Access speaker bios here:
https://files.asprtracie.hhs.gov/documents/monoclonals-and-more-issues-and-opportunities-speaker-bios.pdf

Access the recording here: https://attendee.gotowebinar.com/recording/2965502026372652300

Access the transcript here: https://files.asprtracie.hhs.gov/documents/monoclonal-antibodies-webinar-transcript.pdf

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Monoclonals and More: Issues and Opportunities with Early COVID-19 Treatment Options

November 12, 2021

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Resources

- ASPR TRACIE COVID-19 Page
- ASPR COVID-19 Page
  - COVID-19 Monoclonal Antibody Therapeutics
- CDC COVID-19 Page
- FDA COVID-19 Page
- NIH COVID-19 Page
  - COVID-19 Treatment Guidelines
  - Updated COVID-19 Treatment Guidelines on Prioritization of Anti-SARS-CoV-2 Monoclonal Antibodies for the Treatment or Prevention of SARS-CoV-2 Infection when there are Logistical or Supply Constraints
- Coronavirus.gov

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HEALTHCARE EMERGENCY PREPAREDNESS INFORMATION GATEWAY

John Hick, MD
Hennepin Healthcare
Moderator

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HEALTHCARE EMERGENCY PREPAREDNESS INFORMATION GATEWAY

Dan Hanfling, MD
Co-Chair, National Academy of Medicine
Forum on Medical and Public Health Preparedness

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Therapeutics in Limited Supply – Who Gets Access?

- Applying the “Crisis Standards of Care” Framework

- We’ve been down this road before (EMS, oncology)
  - Conserve – Substitute – Adapt

- Accountability – Reciprocity – Duty to Plan – Duty to Treat
  - Balance maximal medical benefit AND equity

Therapeutics in Limited Supply -- Who Gets Access?

- "The goal of equitable mAb allocation is not to get every eligible patient to accept mAb therapy, but to identify the right patients at the right time." [NAM, Standing Committee, January 2021]
    - Transparency, Fairness – over place and time
- Utilitarian framework --- patients who have the greatest risk of hospitalization and death
    - Identify impacted populations
    - Target areas with high incidence of disease in community
    - Prioritize treatment over prophylaxis
- Equity lens – recognize and support the disadvantaged

COVID-19 Outpatient Therapeutics

Rajesh T. Gandhi, MD

Massachusetts General Hospital

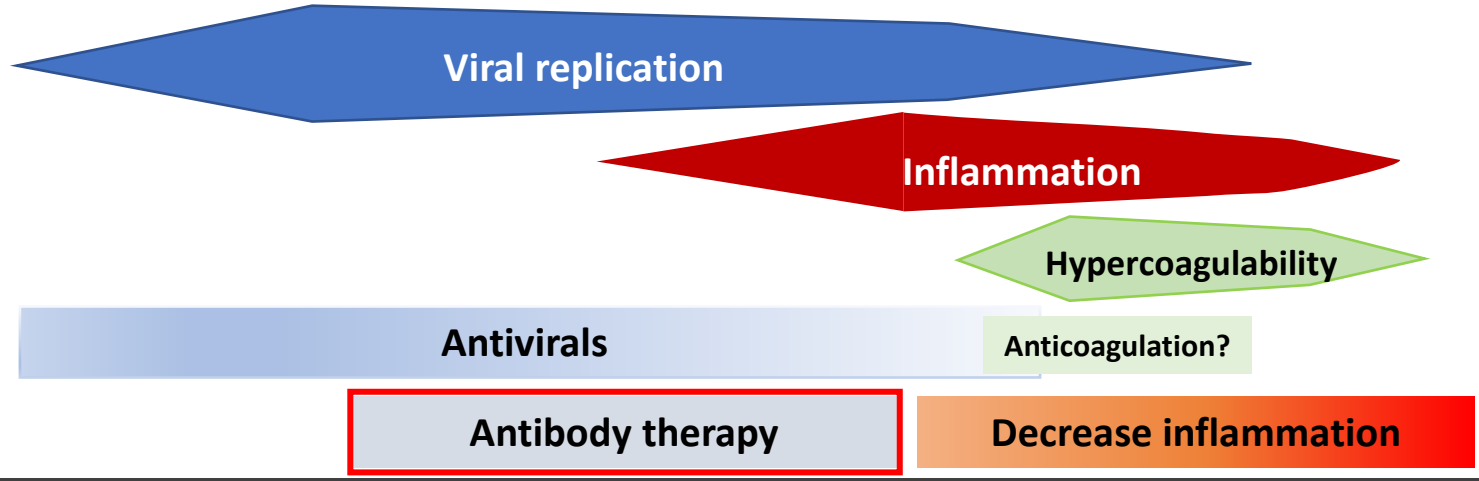
Harvard University Center for AIDS Research

