COVID-19 Update September 1, 2021

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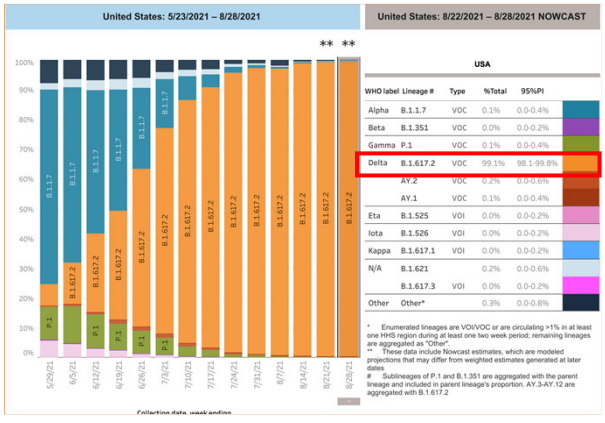
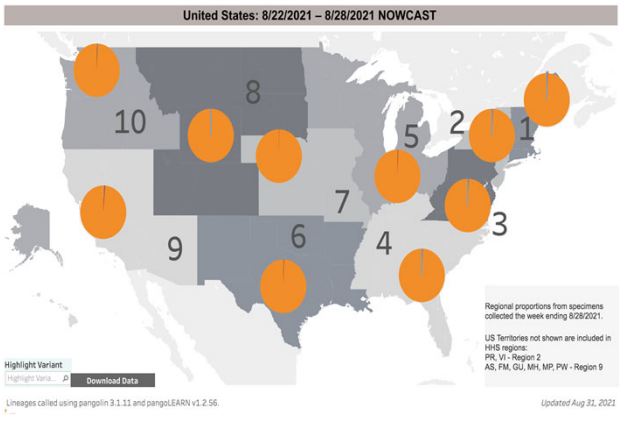
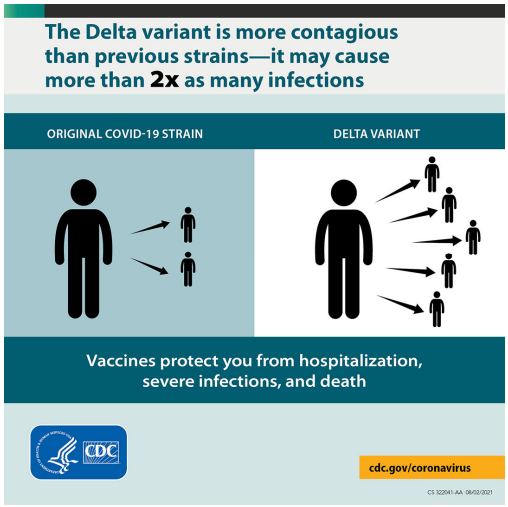
COVID-19 Variants in the United States





Source: CDC

DELTA VARIANT



May cause more severe illness	In two different studies from Canada and Scotland, patients infected with the Delta variant were more likely to be hospitalized than patients infected with Alpha or the original virus strains.
Unvaccinated people remain the greatest concern:	However, the greatest risk of transmission is among unvaccinated people who are much more likely to contract, and therefore transmit the virus.
Fully vaccinated people are likely infectious for less time than unvaccinated people	They can have breakthrough infections and spread the virus to others but are infectious for a shorter period

Hospital admission and emergency care attendance risk for SARS-CoV-2 delta (B.1.617.2) compared with alpha (B.1.1.7) variants of concern: a cohort study

Background

- The SARS-CoV-2 delta (B.1.617.2) variant was first detected in England in March 2021.
- It has become the predominant lineage, owing to high transmissibility.
- It is suspected that the delta variant is associated with more severe disease than the previously dominant alpha (B.1.1.7) variant.

