
I-ACT
INSTITUTE FOR ADVANCED CLINICAL TRIALS
FOR CHILDREN
DEVELOPING PEDIATRIC
TREATMENTS FOR COVID-19
VIRTUAL WORKSHOP
May 28, 2020

WELCOME

INSTITUTE FOR ADVANCED CLINICAL TRIALS FOR CHILDREN

DEVELOPING PEDIATRIC TREATMENTS FOR COVID-19

I-ACT FOR CHILDREN VIRTUAL WORKSHOP

Laura Gordon

CHIEF EXECUTIVE OFFICER

I-ACT for Children

OUR MODERATORS

INSTITUTE FOR ADVANCED CLINICAL TRIALS FOR CHILDREN

DEVELOPING PEDIATRIC TREATMENTS FOR COVID-19

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Ed Connor, MD, MBE, FAAP

FOUNDER AND CHAIR

I-ACT for Children

Susan McCune, MD

DIRECTOR, OFFICE OF PEDIATRIC THERAPEUTICS

US Food and Drug Administration

AGENDA

INSTITUTE FOR ADVANCED CLINICAL TRIALS FOR CHILDREN

DEVELOPING PEDIATRIC TREATMENTS FOR COVID-19

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- **INTRODUCTION**
- PART 1: COVID-19 in Children
- PART 2: Therapeutics Development

  Antiviral Agents and Immune Modulators
- PART 3: Panel Discussion and Q&A

INTRODUCTION

INSTITUTE FOR ADVANCED CLINICAL TRIALS FOR CHILDREN

DEVELOPING PEDIATRIC TREATMENTS FOR COVID-19

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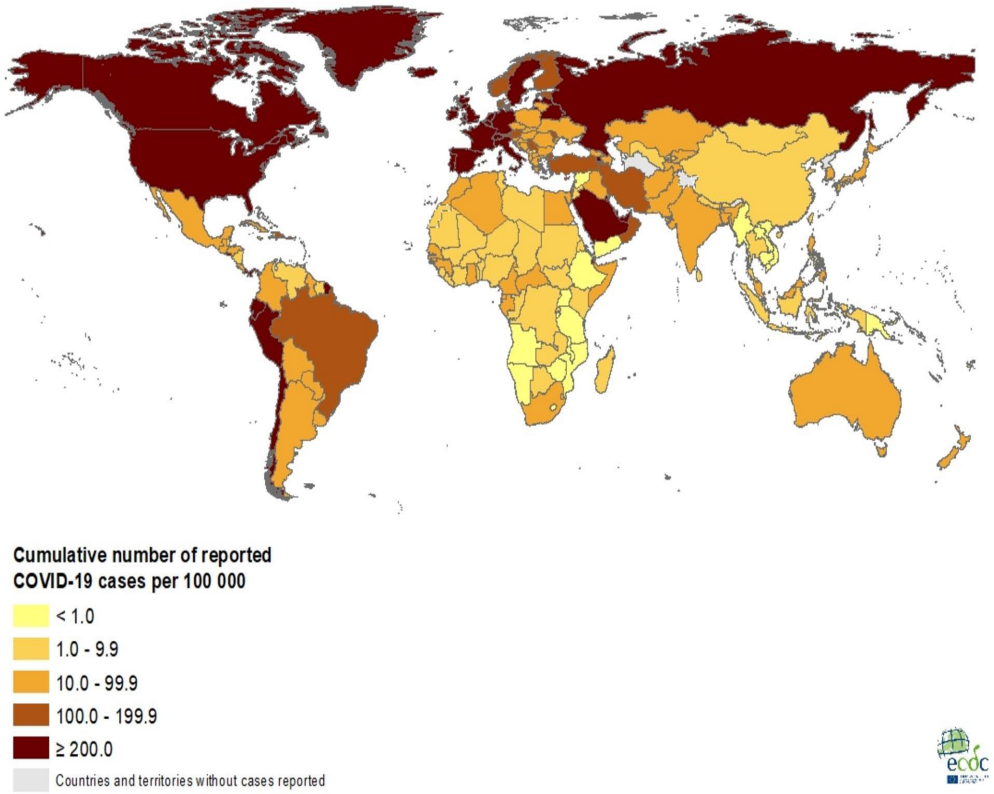
FOCUSING ON COVID-19 RESEARCH IN CHILDREN

Ed Connor, MD, MBE, FAAP
FOUNDER AND CHAIR
I-ACT for Children

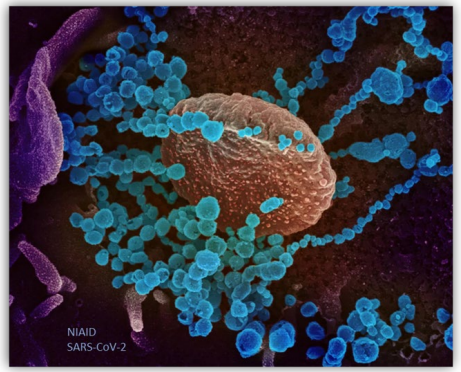
Developing Pediatric Treatments for SARS-CoV-2



- > 5M COVID-19 cases worldwide
- >1.6 M cases in the US with >200 cases per 100,000
- Estimated that 1-2% reported to date are children
- Children appear to be at lower risk for serious disease, but…
- The scope of pediatric COVID-19 is still emerging…
- Thus far testing has been limited in children
- More children reported who require hospitalization, ICU
- New manifestations described – MSID-C
- Hundreds of candidate therapeutics being evaluated
- Essential that high-quality safety & efficacy data be available

COVID-19 Pediatric Therapeutics Research Challenges

- Therapeutics are urgently needed in the face of scientific gaps
- A coordinated approach is needed among diverse stakeholders
- “Accelerators” to advance therapeutics are being formed, but pediatrics is not a visible element to date

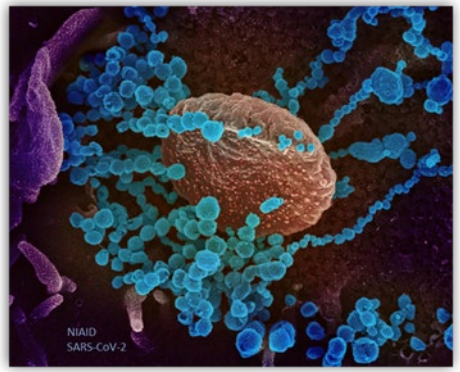


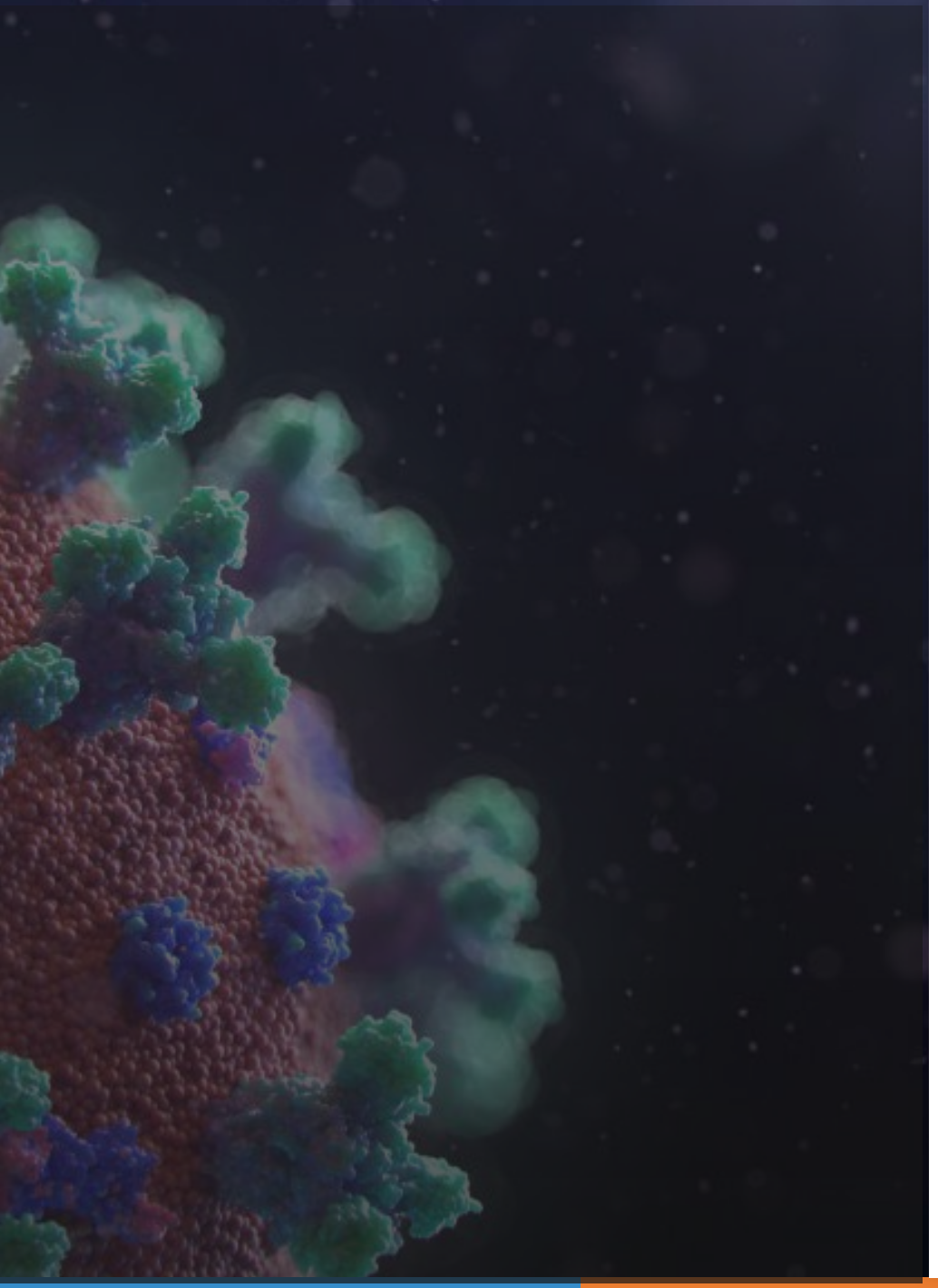
Key COVID-19 Research Priorities	
Pathophysiology and Natural History	✓ Characteristics in neonates, children, adolescents ✓ Correlates of risk, progression, recovery, protection ✓ Studies of transmission to and from children
Viral Diagnosis	✓ Rapid point of care diagnostics ✓ Methods for viral load assessment and shedding ✓ Large-scale testing to determine rates of infection and coinfection ✓ Multi-year assessment for re-infection
Detection of Antibodies	✓ Rapid point of care tests for SARS-CoV-2 Ab response ✓ Methodology for quantifying neutralizing Ab ✓ Longitudinal assessment of antibody durability
Framework for Therapeutics Development	✓ Knowledge base of candidates in development ✓ Early pediatric engagement in planning & evaluation of risk : benefit
Evaluation of Vaccine Candidates	✓ Framework for pediatric development, risk : benefit ✓ Developmental aspects of vaccine response ✓ Risk for disease enhancement

Gary J. Noel, Jonathan M. Davis , Octavio Ramilo , John S. Bradley and Edward Connor
Pediatric Research https://doi.org/10.1038/s41390-020-0962-y

Developing Pediatric Treatments for SARS-CoV-2

- Significant advances have been made in development of therapeutics for viral disease over the past several decades
- Innovative methodologies can be used in pediatric drug development
- Infrastructure of conducting global regulatory grade trials has evolved
- To date, Emergency Use Authorization for therapeutics has included consideration of pediatric patients… but this is only the beginning…
- Pediatric “voice” needs to be at the table early and therapeutics need to be developed with the same urgency and quality as for adults





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DEVELOPING PEDIATRIC TREATMENTS FOR COVID-19

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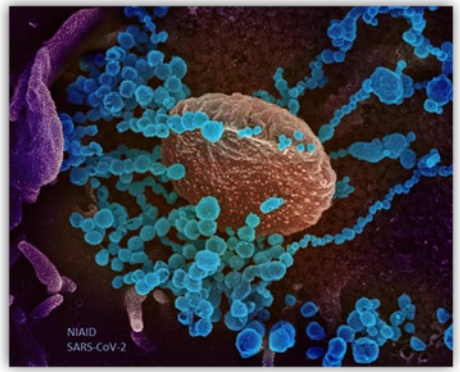
- **PART 1: COVID-19 in Children**
- PART 2: Therapeutics Development

  Antiviral Agents and Immune Modulators
- PART 3: Panel Discussion and Q&A

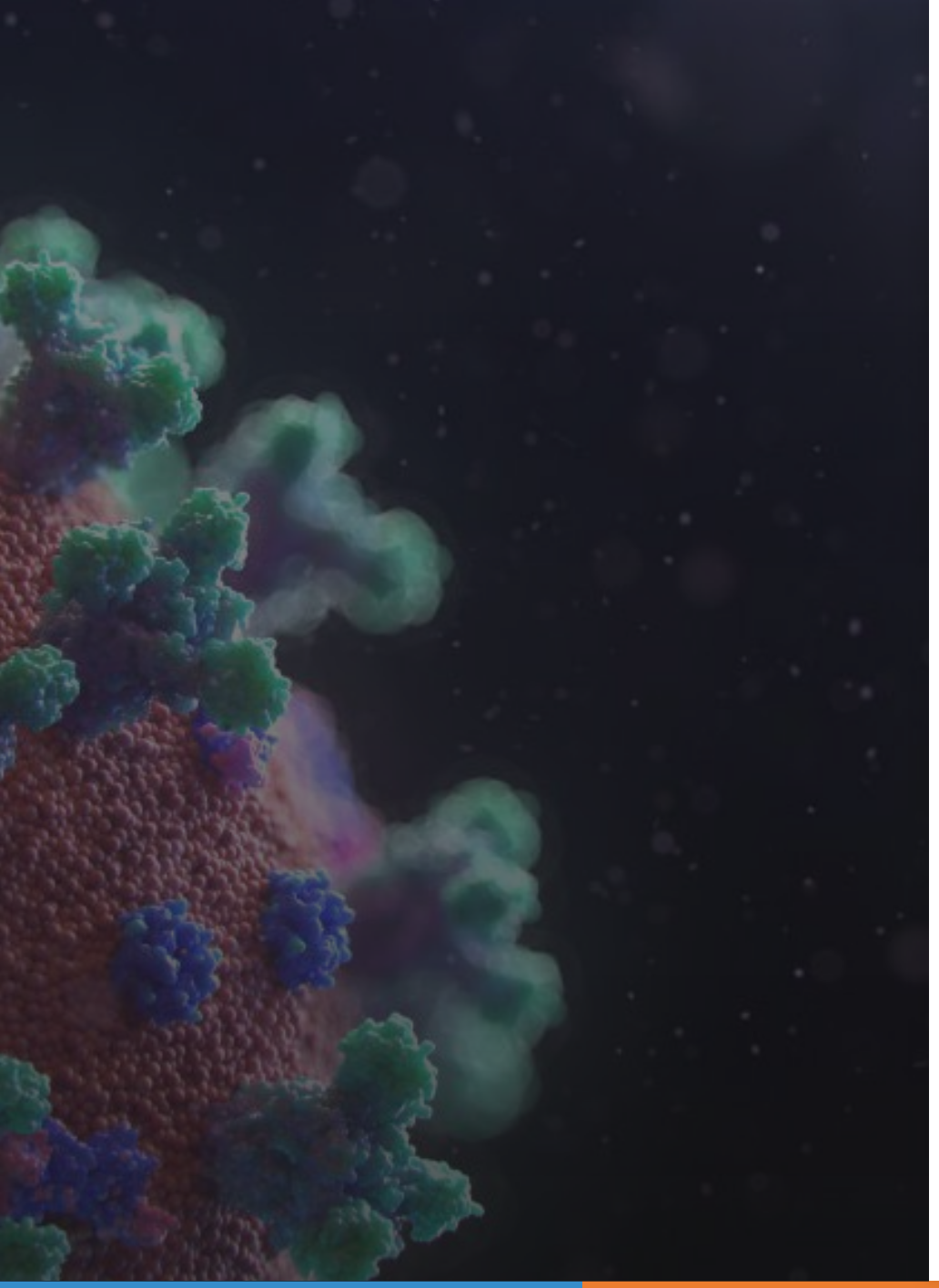
PART 1: Epidemiology of Pediatric COVID-19

- The epidemiology of COVID-19 in pediatric patients is limited by sparse testing in children
- Data are available from CDC surveillance, series of patients from China, Italy, US and elsewhere
- *Human Epidemiology and Response to SARS-CoV-2 (HEROS)* launched (NIAID) in 6,000 people in 2,000 families
- Evolving insight from EHR and other real-world sources

Collin Hovinga, PharmD, MS, FCCP
SVP Clinical and Scientific Development
Institute for Advanced Clinical Trials for Children



Seth Kuranz, PhD
Principal Epidemiologist, Clinical Sciences
TriNetX



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COVID-19 IN PEDIATRIC POPULATIONS

REAL-WORLD DATA

Collin Hovinga, PharmD

SVP, CLINICAL & SCIENTIFIC DEVELOPMENT

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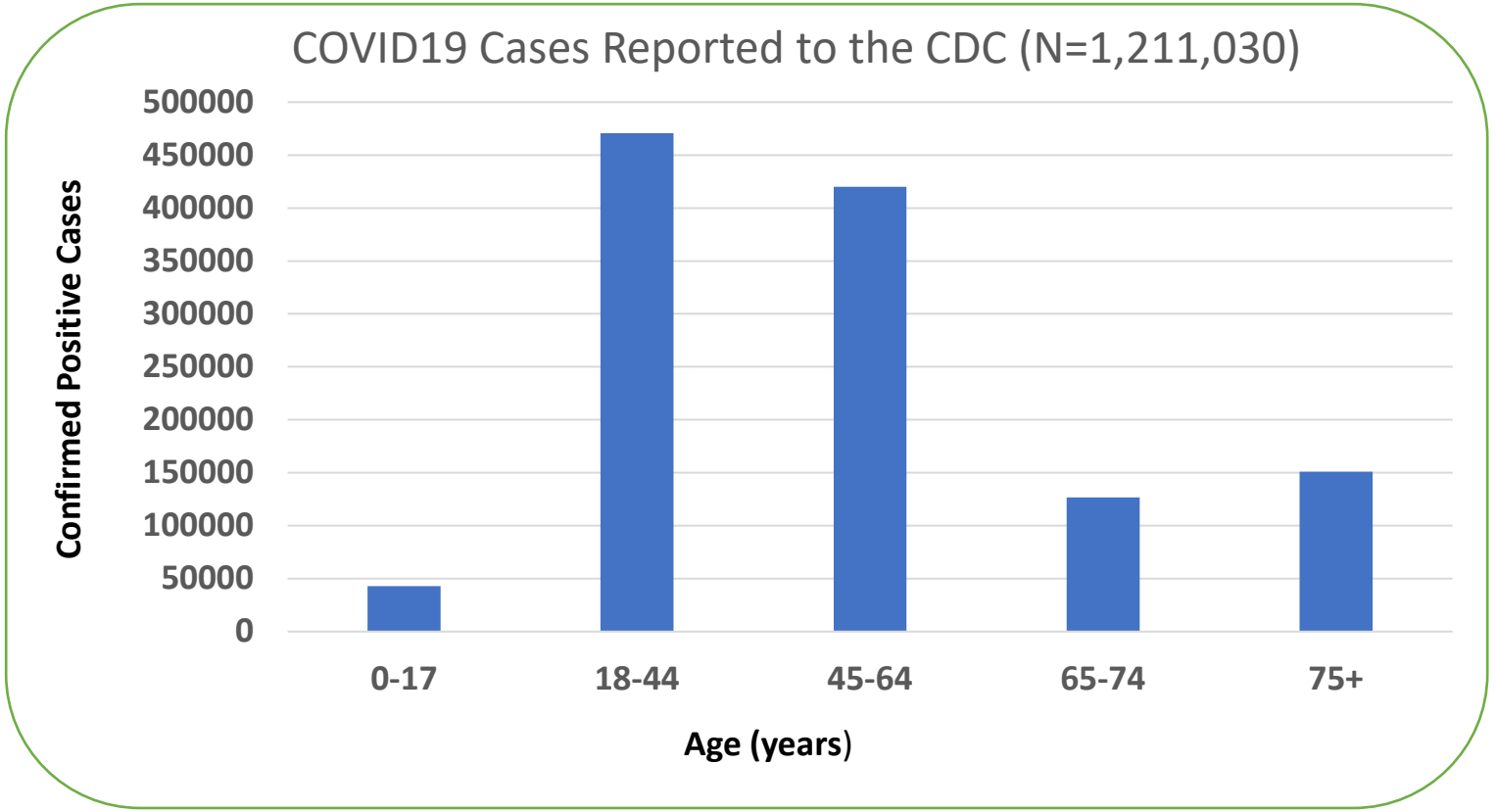
Confirmed COVID-19 Cases by Age

CDC Data: Updated May 25, 2020

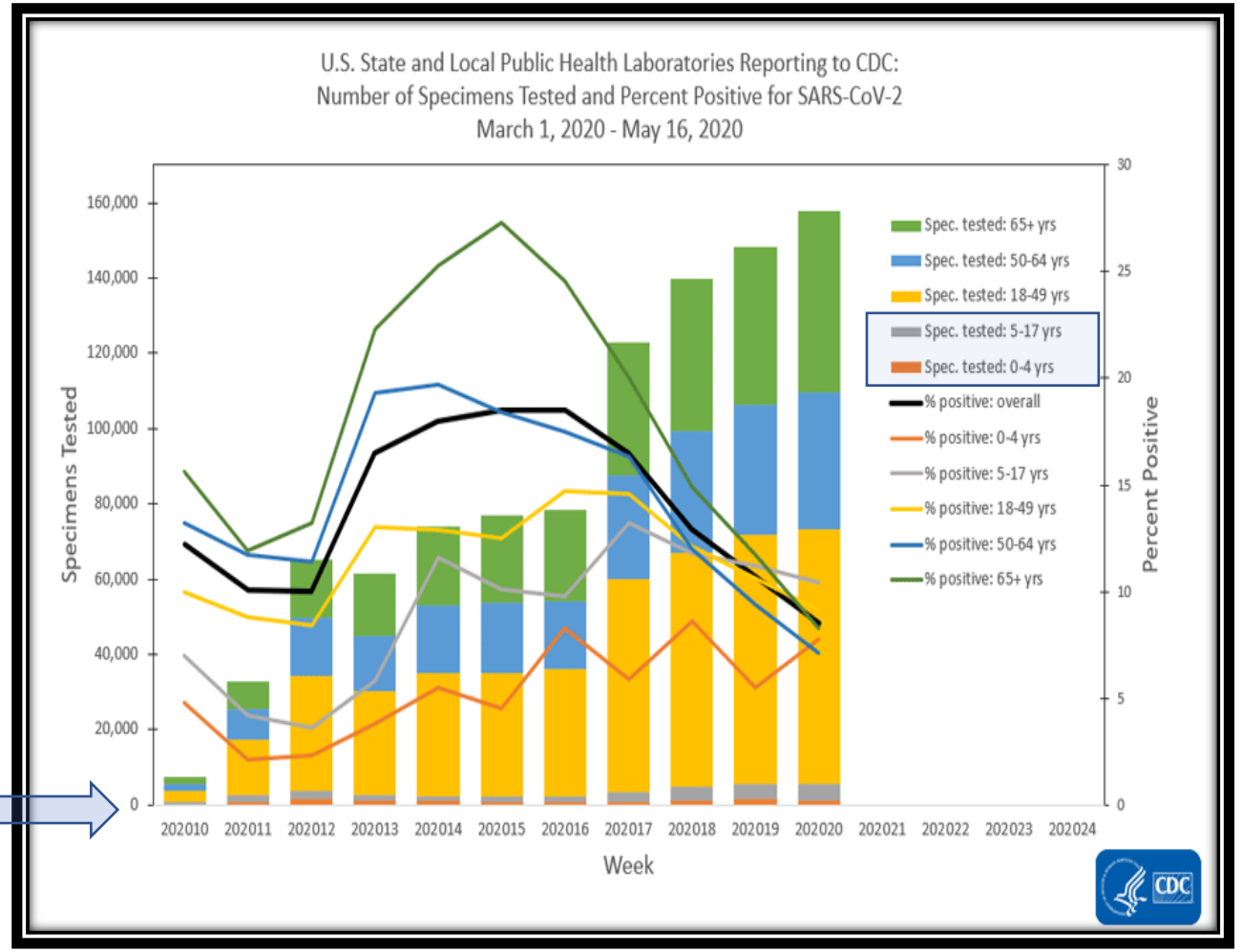
- Age was reported in 1.2M cases of COVID-19
- Cumulatively, 42,810 cases have been reported in patients < 18 years of age



https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/cases-in-us.html
Accessed 5-26-2020

CDC Data: Number of Specimens and Percent Positive

- Total number of COVID-19 tests in pediatrics is small
- Number of tests is increasing, as is the rate of positivity in children
- Rates in adults are decreasing

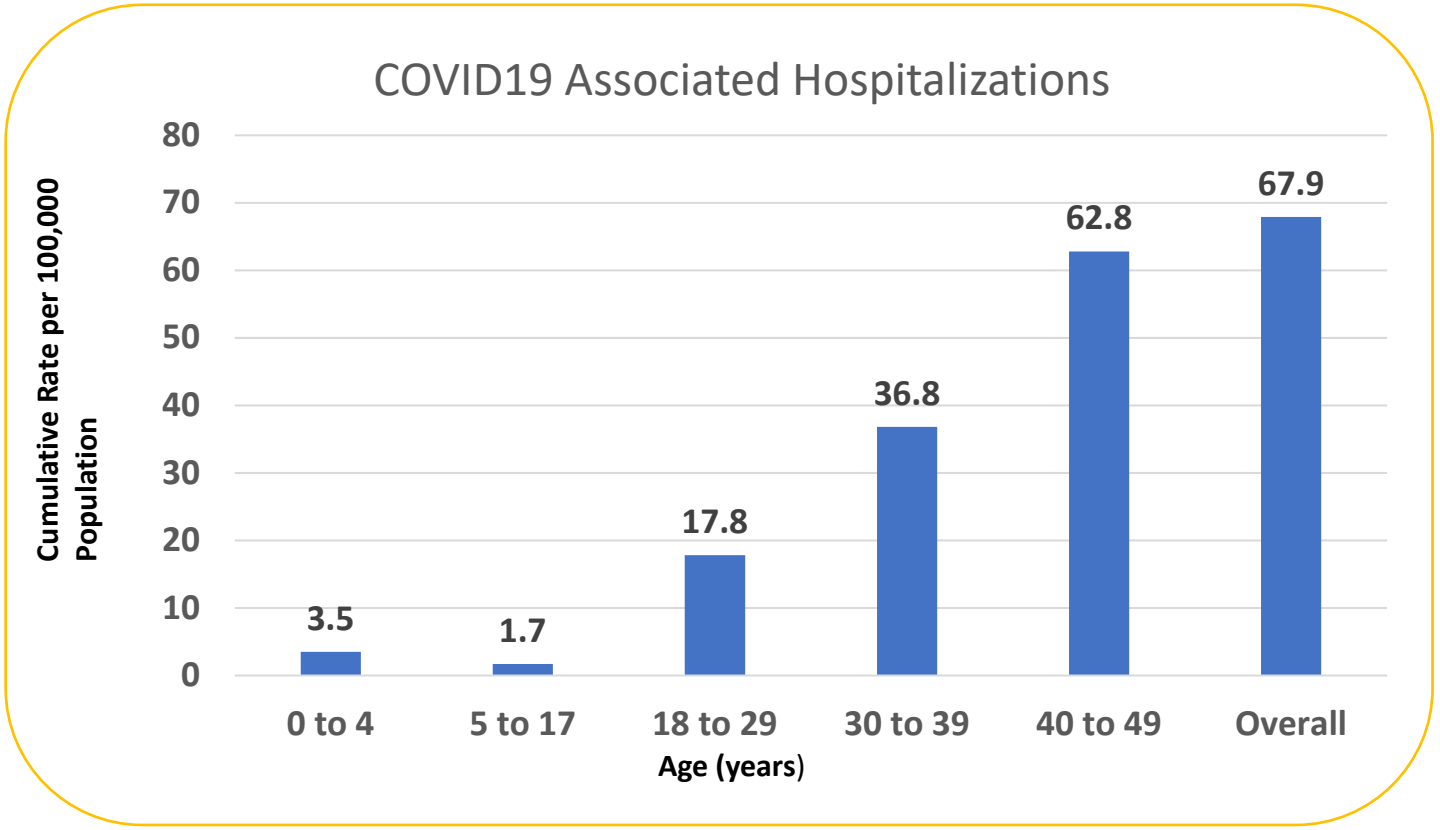


1 https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html
Accessed 5-26-2020

COVID-19-Related Hospitalizations

CDC Data Updated May 25, 2020

- COVID-NET survey
- Represents ~10% of US population
- COVID-19 hospitalizations lower in pediatric patients thus far….



https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html
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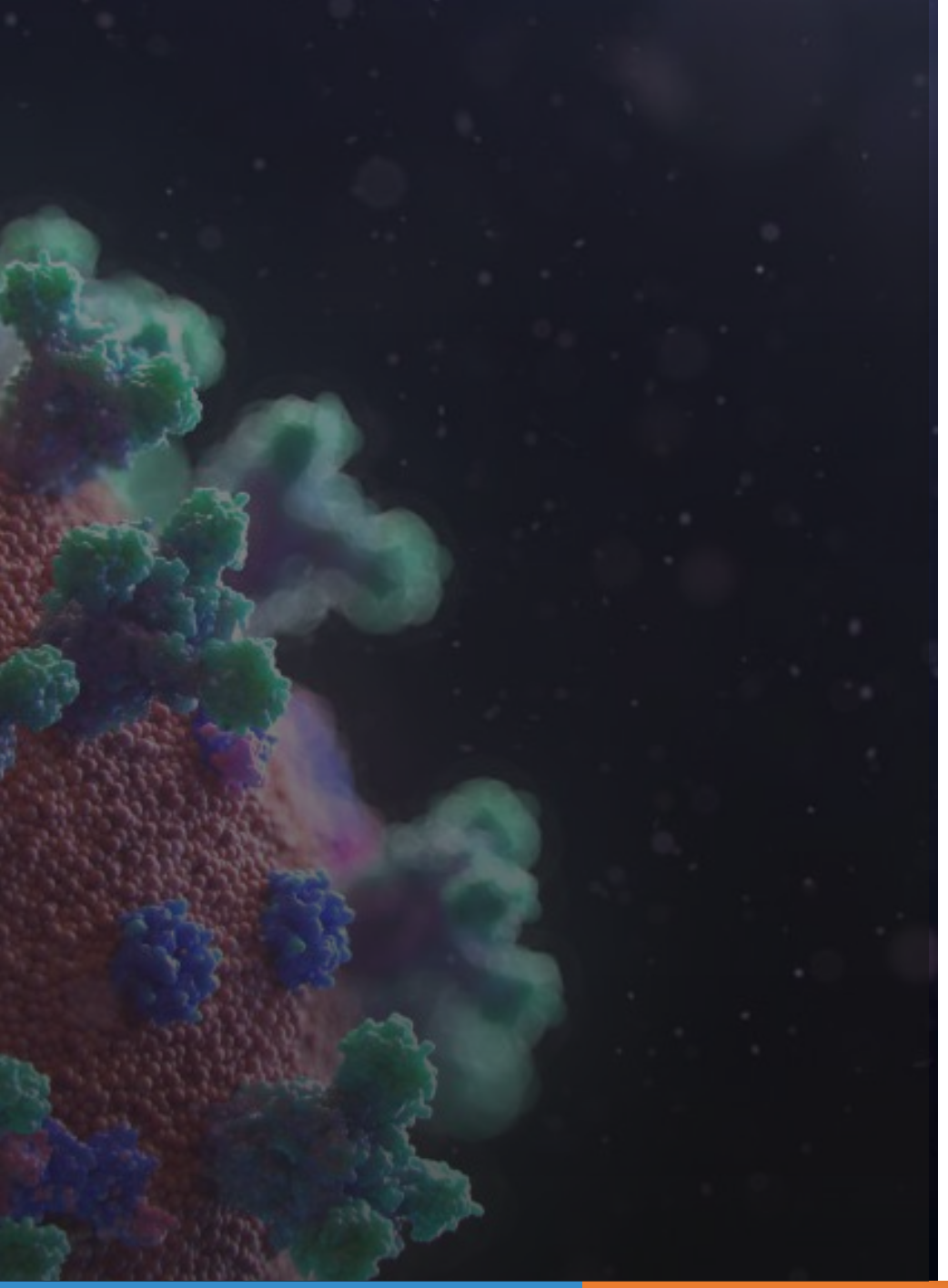

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COVID-19 IN PEDIATRIC POPULATIONS

REAL-WORLD DATA

Seth Kuranz

PRINCIPAL EPIDEMIOLOGIST

TriNetX

TriNetX

VARIOUS AND DISPARATE DATA

- Demographics
- Diagnoses
- Procedures
- Lab Results
- Vitals
- Medications
- Cardiology
- Genomics
- Oncology
- Pulmonology
- Patient Location
- Mortality

MAPPED TO INDUSTRY STANDARD TERMINOLOGIES

Healthcare Org.

