# Elizabeth Glaser Pediatric AIDS Foundation

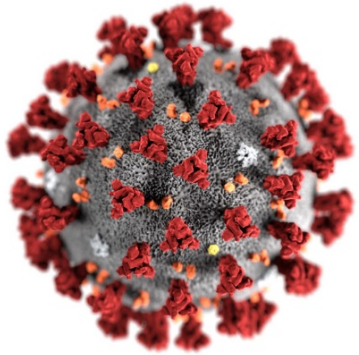
## Fighting for an AIDS-free generation

# SARS-CoV-2 Infection and COVID-19 Disease in Children - An Evolving Picture

Dr. Lynne Mofenson

This overview of relevant new data published to date will be followed by a discussion centered around how we advocate for children and their specific needs as this pandemic unfolds.

- Although everyone is muted, we encourage all to participate digitally using the **Q&A function** of Zoom.




# SARS-CoV-2 Infection and COVID-19 Disease in Children – An Evolving Picture

Lynne M. Mofenson, M.D.
Senior HIV Technical Advisor

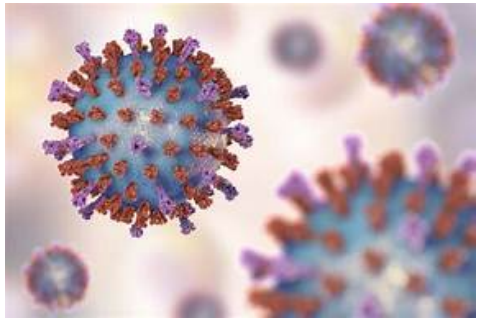
Elizabeth Glaser
Pediatric AIDS Foundation
Fighting for an AIDS-free generation

*June 7, 2020*

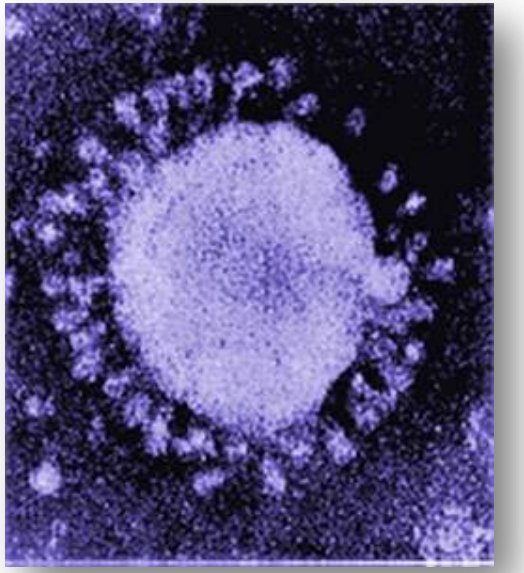

# Please Note that Data Continue to be Preliminary, Some of Poor Quality, and Change Almost Daily

**HOW TO INTERPRET THE DELUGE OF DATA?**





# Epidemiology of SARS-CoV-2/ COVID-19 in Children



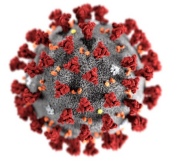
# Race/Ethnicity and SARS-CoV-2 Infection

- In US and UK, COVID-19 disease more common among black and ethnic minority adults *(Price-Haywood EG. NEJM. 2020 May 27,de Lusignan S. Lancet Infect Dis. 2020 May 15).*
- Limited data in children (most pediatric studies do not report race/ethnicity).
- 5 studies suggest similar race/ethnicity disproportonality in children:
  - Chicago: 474 children tested Mar-Apr; 25 (5.2%) were +: 6.8% black, 6.6% Hispanic, 1.7% white; on logistic regression, black race and older age were risk factors for SARS-CoV-2 positivity *(Bandi S. Pediatr Allergy Immunol. 2020 May 29).*
  - New York City: 96 children hospitalized with COVID-19, 56% were Hispanic *(Zachariah P. JAMA Pediatr. 2020 June 3; Chao JY. J Pediatr. 2020 May).*
  - Texas: 57 children diagnosed COVID-19; 37% black, 46% Hispanic, 7% white *(Foster CE. JPIDS. 2020 June 6)*
  - United Kingdom: 9/12 children with COVID-19 admitted to King's College Hospital Feb-Apr 2020 were black or other ethnic minority *(Harman K . Lancet Child Adolesc Health. 2020 May 28).*

# Race/Ethnicity and SARS-CoV-2 Infection

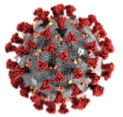
- Racial disparity in COVID-19 disease may reflect
  - socioeconomic and environmental factors increasing exposure
  - higher prevalence chronic comorbidities (e.g., hypertension) in minority populations
  - undefined biologic factors
- Disproportionate representation of children of color in both the United States and the United Kingdom is concerning given the expansion of the pandemic to Africa.
- At a minimum, studies of SARS-CoV-2 in children (and adults) should report on race/ethnicity, and further studies need to evaluate reasons for this disparity in infection/disease.

# Prevalence of COVID-19 Disease in Children



- Prevalence of COVID-19 in children has been cited as 1-2% of all COVID-19 cases.
- However, this is based on initial data from China.
- There is **no easy way** to get global age-related data for pediatric age groups.
- When examine individual data by country, prevalence may actually be higher than often cited 1-2%.
- Additionally, under-reporting of pediatric COVID-19 from Africa may be happening.

# Prevalence of COVID-19 Reported in Children – 13 Countries



| Country (date of data) | Total # cases | 0-19 Years | | 0-9 Years | | 10-18 Years | |
|---|---|---|---|---|---|---|---|
| Africa (June 6) [1] | 124,289 | 469 | **0.4%** | *189* | *0.2%* | *280* | *0.2%* |
| China (Feb 11) [2] | 44,672 | 965 | **2.1%** | *416* | *0.9%* | *549* | *1.2%* |
| Mexico (June 6) [3] | 110,026 | 3,008 | **2.7%** | *1,038* | *0.9%* | *1,970* | *1.8%* |
| Brazil (May 23) [4] | 117,598 | 4,019 | **3.4%** | *1,973* | *1.7%* | *2,046* | *1.4%* |
| United States (June 6) [5] | 1,516,175 | 64,177 | **4.2%** | | - | | - |
| EU/EEA/UK (June 4) [6] | 635,274 | 26,817 | **4.2%** | *8,906* | *1.4%* | *17,911* | *2.8%* |
| Australia (June 5) [7] | 7,173 | 336 | **4.4%** | *104* | *1.3%* | *232* | *3.1%* |
| Canada (June 5) [8] | 92,264 | 6,025 | **6.5%** | | - | | - |
| Japan (May 28) [9] | 11,344 | 799 | **7.1%** | *155* | *1.4%* | *644* | *5.7%* |
| South Korea (May 22) [10] | 11,402 | 806 | **7.1%** | *156* | *1.4%* | *650* | *5.7%* |
| Moscow (new cases May 21) [11] | 2,830 | 201 | **7.1%** | | - | | - |
| New Zealand (May 22) [12] | 1,504 | 157 | **10.4%** | *36* | *2.4%* | *121* | *8.0%* |
| India (April 26) [13] | 2,344 | 326 | **13.9%** | *98* | *4.2%* | *228* | *9.7%* |
| **TOTAL** | **2,676,982** | **108,105** | **4.0%** | ***13,071*** | ***1.2%**** | ***24,631*** | ***2.3%**** |

[1] https://www.afro.who.int/health-topics/coronavirus-covid-19
[2] https://www.statista.com/statistics/1095024/china-age-distribution-of-wuhan-coronavirus-covid-19-patients/
[3] https://coronavirus.gob.mx/datos/
[4] https://portalarquivos.saude.gov.br/images/pdf/2020/May/21/2020-05-19---BEE16---Boletim-do-COE-13h.pdf
[5] https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/cases-in-us.html
[6] https://covid19-surveillance-report.ecdc.europa.eu/
[7] https://www.health.gov.au/news/health-alerts/novel-coronavirus-2019-ncov-health-alert/coronavirus-covid-19-current-situation-and-case-numbers#cases-and-deaths-by-age-and-sex
[8] https://health-infobase.canada.ca/covid-19/epidemiological-summary-covid-19-cases.html
[9] https://www3.nhk.or.jp/news/special/coronavirus/data-rate/
[10] https://www.statista.com/statistics/1102730/south-korea-coronavirus-cases-by-age/
[11] https://www.statista.com/statistics/1109859/covid-19-cases-by-age-group-moscow/
[12] https://www.health.govt.nz/our-work/diseases-and-conditions/covid-19-novel-coronavirus/covid-19-current-situation/covid-19-current-cases
[13] https://www.covid19india.org/deepdive

* denominator 1,065,626

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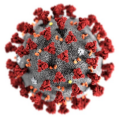

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| Chi | | | | | | | |
| Mex | | | | | | | |
| Bra | | | | | | | |
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| EU/ | | | | | | | |
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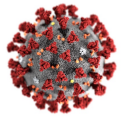
| Can | | | | | | | |
| Jap | | | | | | | |
| Sou | | | | | | | |
| Mos | | | | | | | |
| New | | | | | | | |
| Ind | | | | | | | |
| TOTAL | 2,676,982 | 108,105 | 4.0% | 13,071 | 1.2% | 24,631 | 2.3% |

# It Shouldn't Be This Hard to Get Age-Related Data

[1] https://www.afro.who.int/health-topics/coronavirus-covid-19
[2] https://www.statista.com/statistics/1095024/china-age-distribution-of-wuhan-coronavirus-covid-19-patients/
[3] https://coronavirus.gob.mx/datos/
[4] https://portalarquivos.saude.gov.br/images/pdf/2020/May/21/2020-05-19---BEE16---Boletim-do-COE-13h.pdf
[5] https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/cases-in-us.html
[6] https://covid19-surveillance-report.ecdc.europa.eu/
[7] https://www.health.gov.au/news/health-alerts/novel-coronavirus-2019-ncov-health-alert/coronavirus-covid-19-current-situation-and-case-numbers#cases-and-deaths-by-age-and-sex
[8] https://health-infobase.canada.ca/covid-19/epidemiological-summary-covid-19-cases.html
[9] https://www3.nhk.or.jp/news/special/coronavirus/data-rate/
[10] https://www.statista.com/statistics/1102730/south-korea-coronavirus-cases-by-age/
[11] https://www.statista.com/statistics/1109859/covid-19-cases-by-age-group-moscow/
[12] https://www.health.govt.nz/our-work/diseases-and-conditions/covid-19-novel-coronavirus/covid-19-current-situation/covid-19-current-cases
[13] https://www.covid19india.org/deepdive

* denominator 1,065,626

# Among Children with COVID-19, Difficult to Get Disaggregated Data to Evaluate Proportional Representation by Age



| Country/Reference | # Children 0-19 yr | Number/Proportion of Pediatric Cases by Age | | | | |
|---|---|---|---|---|---|---|
| | | <1 yr | 1-4/5yr | 6/5-9/10 yr | 10/11-14/15 yr | 15/16-17/18yr |
| Africa *(website)* [1] | 469 | 21 (4%) | 1-5<br>100 (21%) | 6-10<br>96 (21%) | 11-15<br>135 (29%) | 16-18<br>117 (25%) |
| US *(MMWR)* [2] | 2,572 | 393 (15.2%) | 1-4<br>291 (11%) | 5-9<br>388 (15%) | 10-14<br>682 (27%) | 15-17<br>813 (32%) |
| China *(Cui X, J Med Virol)* [3] *(analysis all China reports incl Dong)* | 2,492 | 446 (17.9%) | 1-5<br>593<br>(23.8%) | 6-10<br>626 (25.1%) | 11-15<br>492 (19.7%) | 16-18<br>335 (19.7%) |
| Brazil *(website)* [4] | 4,019 | 0-4<br>1,352 (34%) | | 5-9<br>621 (15%) | 10-14<br>687 (17%) | 15-19<br>1,359 (34%) |
| Mexico *(website)* [5] | 3,008 | 0-4<br>591 (20%) | | 5-9<br>447 (15%) | 10-14<br>667 (22%) | 15-19<br>1,303 (43%) |
| **TOTAL** | **12,560** | **Age 0 - 4/5<br>3,787 (31%)** | | **Age 5/6 - 9/10<br>2,178 (17%)** | **Age 10/11 - 14/15<br>2,663 (21%)** | **Age 15/16 - 19/19<br>3,927 (30%)** |

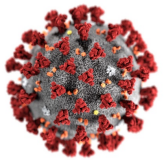
**About 1/3 cases are 0-5 years**

**Over half of cases are 10-18 years**

[1] https://www.afro.who.int/health-topics/coronavirus-covid-19
[2] CDC COVID-19 Response Team. MMWR 2020 Apr 6
[3] Cui X et al. J Med Virol. 2020 May 17 (includes Dong Y et al. Pediatrics. 2020 Mar 16)
[4] https://portalarquivos.saude.gov.br/images/pdf/2020/May/21/2020-05-19---BEE16---Boletim-do-COE-13h.pdf
[5] https://coronavirus.gob.mx/datos/

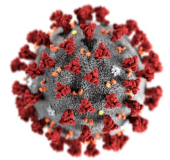
**Caveat: Younger children may have less typical symptoms and therefore be less likely to be tested**

# Why is There Low Prevalence of SARS-CoV-2 in Children?



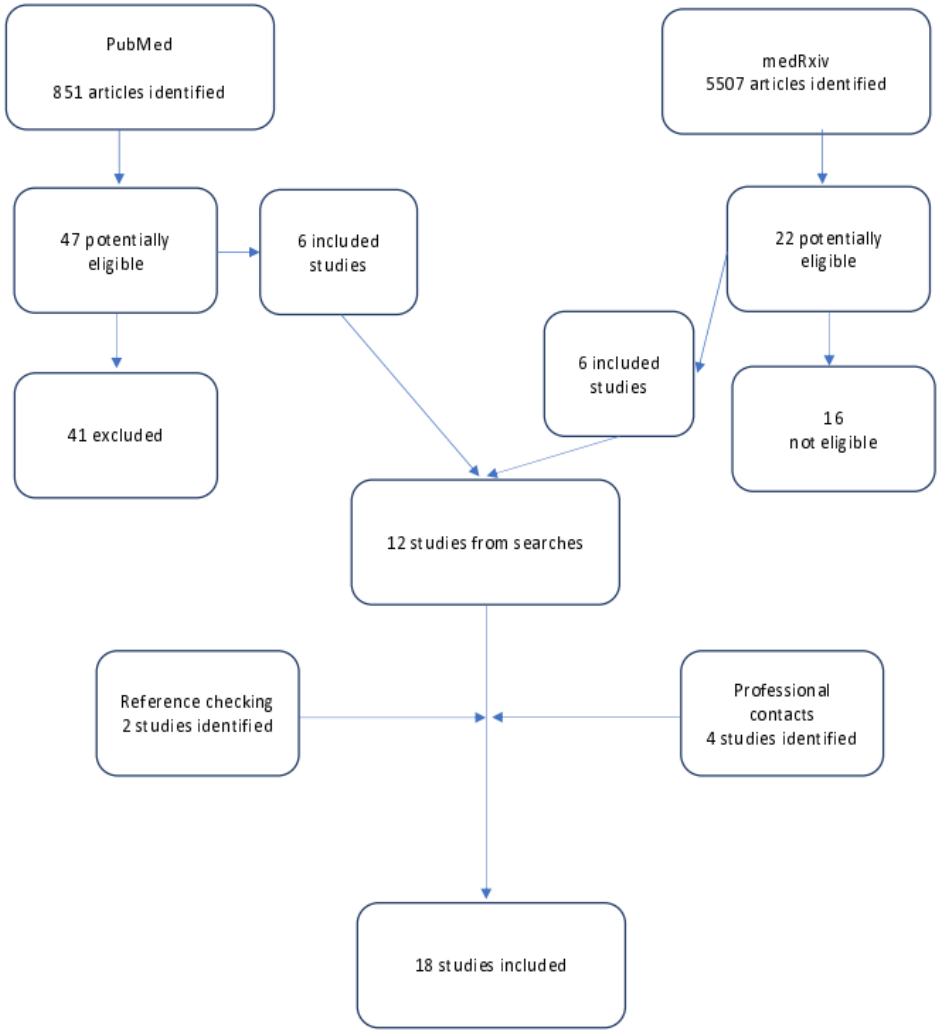
- Surveillance data have predominantly reflected individuals diagnosed with COVID-19 disease and hence reflect selective testing of only the most symptomatic persons.
- However, children may be less likely to have typical symptoms.
- Is low incidence of SARS-CoV-2 in children because they are more likely asymptomatic or have atypical/mild symptoms and hence are **less likely to be tested**? ***OR***
- Is low incidence of SARS-CoV-2 in children because of mitigation measures (e.g., closure schools) and hence they are **less likely to be exposed to infected individuals**? ***OR***
- Is low incidence SARS-CoV-2 in children reflective of a **true lower susceptibility to infection** compared to adults?

# Susceptibility to SARS-CoV-2 in Children and Adolescents Systematic Review and Meta-Analysis



*Viner RM et al. MedRxiv 2020 May 24* (https://www.medrxiv.org/content/10.1101/2020.05.20.20108126v1)

- Systematic review:
  - Contact-tracing studies (secondary infection)
  - Population prevalence studies (virologic testing or serologic testing)
- 18 studies were identified
  - 9 contact-tracing; 1 review of household contact-tracing; 8 population-screening
  - 6 China; 1 each from Taiwan, Japan, Iceland Italy, Netherlands, Sweden, Germany, Spain, Switzerland, Australia and UK, and one multiple countries