Note: I am speaking on my own behalf and NOT on behalf of the NIH COVID-19 Treatment Guidelines Panel

Disclosures (for past two years):
Member, NIH & Infectious Diseases Society of America COVID-19 Treatment Guidelines Panels; Investigator, AIDS Clinical Trials Group and COVID-19 Prevention Network trials on anti-SARS CoV-2 monoclonal antibodies

Treatment Across the COVID-19 Spectrum

Stage/ Severity:	Asymptomatic/ Presymptomatic	Mild Illness	Moderate Illness	Severe Illness	Critical illness
	+ SARS-CoV-2 test but no symptoms	Mild symptoms (e.g., fever, cough, taste/smell changes); no dyspnea	O_2 saturation >=94%, lower respiratory tract disease	O_2 saturation <94%, respiratory rate >30/min; lung infiltrates >50%	Respiratory failure, shock, multi-organ dysfunction/failure



Gandhi RT, CID, 2020
Gandhi RT, Lynch J, del Rio C. NEJM 2020

Anti-SARS CoV-2 Monoclonal Ab for Treatment

- Phase 3 placebo controlled clinical trials in non-hospitalized patients with mild to moderate COVID and with at least one risk factor for severe COVID

Antibody	% Reduction Hospitalization/Death
Bamlanivimab/etesevimab*	70%
Casirivimab/Imdevimab*	70%
Sotrovimab*	85%

*Authorized in the US

Dougan M et al, NEJM, 2021; Weinreich et al., NEJM 2021; Gupta A et al, medRxiv, 2021; https://doi.org/10.1101/2021.05.27.21257096; Evering T et al, IDWeek 2021; https://www.astrazeneca.com/media-centre/press-releases/2021/azd7442-phiii-trial-positive-in-covid-outpatients.html; Ison MG et al, IDWeek 2021

Anti-SARS CoV-2 Monoclonal Antibodies for Treatment

- Antibodies authorized for treatment of non-hospitalized patients with mild to moderate COVID at high risk of progression and within 10 d of symptom onset:
  - Bamlanivimab + Etesevimab (700/1400 mg)
  - Casirivimab + Imdevimab (600/600 mg)
  - Sotrovimab

Anti-SARS CoV-2 Antibodies for Prevention

Anti-SARS CoV-2 Monoclonal Antibodies for Post-Exposure Prophylaxis

- Casirivimab/imdevimab (subcutaneous or intravenous) and bamlanivimab/etesevimab (iv) authorized for post-exposure prophylaxis in individuals who are at high risk for progression to severe COVID-19 and are:
  - Not fully vaccinated or not expected to mount adequate immune response to COVID vaccination (e.g., immunosuppressed individuals) AND
    - Have been exposed* to individual with COVID-19

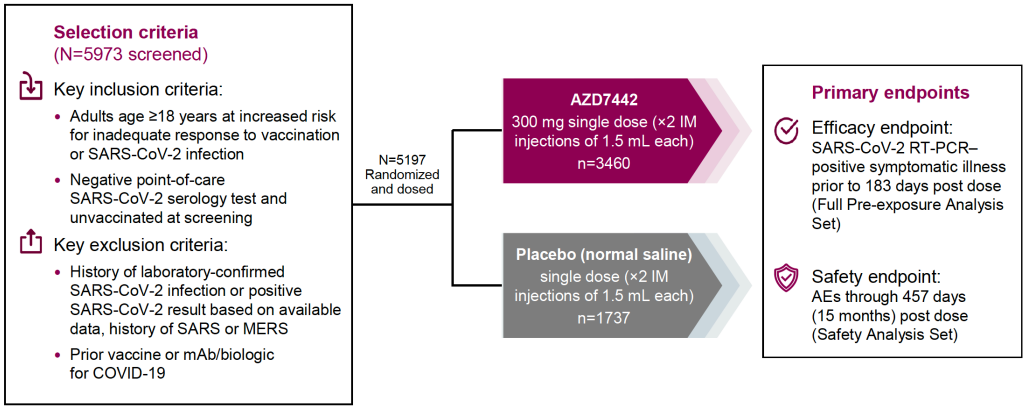
      or

    - At high risk of exposure because of occurrence of COVID-19 in same institutional setting (e.g., nursing home, prison)

*Within 6 feet for >=15 min, providing care at home, direct contact, exposed to respiratory droplets of infected person