TriNetX

- HL7
- ICD-10, ICD-9
- CPT
- RxNorm, NDF-RT
- LOINC
- NAACCR, ICD-O
- HGNC, HGVS, ClinVar, dbSNP

MASTER TERMINOLOGY/ INTELLIGENT SYNONYM SEARCH

MUST Have: HbA1c

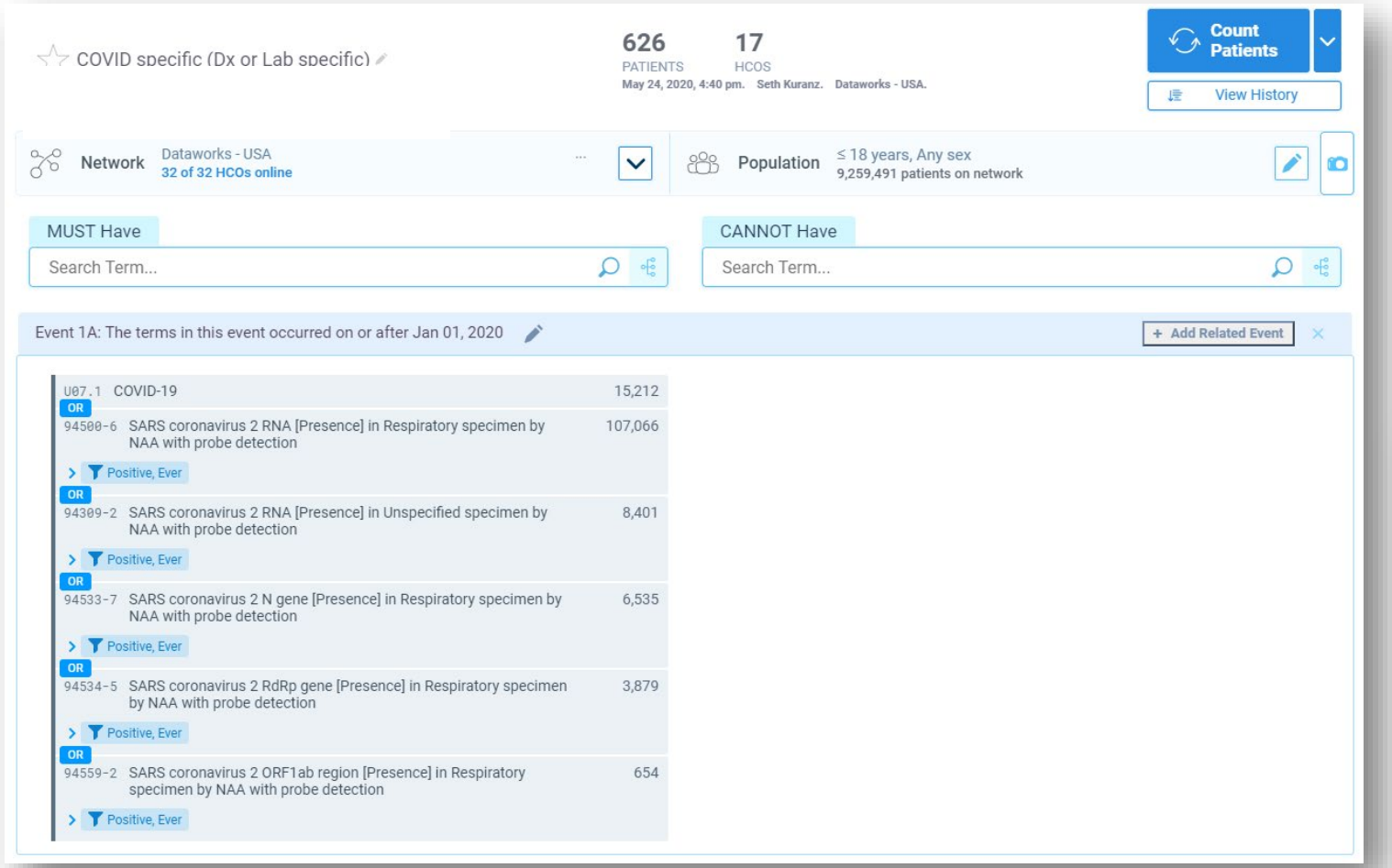
CANNOT Have: Search Term…

Code		Term Description	Patients
TNX:LAB:9037	L	Hemoglobin a1c/hemoglobin.total in blood	3,294,500

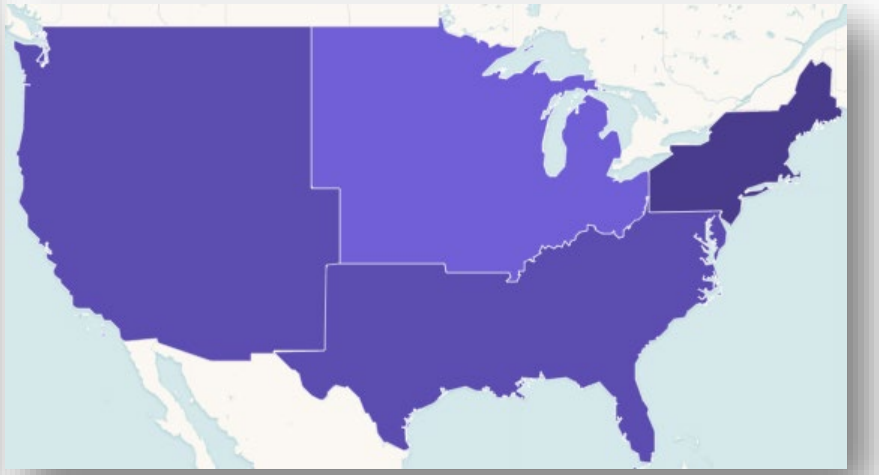
D Demographics | Dx Diagnoses | L Labs

M Medications | P Procedures | G Genomics

COVID-19 Definition



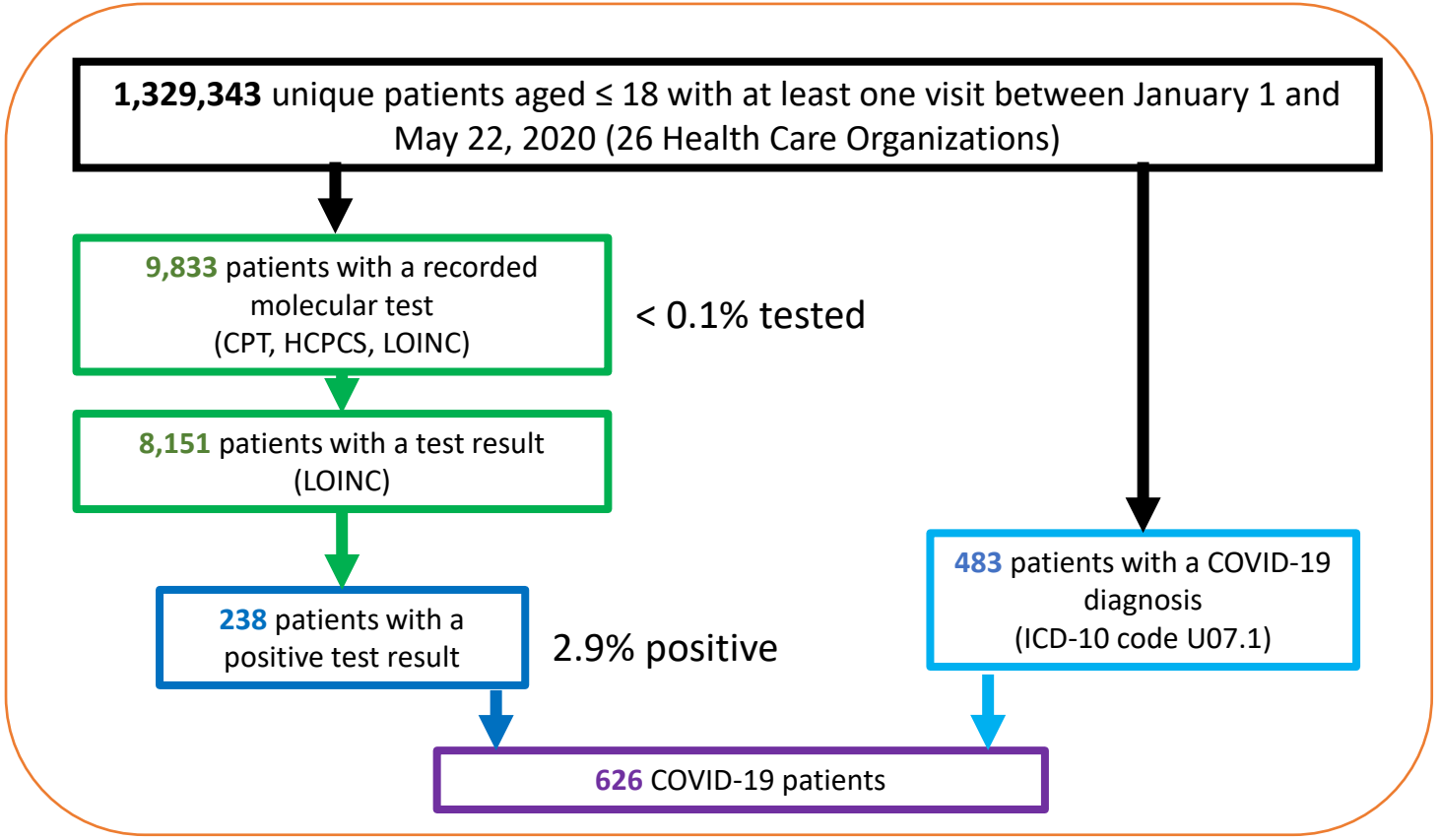
US Region	Percentage
Northeast	39
Midwest	12
South	21
West	28



The COVID-19 Pediatric Population in TriNetX

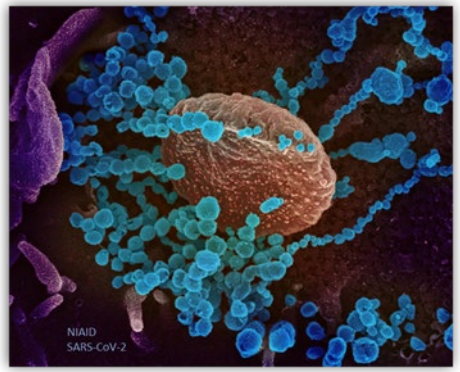
- 1.3M patients ≤ 18 years of age
- < 0.1% tested
- 2.9% positive among those with test results available
- 626 pediatric patients identified when testing and diagnostic codes were used
- Age distribution (n=626)

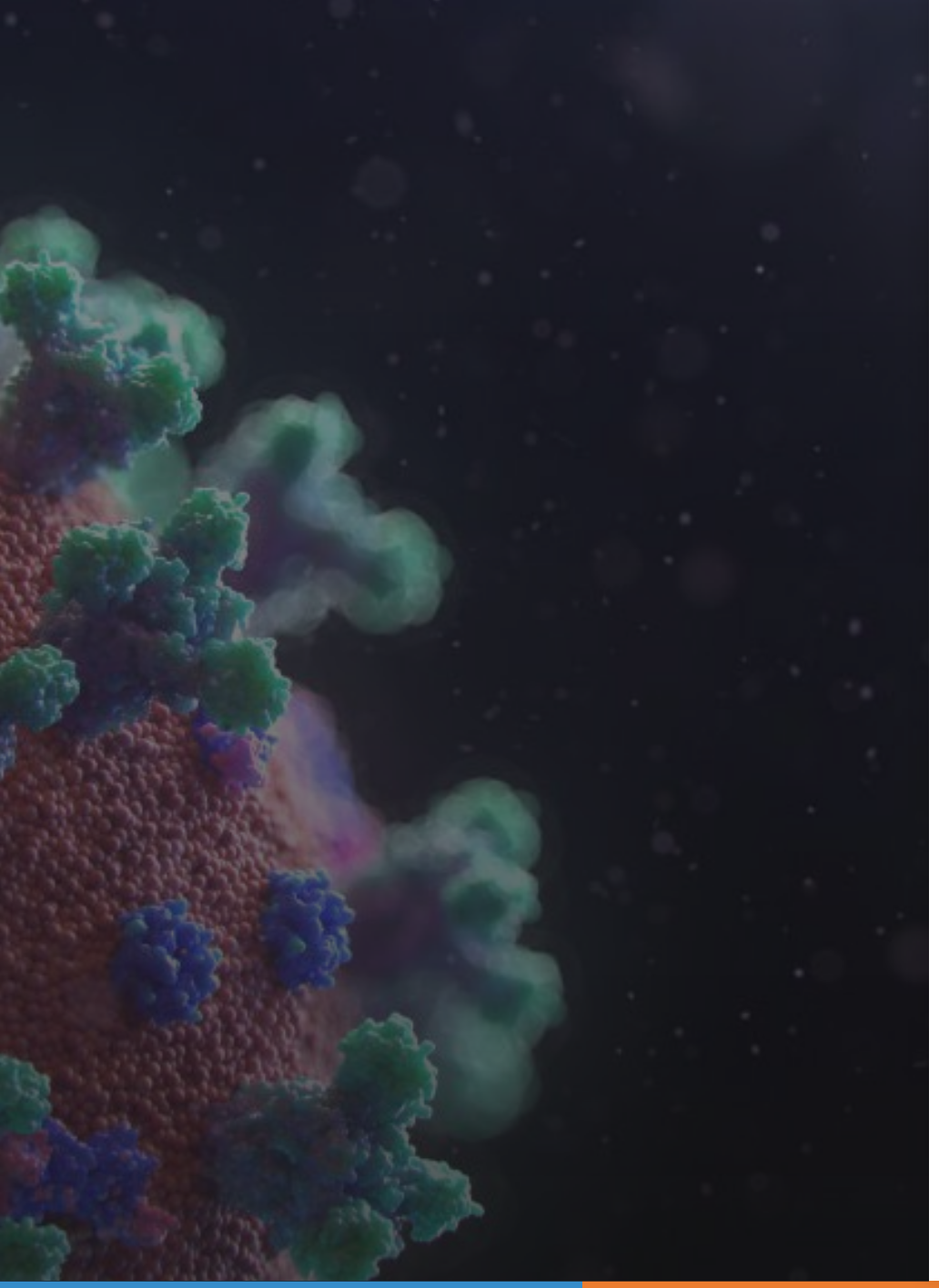
Age (YEARS)	PERCENT
0-4	30
5-9	13
10-14	20
15-18	36



PART 1: Summary

- The epidemiology of COVID-19 in children is still unfolding.
- The number of children being testing for COVID-19 is proportionally lower than that being done in adults.
- A more accurate estimate of the frequency of SARS-CoV-2 infection in children is pending as testing rates begin to increase.
- Despite low rates of testing, the number of pediatric patients with COVID-19 is sufficient to start clinical trials involving children.





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DIAGNOSIS, CLINICAL PRESENTATION AND OUTCOMES IN CHILDREN WITH COVID-19

Roberta DeBiasi, MD, MS

CHIEF, DIVISION OF PEDIATRIC INFECTIOUS DISEASES

Children's National Medical Center

Diagnosis, Clinical Presentation and Outcomes of Children with COVID-19:

Severe Disease in Children and Young Adults in the Washington DC Metropolitan Region

Roberta L. DeBiasi, MD, MS
Chief, Division of Pediatric Infectious Diseases
Children's National Hospital and Research Institute
Professor, Pediatrics and Microbiology, Immunology and Tropical Medicine
The George Washington University School of Medicine

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Children's National Hospital COVID-19

- March 15- May 27, 2020
- Approximately 9.4% of 4000 tested
- 376 SARS-CoV-2 PCR positive, symptomatic patients seeking care at Children's National
  - **93 (25%) hospitalized**
    - **28 (30%) Critical – Pediatric Intensive Care Unit**
    - **64 (70%) Acute – Special Isolation Unit**

- Daily Hospitalized Census: 12-17 COVID + patients
  - Additional PUI
- Since late April 2020 - Multisystem inflammatory Disease – Children (MIS-C)
  - 26 additional hospitalized patients

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Interim Analysis of first 177 symptomatic COVID+ patients: Published online May 12, 2020 in *The Journal of Pediatrics*

Severe COVID-19 in Children and Young Adults in the Washington, DC Metropolitan Region

DeBiasi RL, Song X, Delaney M, Bell M, Smith K, Pershad J, Ansusinha E, Hahn A, Hamdy R, Harik N, Hanisch B, Jantausch B, Koay A, Steinhorn R, Newman K, Wessel D.

The Journal of Pediatrics (2020), doi: https://doi.org/10.1016/j.jpeds.2020.05.007

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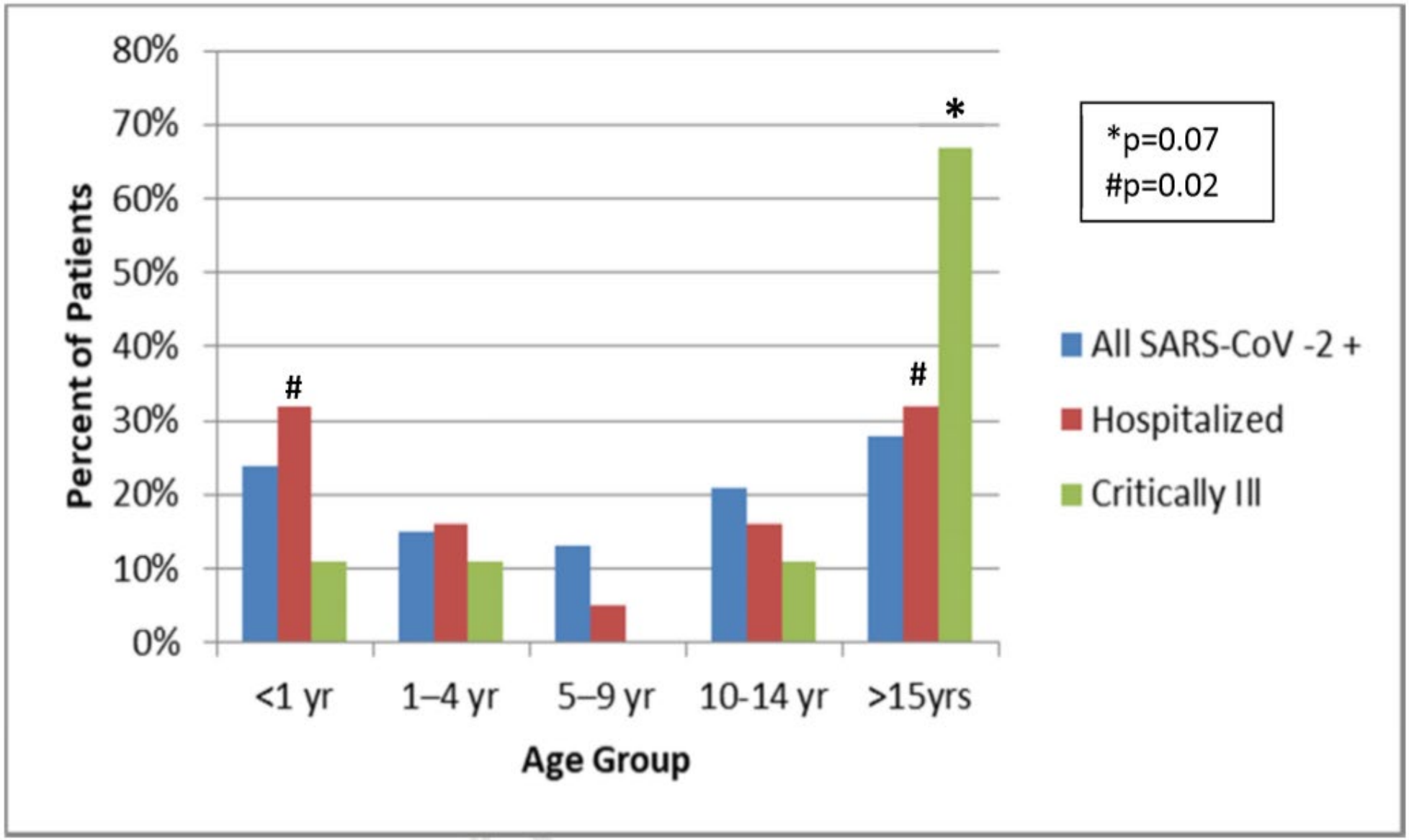
Table 1: Epidemiologic Characteristics and Clinical Features of 177 Children and Young Adults with Symptomatic SARS-CoV-2 Infection

Characteristic	Total, Non-hospitalized and Hospitalized (N=177)	Non-Hospitalized (N=133)	Hospitalized (N=44)	p value	Hospitalized, Non-Critical Care (N=35)	Hospitalized, Critical Care (N=9)	p value
Age (years)							
Median (range)	9.6 (0.1-34.2)	9.5 (0.1-34.2)	9.6 (0.1-25.6)	0.75	3.6 (0.1-21.5)	17.3 (0.1-25.6)	**0.04**
Distribution — no. (%)							
<1 yr	43 (24%)	29 (22%)	14 (32%)	0.22	13 (37%)	1 (11%)	0.15
1–4 yr	26 (15%)	19 (14%)	7 (16%)		6 (17%)	1 (11%)	
5–9 yr	23 (13%)	21 (16%)	2 (5%)		2 (6%)	0 (0%)	
10-14 yr	36 (21%)	29 (22%)	7 (16%)		6 (17%)	1 (11%)	
15-20 yr	37 (21%)	28 (21%)	9 (20%)		6 (17%)	3 (33%)	
>20 yr	12 (7%)	7 (5%)	5 (11%)		2 (6%)	3 (33%)	
Sex – no (%)							
Male	92 (52%)	70 (53%)	22 (50%)	0.76	16 (46%)	6 (67%)	0.26
Female	85 (48%)	63 (47%)	22 (50%)		19 (54%)	3 (33%)	
Underlying Medical Condition							
Yes	69 (39%)	42 (32%)	27 (63%)	**0.001**	20 (57%)	7 (78%)	0.45
No	96 (55%)	80 (60%)	16 (37%)		14 (40%)	2 (22%)	
Unknown	11 (6%)	11 (8%)	0	-	0	0	-

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



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Reported underlying medical condition							
Asthma	35 (20%)	28 (21%)	7 (16%)	0.46	5 (14%)	2 (22%)	0.62
Diabetes	5 (3%)	3 (2%)	2 (5%)	0.43	1 (3%)	1 (11%)	0.37
Neurologic	11 (6%)	3 (2%)	8 (19%)	**<0.001**	5 (14%)	3 (33%)	0.33
Obesity	4 (2%)	3 (2%)	1 (2%)	1.00	0 (0%)	1 (11%)	0.21
Cardiac	5 (3%)	1 (1%)	4 (9%)	**0.004**	2 (6%)	2 (22%)	0.18
Hematologic	6 (3%)	2 (2%)	4 (9%)	**0.004**	4 (11%)	0 (0%)	0.57
Oncologic	2 (1%)	0 (0%)	2 (5%)	**0.013**	2 (6%)	0 (0%)	1.00
Symptoms Present at the time of visit							
Fever	116 (66%)	82 (62%)	34 (77%)	0.06	27 (77%)	7 (78%)	0.97
Sore throat or congestion	77 (44%)	66 (50%)	11 (25%)	**0.004**	10 (29%)	1 (11%)	0.28
Cough	99 (56%)	83 (62%)	16 (37%)	**0.003**	12 (34%)	4 (44%)	0.57
Shortness of breath	27 (15%)	16 (12%)	11 (26%)	**0.04**	7 (20%)	4 (44%)	0.13
Diarrhea or vomiting	27 (15%)	20 (15%)	7 (15%)	0.89	5 (14%)	2 (22%)	0.56
Myalgia	25 (14%)	21 (16%)	4 (9%)	0.27	2 (6%)	2 (22%)	0.59
Chest Pain	16 (9%)	10 (8%)	6 (14%)	0.22	4 (11%)	2 (22%)	0.40
Loss of Sense of Taste and/or Smell	15 (9%)	13 (10%)	2 (5%)	0.28	2 (6%)	0 (0%)	1.00
Headache	25 (14%)	24 (18%)	1 (2%)	**0.01**	1 (3%)	0 (0%)	1.00

MIS-C

Multisystem Inflammatory Syndrome in Children

- Fever **+** Inflammation on labs **+** clinically severe illness requiring hospitalization with multisystem organ involvement

AND

- Positive for SARS-CoV-2 via PCR, Antibody or Antigen **OR**
- COVID-19 exposure within 4 weeks of onset of symptoms

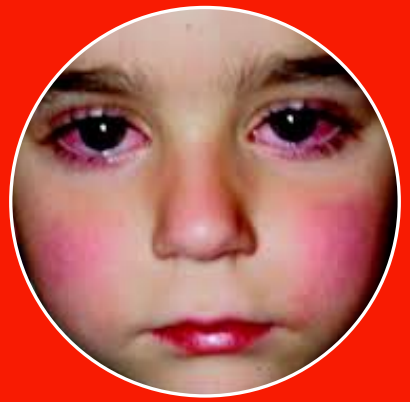
AND

- No alternative plausible diagnosis*

MIS-C Presentations

Fever +

Severe Abdominal Pain



Fever + KD-like Features

Fever + Multisystem Organ Dysfunction

MIS-C Type 1 Presentation : Kawasaki Shock-like , COVID +

- 4 yo male, no underlying past medical history
- Symptom onset 5 days prior to admission
  - **Complete KD** (High Fever, Rash, Strawberry tongue, Cervical lymphadenopathy Peripheral Extremity Edema)
- Presented in **hypotensive shock**
- No respiratory symptoms
- **Markedly decreased myocardial function** consistent with myocardial injury
  - **BNP 16,000 to 78,000; Troponin peaked 0.32**
  - **ECHO: No coronary involvement**
- Initial 2 COVID tests negative (NP), 3rd test positive (lower respiratory specimen)
- Presentation consistent with severe hyperinflammatory state
- Required intubation/mechanical ventilation, fluids, pressors, milrinone
- Treated with **IVIG, Aspirin, Anakinra**
- Good clinical response – Echocardiogram – repeat no coronary involvement (acute)

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MIS-C Type 2 Presentation - Severe Abdominal Pain + Shock - COVID+