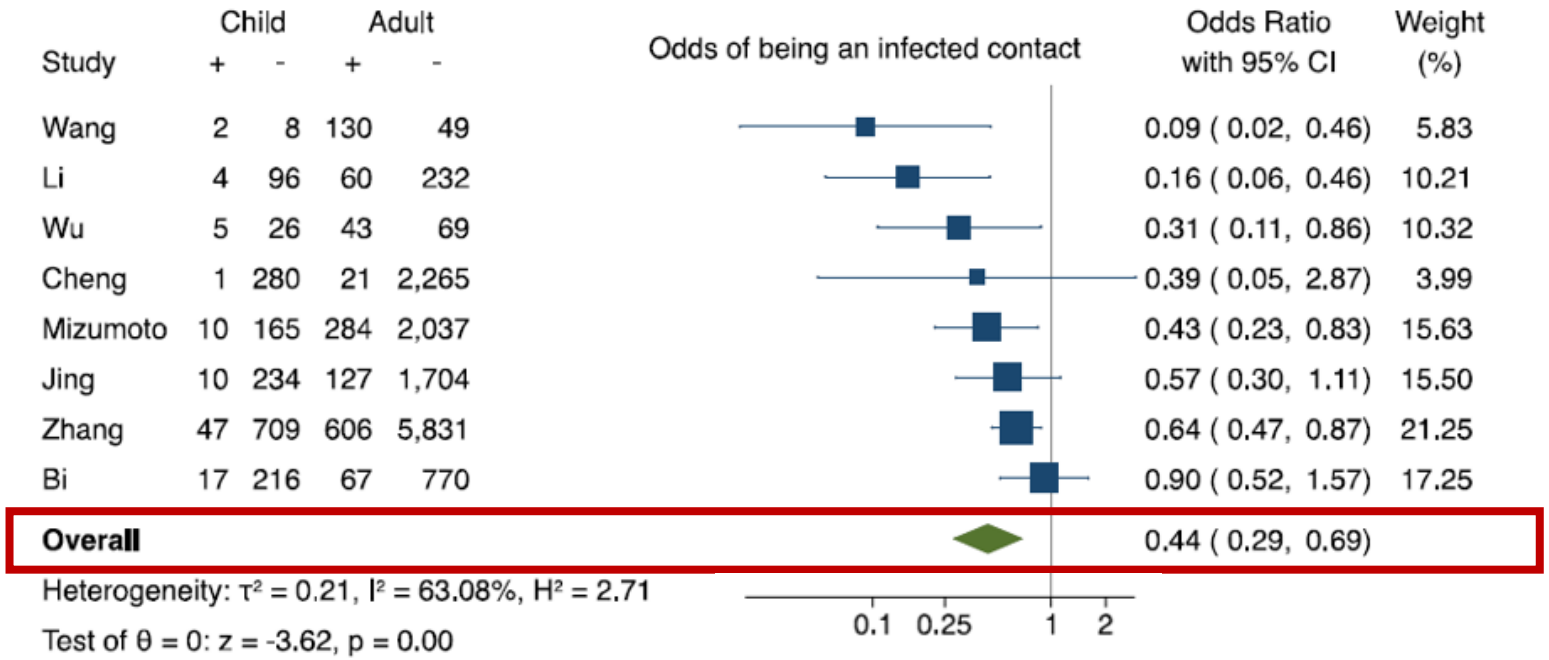


# 8 Contact/Household Contact Tracing Studies

## Preliminary Data Suggest Lower Odds Infection in Children vs Adults

*Viner RM et al. MedRxiv 2020 May 24 (https://doi.org/10.1101/2020./05/20108126*

**Pooled Odds Estimate of Being Infected Contact in Children vs Adults, All Contact Studies**



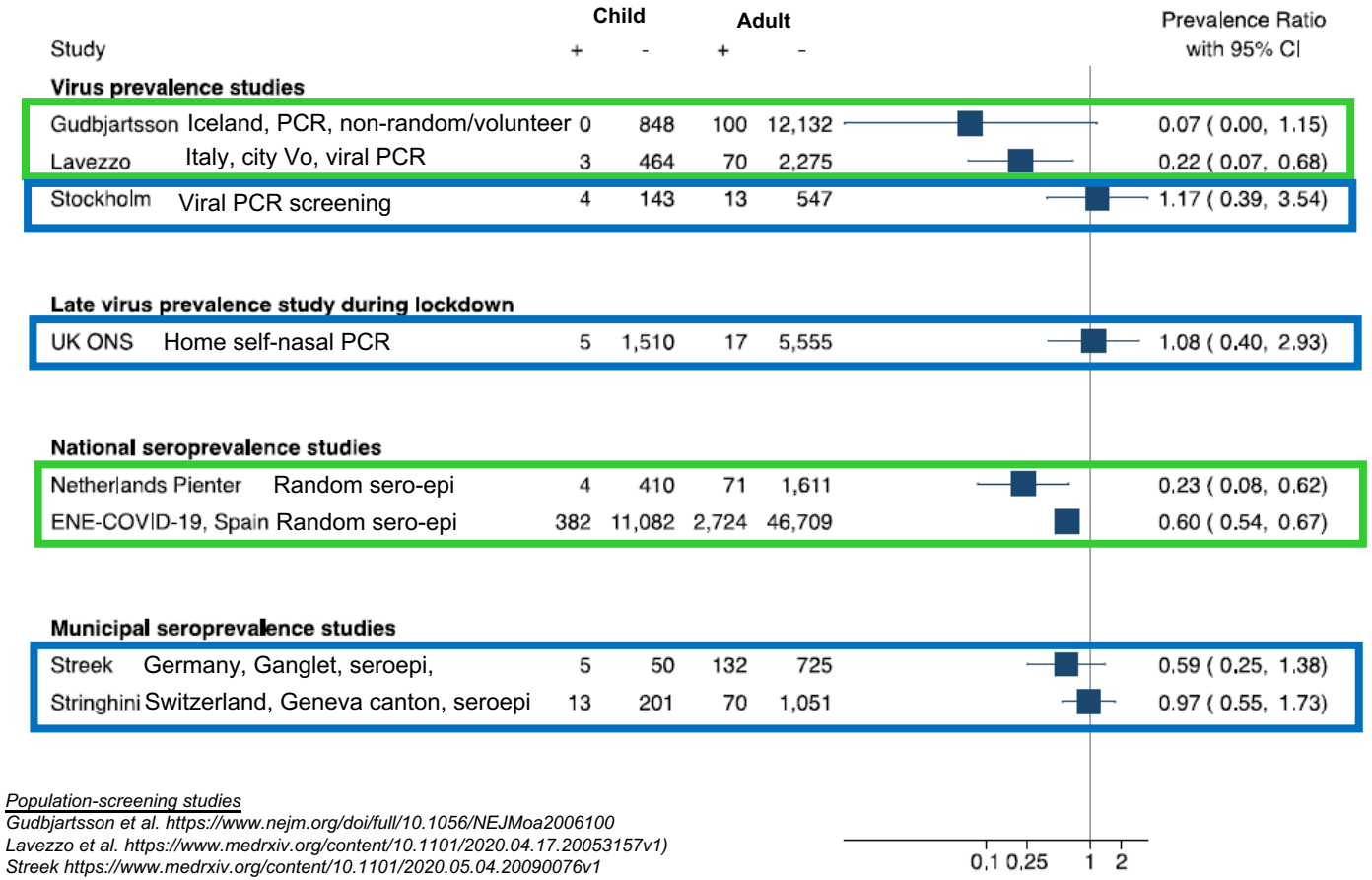

- Child contacts (age <18-20 yrs) had **56% lower odds of becoming infected after contact with an infected individual** (OR 0.44) than adult contacts.
- Little difference when include only better-quality studies with lower bias (OR 0.51).
- Data insufficient to explore differences between younger children vs adolescents.

# 8 Population-Based Surveillance Studies

## Heterogeneous Data, Mixed Results – Insufficient to Draw Conclusions

*Viner RM et al. MedRxiv 2020 May 24 (https://doi.org/10.1101/2020./05/20108126*

**Ratios of Prevalence SARS-CoV-2 Infection in Children Compared to Adults**




*Population-screening studies*
*Gudbjartsson et al. https://www.nejm.org/doi/full/10.1056/NEJMoa2006100*
*Lavezzo et al. https://www.medrxiv.org/content/10.1101/2020.04.17.20053157v1)*
*Streek https://www.medrxiv.org/content/10.1101/2020.05.04.20090076v1*
*Netherlands Pienter: https://www.rivm.nl/en/novel-coronavirus-covid-19/children-and-covid-19*
*UK ONS: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/coronaviruscovid19infectionsurveypilot/england14may2020*
*Stockholm: https://www.folkhalsomyndigheten.se/publiceratmaterial/publikationsarkiv/f/forekomsten-av-covid-19-i-region-stockholm-26-mars3-april-2020/*
*ENE-COVID-19, Spain: https://www.mscbs.gob.es/gabinetePrensa/notaPrensa/pdf/ENEC140520115618104.pdf*

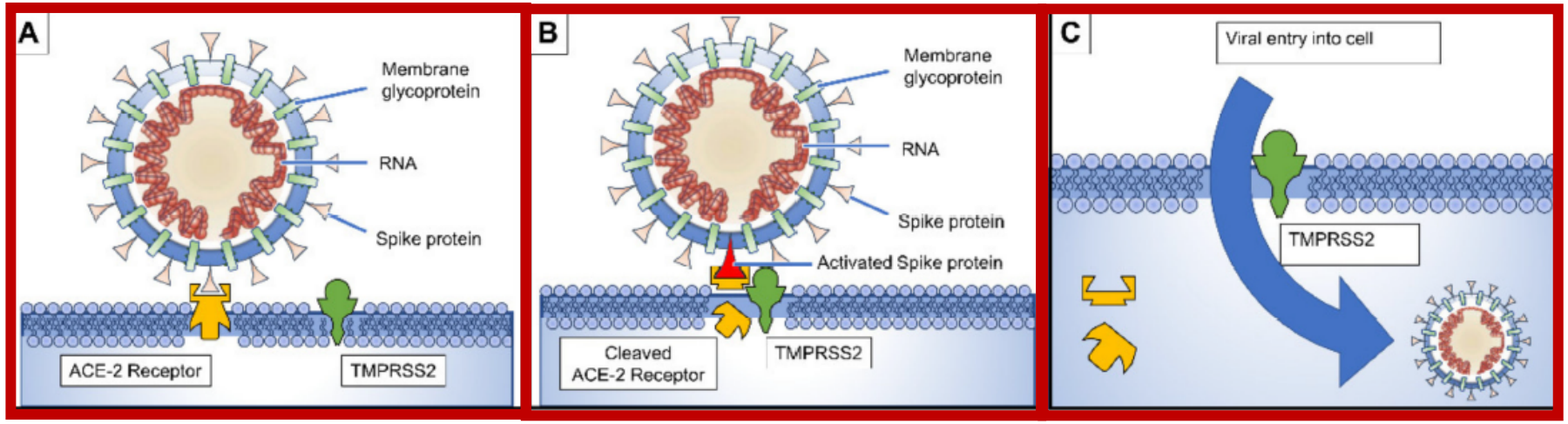
- Data more heterogeneous and not suitable for meta-analysis; mixed results.
- Two viral-detection studies and two national sero-prevalence surveys (Netherlands, Spain) show **lower prevalence in children** than adults.
- Two viral-detection studies (Stockholm, UK) and two municipal sero-prevalence studies (Germany, Switzerland) show prevalence of infection was **similar in children and adults**.
- Significant uncertainty of estimates; issues including timing of survey and timing of COVID-19 interventions.

# New Insights into SARS-CoV-2 Cell Entry

## Differences in Receptor Levels May Be Biologic Mechanism for ↓ Susceptibility in Children?

*Rabi FA et al. Pathogens. 2020;9:231*

- Two cellular proteins on the cell surface are involved in viral entry: angiotensin-converting enzyme 2 (ACE-2) and type II transmembrane serine protease (TMPRSS2); TMPRSS2 expression increases cellular uptake of coronavirus




→Spike protein on virus binds to ACE-2 on surface target cell

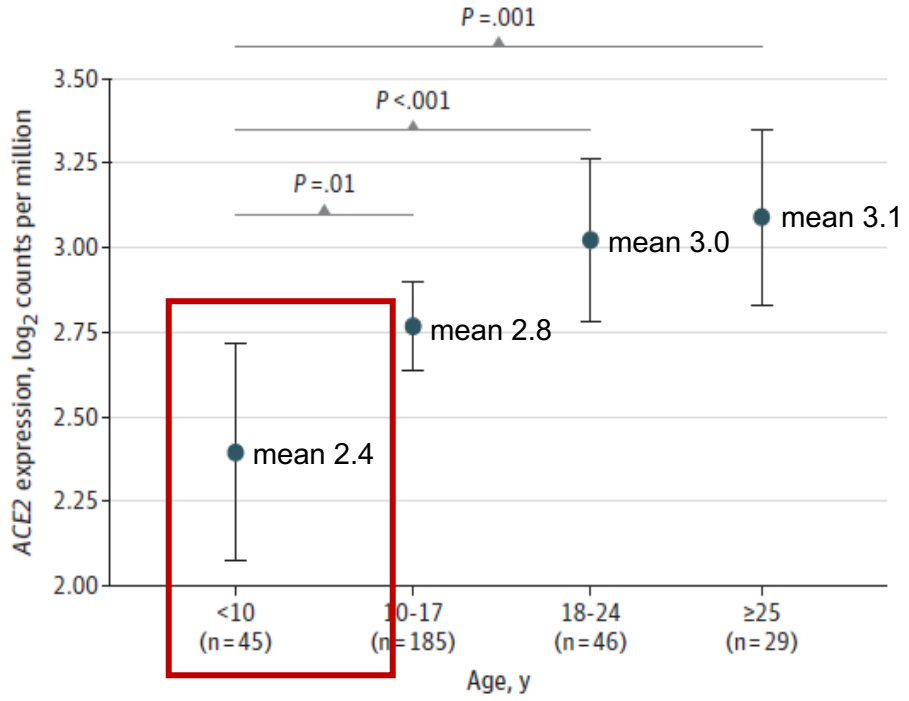
→Cellular protease TMPRSS2 binds to and cleaves ACE2 receptor and cleaves the spike protein, activating/priming the virus for cell entry

→Cleaved ACE-2 and activated spike protein enables cell fusion

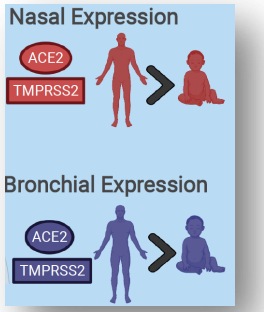
# Children May Have Lower Levels of Nasal ACE-2 than Adults, Potentially Making Them Less Susceptible to Infection and/or Replication

*Bunyavanich S et al. JAMA. 2020 May 20 (epub)*

- Retrospective exam stored nasal epithelium from 305 persons age 4-60 years from a study evaluating nasal markers of asthma 2015-2018 (50% of sample had asthma and 50% did not).
- Evaluated ACE-2 enzyme gene expression in stored samples.



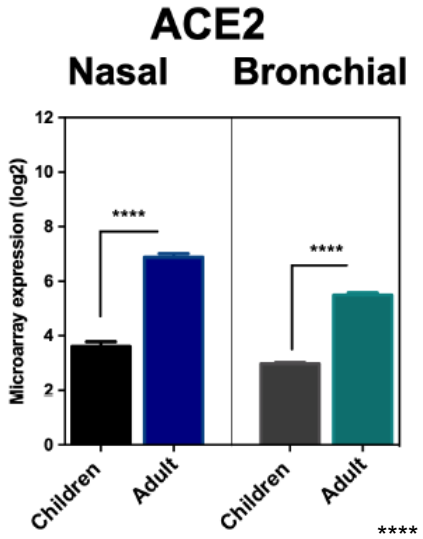

- ACE-2 enzyme gene expression was age-dependent, being lowest in children <10 years, then ↑ with age.
- ACE-2 was significantly lower in children <10 year than older persons, independent of sex and asthma.




# Children May Have Lower Levels of Nasal and Bronchial ACE-2 and TMPRSS2 than Adults

*Sharif-Askari NS et al. Molec Ther Methods Clin Develop. 2020 Sept; Vol 18*

- Used public gene expression datasets.
- Differential expression of both ACE2 and TMPRSS2 in nasal and bronchial airways relative to age and in certain diseases.
- **Children had significantly lower expression of both ACE2 and TMPRSS2 in the upper and lower airways** (nasal and bronchial) compared to adults.
- Expression of both ACE 2 and TMPRSS2 in lung biopsy tissues was significantly upregulated in smokers and persons with COPD, both associated with more severe COVID-19 disease.

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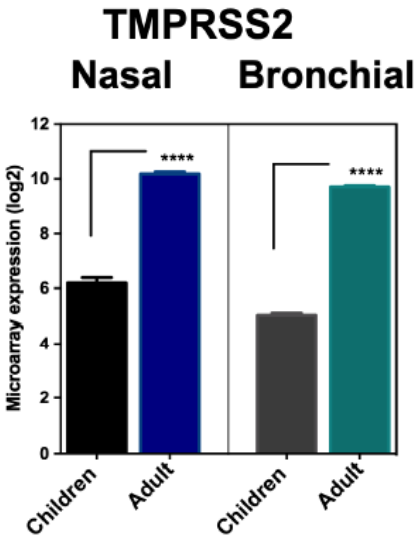


# What About Transmission of SARS-CoV-2 from Children to Others?

- The role that children and young people play in transmission of SARS-CoV-2 depends on multiple factors:
  - Risk of exposure to infected individual: children less likely to be exposed during mitigation interventions
  - Probability of being infected upon exposure: children may have lower susceptibility
  - Extent develops symptoms: children more likely asymptomatic
  - Propensity to make potentially infectious contact with others (number of social contacts across age groups): school re-openings increase possibility
  - Extent develops viral load sufficiently high to transmit and duration of infectiousness: mixed data on viral load in children vs adults


# COVID-19 Investigation, Schools, New South Wales, Australia

## Low Rate Infection in Students, None in Teachers/Staff

http://ncirs.org.au/sites/default/files/2020-04/NCIRS%20NSW%20Schools%20COVID_Summary_FINAL%20public_26%20April%202020.pdf

- 9 students/9 staff from 5 primary and 10 high schools had COVID-19 dx
  - 735 students and 128 staff viewed as close contacts of cases.
- 288 students/staff agreeing to participate had SARS-CoV-2 rtPCR swab taken 5-10 days after last contact with case and 96 had blood sample taken to detect antibodies to virus.

→ Of those evaluated for infection:

- 1/288 (0.3%) students had positive rtPCR viral test
- 1/96 (1%) students with negative rtPCR had SARS-CoV-2 antibody

→Overall:

- 2/735 (0.3%) students and 0/128 staff had possible secondary infection from exposure to case

# However, We Are in the Midst of a “Grand Experiment”

May 18 2020

CORONAVIRUS | News

## 70 cases of COVID-19 at French schools days after reopening

Thomas Adamson

The Associated Press Staff
Contact

Published Monday, May 18, 2020 11:37AM EDT

PARIS -- Just one week after a third of French schoolchildren went back to school in an easing of the coronavirus lockdown, there has been a worrying flareup of about 70 COVID-19 cases linked to schools, the government said Monday.

June 3 2020

CORONAVIRUS

## France closes 120 schools as Morbihan becomes third Covid-19 hotspot

Issued on: 03/03/2020 - 15:38 Modified: 03/03/2020 - 18:05

**France has closed some 120 schools in areas with the largest numbers of coronavirus infection, with more likely to follow in the coming days. As a fourth Covid-19 death was reported on Tuesday, the northwestern department of Morbihan became the third epidemic hotspot, with parts placed under confinement.**

June 1 2020

PEOPLE.COM › HEALTH

## Spike in Coronavirus Cases Causes Hundreds of Schools in South Korea to Close After Reopening

South Korea began relaxing social distancing guidelines in May

By **Maria Pasquini** | June 01, 2020 12:33 PM

June 3 2020

THE CORONAVIRUS CRISIS

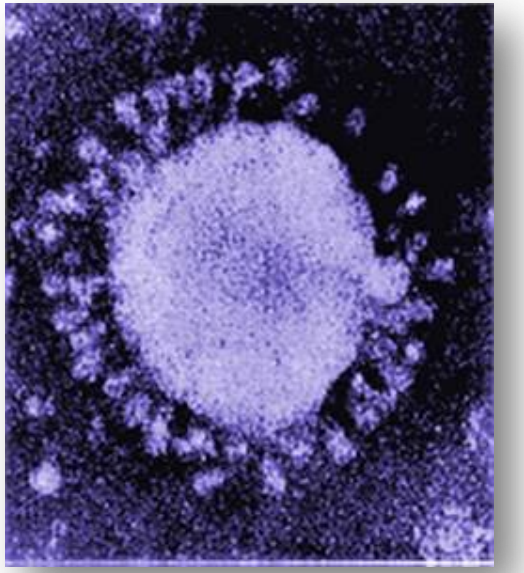
## After Reopening Schools, Israel Orders Them To Shut If COVID-19 Cases Are Discovered

June 3, 2020 · 11:32 AM ET

Two weeks after Israel fully reopened schools, a COVID-19 outbreak sweeping through classrooms — including at least 130 cases at a single school — has led officials to close dozens of schools where students and staff were infected. A new policy orders any school where a virus case emerges to close.

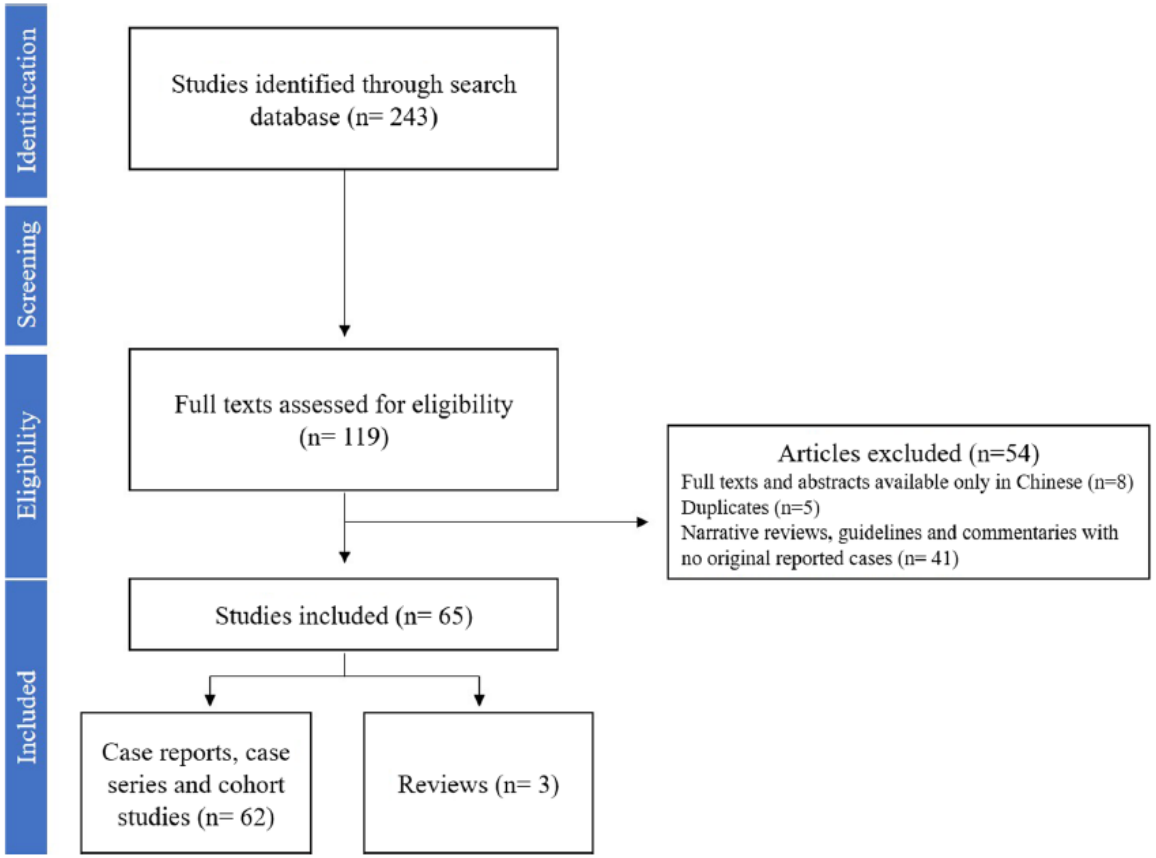
The government decision, announced Wednesday evening, comes after more than 200 cases have been confirmed among students and staff at various schools. At least 244 students and school employees have tested positive for the coronavirus, according to the education ministry. At least 42 kindergartens and schools have been shuttered indefinitely. More than 6,800 students and teachers are in home quarantine by government order.

