Coronavirus Update

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July 21, 2021

Evidence of Severe Acute Respiratory Syndrome Coronavirus 2 Replication and Tropism in the Lungs, Airways, and Vascular Endothelium of Patients With Fatal Coronavirus Disease 2019: An Autopsy Case Series

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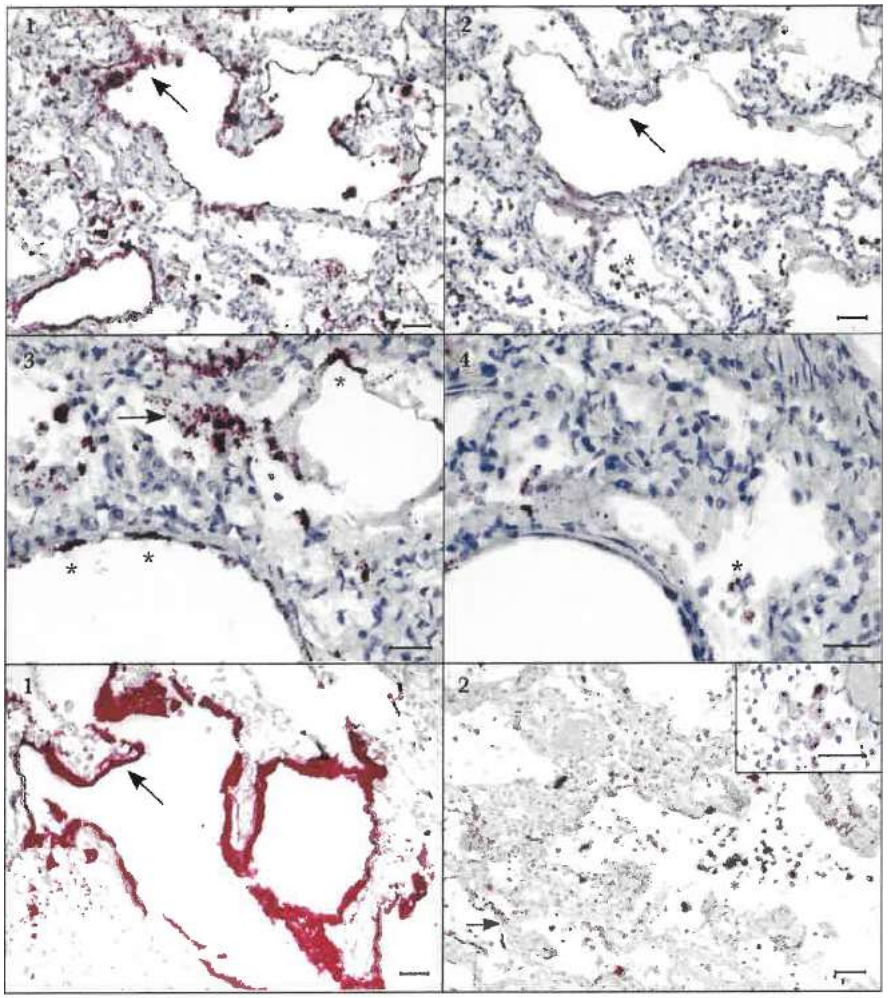
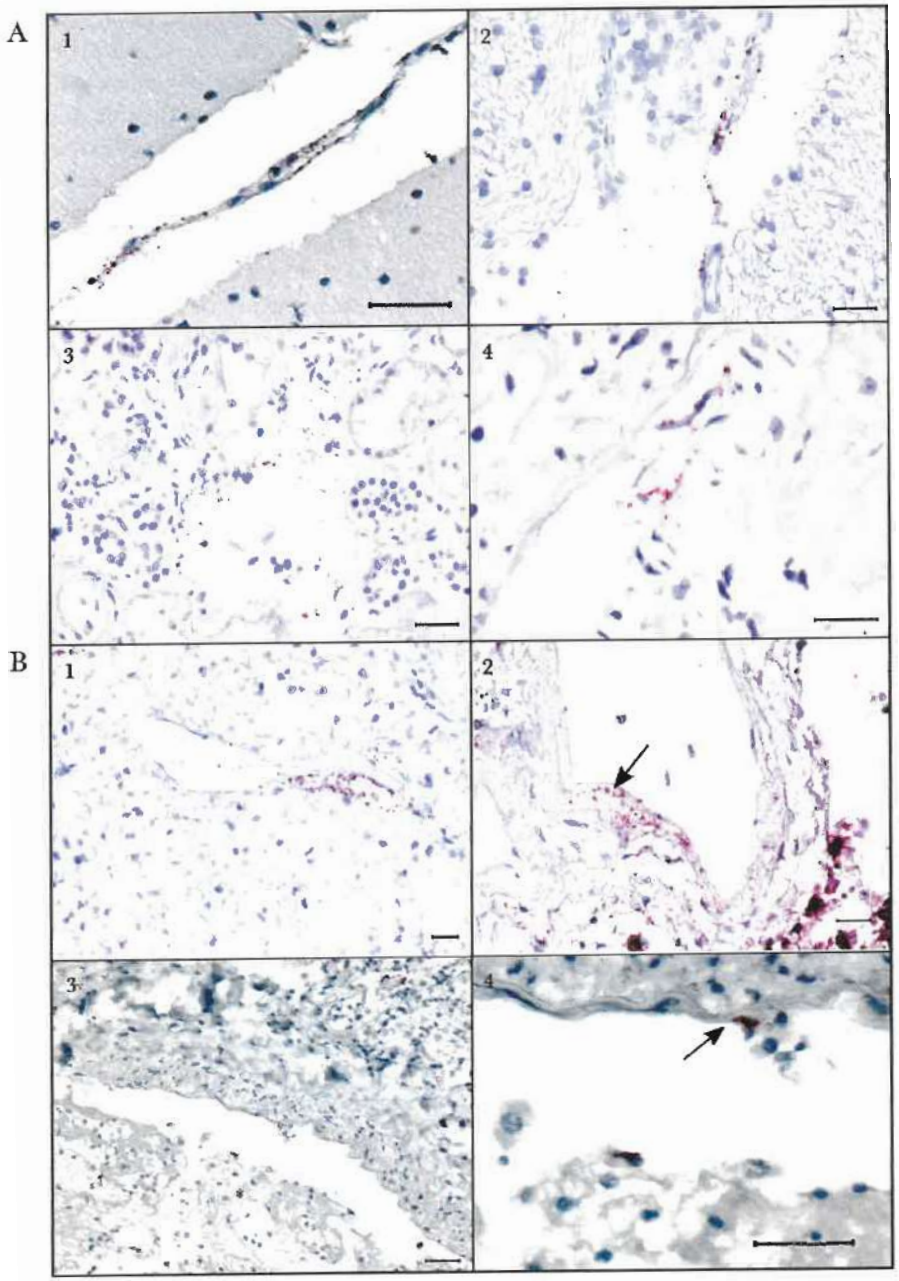
The Journal of Infectious Diseases® 2021;223:752–64