- 8 year old, previously healthy male, no underlying medical conditions
- 5 days PTA had fever, sore throat, cough, SOB, abdominal pain
- Presented back to ED with **severe worsening abdominal pain**, and **hypotensive shock**
    - Minimal conjunctival injection, Minimal rash, no other KD findings
- CXR with cardiomegaly, mild pulmonary edema
- EKG no segmental changes, troponin 1.04 peaked at 2.83, BNP 12,500
- Echo with moderately decreased LV function
    - **Moderately dilated RCA (Z score +2.3, mildly dilated LMC (Z score + 2.8)**
- COVID swab 1 negative, COVID swab 2 positive
- Treated with 60 ml/Kg fluids, **IVIG X 2, Asprin, and Anakinra**
- Improving

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MIS-C Type 3 Presentation: Respiratory, Shock, Multi-organ Failure – COVID +

- 16 year old male
- Underlying Neurological Disorder: Microcephaly, Global Devel Delay, Seizure Disorder
- Symptom onset 3 days prior to admission: Fever and increased seizure frequency
- Presented with **Hypotensive Shock**, **CXR with lobar pneumonia**
  - Intubated, Mechanically Ventilated (Highest FiO2 0.6; Highest PEEP 10)
  - Fluids, Pressors, Milrinone, Hydrocortisone, Transfusions, FFP
  - Received hydroxychlororoquine - QTC prolongation/VTach - discontinued
  - Multisystem organ failure:
    - **Heme: DIC, Coagulopathy, Thrombocytopenia**
    - **Kidney: Hemodialysis**
    - **Hepatic Injury**
    - **Myocardial Depression: Troponin 5.4 to 10 to peak 32**

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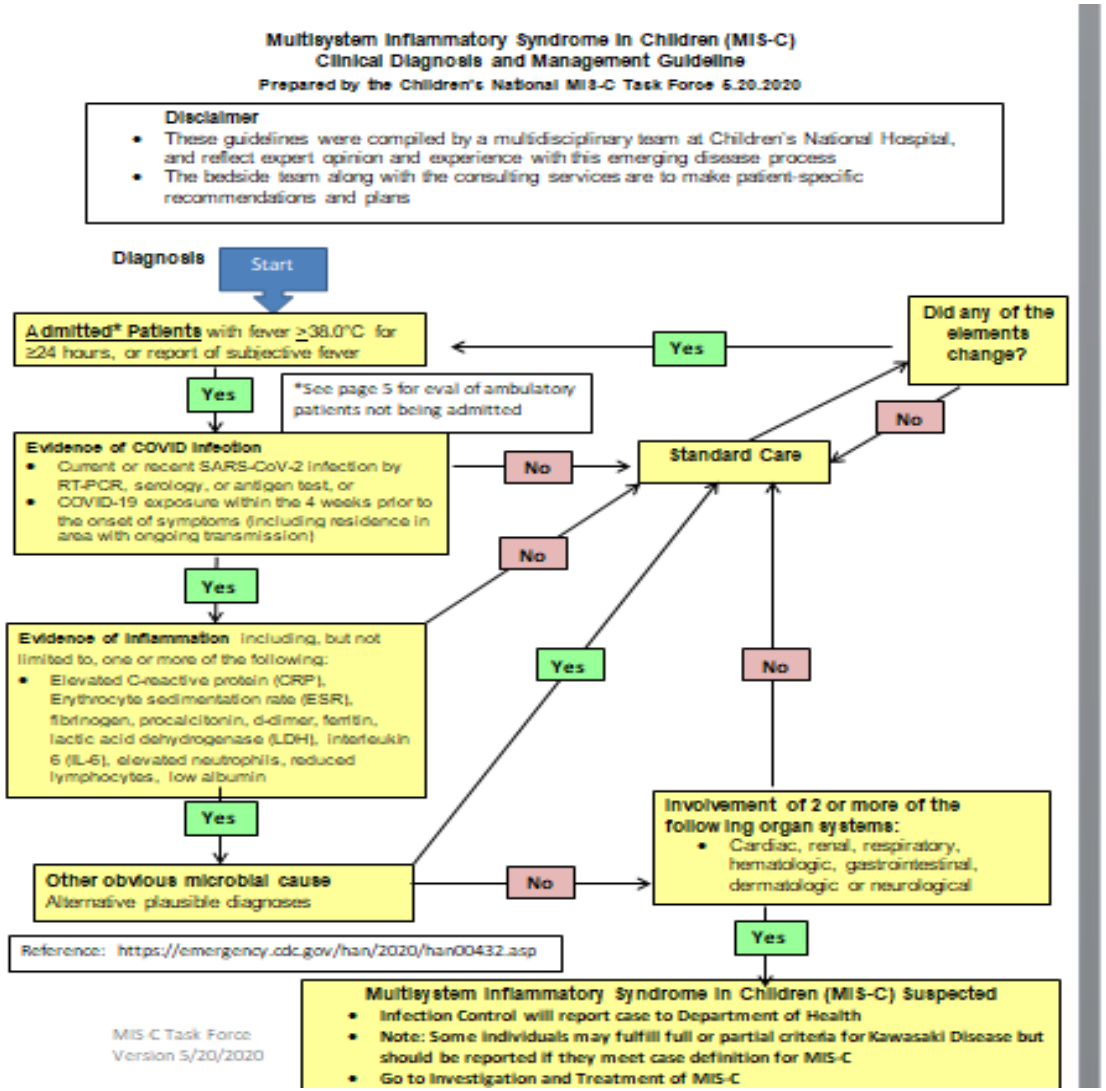
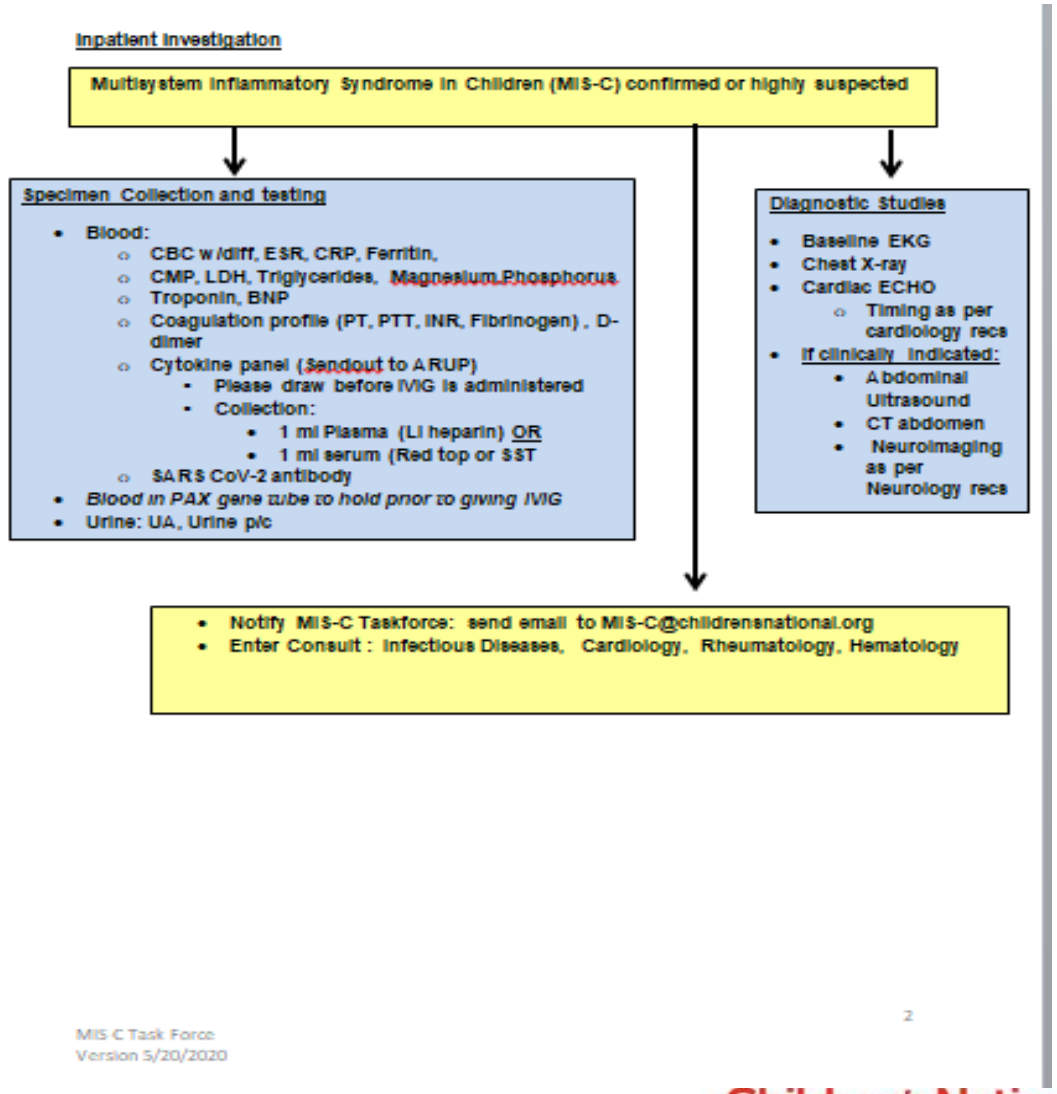
Children's National MIS-C Taskforce email: MIS-C@childrensnational.org





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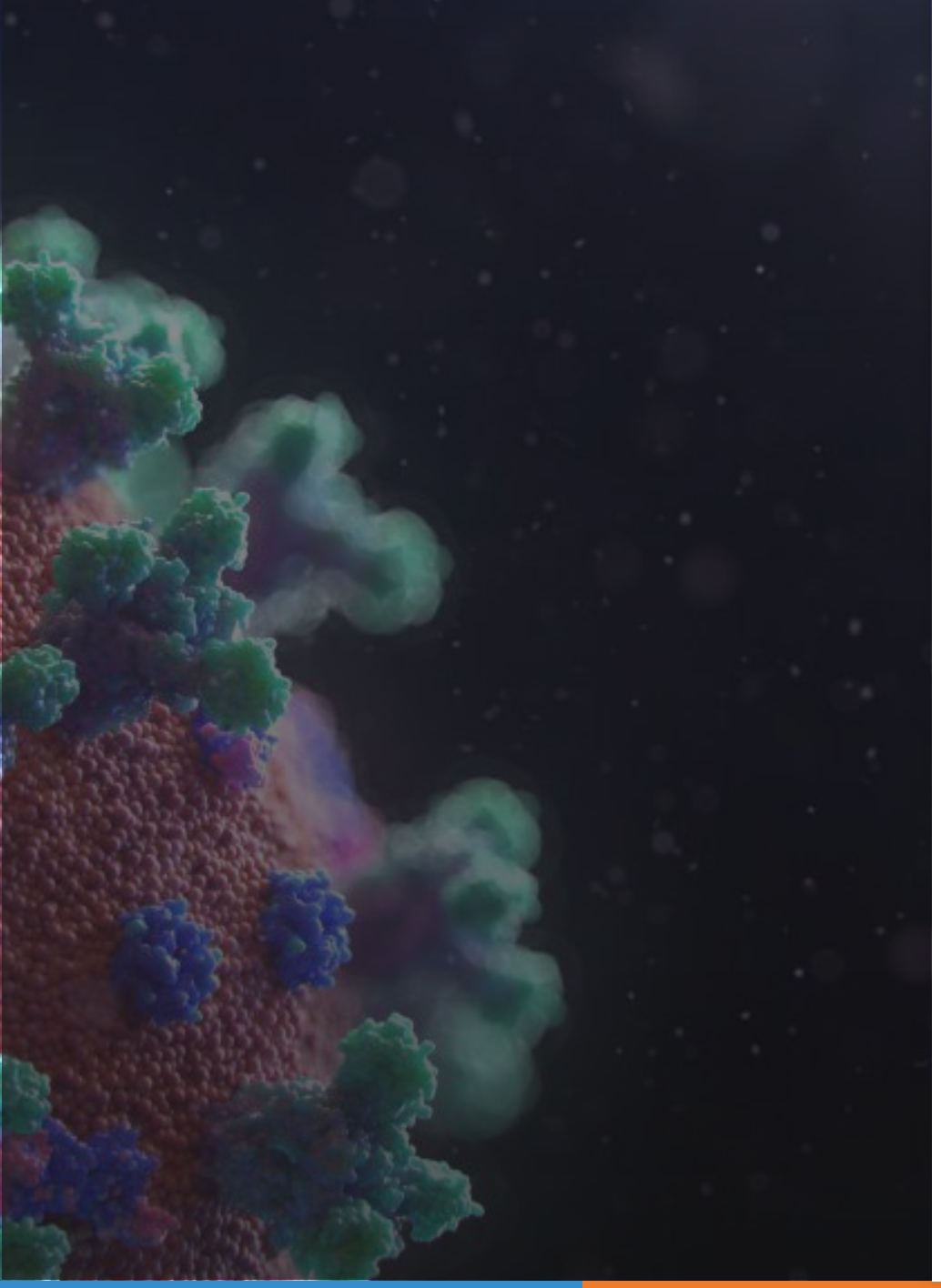
Children's National Hospital COVID-19 Research Focus

- Centralized de-identified institutional database with validated data
  - Lab, clinical, demographic, outcomes
- Central Wiki catalogues all COVID-focused projects: resource management (lab specimens and data), facilitates collaborations
  - Genetics of Host and Virus
  - Convalescent Plasma
  - T cell therapies
  - Fetal/Maternal interface, placenta, neurodevelopmental outcomes
  - Diagnostics – Rapid POC
  - Seroprevalence in children and health care workers
  - MIS-C pathogenesis



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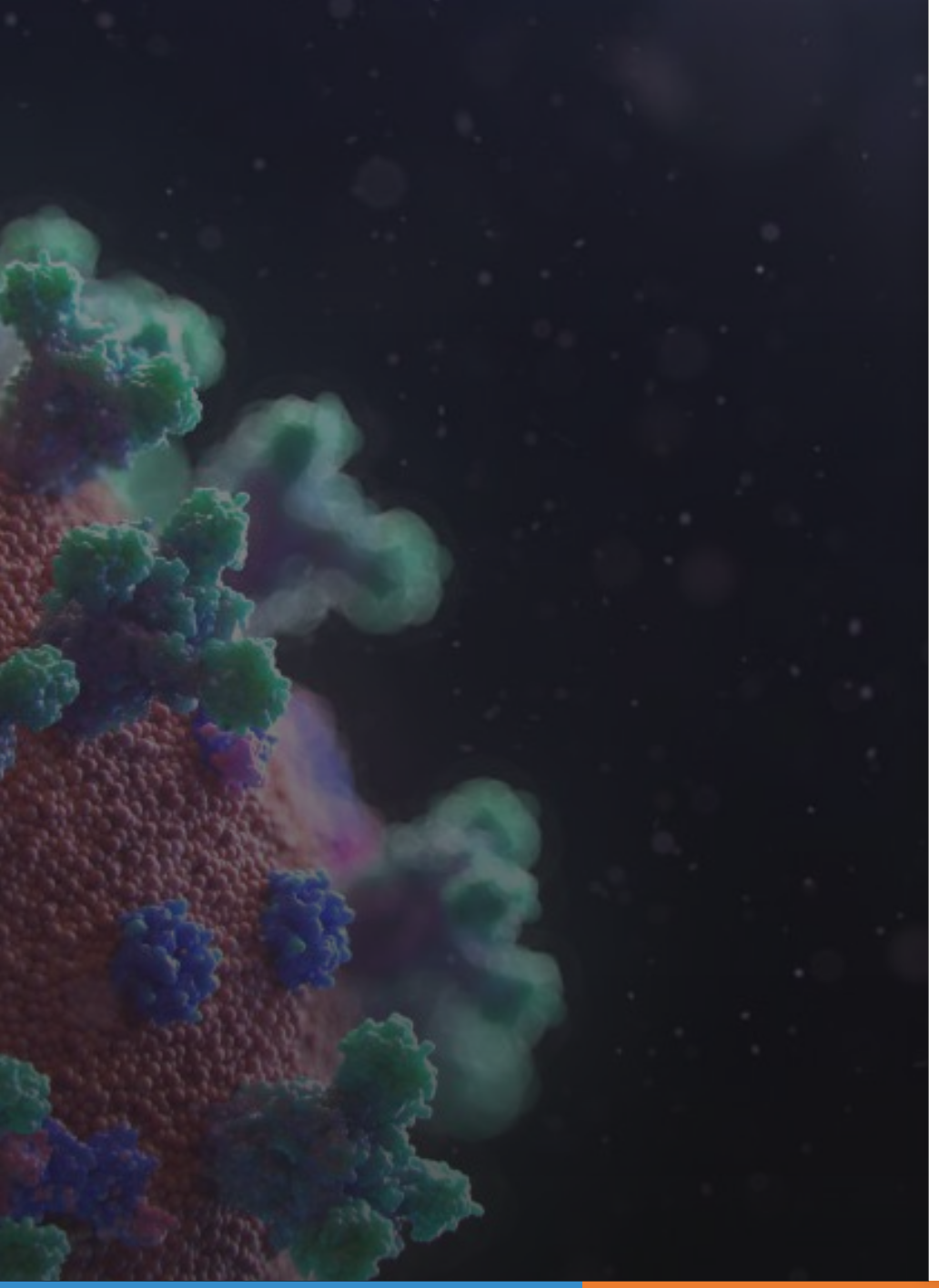

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STATE OF DRUGS/BIOLOGICS DEVELOPMENT

Gary Noel, MD, FAAP, FIDSA
CHIEF MEDICAL OFFICER
I-ACT for Children

"The good physician treats the disease; the great physician treats the patient who has the disease."

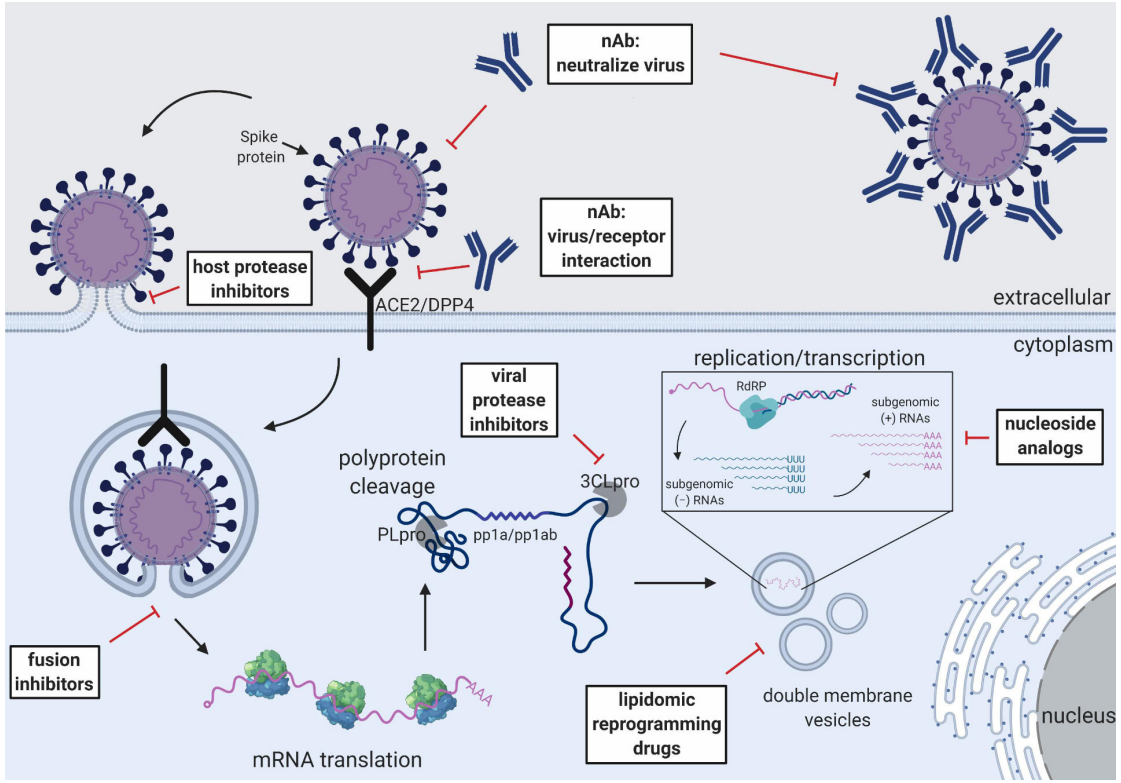
-- Sir William Osler

Research Priorities

Pediatric Research Nature 2020: https://www.nature.com/articles/s41390-020-0962-y

- Understand the virology, innate and acquired immune responses and pathogenesis and sequelae of SARS- CoV-2 infections in infants, children and adolescents.
- Rapidly develop therapies that improve the outcomes in infected children.
- Decrease the frequency and spread of SARS-CoV-2 infection.

Many Potential Antiviral Targets



http://www.sci-news.com/medicine/strategies-combating-sars-cov-2-other-coronaviruses-08363.html

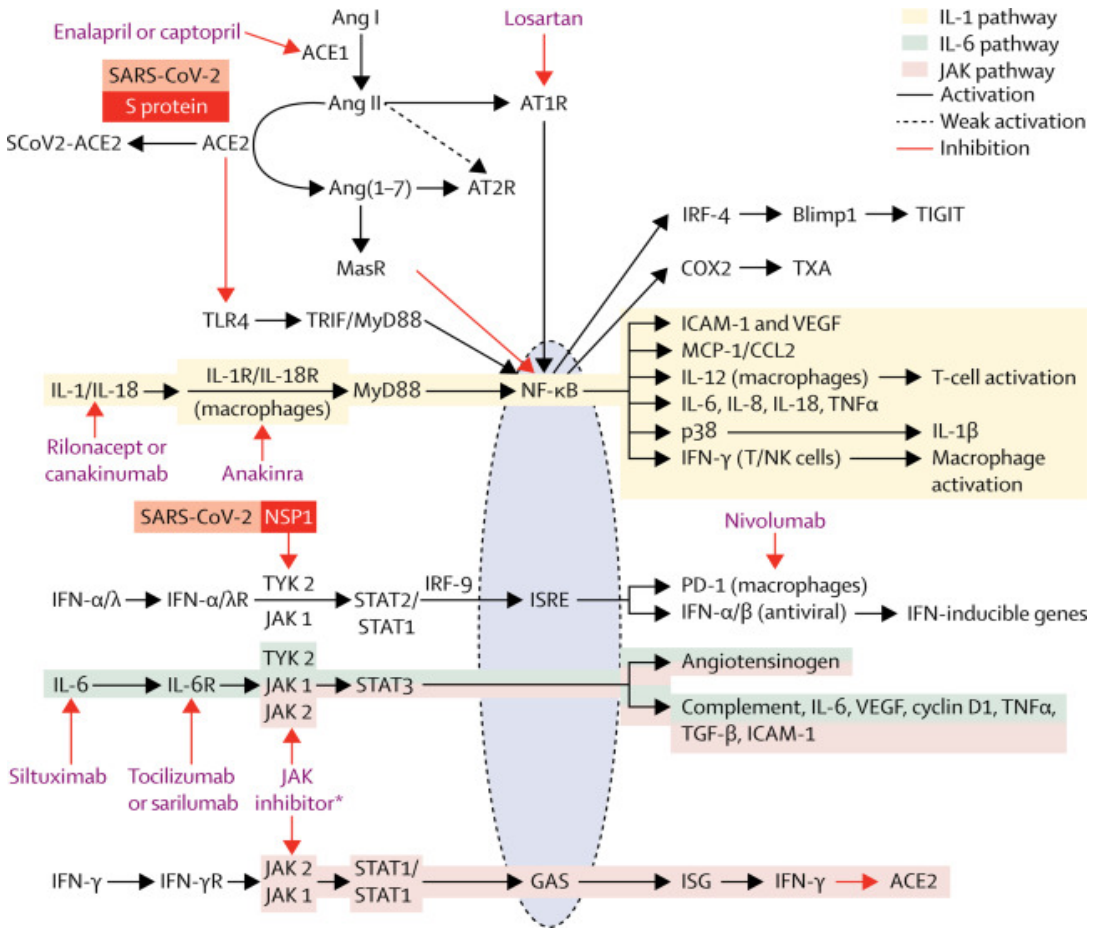
Neutralizing antibodies

Viral protease inhibitors

RNA polymerase inhibitors
(Nucleoside analogs)

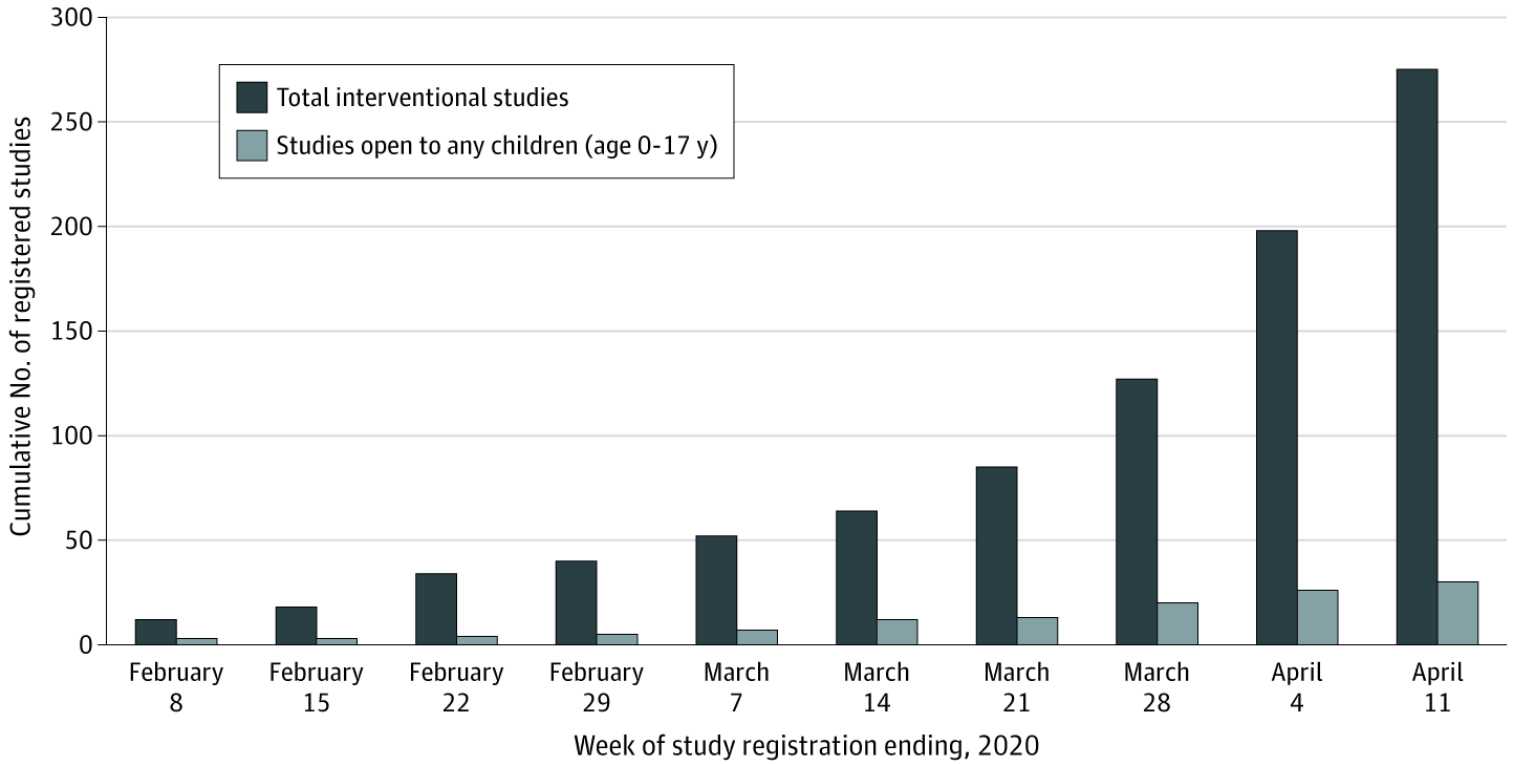
Fusion inhibitors

Even More Immune Modulating Targets



https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30226-5/fulltext

Involving Children in Clinical Trials - Getting it Right

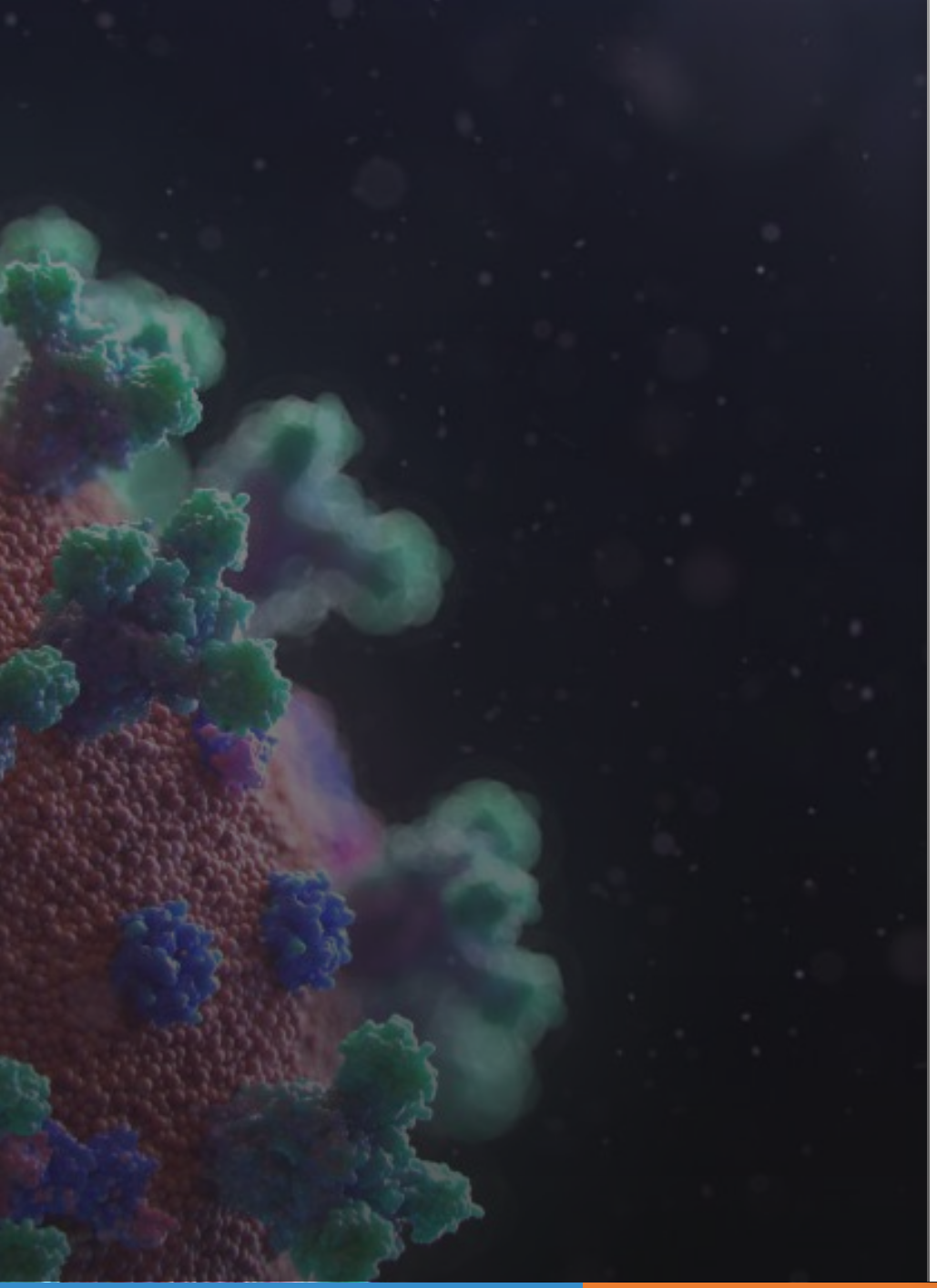


JAMA Pediatr. Published online May 7, 2020. doi:10.1001/jamapediatrics.2020.1888

Plenty of Room to Improve

- Designing initial trials that will optimize transition from adult to pediatric trials
  - Pharmacokinetics/pharmacodynamics
  - Drug metabolism
- Involving adolescents in early clinical trials
- Establishing the similarities and differences between adults and children in host response to SARS-CoV-2
  - Viral dynamics in acute infection
  - Transcriptional immune profiles


