COVID-19 Looking Back, Looking Ahead

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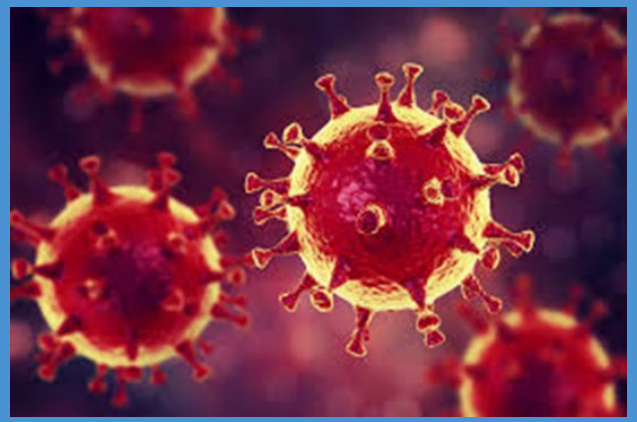


(BACK TO THE) **FUTURE OF PEDIATRICS**

Disclosures

COVID-focused Research Funding:

- NIAID: PECOS study (Pediatric COVID and MIS-C Outcomes Study)
- NICHD/UCSF: RadX Consortium/ PREVAIL
- NHLBI/UCSD: CHARMS/KIDCARE (MIS-C consortium)
- HHS/DC DOH: COVID Preparedness Funding

- **No unapproved or investigational use of any drugs, commercial products or devices.**

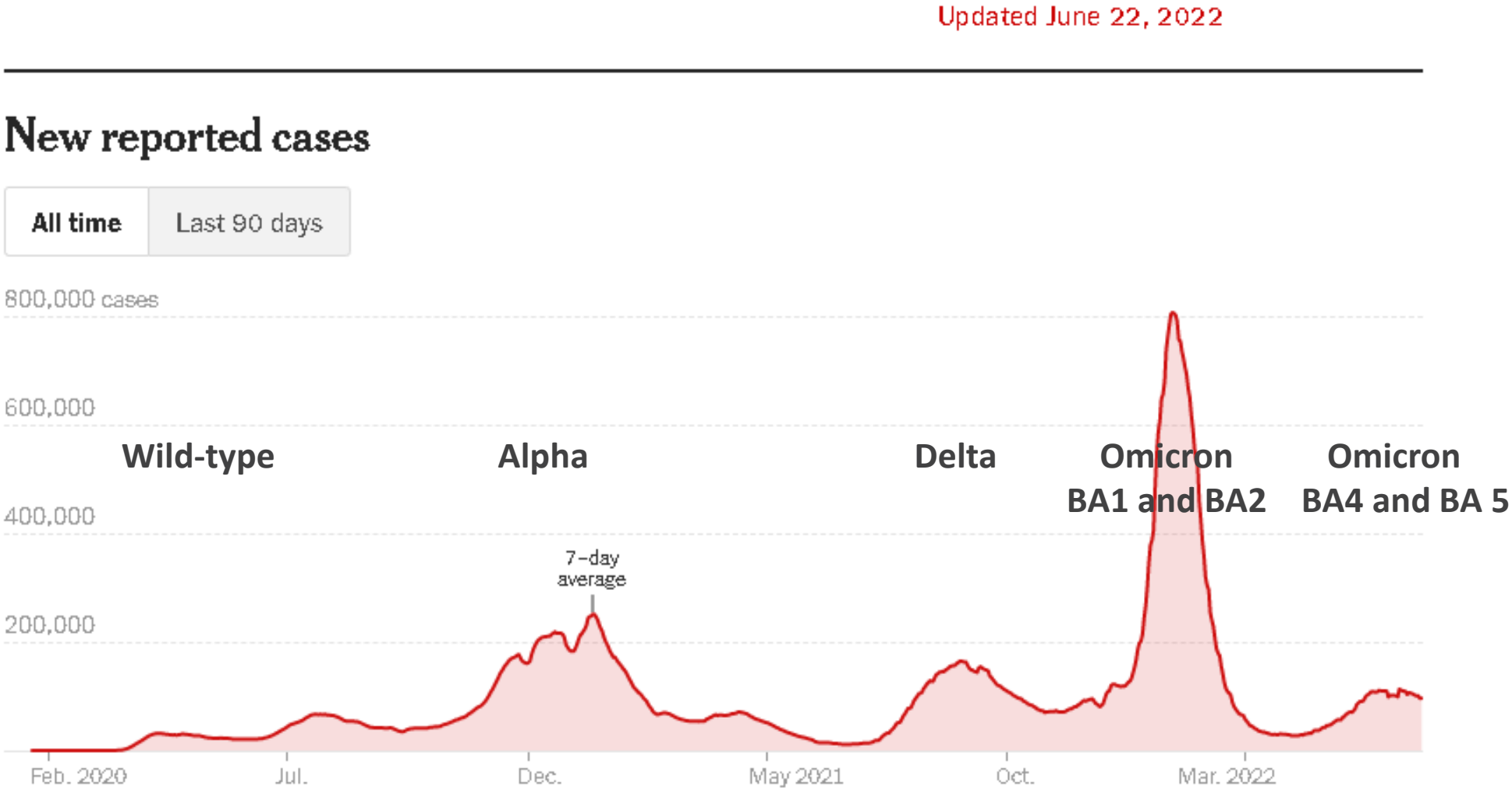
Overview

- **Epidemiology –**
  - SARS CoV-2 virus and variants
  - Impact on the Pediatric population
- **Children's National Experience with COVID and MIS-C**
  - Clinical and Research
- **Testing**
- **Therapeutics**
- **Vaccination**
- **Long Term Effects**
  - PECOS Study and POCO Clinic

EPIDEMIOLOGY

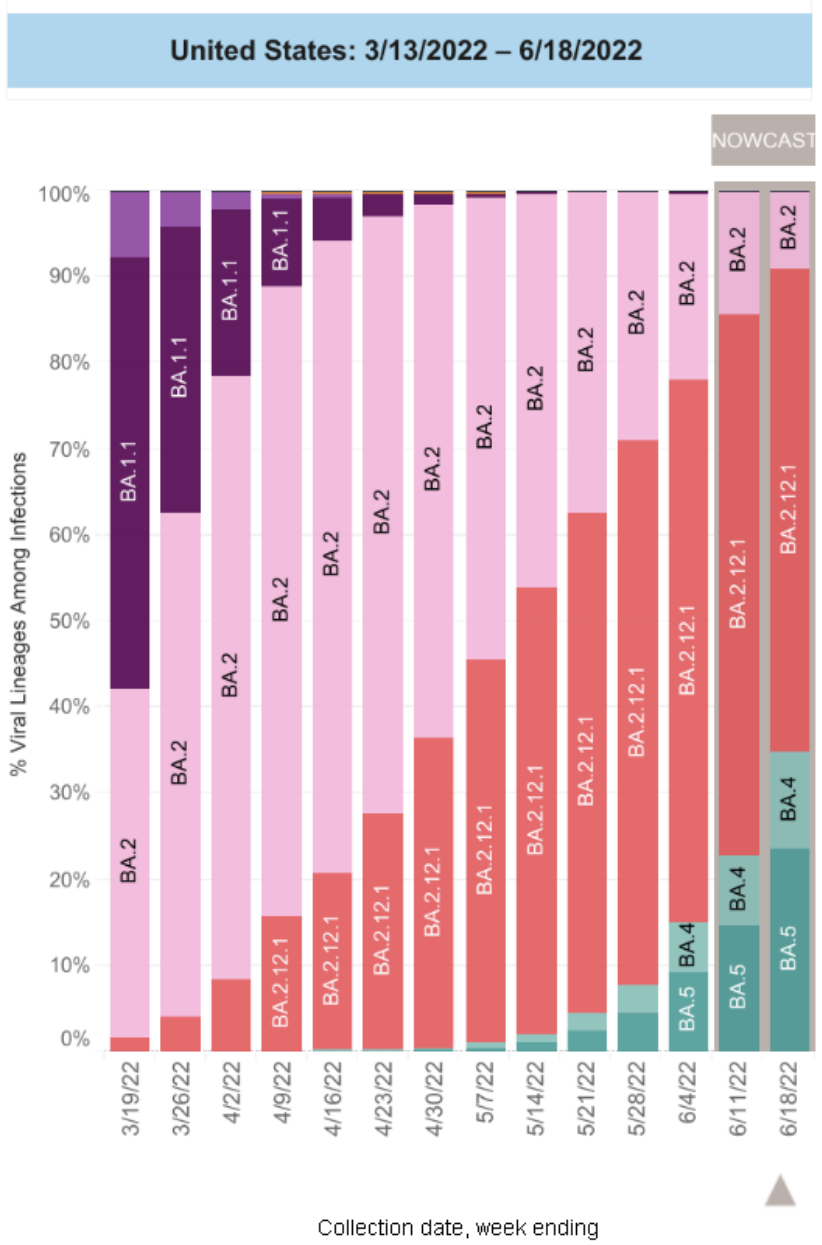
- The Virus and Variants
- Impact on the Pediatric Population

SARS CoV-2 Cases in the United States March 2020 - Present



NYTimes - https://www.nytimes.com/interactive/2021/us/covid-cases.html

Omicron Sub-Variant Emergence/Circulation: March –June 2022



United States: 6/12/2022 – 6/18/2022 NOWCAST

USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	BA.2.12.1	VOC	56.0%	51.4-60.5%
	BA.5	VOC	23.5%	20.3-27.0%
	BA.4	VOC	11.4%	8.8-14.5%
	BA.2	VOC	9.1%	7.9-10.5%
	BA.1.1	VOC	0.0%	0.0-0.0%
	B.1.1.529	VOC	0.0%	0.0-0.0%
Delta	B.1.617.2	VBM	0.0%	0.0-0.0%
Other	Other*		0.0%	0.0-0.0%

* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.

** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates

AY.1-AY.133 and their sublineages are aggregated with B.1.617.2. BA.1, BA.3 and their sublineages (except BA.1.1 and its sublineages) are aggregated with B.1.1.529. For regional data, BA.1.1 and its sublineages are also aggregated with B.1.1.529, as they currently cannot be reliably called in each region. Except BA.2.12.1, BA.2 sublineages are aggregated with BA.2. BA.5.1 is aggregated with BA.5.