Localization of SARS-CoV-2 RNA in the lung

- Hyaline membranes
- Pneumocytes
- Alveolar macrophages

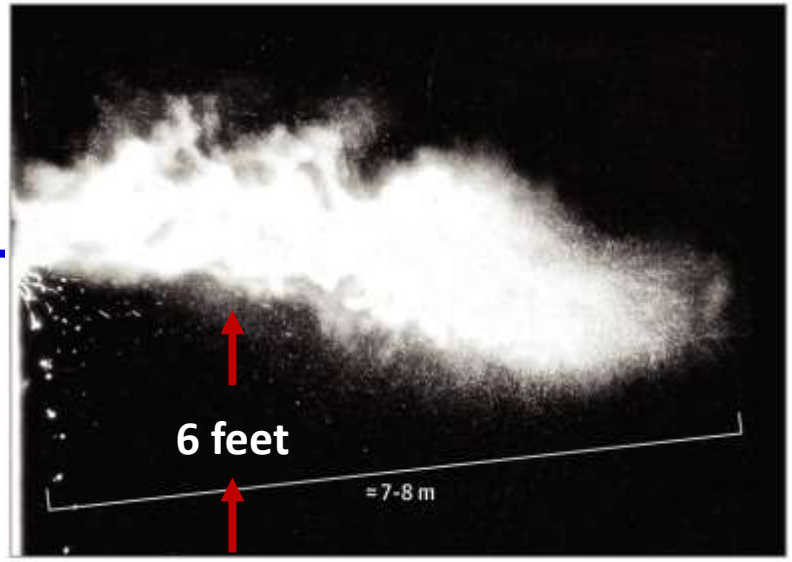


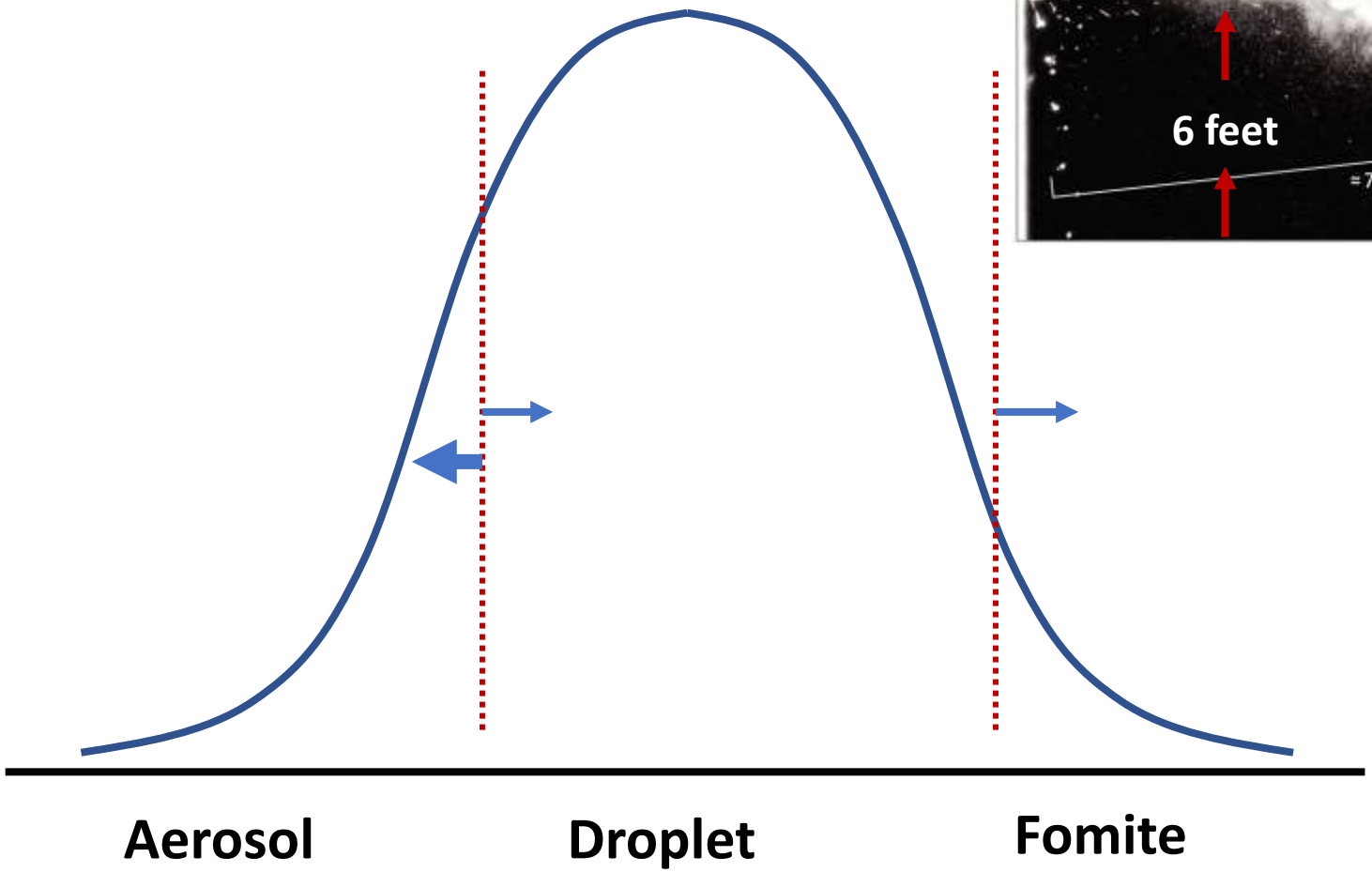


Localization of SARS-CoV-2 RNA

- Endothelial cells with and without associated with thrombus
  - Tunica media of a cerebellar leptomeningeal vessel (A1)
  - Vascular endothelium brain stem parenchyma (A2)

Transmission

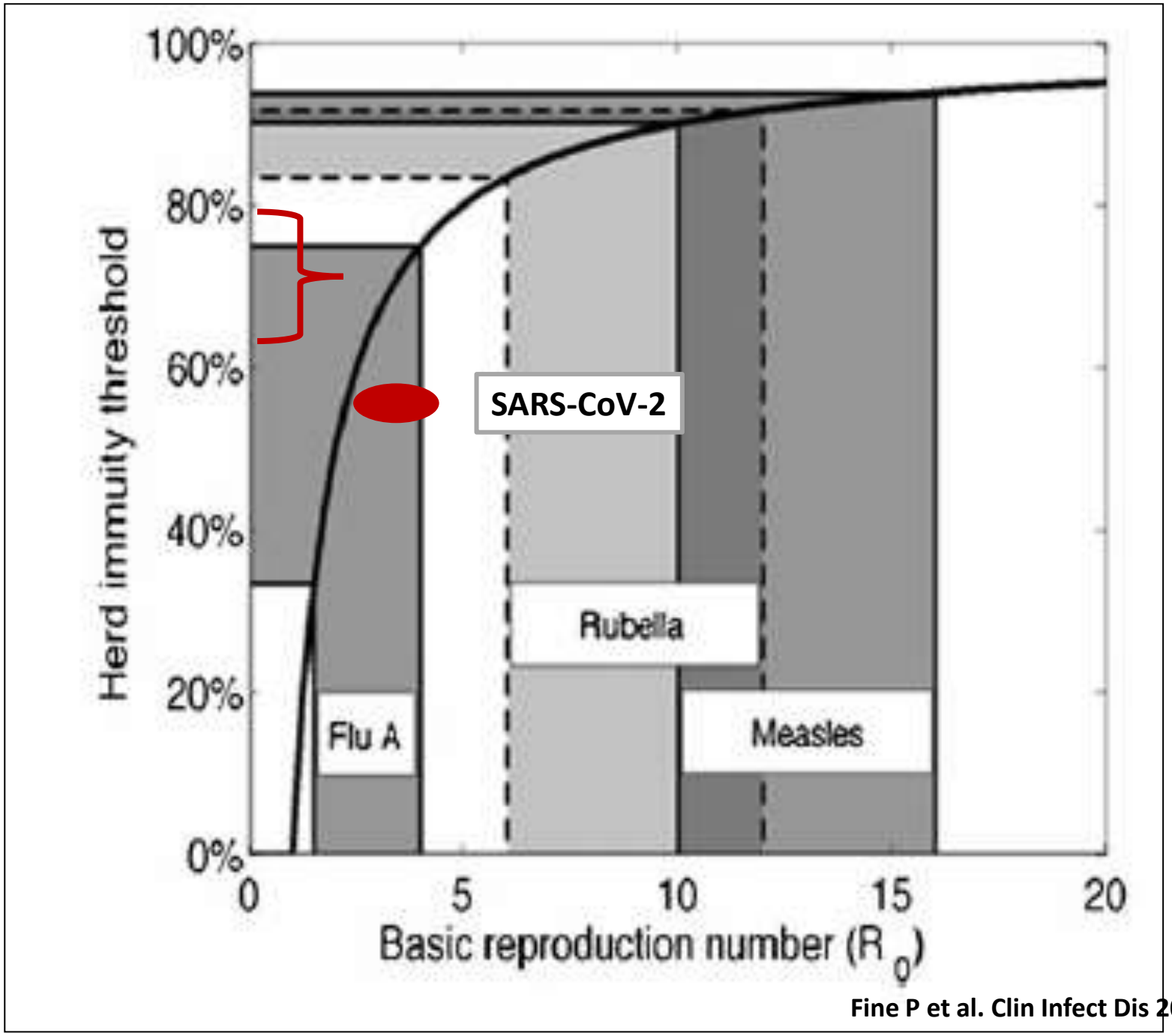




Turbulent gas cloud model

- False dichotomy of “droplet” vs “aerosol”
  - 5 to 10 μm dividing line
  - Larger droplets settle faster than evaporate; smaller = vice versa
- Many factors influence “contagion from the cloud”
  - Force of forward momentum of expelled air
  - Moisture & temperature of the cloud
  - Ambient temperature & humidity
  - Airflow (wind, interior air exchange rate)
  - Settling out of larger droplets onto surfaces
  - Residue nuclei (droplet to aerosol size)
    - May desiccate or remain suspended with “viable payload”
- Evaporation of complex biological liquids poorly understood
  - Lab tests may or may not reflect reality (CW)