# Clinical Findings of SARS-CoV-2/ COVID-19 in Children



# Updated Data on Clinical Characteristics and Outcome

- Systematic review of pediatric SARS-CoV-2 publications Jan 1 to May 1 2020 , included 62 studies and 3 reviews and 7,480 children 0-18 years.

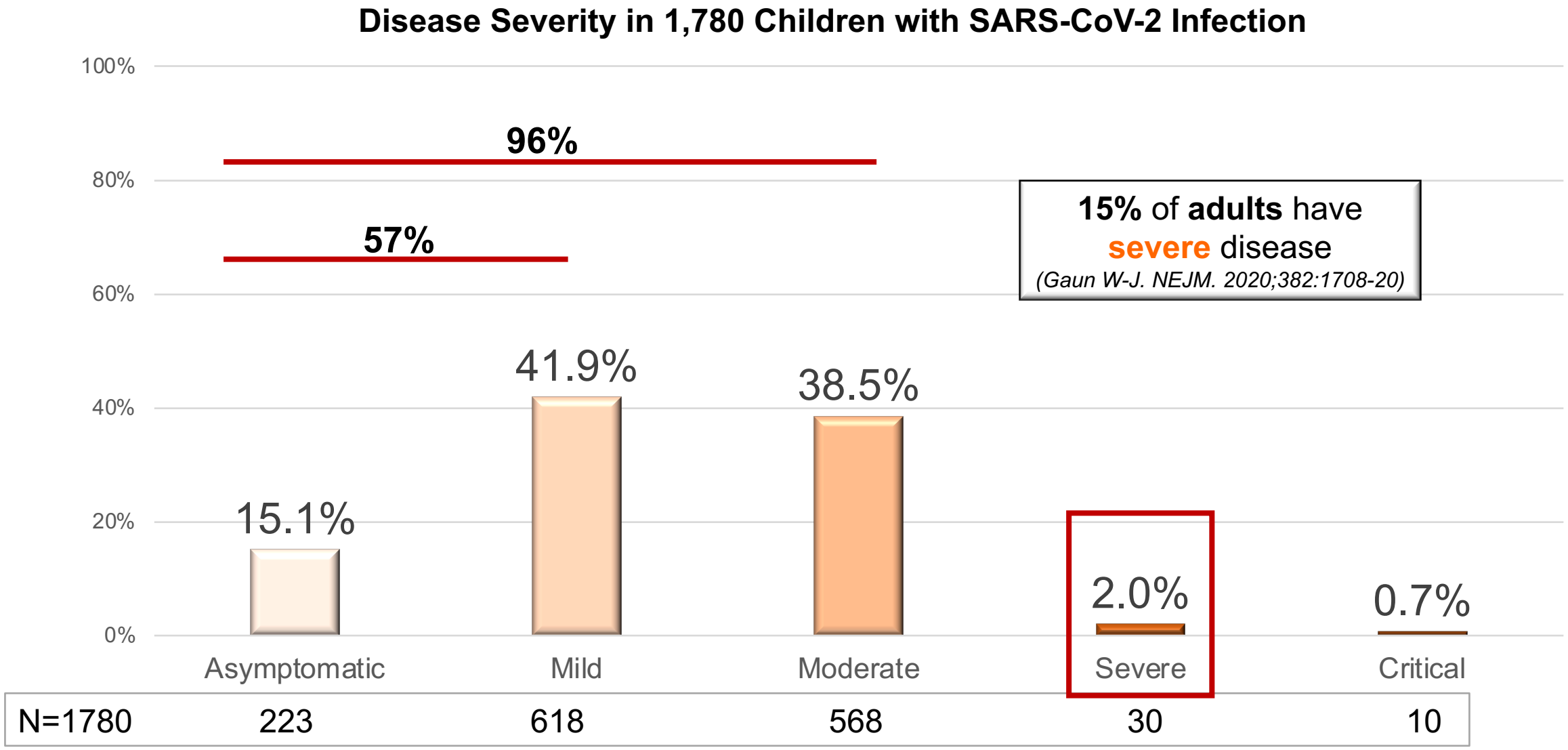



- Mean age 7.6 years, 52% male
- 44% Italy, 34% US, 18% China
- 73.3% exposed in family, 13.5% unknown exposure
- Only confirmed cases considered in the review

*Liguoro I et al. Eur J Pediatr. 2020 May 18*

# Data Continue to Show Children Generally Have Mild-Moderate Disease

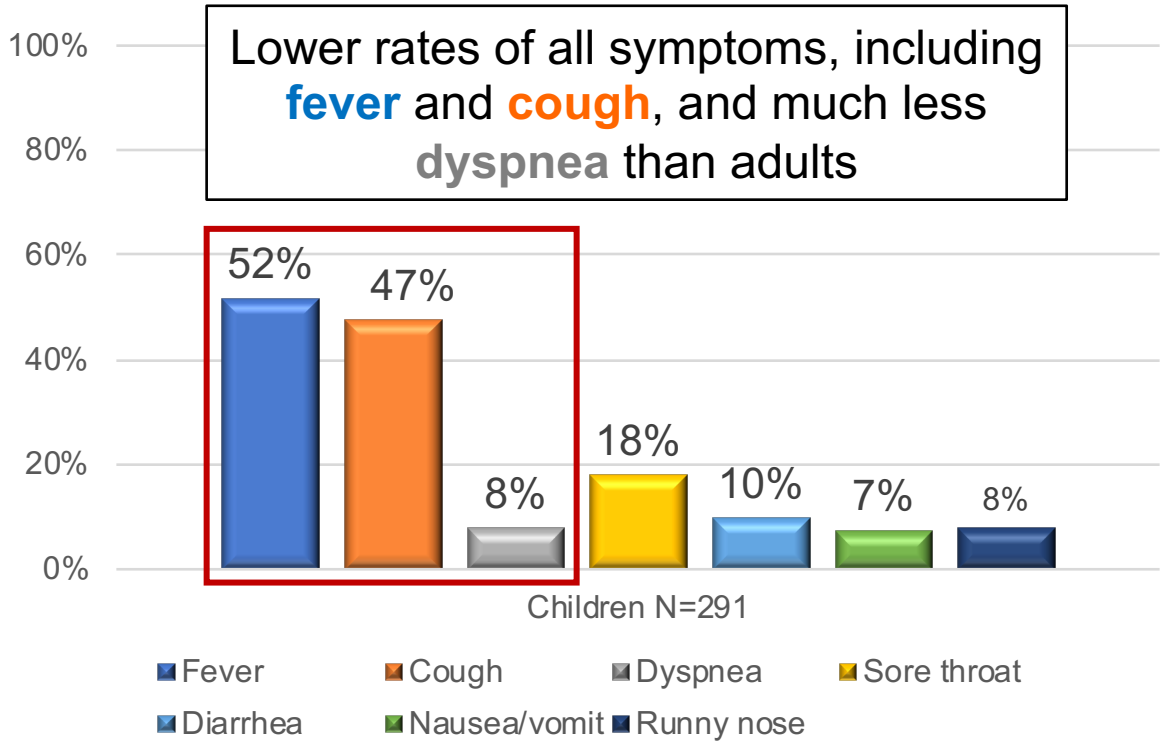
*Liguoro I et al. Eur J Pediatr. 2020 May 18*



# Children Have Fewer Symptoms Than Adults Most Common Fever and Cough

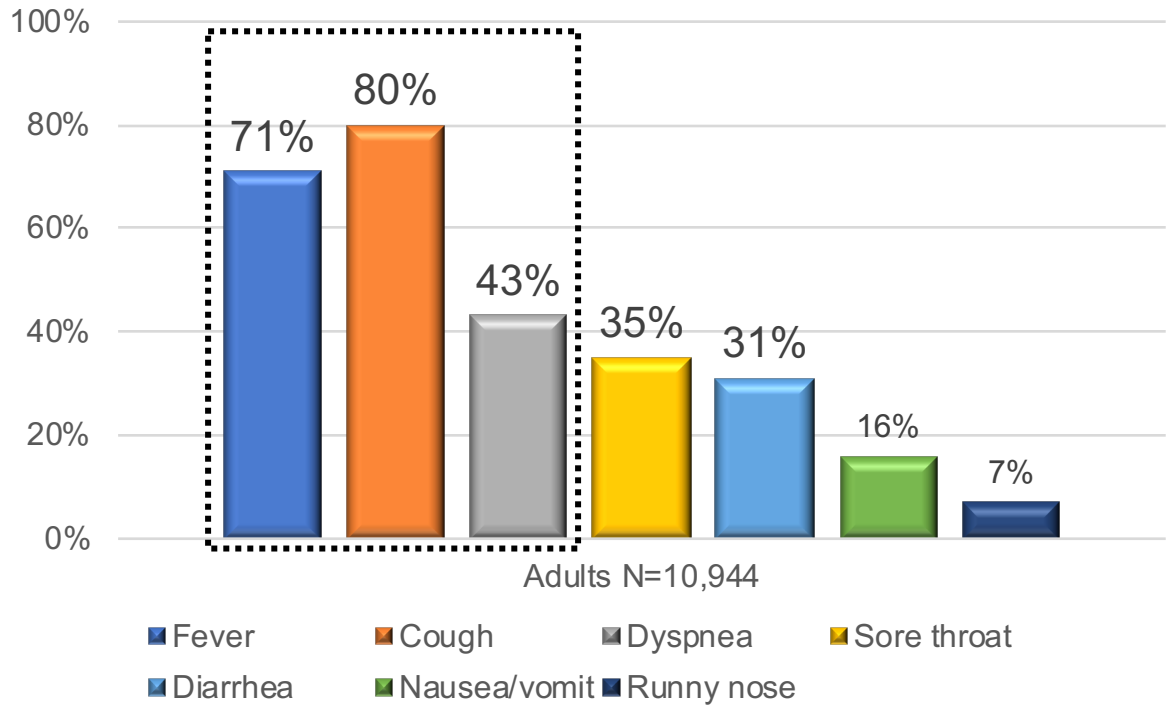
*Liguoro I et al. Eur J Pediatr. 2020 May 18*

**Disease Symptoms in 1,780 Children 0-18 Years with SARS-CoV-2 Infection**




*Systematic Review - Liguoro I et al. Eur J Pediatr. 2020 May 18*

**Disease Symptoms in 10,944 Adults 18-64 Years in US with SARS-CoV-2 Infection**

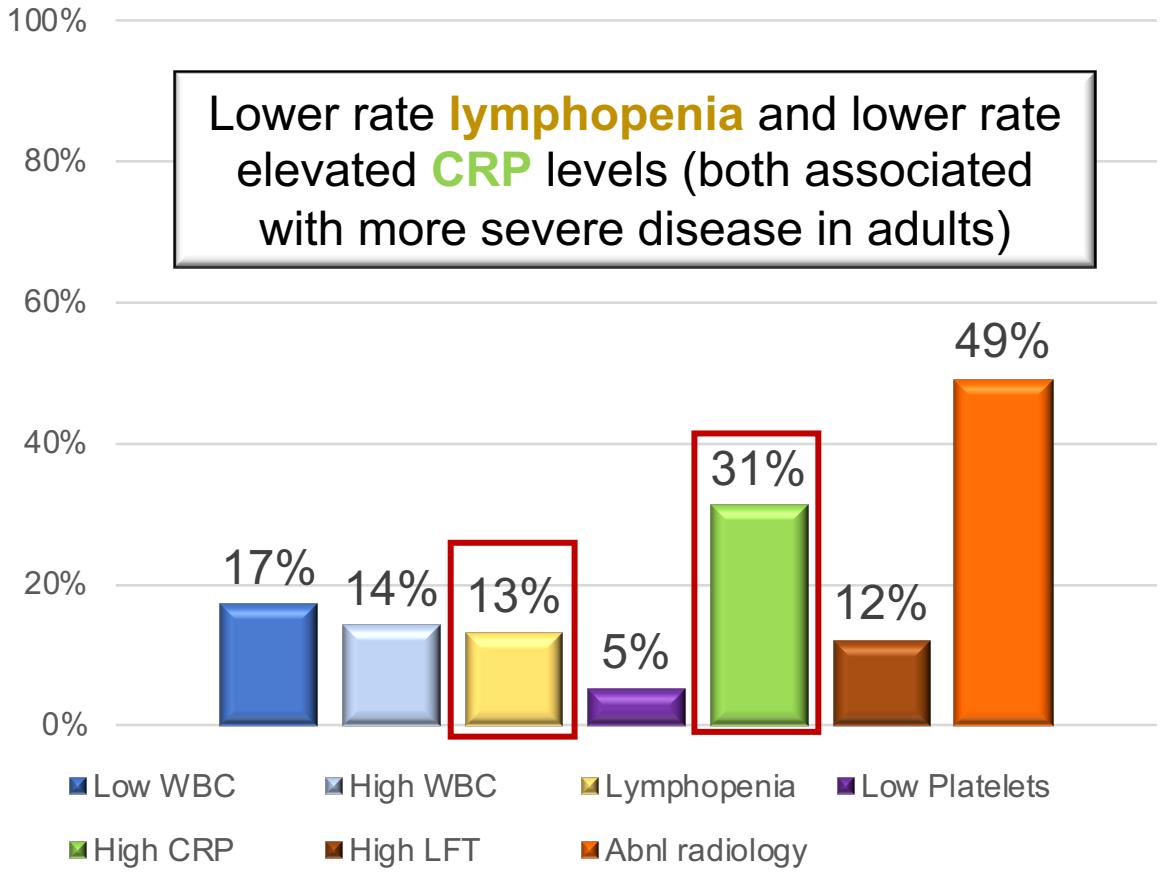



*CDC COVID-19 Response Team. MMWR 2020 Apr 6;69 (US data)*

# Consistent with Less Severe Disease, Laboratory Findings in Children with COVID-19 Less Abnormal than in Adults

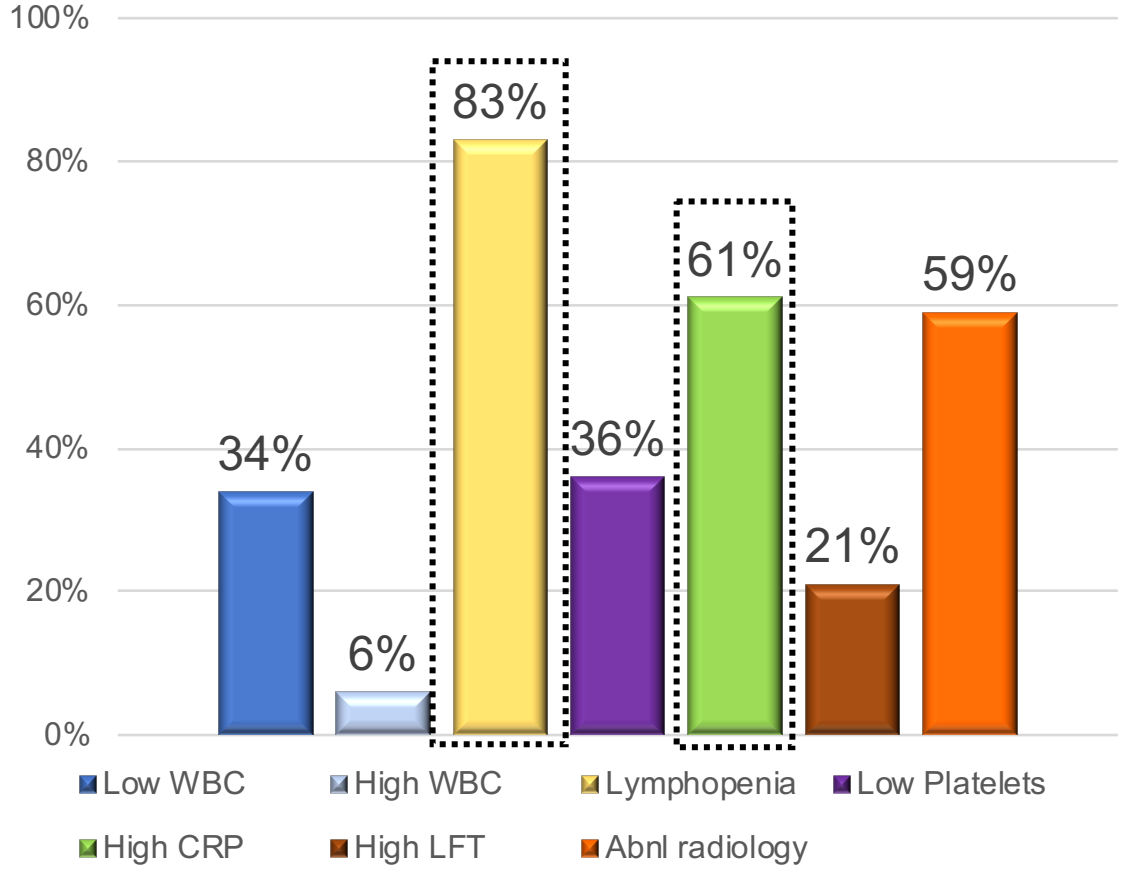
*Liguoro I et al. Eur J Pediatr. 2020 May 18*

