EMILY T. KUWAHARA (SBN 252411)
ekuwahara@crowell.com
URI NIV (SBN 307487)
univ@crowell.com
CROWELL & MORING LLP
515 South Flower Street, 40th Floor
Los Angeles, CA 90071
Telephone: 213.622.4750
Facsimile: 213.622.2690

KRISTIN J. MADIGAN (SBN 233436)
kmadigan@crowell.com
SUZANNE E. RODE (SBN 253830)
srode@crowell.com
CROWELL & MORING LLP
3 Embarcadero Center, 26th Floor
San Francisco, CA 94111
Telephone: 415.986.2800
Facsimile: 415.986.2827

[Additional Counsel Listed on Next Page]

Attorneys for Defendants
THE REGENTS OF THE UNIVERSITY OF CALIFORNIA and MICHAEL V. DRAKE

UNITED STATES DISTRICT COURT

CENTRAL DISTRICT OF CALIFORNIA

SOUTHERN DIVISION

AARON KHERIATY, M.D.,

Plaintiff,

v.

THE REGENTS OF THE UNIVERSITY OF CALIFORNIA, a corporation, and MICHAEL V. DRAKE, in his official capacity as President of the UNIVERSITY OF CALIFORNIA,

Defendants.

Case No. 8:21-cv-01367-JVS-KES

DECLARATION OF CARRIE L. BYINGTON, M.D., IN SUPPORT OF DEFENDANTS' OPPOSITION TO PLAINTIFF'S MOTION FOR PRELIMINARY INJUNCTION

Date: September 27, 2021
Time: 1:30 p.m.
Place: Courtroom 10 C
Judge: Hon. James V. Selna

CHARLES F. ROBINSON (SBN 113197)
charles.robinson@ucop.edu
NORMAN J. HAMILL (SBN 154272)
norman.hamill@ucop.edu
KATHARINE ESSICK (SBN 219426)
katharine.essick@ucop.edu
UNIVERSITY OF CALIFORNIA
Office of General Counsel
1111 Franklin Street, 8th Floor
Oakland, CA 94607
Telephone: 510.987.9800
Facsimile: 510.987.9757

Attorneys for Defendants
THE REGENTS OF THE UNIVERSITY OF CALIFORNIA AND MICHAEL V. DRAKE

I, Carrie L. Byington, M.D., declare:

1. I provide this declaration in support of Defendants The Regents of the University of California and President Michael V. Drake's ("Defendants") Opposition to Plaintiffs' Motion for Preliminary Injunction. I base this declaration on my expertise as outlined below and facts within my personal knowledge, to which I could and would testify competently if called upon to do so.

2. I am Executive Vice President, University of California Health (**UCH**), and a tenured Professor of Pediatric Infectious Diseases at the University of California, San Francisco. I am a medical doctor, specializing in pediatric infectious diseases. My research has focused on the clinical diagnosis, management and prevention of respiratory infection and the development of diagnostic technology for the recognition of pathogens with pandemic potential. I have worked on the prevention and control of infectious diseases in the United States and internationally. Among other experience, I have planned emergency infrastructure for universities, was responsible for protecting Team USA athletes and staff from Zika Virus during the 2016 Olympic Games in Brazil, and chaired the American Academy of Pediatrics Committee on Infectious Diseases during the Ebola and Zika outbreaks (2014-2018). I have authored numerous peer-reviewed articles (n=210) including national policy statements (n=70) on the prevention and control of infectious diseases in children in my capacity as a faculty researcher (1995-present) and member, vice chair, and chair of the American Academy of Pediatrics Committee on Infectious Diseases from 2007-2018.

EDUCATION AND PROFESSIONAL BACKGROUND

3. I received my B.S. in biology from Texas A&M University, cum laude, in 1985, and my M.D. from Baylor College of Medicine in 1989 with honors. I completed a pediatric residency at Baylor College of Medicine, where I served as neonatal chief resident in 1992, and I completed a fellowship in Pediatric Infectious Diseases at the University of California, San Francisco.

4. My research focus has been on respiratory pathogens including pathogens of pandemic potential. My career in academic medicine has bridged clinical care and public health. Before I began my position at UC (2019), I was, simultaneously, the Dean of the College of Medicine and Senior Vice President for Health Sciences at Texas A&M University and Vice Chancellor for Health Services for the 11-campus Texas A&M University System (2017-2019). Prior to that, I was a faculty member for 21 years (1995-2016) at the University of Utah. I served as Distinguished Service Professor at University of Utah (2015); Director and Principal Investigator, Utah Center for Clinical and Translational Science (2015-2016); Associate Vice President of Faculty and Academic Affairs at the University of Utah Health Sciences Center (2013-2016); Co-Director and Principal Investigator at the Utah Center for Clinical and Translational Science (2013-2015); Benning Presidential Professor of Pediatrics at the University of Utah Health Sciences Center (2010-2016); Vice Chair (Oversight Research Enterprise) of the Department of Pediatrics at the University of Utah Health Sciences Center (2009-2013); Associate Director of the University of Utah Center for Clinical and Translational Science (2008-2013); Associate Chair for Clinical Research of the Department of Pediatrics at the University of Utah Health Sciences Center (2007-2009); Professor of Pediatrics, Division of General Pediatrics and Division of Pediatric Infectious Diseases at the University of Utah Health Sciences Center (2006-2016); Lowell Bennion Public Service Professor at the University of Utah (2001-2002); Associate Professor, Division of General Pediatrics and Division of Pediatric Infectious Diseases at the University of Utah Health Sciences Center (2000-2006); Assistant Professor, Division of General Pediatrics and Division of Pediatric Infectious Diseases at the University of Utah Health Sciences Center (1995-2000); Fellow in Pediatric Infectious Diseases, University of California, San Francisco (1993-1995), and Assistant Professor for the Division of Ambulatory Pediatrics at Baylor College of Medicine (1992-1993).