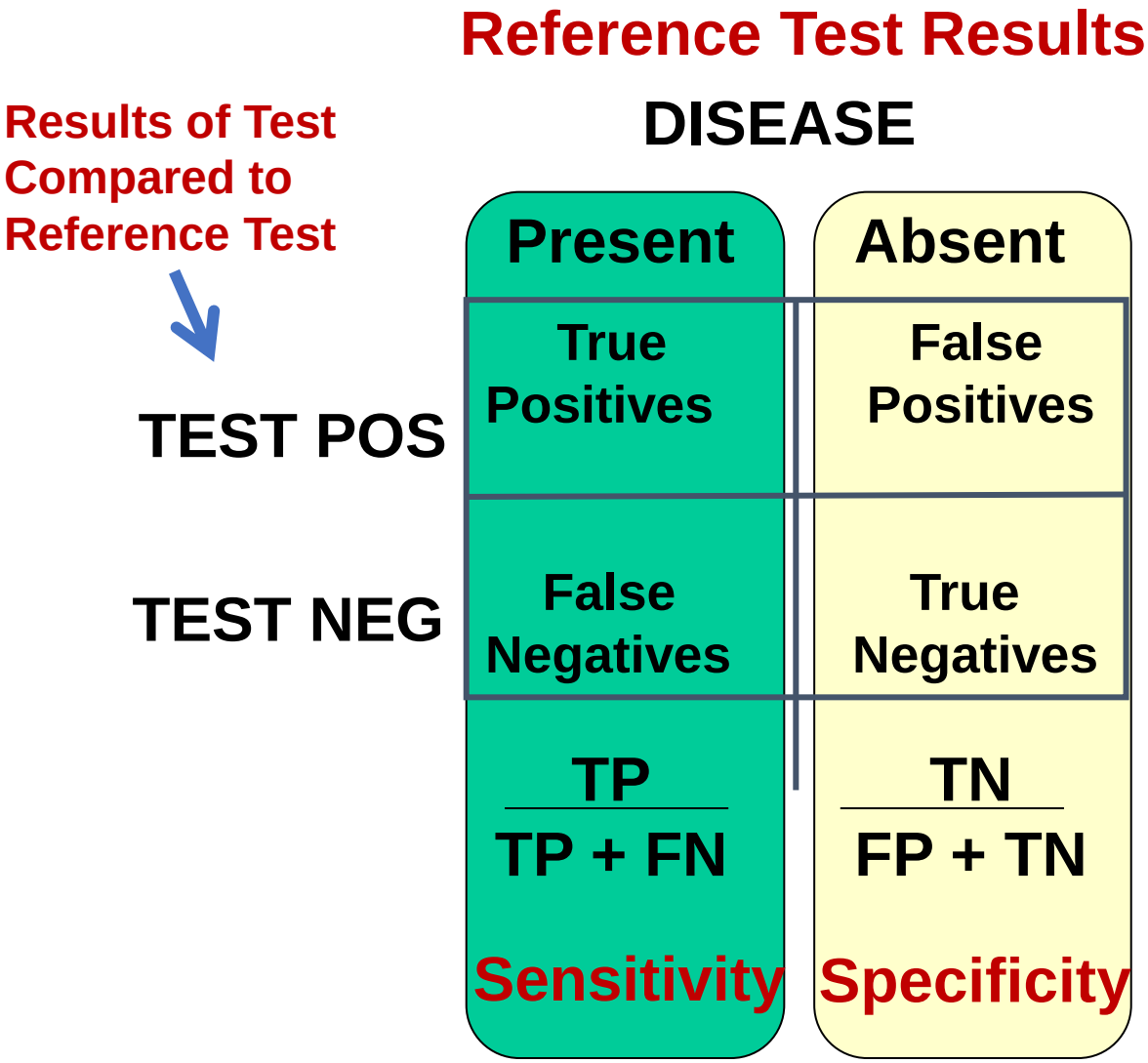
Bourouiba L. JAMA 2020;323:1837



Fine P et al. Clin Infect Dis 2011;52:911

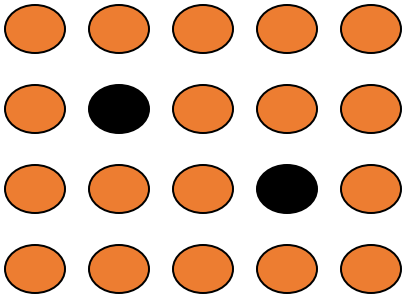
The 2 x 2 Table: Sensitivity & Specificity

EBM "Torture"