**Laboratory Findings in 655 Children 0-18 Years with SARS-CoV-2 Infection**




*Systematic Review - Liguoro I et al. Eur J Pediatr. 2020 May 18*

**Laboratory Findings in 1,099 Adults 18-64 Years in China with SARS-CoV-2 Infection**

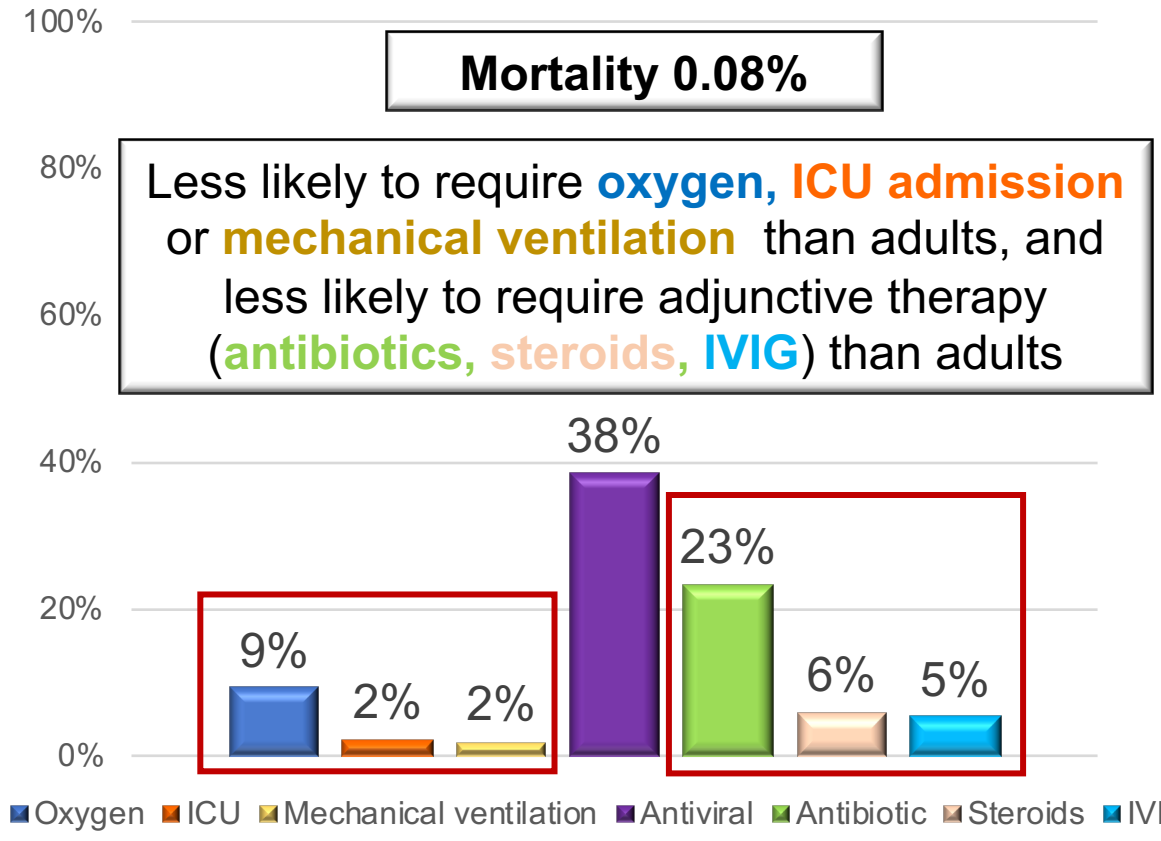



*Guan W et al. N Engl. J Med. 2020 Feb 28 (China data)*

# Consistent with Less Severe Disease, Children Were Less Likely to Require ICU or Significant Treatments

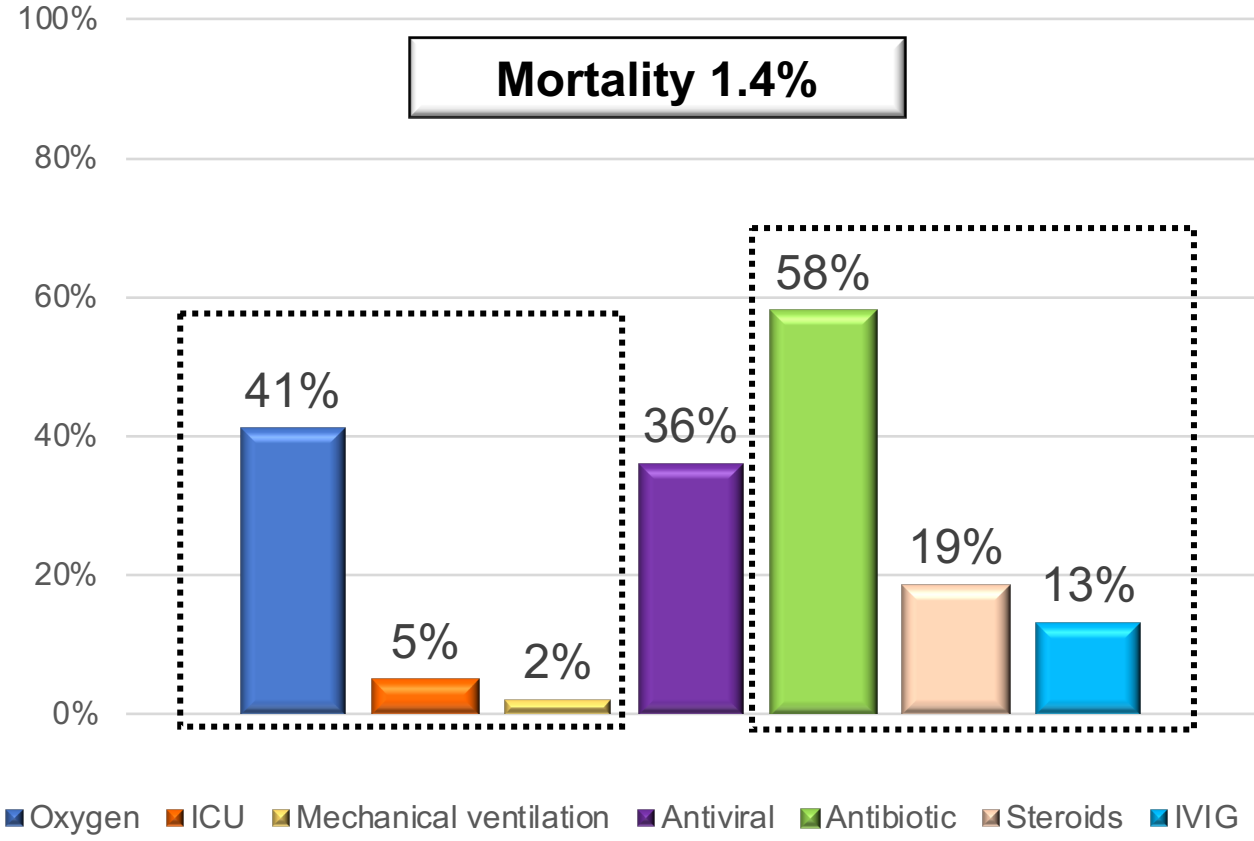
*Liguoro I et al. Eur J Pediatr. 2020 May 18*

**Treatment in 1,402 Children 0-18 Years with SARS-CoV-2 Infection**




*Systematic Review - Liguoro I et al. Eur J Pediatr. 2020 May 18*

**Treatment in 1,099 Adults 18-64 Years in China with SARS-CoV-2 Infection**

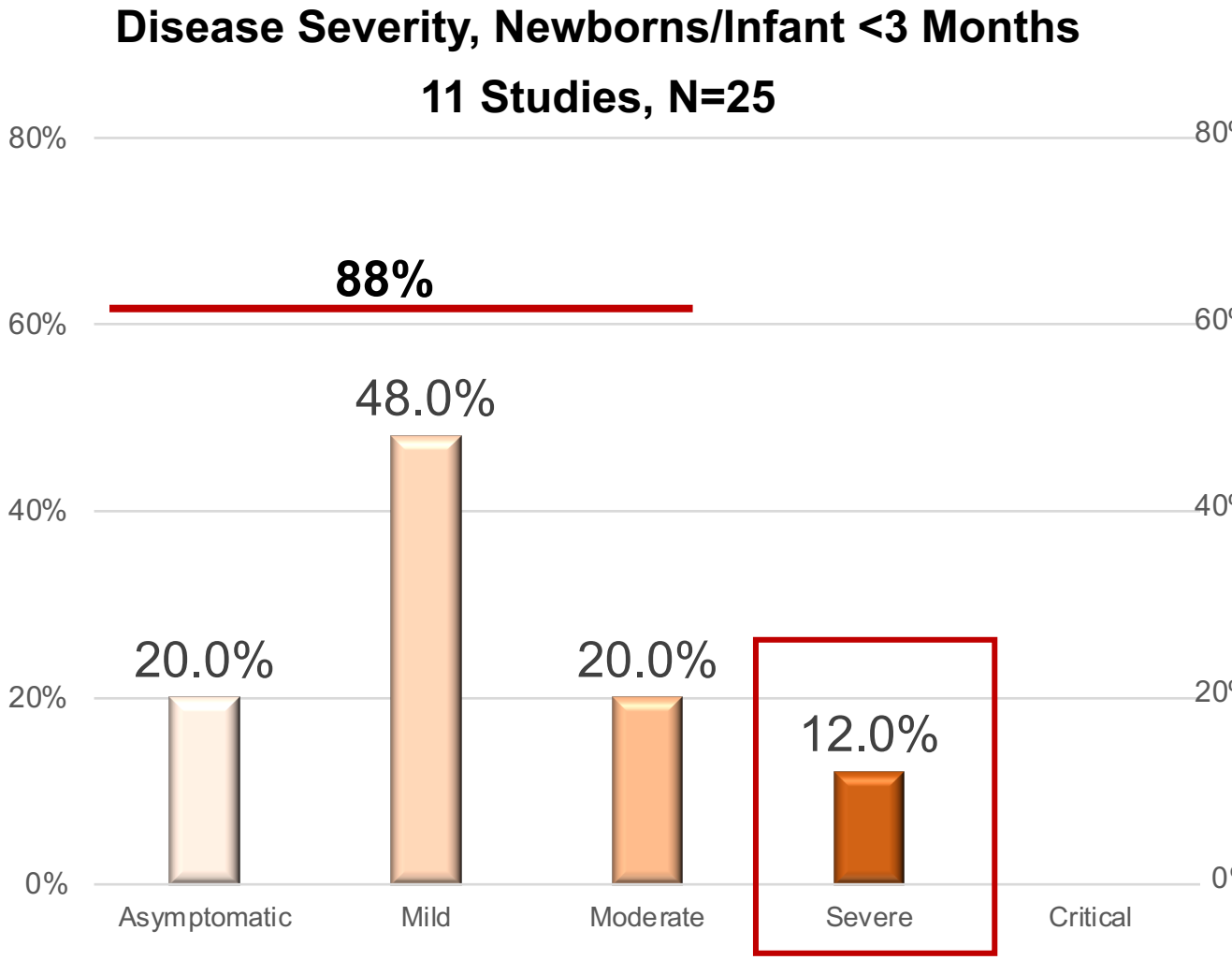


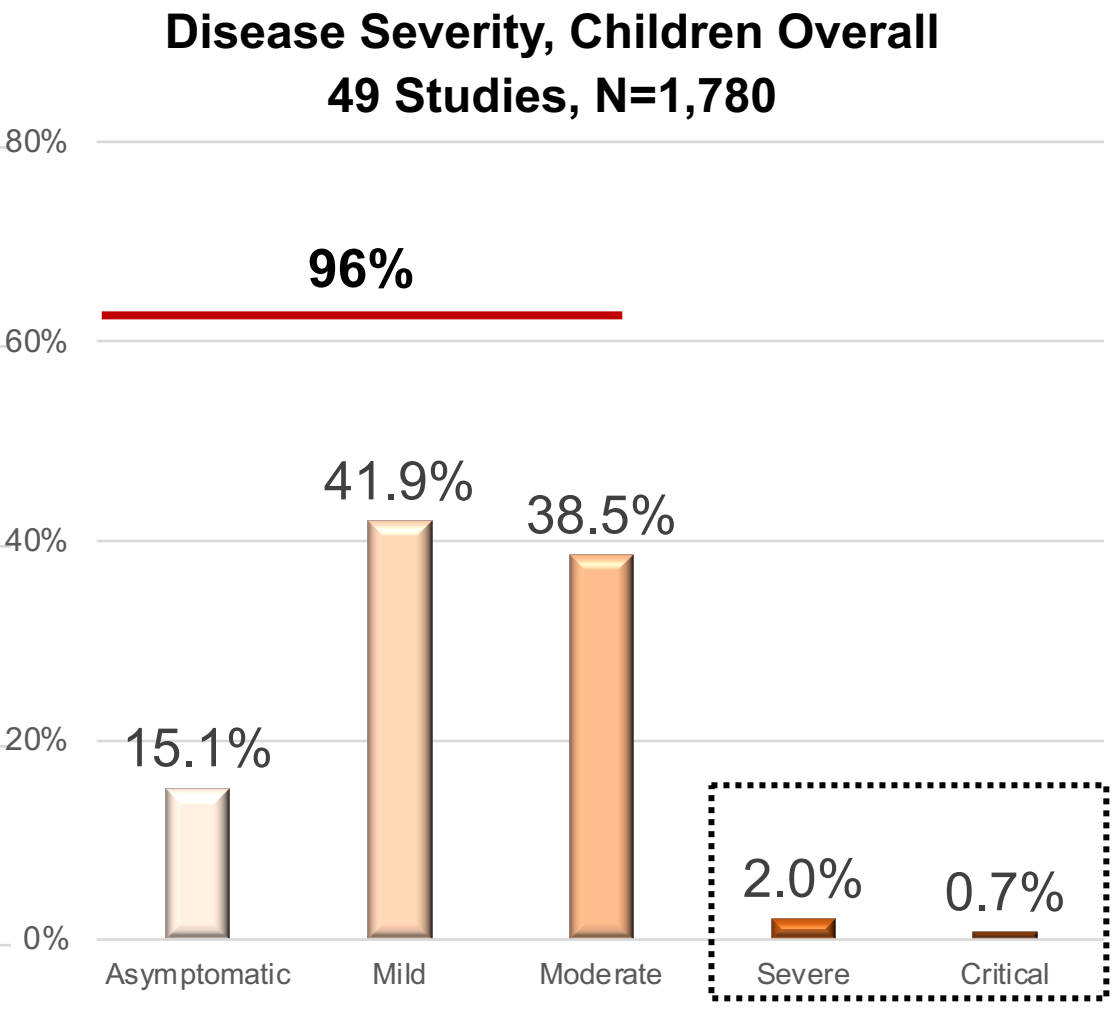

*Guan W et al. N Engl. J Med. 2020 Feb 28 (China data)*

# Do Symptoms Differ in Youngest Infants Compared to Older Children?

# Higher Proportion Newborns/Children Age <3 Months Have Severe Disease than Older Children

*Liguoro I et al. Eur J Pediatr. 2020 May 18*

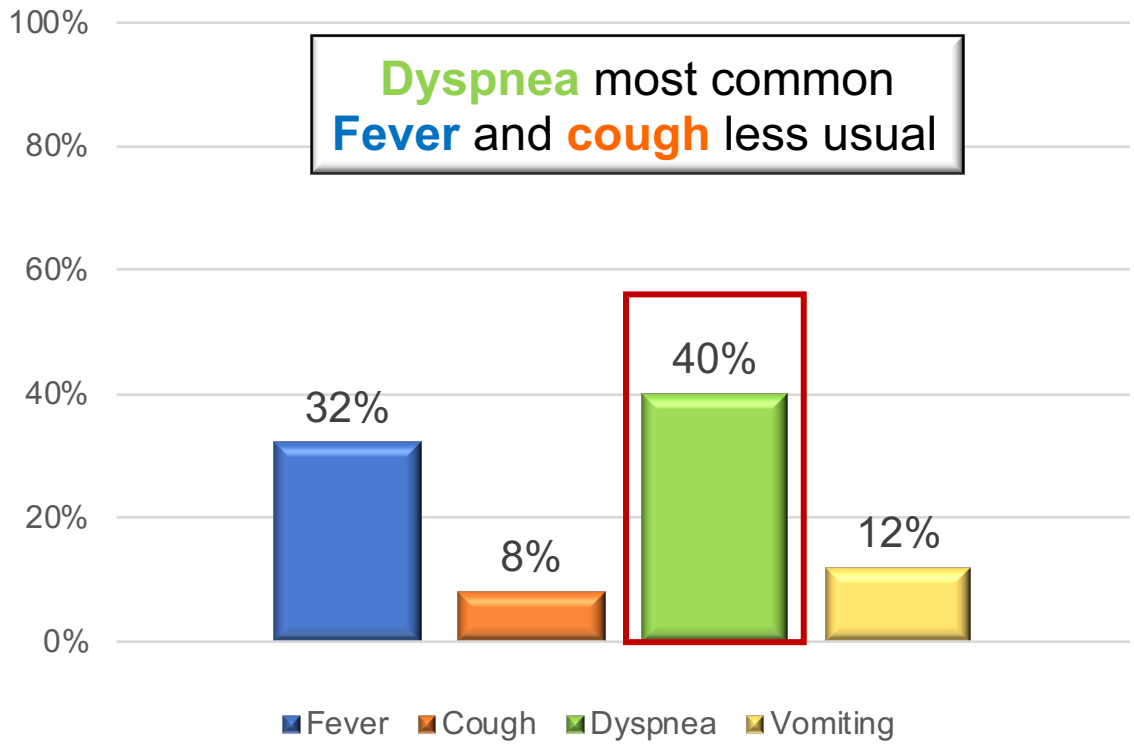


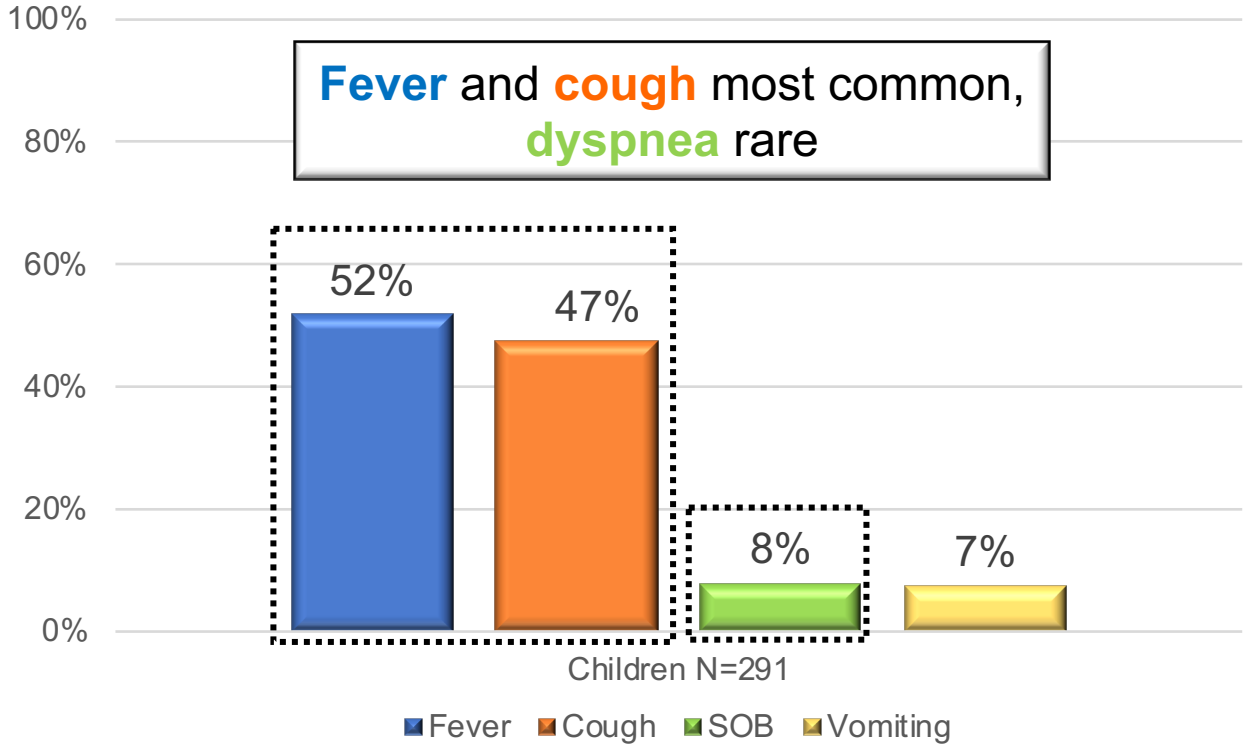
# Newborns/Infants Age <3 Months Less Likely Fever/Cough but More Likely Dyspnea Than Older Children

