

Right Patient, Right Time, Right Place: A Critical Challenge of COVID-19 Monoclonal Antibodies

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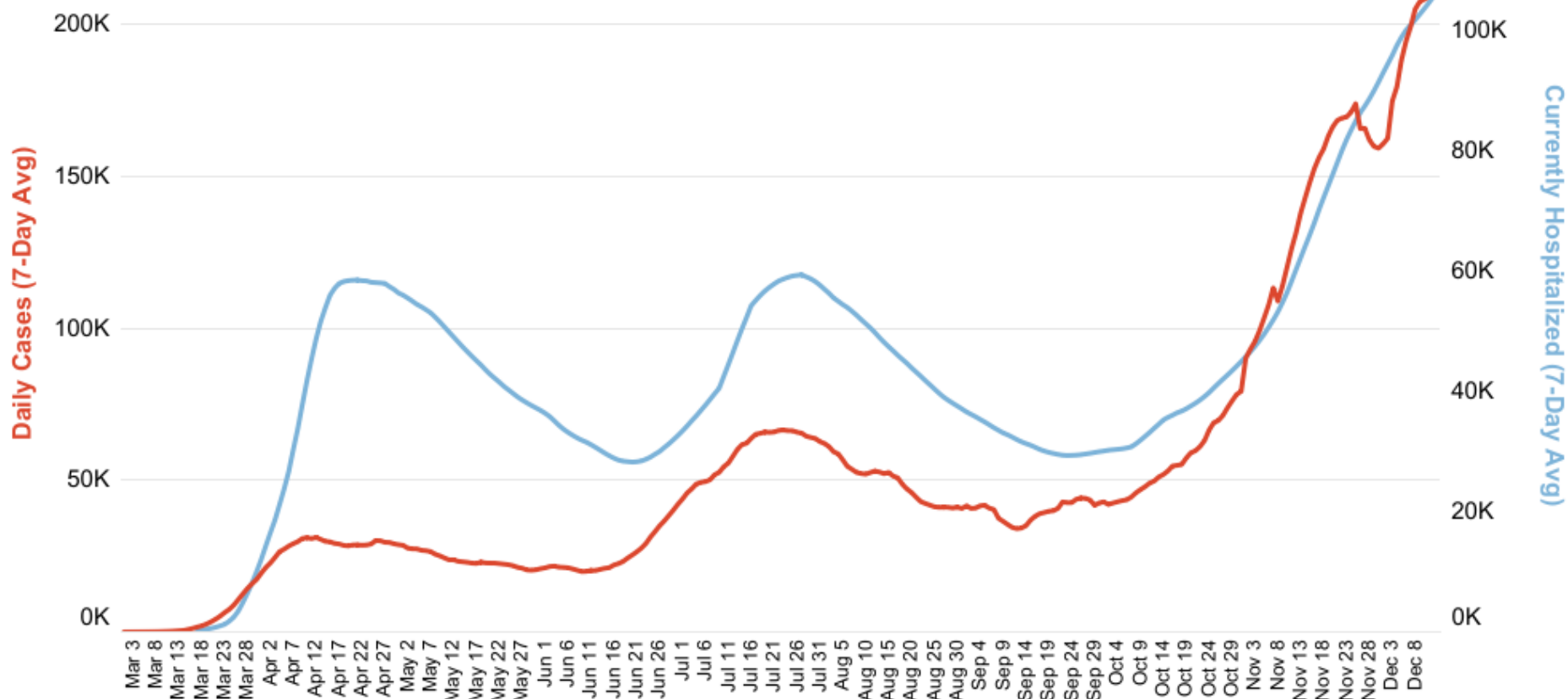
Prepared for NASEM 12/16/2020 meeting

COVID-19 mAbs: great but uncertain potential

- Trial submitted for EUA show statistically significant reduction of hospitalizations in high-risk patients
 - 75% for bamlanivimab, 67% for casirivimab + imdevimab
- Small trials and low baseline risk raise uncertainty
 - IDSA: Conditional recommendation against the **routine** use of bamlanivimab due to "very low certainty of evidence"
 - NIH: "At this time, there are insufficient data to recommend either for or against the use of bamlanivimab for the treatment of outpatients with mild to moderate COVID-19."

Daily Cases & Currently Hospitalized. 7-Day Average Lines

Mar 1 to Dec 13



Left Axis
DAILY CASES

Right Axis
CURRENTLY HOSPITALIZ..

All States Included

All Regions Included

The COVID-19 mAb allocation challenge

To help the patients who could benefit the most, we need:

- Identify the right patients
- At the right time (early in disease progression)
- And at the right place (provider burden, patient location)

This is not remdesivir...