PROVENT: Phase 3 Pre-exposure Prophylaxis Trial

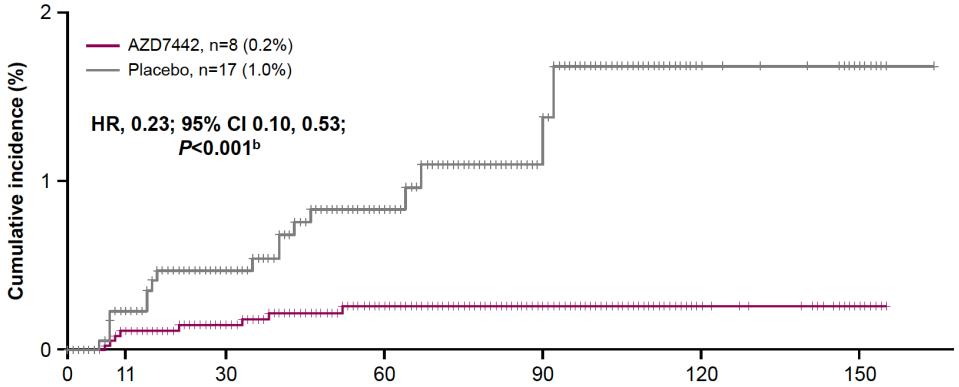
IM Tixagevimab/cilgivimab (AZD7442) vs. Placebo



Who was in PROVENT (n=5197)?

- Age >=60 yrs: 43%
- Obese: 41.7%. CVD: 8%; COPD 5%; CKD: 5%; Liver disease 4.6%
- Immunosuppressed: 3.8%

Symptomatic COVID-19: 77% Reduction



Levin M et al, IDWeek 2021, LB5

Small Molecule Antiviral for SARS CoV-2: Molnupiravir

- Oral inhibitor of SARS-CoV-2 replication: viral error catastrophe
- Phase 3 MOVe-OUT Trial
  - Non-hospitalized adults, mild to moderate COVID-19
  - ≥1 risk factor for severe disease
  - Symptom onset within 5 days of study randomization
- Molnupiravir 800 mg twice a day or placebo for 5 days
  - 4 (200 mg) pills twice a day
- Interim analysis (n=775)

https://www.gov.uk/government/publications/regulatory-approval-of-lagevrio-molnupiravir/summary-of-product-characteristics-for-lagevrio

Small Molecule Antiviral for SARS CoV-2: Molnupiravir

- Who was in the trial?
  - Median age 44 years
  - Age 60 years or older: 14%
  - Obesity (77%); diabetes (14%)

	Hospitalization or death	Deaths	% Reduction
Molnupiravir	**28/385 (7.3%)**	**0**	**48% (p=0.0012)**
Placebo	**53/377 (14%)**	**8**	

- Appeared to be active against Gamma, Delta and Mu variants
- No dose adjustments for renal, hepatic impairment; no drug interactions identified
- Recently authorized in the UK. FDA Advisory Meeting: November 30, 2021

https://www.gov.uk/government/publications/regulatory-approval-of-lagevrio-molnupiravir/summary-of-product-characteristics-for-lagevrio

Small Molecule Antiviral for SARS-CoV-2: PF-07321332 (‘332)

- Oral SARS CoV-2-3CL protease inhibitor (given with ritonavir)
- Phase 2/3 EPIC trial in high-risk non-hospitalized patients
- Randomized to receive ‘332/rtv (3 pills) every 12 h or placebo, 5 days
- Interim analysis of patients treated within 3 days of symptom onset (n=774)

	Hospitalization or death	% Reduction
332/rtv	3/389 (0.8%) 0 deaths	89% P<0.0001
Placebo	27/385 (7%) 7 deaths	

- Similar reductions in hospitalization or death among people treated within 5 days of symptom onset (n=1219)
- Also being evaluated in lower risk patients and for post-exposure prophylaxis

Owen DR et al, Science, 2021; https://www.pfizer.com/news/press-release/press-release-detail/pfizers-novel-covid-19-oral-antiviral-treatment-candidate

What About People who Develop COVID-19 After Vaccination?

- *For people who develop COVID-19 after receiving SARS-CoV-2 vaccination, prior vaccination should not affect treatment decisions, including use of and timing of treatment with monoclonal antibodies.*

Prophylaxis and Treatment Across the COVID-19 Spectrum

Exposure	Asymptomatic/ Presymptomatic	Mild Illness	Moderate Illness	Severe Illness	Critical illness
	+ SARS-CoV-2 test but no symptoms	Mild symptoms (e.g., fever, cough, taste/smell changes); no dyspnea	O_2 saturation ≥ 94%, lower respiratory tract disease	O_2 saturation <94%, respiratory rate >30/min; lung infiltrates >50%	Respiratory failure, shock, multi-organ dysfunction/failure

Pre-exposure prophylaxis: VACCINE Tixagevimab/ Cilgavimab?

Post-exposure prophylaxis: Bam/Ete,Casi/Imdev (high risk, not fully vaccinated or immunosuppressed)

Viral replication

Inf

Remdesivir Casi/imdev?

Therapeutic anticoagulation?

Bam/Ete, Casi/Imdev or Sotrovimab (high risk outpatients with mild-mod COVID-19) Molnupiravir?