Gone:

- **BA1.1.529 and BA1.1**

Going:

- **BA2= 9%**

Predominant

- **BA 2.12.1 = 56%**

Rising:

- **BA5 23.5%**
- **BA4 11.4%**

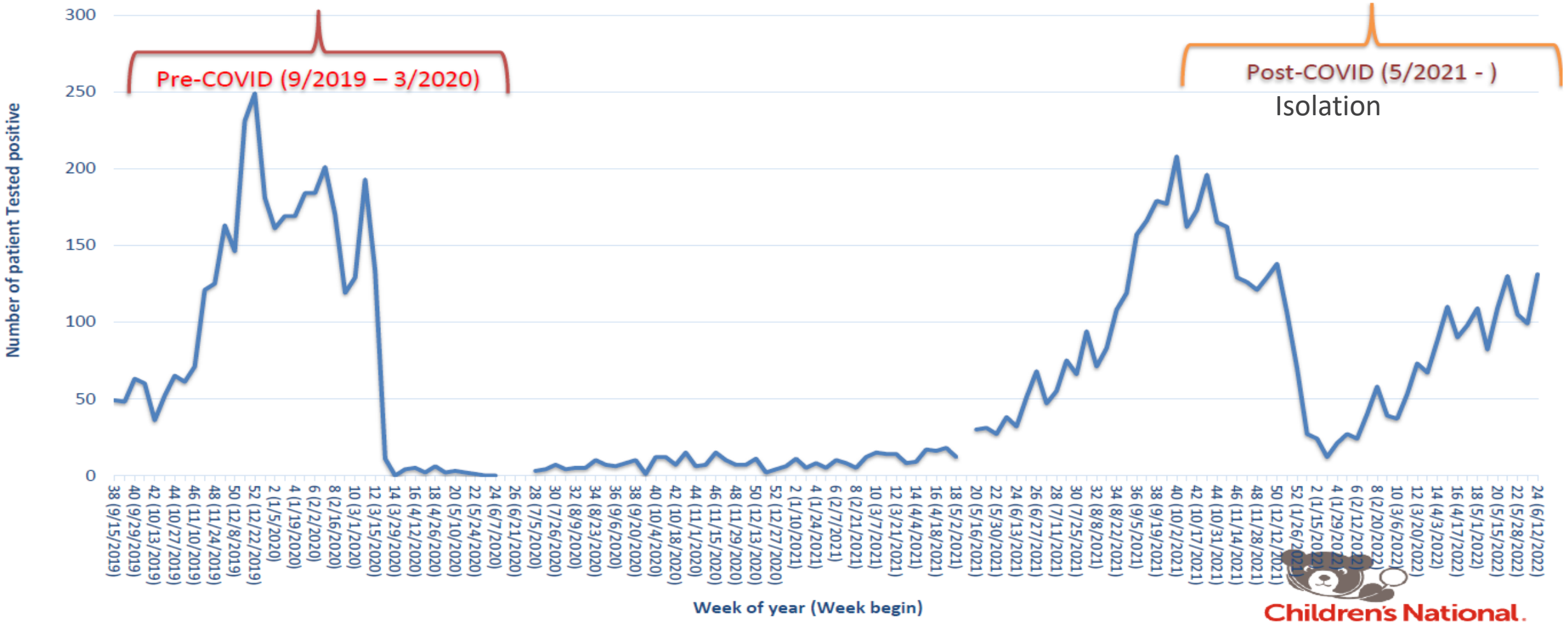
COVID DASHBOARD: Cumulative Global, National, Regional as of June 20, 2022

	Global	US	DC/MD/VA
Total Cases	538,831,378	86,127,070	3,107,158
Percent Change (since last week)	7.2%	-2.3%	-12.7%
Total Hospitalizations		4,818,395	173,260
Percent Change (since last week)		1.8%	-8.8%
Total Deaths	6,315,117	1,009,893	36,521
Percent Change (since last week)	-12.9%	-5.4%	-4.4%
Case Fatality Rate (7 day average)	0.2%	0.3%	0.2%
New Cases Per 100K (7 day average)	6.8	30.8	27.1
Test Positive Rate (7 day average)		14.0%	13.6%

CNH Data Team: Jacob Cheng, Thomas Chang

CNH Lab-confirmed Seasonal Respiratory Viral Infections,

9/8/2019 – 6/18/2022



Courtesy of Dr. Song , Hospital Epidemiology and Infection Control Division

Impact on Pediatric Population

Pediatric SARS CoV2 Infection through June 2022

Children's Hospital Association/American Academy of Pediatrics

- **13.6 million SARS-CoV-2** lab confirmed cases in children
  - Children make up **18.8% of all cases**

- **43,000 Hospitalizations in children**
  - Children make up **3.2% of all COVID-19 hospitalizations**
  - **Hospitalization rate in children as high as 3.2%; Currently 0.7%**

- **1055 Deaths in US Children**
  - Children make up **0.1% of all deaths**

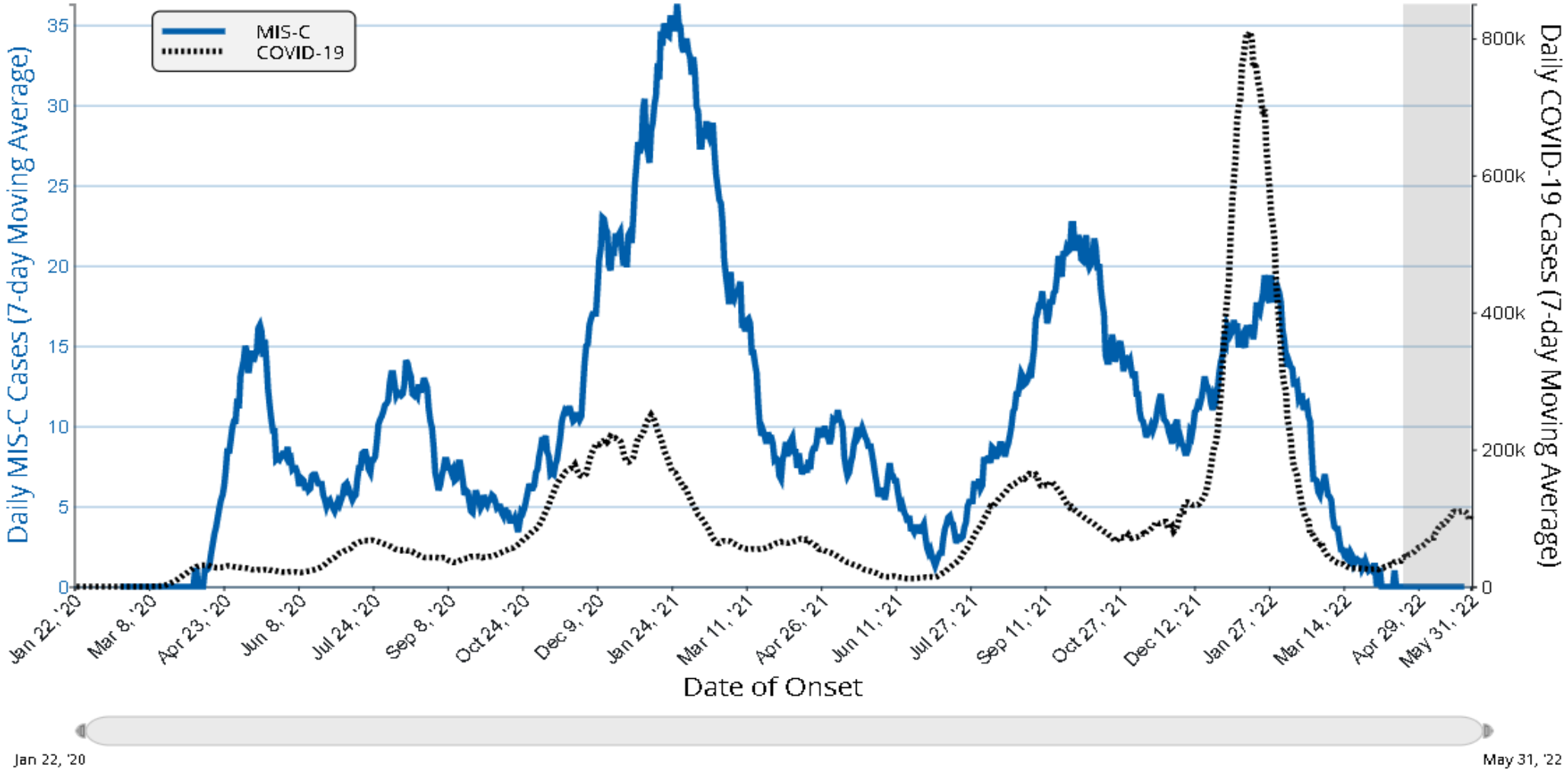
- **8,525 MIS-C cases; 69 deaths**

See detail in Appendix: Data from 49 states, NYC, DC, PR, and GU
Analysis by American Academy of Pediatrics and Children's Hospital Association
All data reported by state/local health departments are preliminary and subject to change

CHILDREN'S HOSPITAL ASSOCIATION

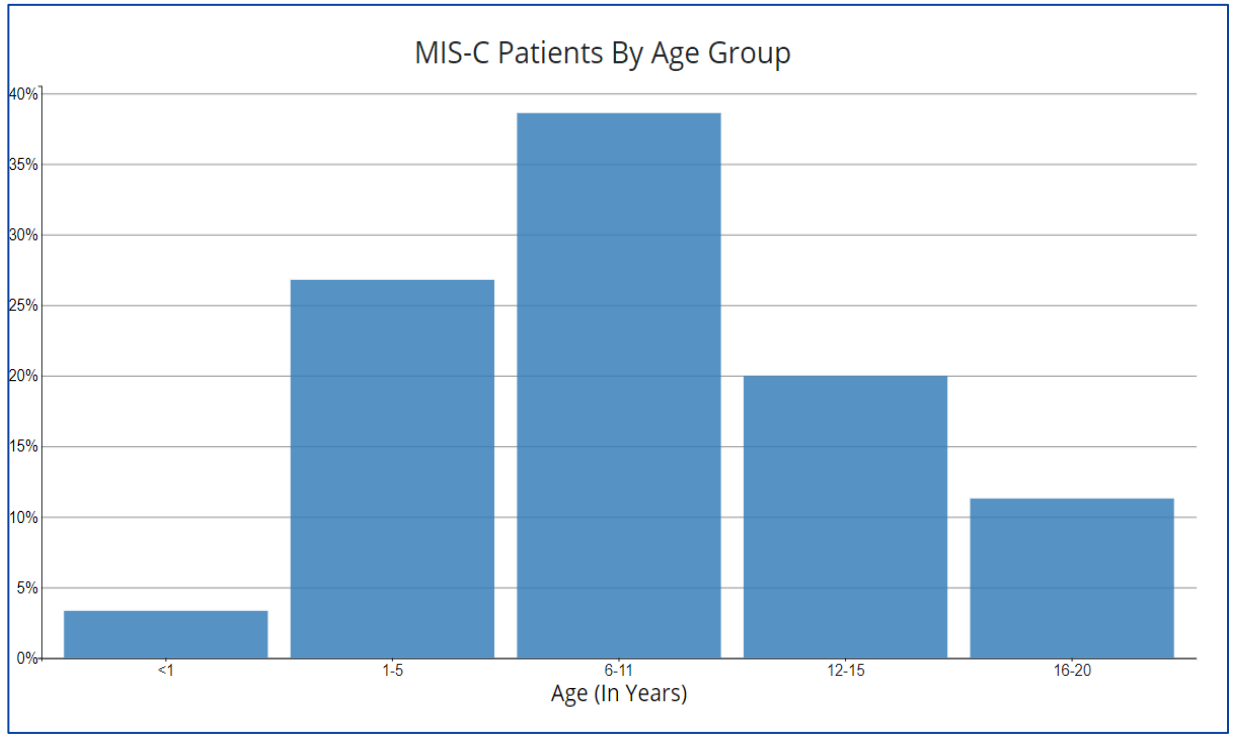
American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN®