Right patient challenge: Number of eligible patients exceeds supply

- EUA criteria are very broad
 - Over 65 or
 - BMI>35 or
 - certain comorbidities
- Supply is limited
 - Over 1.2M doses should be available by end of January

5,207,541 new cases reported Nov 9-Dec 9



337,182 courses of mAbs allocated Nov 9-Dec 9



Right patient challenge

- In a typical shortage, providers narrow eligibility criteria using information on future supplies and clinical data
- But remdesivir and mAbs have been different:
 - Federal government and states are involved
 - Available future supplies not known outside HHS
 - Limited clinical data to support narrowing eligibility beyond EUA high-risk
- States have differentially embraced their new role:
 - Many set up allocation boards that involved health system participants
 - For mAbs, generally did little to narrow eligibility criteria

With limited data, providers seem to use two approaches for narrowing criteria

- Rely on lottery
 - Usually based on state guidance
- Rely on baseline risk
 - Needed to treat (NNT) to prevent an ER visit or hospitalization with bamlanivimab was about 10 patients for the high-risk group versus about 21 patients in the full study cohort
 - The differential appears related to baseline risk rather than differential efficacy of the drug with hospitalizations dropping (71%) for high-risk vs the overall group (75%)

Predict Hospitalization Risk for COVID-19 Positive

The screenshot shows a web-based calculator interface for predicting hospitalization risk for COVID-19 positive patients. The interface is divided into two main sections: a form for inputting patient data and a results section.

Form Section:

- Age:** A text input field containing the value "18".
- Race:** A dropdown menu with "White" selected.
- Ethnicity:** A dropdown menu with "Non-Hispanic" selected.
- Gender:** A dropdown menu with "Male" selected.
- Smoking:** A dropdown menu with "No" selected.
- BMI:** A text input field containing the value "21".
- ZIP?** A toggle switch that is currently turned off.
- Symptoms and risks:** A text input field.
- Comorbidities:** A text input field.
- Pre-testing medications:** A text input field.
- Platelets?** A toggle switch that is currently turned off.
- AST?** A toggle switch that is currently turned off.
- BUN?** A toggle switch that is currently turned off.
- Chloride?** A toggle switch that is currently turned off.
- Potassium?** A toggle switch that is currently turned off.

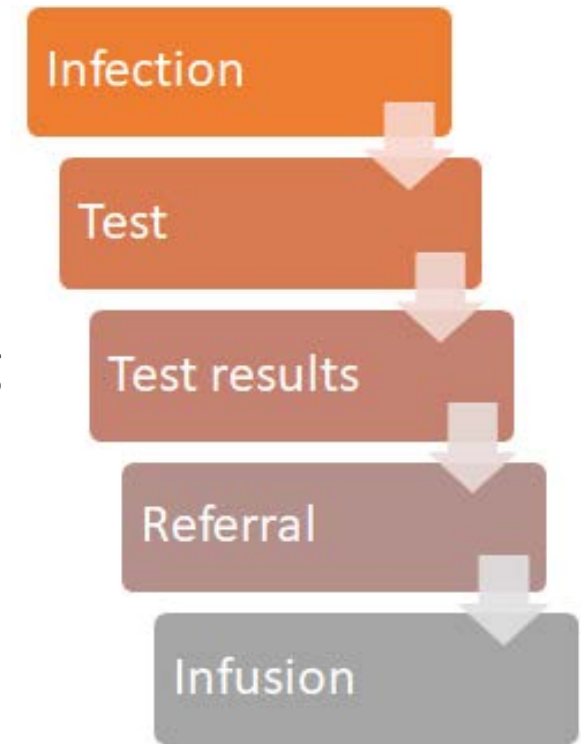
Results Section:

- Run Calculator:** A button to initiate the calculation.
- Reference:** A section containing a citation: "Jehi, L., Ji, X., Milinovich, A., Erzurum, S., Merlino, A., Gordon, S., Young, J. B., & Kattan, M. W. (2020). Development and validation of a model for individualized prediction of hospitalization risk in 4,536 patients with COVID-19. PLoS one, 15(8), e0237419."
- Disclaimer:** A section containing a disclaimer: "No Medical Advice. ALTHOUGH SOME CONTENT MAY BE PROVIDED BY INDIVIDUALS IN THE MEDICAL PROFESSION, YOU ACKNOWLEDGE THAT PROVISION OF SUCH CONTENT DOES NOT CREATE A MEDICAL PROFESSIONAL-PATIENT RELATIONSHIP AND DOES NOT CONSTITUTE AN OPINION, MEDICAL ADVICE, PROFESSIONAL DIAGNOSIS, SERVICE OR TREATMENT OF ANY CONDITION. Access to general information is provided for educational purposes only, through this site and links to other sites. Content is not recommended or endorsed by any doctor or healthcare provider. The information and Content provided are not substitutes for medical or professional care, and you should not use the information in place of a visit, call, consultation or the advice of your physician or other healthcare provider. You are liable or responsible for any advice, course of treatment, diagnosis or any other information, services or product obtained through this site."
- Homepage | Contact Us:** A link to the homepage or contact information.
- Cleveland Clinic | Department of Quantitative Health Sciences:** A logo and text indicating the source of the calculator.