THANK YOU



INSTITUTE FOR ADVANCED CLINICAL TRIALS FOR CHILDREN

DEVELOPING PEDIATRIC TREATMENTS FOR COVID-19

I-ACT FOR CHILDREN VIRTUAL WORKSHOP

CURRENT STATE OF DRUGS & BIOLOGICS DEVELOPMENT

Lynne P. Yao, MD

DIRECTOR, DIVISION OF PEDIATRICS AND MATERNAL HEALTH

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Office of New Drugs

Center for Drug Evaluation and Research

US Food and Drug Administration

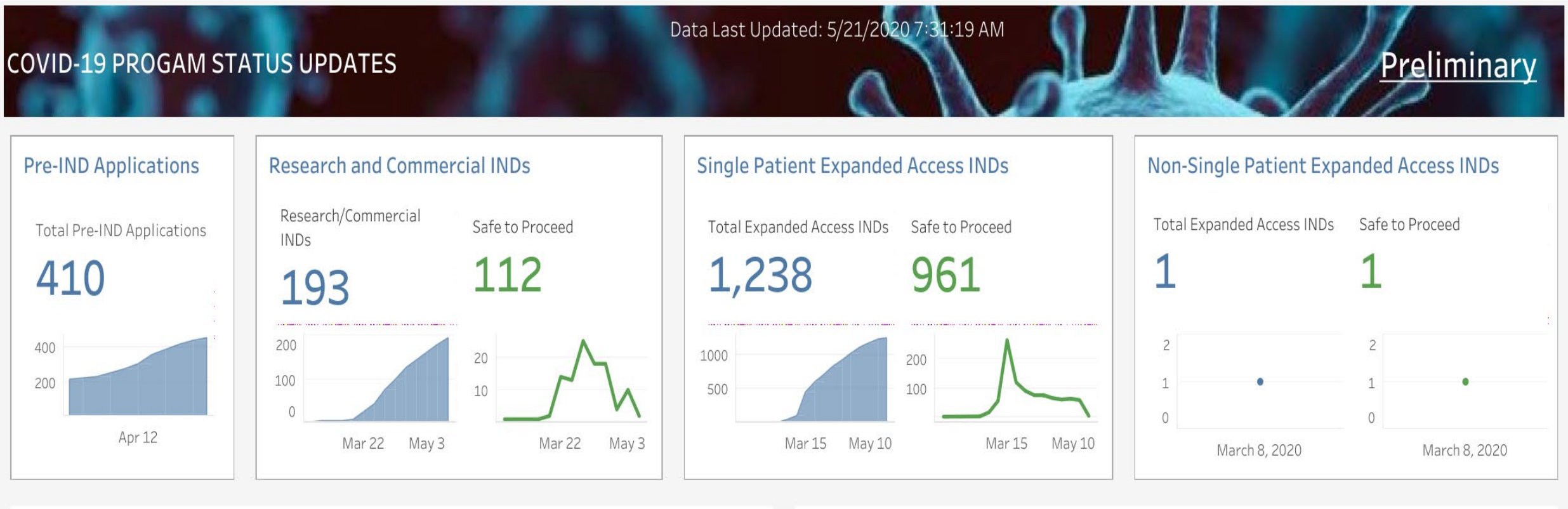
Disclosure Statement

- I have no financial relationships to disclose relating to this presentation
- The views expressed in this talk represent my opinions and do not necessarily represent the views of FDA
- Acknowledgments:
  - Susan McCune, M.D., Director, Office of Pediatric Therapeutics, OC
  - John Alexander, M.D., Deputy Director, Division of Pediatric and Maternal Health
  - Khushboo Sharma, M.B.A., RAC, Deputy Director for Operations, OND Immediate Office

FDA Coronavirus Treatment Acceleration Program (CTAP)

- Immediate triage of requests from developers and scientists seeking to develop or evaluate new drug and biologic therapies.
  - Identify appropriate FDA staff
  - FDA will generally respond within a day
- Provided ultra-rapid, interactive input on most development plans.
  - Interactions have generally been prioritized
- Provided ultra-rapid protocol review – within 24 hours of submission, in some cases.
- Completed review of single patient expanded access requests around-the-clock – and generally within 3 hours.
- Worked closely with applicants and other regulatory agencies to expedite quality assessments for products to treat COVID-19 patients.
  - Transfer manufacturing to alternative or new sites to avoid supply disruption.

OND COVID-19 Application Tracker*



As of 21 May 2020

COVID-19: FDA Guidances

- COVID-19: Developing Drugs and Biological Products for Treatment or Prevention – Guidance for Industry
- COVID-19 Public Health Emergency: General Considerations for Pre-IND Meeting Requests for COVID-19 Related Drugs and Biological Products – Guidance for Industry
- Investigational COVID-19 Convalescent Plasma – Guidance for Industry
- FDA Guidance on Conduct of Clinical Trials of Medical Products during the COVID-19 Public Health Emergency

Available at https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs

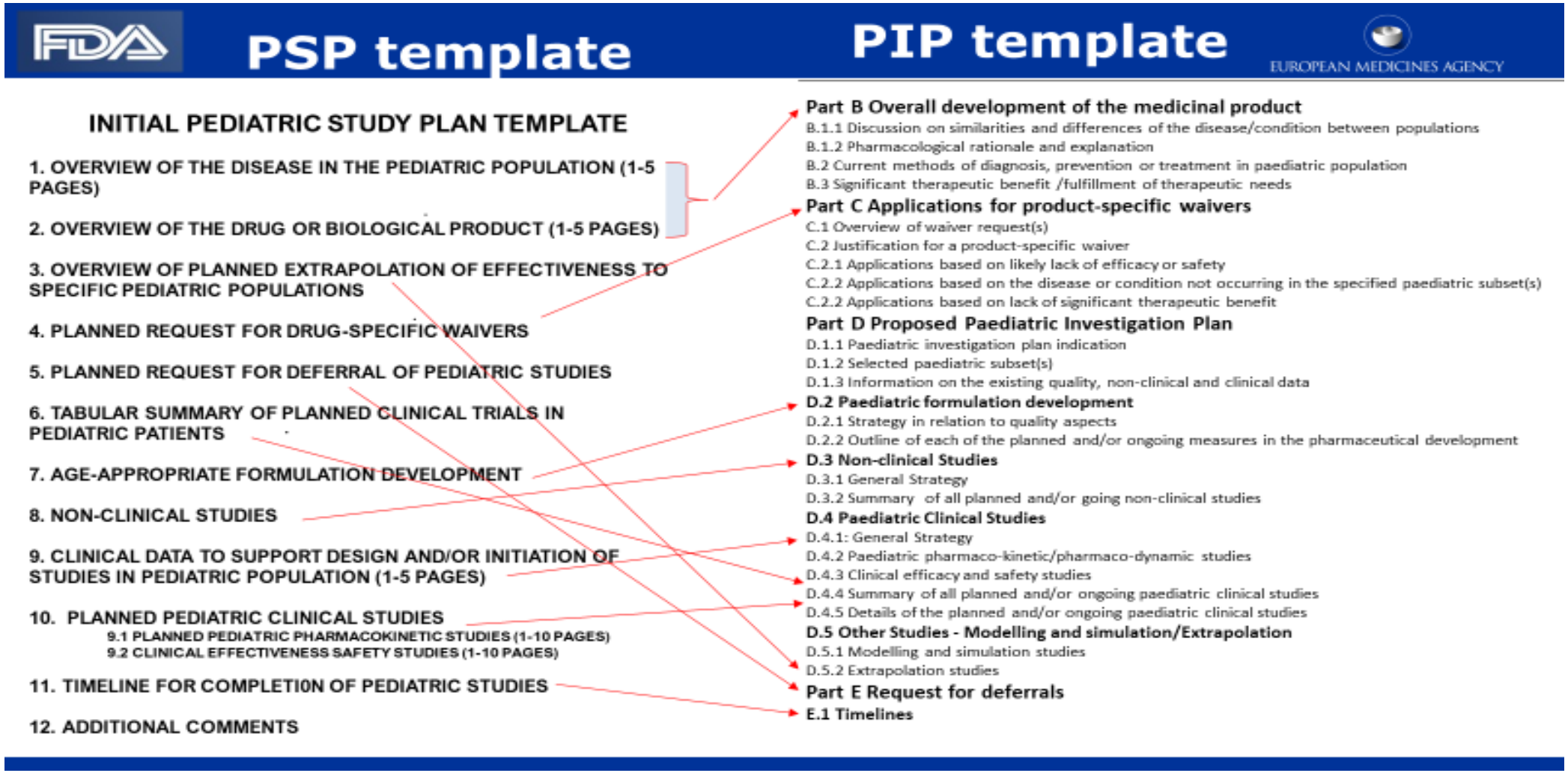
COVID-19: Developing Drugs and Biological Products for Treatment or Prevention

- Final Guidance published May 11, 2020.
- Children should not be categorically excluded from clinical trials of investigational COVID-19 products in which there is a prospect for direct benefit.
  - Potential for use of pediatric extrapolation of adult efficacy data
  - If dosing recommendations for a drug are the same for adults and adolescents and there is sufficient prospect of benefit to justify the risks, then it may be appropriate to include adolescents in the initial phase 3 clinical trials
  - Sponsors are encouraged to submit an initial pediatric study plan as soon as practicable
  - FDA intends to work with sponsors to reach agreement on the initial pediatric study plan and any pediatric trial protocols as quickly as possible to avoid any unnecessary delays in the initiation of trials or submission of any marketing application
- FDA encourages the enrollment of pregnant and lactating individuals in the phase 3 (efficacy) clinical trials if appropriate.

International Collaborations

- Strong sense of shared responsibility across regulatory authorities related to pediatric COVID-19 therapeutics development
- Use of scheduled and *ad hoc* Pediatric Cluster calls to discuss pediatric-related COVID-19 therapeutics development issues
- Goal is to achieve high degree of consistency with pediatric development plans (iPSP and PIP) for COVID-19 treatments with rapid turnaround time
- Developed a Common Commentary to aid sponsors with administrative process for submission of iPSP and PIP

Common Commentary for Submission of Pediatric Development Plans for Treatment and Prevention of COVID-19 to FDA and EMA



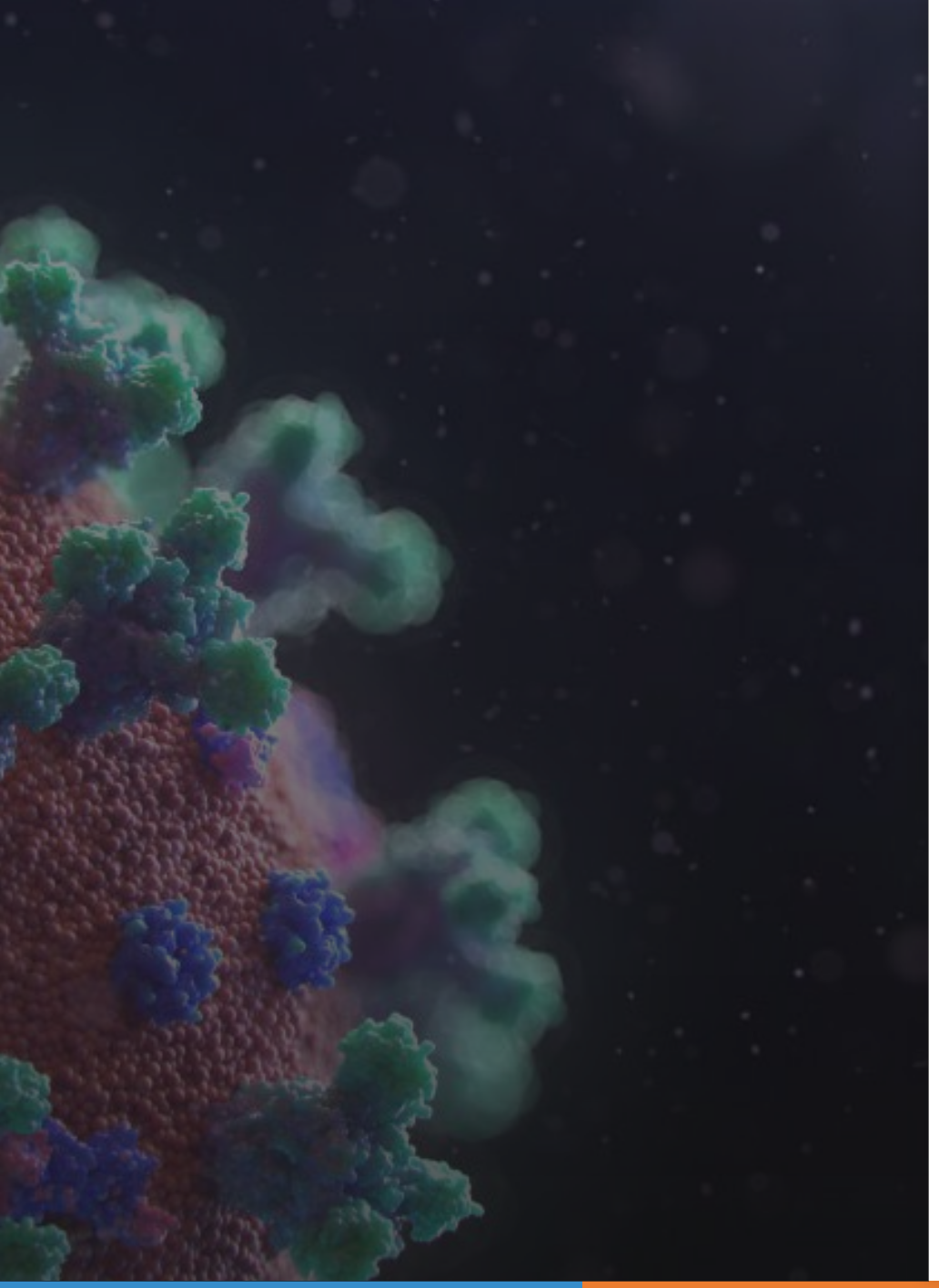
Selected Comparison of iPSP and PIP for COVID-19 therapies

	iPSP	PIP Some sections of the PIP template can be used in a simplified way as described below.
Overview Of The Disease In The Pediatric Population **Overview Of The Drug Or Biological Product**	Section 1: Brief overview of COVID-19 disease in the pediatric population (1-2 pages) (can be based on publication). Section 2: Brief overview of the drug/biological product (1-2 pages)	Part B1: Short overview on the disease, the medicinal product and the pharmacological rationale (can be based on publication). Focus should be on - most recent research findings related to COVID-19 in relation to the pharmacological rationale of the IMP (entry into cells, binding receptors, virulence, shedding, etc.) - (dis)similarity of disease/severity between adults and various paediatric age subsets as basis for potential extrapolation in view of their target population and mode of action of medicinal product Part B2: Very short overview on current treatment. No need to fill in Part B.3

	iPSP	PIP Some sections of the PIP template can be used in a simplified way as described below.
Overview Of Planned Extrapolation Of Effectiveness To Specific Pediatric Populations	Section 3: Discuss use of extrapolation to support effectiveness of the product in the pediatric population (1-2 pages).	This aspect should be discussed in part D 5.2
Planned Request For Drug-Specific Waivers	Section 4: This can be concise with only the age, the grounds and arguments to support the grounds for the waiver included in the general paragraph (< 1 page).	Part C: This can be concise with only the age, the grounds and arguments to support the grounds for the waiver included in the general paragraph with no need to complete C2.1, C2.2, C.2.3
Planned Request For Deferral Of Pediatric Studies	Section 5: This can be concise with only the age, the grounds and arguments to support the grounds for the deferral included in the general paragraph (< 1 page).	Part E: This can be concise with only the age, the grounds and arguments to support the grounds for the deferral included in the general paragraph.

Final Thoughts

- Unprecedented time in our history
- Obligation to collaborate globally to protect our children by providing timely access to safe and effective therapeutic products for COVID-19
- This global collaboration must include industry, clinical trial networks, academic institutions, researchers, health authorities, and regulators



I-ACT INSTITUTE FOR ADVANCED CLINICAL TRIALS FOR CHILDREN

DEVELOPING PEDIATRIC TREATMENTS FOR COVID-19

I-ACT FOR CHILDREN VIRTUAL WORKSHOP

INNOVATIVE METHODS FOR CONDUCTING PEDIATRIC CLINICAL TRIALS

Lily Mulugeta, PharmD

ASSOCIATE DIRECTOR FOR SCIENCE

Division of Pediatrics and Maternal Health

Center for Drug Evaluation and Research

US Food and Drug Administration

Disclaimer: I have no financial interests or relationships to disclose. These views do not necessarily reflect the views of the Food and Drug Administration

Timely Access to Therapies for Pediatric Patients

Pediatric development program should provide **timely access to**:

- **Clinical trials**:
  - Should begin once prospect of direct benefit is determined and overall risk benefit has been considered to allow enrollment of children into a clinical trial.
- **Approved therapies**:
  - Pediatric trials should be completed and assessment of the data submitted concurrently with adults or alternatively, complete enrollment before off-label use makes clinical trials difficult to complete (~2 to 3 years after approval in adults).
  - One potential solution: include pediatric patients into adult phase 3 trials pre-approval; alternatively, pediatric patients can be enrolled in a separate and concurrent trial when appropriate.

Use of innovative approaches is critical for expediting drug development in pediatric patients

Some Challenges in Pediatric Drug Development

- Small population
  - May limit study design
- Phenotypic variability adds to complexity
- Natural history often poorly understood
- Biomarkers, outcome measures, and endpoints often lacking
- Lack of a suitable control and ethical concerns
- Lack of clinical research infrastructure

Use of Pediatric Extrapolation in Drug Development

- What data, if any, could be leveraged and to which pediatric population/subgroup does it apply?
- What additional data are needed in the target pediatric population?
- What is the optimal trial design to obtain the necessary data?

Pediatric Extrapolation: Disease/Response "Similarity" is a Continuum

Different	Dissimilar	Similar	Same
No overlap between adult and pediatric condition/response	Some degree of overlap with significant differences between adult and pediatric condition/response	Large degree of overlap with some differences between adult and pediatric condition/response	Significant overlap; no known significant differences between adult and pediatric condition/response

Increasing relevance of adult information to pediatric population with increasing confidence in similarity between adult and pediatric condition

Innovative Approaches??

AWC Pediatric Trial

Exposure Matching

Innovative Approaches for Expediting Pediatric Drug Development

Study Designs

- Randomized withdrawal
- Bridging biomarker strategies
- **Enrolling pediatric patients in adult trials**
- Externally controlled studies
- Adaptive designs (dose, trial duration, etc.)
- **Master protocols**

Statistical Methodologies

- Bayesian approaches

Modeling and Simulation

- Clinical trial simulation
- **Dose selection and refinement**

Enrolling Pediatric Patients in Adult Trials

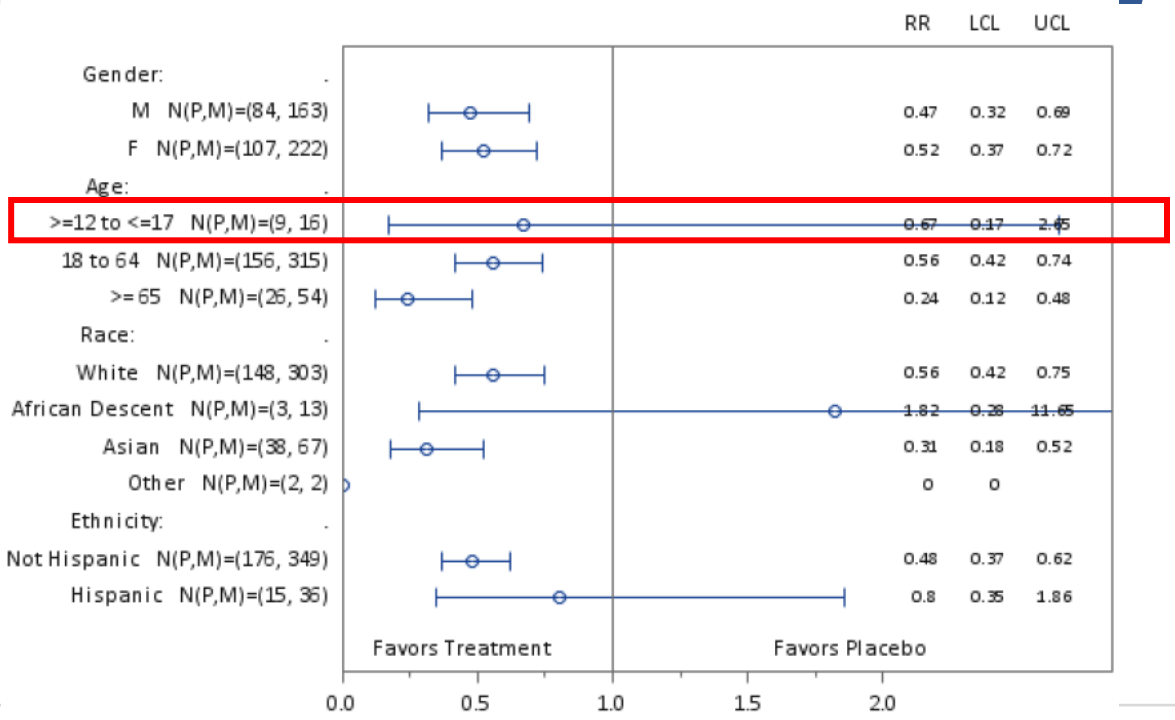
- **Should be considered on case-by-case basis:**
  - Strong evidence of disease similarity between adults and pediatrics
  - Sufficient data to support dose selection including availability of a formulation
  - Evidence of preliminary clinical efficacy and safety data in adults
- **If enrolled in adult phase 3 trial:**
  - Include pediatric patients in the primary endpoint analysis
  - (Pre-specified) subgroup analysis focused on direction rather than magnitude of effect
  - Adequate safety monitoring required
- **Additional considerations:**
  - Evaluation of the adult trial design
    - Ease and suitability of the endpoint in pediatric patients and the timing of the endpoint
    - Choice of the comparator
    - Frequency of blood draws and other invasive procedures; frequency of visits and assessments
- **Operational considerations including site selection**

FDA Guidance https://www.fda.gov/media/113499/download

https://www.fda.gov/media/113319/download

Enrolling Adolescents in Adult Trials: Case Example

Data supported approval in adults and adolescents



Exacerbation rate ratios by demographics including age (mepolizumab)

Source: FDA statistical review (dated 07/10/2015)
https://www.fda.gov/drugs/development-resources/reviews-pediatric-studies-conducted-under-bpca-and-prea-2012-present

Mepolizumab (Nucala®): mAb directed against IL-5 (1st in class); approved for severe asthma with eosinophilic phenotype

Strong evidence of disease similarity and early development did not indicate development-related safety signals

Trial design appropriate: Similar endpoint and comparator
Dose selection addressed

Dosing: Same dose as in adults; PK data were collected in the phase 3 trial

Results and analyses

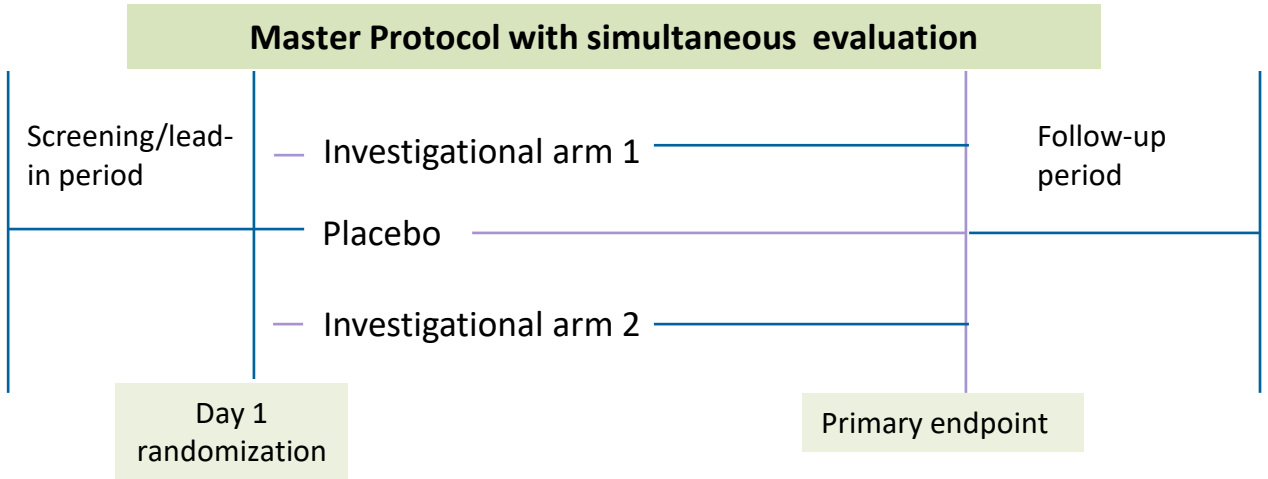
Three pivotal phase studies included patients
Adolescents: N=28 across three studies ≥ 12 years

Adolescents included in the ITT population for primary efficacy analysis

Subgroup analysis: Point estimates of treatment effect favored mepolizumab (confidence intervals wide);
Safety profile similar

Master Protocols

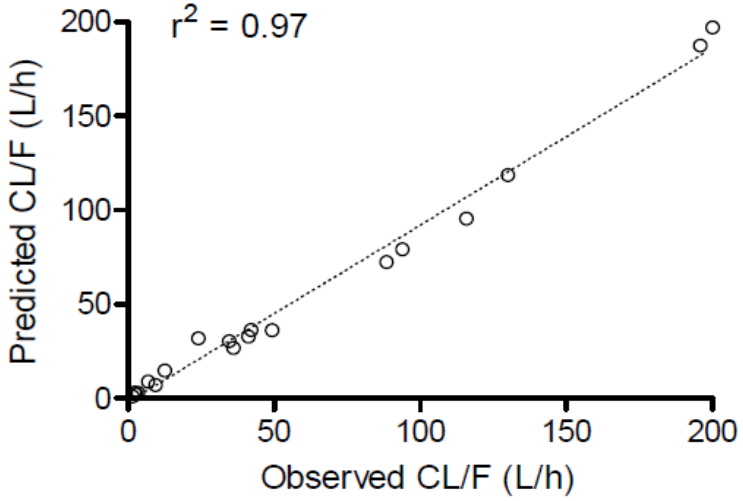
- Enables multiple drugs to be evaluated in a clinical trial in either a simultaneous or sequential manner
- New compounds are added as they are available; compounds leave the trial for either success or futility
- Master protocol governs the entire study, including key study design elements
- Benefits:
  - Operational efficiencies (reduces study start-up costs)
  - Shared control group (reduces pts exposed to placebo)
  - Uniform collection of data
- May require collaboration across companies



Use of Modeling and Simulation to Estimate Dosing for Pediatric Patients

Adult data can be used to predict adolescent doses well, patient > 2 years typically adequately

Orally Administered Drugs (*n*=19)



Adolescent PK Studies Under **PREA** and **BPCA**.
FDA Advisory Committee for Pharmaceutical Science and Clinical Pharmacology Meeting
March 14, 2012, National Harbor, MD

Separate PK studies may NOT be needed in pediatric patients > 2 years for drugs/biological products

- Can be rolled into efficacy/safety studies or open label safety study
- Implementation of sparse PK strategies
- Potentially leverage PK information from pediatric patients with different diseases

Considerations

- Drugs with narrow therapeutic range
- Non-linearity PK
- Potential differences in the pediatric and adult populations (intrinsic factors)
- E-R/Dose-response data in adults foundation for dose selection in pediatric patients