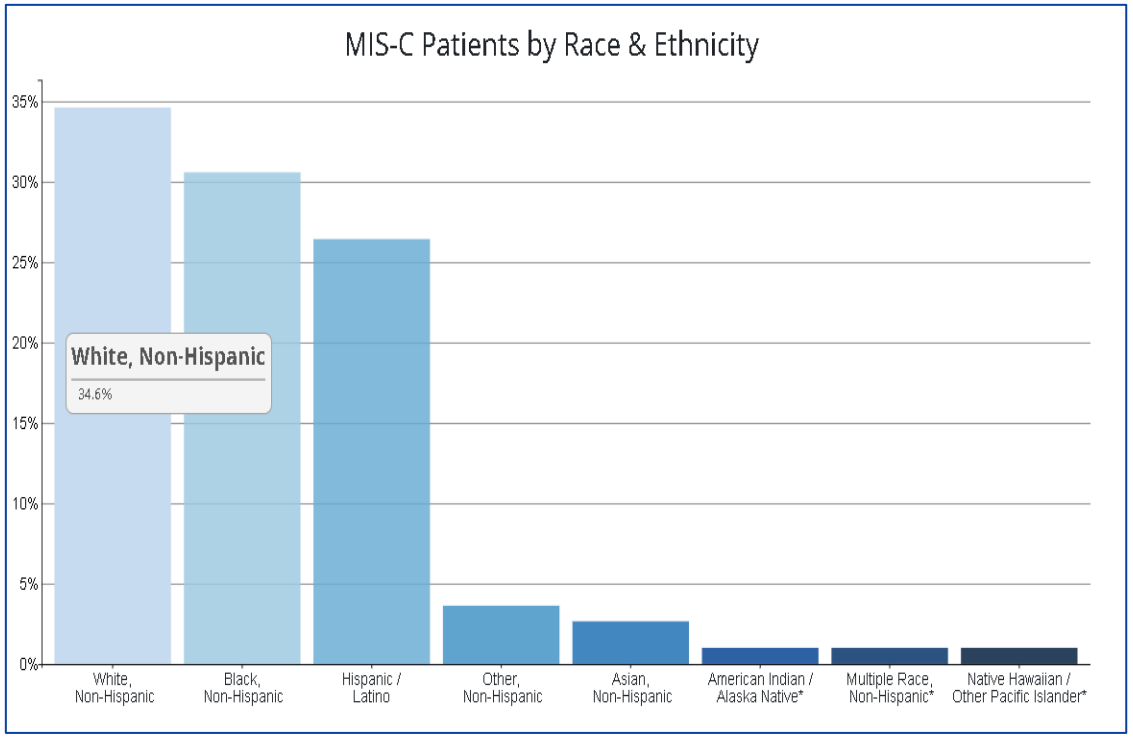
CDC Summary Data for MIS-C in the United States



https://covid.cdc.gov/covid-data-tracker/#mis-national-surveillance

CDC Summary Data for MIS-C in the United States





https://covid.cdc.gov/covid-data-tracker/#mis-national-surveillance

- **Children's National COVID Experience**
  - **Clinical Care**
  - **Research**

Children's National COVID-19 and MIS-C:

March 15, 2020- June 22, 2022

Primary COVID-19 Disease

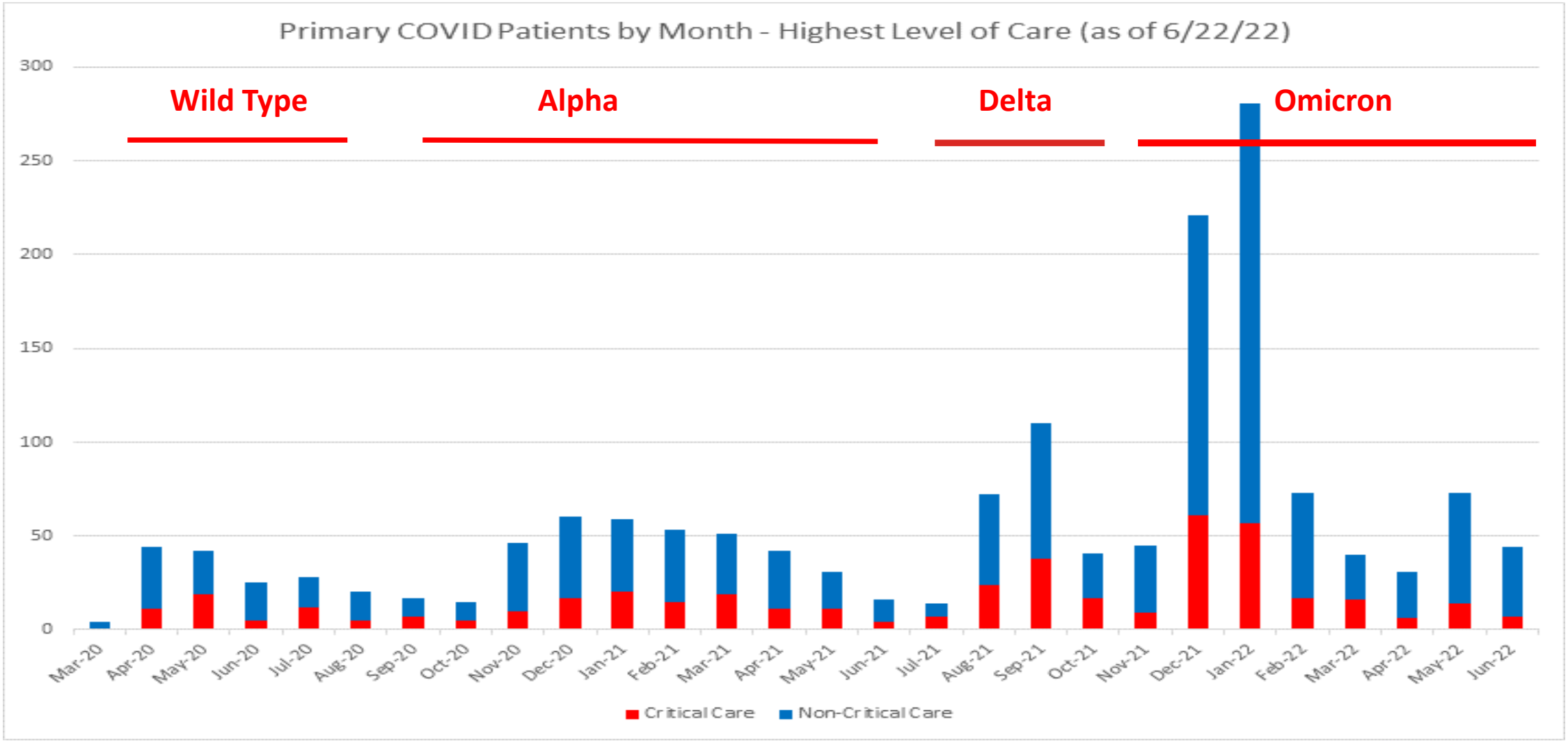
- Cumulative **9059** COVID+ symptomatic patients
  - **Peak of 24 admissions per day 1.29.22**
- Cumulative **1594** COVID+ patients admitted
  - 443 (28%) critical care (380 PICU, 55 NICU, 8 CICU)
  - 1151 (72%) acute care
- **Current COVID+ Census = 12** (all Acute)
  - **Peak Census of 67 on 1.6.22**

Multisystem Inflammatory Disease of Children (MIS-C)

- Cumulative **225**
  - **Peak of 3-4 MISC admissions per day**
- **Current MIS-C Census = 0**

Children's National

Children's National COVID Admissions through June 22, 2022



Children's National Early Leadership in Highlighting Symptomatic and Severe COVID in Children May 12, 2020 - First Wave

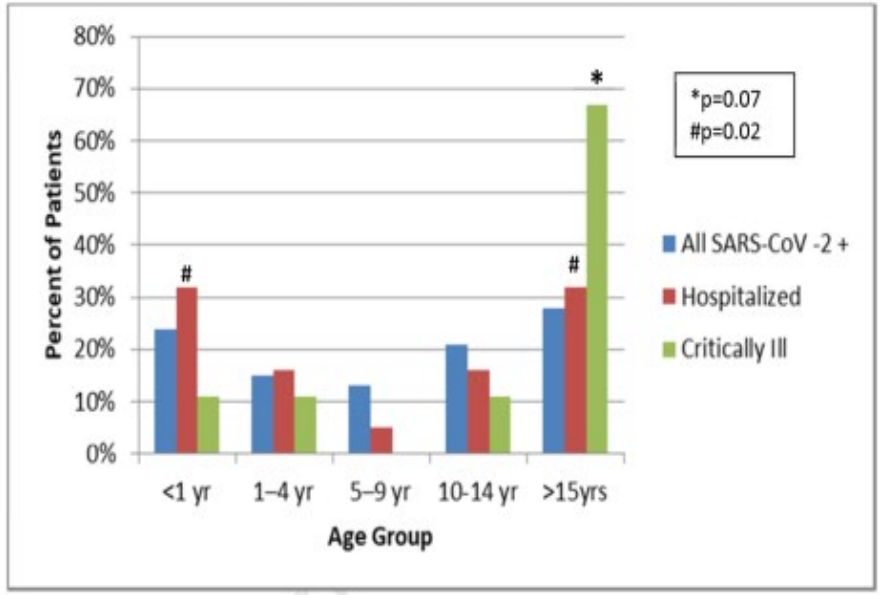
THE JOURNAL OF PEDIATRICS • www.jpeds.com BRIEF REPORTS