*Liguoro I et al. Eur J Pediatr. 2020 May 18*

**Disease Symptoms Newborns/Infants <3 Months**
**11 Studies, N=25**



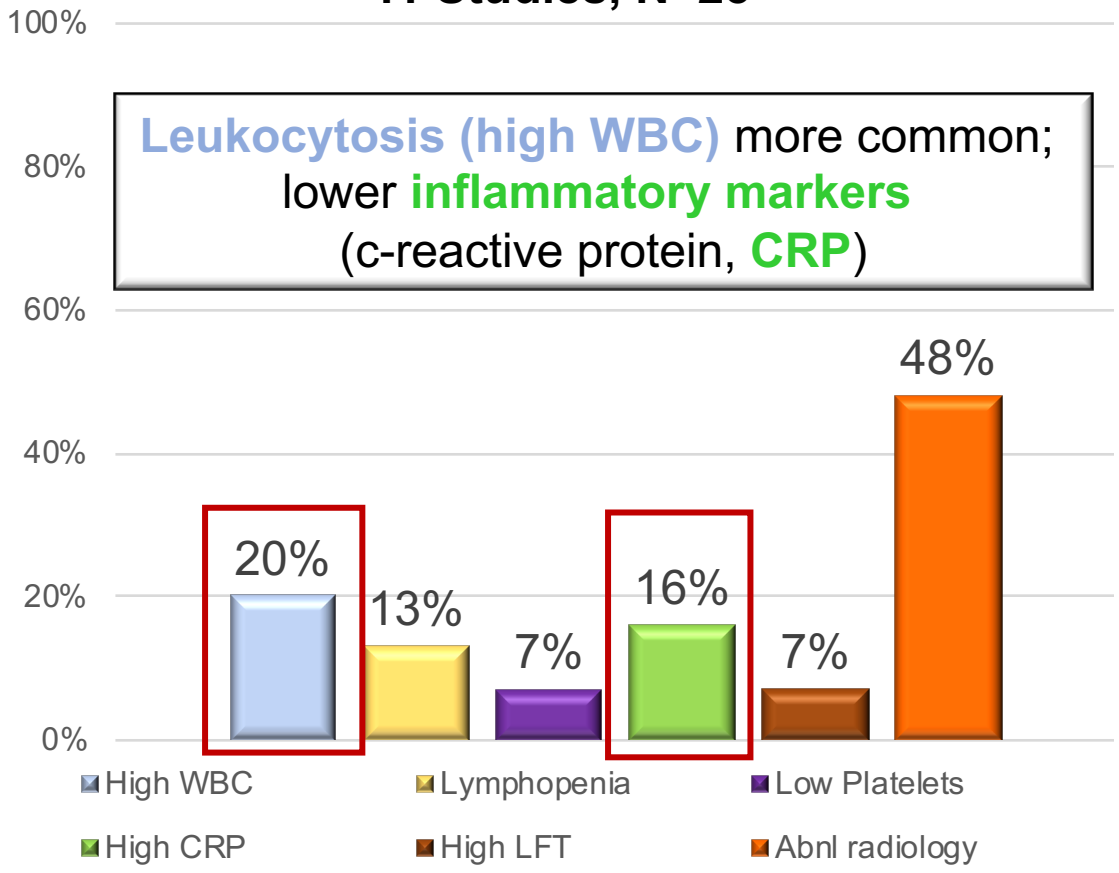

**Disease Symptoms in Children 0-18 Years**
**49 Studies, N=1,780**



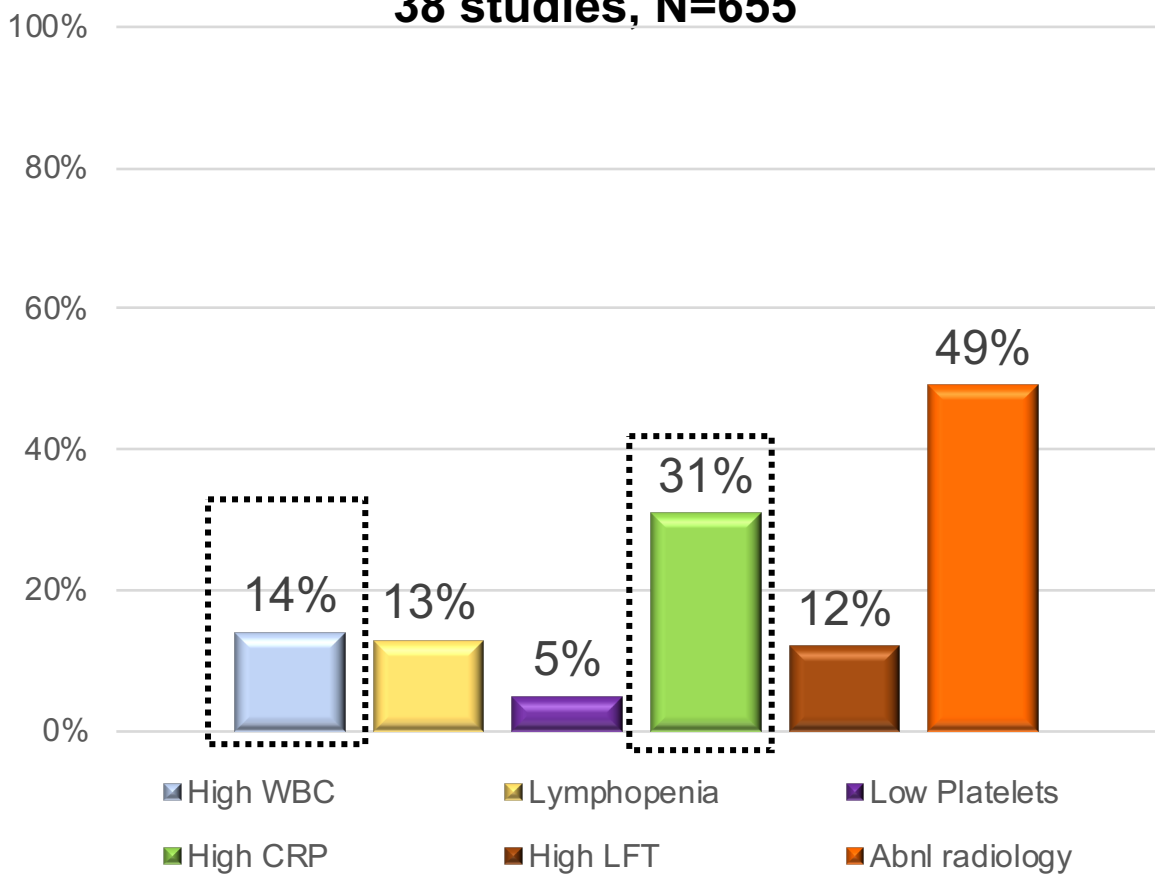
# Laboratory: Newborns/Infants Age <3 Months Have Lower Markers of Inflammation than Older Children

*Liguoro I et al. Eur J Pediatr. 2020 May 18*

## Lab Findings in Newborns/Infants <3 Months Old
## 11 Studies, N=25




## Lab Findings in Children 0-18 Years
## 38 studies, N=655

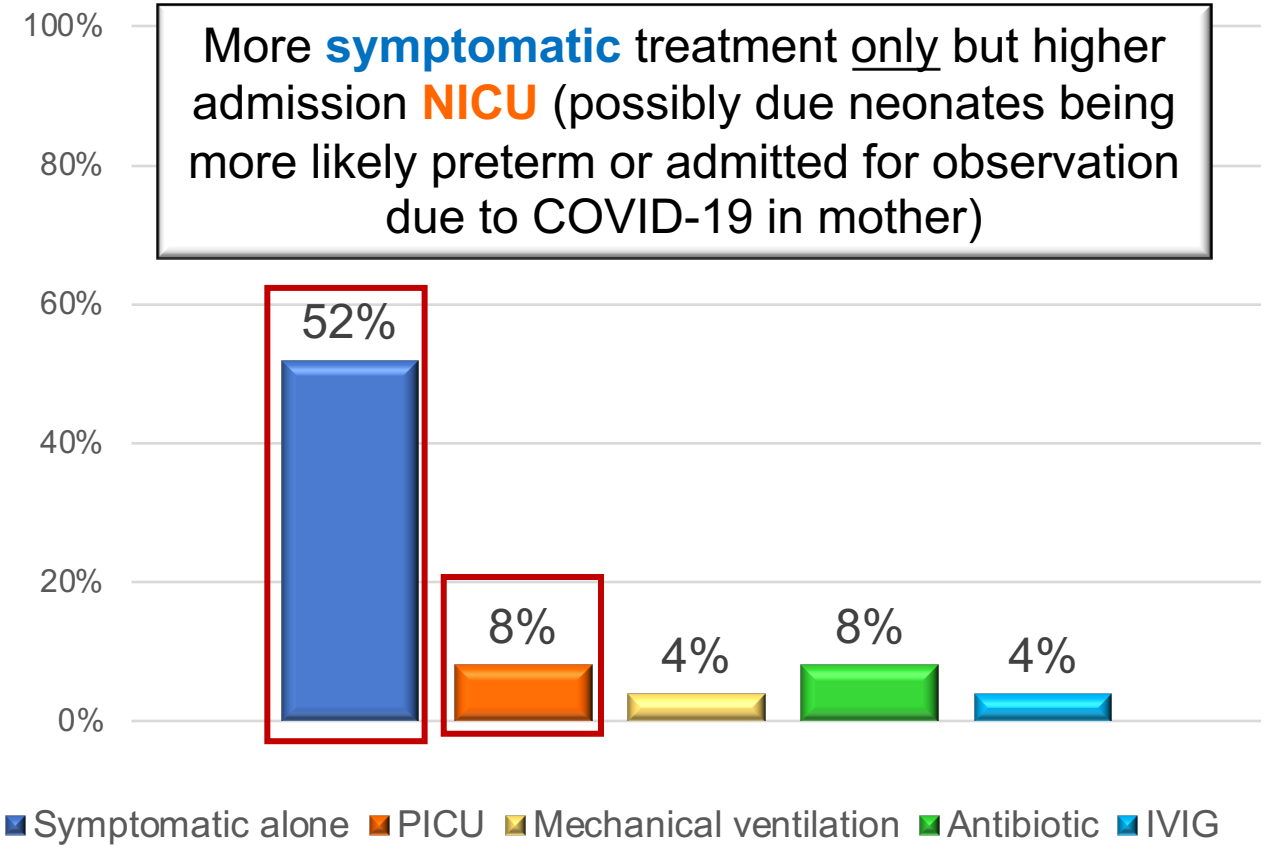


# Newborns/Infants Age <3 Months Less Likely to Require Specific Treatment but More Go to Neonatal ICU

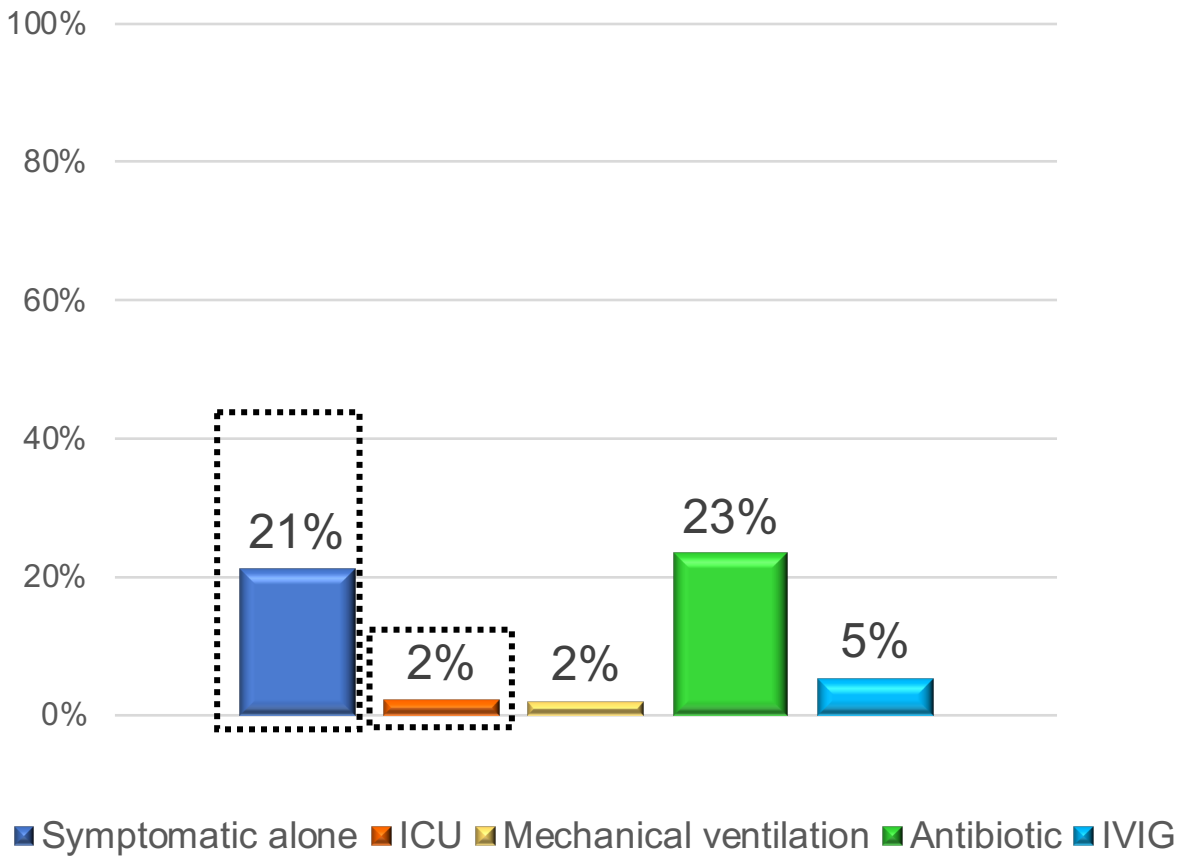
*Liguoro I et al. Eur J Pediatr. 2020 May 18*

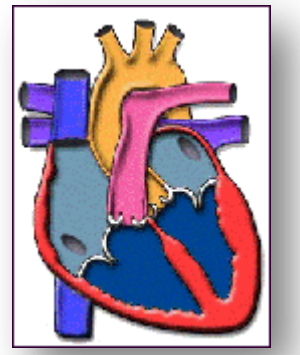
**Treatment in Newborns/Infants <3 Months**
**11 studies, N=25**

More **symptomatic** treatment only but higher admission **NICU** (possibly due neonates being more likely preterm or admitted for observation due to COVID-19 in mother)

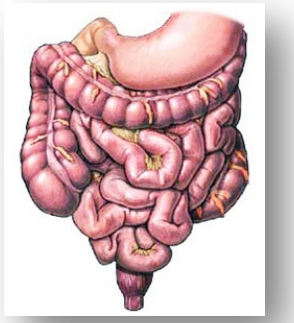



**Treatment in Children 0-18 Years**
**40 Studies, N=1,402**

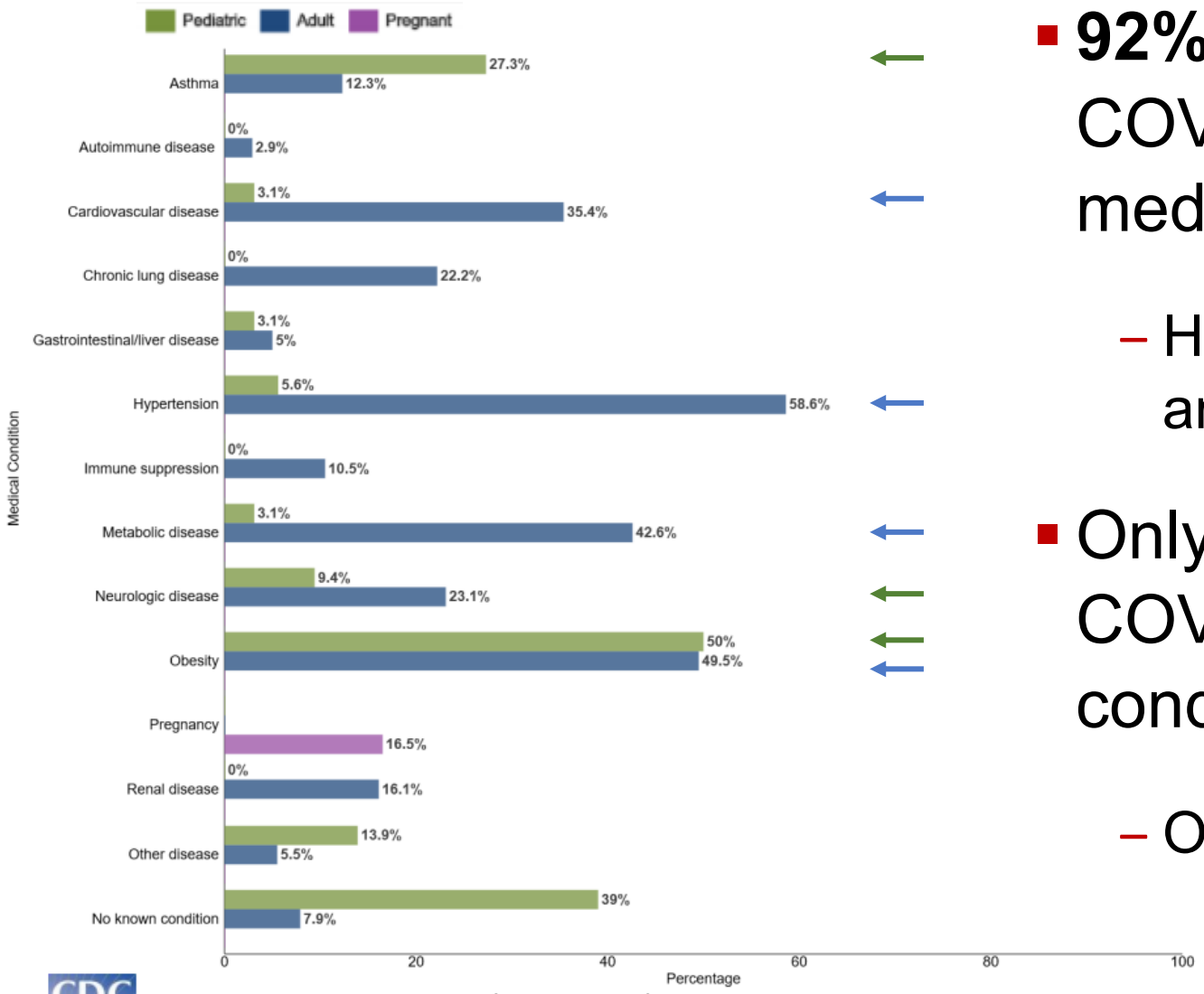




# Comorbidities and Hospitalization for COVID-19 in Children




# Underlying Conditions in Children Hospitalized with COVID-19, While Less Frequent than in Adults, Occurs in Significant Proportion




- **92%** of hospitalized adults with COVID-19 had at least one underlying medical condition; most common:
  - Hypertension, obesity, metabolic disease and cardiovascular disease
- Only **61%** of hospitalized children with COVID-19 had at least one underlying condition; most common:
  - Obesity, asthma, neurologic disease

CDC

COVIDView Week 20, ending May 16 2020

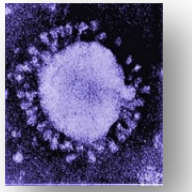
# Underlying Medical Conditions and COVID-19 in Children

- Asthma: While one of the common comorbidies in infected children, does not appear to predispose children to infection or increase hospitalization risk in those infected; nasal epithelium of children and adults with asthma has decreased ACE2 gene expression compared to those without asthma *(Bandi S et al. Pediatr Allergy Immunol. 2020 May 29: DeBasi et al. J Pediatr May 13; Jackson DJ et al. J Allergy Clin Immunol. 2020 Apr 22)*

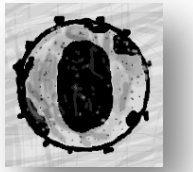
- Cancer: Memorial Sloan Kettering, NYC – screened 178 children with cancer for SARS-CoV-2; 20 (11%) infected, only 5% required hospitalization for symptoms. *(Boulad F et al. JAMA. 2020 May 13)*

- Nutritional status, malnutrition: No data on SARS-CoV-2 in malnourished pt.

- Nutritional status, obesity: **Associated with increased morbidity and mortality of COVID-19 in both children and adults**; obesity is associated with chronic low-grade inflammation and disrupted immune response *(Zachariah P et al. JAMA Pediatr. 2020 June 3; Simmonnet A et al. Obesity. 2020 May 25; Korakas E et al. Am J Physiol Endocrinol Metab. 2020 May 27).*



# COVID-19 and HIV
# Review of Literature through May 30



- 22 published reports on HIV/SARS-CoV-2 coinfection as of May 30
  - 182 HIV+ persons with coinfection, **all adults**
- 98% on ART (9% NNRTI, 18% PI; 73% InSTI)
- Majority CD4 >350 (only 10, 5%, had CD4 <200)
- Of those with VL data, 94% suppressed
- 63% had comorbidity
- Most had mild-moderate COVID-19; 8 (4%) required mechanical ventilation, 12 deaths (6.6%)
- Overall COVID-19 outcome in HIV+ adults similar to overall adults, with mortality associated with comorbidity and age and not HIV per se
- **No data on children with HIV and SARS-CoV-2/COVID-19 to date**

# What Do Children With Severe COVID-19 Look Like?

## Characteristics and Outcomes of Children with COVID-19 Disease Admitted to US/Canadian Pediatric Intensive Care Units

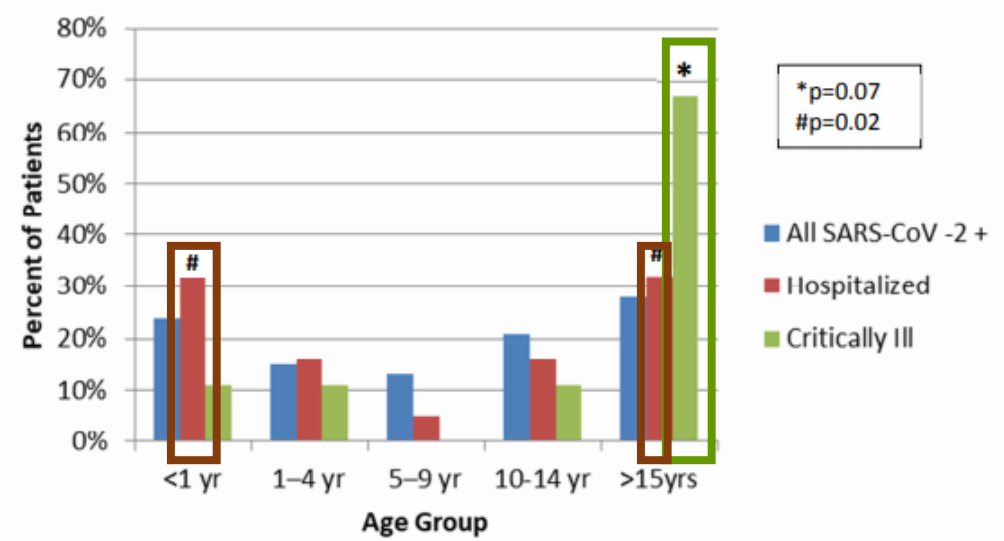
*Shekerdemian LS et al. JAMA. 2020 May 11 (epub)*

- Cross-sectional study of 48 children with COVID-19 admitted to 46 North American PICUs between March 14 and April 3 2020
- 40 (**83%**) had preexisting underlying medical conditions
- 35 (**73%**) presented with respiratory symptoms
- 18 (**38%**) required invasive mechanical ventilation
- Hospital mortality was **4.2%** (vs 0.08% overall in systematic review)
- While children have milder disease than adults, they can be extremely ill and if admitted to PICU, have elevated mortality