Modeling and Simulation to Estimate Dosing for Pediatric Patients: Case Example

Levomilnacipran (Fetzima®)

Approved for major depressive disorder in adults (2013)

Pharmacokinetics: **Linear**; primarily metabolized by CYP3A4

Pediatric dose selection: Match exposures in adults at approved doses

Pediatric study requirements under PREA

Study 1: PK, efficacy, safety **study in patients 12-17 years** (placebo and active-controlled fixed dose)

- Pop PK modeling in adults to justify dose selection
- An interim PK analysis to determine dose for patients 7-<12 yrs

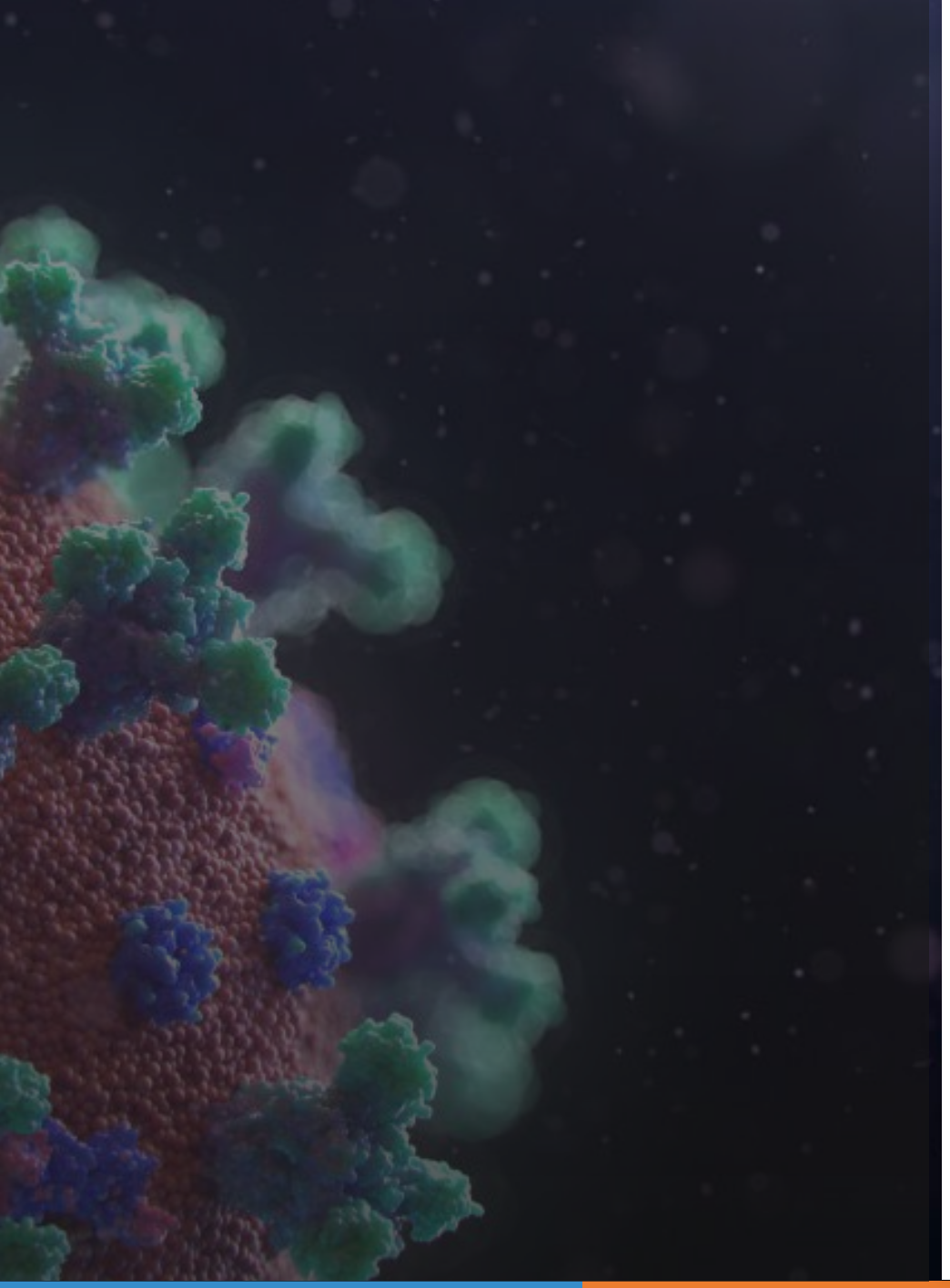
Study 2: Efficacy and safety study **in patients 7 to 17 years**

- Include sparse PK sampling

M&S to support dose selection for clinical study; alleviate need to conduct a separate PK study

Conclusion

- Pediatric development program should provide timely access to approved therapies.
- Pediatric trials should be designed within the context of available data (usually adults) and to address data gaps
- Adult trials should be designed to collect data that can expedite the pediatric program (e.g., robust dose exploration)
- Innovative approaches such as joint adult-pediatric trials, modeling and simulation, and master protocols should be considered to expedite the development of therapies for pediatric patients, including those with COVID-19



INSTITUTE FOR ADVANCED CLINICAL TRIALS FOR CHILDREN

DEVELOPING PEDIATRIC TREATMENTS FOR COVID-19

I-ACT FOR CHILDREN VIRTUAL WORKSHOP

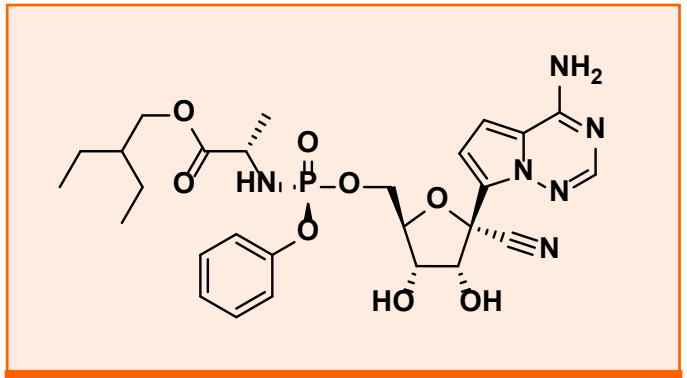
REMDESIVIR PEDIATRIC CLINICAL DEVELOPMENT STRATEGY

Cheryl Pikora, MD, PhD
SENIOR MEDICAL DIRECTOR
Gilead Sciences, Inc.

Topics in Development of RDV for Children

1. Remdesivir background
2. Challenges of pandemic and development strategy
3. Efficacy extrapolation to adults
4. PK as a co-primary endpoint
5. Final study plan
6. Regulatory timeline

Remdesivir: Broad-Spectrum Antiviral Activity



Remdesivir
(GS-5734)

- Warren TK, et al. Nature 2016;531:381-5.
- Lo MK, et al. Sci Reports 2017;7:43395.
- Sheahan TP, et al. Sci Transl Med 2017;9:eaal3653.
- Agostini ML, et al. MBio 2018;9(2):e00221-18.
- Neyts et al., unpublished

Virus Family	Virus	EC_{50} (μM)
Filoviruses	Ebola (Makona)	0.19
	Ebola (Kikwit)	0.14
	Bundibugyo	0.19
	Sudan	0.24
	Marburg	0.06
Coronaviruses	MERS	0.03
	SARS	0.10
Paramyxoviruses	Nipah	0.05
	Measles	0.04
	Hendra	0.06
Flaviviruses	Dengue	0.20
	Yellow fever	0.13
	Zika	0.10
	West Nile	1.0
Arenaviruses	Lassa	4.5
Bunyaviruses	CCHF	>50
Togaviruses	Chikungunya	>20

Challenges in Designing a Strategy for RDV in Children During a Pandemic

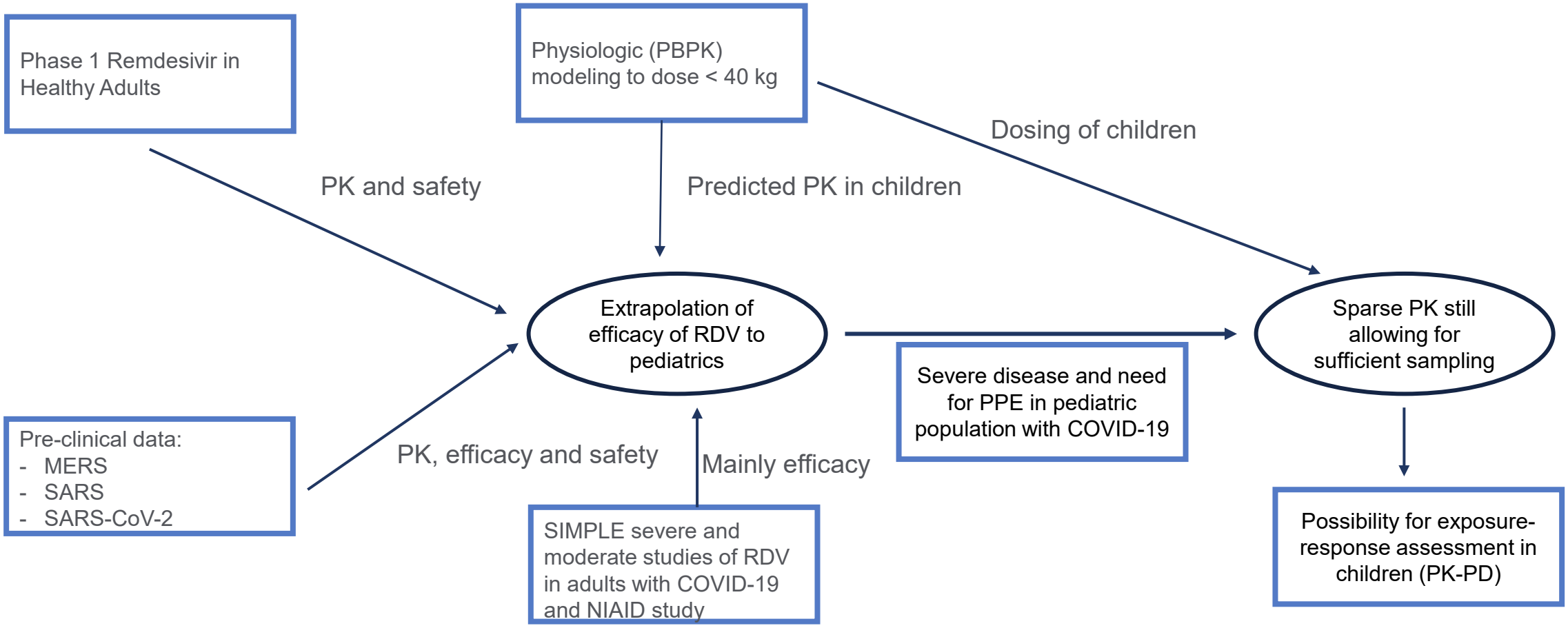
Challenge	Mitigation Strategy	Benefit	Risk
Little known about COVID-19 in children	Include all hospitalized children diagnosed with COVID-19	Enroll at a faster pace and possibly capture benefit in various presentations	Benefit difficult to assess with too much variation in presentation
PK data in adults is mainly from healthy adult studies	PK modeling and extrapolation where possible	Aligns with extrapolating efficacy based on PK from adults to children	No strong PK-PD of RDV in adults with COVID-19 PK
PK in children not known	PBPK modeling for Ebola Virus treatment	Use of doses derived from PBPK model for CUP and EUA	Unknown PK-PD in children
Planning for RDV study in children prior to outcomes in adults known	Wait to start study until primary endpoint readout for adult studies	Equipoise in pediatric study design	Protocol and pediatric plans in place need to change quickly as information is obtained
Fewer severe pediatric cases and flattening of curve	Establish approximately 30 sites for study (US and EU)	More sites relates to faster enrollment	More time could be needed to get this many sites up (IRB, CTA TATs)
Need a single plan for both US and EU	FDA and EMA/PDCO conversations and meetings	Aligning the plan across the regions	Areas of disagreement between the 2 agencies

Approaches to the Use of Extrapolation of Efficacy from Adult to Pediatric Population

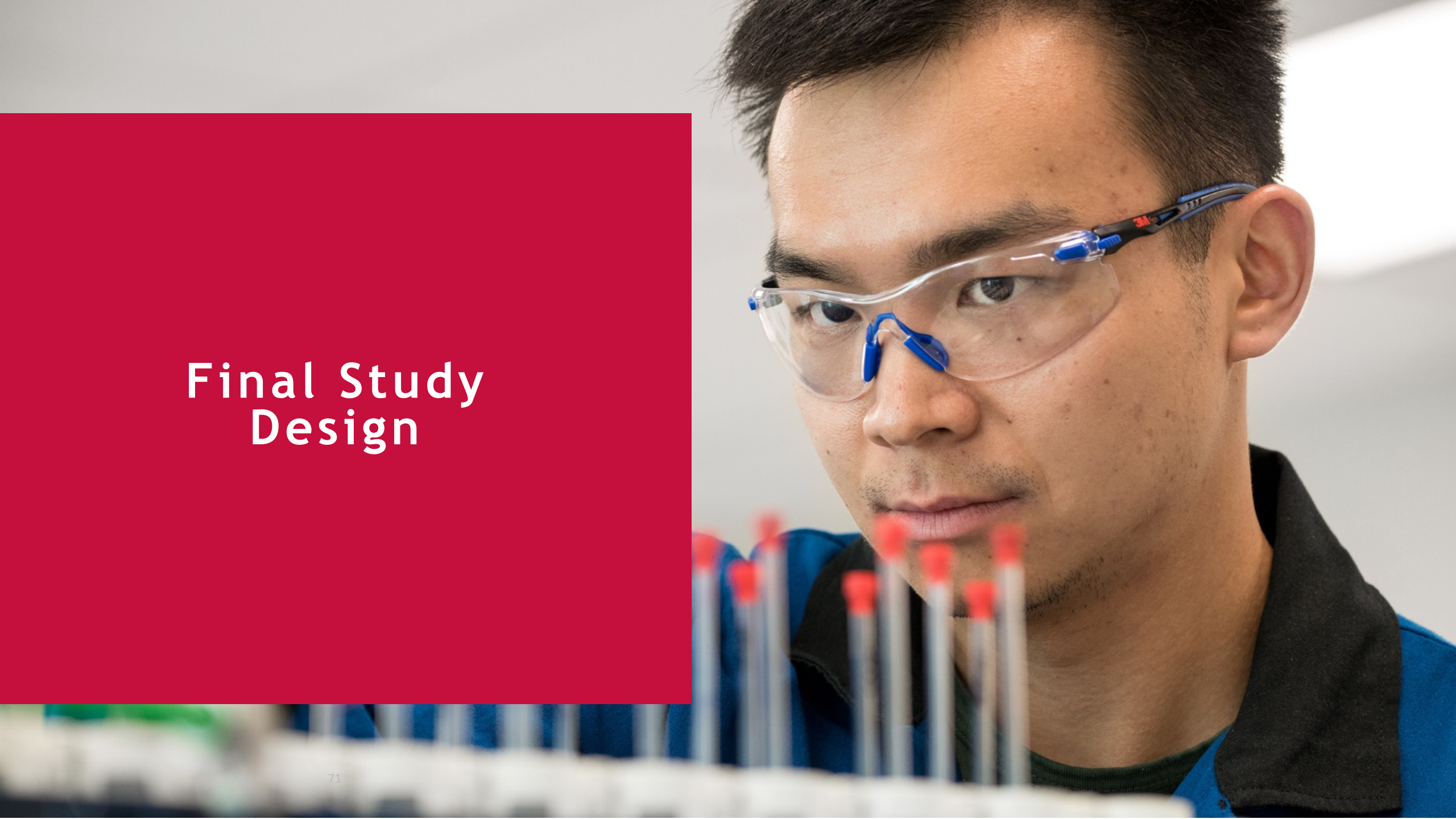
Pediatric Rule (1998): Where the course of the disease and the product's effects are similar in adults and pediatric patients, FDA may conclude that pediatric safety and effectiveness can be supported by effectiveness data, such as dosing, pharmacokinetic, and safety data in pediatric patients.

Level of Extrapolation	Design Requirements
No extrapolation	Two adequate well-controlled efficacy and safety trials in children plus pharmacokinetic data
Partial extrapolation	Single adequate, well-controlled efficacy and safety trial plus pharmacokinetic data or demonstration of exposure/response in defined situations
Complete extrapolation	Pharmacokinetic and safety data

PK as a Co-Primary Endpoint



Final Study Design



Paediatric Study: Birth to < 18 Years of Age

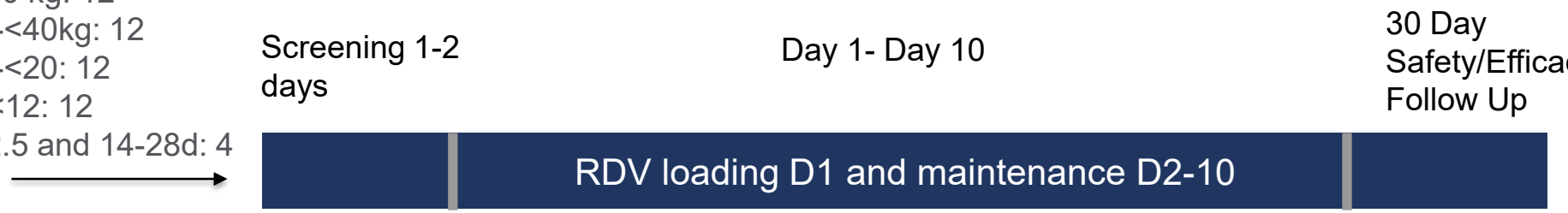
Key Inclusion
- Laboratory proven SARS-CoV-2 infection
- Hospitalization with or without respiratory support and with respiratory symptoms
- Age birth to < 18 yrs (including preterm neonates/infants < 56 days of age)
- Weight:
  - 12-<18y; ≥ 40 kg
  - 14 days and GA ≥ 37 wks to < 18 y; 2.5-<40kg
  - 0-14 days, BW≥ 2.5 kg and GA ≥ 37 wks
  - 0-56 days, BW≥ 1.5 kg and GA ≥ 32 wks

Key Exclusion
- eGFR < 30 ml/min/m2 for ≥ 1 yr of age and Cr > threshold limits for < 1 yr
- ALT > 5X ULN

Primary endpoint:
- Safety and tolerability of remdesivir
- PK parameters

Secondary endpoints:
- Efficacy – mechanical ventilation, days of hospitalization, improvement on ordinal scale, PEWS score (exploratory)
- Antiviral activity assessed by cycle threshold of real time PCR of respiratory and rectal swabs and days to loss of PCR positivity
- Exploratory – serologic response and correlation to antiviral activity

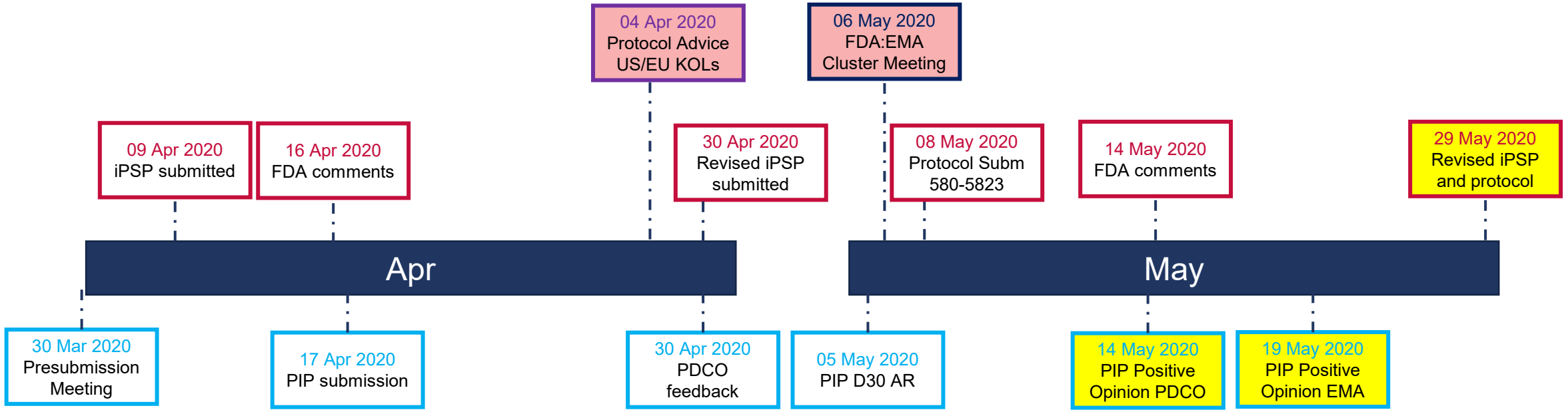
Sample size: 52
≥ 40 kg: 12
20-<40kg: 12
12-<20: 12
3-<12: 12
≥ 2.5 and 14-28d: 4



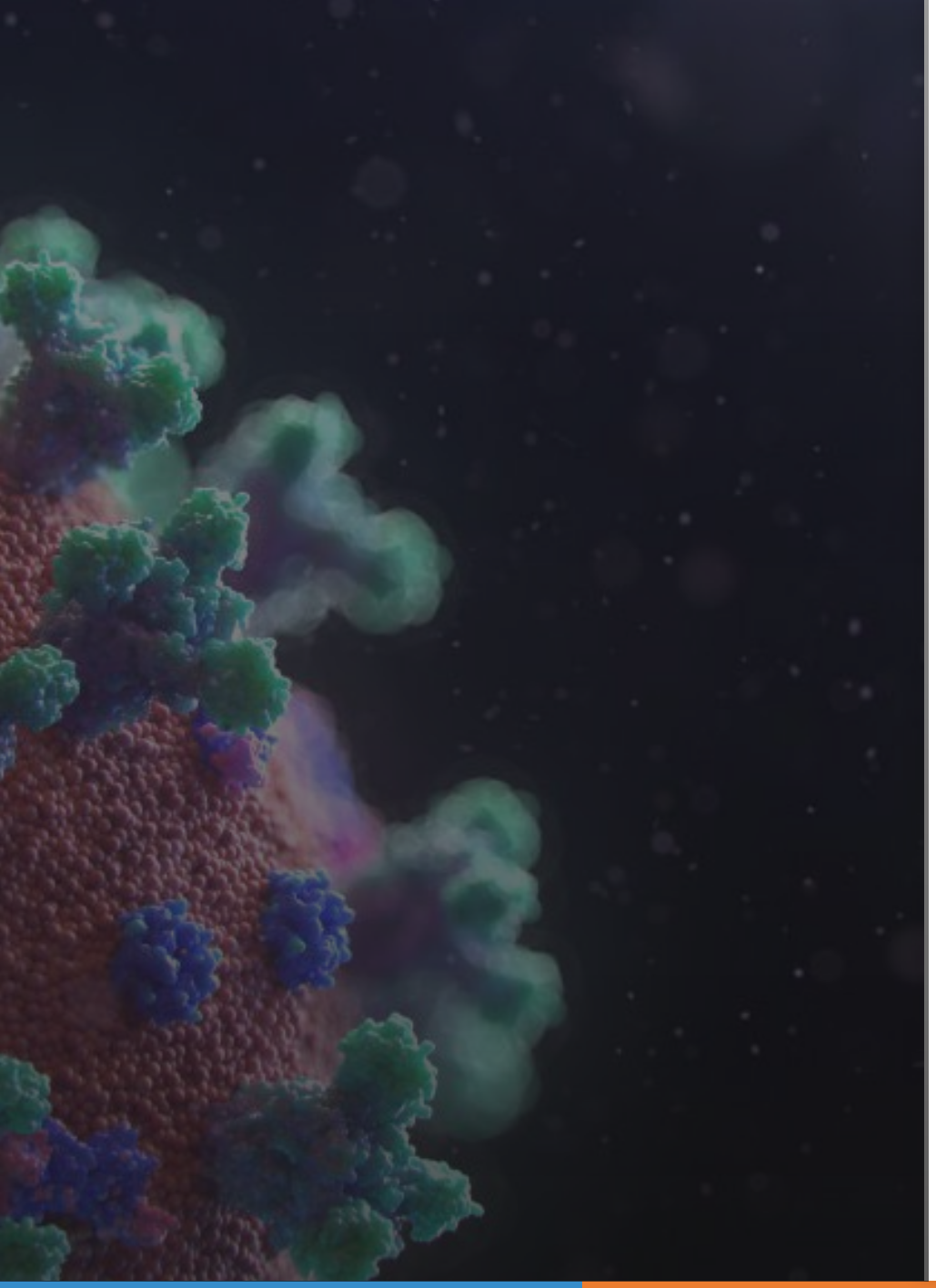
Safety: AEs, SAEs, Grade 3/4 laboratories
Efficacy and antiviral outcomes: Clinical score (PEWS), SARS-CoV-2 PCR from resp and rectal swabs Day 2, 4, 6, 8, 10 and 30
PK: Sparse PK sampling
Exploratory: Biomarkers – inflammatory markers (CRP, PCT)

Remdesivir dose:
Baseline weight < 40 kg and age ≥ 14 days, loading dose of 5 mg/kg IV on Day 1 and 2.5 mg/kg IV Days 2-10 (or until discharge – whichever comes first) and ≥ 40 kg is loading dose of 200 mg and maintenance of 100 mg.

RDV Pediatric Regulatory Timeline – FAST!!




THANK YOU



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I-ACT FOR CHILDREN VIRTUAL WORKSHOP

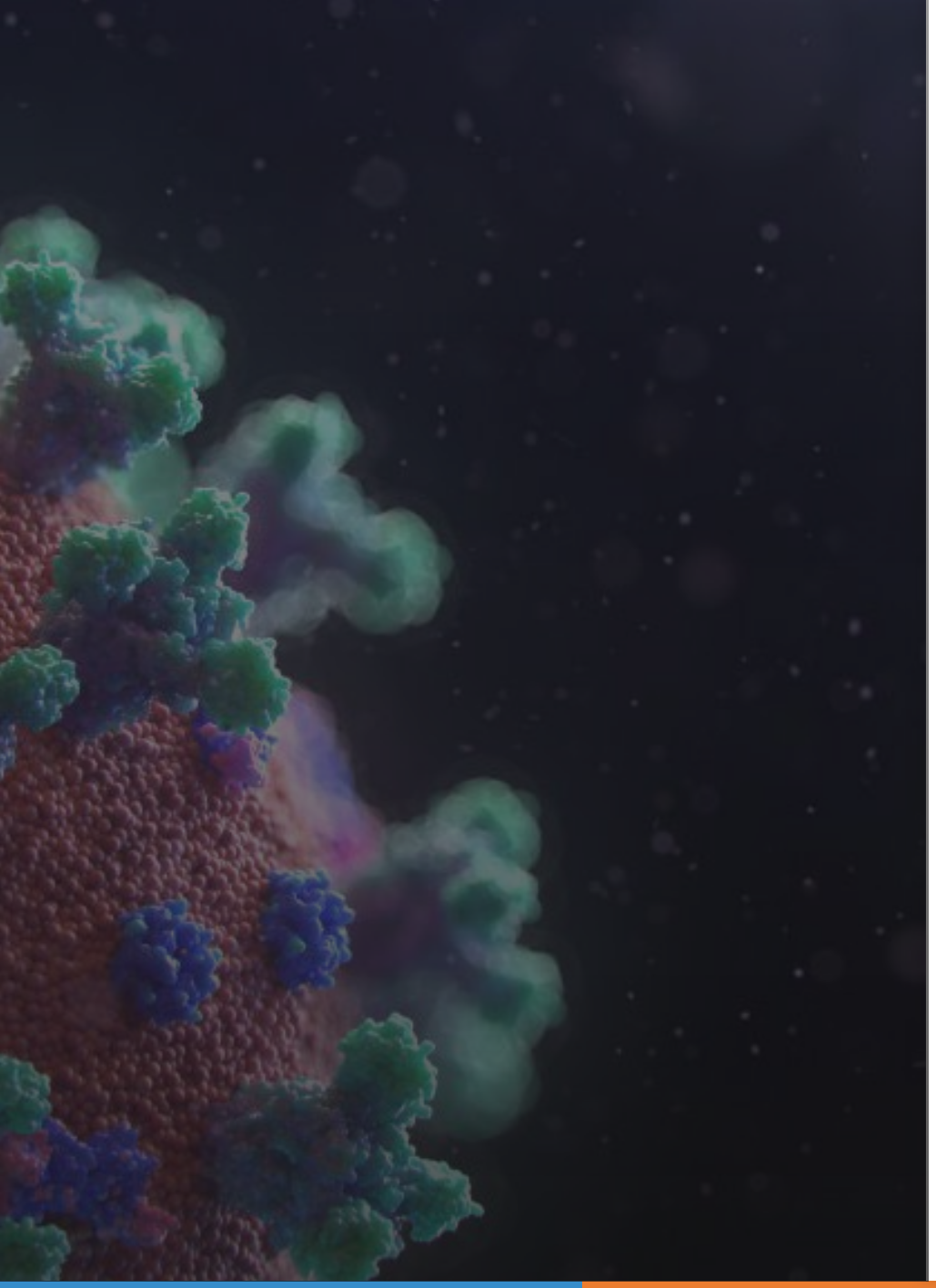
ANTIVIRAL DRUG DEVELOPMENT: DRUGS AND BIOLOGICS

Yodit Belew, MD

SENIOR MEDICAL OFFICER

DIVISION OF ANTIVIRAL PRODUCTS

CDER, US Food and Drug Administration



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DEVELOPMENT OF IMMUNOMODULATORS