Severe Coronavirus Disease-2019 in Children and Young Adults in the Washington, DC, Metropolitan Region

Roberta L. DeBiasi, MD, MS[1,2,3], Xiaoyan Song, MBBS, PhD[2,4], Meghan Delaney, MD[2,5], Michael Bell, MD[2,6], Karen Smith, MD[2,7], Jay Pershad, MD[2,8], Emily Ansusinha, MA[1], Andrea Hahn, MD, MS[1,2], Rana Hamdy, MD, MPH[1,2], Nada Harik, MD[1,2], Benjamin Hanisch, MD[1,2], Barbara Jantausch, MD[1,2], Adeline Koay, MBBS[1,2], Robin Steinhorn, MD[2,9], Kurt Newman, MD[2,10], and David Wessel, MD[2,6]

Despite worldwide spread of severe acute respiratory syndrome coronavirus-2, few publications have reported the potential for severe disease in the pediatric population. We report 177 infected children and young adults, including 44 hospitalized and 9 critically ill patients, with a comparison of patient characteristics between infected hospitalized and nonhospitalized cohorts, as well as critically ill and noncritically ill cohorts. Children <1 year and adolescents and young adults >15 years of age were over-represented among hospitalized patients (P = .07). Adolescents and young adults were over-represented among the critically ill cohort (P = .02). *(J Pediatr 2020;223:199-203).*

Age Distribution of All SARS-CoV-2 Positive, Hospitalized and Critically Ill Patients



DeBiasi et al. *The Journal of Pediatrics* 2020: 223:199-203

Children's National

Children's National Leadership in Evaluation and Care of Children with MIS-C

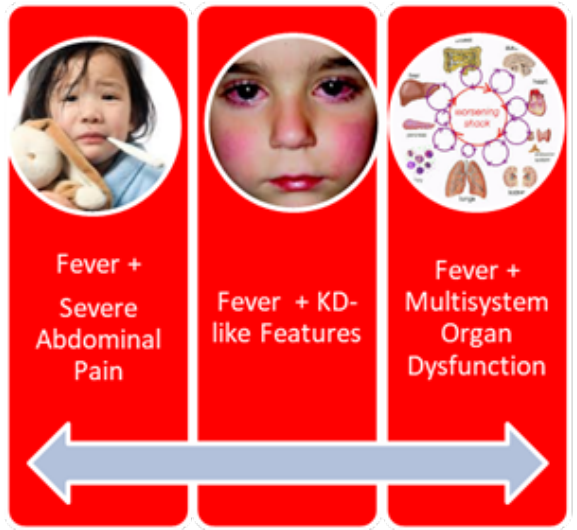
ARTICLE IN PRESS

THE JOURNAL OF PEDIATRICS • www.jpeds.com

ORIGINAL ARTICLES

Multisystem Inflammatory Syndrome of Children: Subphenotypes, Risk Factors, Biomarkers, Cytokine Profiles, and Viral Sequencing

Roberta L. DeBiasi, MD, MS[1,2,3,4], Ashraf S. Harahsheh, MD[2,3], Hemalatha Srinivasalu, MD[3,5], Anita Krishnan, MD[2,3], Matthew P. Sharron, MD[3,6], Kavita Parikh, MD[3,7], Karen Smith, MD[3,7], Michael Bell, MD[3,6], Drew Michael, PhD[3,8,9,10], Meghan Delaney, DO[3,8], Joseph Campos, PhD[3,8], Eric Vilain, MD, PhD[10,11], Jonathan LoTiempo, BS[10,11], Jaclyn N. Kline, MD[3,12], Tova Ronis, MD[3,5], Suvankar Majumdar, MD[6,13], Eleanor Sadler, PharmD[14], Susan R. Conway, MD[3,6], Charles I. Berul, MD[2,3], Sangeeta Sule, MD[3,5], Rebeca Lahoz, MD[1], Emily Ansusinha, MS[1], Jay Pershad, MD[12], Vanessa Bundy, MD[3,15], Elizabeth Wells, MD[3,16], James E. Bost, PhD[17], and David Wessel, MD[2,3,6], on behalf of the Children's National Hospital MIS-C Taskforce



- MIS-C Multidisciplinary Taskforce and Huddles
- Establishes well-characterized large cohort of MIS-C evaluated and treated following a standardized protocol with opportunity for long-term systematic follow-up to determine sequelae

The NEW ENGLAND JOURNAL of MEDICINE

EDITORIALS

Immunotherapy for MIS-C — IVIG, Glucocorticoids, and Biologics

Roberta L. DeBiasi, M.D.

MIS-C Cardiac Involvement

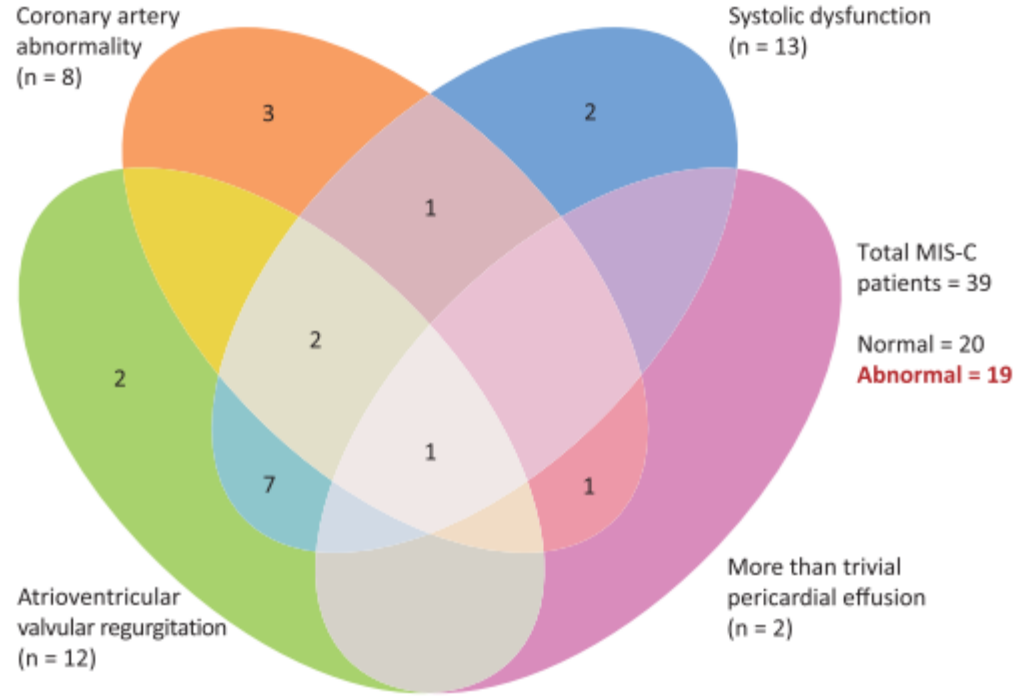


Figure 1. Distribution of cardiac complications in multi-system inflammatory syndrome in children.

Harahsheh et al, Cardiology in the Young, 2021

Cardiology in the Young

cambridge.org/cty

Cardiac echocardiogram findings of severe acute respiratory syndrome coronavirus-2-associated multi-system inflammatory syndrome in children

Original Article

Cite this article: Harahsheh AS, Krishnan A, DeBiasi RL, Olivieri LJ, Spurney C, Donofrio MT, Cross RR, Sharron MP, Frank LH, Berul CI, Christopher A, Dham N, Srinivasalu H, Ronis T, Smith KL, Kline JN, Parikh K, Wessel D, Bost JE, Litt S, Austin A, Zhang J, and Sable CA (2021). Cardiac echocardiogram findings of severe acute respiratory syndrome coronavirus-2-associated multi-system inflammatory syndrome in children. *Cardiology in the Young*, page 1 of 9. doi: 10.1017/S1047951121003024

Ashraf S. Harahsheh[1,2], Anita Krishnan[1,2], Roberta L. DeBiasi[2,3,4], Laura J. Olivieri[1,2], Christopher Spurney[1,2], Mary T. Donofrio[1,2], Russell R. Cross[1,2], Matthew P. Sharron[2,5], Lowell H. Frank[1,2], Charles I. Berul[1,2], Adam Christopher[1], Niti Dham[1,2], Hemalatha Srinivasalu[2,6], Tova Ronis[2,6], Karen L. Smith[2,7], Jaclyn N. Kline[2,8], Kavita Parikh[2,7], David Wessel[1,2], James E. Bost[2,9,†], Sarah Litt[1], Ashley Austin[1], Jing Zhang[1] and Craig A. Sable[1,2]