# Severe COVID-19 in Children and Young Adults, Washington DC

*DeBiasi RL et al. J Pediatr. 2020 May 13 (epub)*

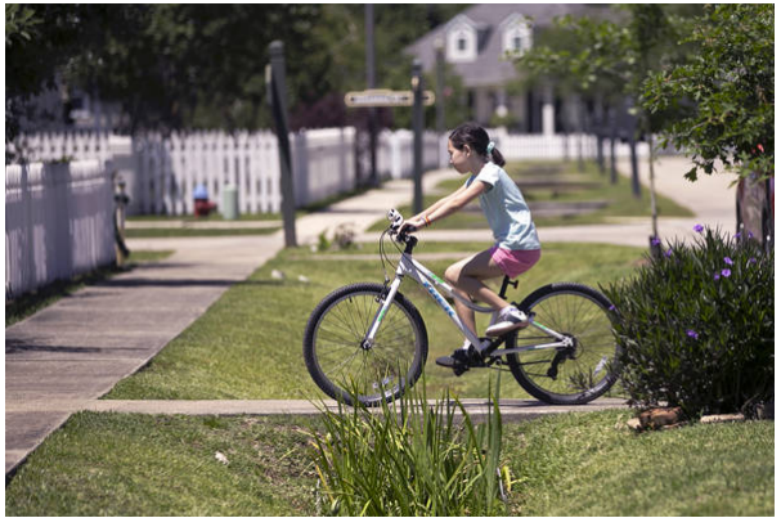
- 177 children with COVID-19 symptoms seen DC Children's Hospital
  - 133 not hospitalized, 44 (25%) hospitalized - 5%(9) needing critical care including mechanical ventilation (4)
  - Comorbidity in 39% - more common in those hospitalized (63% vs 32%)
  - Median age 9.6 years, however youngest (<1 year) and oldest (15-25 years) most likely to need hospitalization
    - Critically ill patients more likely to adolescent/young adult (mean 17.3 years)




→Adolescents and young adults with COVID-19 disease may be more likely to have "cytokine storm" picture seen in adults

# Multi-System Inflammatory Syndrome Temporally Associated with COVID-19 in Children

The Post Most



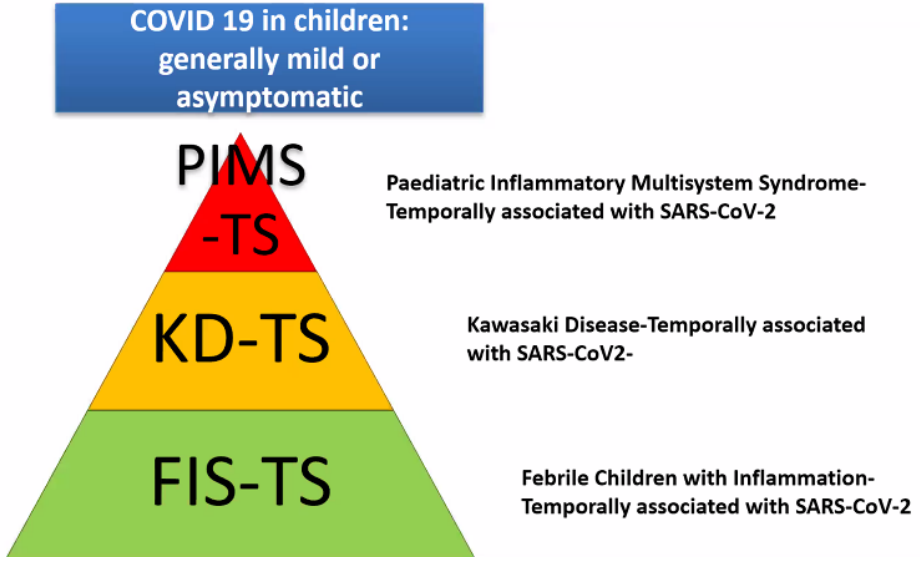
(Gerald Herbert/AP)

## The girl who died twice

Juliet Daly, from Covington, La., was a healthy 12-year-old before the coronavirus infected her heart, causing its electrical signals to go haywire until suddenly it stopped working.

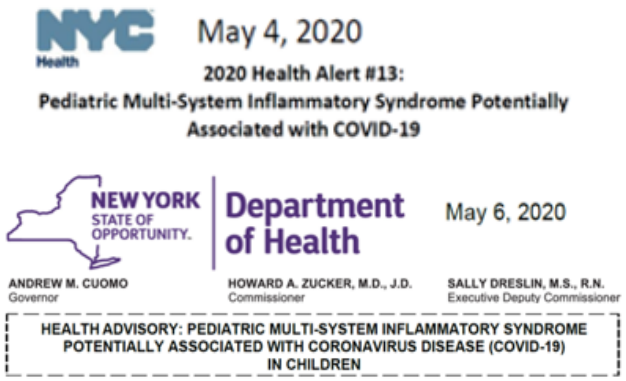
By Ariana Eunjung Cha and Chelsea Janes • **Read more »**

An emerging new spectrum of SARSCov2 in children- not just COVID



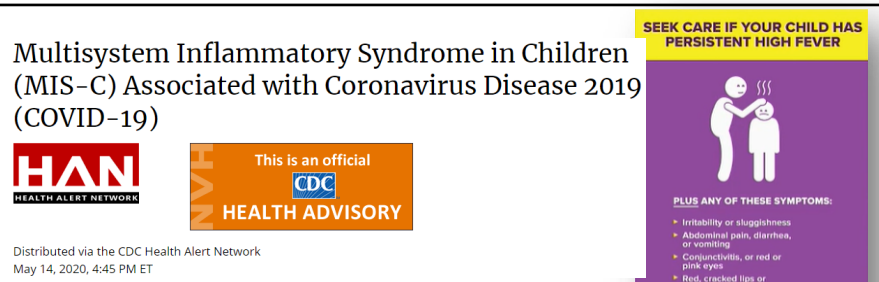
# Emerging Potential New Manifestation of SARS-CoV-2 in Children Pediatric Multi-System Inflammatory Syndrome (MSIS)


- In mid-late April reports from Western Europe identified a new febrile pediatric entity involving:
  - systemic hyperinflammation, multi-organ involvement, abdominal pain and GI symptoms, features similar to Kawasaki disease, with prominent cardiogenic shock and myocardial dysfunction.
  - Most children tested + rtPCR and/or had IgG/IgM antibody to SARS-CoV-2 although may not have had symptoms.

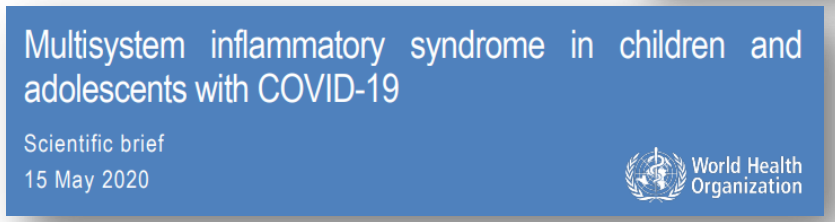


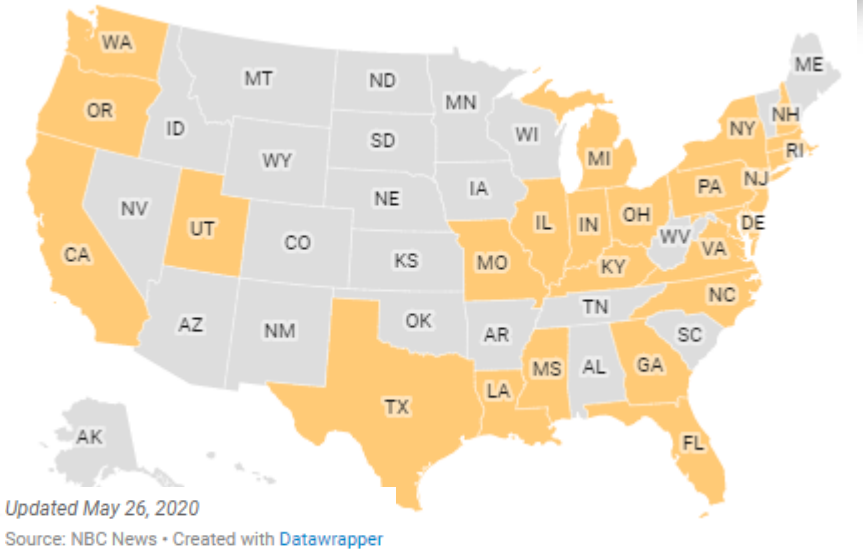

- By early May, cases reported in NYC, with health alert issued 1st by NYC May 4, then NY State on May 6 after 64 cases; by May 12, 102 cases reported with **3 deaths** in NY State.

# Emerging Potential New Manifestation of SARS-CoV-2 in Children Multi-System Inflammatory Syndrome in Children (MSIS)








- May 14, CDC issued health advisory with case definition and requested reporting of cases in US.
- May 15, WHO issued scientific brief, preliminary case definition, request for reporting to Global COVID-19 Clinical Data Platform and set up a global collaborative research forum.
- By May 26, MIS-C reported in children from 23 states in the US.

# Since First Published Report on MSIS in April, Explosion of Publications From US and Europe – 24 in <4 Weeks!

Hospital Pediatrics

Hospital Pediatrics »Insight

## Acute myocardial injury: a novel clinical pattern in children with COVID-19

*Andrea Wolfler, Savina Mannarino, Vania Giacomet, Anna Camporesi, Gianvincenzo Zuccotti

Lancet Child Adolesc Health 2020
Published Online
June 1, 2020
https://doi.org/10.1016/S2352-4642(20)30168-1

Alan R. Schroeder, Karen M Wilso

Hospital Pediatrics, May 2020, hpeds.2020-000356

in the Noise

The Pediatric Infectious Disease Journal

Pediatric Infectious Diseases Society

Indian

The Indian Journal of Pediatrics
https://doi.org/10.1007/s12098-020-03357-1

CLINICAL BRIEF

## Multisystem Inflammato Kawasaki Disease during

Abdul Rauf[1] · Ajay Vijayan[1] · Shaji Thomas John[1] · Raghuram Krishnan[2] · Abdul Lat

JAMA | Original Investigation JAMA Published online June 8, 2020

## Clinical Characteristics of 58 Children With a Pediatric Inflammatory Multisystem Syndrome Temporally Associated With SARS-CoV-2

Elizabeth Whittaker, MD; Alasdair Bamford, MD; Julia Kenny, MD; Myrsini Kaforou, PhD; Christine E. Jones, MD; Priyen Shah, MD; Padmanabhan Ramnarayan, MD; Alain Fraisse, MD; Owen Miller, MD; Patrick Davies, MD; Filip Kucera, MD; Joe Brierley, MD; Marilyn McDougall, MD; Michael Carter, MD; Adriana Tremoulet, MD; Chisato Shimizu, MD; Jethro Herberg, MD; Jane C. Burns, MD; Hermione Lyall, MD; Michael Levin, MD; for the PIMS-TS Study Group and EUCLIDS and PERFORM Consortia

JAMA Published online June 8, 2020

RESEARCH LETTER

## Multisystem Inflammatory Syndrome Related to COVID-19 in Previously Healthy Children and Adolescents in New York City

Eva W. Cheung, MD
Philip Zachariah, MD, MS
Mark Gorelik, MD
Alexis Boneparth, MD
Steven G. Kernie, MD
Jordan S. Orange, MD, PhD
Joshua D. Milner, MD

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

ELSEVIER

Cardiology in the Young

Circulation

## Features of COVID-19 post-infectious cytokine release syndrome in children presenting to the emergency department

Temima Waltuch, MD *, Prakriti Gill, MD, Lauren E. Zinns, MD, Rachel Whitney, MD, Julia Tokarski, MD, James W. Tsung, MD, MPH, Jennifer E. Sanders, MD

## Novel paediatric presentation of COVID-19 with ARDS and cytokine storm syndrome without respiratory symptoms

Clare E Pain, Susanna Felsenstein, Gavin Cleary, Sarah Mayell, Karsten Conrad, Srikrishna Harave, Phuoc Duong, Ian Sinha, David Porter, *Christian M Hedrich

Lancet Rheumatol 2020
Published Online
May 15, 2020
https://doi.org/10.1016/S2665-9913(20)30137-5

The Lancet
Published: May 13, 2020

Roberta L. DeBiasi MD, MS[1, 10, 11], Xiaoyan Song MBBS, PhD[2, 10], Meghan Delaney MD[3, 10], Michael Bell MD[4, 10], Karen Smith MD[5, 10], Jay Pershad MD[6, 10], Emily Ansusinha[1], Andrea Hahn[1, 10], Rana Hamdy[1, 10], Nada Harik[1, 10], Benjamin Hanisch[1, 10], Barbara Jantausch[1, 10], Adeline Koay[1, 10], Robin Steinhorn MD[7, 10], Kurt Newman MD[8, 10], David Wessel MD[4, 9, 10]

Metropolitan Region

Loomba, Enrique Villarreal, Saul Flores

d online by Cambridge University Press: 15 May 2020, pp. 1-5

art failure in multisystem inflammatory syndrome in children (MIS-C) in ext of global SARS-CoV-2 pandemic

djer, Mathilde Méot, Fanny Bajolle, Diala Khraiche, Antoine Legendre, Samya Abakka, Johanne Auriau, aud, Mehdi Oualha, Maurice Beghetti, Julie Wacker, Caroline Ovaert, Sebastien Hascoet, gny, Sophie Malekzadeh-Milani, Alice Maltret, Gilles Bosser, Nathan Giroux, Laurent Bonnemains, det, Sylvie Di Filippo, Pierre Mauran, Sylvie Falcon-Eicher, Jean-Benoît Thambo, Bruno Lefort, eri, Lucile Houyel, Sylvain Renolleau, and Damien Bonnet

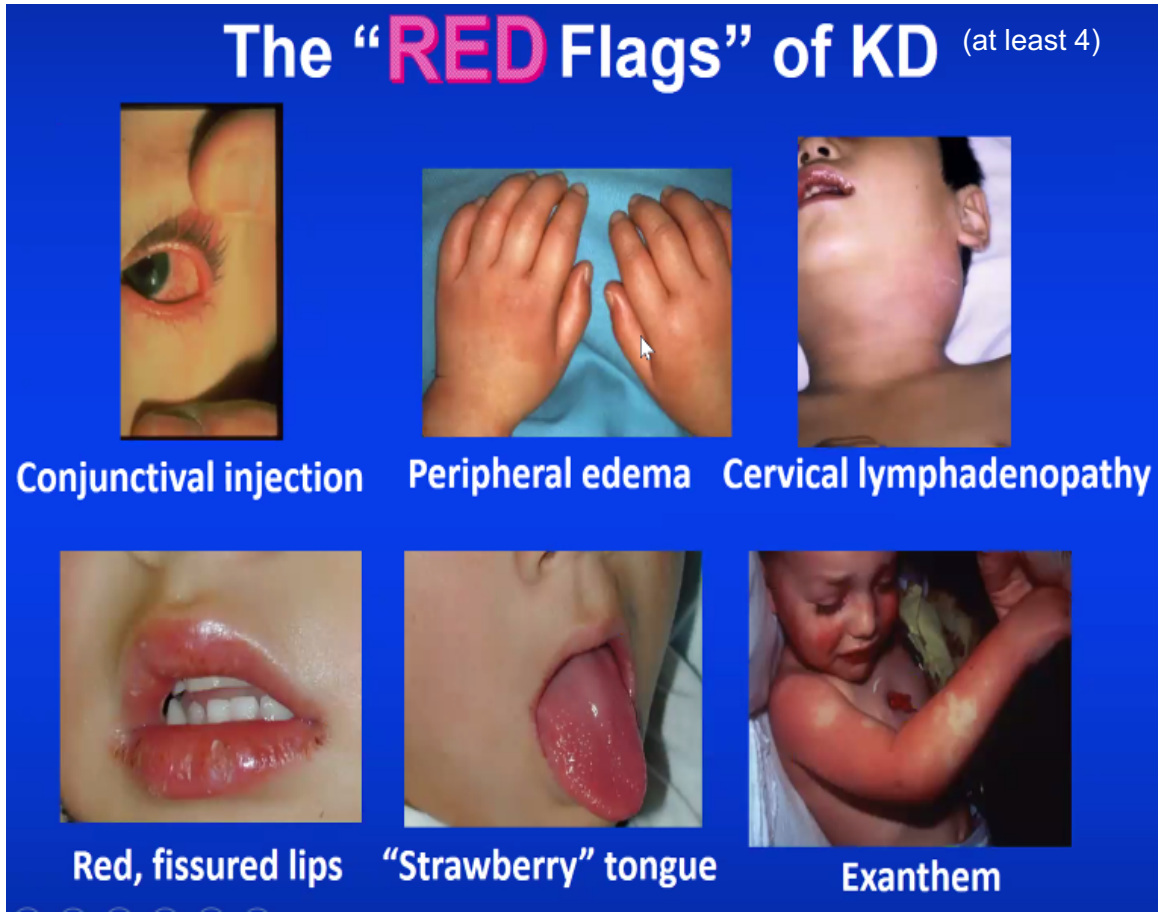
Circulation. 2020, https://doi.org/10.1161/CIRCULATIONAHA.120.048360

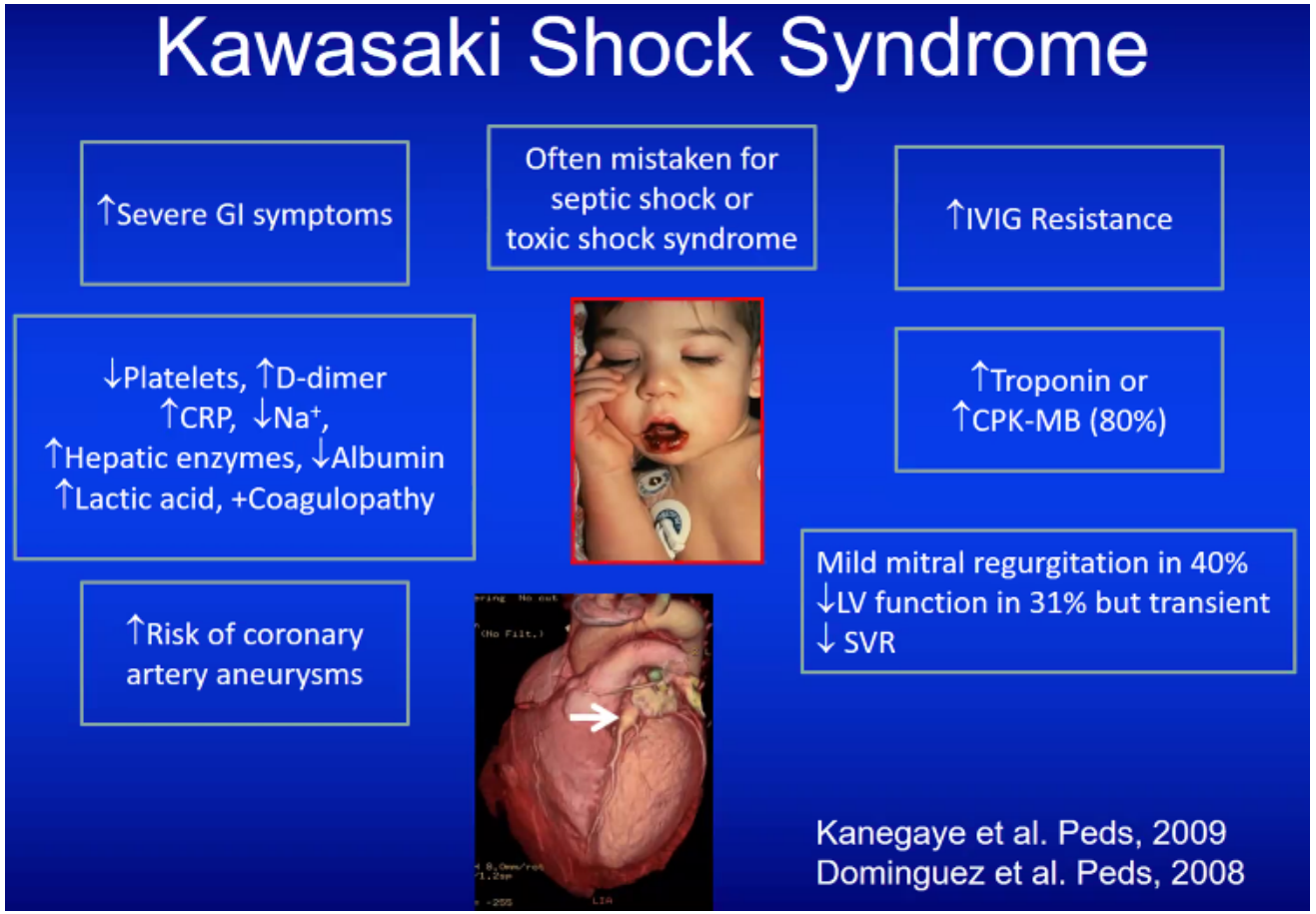
# Pediatric Multi-System Inflammatory Syndrome

- Temporally, MSIS began to manifest approximately ~1 month after the peak of COVID-19 cases in Europe and US rather than contemporaneously with epidemic peak.
- Most children have evidence of SARS-CoV-2 but not necessarily current infection (rtPCR+) but IgG/IgM indicating past infection.
- Suggests a post-infectious inflammatory process that may be immune complex-mediated.
- Resemblance to Kawasaki Disease/Shock Syndrome.
- Clinical picture possibly resembles later phase of adult COVID-19 characterized by cytokine storm, hyperinflammation, multi-organ damage including severe myocarditis and acute kidney injury.