Dexamethasone In some patients: IL-6 inhibitor (tocilizumab) or Jak inhibitor (baricitinib)

Gandhi RT, CID, 2020
Gandhi RT, Lynch J, del Rio C. NEJM 2020

Monoclonals and More: Issues and Opportunities with Early COVID-19 Treatment Options

Jay S. Epstein, MD
COVID-19 Therapeutics Response,
HHS/ASPR

November 12, 2021

USG Role in Procurement and Distribution of Monoclonal Antibodies (mAbs) Against SARS-CoV-2

- The USG is responsible for ensuring rapid and equitable access to medical countermeasures (MCM) in a public health emergency
  - Strategies may include development, procurement, distribution, guidance, administration, and reporting, especially for novel products

- When demand exceeds supply, allocation strategies allow for equitable access by ensuring consistent supply, broad availability, and the capability for jurisdictions to target the delivery and administration of product to meet their unique needs (e.g., high risk populations, disease burden)
  - Historic examples of government allocation included oseltamivir (2009-2010 H1N1 pandemic) and initial distribution of COVID-19 vaccines

Equitable Access to mAbs in Times of Limitations

- Equity is a cornerstone of the federal approach to the distribution and administration of MCM
- USG believes that when supplies are scarce, jurisdictional partners are best positioned to determine how to ensure access to MCM for their populations
  - USG allocates mAbs to jurisdictions based on relative need
  - Jurisdictions understand the need in their areas and can use advanced tools (e.g., CDC social vulnerability index and geo-spatial mapping of provider locations) to address equities through prioritization of ordering sites

Equitable Allocation of mAbs

- ASPR began allocating mAbs after FDA authorizations in Nov. 2020
- NIH ethics was consulted on equitable allocation of a limited supply
- Unrestricted ordering commenced in Feb. 2021 when demand was low; over time ~7,000 individual sites submitted orders
- With the surge of the delta variant in July-August, a dramatic increase in orders threatened to exhaust supplies of mAbs within weeks
  - In Sept. 2021, ASPR reinstituted allocations and began massive procurements to ensure ongoing supply both geographically and temporally
  - Jurisdictions receive proportionate shares of a weekly weighted average of newly diagnosed cases and hospitalizations

Evolving Landscape

- ASPR balances allocation of mAbs in response to product availability and user preferences for products with different logistical complexity
- mAbs for pre-exposure prophylaxis are under FDA review and may warrant different distribution strategies than for early therapy
- ASPR anticipates a transition to commercialization of mAbs when crisis conditions resolve and mAbs are no longer in limited supply
- Equitable distribution strategies will be needed for authorized oral antivirals
- Availability of oral antivirals may impact demand and supply of mAbs

HHS/ASPR will continue to provide access to USG-procured MCMs for COVID-19, but challenges persist with broad and equitable distribution and prioritized clinical use when products are in limited supply

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HEALTHCARE EMERGENCY PREPAREDNESS INFORMATION GATEWAY

Anne Zink, MD, FACEP
Chief Medical Officer, Alaska Department of Health and Social Services
President-Elect, ASTHO