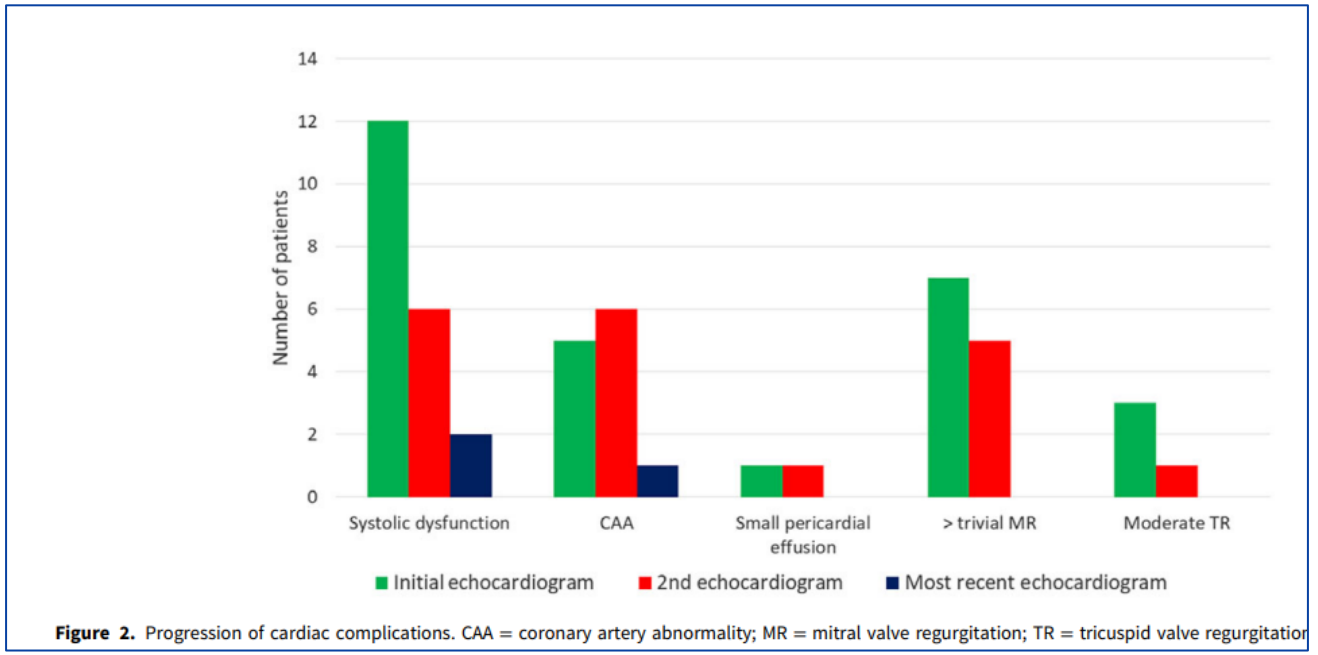


Figure 2. Progression of cardiac complications. CAA = coronary artery abnormality; MR = mitral valve regurgitation; TR = tricuspid valve regurgitation

Testing

Children's National Lab COVID-19 Testing Timeline

Many publications along the way…

Frontier days: 2020

- March 6: **PCR Testing Send Out with ID Review/Approval Pager**
- March 13: **CNH First In-House Validated PCR**
- March 15: First positive patient and employee
- Late March –June: **Walk- up/drive-up dedicated pediatric esting site**
  - 2,439 patients tested with 29% positive rate
- March 27: PCR capacity increases to **2 in-house platforms**
- April-June
  - Expansion to **4 different in-house PCR platforms**
  - In-House **COVID antibody test**
  - Supply chain issues for reagents
    - CRI (Dr Eric Vilain) laboratory manufactures test media
  - Testing commences for CNPA practices
- July: Enrollment of first pts into **COVID specimen biorepository**
- October 5: Launch of **COVID PCR using saliva sample**

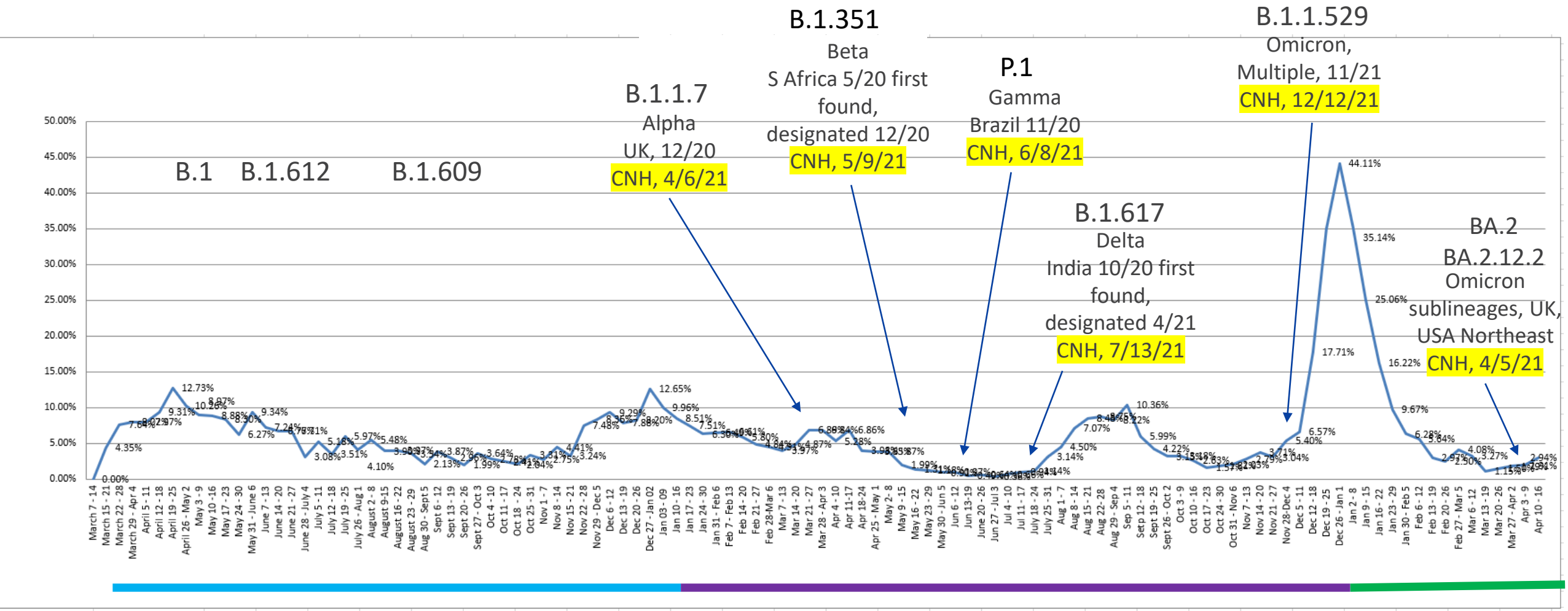
2021

- April 23, 2021: **In-house viral sequencing**
- **Pre-surgical and Pre-procedural testing program**

(BACK TO THE) **FUTURE OF PEDIATRICS**

Courtesy of Meghan Delaney

173,429 SARS-CoV-2 PCR tests at CNH Lab since March 13, 2020



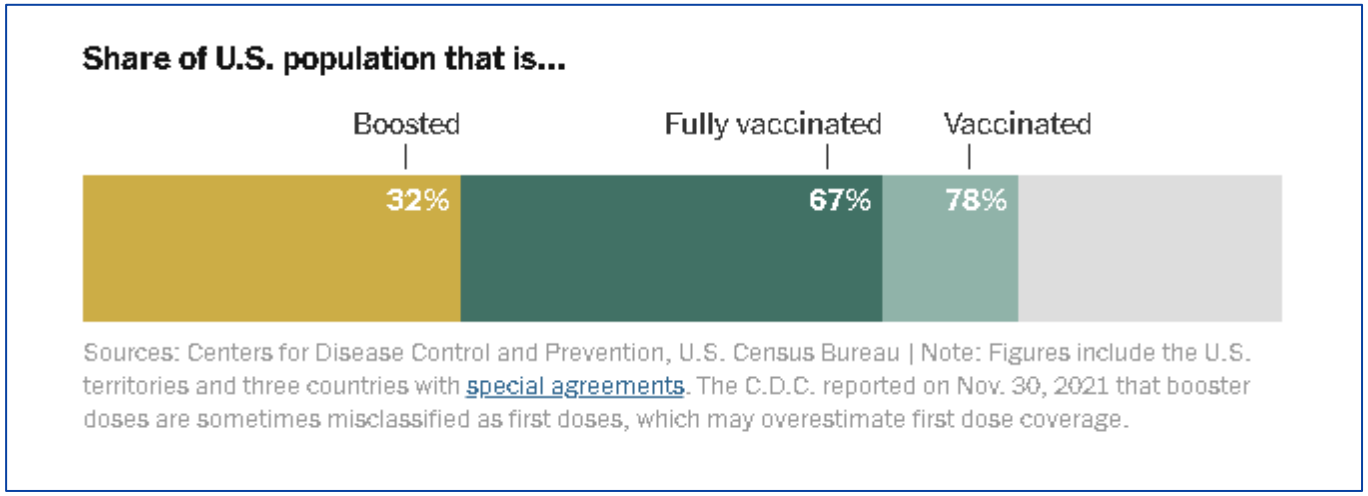
(BACK TO THE) **FUTURE OF PEDIATRICS**

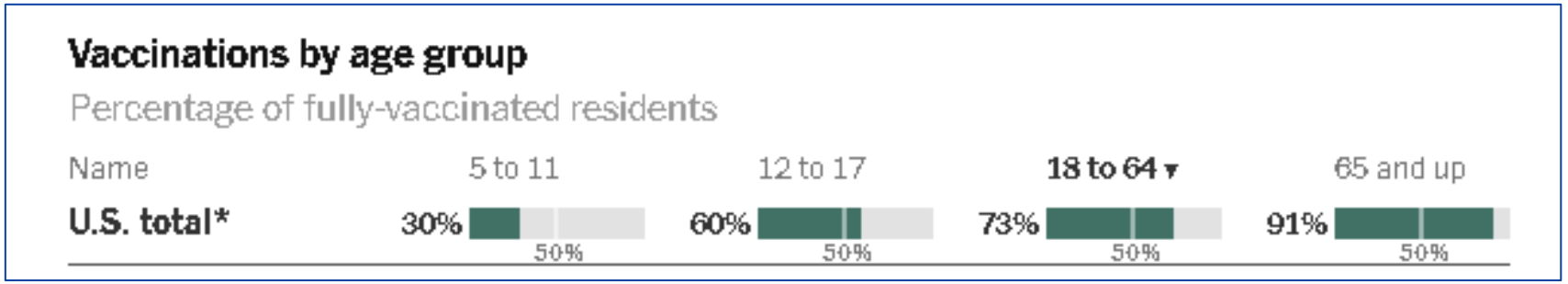
Courtesy of Meghan Delaney

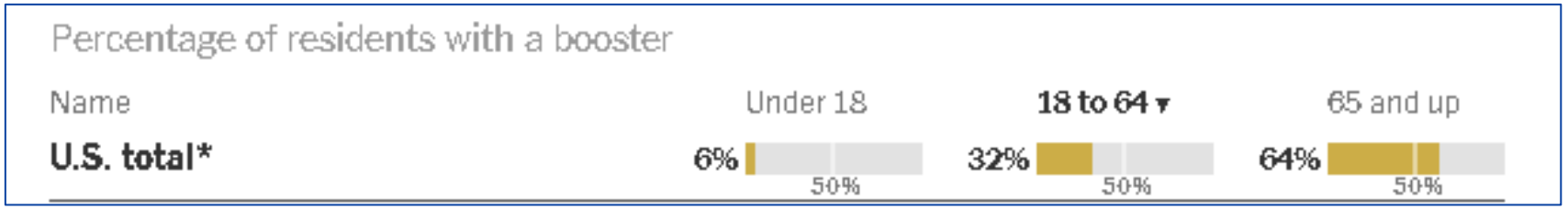
www.who.int/en/activities/tracking-SARS-CoV-2-variants/

Vaccination

SARS-CoV-2 Vaccination in the United States as of June 2022







NYTimes - https://www.nytimes.com/interactive/2021/us/covid-cases.html

Vaccination: What's Next?