# Kawasaki Disease (KD) and Kawasaki Shock Syndrome

- Self-limited vasculitis of childhood, thought precipitated by common infection pathogen resulting in immune-mediated response in genetically pre-disposed children; most important complication coronary artery aneurysms.




*Adriana Tremoulet, Kawasaki Disease Research Center, UCSD*

# Differences Kawasaki Disease and Multi-System Inflammatory Syndrome

- **Demographic features** differ from KD, where 50% are <24 months and 80% <5 years, compared to mean age 8-10 years with MIS-C including adolescents. KD more frequent in Asian countries but MIS-C not seen in Asia yet; in several series, more often in children of African ancestry.
- **Clinical features** include more impressive abdominal pain, diarrhea, vomiting and multi-organ involvement including acute kidney injury.
- **Cardiac features** show moderate to severe myocardial involvement (by imaging and very high NT-pro-BNP and troponin levels), greater than KD or KD shock syndrome.
- **Laboratory features** distinct from KD with hyperinflammation with elevated ferritin, D-dimers,  IL-6, CRP, lymphopenia, thrombocytopenia.

JAMA | Original Investigation *epub June 8 2020*

# Clinical Characteristics of 58 Children With a Pediatric Inflammatory Multisystem Syndrome Temporally Associated With SARS-CoV-2

Elizabeth Whittaker, MD; Alasdair Bamford, MD; Julia Kenny, MD; Myrsini Kaforou, PhD; Christine E. Jones, MD; Priyen Shah, MD; Padmanabhan Ramnarayan, MD; Alain Fraisse, MD; Owen Miller, MD; Patrick Davies, MD; Filip Kucera, MD; Joe Brierley, MD; Marilyn McDougall, MD; Michael Carter, MD; Adriana Tremoulet, MD; Chisato Shimizu, MD; Jethro Herberg, MD; Jane C. Burns, MD; Hermione Lyall, MD; Michael Levin, MD; for the PIMS-TS Study Group and EUCLIDS and PERFORM Consortia


- Largest case series published: 58 children from 8 hospitals England
- Presented with fever, non-specific sx (most common GI), inflammation
  - 13 had sx meeting definition KD (+- shock)
  - 23 had fever and inflammation without shock or KD
  - 29 developed shock/myocardial dysfunction, 23 mechanical ventilation
  - 8 developed coronary artery dilatation or aneurysm
- 78% had evidence current or prior SARS-CoV-2
- They compared to database of >1,000 children with KD/KD-shock syndrome to evaluate similarities and differences

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**MSIS**

**Older**

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**MSIS**

Older

**Higher WBC**

**Higher neutrophils**

JAMA | Original Investigation

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**MSIS**

Older

Higher WBC

Higher neutrophils

**Lower lymphocytes**

**Lower hemoglobin**

**Lower platelets**

**Lower albumin**

JAMA | Original Investigation

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**MSIS**

Older

Higher WBC

Higher ANC

More lymphopenia

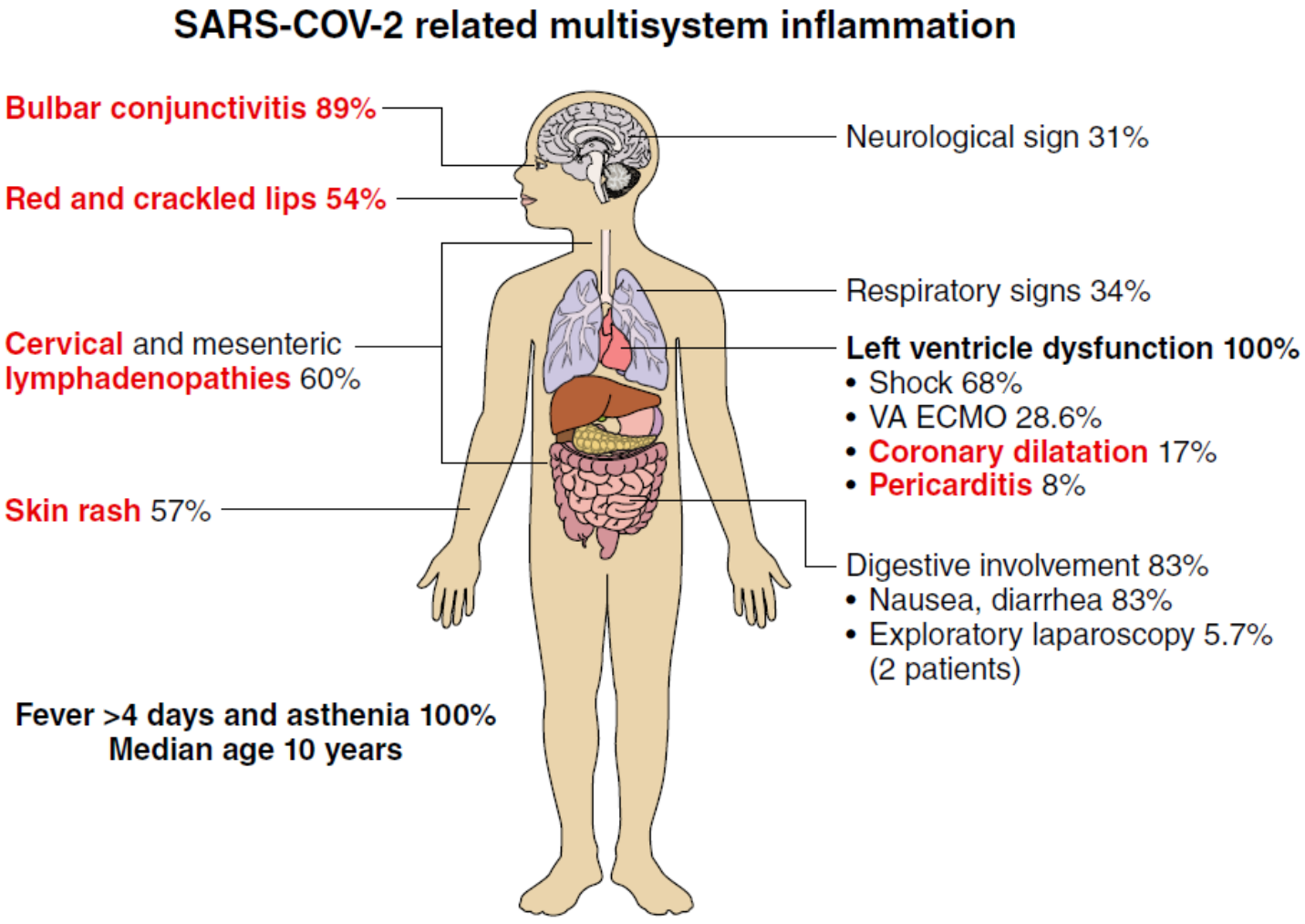
More anemia

Lower platelets

Lower albumin

**Markedly elevated inflammatory markers**

# Manifestations of Multi-System Inflammatory Syndrome



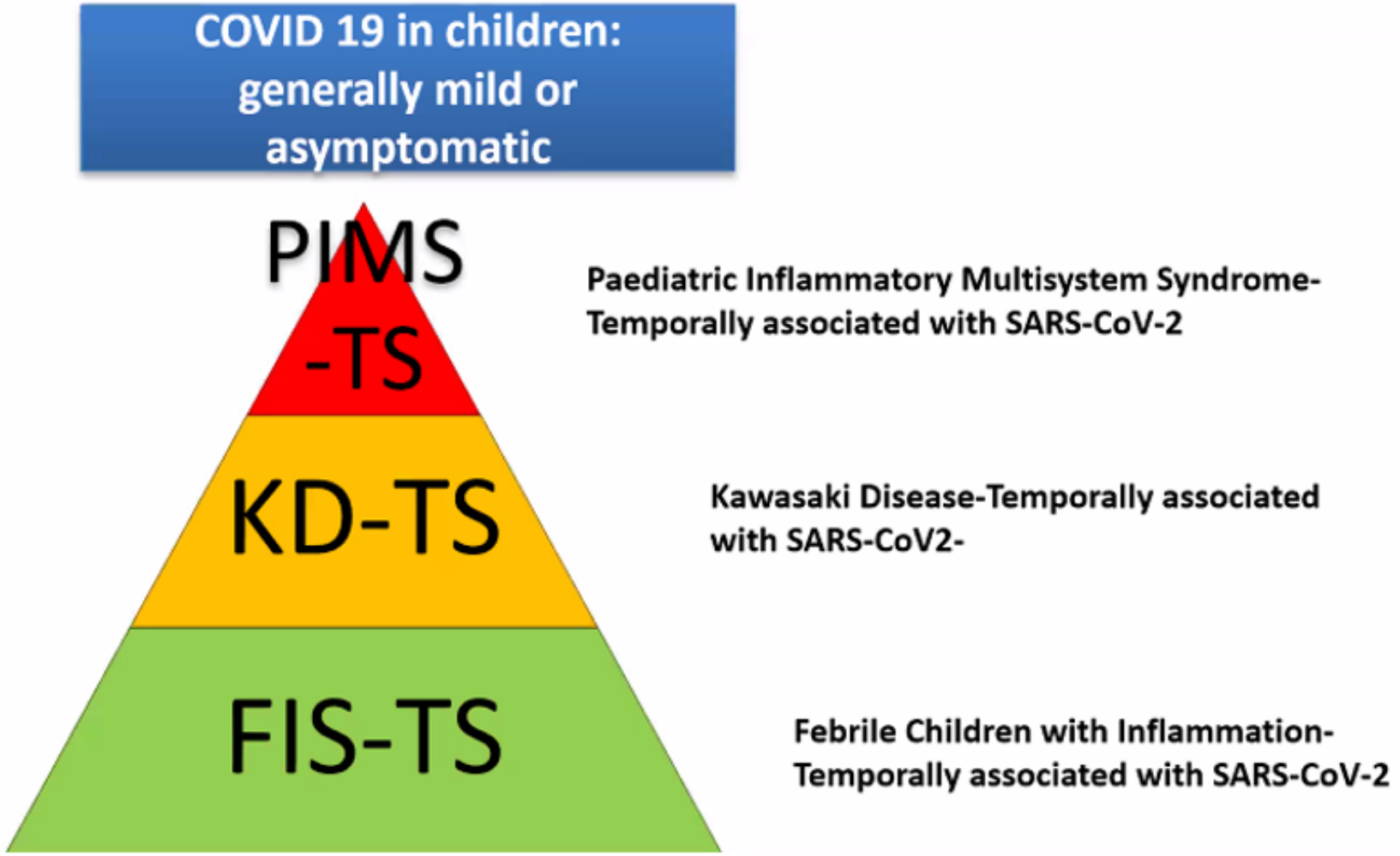

*Belhadjer Z et al. Circulation 2020 May 17 (epub)*

- Red=signs/symptoms consistent with Kawasaki Disease
- Black=signs that are rare in Kawasaki Disease
- Percentages come from case series of 35 cases over 2 months from 14 centers France and Switzerland *(Belhadjer Z et al. Circulation 2020 May 17)*


# Treatment of Multi-System Inflammatory Syndrome


- Primary supportive care of acute organ dysfunction and shock.
- Most improve with IVIG with or without steroids, which act to modulate cytokine activation.
- Other immune modulators have been used if non-responsive to IVIG/steroids (anakinra – IL1 blockade; sarilumab/tocilizumab – IL6 blockade).
- Not reported from Asian countries at this time, or from Africa – but surveillance for the syndrome has also been limited to non-existent until now.

# Possible Widening Spectrum of Disorders in Children that May be Associated with SARS-CoV-2 Infection




*Dr. Michael Levin, Imperial College, United Kingdom*

# WHO Website for Multi-System Inflammatory Syndrome

https://www.who.int/news-room/commentaries/detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19

- Preliminary case definition and global reporting clinical data platform.

## Multisystem inflammatory syndrome in children and adolescents with COVID-19

Scientific brief
15 May 2020

World Health Organization

### Preliminary case definition[a]

Children and adolescents 0–19 years of age with fever ≥ 3 days

**AND** two of the following:

a) Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet).

b) Hypotension or shock.

c) Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP),

d) Evidence of coagulopathy (by PT, PTT, elevated d-Dimers).

e) Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain).

**AND**

Elevated markers of inflammation such as ESR, C-reactive protein, or procalcitonin.

**AND**

No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes.

**AND**

Evidence of COVID-19 (RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19.

[a] Consider this syndrome in children with features of typical or atypical Kawasaki disease or toxic shock syndrome.

World Health Organization

PARTICIPANT ID I__I I__I I__I I__I I__I -- I__I I__I I__I I__I

**Global COVID-19 Clinical Platform: Case Report Form for suspected cases of Multisystem inflammatory syndrome (MIS) in children and adolescents temporally related to COVID-19**

**Preliminary case definition**

Children and adolescents 0–19 years of age with fever ≥ 3 days

*AND* two of the following:

a) Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet)
b) Hypotension or shock
c) Features of myocardial dysfunction, or pericarditis, or valvulitis, or coronary abnormalities (ECHO findings or elevated Troponin/NT-proBNP)
d) Evidence of coagulopathy (abnormal PT, PTT, elevated d-Dimers)
e) Acute gastrointestinal problems (diarrhoea, vomiting or abdominal pain)

***AND***

Elevated markers of inflammation such as ESR, C-reactive protein or procalcitonin

***AND***

No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes

***AND***

Evidence of COVID (RT-PCR, antigen test or serology positive) or likely contact with patients with COVID

**MODULE 1. Complete this form for all children aged 0–19 suspected to have multisystem inflammatory disorder (even if all criteria in the case definition are not met – to capture full spectrum of the condition). Initiate the form at the time the disorder is suspected. Submit Module 1 when initial investigations included in case definition are available.**

**Facility name**_____ **Country**_____

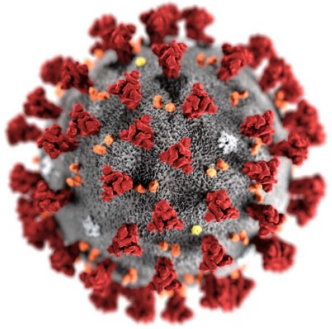
**Date of completing module** [_D_][_D_]/[_M_][_M_]/[_2_][_0_][_Y_][_Y_]
**Date of admission to hospital** [_D_][_D_]/[_M_][_M_]/[_2_][_0_][_Y_][_Y_]

**1a. CLINICAL FEATURES OF CURRENT ILLNESS** *(complete when MIS is first suspected)*

| | | | |
|---|---|---|---|
| Fever | ☐Yes | ☐No | ☐Unknown |
| Duration of fever ___ days | | | |
| Rash | ☐Yes | ☐No | ☐Unknown |
| Bilateral non-purulent conjunctivitis | ☐Yes | ☐No | ☐Unknown |
| Oral mucosal inflammation signs | ☐Yes | ☐No | ☐Unknown |
| Peripheral cutaneous inflammation signs (hands or feet) | ☐Yes | ☐No | ☐Unknown |
| Hypotension (age-appropriate) | ☐Yes | ☐No | ☐Unknown |
| Tachycardia (age-appropriate) | ☐Yes | ☐No | ☐Unknown |
| Prolonged capillary refill time | ☐Yes | ☐No | ☐Unknown |
| Pale/mottled skin | ☐Yes | ☐No | ☐Unknown |
| Cold hands/feet | ☐Yes | ☐No | ☐Unknown |
| Urinary output < 2 mL/kg/hr | ☐Yes | ☐No | ☐Unknown |
| Chest pain | ☐Yes | ☐No | ☐Unknown |
| Tachypnoea (age-appropriate) | ☐Yes | ☐No | ☐Unknown |
| Respiratory distress | ☐Yes | ☐No | ☐Unknown |
| Abdominal pain | ☐Yes | ☐No | ☐Unknown |
| Diarrhoea | ☐Yes | ☐No | ☐Unknown |
| Vomiting | ☐Yes | ☐No | ☐Unknown |

# COVID-19 Disease in Children

- While COVID-19 seems relatively less frequent and more benign in pediatric populations, severe cases have been reported and this appearance may be biased by our incomplete knowledge of this new disease.
- Similar to adults, children with comorbidities appear over-represented in those with more severe disease.
- Recent emergence of multi-system inflammatory syndrome in children with SARS-CoV-2 infection (either current infection or infection in recent past) demonstrates how disease due to SARS-CoV-2 in children remains yet to be defined.



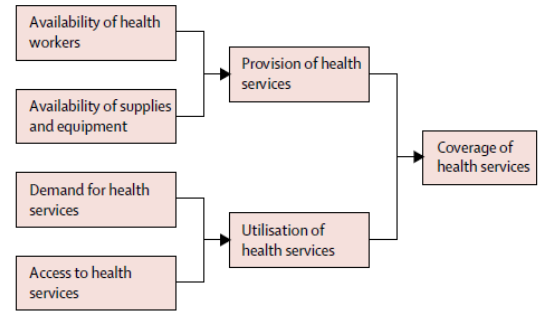
# Impact of COVID-19 Response on HIV and Maternal and Child Health Services

Modeling Exercises

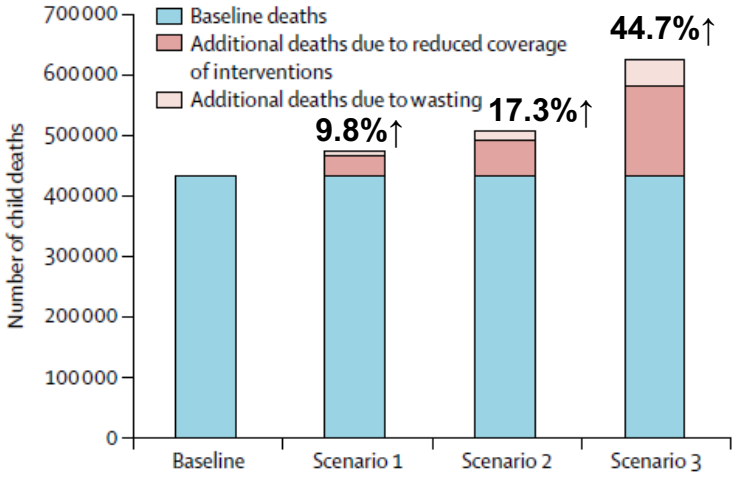
# Potential Impact of COVID-19 Responses on Maternal/Child Mortality

- *Robertson T et al. Lancet Global Health. 2020 May 12* – modeled 3 scenarios where coverage of essential maternal and child health interventions are reduced by 5-10-15% and child wasting increases by 5-10-15% in 118 LMIC.

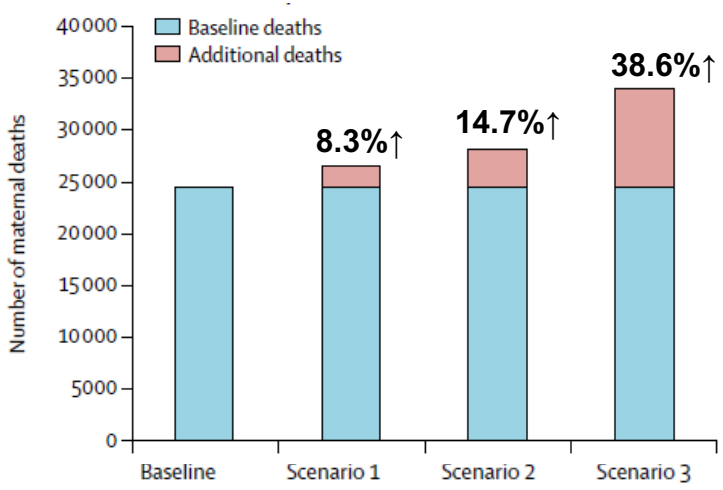
**Framework Effects of Health System Components on Health Service Coverage**




**Child Deaths per Month**




**Maternal Deaths per Month**




Disruption in service coverage:

Scenario 1: Small ↓ services

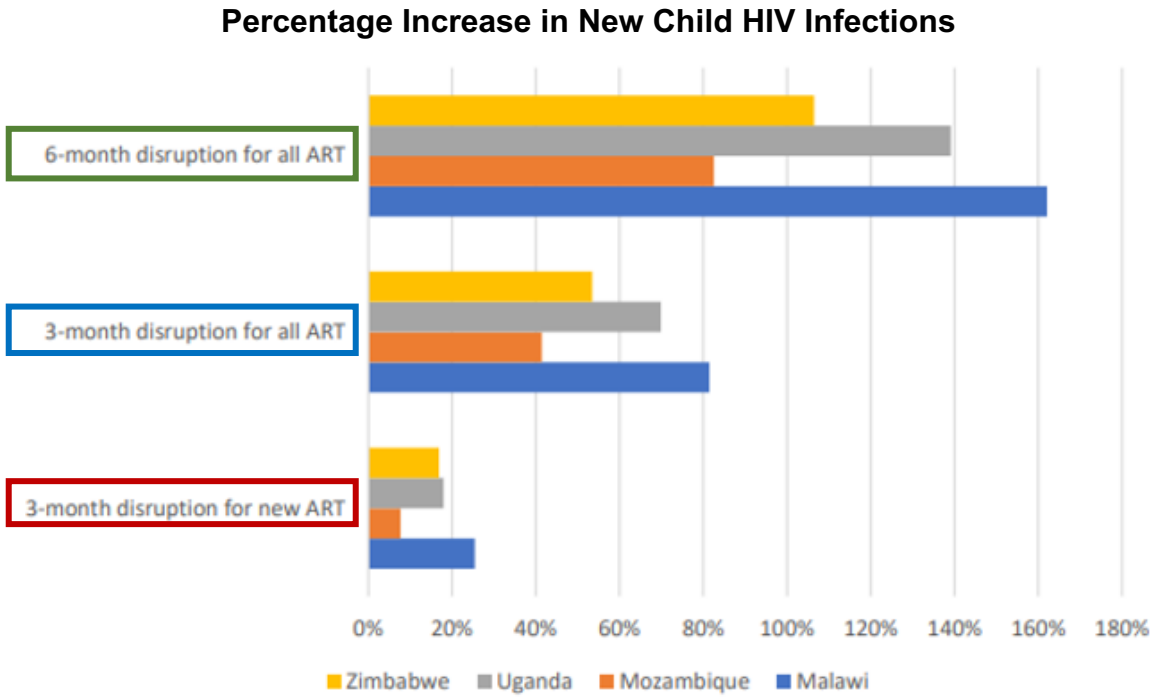
Scenario 2: Moderate ↓ services

Scenario 3: Large ↓ service

- Depending on scenario, there could be an increase of 9.8 to 44.7% in under age 5-child deaths per month and 8.3% to 38.6% increased in maternal deaths per month across 118 countries.