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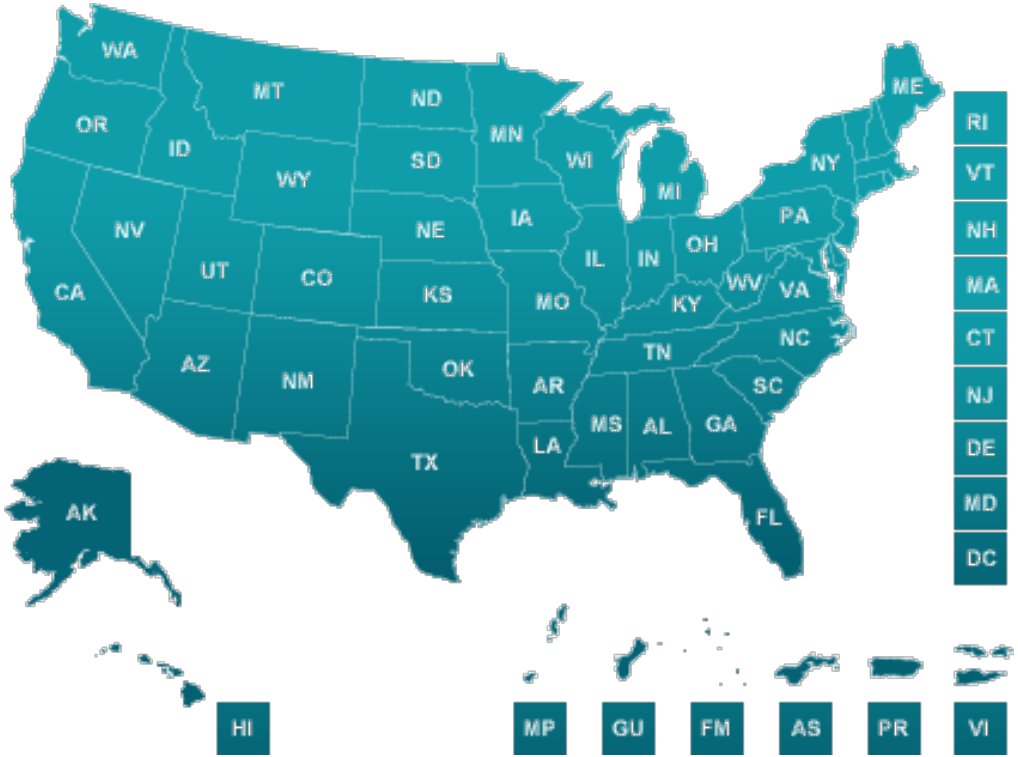
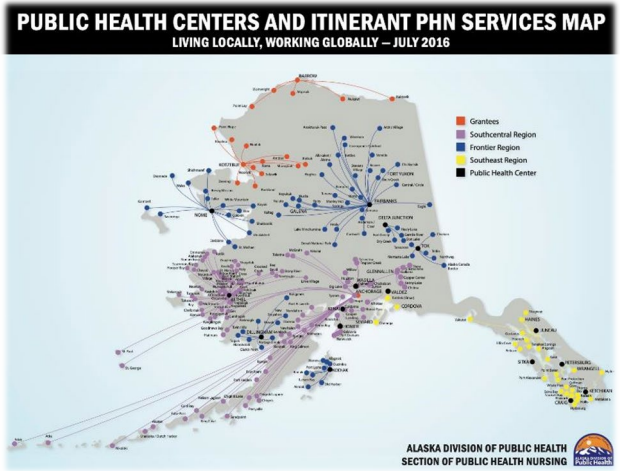
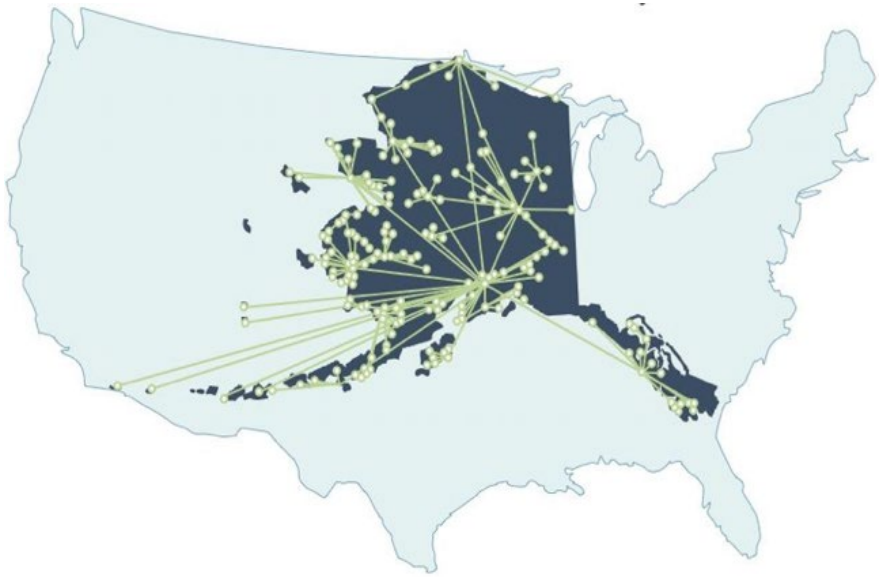
State-level Issues and Considerations



Alaska – Strengths and Challenges



Alaska Native Health Care System
Referral Pattern and Telehealth Network

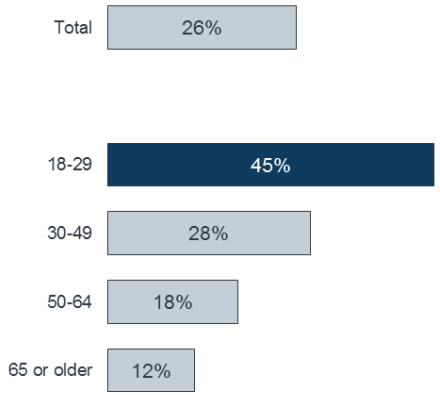


Where People Get Care

According to a 2019 Kaiser Health Foundation Tracking Poll, **one fourth of all adults** and **nearly half of adults under age 30** don't have a primary care doctor.