Vaccination of Younger Kids Aged 6 months – 5 years

- **Moderna mRNA: 6 months – 5 years of age**
  - 2 dose primary series (25 mcg)
    - Dose 2 given 4 weeks after Dose 1
    - Efficacy
      - 6–23 months: 50.6% (2–69%)
      - 2–5 years: 36.5% (13–54%)
      - Overall 6 months–5 years: 41.5% (24–55.0%)

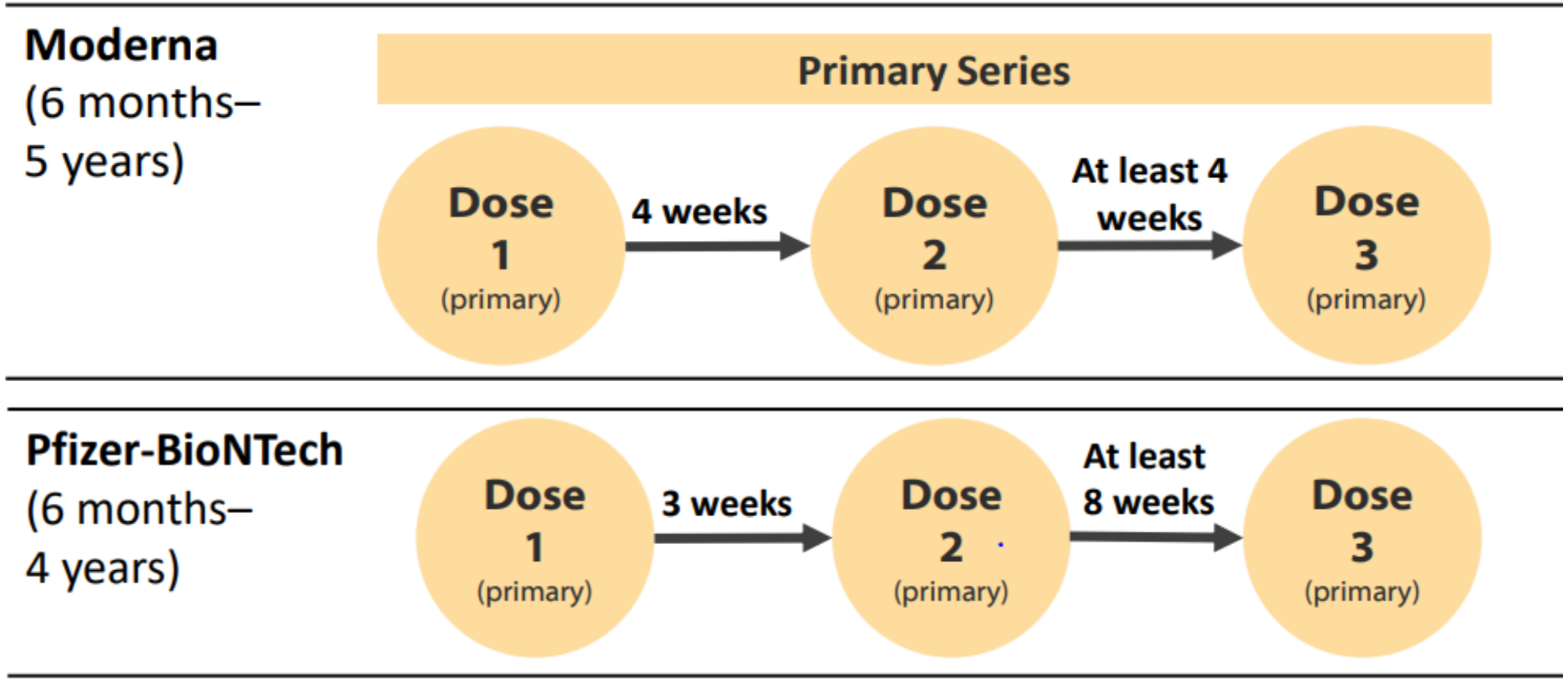
- **Pfizer mRNA: 6 months – 4 years of age**
  - 3 dose primary series (3 mcg)
    - Dose 2 given 3 weeks after Dose 1
    - Dose 3 given 8 weeks after Dose 2
    - Efficacy
      - 6–23 months: 75.5% (37-99.%)
      - 2–4 years: 82.3% (8-93%)
      - Overall 6 months–4 years: 80.3% (14-97%)

Other Vaccine Developments

- **Mix and Match Approach for Boosting**
  - mRNA and vector-based vaccines
- **Vaccines incorporating new SARS-CoV-2 Variants**
- **Intranasal Vaccines**
- **Combination vaccines for SARS-CoV-2 and Influenza**

NOTE: Three dose primary series is authorized for both products for Moderate or Severe Immunocompromised Host

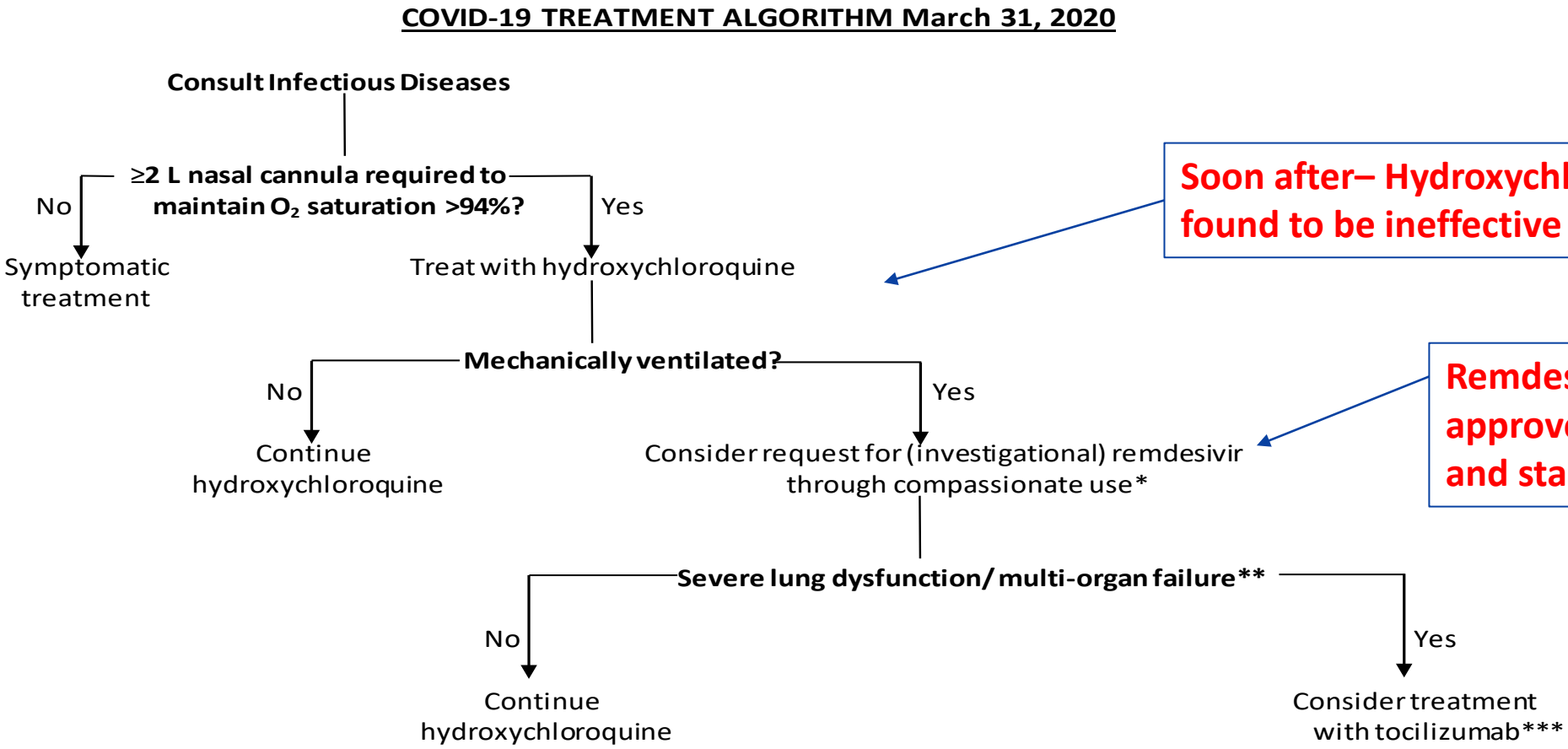
People who **ARE** moderately or severely immunocompromised



CDC COCA Call June 22
https://emergency.cdc.gov/coca/ppt/2022/062222_slides_updated_post_live_webinar.pdf

Therapeutics

THEN (March 2020)…… Focus on Inpatient Amelioration



Soon after– Hydroxychloroquine found to be ineffective

Remdesivir now approved and standard of care

- Corticosteroid now standard for severe disease
- Immune Plasma tried but limited efficacy
- Tocilizumab second-line

*Note: Hydroxychloroquine must be discontinued once treatment with remdesivir begins
**Clinically deteriorating requiring increasing mechanical support or inotropes with CRP >1 mg/dL
***In addition to remdesivir OR hydroxychloroquine

And NOW (June 2022)…… Focus on Outpatient Prevention of Disease Progression for Highest Risk Patients