Wallace Crandall, MD, MMM

MEDICAL FELLOW

SENIOR MEDICAL LEADER FOR PEDIATRIC IMMUNOLOGY

Eli Lilly and Company

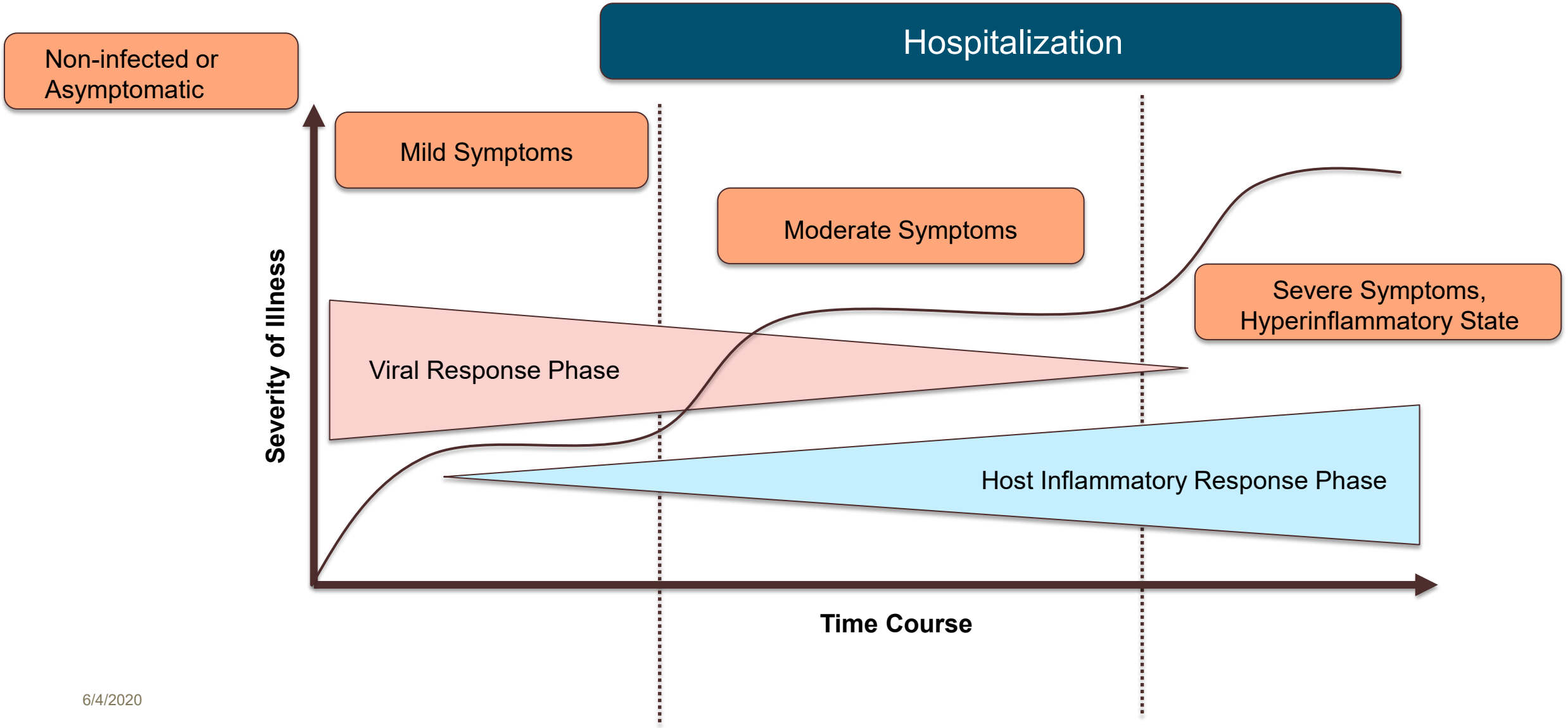
Overview

- Target sub-population(s)
  - “Traditional” (pulmonary, adult-like) presentation
  - Multi-System Inflammatory Syndrome in Children (MIS-C)
- Select study design issues
  - Study population
  - Timing of pediatric trials

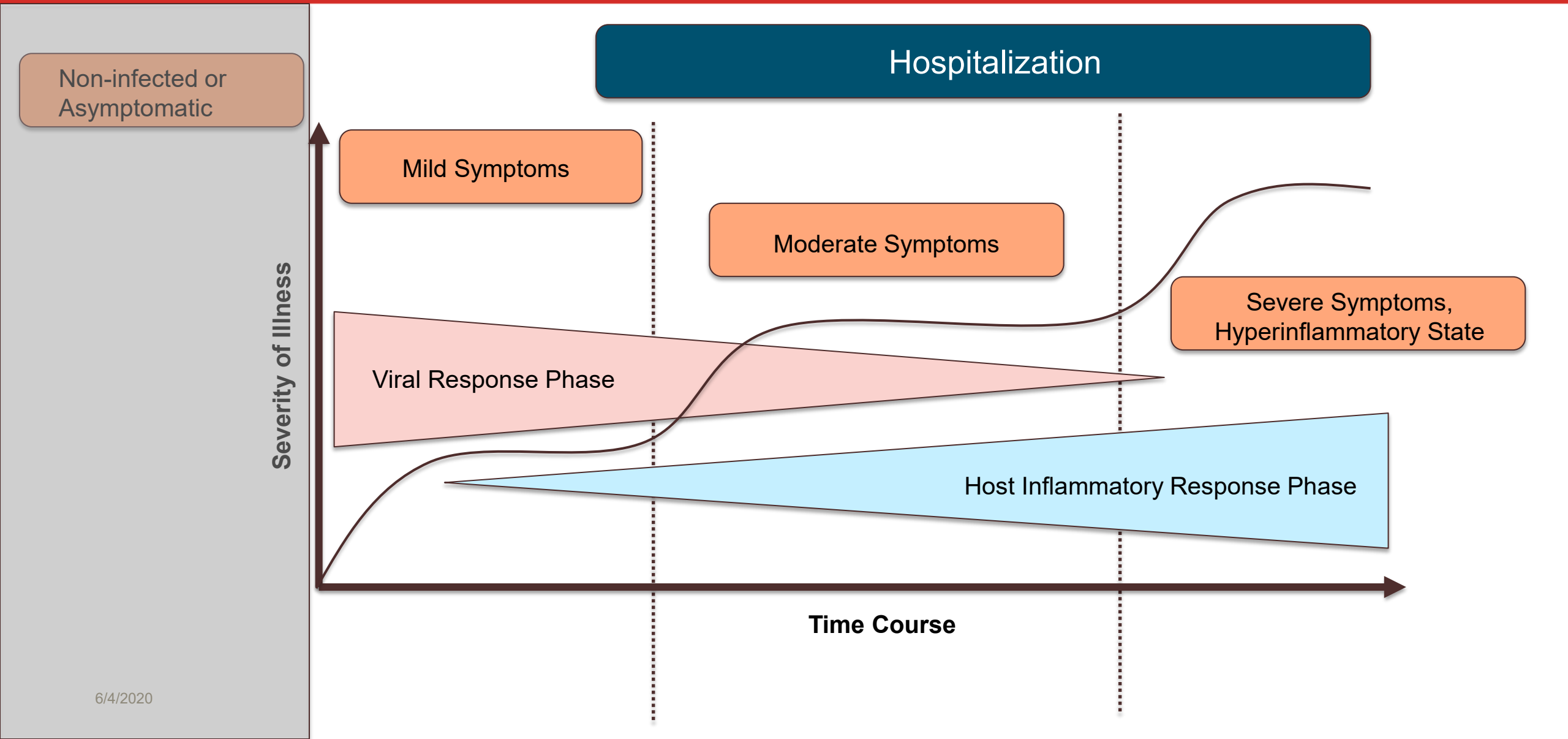
Overview

- Target sub-population(s)
  - “Traditional” (pulmonary, adult-like) presentation
  - Multi-System Inflammatory Syndrome in Children (MIS-C)
- Select study design issues
  - Study population
  - Timing of pediatric trials

Disease Stage



Disease Stage



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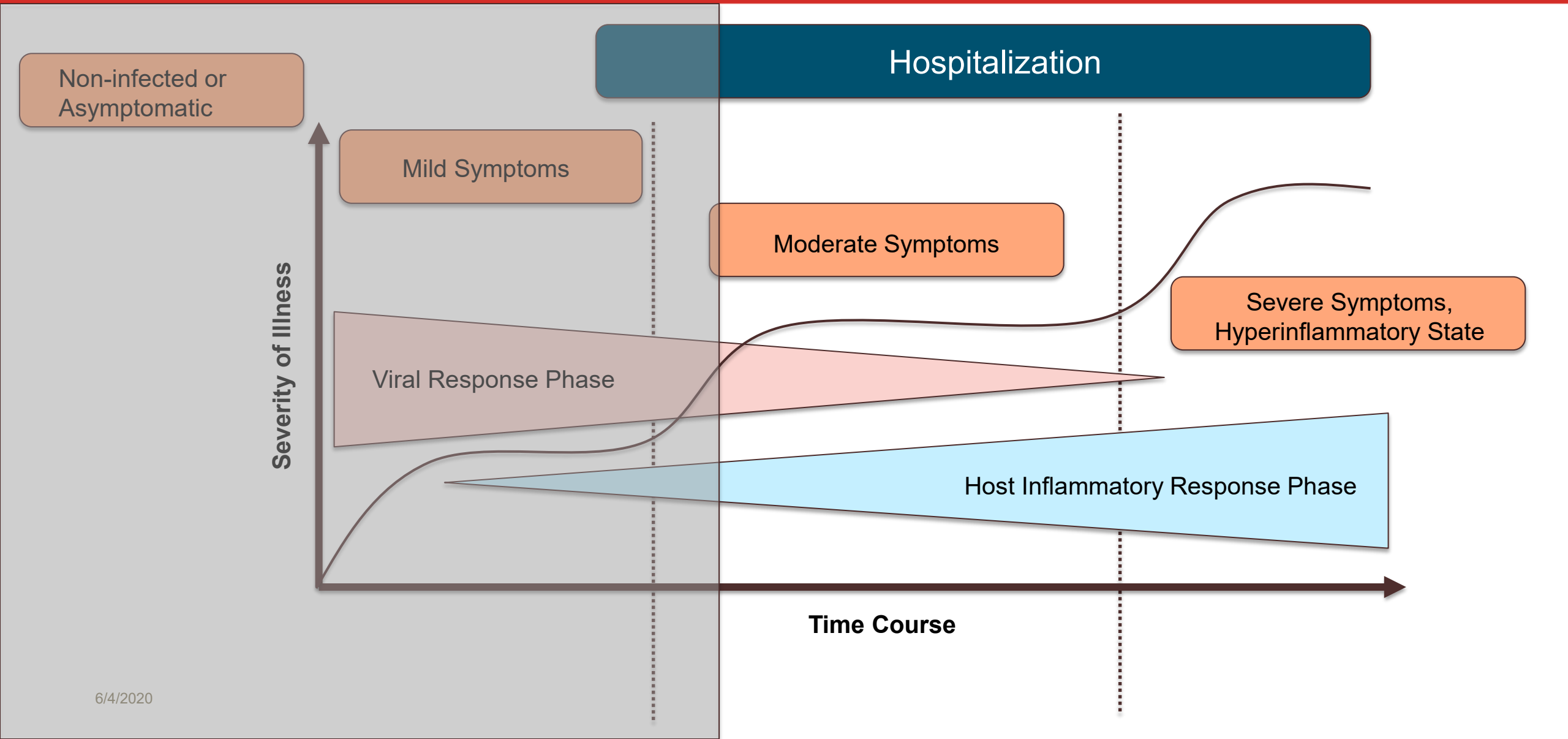

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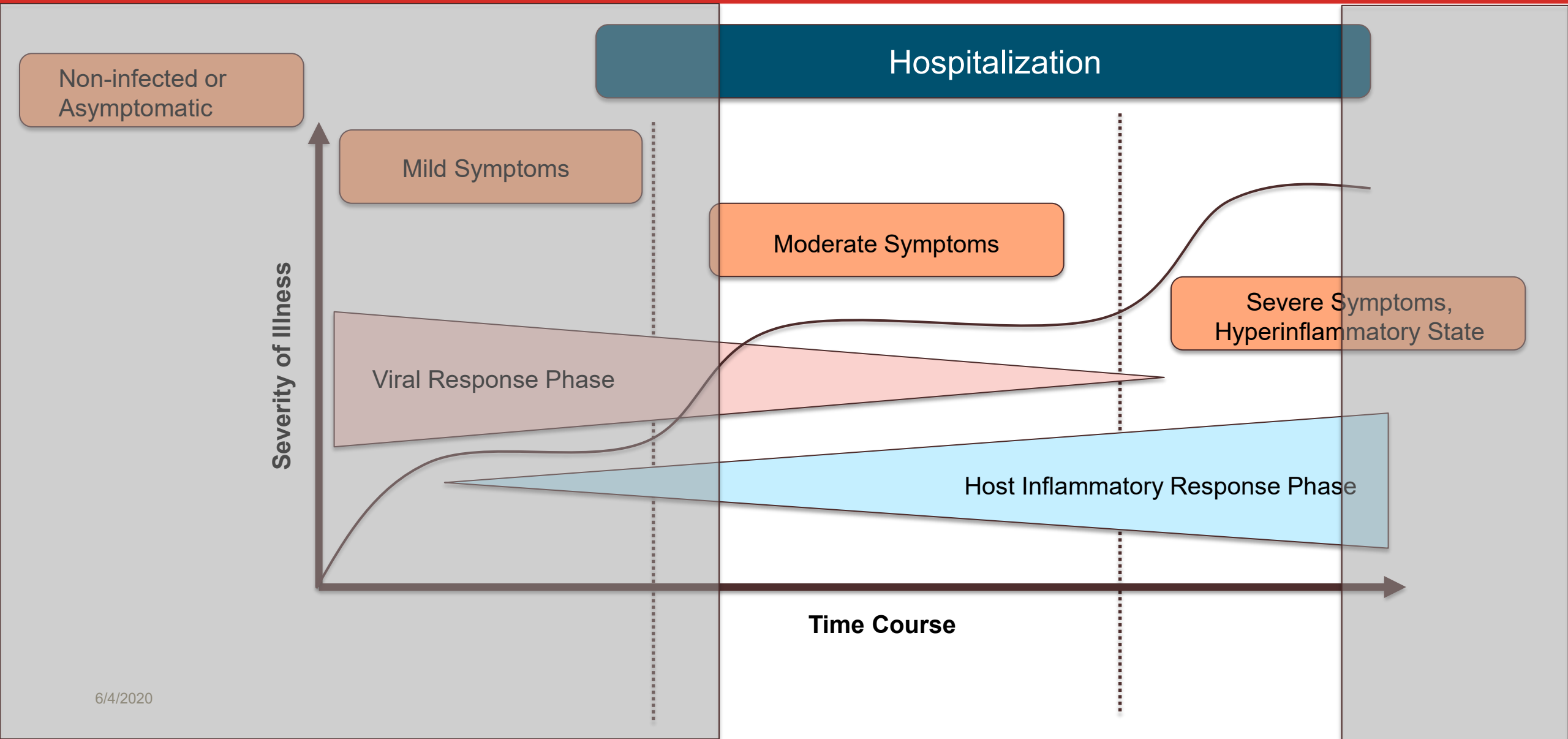
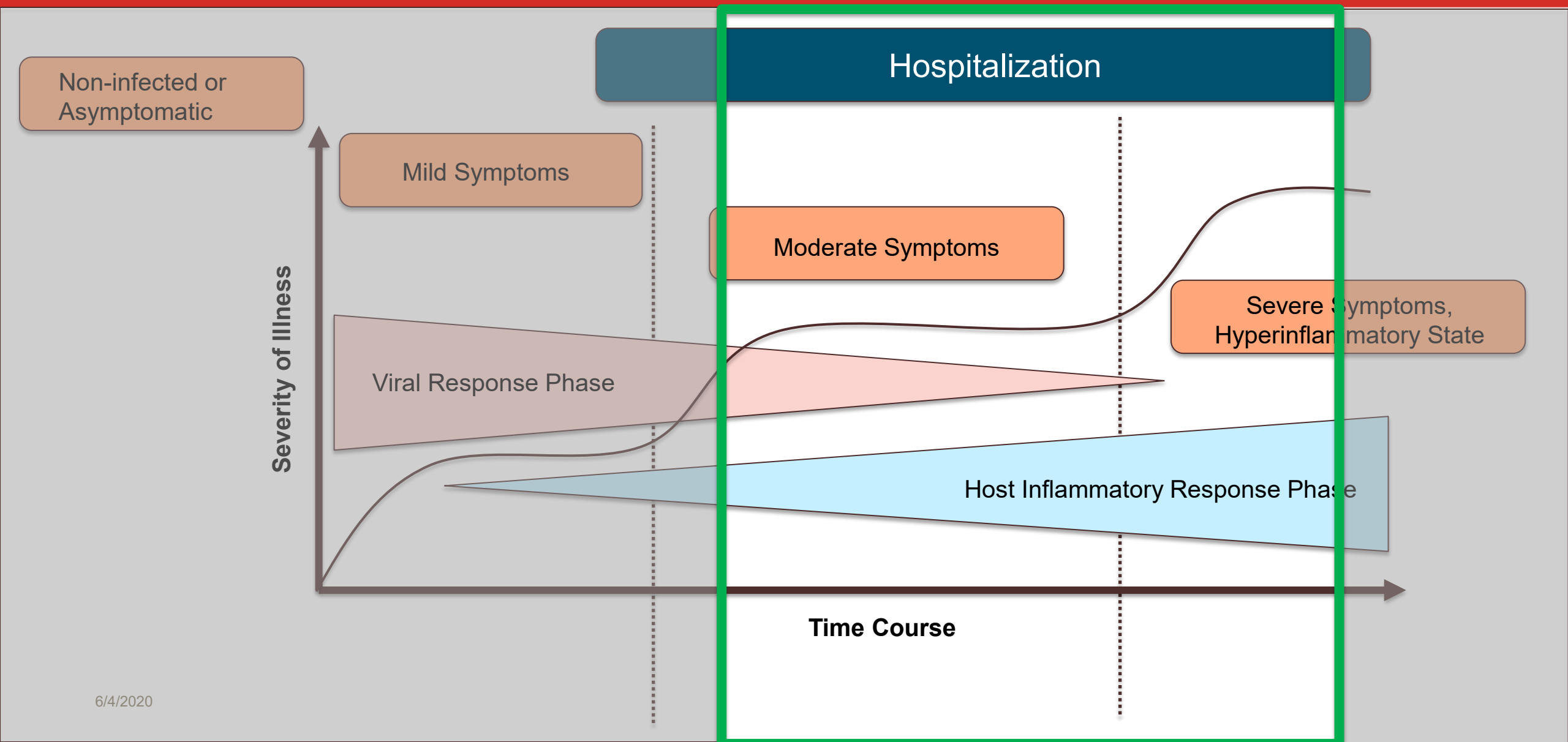


Immunomodulator Window?



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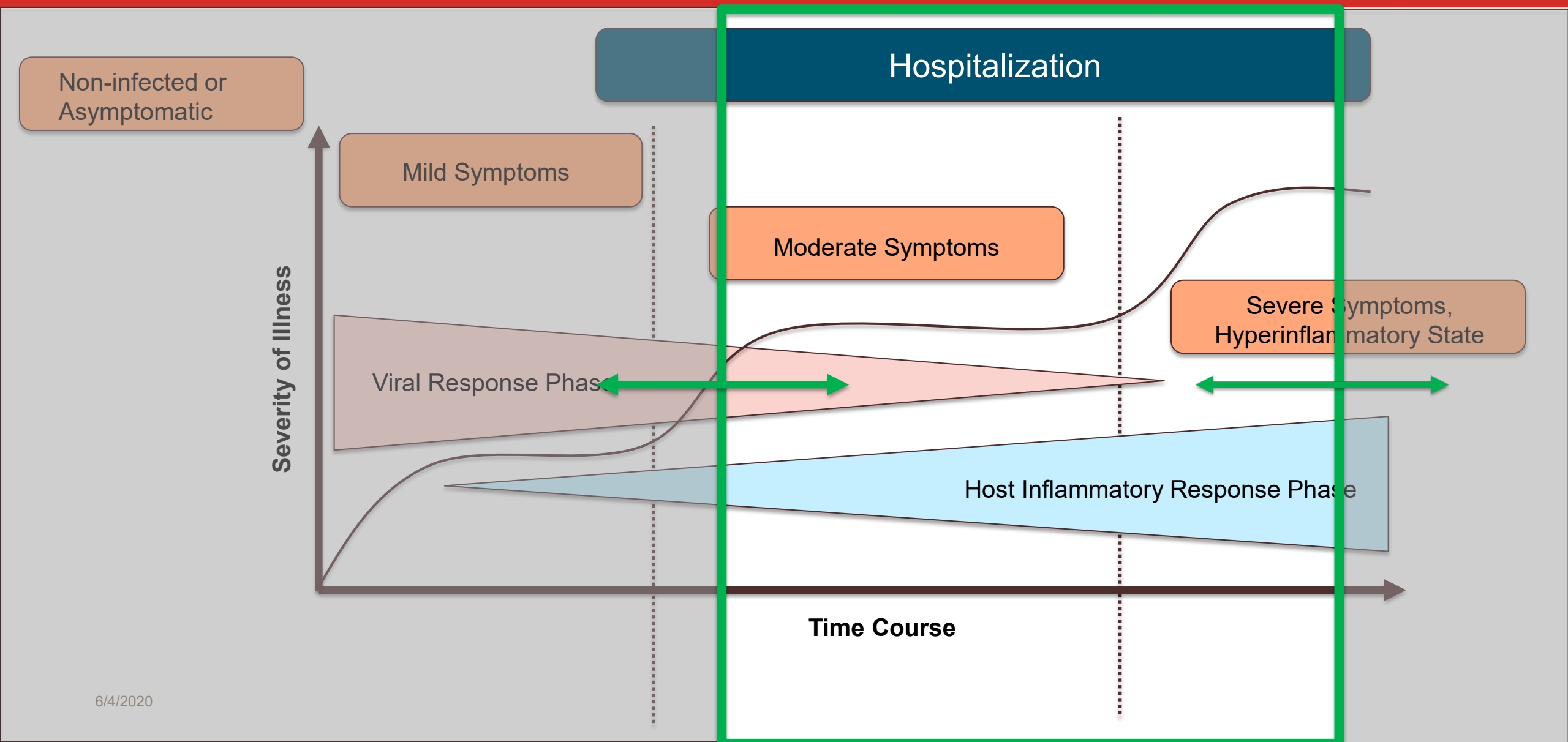

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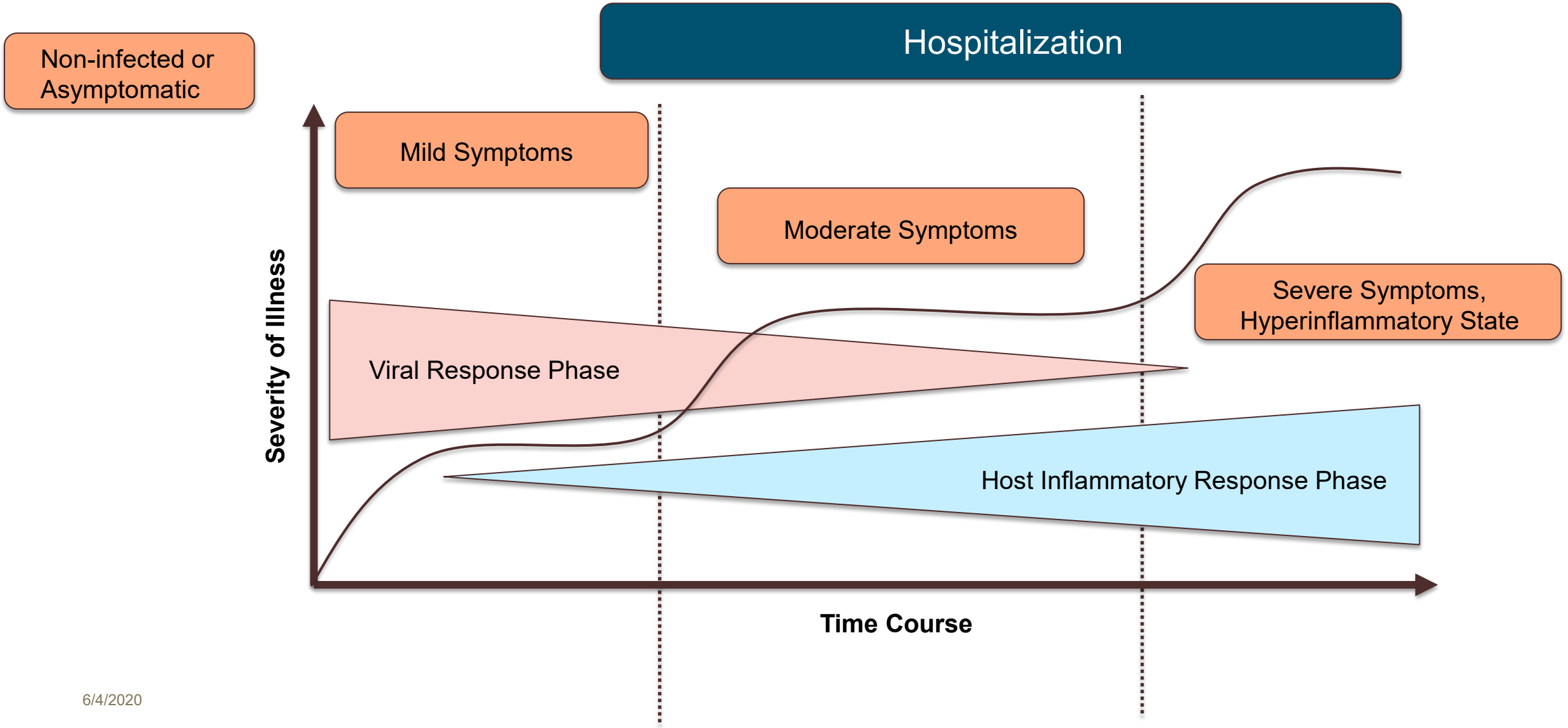

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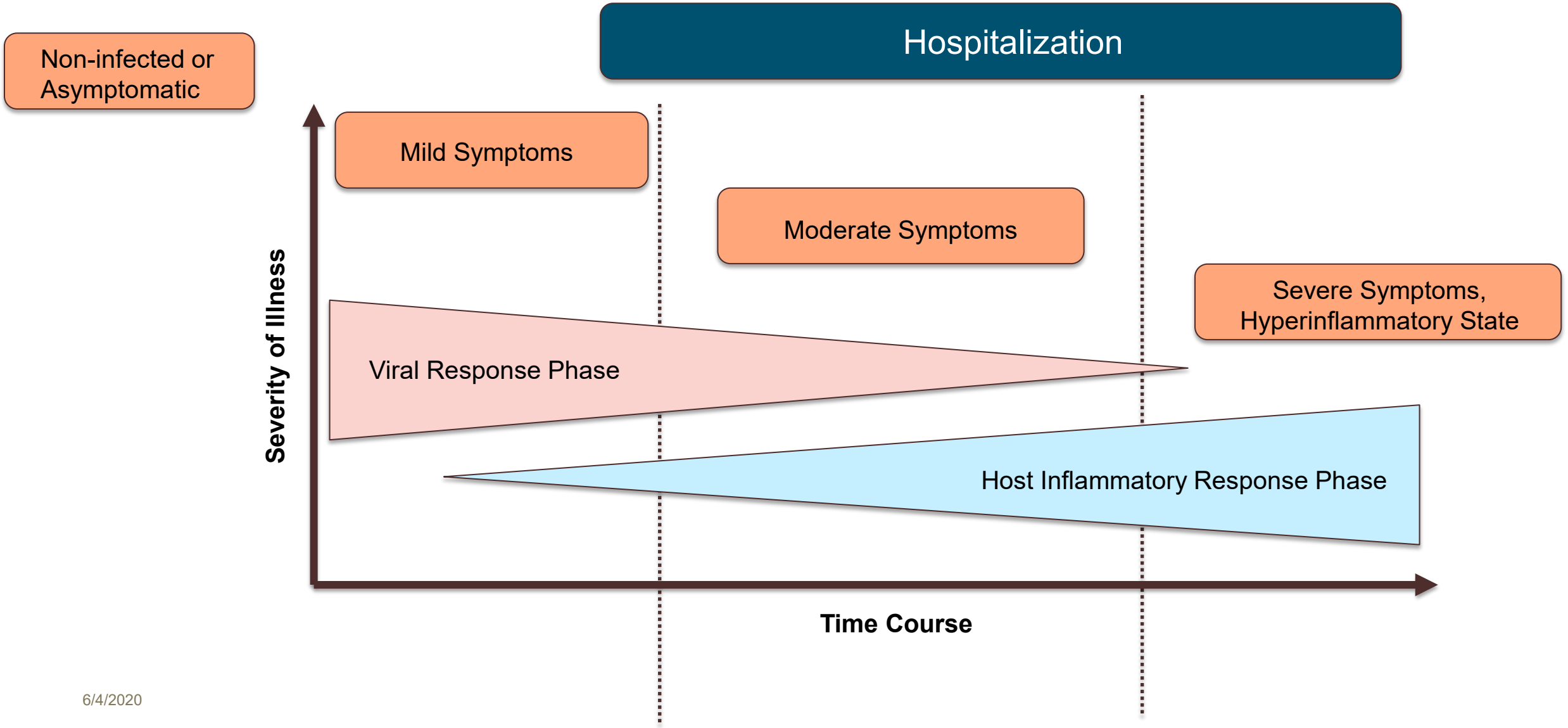
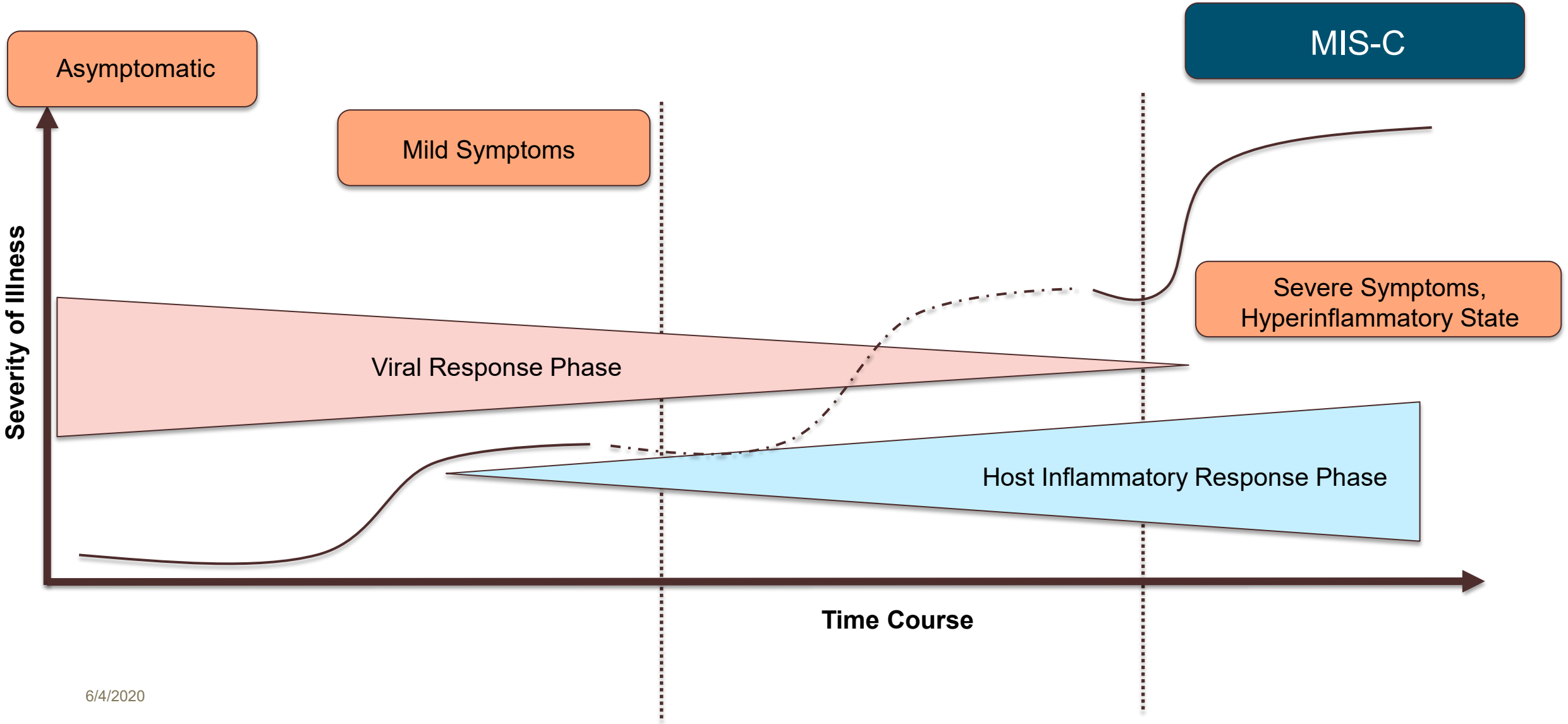


Unclear Disease Stages?