One-Fourth Of Adults And Nearly Half of Adults Under 30 Don't Have A Primary Care Doctor

Percent who say they **currently do not have** one person they think of as their primary care doctor or health care provider that they usually go to when they are sick or need health care:



SOURCE: KFF Health Tracking Poll (conducted July 17-22, 2018)

Health Care Partnerships

Partnerships are Key:

- Pharmacies
- Drive-up/walk-through clinics
- Regional Tribal clinics
- Schools
- Industry/workplace clinics
- Department of Corrections
- Cruise ships/travel industry

The State's Role in Treatment Distribution

- State-run MAB sites
- State-run redistribution
- Outbreak response

Photo courtesy of UAA

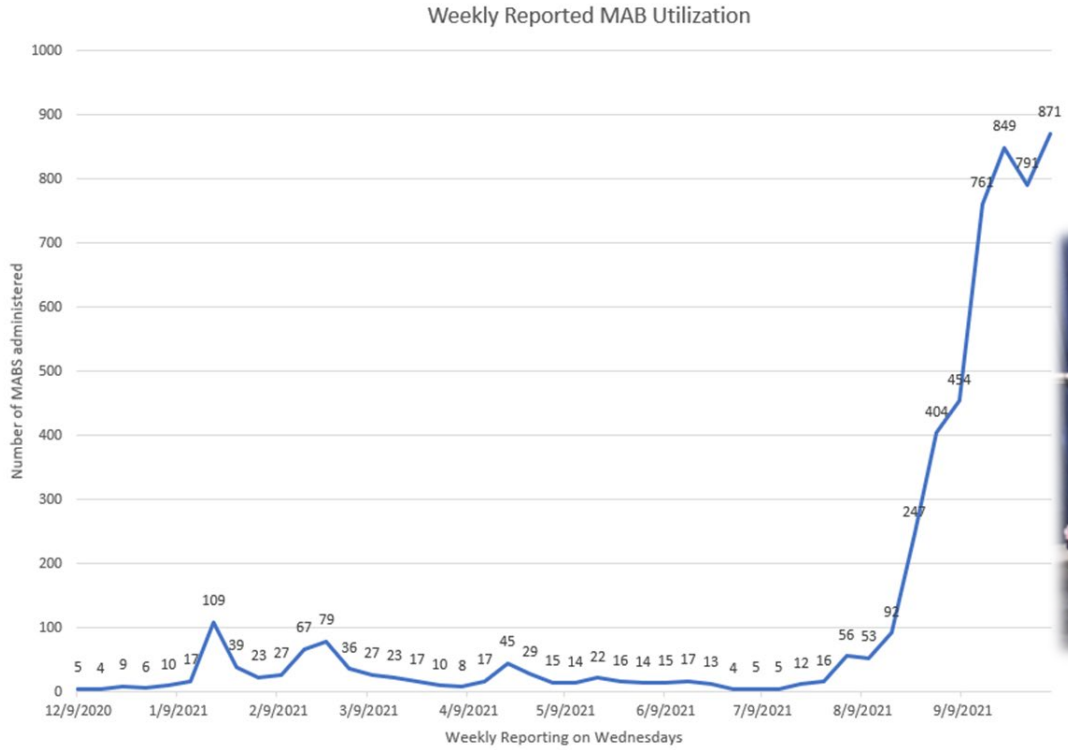
Alaska – Logistics

Cooperation and Efficiencies

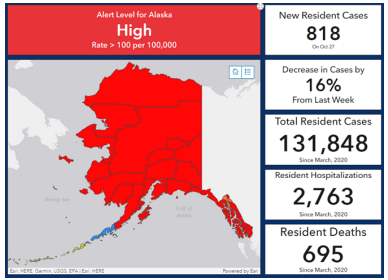
- Movement within a hospital system – Providence Alaska
- Iluiliuk Family and Health Services + American Seafoods
- ConocoPhillips flights to Alpine Medical and Kuparak
- Sharing mAbs – Juneau Pioneer Home and Department of Corrections, Weka and Fairweather