The aim of the study was to characterize the severity of the delta variant compared with the alpha variant

Methods

- Cohort of patients with alpha or delta SARS-Cov-2 variant diagnosed between March and May 2021 in England
- Outcomes: Risk for hospital admission and ED visits were compared and stratified by vaccination status

www.thelancet.com/infection

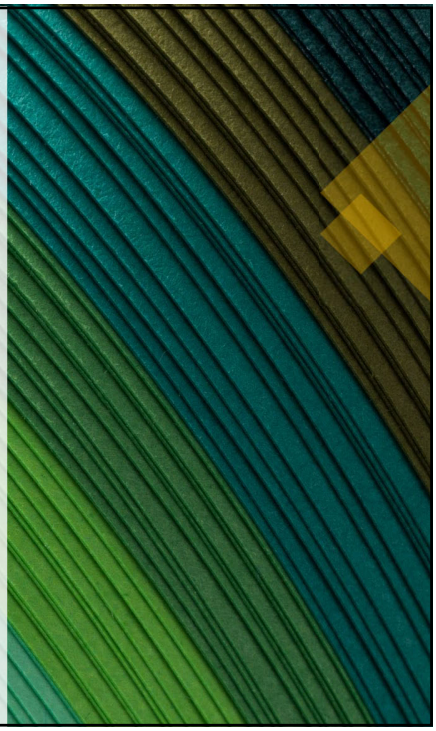
August 27, 2021, https://doi.org/10.1016/S1473-3099(21)00475-8

Hospital admission and emergency care attendance risk for SARS-CoV-2 delta (B.1.617.2) compared with alpha (B.1.1.7) variants of concern: a cohort study

Data on 43,338 COVID-19-positive patients was available	8682 with the delta variant, 34656 with the alpha variant were analyzed
More patients with delta variant required hospital admissions within 14 days of sampling (HR 2.26) [95% CI 1·32–3·89]).	
More patients with delta variant required hospital admission OR ED care withing 14 days of sampling (HR 1.45)	498 (5·7%) patients with the delta variant versus 1448 (4·2%) patients with the alpha variant were admitted to hospital or attended emergency care within 14 days (adjusted HR 1·45 [1·08–1·95]).
Most patients were unvaccinated (32 078 [74·0%] across both groups).	The HRs for vaccinated patients with the delta variant versus the alpha variant were similar to the HRs for unvaccinated patients (2·32 [1·29–4·16] but the precision for the vaccinated subgroup was low.

www.thelancet.com/infection

August 27, 2021, https://doi.org/10.1016/S1473-3099(21)00475-8



Hospital admission and emergency care attendance risk for SARS-CoV-2 delta (B.1.617.2) compared with alpha (B.1.1.7) variants of concern: a cohort study

Interpretation

- This large national study found a higher hospital admission or emergency care attendance risk for patients with COVID-19 infected with the delta variant compared with the alpha variant.
- Results suggest that outbreaks of the delta variant in unvaccinated populations might lead to a greater burden on health-care services than the alpha variant.

COVID-19 EUA Treatment Guidelines

Pre-Exposure Prophylaxis

- Nothing approved

Pot-Exposure Prophylaxis

- **Monoclonal antibodies** (Casirivimab plus imdevimab)

Symptomatic patients that do not require hospitalization and pulse oximetry is ≥ 94%

- **Anti SARS-CoV-2 monoclonal antibodies (**Casirivimab + imdevimab or sotrovimab)

GREY ZONE (Patients with exertional hypoxemia)

Symptomatic patients with pulse oximetry < 94% that require hospitalization

- **Antiviral** (Remdesivir)
- **Immunomodulatory agents** (Dexamethasone, Tocilizumab with dexamethasone, baricitinib with dexamethasone)

Treatment of concomitant conditions

- Thromboembolic disease
- Bacterial and fungal coinfections

IDSA/NIH Guidelines

Post Exposure Prophylaxis (PEP) for people who are at high risk for progression to severe COVID-19

Casirivimab 600 mg plus imdevimab 600 mg administered as subcutaneous injections **(AI)** or an intravenous infusion **(BIII)** as PEP for people who are at **high risk for progression** to severe COVID-19 if infected with SARS-CoV-2 **AND** who have the following vaccination status **AND** exposure history:

Vaccination Status:

- Not fully vaccinated (defined as people who were never vaccinated or those who received the second vaccine dose in a two-dose series or a single-dose vaccine <2 weeks ago); *or*
- Fully vaccinated, but not expected to mount an adequate immune response (e.g., those with immunocompromising conditions, including those who are taking immunosuppressive medications) **AND**

Exposure History to SARS-CoV-2:

- Had a recent exposure to an individual with SARS-CoV-2 infection that is consistent with the Centers for Disease Control and Prevention close contact criteria; *or*
- At high risk of exposure to an individual with SARS-CoV-2 infection because of recent occurrence of SARS-CoV-2 infection in other individuals in the same institutional setting (e.g., nursing homes, prisons)

Sixty two percent less symptomatic disease in those who receive treatment compared to placebo

https://www.covid19treatmentguidelines.nih.gov/about-the-guidelines/whats-new/

Casirivimab 600 mg plus Imdevimab 600 mg I: Double-blind, placebo-controlled randomized trial in outpatients with mild to moderate COVID-19

Participants aged ≥18 years who had a positive SARS-CoV-2 PCR and one or more risk factors for progression to severe COVID-19.