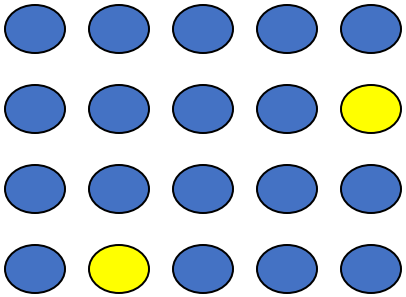
The Intrinsic Test Properties

Persons with Disease



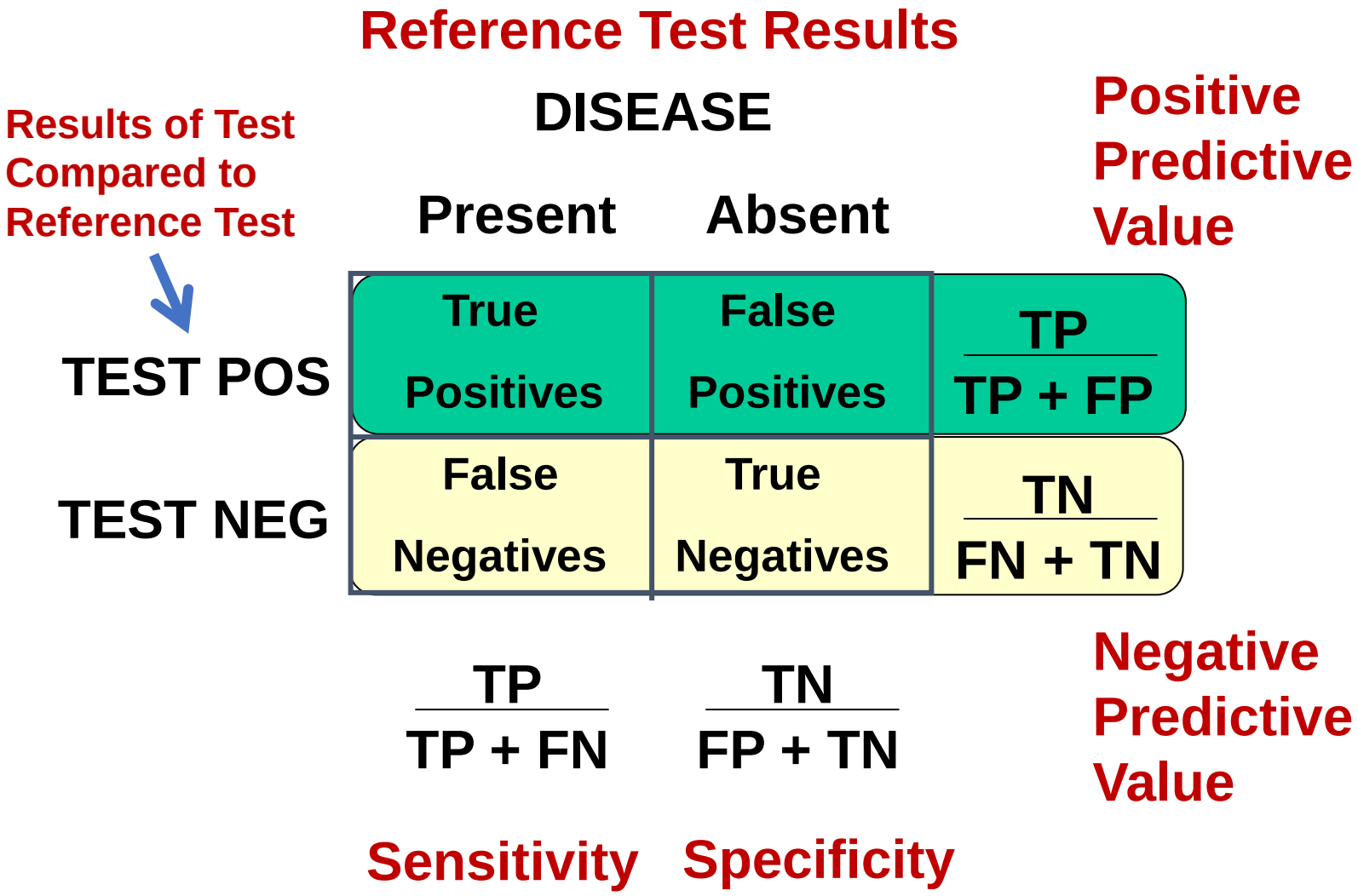
90% Sensitivity

Persons w/o Disease

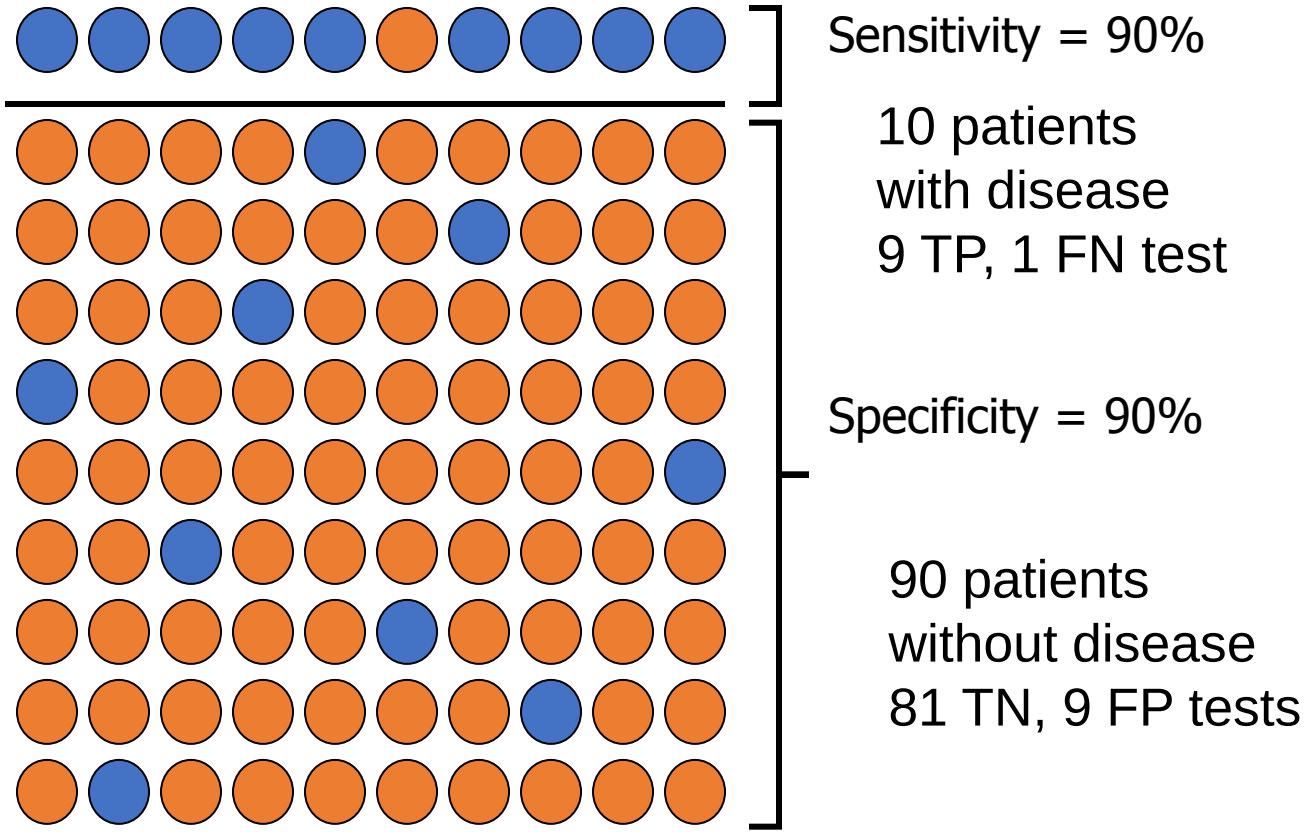


90% Specificity

The 2 x 2 Table: Predictive Values



Sample of 100 persons, 10% disease prevalence



Positive Predictive Value = 50%
Negative Predictive Value = 99%

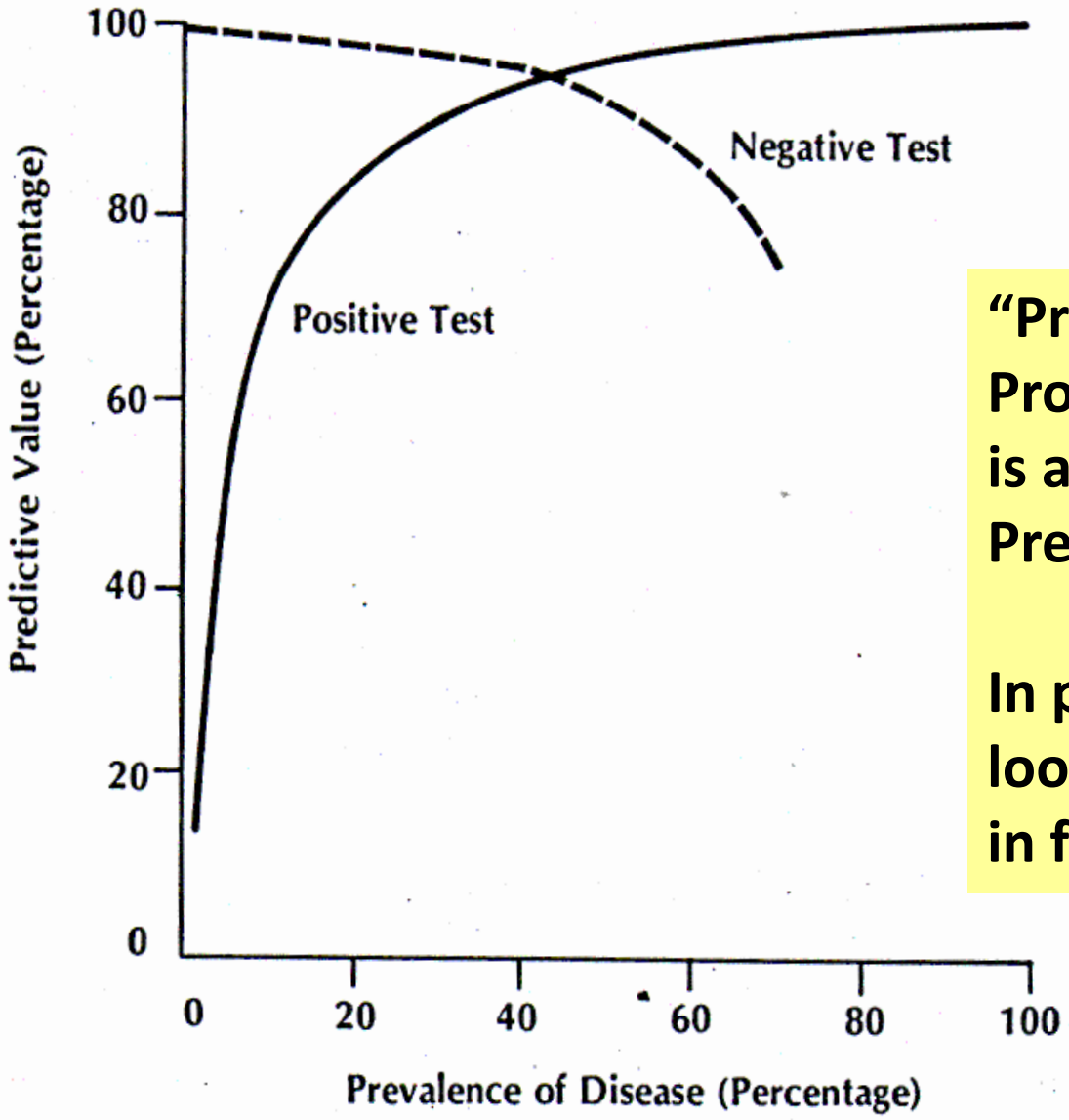


Figure 9–6 Relationship between prevalence of disease and predictive value, with sensitivity and specificity held constant at 95 per cent. (Adapted from Vecchio, 1966.)

"Pre-test Probability" is an estimate of Prevalence…

In patients who look like the one in front of you

Laboratory Validation		Clinical Validation		Additional Factors in Practice	
Sensitivity	**Specificity**	**Sensitivity**	**Specificity**	**Test-Related**	**Results Interpretation**
Artificial samples spiked with varying concentrations of SARS-CoV-2	Artificial samples spiked with varying concentrations of other coronaviruses Artificial samples spiked with varying concentrations of other common viruses	Samples from patients confirmed SARS-CoV-2 infection 1) Asymptomatic persons 2) Symptomatic persons within the first 7 days of symptoms 3) Symptomatic persons on the 8th to 14th day after onset of symptoms 4) Symptomatic persons on the 15th to 21st day after onset of symptoms Confirmed by 1) Positive viral cx OR 2) Positive PCR tests against other molecular targets for SARS-CoV-2 (two or more, preferably)	Samples from patients 1) Positive tests for acute infection with other human coronaviruses 2) Positive tests for acute infection with other common viruses 3) Selected clinical syndromes compatible with SARS-CoV-2 infection (e.g., ARDS, pneumonia) 4) Asymptomatic WITH* Negative viral culture for SARS-CoV-2 AND* Two or more negative PCR tests for other molecular targets for SARS-CoV-2 *Unless samples are pre-pandemic	• Timing within course of illness or time-lapsed since exposure if known • Adequacy of collected specimen • Specimen handling and processing • Function of test kit/cartridge • Function of machine/test platform • Communication of test result to provider	• Role of infection prevalence • Role of cycle threshold, if any • Provider understanding of test limitations and communication of test result in proper context to patient • Patient/family understanding of test limitations and subsequent behaviors based on understanding of test results

Sensitivity (%)	Specificity (%)	LR +	LR -	Disease Prevalence* (%)	PPV (%)	False Pos. One in X	NPV (%)	False Neg. One in X	Risk of infection, neg x2
70	99.8	350	0.30	1	78.0	4.5	99.7	333	<.001%
				10	97.5	40	96.8	31	0.1%
				25	99.2	118	90.9	11	0.8%
				50	99.7	357	76.9	4.3	5.4%
70	98	35	0.31	10	79.5	4.9	96.7	30	0.1%
				50	97.2	36	76.6	4.3	5.4%
50	99.8	250	0.50	10	96.5	29	94.7	19	0.3%
				50	99.6	251	66.6	3	11%

*Best measure is weekly period prevalence: new cases + previous “still contagious” cases

Test interpretation “paradox”

- At very low period prevalence (<1%) in a community…
  - Many positive results = false positives
  - NPV is >99% (may add little value if asymptomatic)
- Among ill patients who have features suggestive of COVID-19, prevalence may be 40% to 60%...
  - PPV = good
  - NPV = less so – may need 2 or 3 negative tests to “exclude”
- Prevalence = pretest probability
  - “Period prevalence” = number of infectious cases this week
    - Weekly incidence (new cases) ~ weekly period prevalence