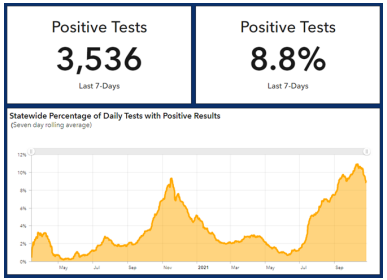
Unalaska/Dutch Harbor

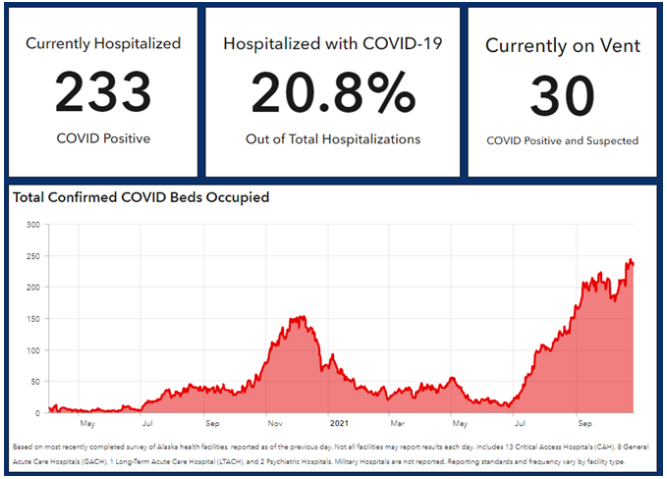
Responding to Changing Demand

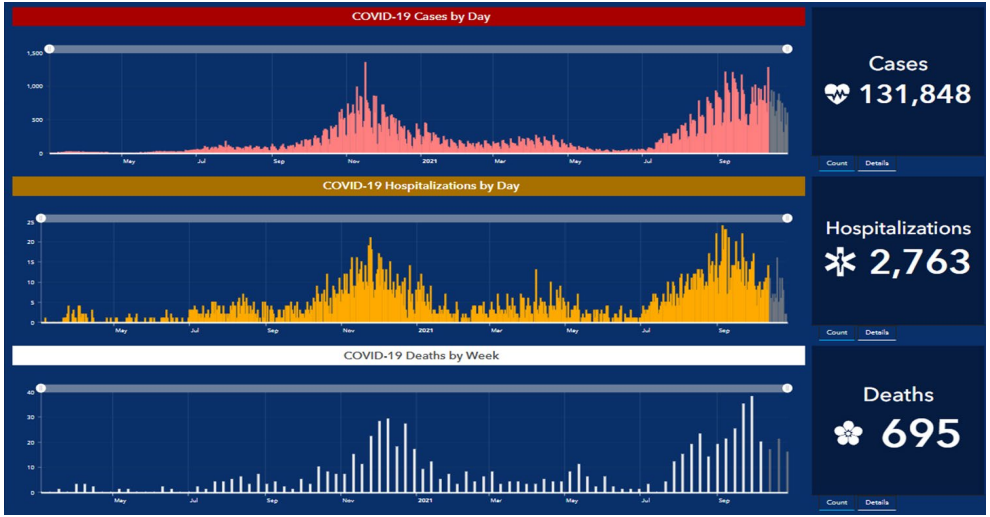


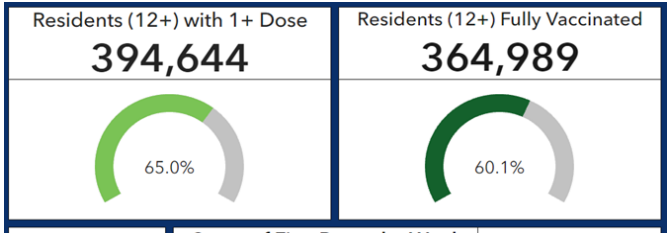
Changing Clinical Dynamic











Allocation of State Resources – NIH Guidance

The State of Alaska's Crisis Care Committee is recommending adopting a modified recommendation based on these national NIH guidelines, as follows:

Prioritizing the treatment of COVID-19 over post-exposure prophylaxis of SARS-CoV-2 infection prioritizing

- Unvaccinated "high risk" for progression
- Vaccinated who are:
  - Age ≥ 65 years old
  - Pregnancy
  - Individuals who are not expected to mount an adequate immune response (e.g., people that meet 3rd dose vaccine criteria)

Challenges to National Guidelines

- Interpretation of NIH guidance
- Diverse health authorities/diverse tools
- Standing orders
- Education, work-flow of clinicians working within and without the State's guidance

Examples from Other States

Alabama

- Separate outpatient infusion sites
- Partnership to educate providers

Maryland

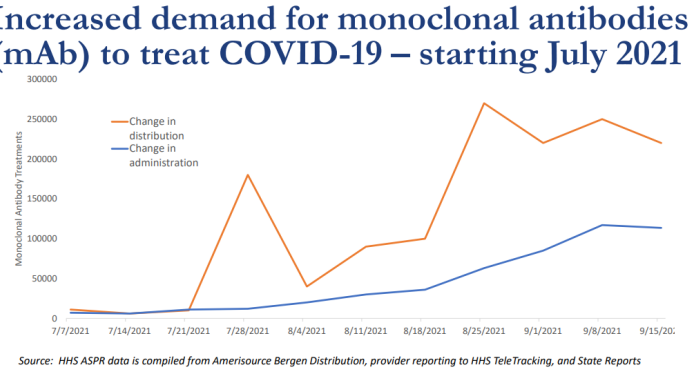
- Co-located infusion with testing
- Engaged with network of antigen tests

Michigan

- Created regional centers for allocation
- Partnered with local public health and regional health care teams

Texas

- Multi-stakeholder approach including health systems, nursing homes, rural hospitals, and medical staffing companies
- Incorporate home infusion channels and administration by SQ injection