The primary outcome: COVID-19-related hospitalization or death from any cause

Occurred in 7 of 736 participants (**1.0%**) in the casirivimab 600 mg plus imdevimab 600 mg IV arm and in 24 of 748 participants (**3.2%**) in the placebo arm (P = 0.0024)

Demonstrating a 2.2% absolute reduction and a 70% relative reduction in hospitalization or death among the casirivimab plus imdevimab recipients compared to the placebo recipients.

Monoclonal Antibodies

for COVID-19

Our Experience

Jorge Mera, MD, FACP
Whitney Essex, APRN-CNP

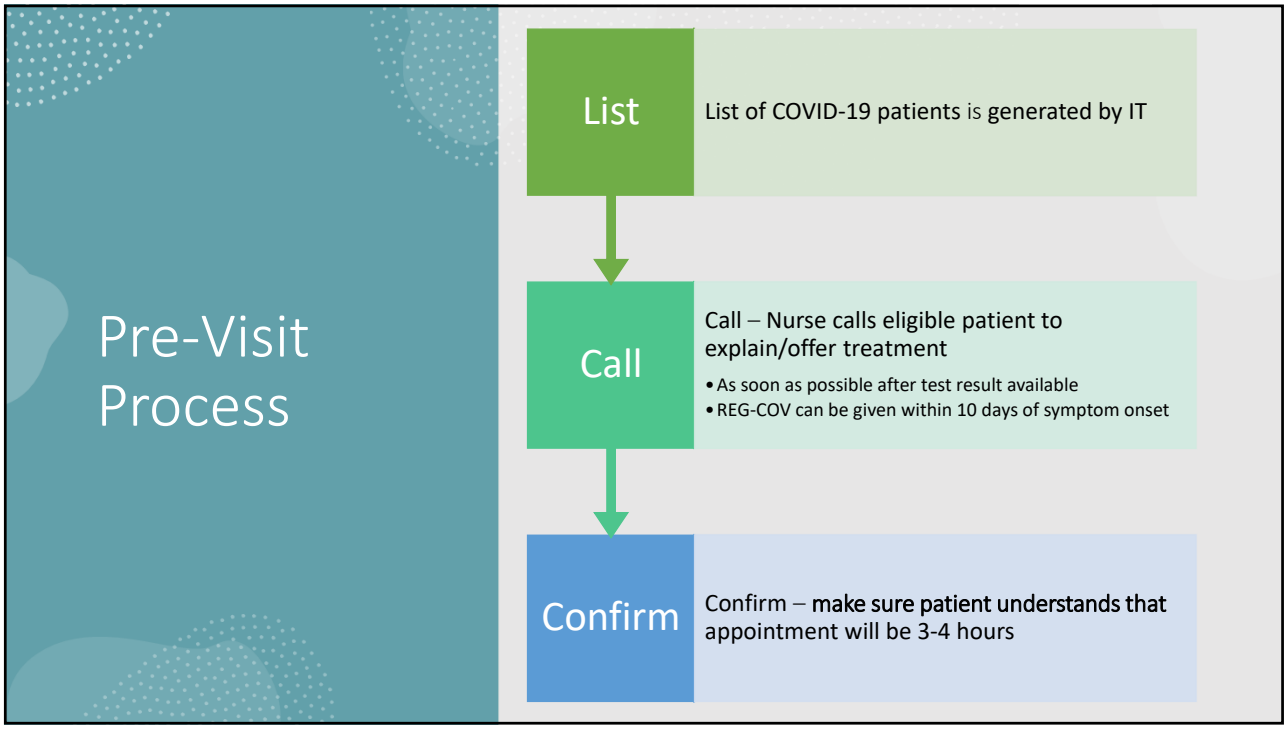
September 1, 2021

EUA – REGEN-COV (casirivimab 600mg + imdevimab 600mg)
Authorized for emergency use for:

- ***Treatment***
  - of mild to moderate COVID-19 in adult and pediatric patients (12 years of age and older weighing at least 40 kg) who are at high risk for progression to severe COVID-19, including hospitalization or death
- ***Post-exposure Prophylaxis***
  - of COVID-19 in adult and pediatric individuals (12 years of age and older weighing at least 40 kg) who are at high risk for progression to severe COVID-19, including hospitalization or death, ***AND***
    - Are not fully vaccinated *or* fully vaccinated but not expected to have an adequate immune response to the vaccine, ***AND***
      - Is a close contact of a positive case, *or*
      - High risk of exposure due to institutional setting (NH, Prison, etc.)

EUA – REGEN-COV (casirivimab 600mg + imdevimab 600mg)
Qualifying Risk Factors

- Older age (for example, age ≥65 years of age)
- Obesity or being overweight (BMI >25 kg/m2 , or if age 12-17, have BMI ≥85th percentile for their age and gender)
- Pregnancy
- Chronic kidney disease
- Diabetes
- Immunosuppressive disease or immunosuppressive treatment
- Cardiovascular disease (including congenital heart disease) or hypertension
- Chronic lung diseases (for example, COPD, asthma [moderate-to-severe], interstitial lung disease, CF and pulmonary hypertension)
- Sickle cell disease
- Neurodevelopmental disorders (for example, cerebral palsy) or other conditions that confer medical complexity
- Having a medical-related technological dependence (for example, tracheostomy)
- Other medical conditions or factors (for example, race or ethnicity) may also place individual patients at high risk for progression to severe COVID-19 and authorization of REGEN-COV under the EUA is not limited to the medical conditions or factors listed above.



Day of Visit

- Patient arrives – Nurse performs intake, including O2 Sat (~10 minutes)
- Prescriber:
  - Confirms eligibility with patient
  - Explains EUA (~15 minutes) – provides copy of fact sheet
  - Orders IV Start and confirms IV access prior to ordering bamlanivimab
  - Place order for REGEN-COV – informs pharmacy
- Pharmacy prepares REGEN-COV – delivers to clinic (~30 minutes)
  - REGEN-COV is stored in refrigerator
  - Room temperature for administration
    - More "infusion reactions" if too cold

Day of Visit continued… and Follow up

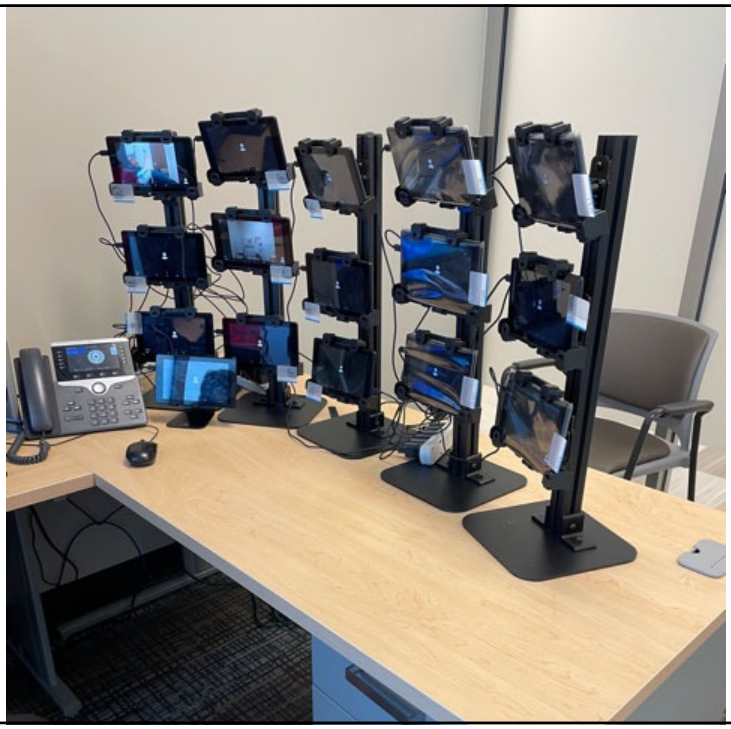
- Nurse starts infusion
  - Use inline filter
  - Can be by gravity or pump
  - Confirms monitor (or self-monitors)
  - Monitor VS during and after infusion (per site protocol)
- Follow-up 1-3 days after via phone, Day 14 to confirm serious adverse events (hospitalization)