Basics of Available Diagnostic Tests

- PCR tests
  - We still do not really know sensitivity and specificity
  - Period prevalence – need more testing to understand locally
  - **Lower respiratory > Nasopharyngeal/Pharyngeal > Saliva**
- Antigen tests – less accurate than PCR
- Serologic tests
  - IgG serologies likely reliable – 2 to 4 weeks after onset of illness
    - Need to ensure no cross-reaction with other human coronaviruses
    - Sensitivities may be **????**
  - IgM or IgM+IgG
    - Higher false positive rate (poorer specificity in general) re IgM
  - Spike Ag vs other 'non-vaccine' components

Comparison of Mid-Turbinate and Nasopharyngeal Specimens for Molecular Detection of SARS-CoV-2 Among Symptomatic Outpatients at a Pediatric Drive-Through Testing Site

Leila C. Sahni,[1,2] Vasanthi Avadhanula,[3] Camerin S. Ortiz,[2] Karen E. Feliz,[3] Rebekah E. John,[2] Cameron A. Brown,[4] Joana Y. Lively,[5,6] Brian Rha,[5] Flor M. Munoz,[1,3] Pedro A. Piedra,[1,3] James J. Dunn,[4] and Julie A. Boom[1,2]

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Journal of the Pediatric Infectious Diseases Society 2021;XX(XX):1–8

Conclusions:

- MT specimens, compared to less-tolerated NP specimens in children, especially in the first week of illness, have
  - moderately reduced sensitivity
  - equivalent specificity
- MT specimens may represent a viable alternative… ???

JAMA Pediatrics | Original Investigation

Assessment of Maternal and Neonatal Cord Blood SARS-CoV-2 Antibodies and Placental Transfer Ratios

Dustin D. Flannery, DO, MSCE; Sigrid Gouma, PhD; Miren B. Dhudasia, MBBS, MPH; Sagori Mukhopadhyay, MD, MMSc; Madeline R. Pfeifer, BS; Emily C. Woodford, BA; Jourdan E. Triebwasser, MD, MA; Jeffrey S. Gerber, MD, PhD; Jeffrey S. Morris, PhD; Madison E. Weirick, BS; Christopher M. McAllister, BS; Marcus J. Bolton, BS; Claudia P. Arevalo, BS; Elizabeth M. Anderson, PhD; Eileen C. Goodwin, BA; Scott E. Hensley, PhD; Karen M. Puopolo, MD, PhD

JAMA Pediatr 2021;175:594

Maternal IgG antibodies to SARS-CoV-2 are transferred across the placenta after asymptomatic and symptomatic infection

Cord blood Ab correlates with

- Maternal antibody concentration
- Duration between onset of infection and delivery

Maternally-derived Ab may provide neonatal protection…

Safety, Immunogenicity, and Efficacy of the BNT162b2 Covid-19 Vaccine in Adolescents

Robert W. Frenck, Jr., M.D., Nicola P. Klein, M.D., Ph.D., Nicholas Kitchin, M.D., Alejandra Gurtman, M.D., Judith Absalon, M.D., Stephen Lockhart, D.M., John L. Perez, M.D., Emmanuel B. Walter, M.D., Shelly Senders, M.D., Ruth Bailey, B.Sc., Kena A. Swanson, Ph.D., Hua Ma, Ph.D., Xia Xu, Ph.D., Kenneth Koury, Ph.D., Warren V. Kalina, Ph.D., David Cooper, Ph.D., Timothy Jennings, D.O., Donald M. Brandon, M.D., Stephen J. Thomas, M.D., Özlem Türeci, M.D., Dina B. Tresnan, D.V.M., Ph.D., Susan Mather, M.D., Philip R. Dormitzer, M.D., Ph.D., Uğur Şahin, M.D., Kathrin U. Jansen, Ph.D., and William C. Gruber, M.D., for the C4591001 Clinical Trial Group*

Pfizer-BioNTech mRNA vaccine

N ENGL J MED 385;3 NEJM.ORG JULY 15, 2021

2260 adolescents 12 to 15 yrs old

- 1131 received vaccine

Mild to moderate reactogenicity in 79% to 86%

- Injection site pain
- Fatigue
- Headache

No vaccine-related SAEs

Post vaccine neutralizing titers

met non-inferiority criteria

Vaccine efficacy

(case ≥ 7 d after dose 2)

- 100%
- 95% CI: 75.3% – 100%

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Early Release / Vol. 70
July 6, 2021

Use of mRNA COVID-19 Vaccine After Reports of Myocarditis Among Vaccine Recipients: Update from the Advisory Committee on Immunization Practices — United States, June 2021

Julia W. Gargano, PhD[1,*]; Megan Wallace, DrPH[1,*]; Stephen C. Hadler, MD[1]; Gayle Langley, MD[1]; John R. Su, MD, PhD[1]; Matthew E. Oster, MD[1]; Karen R. Broder, MD[1]; Julianne Gee, MPH[1]; Eric Weintraub, MPH[1]; Tom Shimabukuro, MD[1]; Heather M. Scobie, PhD[1]; Danielle Moulia, MPH[1]; Lauri E. Markowitz, MD[1]; Melinda Wharton, MD[1]; Veronica V. McNally, JD[2]; José R. Romero, MD[3]; H. Keipp Talbot, MD[4]; Grace M. Lee, MD[5]; Matthew F. Daley, MD[6]; Sara E. Oliver, MD[1]

As of June 1, 2021, 1226 reports, with age known for 1194

- 923 male, 298 female
- 687 cases < 30 yrs old
- 76% after 2nd dose

484 < 30 yrs old May 1 – June 11, median age 19 yrs (12-29)

- 291 male, 32 female
- 92% within 7 days of vaccination
- 304 hospitalized, but generally mild clinical course
- No deaths

40.6 cases / million does of mRNA vaccine (both versions)

- 62.5 per million 2nd doses – males 12 - 17 yrs old
- 50.5 per million 2nd doses – males 18 - 24 yrs old
- 4.2 per million 2nd doses – females 12-17 yrs old

Adverse events prevented per million 2nd doses, males < 30

- **11,000 cases**
- **560 hospitalizations**
- **138 ICU admissions**
- **6 deaths**

Some will have cardiac involvement

- **Acute infection**
- **Post-infectious**

…as prevalence falls, the math may change

Mandatory SARS-CoV-2 Vaccinations in K-12 Schools, Colleges/Universities, and Businesses

The Centers for Disease Control and Prevention (CDC) recently issued guidance that fully vaccinated individuals can safely remove masks and end social distancing in most indoor settings.[1] Educational facilities and businesses are

vaccines. The FDA recently extended its EUA for the BNT162b2 (Pfizer-BioNTech) vaccine to 12- to 15-year-olds. The American Academy of Pediatrics also recommends SARS-CoV-2 vaccinations for all eligible youths. The

JAMA July 6, 2021 Volume 326, Number 1

- Ethical frameworks
- Political environments
- Newness of products
- Human nature
- Unanswered questions

Benefit vs risk calculation – with incomplete knowledge…

SARS-CoV-2 Antibody Response in Persons with Past Natural Infection

TO THE EDITOR: Whether or not persons who have already been infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) should be vaccinated is unclear. Only a few stud-

N Engl J Med 385:1 July 1, 2021

Natural infection + one dose of vaccine

>

Two doses of vaccine without prior infection

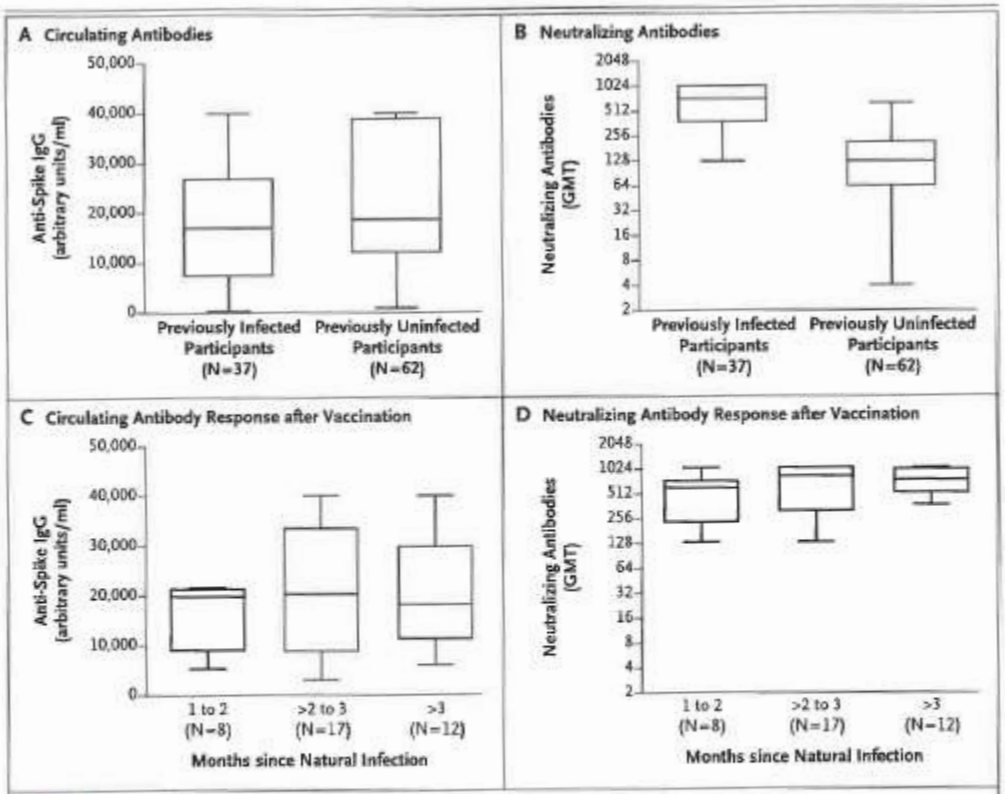


Figure 1. Immune Response in Participants with or without Previous SARS-CoV-2 Infection.