Areas of Focus Moving Forward

- State visibility and partnership with distribution (Pharmacy, VA/DOD, IHS) and reporting
- Building sustainable treatment infrastructure within and outside of traditional health care
- Education and clinical resources (standing orders, telehealth, consult line etc.)
- Strategies for responding to COVID-19 surges including personnel
- Preparing for future pandemic responses to incorporate treatment – streamline federal response

Moderator Roundtable Topic 1

Monoclonal Antibody Allocation Guidance

Updated COVID-19 Treatment Guidelines Panel's Statement on the Prioritization of anti-SARS CoV-2 Monoclonal Antibodies for the Treatment or Prevention of SARS CoV-2 Infection When There Are Logistical or Supply Constraints - 1

- The Panel recommends the use of anti-SARS CoV-2 monoclonal antibodies (mAbs) for treatment of mild-to-moderate COVID-19 and for post-exposure prophylaxis (PEP) of SARS CoV-2 infection in individuals at high risk for progression to severe COVID-19 (as outlined in the FDA EUA).
- The anti-SARS CoV-2 mAbs are of greatest benefit as treatment or PEP for people who have risk factors for progression to severe COVID-19. Among individuals at high risk for progressing to severe COVID-19, the risks are lower for those who have been fully vaccinated and are immunocompetent than for those who are either not fully vaccinated or are fully vaccinated but not expected to mount an adequate immune response to the vaccine.

National Institutes of Health, 2021, https://www.covid19treatmentguidelines.nih.gov/therapies/updated-statement-on-the-prioritization-of-anti-sars-cov-2-mabs/

Updated COVID-19 Treatment Guidelines Panel's Statement on the Prioritization of anti-SARS CoV-2 Monoclonal Antibodies for the Treatment or Prevention of SARS CoV-2 Infection When There Are Logistical or Supply Constraints - 2

- **The Panel issued guidance on which individuals might receive the greatest benefit from anti-SARS CoV-2 mAb therapy when logistical or supply constraints make it impossible to offer the therapy to all eligible patients and triage becomes necessary.**
- **Only when it becomes necessary to triage use of the anti-SARS-CoV-2 mAbs**, the Panel suggests:
  - Prioritizing the treatment of COVID-19 over PEP of SARS-CoV-2 infection; *and*
  - Prioritizing anti-SARS-CoV-2 mAb therapy for unvaccinated or incompletely vaccinated individuals and vaccinated individuals who are not expected to mount an adequate immune response (e.g., individuals who are immunocompromised or on immunosuppressive medications or individuals aged ≥65 years).
- Providers should use their clinical judgment when prioritizing the use of anti-SARS CoV-2 mAbs for treatment or PEP in a specific situation.
- The availability and distribution of authorized anti-SARS CoV-2 mAbs should be monitored to ensure that access to products is equitable.

National Institutes of Health, 2021, https://www.covid19treatmentguidelines.nih.gov/therapies/updated-statement-on-the-prioritization-of-anti-sars-cov-2-mabs/

Updated COVID-19 Treatment Guidelines Panel's Statement on the Prioritization of anti-SARS CoV-2 Monoclonal Antibodies for the Treatment or Prevention of SARS CoV-2 Infection When There Are Logistical or Supply Constraints - 3

- When logistical or supply constraints limit the availability of anti-SARS CoV-2 antibodies, the Panel recommends that, in addition to the prioritization previously listed, clinicians consider prioritizing their use for patients at highest risk for clinical progression.
- CDC provides a list of risk factors for severe illness from COVID-19.
- Some of the most important risk factors include (listed alphabetically): age (risk increases with each decade after age 50); cancer; cardiovascular disease; chronic kidney disease; chronic lung disease, diabetes, immunocompromising conditions or receipt of immunosuppressive medications, obesity (body mass index ≥30); pregnancy; and sickle cell disease. CDC provides a complete list of risk factors, including information on relative risk of severe disease: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html
- Likelihood of developing severe COVID-19 increases when a person has multiple comorbidities.
- Review individual FDA EUAs for a complete list of medical conditions or other factors as criteria for use of anti-SARS CoV-2 mAbs as treatment or PEP.

National Institutes of Health, 2021, https://www.covid19treatmentguidelines.nih.gov/therapies/updated-statement-on-the-prioritization-of-anti-sars-cov-2-mabs/

Moderator Roundtable Topic 2

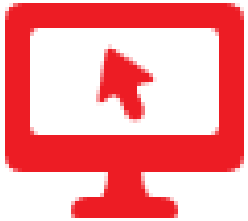
Access and Equity in Allocation of COVID-19 Therapeutics

Moderator Roundtable Topic 3

Fair Distribution and Administration of COVID-19 Therapeutics

Question & Answer

Contact Us



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