# Potential Impact of COVID-19 Responses on Pediatric HIV Epidemic

- *Stover J et al. MedRxiv doi.org/10.1101/2020.05.04.20090399* – examined effects of 3- or 6-month service disruption due to lockdown/health system capacity constraints on HIV incidence, including MTCT, in 4 African countries.

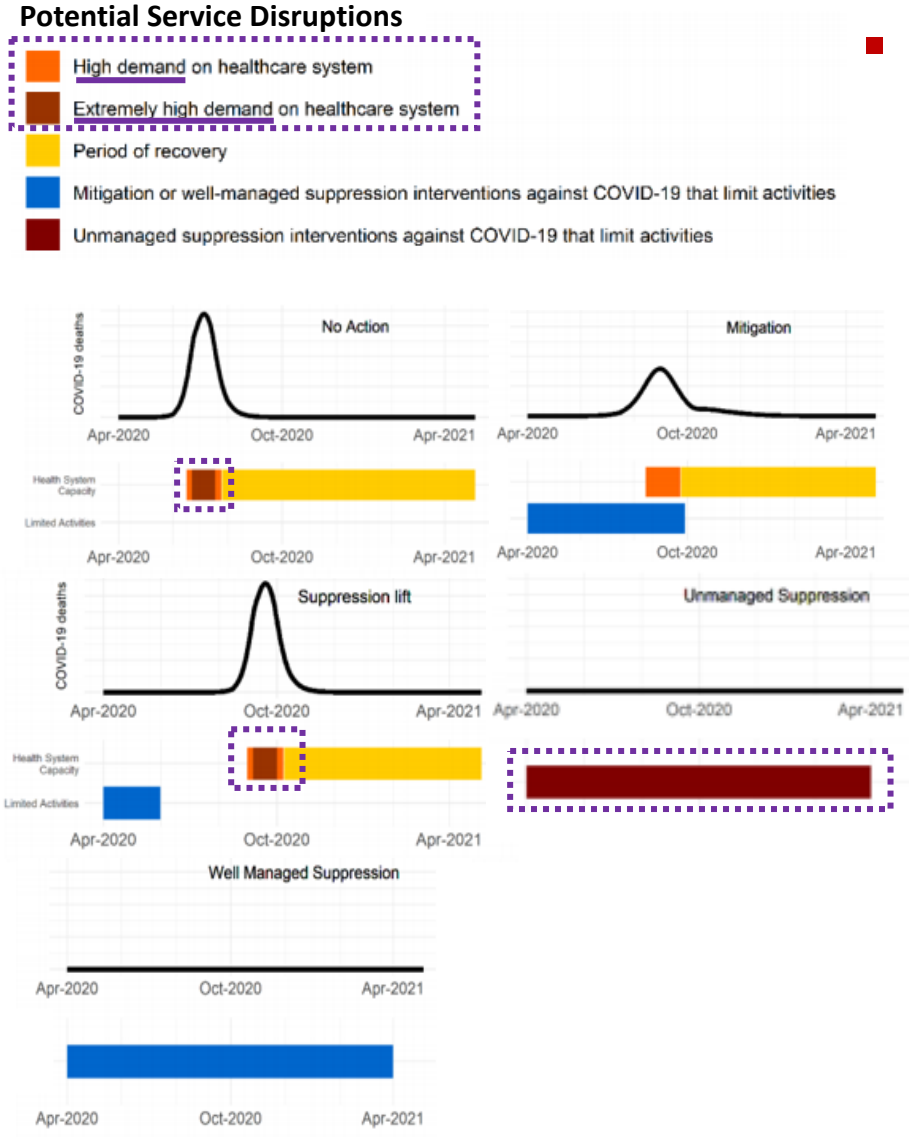



- Currently PMTCT coverage is high in most countries with few new child infections.
- Any disruption in PMTCT services could lead to large increases in new child infections, from about 10% if disruption for new patients only; to ~50% for 3-month if disruptions for all PMTCT services; and 100% or more for 6-month if disruptions to all PMTCT services.

# Impact of COVID-19 Response on HIV, TB and Malaria in LMIC

*Hogan AB et al; Imperial College COVID-19 Response Team 2020 May 1*

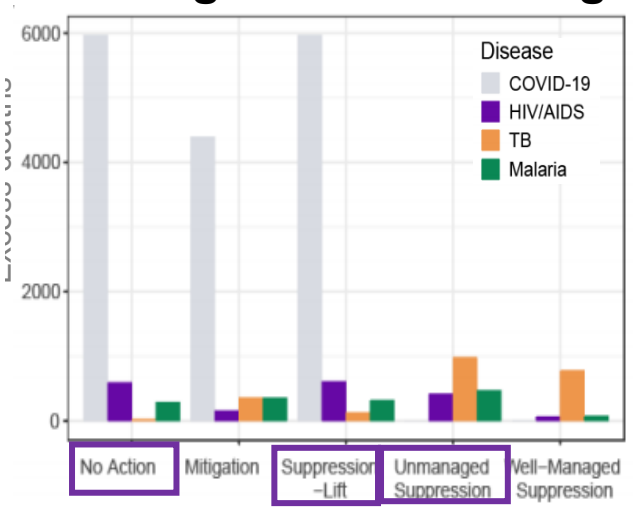
https://www.imperial.ac.uk/media/imperial-college/medicine/mrc-gida/2020-05-01-COVID19-Report-19.pdf




- Modeled 5 intervention scenarios for COVID-19 (no action, mitigation, suppression-lift, unmanaged, and well-managed suppression) and **potential service disruptions**, and impact on extra deaths due to HIV, TB and malaria 2020-2024.

**Excess deaths 2020-2024, COVID-19, HIV, TB or Malaria in Each Scenario**

**High Burden Setting**

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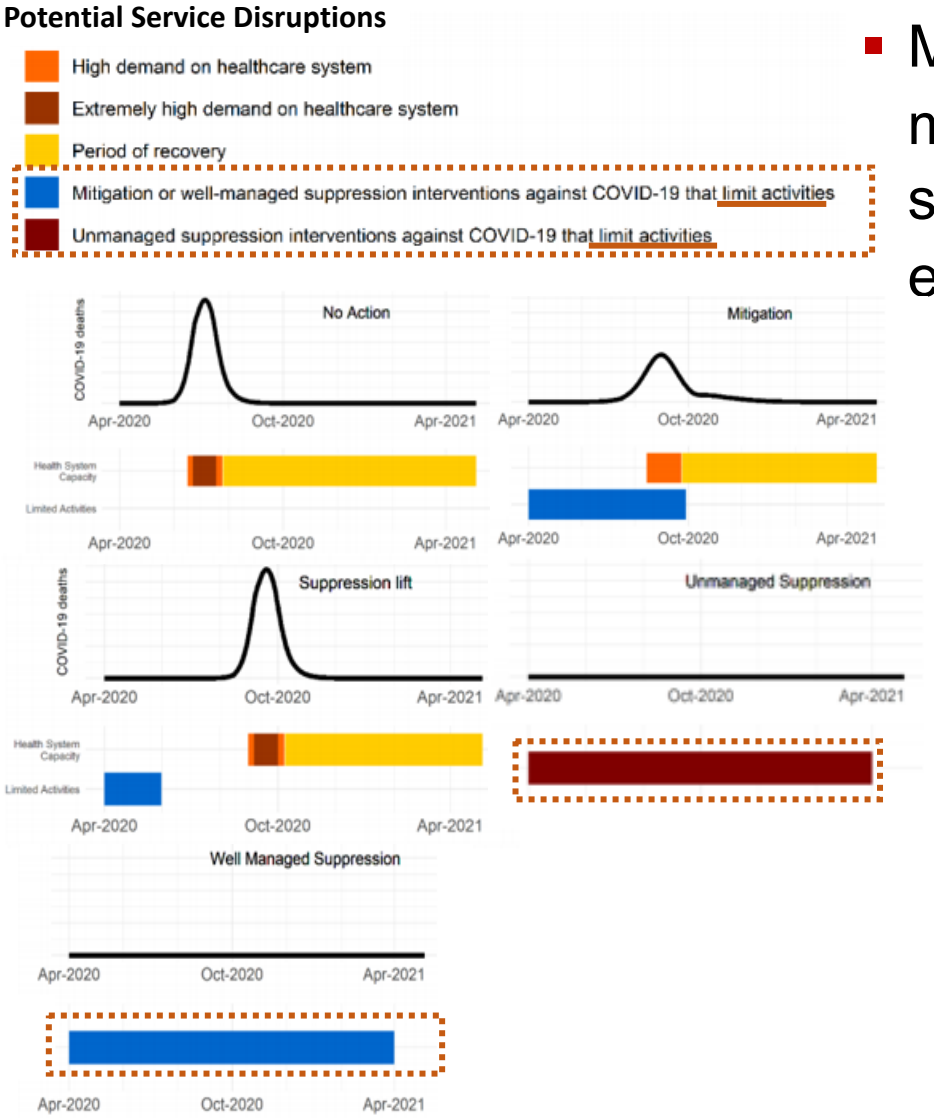


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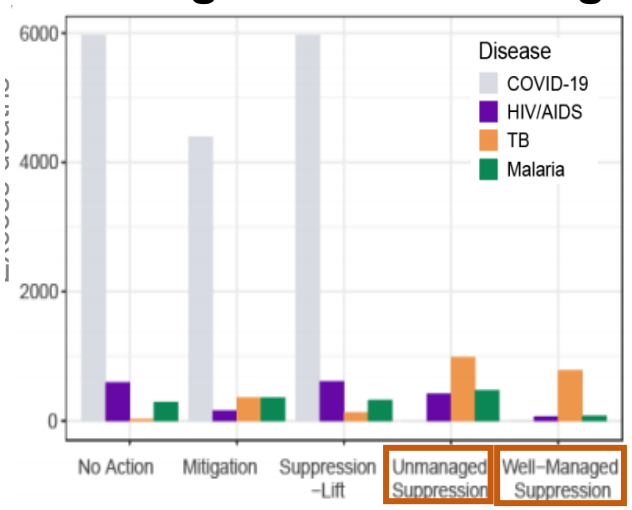


→ For HIV, up to 10% ↑ HIV deaths, primarily ART interruption during high/extreme health system demand.

→ For TB, up to 20% ↑ TB deaths, primarily reductions in timely dx/rx new cases from long period of COVID-19 unmanaged/well-managed suppression interventions that limit activities.

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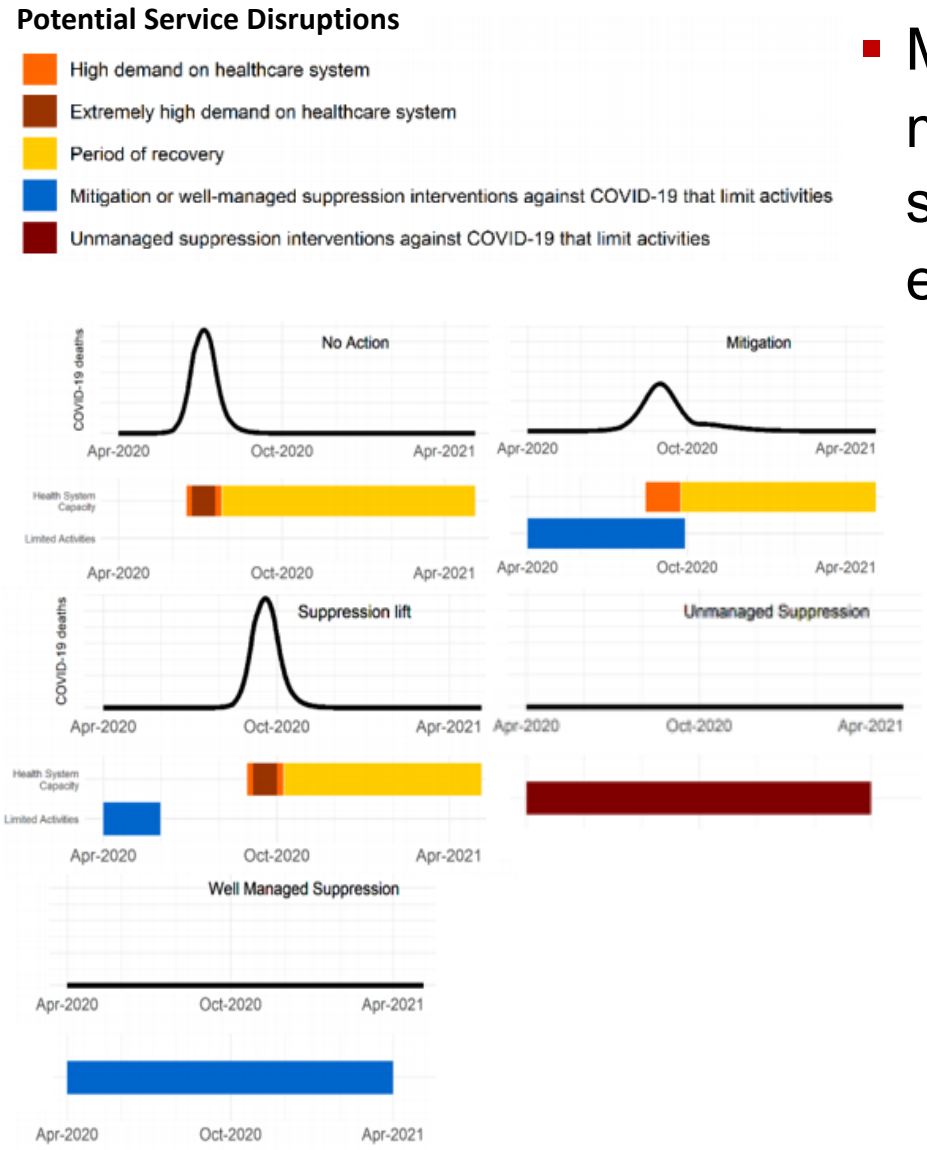
*Hogan AB et al; Imperial College COVID-19 Response Team 2020 May 1*

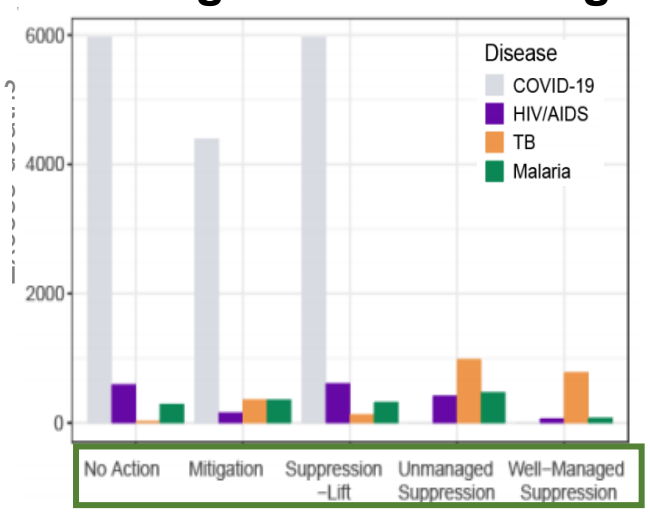
https://www.imperial.ac.uk/media/imperial-college/medicine/mrc-gida/2020-05-01-COVID19-Report-19.pdf




- Modeled 5 intervention scenarios for COVID-19 (no action; mitigation; suppression-lift; well-managed and unmanaged suppression) and potential service disruptions, and impact on extra deaths due to HIV, TB and malaria 2020-2024.

**Excess deaths 2020-2024, COVID-19, HIV, TB or Malaria in Each Scenario**

**High Burden Setting**




→ For HIV, up to 10% ↑ HIV deaths, primarily ART interruption during high/extreme health system demand.

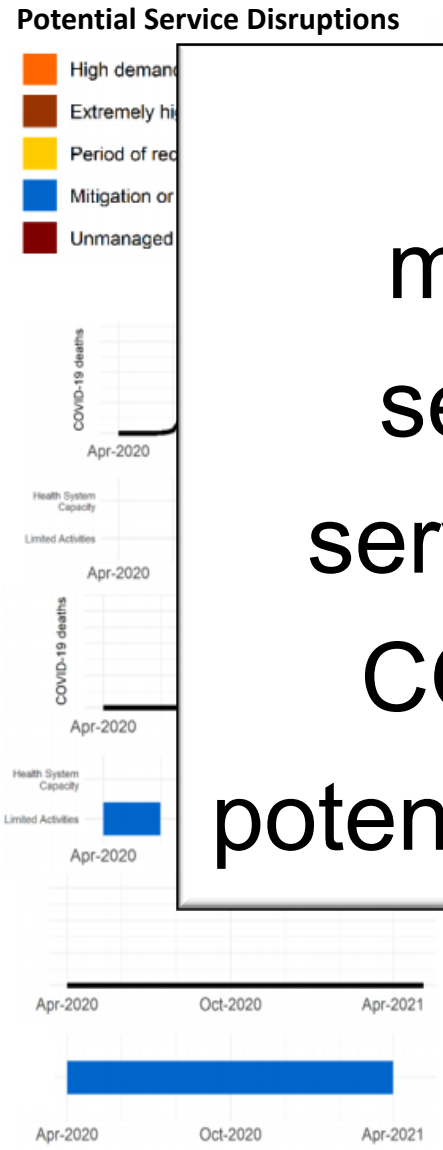
→ For TB, up to 20% ↑ TB deaths, primarily reductions in timely dx/rx new cases from long period of COVID-19 unmanaged/well-managed suppression interventions that limit activities.

→ For malaria, up to 36% ↑ malaria deaths, primarily reduced prevention activities (eg distribution ITN) in all phases of response.

# Impact of COVID-19 Response on HIV, TB and Malaria in LMIC

*Hogan AB et al; Imperial College COVID-19 Response Team 2020 May 1*

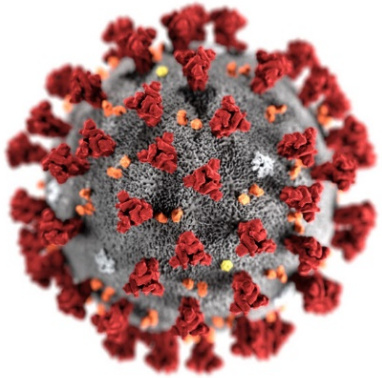
https://www.imperial.ac.uk/media/imperial-college/medicine/mrc-gida/2020-05-01-COVID19-Report-19.pdf




All illustrate the critical importance of maintenance of maternal and child health services and HIV, TB and malaria-specific services as much as possible as a part of the COVID-19 response to reduce the broader potential public health impact of our interventions


→ For malaria, up to 36% ↑ malaria deaths, primarily reduced prevention activities (nets) in all phases of response.

# Thank You For Your Attention!



# Q&A

We encourage all to participate!

- **We will answer messages coming in digitally, first** (through the Q&A box of your screen)
- **Click the Q&A box** at the bottom of the screen, **type in your question(s) and hit send** – hosts will be notified and respond to your question.
- To ask your questions verbally, click "raise hand" in your toolbar, or if dialing in **on the phone, click *9** to raise your hand. The host **will then un-mute you when it is time to take your question.** You will be notified when you are un-muted. **Once un-muted please start with your name and affiliation, then your question**
- We may not be able to get to all questions. If we are unable to get to your question, please email publications@pedaids.org with it. We will respond to all questions by the end of the day.