Shown are titers of circulating severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) anti-spike IgG antibodies (Panel A) and neutralizing SARS-CoV-2 anti-spike IgG antibodies (Panel B) in serum samples obtained from previously infected participants after they received a single dose of vaccine and in samples obtained from previously uninfected participants after they received a second dose of vaccine. Differences in circulating (Panel C) and neutralizing (Panel D) IgG antibodies in samples obtained from previously infected participants were evaluated according to the duration from natural infection to vaccination (1 to 2 months, >2 months to 3 months, or >3 months). In each box-and-whisker plot, the horizontal line represents the median, the top and bottom of the box the interquartile range, and the whiskers the minimum and maximum values. GMT denotes geometric mean titer.

Heterologous ChAdOx1 nCoV-19 and mRNA-1273 Vaccination

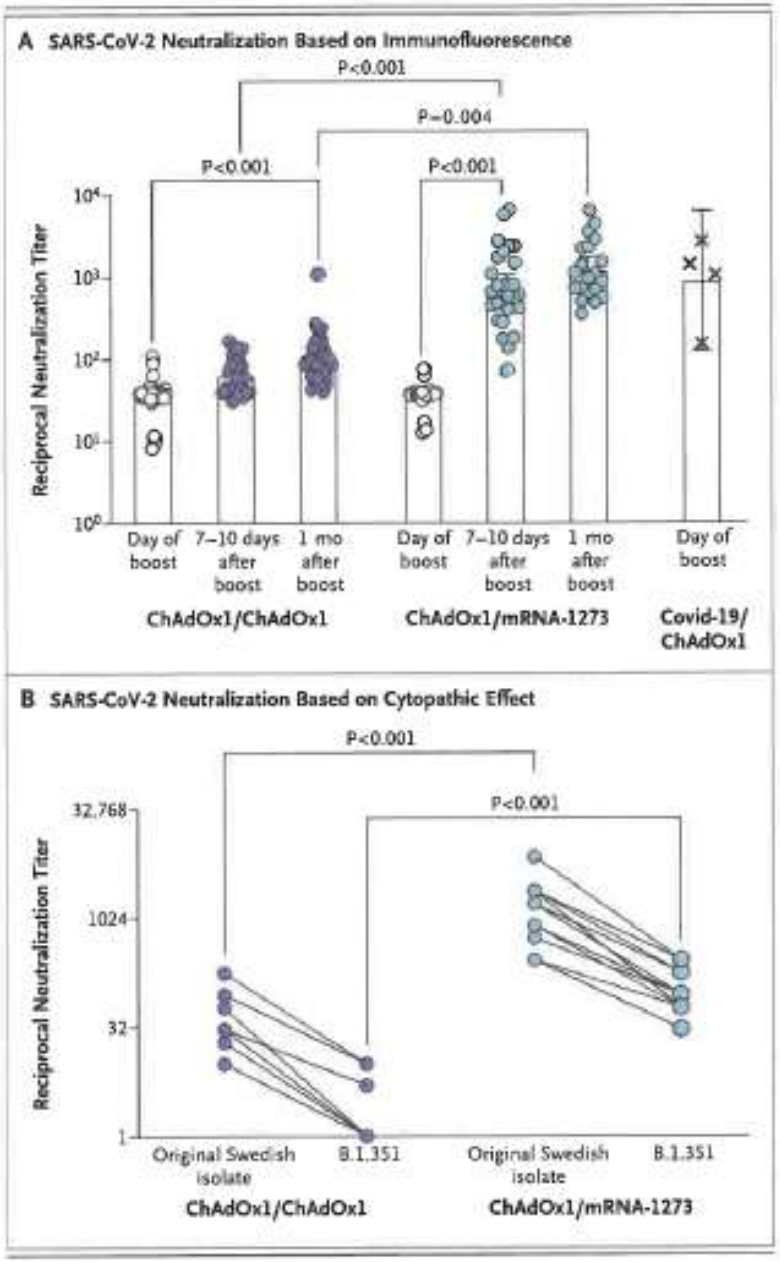
TO THE EDITOR: Because of concerns about thrombotic events after vaccination with ChAdOx1 nCoV-19 (Oxford–AstraZeneca),[1] several European countries have recommended heterologous mes-

provided in the Supplier able at NEJM.org.

On the day of the bo similar levels of SARS-C

Normark J et al
N Engl J Med July 14, 2021

AstraZeneca-Oxford + Moderna



B.1.351 variant

Children and Spread

- Milder illness overall – risk of severe/death ≠ 0

- Early studies –
  - Less likely to transmit, less susceptible to infection
    - Bias re testing, design vs true – **SEEMS TRUE**
    - Physiologic rationale – less ACE2 in nasal epithelium

- More virus in nose (lower PCR Ct)
  - Paradox – less volume of aerosol – less distance?

JAMA Pediatrics | Original Investigation

Prevalence of SARS-CoV-2 Infection in Children and Their Parents in Southwest Germany

Burkhard Tönshoff, MD; Barbara Müller, PhD; Roland Elling, MD; Hanna Renk, MD; Peter Meissner, MD; Hartmut Hengel, MD; Sven F. Garbade, PhD; Meinhard Kieser, PhD; Kathrin Jeltsch, PhD; Jürgen Grulich-Henn, MD; Julia Euler, MA; Maximilian Stich, MD; Kristine Chobanyan-Jürgens, MD; Maria Zernickel, MA; Aleš Janda, MD; Lena Wölfle, MD; Thomas Stamminger, MD; Thomas Iftner, MD; Tina Ganzenmueller, MD; Christian Schmitt, MD; Tessa Göme; Vibor Laketa, PhD; Sylvia Olberg, PhD; Anna Plaszczyca, PhD; Mirko Cortese, PhD; Ralf Bartenschlager, PhD; Constantin Pape, MSc; Roman Remme, MSc; Daniela Huzly, MD; Marcus Panning, MD; Sebastian Weigang, MSc; Sebastian Giese, PhD; Kevin Ciminski, MSc; Jakob Ankerhold; Georg Kochs, PhD; Martin Schwemmle, PhD; Rupert Handgretinger, MD; Charlotte M. Niemeyer, MD; Corinna Engel, MD; Winfried V. Kern, MD; Georg Friedrich Hoffmann, MD; Axel R. Franz, MD; Philipp Henneke, MD; Klaus-Michael Debatin, MD; Hans-Georg Kräusslich, MD

JAMA Pediatr. 2021;175(6):586-593. doi:10.1001/jamapediatrics.2021.0001
Published online January 22, 2021.

CONCLUSIONS AND RELEVANCE In this cross-sectional study, the spread of SARS-CoV-2 infection during a period of lockdown in southwest Germany was particularly low in children aged 1 to 10 years. Accordingly, it is unlikely that children have boosted the pandemic. This SARS-CoV-2 prevalence study, which appears to be the largest focusing on children, is instructive for how ad hoc mass testing provides the basis for rational political decision-making in a pandemic.

COVID-19 Infections Among Students and Staff in New York City Public Schools

PEDIATRICS Volume 147, number 5, May 2021:e2021050605

Jay K. Varma, MD,[a,b] Jeff Thamkittikasem, MPA,[c] Katherine Whittemore, MPH,[c] Mariana Alexander, MSc,[c] Daniel H. Stephens, MD,[d] Kayla Arslanian, JD,[e] Jackie Bray, MPH,[e] Theodore G. Long, MD, MHS[c]

CONCLUSIONS: We found that in-person learning in NYC public schools was not associated with increased prevalence or incidence overall of COVID-19 infection compared with the general community.

Incidence and Secondary Transmission of SARS-CoV-2 Infections in Schools

PEDIATRICS Volume 147, number 4, April 2021:e20200

Kanecia O. Zimmerman, MD,[a,b,c] Ibukunoluwa C. Akinboyo, MD,[a,b] M. Alan Brookhart, PhD,[d] Angelique E. Boutzoukas, MD,[a,b] Kathleen A. McGann, MD,[e] Michael J. Smith, MD, MSCE,[b] Gabriela Maradiaga Panayotti, MD,[b] Sarah C. Armstrong, MD,[a,b] Helen Bristow, MPH,[b] Donna Parker, MPH,[a] Sabrina Zadrozny, PhD,[a] David J. Weber, MD, MPH,[f] Daniel K. Benjamin, Jr, MD, PhD,[a,b,c] FOR THE ABC SCIENCE COLLABORATIVE

CONCLUSIONS: In the first 9 weeks of in-person instruction in North Carolina schools, we found extremely limited within-school secondary transmission of SARS-CoV-2, as determined by contact tracing.