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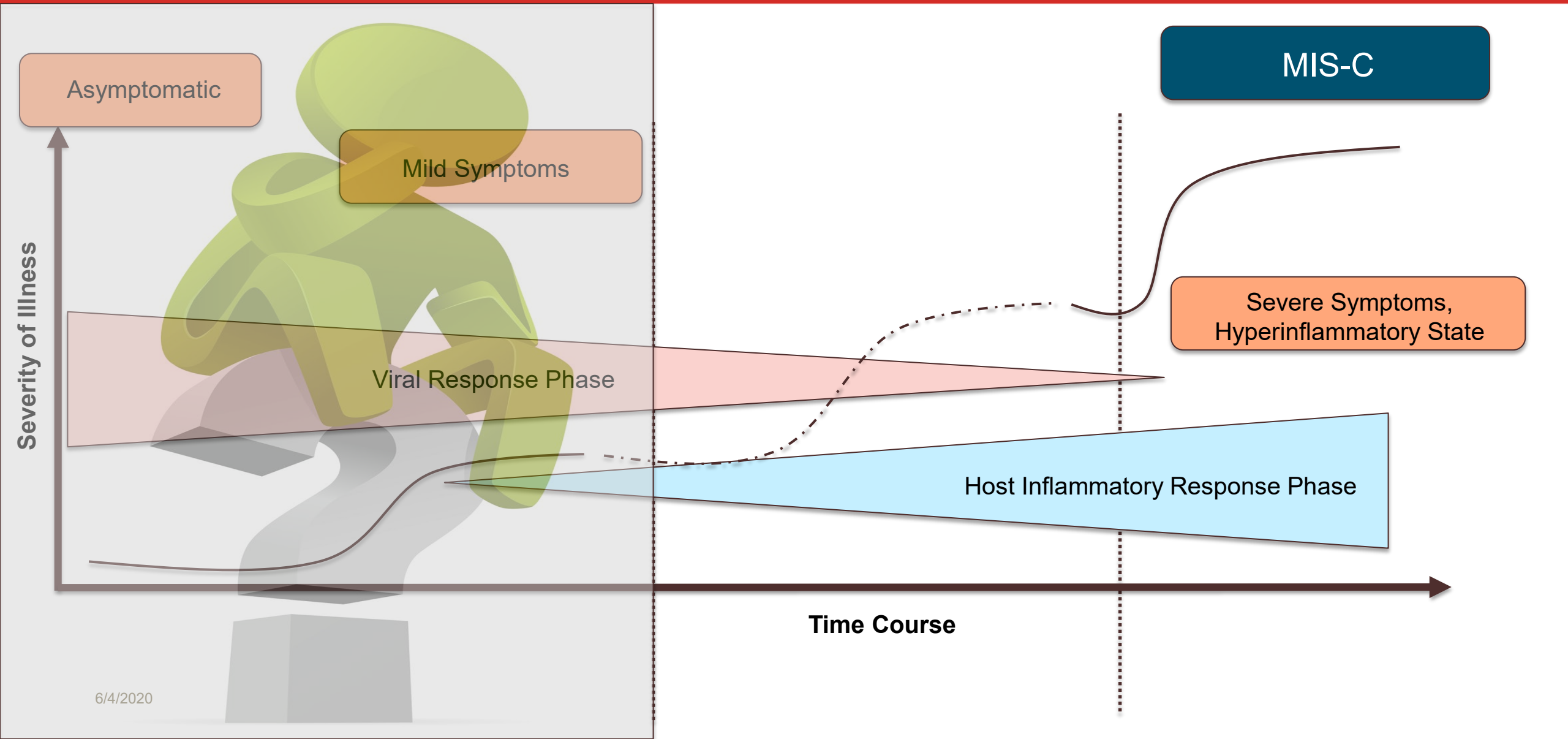

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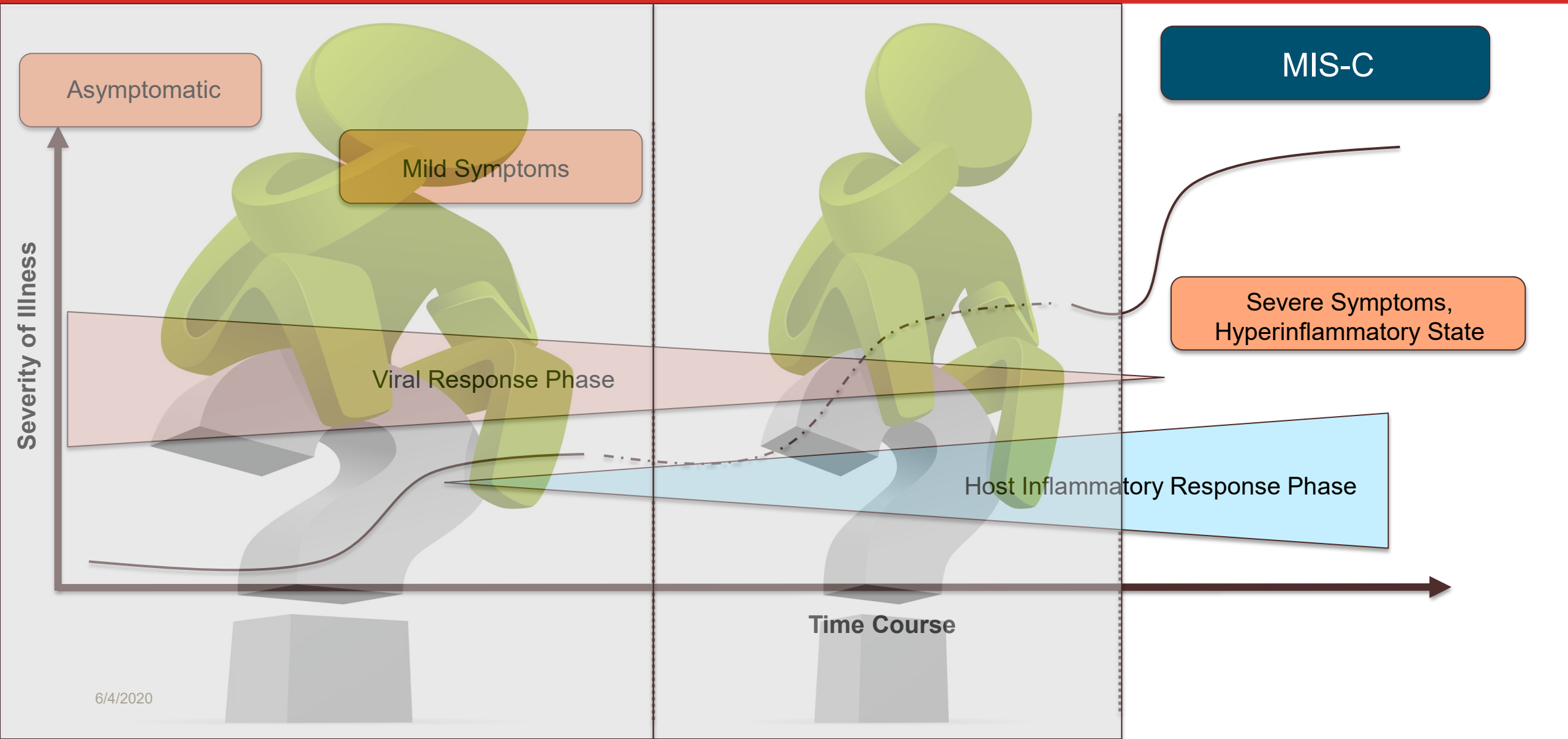

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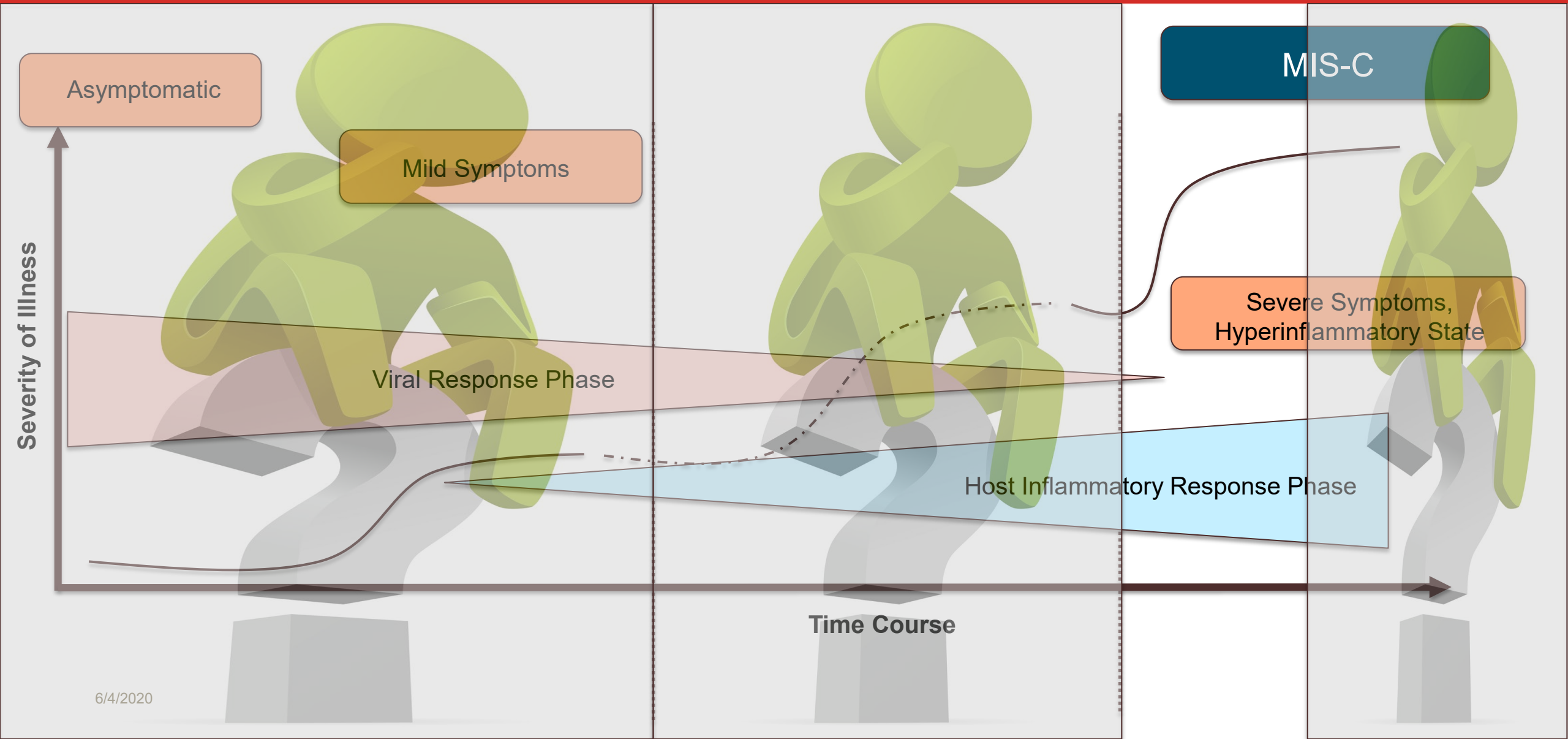

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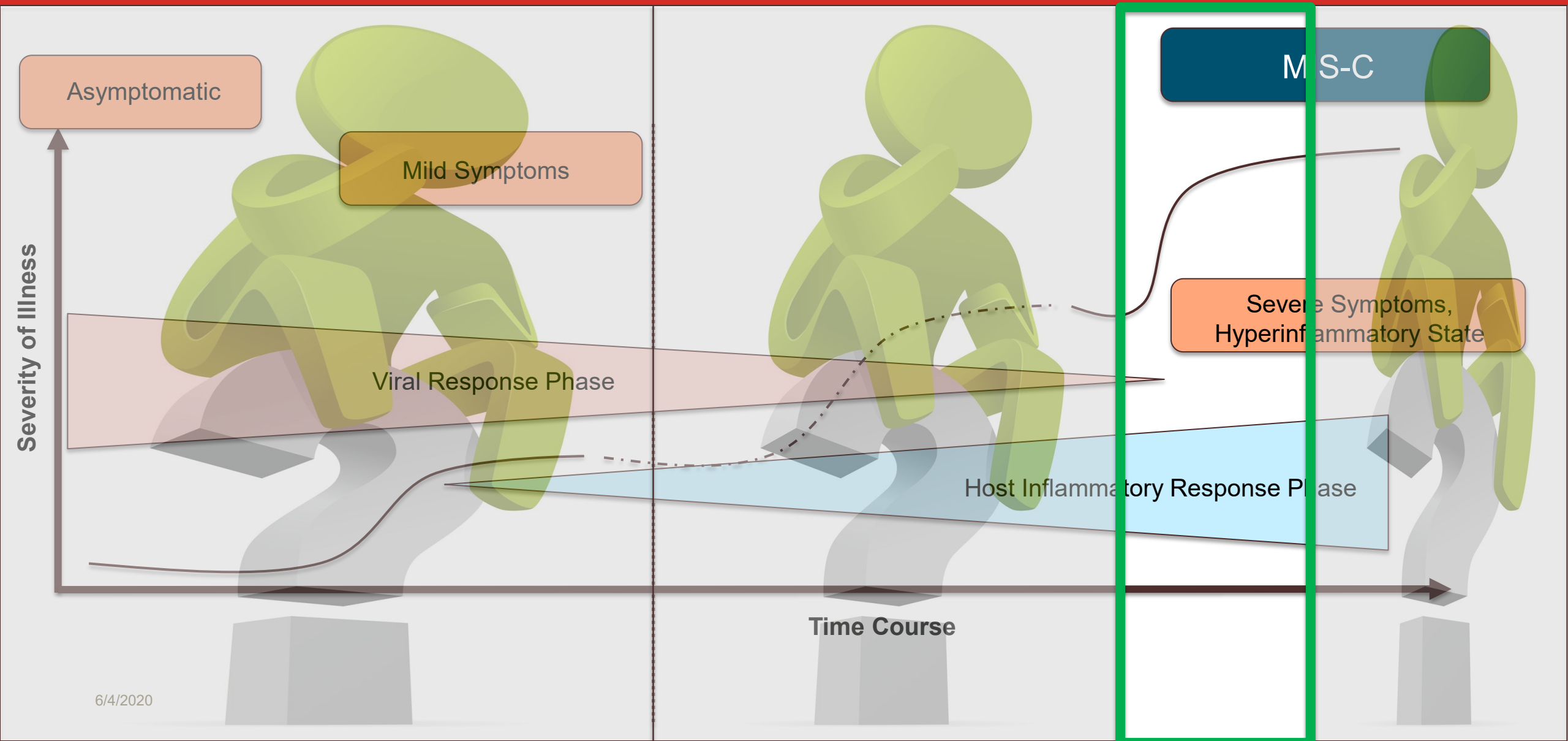

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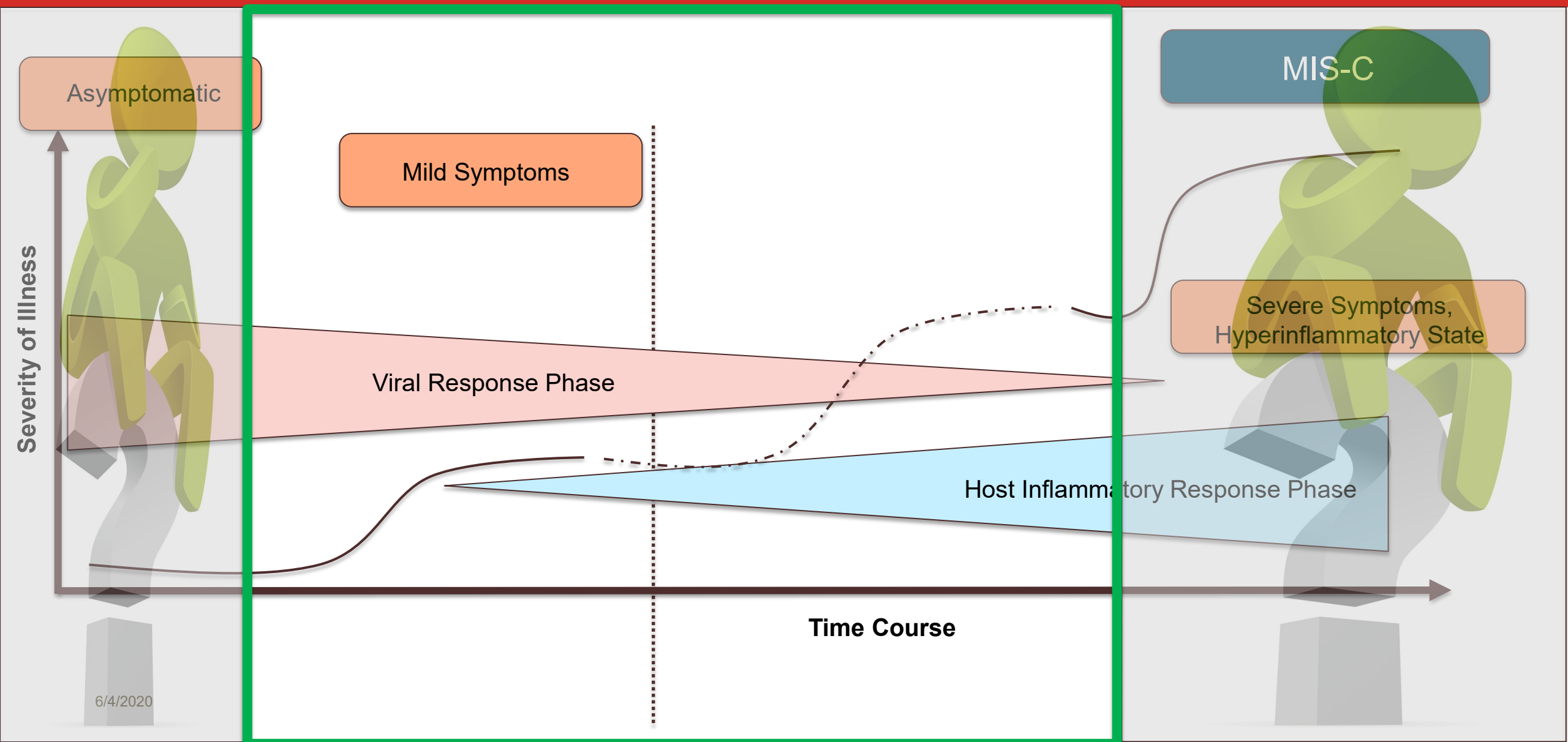


Overview

- Target sub-population(s)
  - “Traditional” (pulmonary, adult-like) presentation
  - Multi-System Inflammatory Syndrome in Children (MIS-C)
- Select study design issues
  - Study population
  - Timing of pediatric trials

Study Design

Study Population: Similarity of Immune Response

- Between adults and children with “traditional” COVID-19?
  - Inclusion of adolescents in adult trials
  - Bayesian borrowing
- Between children with “traditional” COVID-19 and children with MIS-C?
  - Two separate study groups

Study Design

US Study Population: Available Patients

- *Reported* to date:
  - 147 hospitalizations
  - 74 ICU admissions (140-166 hospitals)
  - 8+ deaths
  - Most common in < 1yr, medically complex, malignancy (less information on pK, dosing, risk/benefit)
  - > 100 MIS-C

CDC; Pathak et.al., JPHMP 2020; Shekerdemian et. al., JAMA Peds 2020

Study Design

- What is outcome of interest?
  - Prevention of death (8+ reported deaths)
    - Risk/Benefit of IMs
- Number of patients/study drug?
  - Full extrapolation for anti-viral drugs
  - Several IMs already in testing in adults

Study Design

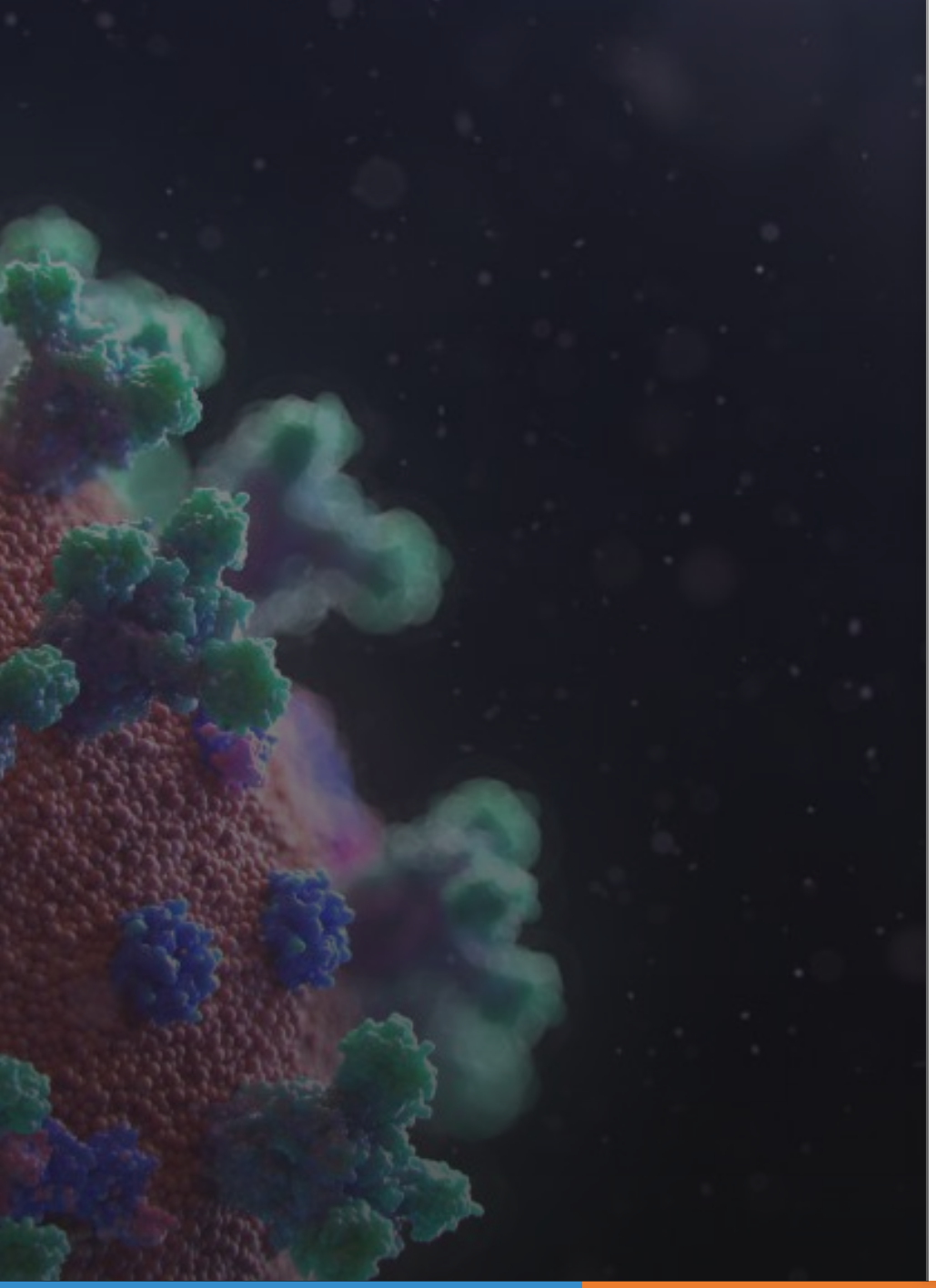
Timing: Concurrent with adult trials

- Time to develop and align pediatric programs
  - Rapid adult development
  - Align on global plan (9 trials on CT.gov, 0 (1) PIPs)

Study Design

Timing: After adult trial(s)

- IM vs SOC
  - "SOC" may already include the study drug if adult trial data is already available, particularly for ill patients (i.e. those needing IMs)
- Open-label
  - Bayesian approach with comparison to?
    - Adult placebo
    - Adult efficacy results



INSTITUTE FOR ADVANCED CLINICAL TRIALS FOR CHILDREN

DEVELOPING PEDIATRIC TREATMENTS FOR COVID-19

I-ACT FOR CHILDREN VIRTUAL WORKSHOP

DEVELOPMENT OF IMMUNOMODULATORS

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Disclosure Statement

- I have no financial interests or conflicts of interest with any pharmaceutical company to disclose relating to this presentation

- This presentation reflects the views of the author and should not be construed to represent FDA's views or policies

Challenges with Clinical Development for Rare Pediatric Diseases

- Small population
- Heterogeneous diseases
- Pathogenesis and natural history not fully elucidated
- Lack of regulatory/drug development precedent
- Endpoints and outcome assessments often uncertain

Extrapolation of Efficacy

The foundation of pediatric extrapolation is the degree of response similarity between adults and pediatric patients, which is informed by:

Disease Similarity

- Natural history
- Pathophysiology
- Diagnostic criteria
- Clinical management
- Response to other therapies
- Placebo response
- Similar endpoints

Pharmacology

- ADME
- Mode of action
- Ontogeny of targets
- Genetics/genomics

Extrapolation of Efficacy:

Disease/response "similarity" is a continuum

Different	Dissimilar	Similar	Same
No overlap between adult and pediatric condition	Some degree of overlap with significant differences between adult and pediatric condition	Large degree of overlap with some differences between adult and pediatric condition	Significant overlap; no known significant differences between adult and pediatric condition

Increasing relevance of adult information to pediatric population with increasing confidence in similarity between adult and pediatric condition

AWC pediatric trial(s)

Bridging biomarker, Bayesian borrowing, etc.