<https://riskcalc.org/COVID19Hospitalization/>

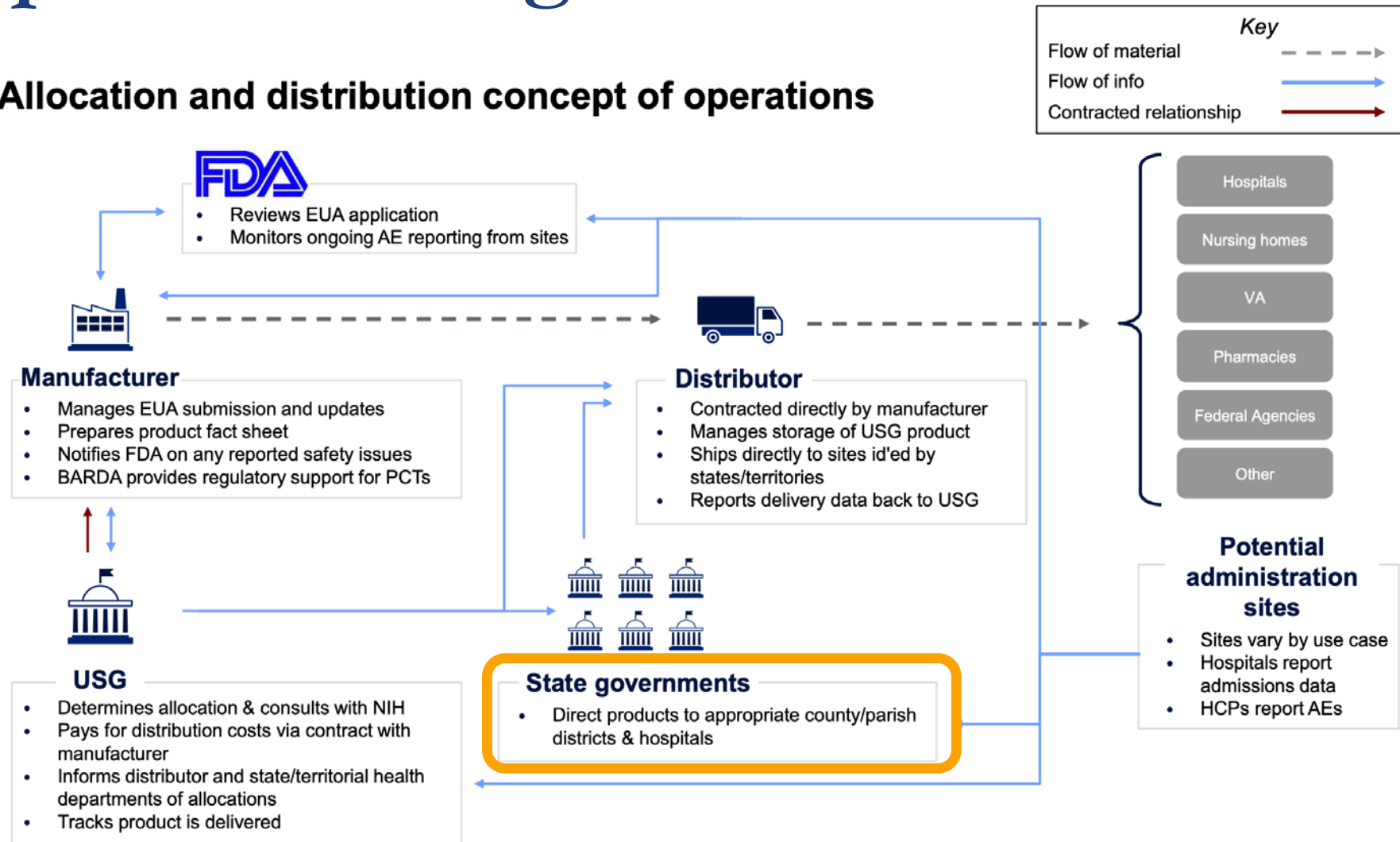
Right time challenge

- Need to infuse within 10 days of symptoms, but...
 - Patients generally don't seek care until quite ill
 - Many other parts of the process can have delays
- Role for providers
 - Check eligibility and discuss treatment options when testing
 - Ensure prompt test turnaround time and rapid referral
- Role for states
 - Enable screening for high-risk patients at testing sites
 - Check for health system and facility readiness and capacity
 - Support efforts to streamline the test-to-infusion timeline



Right place challenge: where to do infusions?