With masking + distancing efforts….

Symptomatic SARS-CoV-2 Transmission in Youth and Staff Attending Day Camps

Emily M. D'Agostino, DPH,[a,b] Sarah C. Armstrong, MD,[a,b,c,d,e] Lisa Humphreys, BS,[f] Stacey Coffman, BS,[f] Gordon Sinclair, MBA,[f] Sallie R. Permar, MD, PhD,[c,g,*] Ibukunoluwa C. Akinboyo, MD[c,*]

PEDIATRICS Volume 147, number 4, April 2021:e2020042416

CONCLUSIONS: Extremely low youth and staff symptomatic SARS-CoV-2 attack and transmission rates were observed over a 147-day period across 54 YMCA camps from March to August 2020, when local coronavirus disease 2019 prevalence peaked. These findings suggest that the benefit of in-person programming in recreation settings with appropriate mitigation may outweigh the risk of viral transmission.

- 5344 children, mean age 8.5 years
- 1486 staff, mean age 22 years
- 9 youth and 8 staff had primary infection
- 2 secondary cases among 3030 contacts

- Screening for symptoms
- Hand hygiene
- Masks for staff and attendees
- Distancing and small cohorts
- Training and cleaning

Morbidity and Mortality Weekly Report
March 19, 2021

Low SARS-CoV-2 Transmission in Elementary Schools — Salt Lake County, Utah, December 3, 2020–January 31, 2021

Rebecca B. Hershow, PhD[1,2,*]; Karen Wu, DVM[1,2,*]; Nathaniel M. Lewis, PhD[1,2,3]; Alison T. Milne, EdD[4]; Dustin Currie, PhD[1,2]; Amanda R. Smith, PhD[1,2]; Spencer Lloyd, MD[1]; Brian Orleans, MS[5]; Erin L. Young, PhD[6]; Brandi Freeman, PhD[1]; Noah Schwartz, MD[1,2]; Bobbi Bryant, MPH[1,7]; Catherine Espinosa, MPH[1]; Yoshinori Nakazawa, PhD[1]; Elizabeth Garza, MPH[1]; Olivia Almendares, MSPH[1]; Winston E. Abara, MD, PhD[1]; Daniel C. Ehlman, ScD[1,2]; Keith Waters, MS[1]; Mary Hill, MPH[8]; Ilene Risk, MPA[8]; Kelly Oakeson, PhD[6]; Jacqueline E. Tate, PhD[1]; Hannah L. Kirking, MD[1]; Angela Dunn, MD[3]; Snigdha Vallabhaneni, MD[1]; Adam L. Hersh, MD, PhD[5]; Victoria T. Chu, MD[1,2]

Despite high community incidence and an inability to space students' classroom seats ≥6 ft apart, this investigation found low SARS-CoV-2 transmission and no school-related outbreaks in 20 Salt Lake County elementary schools with high student mask use (86%) and implementation of multiple strategies to limit transmission.

COVID-19 in Primary and Secondary School Settings During the First Semester of School Reopening — Florida, August–December 2020

Timothy Doyle, PhD[1,2]; Katherine Kendrick, MPH[1]; Thomas Troelstrup, MPH[1]; Megan Gumke, MPH[1]; Jerri Edwards[3]; Shay Chapman, MBA[3]; Randy Propper, PhD[1]; Scott A. Rivkees, MD[4]; Carina Blackmore, DVM, PhD[1]

Although COVID-19 does occur in school settings…

- 60% of cases in school-aged children were not school related
- <1% of registered students had school-related SARS-CoV-2 infection
- <11% of K-12 schools reported outbreaks

MIS-C … not KD … many questions

MMWR August 7, 2020

- Class 1 = 203 – likely true MIS-C – median age 9 yrs
  - abdominal pain, shock, myocarditis, lymphopenia, markedly elevated CRP, ferritin), troponin, BNP
  - Almost all positive SARS-CoV-2 serology ± RT-PCR test results.
  - No overlap with acute COVID-19 or KD
- Class 2 = 169 – likely acute COVID-19 – median age 10 yrs
  - 76.3% had respiratory findings
  - 84% had +RT-PCR with neg. serology
  - Case fatality rate 5.3%
- Class 3 =198 – ?? KD, other – median age 6 yrs
  - 63% had rash, 45% mucocutaneous lesions
  - 6.6% met full KD definition
  - 63% had positive SARS-CoV-2 serology only; 33.8% had both
- Coronary artery dilatations or more in about 20% each…

MIS-C = Multisystem Inflammatory Syndrome – Children **KD = Kawasaki Disease**

JAMA | Original Investigation

Characteristics and Outcomes of US Children and Adolescents With Multisystem Inflammatory Syndrome in Children (MIS-C) Compared With Severe Acute COVID-19

JAMA. 2021;325(11):1074-1087. doi:10.1001/jama.2021.2091
Published online February 24, 2021.

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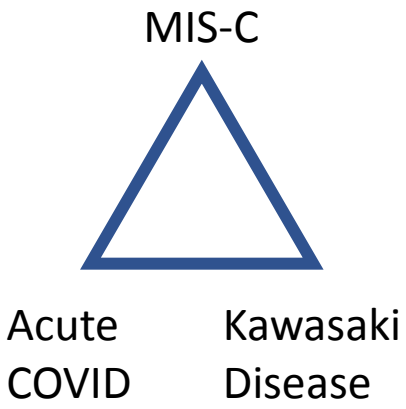

Lots of overlap…timing may help re Acute COVID
Age 6 – 12 years higher risk MIS-C ?

Favors MIS-C

- Cardiac involvement
- Mucocutaneous findings
- Absence of underlying conditions
- Higher neutrophil to lymphocyte ratio
- Thrombocytopenia
- C-reactive protein >100 mg/L

Treatment of Multisystem Inflammatory Syndrome in Children

A.J. McArdle, O. Vito, H. Patel, E.G. Seaby, P. Shah, C. Wilson, C. Broderick, R. Nijman, A.H. Tremoulet, D. Munblit, R. Ulloa-Gutierrez, M.J. Carter, T. De, C. Hoggart, E. Whittaker, J.A. Herberg, M. Kaforou, A.J. Cunnington, and M. Levin, for the BATS Consortium*

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CONCLUSIONS

We found no evidence that recovery from MIS-C differed after primary treatment with IVIG alone, IVIG plus glucocorticoids, or glucocorticoids alone, although significant differences may emerge as more data accrue. (Funded by the European Union's Horizon 2020 Program and others; BATS ISRCTN number, ISRCTN69546370.)

Multisystem Inflammatory Syndrome in Children — Initial Therapy and Outcomes

M.B.F. Son, N. Murray, K. Friedman, C.C. Young, M.M. Newhams, L.R. Feldstein, L.L. Loftis, K.M. Tarquinio, A.R. Singh, S.M. Heidemann, V.L. Soma, B.J. Riggs, J.C. Fitzgerald, M. Kong, S. Doymaz, J.S. Giuliano, Jr., M.A. Keenaghan, J.R. Hume, C.V. Hobbs, J.E. Schuster, K.N. Clouser, M.W. Hall, L.S. Smith, S.M. Horwitz, S.P. Schwartz, K. Irby, T.T. Bradford, A.B. Maddux, C.J. Babbitt, C.M. Rowan, G.E. McLaughlin, P.H. Yager, M. Maamari, E.H. Mack, C.L. Carroll, V.L. Montgomery, N.B. Halasa, N.Z. Cvijanovich, B.M. Coates, C.E. Rose, J.W. Newburger, M.M. Patel, and A.G. Randolph, for the Overcoming COVID-19 Investigators*

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CONCLUSIONS

Among children and adolescents with MIS-C, initial treatment with IVIG plus glucocorticoids was associated with a lower risk of new or persistent cardiovascular dysfunction than IVIG alone. (Funded by the Centers for Disease Control and Prevention.)