Nurse Staffing/Supply details…

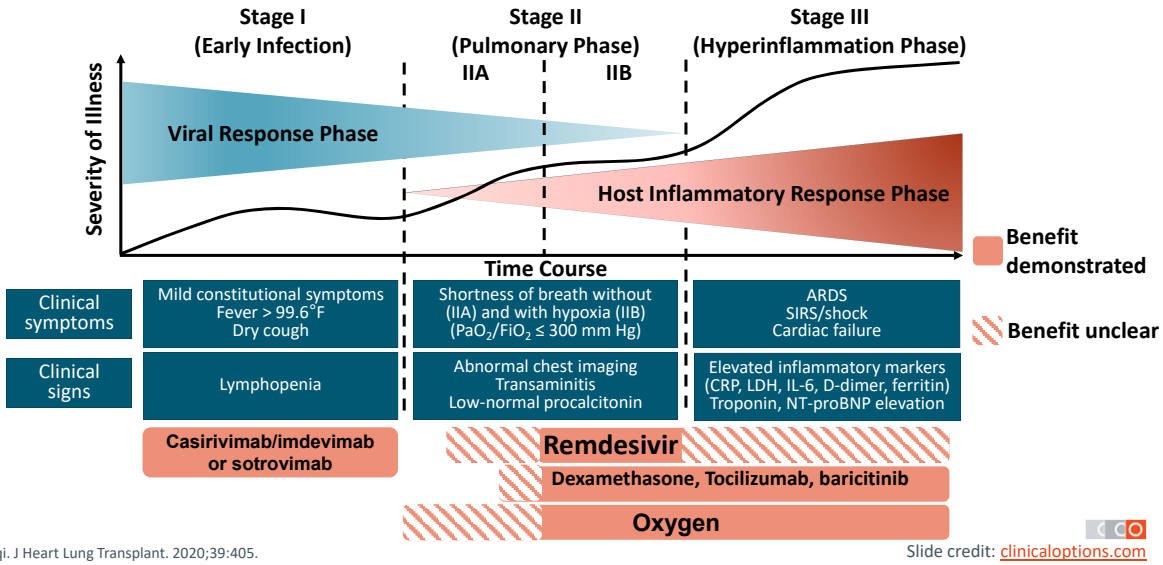
- Nursing
  - Time Intensive
  - IV start
  - Nurse to patient ratio – 1:4 per 8 hour shift
    - With a separate monitor
    - With 2 rooms
  - Nurse to patient ratio – 1:2 per 8 hour shift
    - With no monitor
    - With 1 room
- Supplies
  - Typical IV Infusion supplies **except**: *PVC infusion set containing 0.2 or 0.22 micron polyethersulfone (PES) in-line filter*

Things to Consider

- ACLS trained staff required (at least 1)
- Crash cart or similar present
- Other meds available for in-clinic administration
  - Ondansetron, IV Fluids (NS), Acetaminophen, Ibuprofen, etc.
- Patient is present for up to 4 hours (and they are sick)
  - Snacks, drinks, blankets, etc.
- Monitoring – many ways to do this
  - Tablets
  - Congregate observation room
  - One-on-One



COVID-19 Therapies Predicted to Provide Benefit at Different Stages



Siddiqi. J Heart Lung Transplant. 2020;39:405.

Slide credit: clinicaloptions.com

Special Considerations in Children with COVID-19

SARS-CoV-2 infection is generally milder in children than in adults

- The majority of children with the disease have asymptomatic infection.

Most children with SARS-CoV-2 infection will not require any specific therapy.

- Children with comorbidities as well as nonwhite children and older teenagers may be at increased risk for severe disease.

There are limited data on the pathogenesis, clinical spectrum and treatment of COVID-19 disease in children.

Therapy is based on outcome and safety data for adult patients and the child's risk of disease progression.