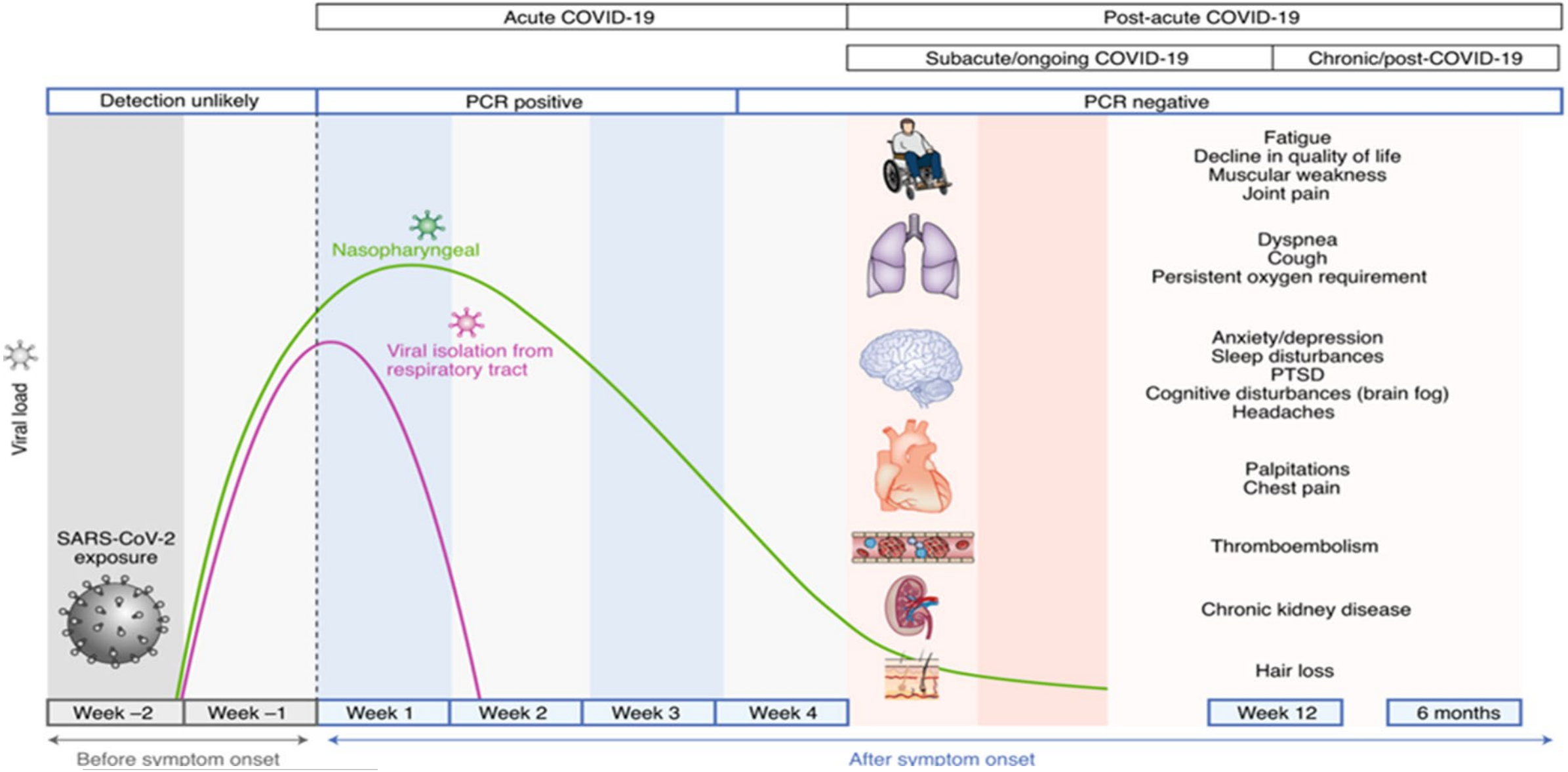
	Paxlovid™ (1)* (ritonavir-boosted irmatrelvir)**	Bebtelovimab (2)***	Veklury™ (3) (Remdesivir)****	Lagevrio™ (4) (Molnupiravir)*****
Age/weight required for use	≥12 years AND ≥ 40 kg	≥12 years AND ≥ 40 kg	≥ 3 kg	≥ 18 years
Initiate within # days of symptom onset	Within 5 days	Within 7 days	Within 7 days	Within 5 days
Route of administration	PO	IV	IV	PO
Duration of therapy	5 days	Once	3 days	5 days
Pros	High efficacy Oral	High efficacy Single IV infusion	High efficacy	Oral No significant drug-drug interactions
Cons	Significant drug-drug interactions	Requires IV infusion	Requires 3 days of IV infusion	Low efficacy Age limitations Not approved in pregnancy
Supply availability	Community pharmacies ONLY: https://healthdata.gov/Health/COVID-19-Public-Therapeutic-Locator/rxn6-qnx8	Available at CNH (ED or cancer/ blood disorders clinic)	Available at CNH (inpatient only)	Community pharmacies ONLY: https://healthdata.gov/Health/COVID-19-Public-Therapeutic-Locator/rxn6-qnx8

Ben Hanisch, MD and Aimee Dassner, PharmD

Long-Term Outcomes of COVID:

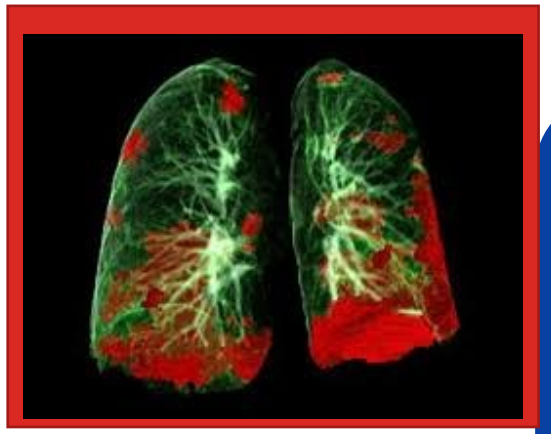
- POCO: Children's National Post-Acute Sequelae of COVID Clinic
- PECOS: Pediatric COVID and MISC Outcomes Study

What About "Long COVID"?



Nalbandian A, et al Nat Med. 2021

Spectrum of Post-COVID Conditions

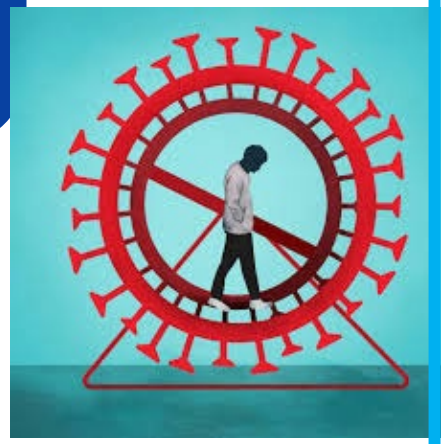


Post-Acute Persistent Symptoms

New-Onset Late Sequelae

Persistent and New Chronic Symptoms

"Long Haulers"



4-12 weeks

MIS-C

>12 weeks

Courtesy of Alexandra Yonts, MD

Children's National
Post-COVID Program Clinic (POCO)

AAP News. 3/1/22

Multidisciplinary clinic: Alexandra Yonts, MD - Director

- Core: ID, Psychology, PM&R
- GI, Neurology, Pain Med, Rheumatology, Cardiology, Pulmonary

Eligibility

- Children/Adolescents (≤ 21 years)
- Prolonged or New, late-onset symptoms
- > 12 weeks since infection
- Lab confirmed (or lab confirmed contact) COVID
  - RT-PCR, Antigen, Serology
- **Wednesday** afternoons at Main Campus
  - **~2 hour appointments**

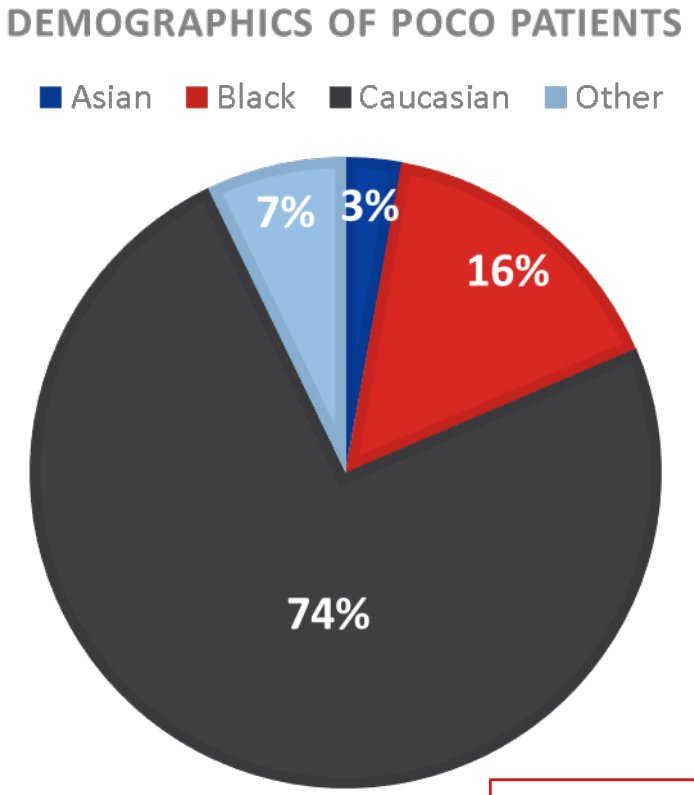
Covid19LongitudinalCareClinic@childrensnational.org

Post-COVID Program Clinic by the Numbers

- **70 new patients** evaluated as of 6/1/22
  - 250+ referrals/inquiries
  - 6-10 new referrals per week
  - Booking into October 2022

- Median Age: 12 years (range 2-20)
- Female > Male (60%)
- Most patients from DMV
  - National: FL, TX, NM, NC, CA, DE, OH