JAMA Neurology | Original Investigation

Neurologic Involvement in Children and Adolescents Hospitalized in the United States for COVID-19 or Multisystem Inflammatory Syndrome

Kerri L. LaRovere, MD; Becky J. Riggs, MD; Tina Y. Poussaint, MD; Cameron C. Young; Margaret M. Newhams, MPH; Mia Maamari, MD; Tracie C. Walker, MD; Aalok R. Singh, MD; Heda Dapul, MD; Charlotte V. Hobbs, MD; Gwenn E. McLaughlin, MD; Mary Beth F. Son, MD; Aline B. Maddux, MD; Katharine N. Clouser, MD; Courtney M. Rowan, MD; John K. McGuire, MD; Julie C. Fitzgerald, MD, PhD; Shira J. Gertz, MD; Steven L. Shein, MD; Alvaro Coronado Munoz, MD; Neal J. Thomas, MD; Katherine Irby, MD; Emily R. Levy, MD; Mary A. Staat, MD; Mark W. Tenforde, MD, PhD; Leora R. Feldstein, PhD; Natasha B. Halasa, MD, MPH; John S. Giuliano Jr, MD; Mark W. Hall, MD; Michele Kong, MD; Christopher L. Carroll, MD; Jennifer E. Schuster, MD; Sule Doymaz, MD; Laura L. Loftis, MD; Keiko M. Tarquinio, MD; Christopher J. Babbitt, MD; Ryan A. Nofziger, MD; Lawrence C. Kleinman, MD, MPH; Michael A. Keenaghan, MD; Natalie Z. Cvijanovich, MD; Philip C. Spinella, MD; Janet R. Hume, MD, PhD; Kari Wellnitz, MD; Elizabeth H. Mack, MD; Kelly N. Michelson, MD; Heidi R. Flori, MD; Manish M. Patel, MD; Adrienne G. Randolph, MD; for the Overcoming COVID-19 Investigators

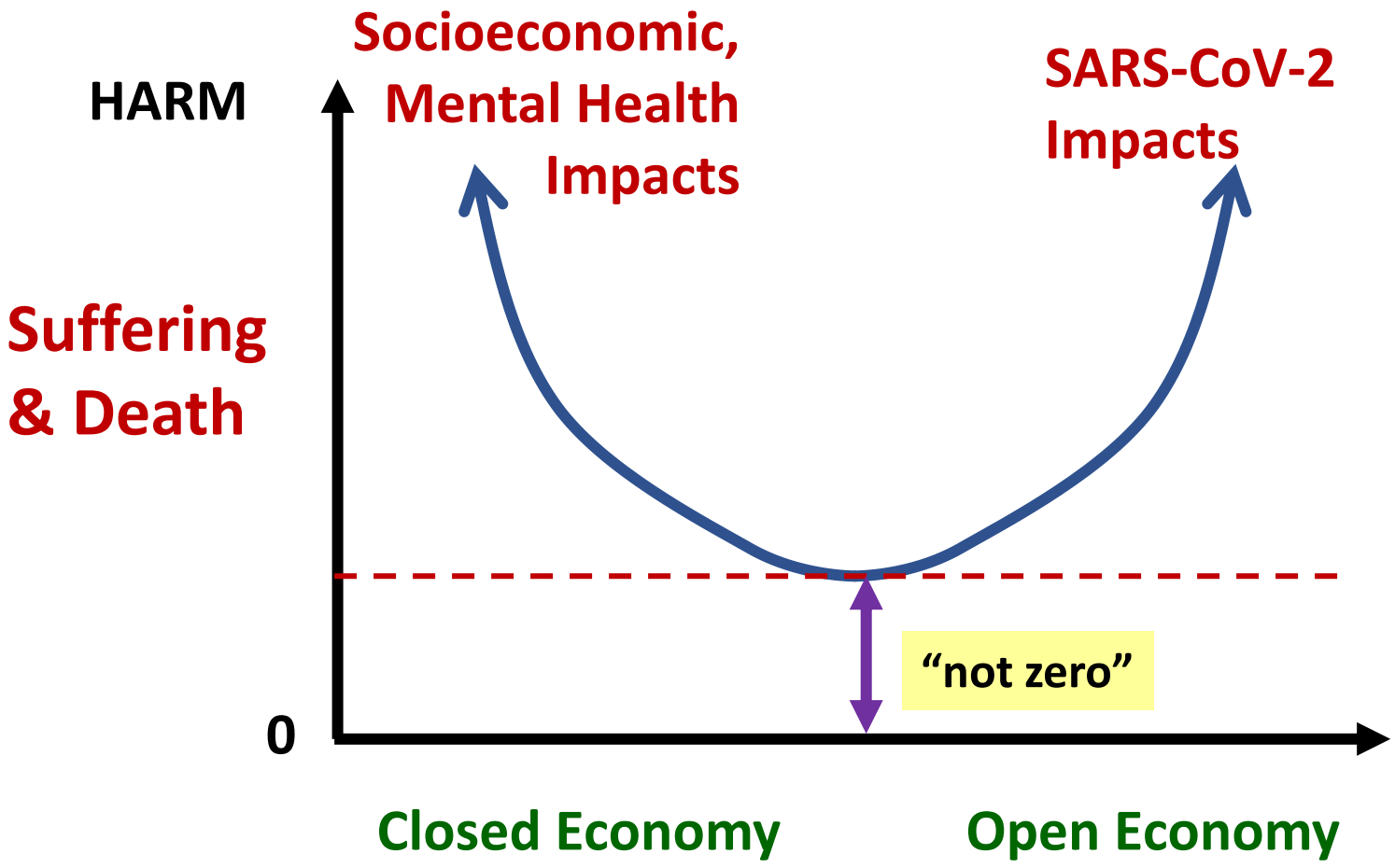
JAMA Neurol. doi:10.1001/jamaneurol.2021.0504
Published online March 5, 2021.

CONCLUSIONS AND RELEVANCE In this study, many children and adolescents hospitalized for COVID-19 or multisystem inflammatory syndrome in children had neurologic involvement, mostly transient symptoms. A range of life-threatening and fatal neurologic conditions associated with COVID-19 infrequently occurred. Effects on long-term neurodevelopmental outcomes are unknown.

Other Issues

- Masks for children in school this year
- Vaccination of younger children once approved…
- Long-haul COVID in children…
- Delta variant… the next variant…

Once this virus reached humans…



Pediatric Hospitalizations During the COVID-19 Pandemic

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PEDIATRICS Volume 146, number 6, December 2020

Looming surge of the "other childhood viruses + influenza" ??

2021

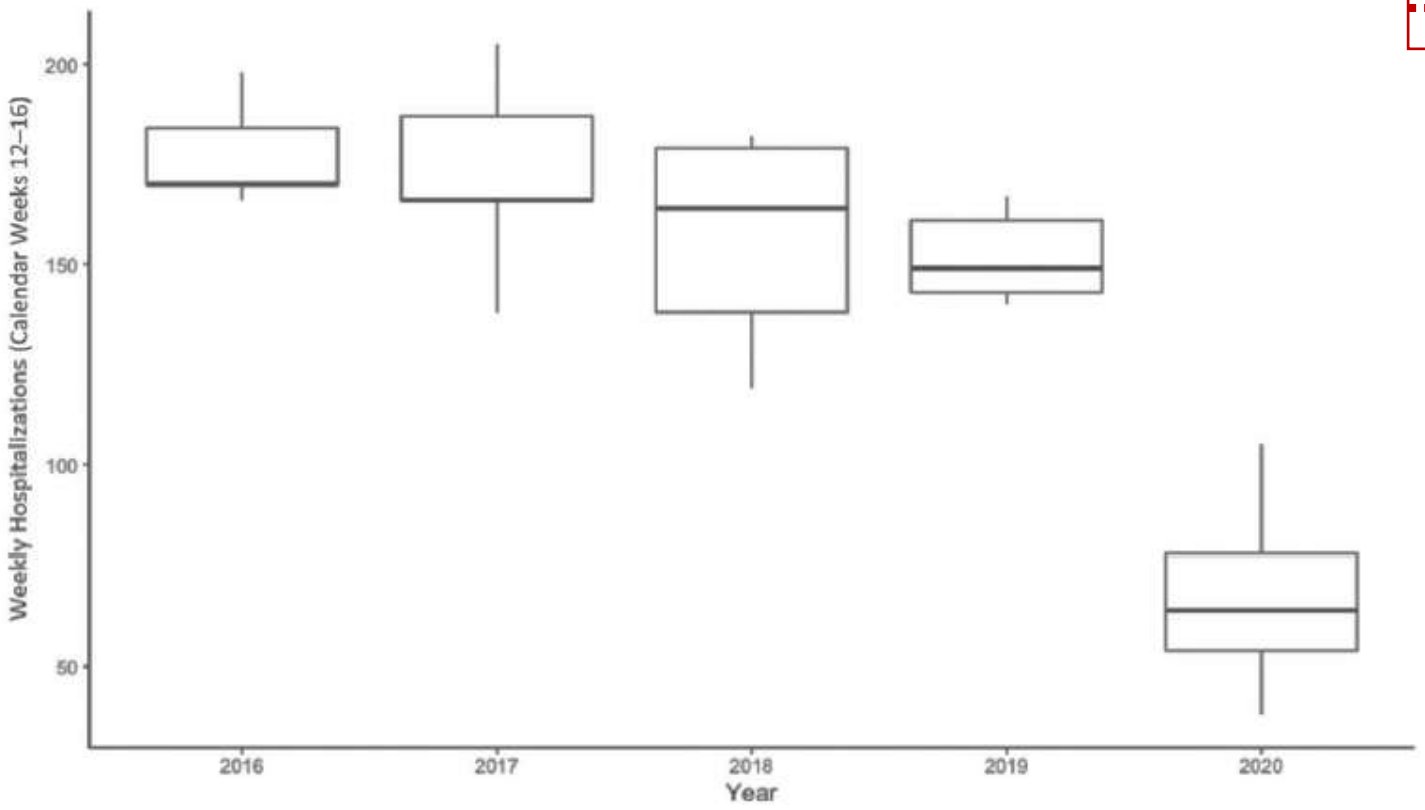

FIGURE 1

Boxplot of weekly pediatric hospitalizations by year. Boxplots depict the medians and interquartile ranges (IQRs) of weekly hospitalizations. Whiskers are 1.5 times the IQR.