MIS-C

Case Definition for Multisystem Inflammatory Syndrome in Children (MIS-C)

- An individual aged <21 years presenting with fever[i], laboratory evidence of inflammation[ii], and evidence of clinically severe illness requiring hospitalization, with multisystem (≥2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological); **AND**
- No alternative plausible diagnoses; **AND**
- Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within the 4 weeks prior to the onset of symptoms

[i]Fever ≥38.0°C for ≥24 hours, or report of subjective fever lasting ≥24 hours
[ii]Including, but not limited to, one or more of the following: an elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, procalcitonin, d-dimer, ferritin, lactic acid dehydrogenase (LDH), or interleukin 6 (IL-6), elevated neutrophils, reduced lymphocytes and low albumin

Additional comments

- Some individuals may fulfill full or partial criteria for Kawasaki disease but should be reported if they meet the case definition for MIS-C
- Consider MIS-C in any pediatric death with evidence of SARS-CoV-2 infection

NIV: Noninvasive ventilation, IMV: Invasive Mechanical Ventilation, ECMO: Extracorporeal Membrane Oxygenation

https://www.covid19treatmentguidelines.nih.gov/special-populations/children/
Accessed August 20, 2021

COVID-19 Treatment in Children

Remdesivir is recommended for:

- Hospitalized children aged ≥12 years who have risk factors for severe disease and have an emergent or increasing need for supplemental oxygen **(BIII)**.
- Hospitalized children aged ≥16 years who have an emergent or increasing need for supplemental oxygen regardless of risks factors for severe disease **(BIII)**.
- Can be considered for hospitalized children of all ages with COVID-19 who have an emergent or increasing need for supplemental oxygen **(CIII)**.

Dexamethasone for hospitalized children who require high-flow oxygen, NIV, IMV, or ECMO **(BIII)**.

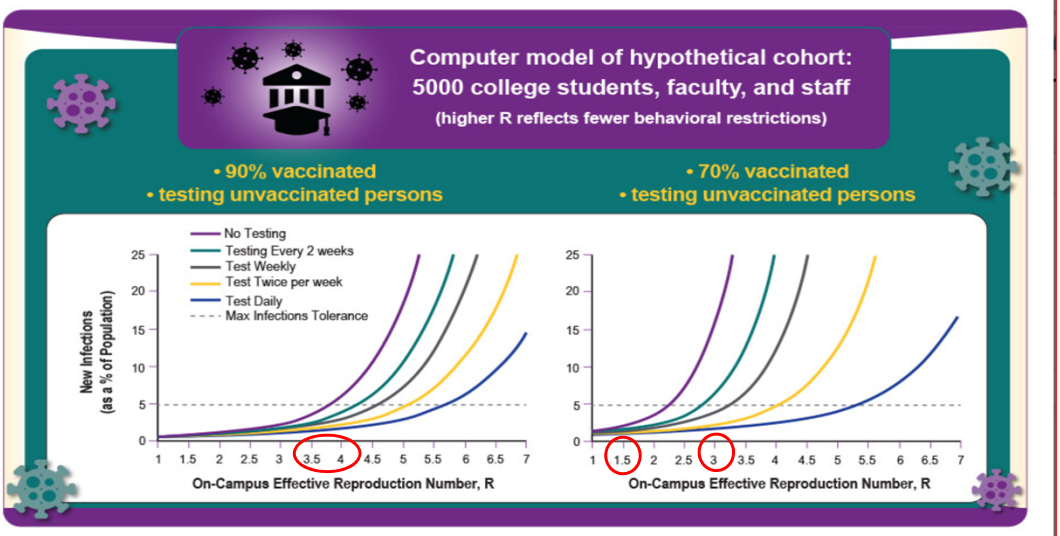
- There is insufficient evidence for the Panel to recommend either for or against the use of anti-SARS-CoV-2 monoclonal antibody products for children with COVID-19 who are not hospitalized but who have risk factors for severe disease.

MIS-C is a serious delayed complication of SARS-CoV-2 infection that may develop in a minority of children and young adults.

- Consultation with a multidisciplinary team is recommended when considering and managing immunomodulating therapy for children with MIS-C **(AIII)**.
- Intravenous immunoglobulin and/or corticosteroids are generally used as first-line therapy, although interleukin-1 antagonists have been used for refractory cases.
- The optimal choice and combination of immunomodulating therapies have not been definitively established.

https://www.covid19treatmentguidelines.nih.gov/special-populations/children/
Accessed August 20, 2021

What is the estimated effect of various COVID-19 safety strategies on cumulative infections over a 120-day college semester?