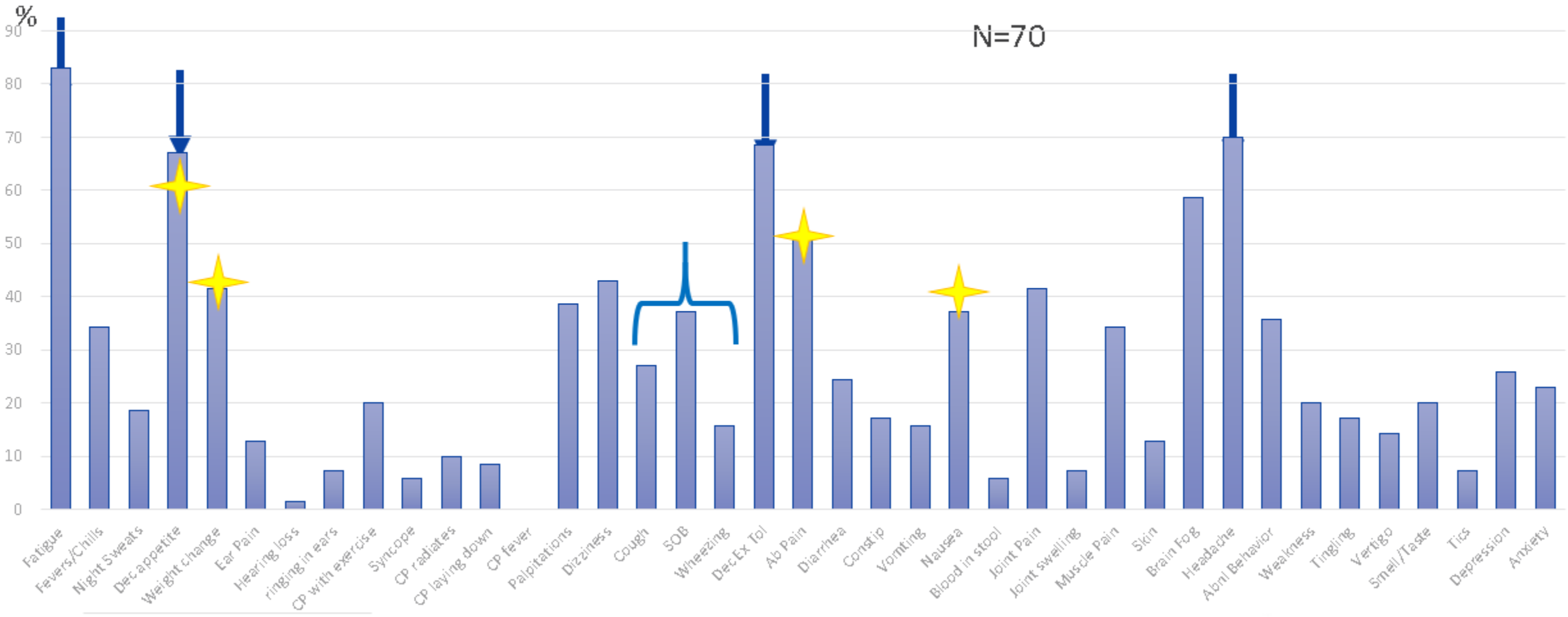
- Avg days from disease onset= 219 (Range 34-714
- Average # symptoms per patient = 10 (Range 2-22)



16%
Hispanic/Latinx
(n=11)

Unpublished Data Courtesy of Alexandra Yonts, MD

POCO Clinic Post-COVID Presenting Symptoms (at intake)



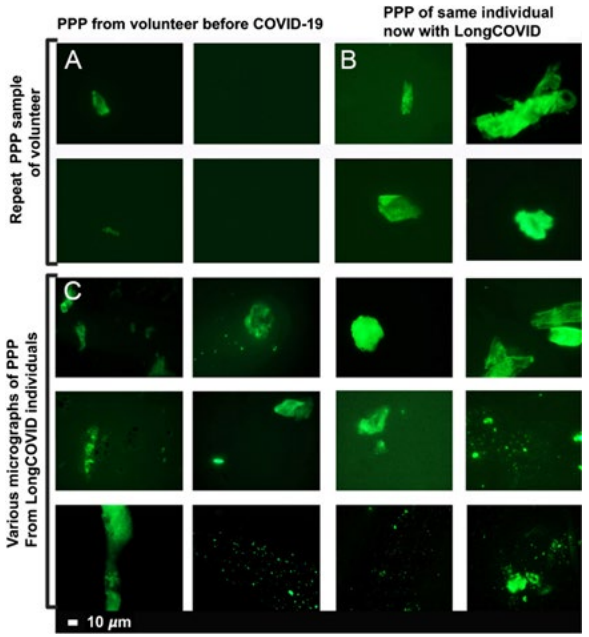
Unpublished Data Courtesy of Alexandra Yonts, MD

Future Clinical Research Questions: Post-COVID

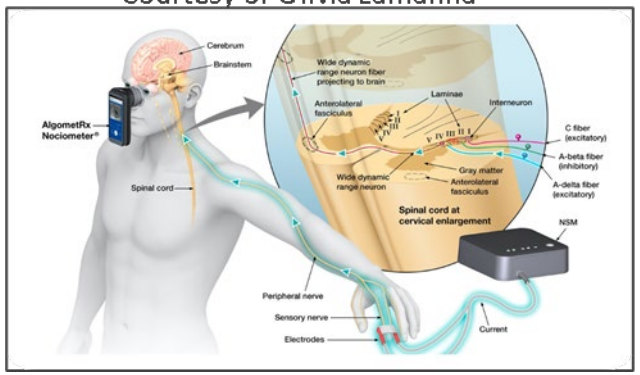
- **Racial disparities and issues of access to Long COVID care**
- **Pediatric Phenotype and Risk factors**

- **New testing and tools for diagnosis**
  - Platelet aggregation ("microclots")
  - Serum amyloid level
  - Mitochondrial function
  - Endothelial damage and capillary dysfunction
  - Small fiber neuropathy
  - Persistent viral proteins in tissues

- **Pharmacologic management and/or treatment**
  - Anticoagulation
  - Supplements
  - Antiviral therapies
  - Anti-inflammatory treatments (IVIG, steroids)



Courtesy of Olivia Lamanna



(BACK TO THE) **FUTURE OF PEDIATRICS**

Pretorius et al. Cardiovasc Diabetol. 2021.

Pediatric COVID Outcome Study (PECOS)

- Recruiting 1000 participants ≤ 21 years of age
  - COVID and MIS-C Survivors
    - Symptomatic and Asymptomatic
    - Hospitalized, Non-hospitalized
  - Healthy Contacts
- 3-year follow-up study
- Detailed evaluation of heart, lung, quality of life neurodevelopment and mental health
  - Echocardiogram, Electrocardiogram, Cardiac MRI
  - Pulmonary Function Testing, Chest/Lung Imaging
  - Validated Surveys
  - Lab evaluation of organ function
- Biorepository of Specimens
  - Antibody Responses overtime
  - Genetics of Disease
  - T-Cell Responses
  - Biomarkers of Severity

SCAN ME

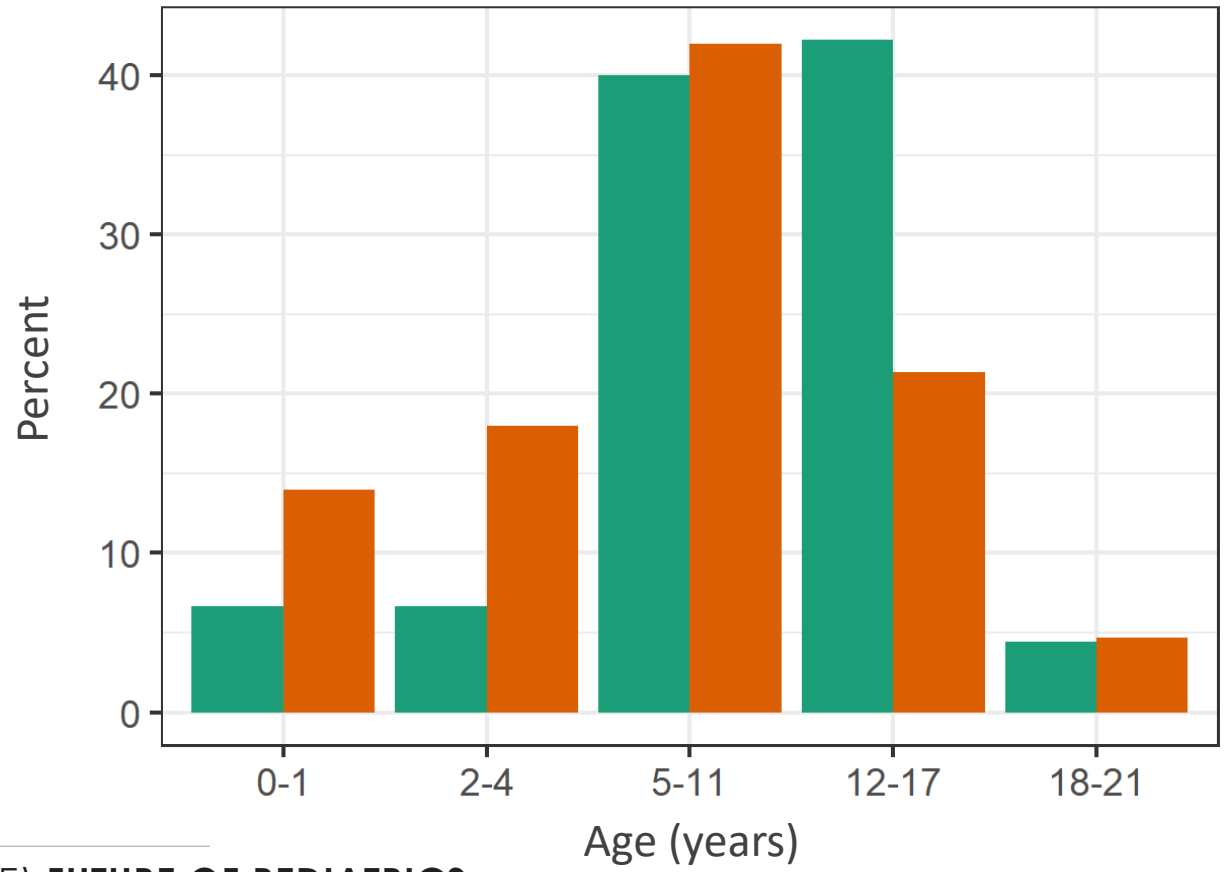
ChildrensNational.org/COVIDstudy

NIH National Institute of Allergy and Infectious Diseases

Children's National

To date, 46% of target enrolled (460/1000)

Age distribution of first 200 Survivors* and Healthy Controls



Interim data analysis in progress

** Excluding MIS-C from survivors*

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Children's National Teams for Emerging Infectious Diseases Response

Special Pathogens Isolation Unit and Response Team

Infectious Diseases and Infection Control Divisions

MIS-C Taskforce

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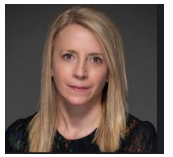
- Cardiology: Harahsheh, Krishnan
- Rheumatology: Srinivasalu, Tovis, Sule
- Hematology: Suvankar,
- Critical Care: Bell, Sharron
- Hospitalist Medicine: Smith, Parikh
- Emergency Medicine: Pershad, Kline
- Lab Medicine: Delaney, Campos











Congenital Zika Program

Acute Flaccid Myelitis Taskforce

Q&A