mean?]. It reports new medical research that has yet to be evaluated and so should not be used to guide clinical practice.

Antiviral Treatments Being Studied As A Way To Alleviate Symptoms of PASC

Paxlovid for Treatment of Long Covid (STOP-PASC)

⚠ The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. [Know the risks and potential benefits](#) of clinical studies and talk to your health care provider before participating. Read our [disclaimer](#) for details.

ClinicalTrials.gov Identifier: NCT05576662

Recruitment Status [1](#) : Recruiting

First Posted [1](#) : October 12, 2022

Last Update Posted [1](#) : November 21, 2022

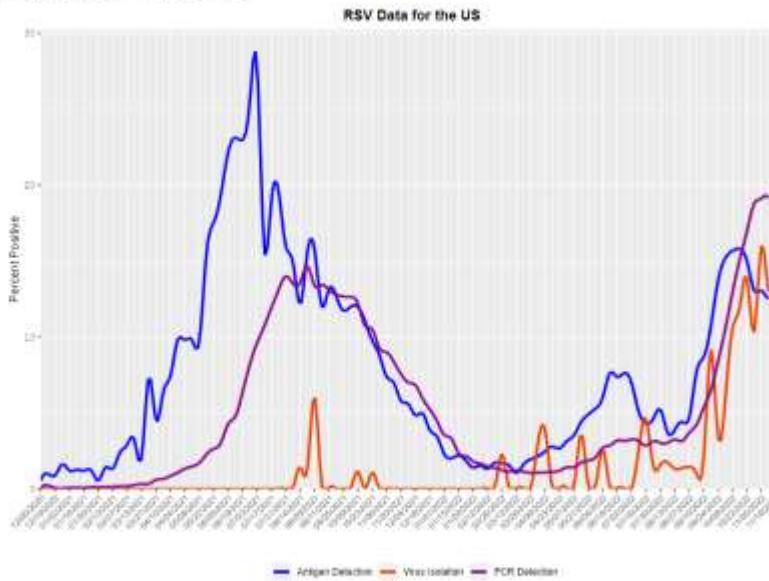
See [Contacts and Locations](#)

[View this study on Beta.ClinicalTrials.gov](#)

Syndemic Respiratory Virus Season

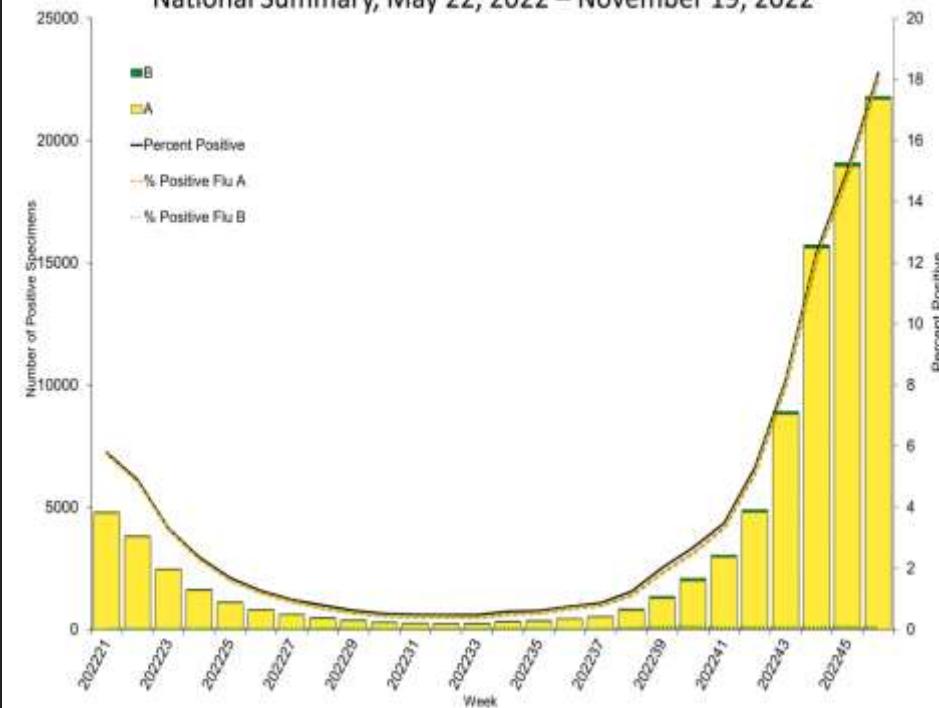
Respiratory Syncytial Virus (RSV)

Percent Positive



[Table: Percent positive respiratory syncytial virus tests in the United States, by week](#)

Influenza Positive Tests Reported to CDC by U.S. Clinical Laboratories, National Summary, May 22, 2022 – November 19, 2022

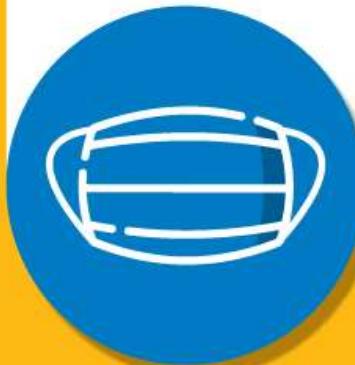


Everything Old Is New Again (redux)

**WASH YOUR
HANDS**



**WEAR A
MASK**



**KEEP YOUR
DISTANCE**