Annals of Internal Medicine

Paltiel AD, Schwartz JL. Assessing COVID-19 prevention strategies to permit the safe opening of residential colleges in fall 2021. Ann Intern Med. 2021. [Epub ahead of print]. doi:10.7326/M21-2965
http://acpjournals.org/doi/10.7326/M21-2965

Investigation of subsequent and co-infections associated with SARS-CoV-2 (COVID-19) in hospitalized patients

Background:

- The burden of co-infections and subsequent infections in patients hospitalized with COVID-19 is not fully understood
- Antimicrobial are used in most patients hospitalized with COVID-19

Aim:

- Describe rates and pathogens of co-infection/ subsequent infections in hospitalized patients with COVID-19
- Describe the impact of these infections on clinical outcomes among hospitalized patients with COVID-19.

Methods:

- Multicenter observational cohort
- Clinical outcomes were compared between patients with a bacterial respiratory co-infection (BRC) and those without.

medRxiv preprint doi: https://doi.org/10.1101/2020.05.29.20117176; this version posted June 2, 2020

Investigation of subsequent and co-infections associated with SARS-CoV-2 (COVID-19) in hospitalized patients

A total of 289 patients were included

- 48 (16.6%) had any co-infection
- 25 (8.7%) had a BRC.
- No significant differences in comorbidities were observed between groups

Patients with BRC had:

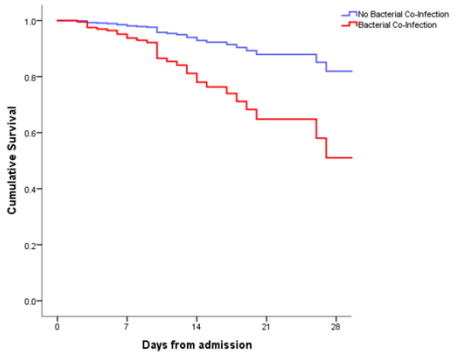
- Significantly higher WBC counts, LDH, CRP, procalcitonin andIL-6 levels
- Higher ICU admission (84.0 vs 31.8%), mechanical ventilation (72.0 vs 23.9%) and in-hospital mortality (45.0 vs 9.8%) compared to those without a co-infection.

Patients with BRC had an increased risk for in-hospital mortality (adjusted HR, 3.37; 95% CI, 1.39 to 8.16; P = 0.007).

- After adjustment for age, ICU admission, mechanical ventilation, corticosteroid administration, and pre-existing comorbidities,

Subsequent infections were uncommon, with 21 infections occurring in 16 (5.5%) patients.

Figure 2. Model-Adjusted Estimated In-Hospital Mortality, by Bacterial Respiratory Co-Infection Status



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Helix

The Viral Early Warning (ViEW) Network

A public-private respiratory disease surveillance and early warning network

September 2021

Helix response to COVID-19 Pandemic

Diagnostic Capability

- Helix quickly established itself as one of the largest and most capable labs (up to 150,000 daily tests) in performing high-throughput diagnostic testing at national scale.

Viral Surveillance Capability

- Partnered with the CDC and is one of the nation's leading viral surveillance organizations (sequencing + analytics)

CDC Centers for Disease Control and Prevention

NIH National Institute of Biomedical Imaging and Bioengineering

Surveillance Dashboard

Helix Sentinel Network

Developing a provider-driven Viral Early Warning System (ViEW) Network will allow us to prepare and respond to respiratory disease threats more robustly and quickly

What it is:

A provider-driven early warning system to proactively monitor respiratory disease

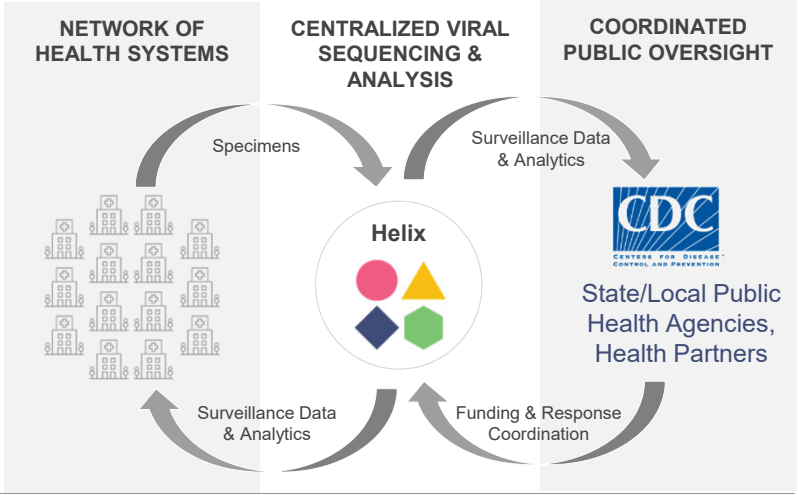
- 50 state sampling of key clinical settings
- Broad viral sequencing panel
- Viral activity visualization both locally and nationally