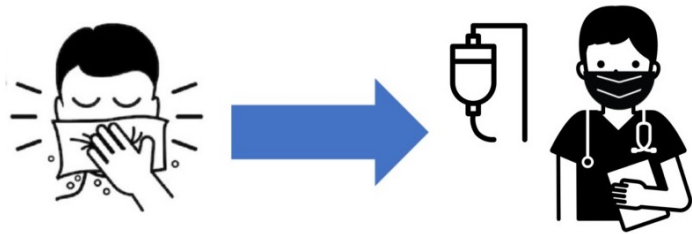
Allocation and distribution concept of operations



Right place challenge: where to do infusions?

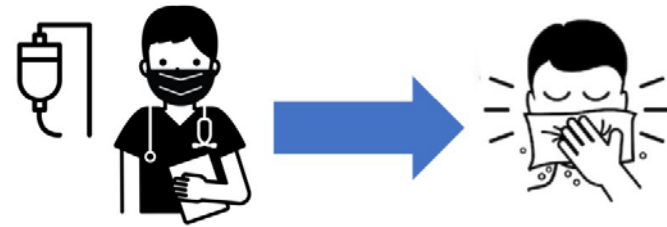
Phase 1 of distribution only included hospital systems and hospital-affiliated locations

Bring patient to infusion site



- How to address need to staffing shortages and COVID precautions?
- How do physicians not affiliated with hospitals refer patients?
- How to reach vulnerable communities?

Bring infusion site to the patient



- How to operationalize the home-infusion model for LTC?
- How to scale home-infusion?

Right place challenge: Where should physicians refer patients to?

The screenshot displays the NICA (National Infusion Center Association) Infusion Center Locator. The interface includes a search bar with the zip code "20815" and a "15 miles" radius, a "SEARCH" button, and a "CLEAR FILTERS" section. The filters section contains checkboxes for "Open Weekends", "Hide hospital based locations", "Accepts Medicare", "Accepts patients from outside doctors", and "Accepts Medicaid". Below the filters, there are dropdown menus for "Medications Available:" (set to "Remicade") and "Specialty:" (set to "Any specialty"). To the right of the filters is a map of the Washington, D.C. area, showing several infusion centers marked with blue dots. The map includes labels for various locations such as Rockville, Aspen Hill, North Bethesda, Bethesda, Silver Spring, Washington, Arlington, and Falls Church. The map also shows major highways like I-495 and I-66.

What does vaccination of high risk groups mean for COVID-19 mAb allocation?

- Should patients who have received one vaccine dose be eligible for COVID-19 mAbs?
- How will priority groups change once vaccines are being administered in settings like LTC facilities?

Duke-Margolis papers on COVID-19 mAbs

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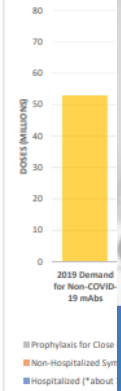
Updated August 2020

COVID-19 Manufacturing for Monoclonal Antibodies

Monoclonal antibodies (mAbs) offer the potential for effective treatments for COVID-19, before and even after a vaccine becomes available. In this issue brief, we estimate the demand for mAb drug products (COVID-19 and otherwise), an overview of the manufacturing process for mAbs, and an analysis of manufacturing capacity currently in use to make mAbs for the North American and European markets. We follow with a discussion of policy implications, with attention to manufacturing issues.

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August 2020 Update
Potential U.S. Demand
(using current epidemic)



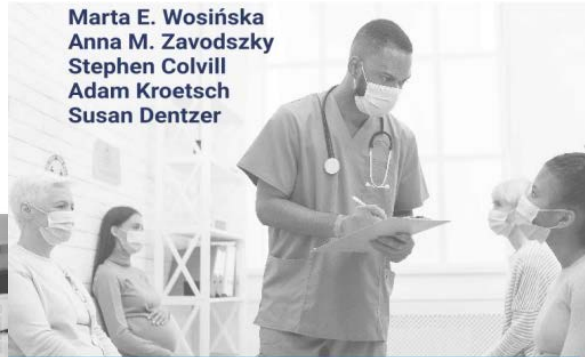
COVID-19 Monoclonal Antibodies: Key Issues After Emergency Use Authorization

NOV 16, 2020

healthpolicy.duke.edu

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DEC 10, 2020

COVID-19 Monoclonal Antibodies: Paying for Administration and Better Evidence

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COVID-19 Monoclonal Antibodies: Feasible Mechanisms for Generating Needed Evidence

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Thank you!

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