Exposure matching

Extrapolation of Efficacy

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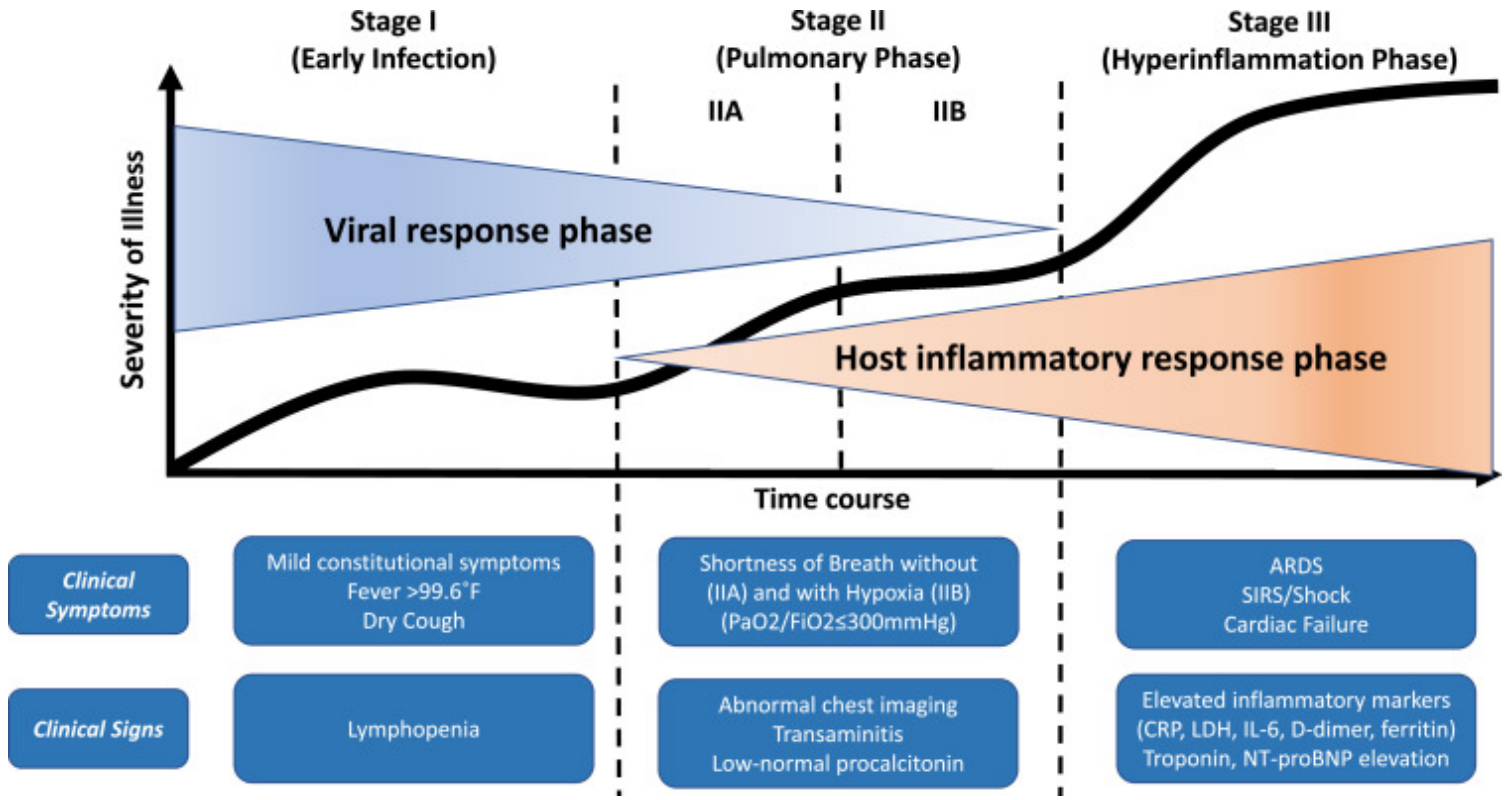
Exposure matching

Challenges with Efficacy Extrapolation for Immunomodulators in Children with COVID-19

- Rapidly evolving understanding of the natural history of COVID-19 in both adults and children
  - Highly variable disease course
  - Timing of therapeutic intervention
  - No established endpoints
- Evolving treatment guidance
- Complexity of underlying inflammatory process
  - When does protective inflammation turn into destructive one

Challenges with Efficacy Extrapolation for Immunomodulators in Children with COVID-19



https://www.jhltonline.org/article/S1053-2498(20)31473-X/fulltext

A minority of COVID-19 patients will transition into the third and most severe stage of the illness, which manifests as systemic hyperinflammation syndrome

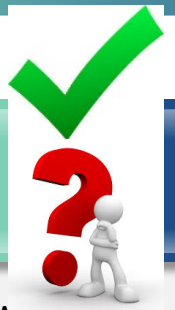
Inflammatory cytokines and biomarkers such as IL-1, IL-6, GM-CSF, macrophage inflammatory protein 1-α, TNF-α, C-reactive protein, ferritin, and D-dimer are significantly elevated in patients with more severe disease

Challenges with Efficacy Extrapolation for Immunomodulators in Children with COVID-19

- Pediatric-specific manifestations, i.e. multisystem inflammatory syndrome in children (MIS-C)*
- Prospect of direct benefit
- Feasibility of conducting dedicated clinical studies in children

*https://emergency.cdc.gov/han/2020/han00432.asp

Extrapolation of Efficacy



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Increasing relevance of adult information to pediatric population with increasing confidence in similarity between adult and pediatric condition

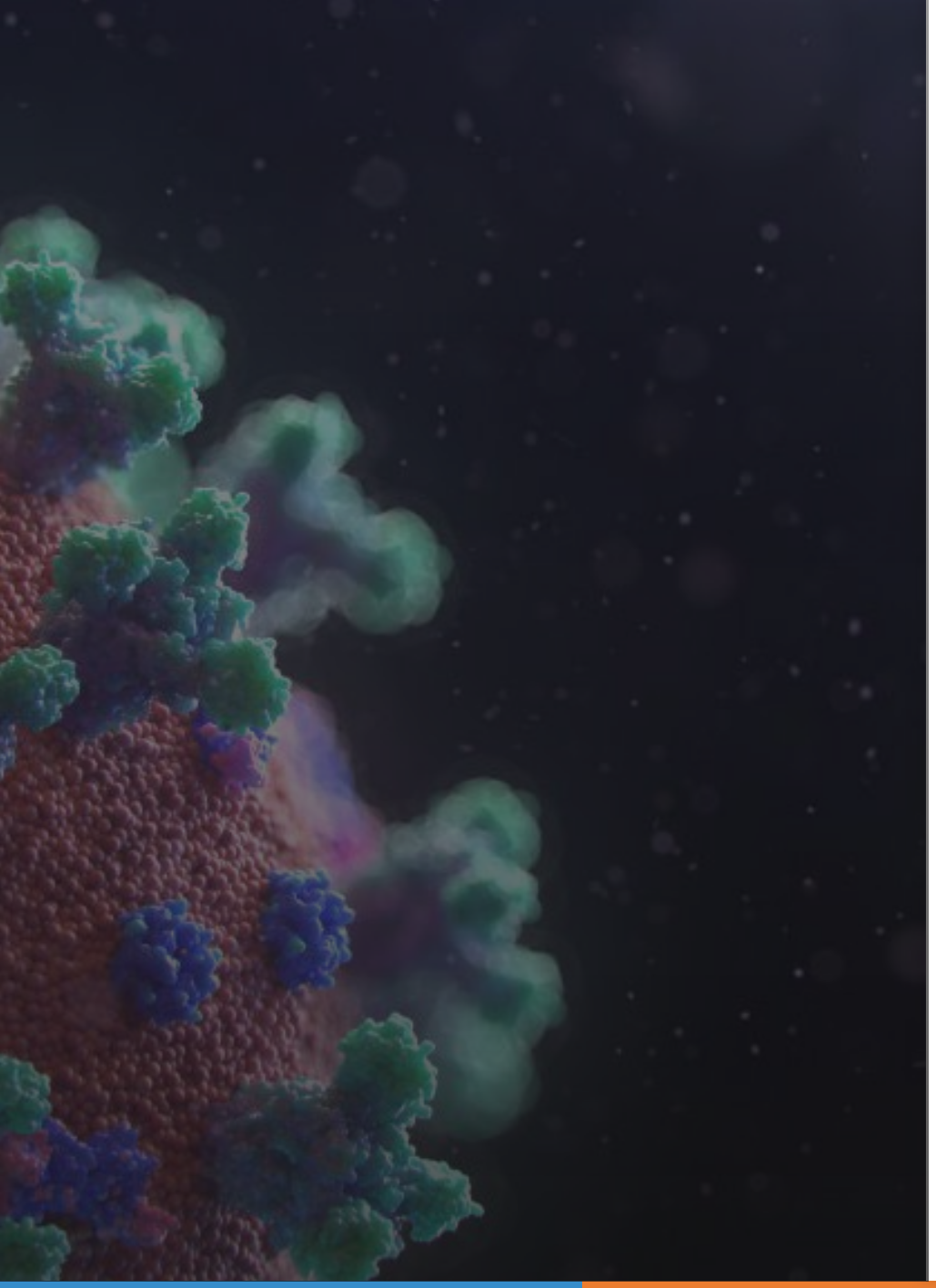
AWC pediatric trial(s)

Bridging biomarker, Bayesian borrowing, etc.

Exposure matching

Considerations for Immunomodulators in Children with COVID-19

- Need for multidisciplinary approach
- Improved understanding of disease manifestations and natural history
- Innovative approaches to assessment of efficacy
- Assessment of safety and, if applicable, immunogenicity
- Coordinated global efforts and multi-stakeholder engagement



INSTITUTE FOR ADVANCED CLINICAL TRIALS FOR CHILDREN

DEVELOPING PEDIATRIC TREATMENTS FOR COVID-19

I-ACT FOR CHILDREN VIRTUAL WORKSHOP

RESEARCH ETHICS IN A PANDEMIC

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No disclosures or financial conflicts of interest

POLICY FORUM | RESEARCH ETHICS: COVID-19

Against pandemic research exceptionalism

Alex John London[1], Jonathan Kimmelman[2]

+ See all authors and affiliations

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DOI: 10.1126/science.abc1731

The “exceptionalist” argument….

- Things are really bad
- Lots of people are dying
- Therefore, we need to throw research standards out the window
- Bad research is ok because some results are better than none.

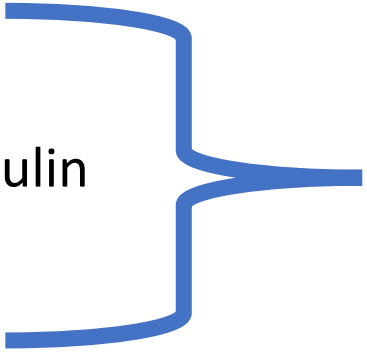
The “exceptionalist” argument….

- Things are really bad
- Lots of people are dying
- Therefore, we need to throw research standards out the window
- Bad research is ok because some results are better than none.

- RESPONSE:
  - Bad data is worse than no data
  - Clinicians have an ethical obligation to be honest about uncertainty and to do research to answer important questions

COVID: What do we need to know

- A new disease
- Plenty of therapies – some new drugs, some re-purposed
  - Chloroquine
  - Steroids
  - Immunoglobulin
  - Antivirals
  - Antibiotics



can be used in various combinations

- Plenty of off-label use
- Natural history varies widely – from asymptomatic infections to complex chronic disease.
- Don’t know which drugs for which patients at what dose or when

COVID highlights existing problems

- Much clinical practice is not evidence-based
- Evidence is expensive:
  - Good studies are difficult economically, technically, psychologically, ethically
- Lots of bad research
- The problems of doing research on COVID highlight the problems doing any clinical research: a broken system

The central problem

- Belief in a clear distinction between “research” and “practice”
- Written into the Belmont report and Common Rule
- Makes clinical innovation easy and rigorous research difficult

An analogy

- What is “Practice?”
  - An intervention to provide diagnosis, preventive treatment, or therapy;
  - Designed solely to enhance the well-being of an individual patient
  - Must have a reasonable expectation of success.

- What is “Practice?”
  - An intervention to provide diagnosis, preventive treatment, or therapy;
  - Designed solely to enhance the well-being of an individual patient
  - Must have a reasonable expectation of success.

- What is ”Research”
  - “An activity, usually with a formal protocol, designed to test a hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge.”

Ethical implications

- "…a fundamental difference between the obligations of clinicians and those of researchers. Doctors are required, even in the face of uncertainty, to do what they view as being best for their individual patients. Researchers do not have that same obligation."

  - Letter from OHRP to University of Alabama at Birmingham. http://www.hhs.gov/ohrp/detrm_letrs/YR13/jun13a.pdf. Accessed 11-19-13.

The alternative view of a clinical researcher

- “I have a fiduciary obligation to provide optimal treatment. I also have a moral obligation to know what the optimal treatment is. And I have a moral obligation to keep trying to find out what the best treatments may be.”
    - Barrington K. www.neonatalresearch.org, 9/18/2013

Intertwined obligations

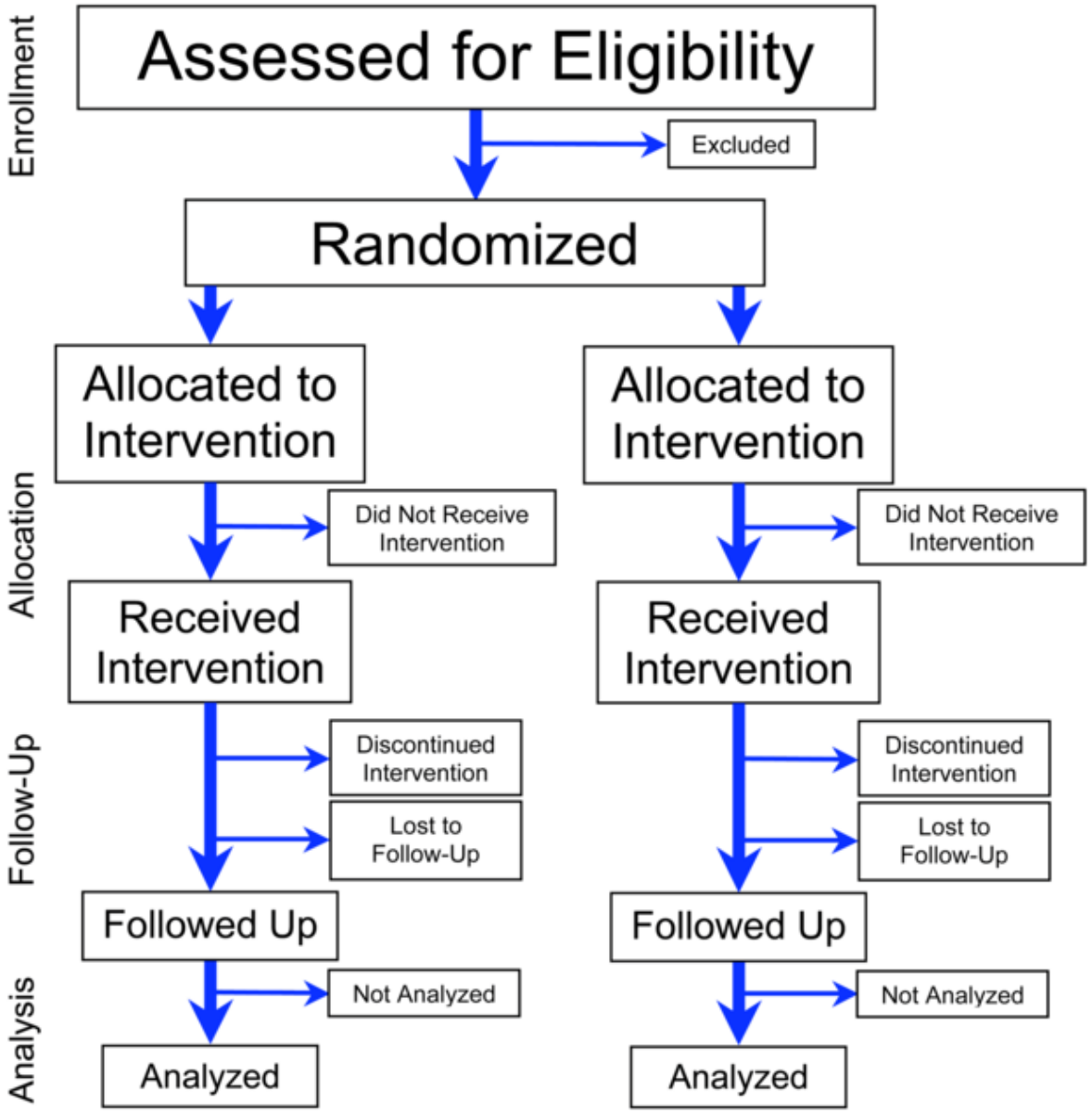
- “The multiple purposes of medical practice, caring for patients, advancing science, improving the health of the community, nations, and future generations cannot be separated clearly.”
- “Research and therapy, pursuit of knowledge and treatment, are not separate but intertwined.”

    - Katz J. The education of the physician-investigator. Daedalus, 1969; 98, 480-501.

Current gray zones

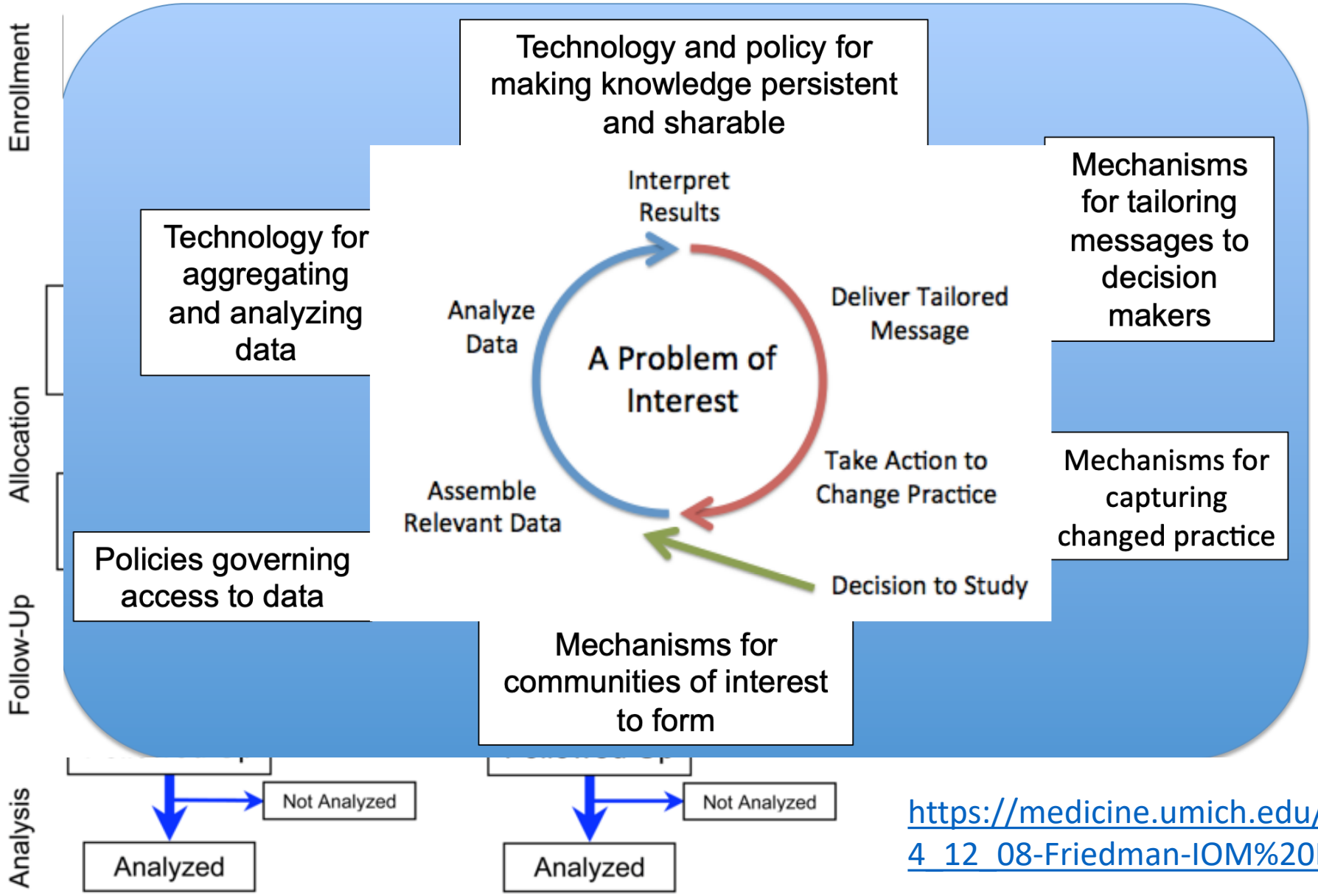
- Learning health care systems
  - Unstudied clinical care is the highest risk activity.
  - Ongoing, embedded research is the mechanism for making that care safer.
  - Doctors and patients both have an obligation to participate.
- Pragmatic clinical trials
  - Not designed to rigorously test a single hypothesis.
  - Instead, they seek to compare the benefits, burdens, risks, and (sometimes) costs of interventions as delivered in the real world, using endpoints that matter to patients and policymakers.

    - Lantos, Perspectives in Biol and Med, 2020.



The traditional RCT

The Learning Health Care System



https://medicine.umich.edu/sites/default/files/2014_12_08-Friedman-IOM%20LHS.pdf

Implications for pediatric research

- Research is considered a risky activity
- Children are considered a vulnerable population
- Thus, they need special protections from the risks of research
- Studies should be done first in adults.

BUT….

- Too much protection will also foreclose the possibility of children benefiting from research.

Why we need pediatric studies

- Not just small adults
  - The disease is different
  - The responses to treatment may be different
  - Children need to not only be included in clinical trials; they may need trials designed specifically for them.
- Can IRBs be convinced?

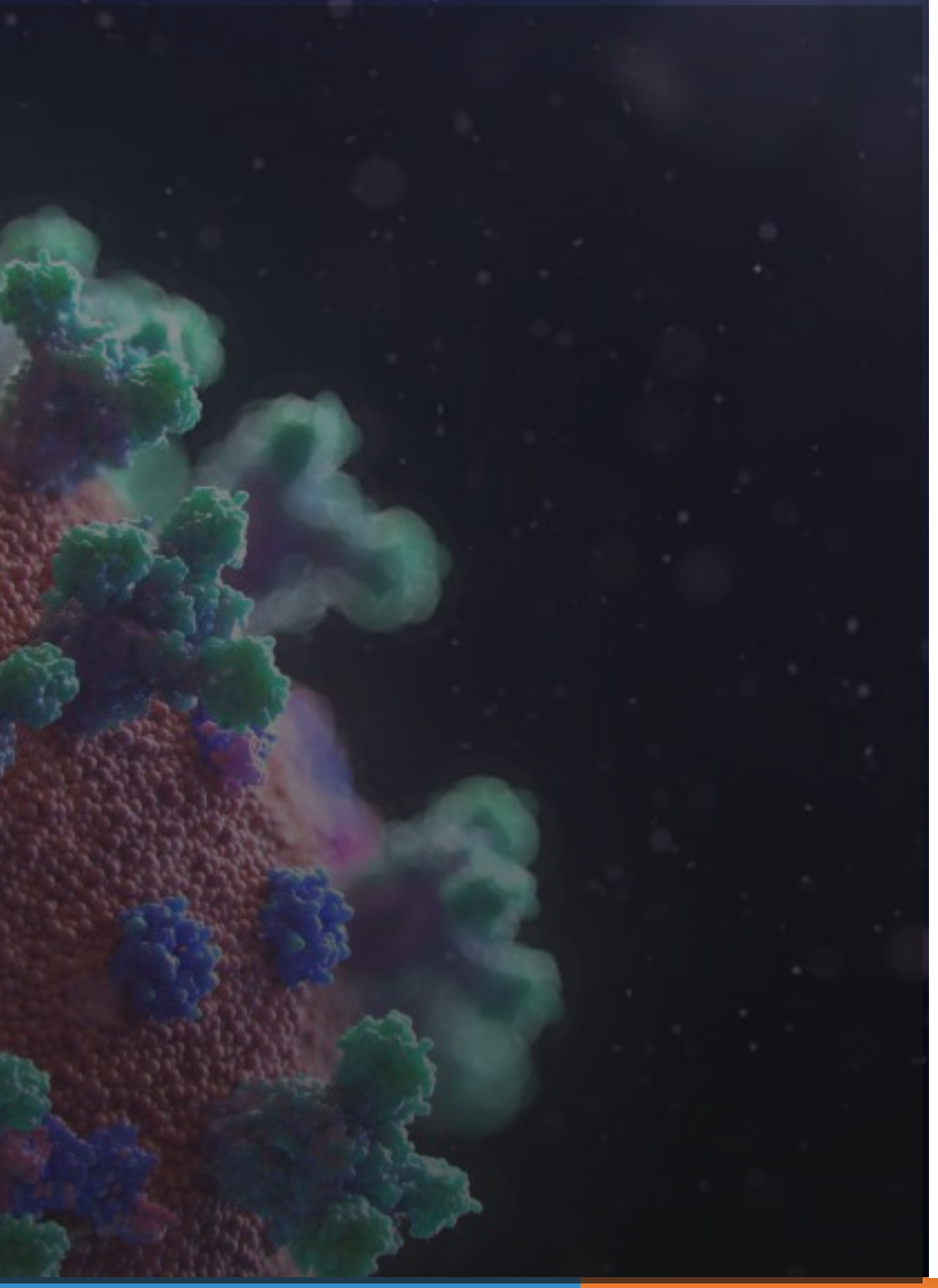
To convince IRBs…

- Children get COVID
- They can be very sick
- The disease is different than disease in adults
- If we don’t study it, children will be at high risk from non-validated tx
- Doing studies is safer than uncontrolled use of innovative tx.

- Perhaps the nudge from COVID will help us move in that direction
- Essential steps (from Rob Califf)
  - Evaluate what has/has not worked in the response to the crisis
  - Allocate funding to transition issues in evidence generation, especially at the interface of medicine and public health
  - Increase purposefulness by creating methods for deciding the most important questions and rewarding behavior that gets those questions answered quickly

    - https://rethinkingclinicaltrials.org/news/may-1-2020-advances-at-the-intersection-of-digital-health-electronic-health-records-and-pragmatic-clinical-trials-keynote-can-the-covid-19-crisis-lead-to-reformation-of-the-evidence-generation-ec/

THANKS!



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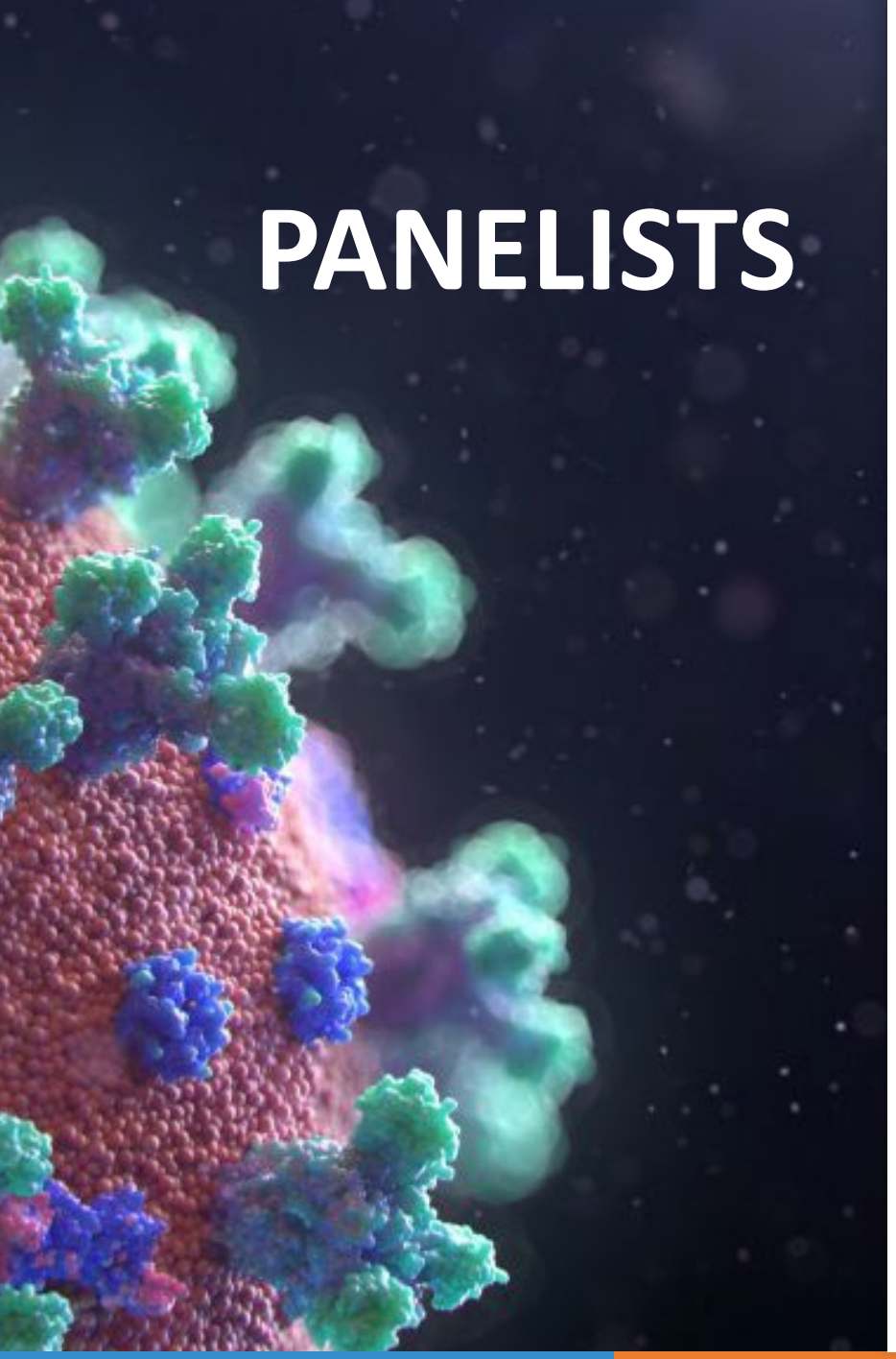
I-ACT FOR CHILDREN VIRTUAL WORKSHOP

- PART 1: COVID-19 in Children
- PART 2: Therapeutics Development

  Antiviral Agents and Immune Modulators
- **PART 3: Panel Discussion and Q&A**



PANELISTS

I-ACT INSTITUTE FOR ADVANCED CLINICAL TRIALS FOR CHILDREN

DEVELOPING PEDIATRIC TREATMENTS FOR COVID-19

I-ACT FOR CHILDREN VIRTUAL WORKSHOP

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Nationwide Children's Hospital

Keira Sorrells

FOUNDER & EXECUTIVE DIRECTOR

NICU Parent Network

Aaron C. Pawlyk, PhD

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Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health


THANK YOU
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