Why it matters

Augments current systems to provide:

1) Centralized and coordinated process
2) Real-time monitoring
3) Improved analytics prediction of circulating respiratory viruses

For the benefit of both public and private systems



Helix

Helix Sentinel Network

Enable End to End Reporting in ~ 1 week from Collection

PILLAR I: SAMPLE COLLECTION

- For patients with respiratory symptoms a second sample collection automatically collected (via EHR)
- Logistics managed by Helix

PILLAR II: SEQUENCE

- Samples undergo full viral sequencing using Helix's VSeq-RP assay (up to 40 viruses) at Helix's San Diego laboratory

PILLAR III: DISTRIBUTE

- CDC, State Departments of Health and Health Partners notified of VOCs weekly
- Dashboards (real-time) for all ViEW health partners to guide operational decision making

PILLAR IV: GENOMIC ANALYSIS

- CDC, public health and health partners receive viral sequence data for deeper analysis
- Inform real-time public health decisions on VOC and VOI and emerging trends

Helix Sentinel Network

National Surveillance Network at no-cost to participating health partners

- Cost recovery for operational activities related to specimen collection
- No charge to institutions for viral sequencing data delivery
- No charge to institutions for dashboard/reporting interface

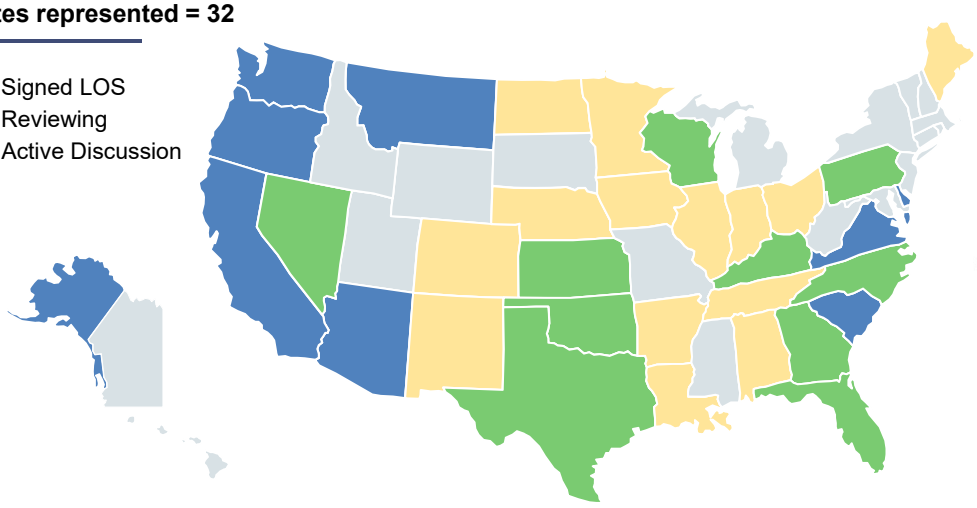
Next Steps/ Commitment

- Helix is finalizing Letters of Support (LOS) for 50 state coverage
- Starting pilot in Q4 2021

And Active Discussions

States represented = 32

= Signed LOS
= Reviewing
= Active Discussion



Renown HEALTH
AdventHealth
TEMPLE HEALTH
Cherokee Nation Health Services

Value to health partners

Real-time insights — Provides real-time surveillance data and analytics to monitor circulating and emerging viral strains across a variety of respiratory viruses

Turnkey — Helix provides all collection materials and integrates into existing workflows without disrupting current diagnostics pathways

No-cost — Full cost recovery provided to each health partner on a per sample basis

Collaborative research — Able to collaborate with Helix and other participating health partners on novel research with robust clinico-genomic dataset

Public Health — Participation in the network and resulting research will drive improved public health

Helix

For more information, please contact:
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