5. Attached as **Exhibit A** is a copy of my Curriculum Vitae.

COVID-19 IS A HIGHLY CONTAGIOUS SERIOUS ILLNESS THAT POSES GREAT RISKS TO HUMAN HEALTH AND VACCINES THAT PREVENT SEVERE DISEASE ARE NOW READILY AVAILABLE

6. SARS-CoV2 is a respiratory virus that easily infects humans and produces an illness referred to as COVID-19. The delta variant is a more infectious form of SARS-CoV2 and was dominant in the U.S. by July 2021. Infections may range from asymptomatic (no symptoms) to life-threatening, or fatal. Patients typically present with acute respiratory signs and symptoms, which can escalate in some patients to respiratory failure and other serious, life-threatening complications with organ damage to the brain, heart and kidneys and blood clotting. Myocarditis, myocardial infarction, and stroke have all been reported following infection. The most common symptoms are fever, cough, and shortness of breath. Other identified symptoms include muscle aches, headaches, chest pain, diarrhea, coughing up blood, sputum production, runny nose, nausea, vomiting, diarrhea, sore throat, confusion, lack of senses of taste and smell, and anorexia. Due to the respiratory impacts of the disease, individuals may require oxygen therapy, and in severe cases, patients may need to be intubated and receive mechanical ventilation or be placed on extracorporeal membrane oxygenation (**ECMO**), a technique of pumping and oxygenating an individual's blood outside of their body, providing prolonged cardiac and respiratory support to persons whose heart and lungs are unable to function properly. Individuals with renal failure may require dialysis.

7. People of every age have contracted COVID-19. Severe cases and deaths have been reported at every age. More than 600,000 deaths attributed to COVID-19 have been reported in the U.S. Geriatric patients are at the greatest risk of severe cases, long-term impairment, and death. Likewise, those with immunologic conditions and with other pre-existing conditions, such as hypertension, certain heart conditions, lung diseases (e.g., asthma, COPD), diabetes

mellitus, obesity, and chronic kidney disease, are at high risk of a life-threatening COVID-19 illness. Pregnant women are also recognized as a group that may have more severe infection with SARS-CoV2 resulting in hospitalization and need for intensive care. In addition, pre-term delivery, which endangers the lives of infants, is now a recognized effect of COVID-19 in pregnancy.

8. SARS-CoV2 is readily spread through aerosols and respiratory droplets. Importantly, asymptomatic person to person transmission of SARS-CoV2 is common. According to the U.S. Centers for Disease Control and Prevention (CDC), the infectiousness of an asymptomatic person is ~75% compared with a symptomatic person; see: https://www.cdc.gov/coronavirus/2019-ncov/hcp/planning-scenarios.html (scenario 5), attached as **Exhibit B**.

9. People may transmit the virus even when they exhibit no symptoms and may transmit in the days before symptoms appear. The viral loads are high in both asymptomatic and pre-symptomatic individuals, especially with the delta variant. All unvaccinated people are susceptible to COVID-19, as it is a novel virus. All unvaccinated people, including previously infected individuals, as well as some vaccinated people are capable of getting COVID-19 because of the ease with which it spreads through person-to-person contact. The virus is spread through aerosols and through droplet transmission; that is, when an infected individual speaks, coughs, sneezes, and the like, they expel droplets that can transmit the virus to others in their proximity. There is growing evidence that COVID-19 is also aerosolized, such that tiny droplets containing the virus remain in the air and can be inhaled by others who come into contact with that air and that COVID-19 can be transmitted in that fashion. See Wang, CC, Prather, KA (UC San Diego) et al., Airborne Transmission of Respiratory Viruses, Science, Aug. 27, 2021: https://science.sciencemag.org/content/373/6558/eabd9149), attached as **Exhibit C**. The virus is also rarely spread through the touching of contaminated surfaces, for example, when an infected person touches a surface with a hand they have coughed

into and then another person touches that same surface before it has been disinfected and then touches their face.

10. Transmission of COVID-19 can occur in any location where there is close proximity (less than six feet) between individuals and in any room where people gather, as with each respiration or utterance, an infected person may generate aerosols. Activities that occur indoors are considered higher risk than those that occur outdoors. And because transmission of the virus can potentially occur via aerosols or environmental surfaces, there is also risk of spread of the virus at any location where multiple individuals have been present and have breathed or touched surfaces. Some individuals who are infected with the virus do not have any symptoms but can transmit the virus and/or are infectious before they develop any symptoms. This means that testing only those with symptoms or isolating only persons known to be infected or quarantining only those exhibiting symptoms of infection will not stop the spread of infection. Young people, including those in the college age group, may be less likely to exhibit symptoms than older individuals. Individuals aged 20 to 29 account for over 20% of cases in the U.S. today and readily transmit infection to others, including older adults, who may have more serious disease.

11. The U.S. by the Food and Drug Administration has granted emergency use authorization for two different COVID-19 vaccines in the United States: the mRNA-1273 (Moderna COVID-19 vaccine) and the adenoviral vector vaccine Ad26.COV2.S (Janssen COVID-19 vaccine, also referred to as the Johnson & Johnson vaccine). The U.S. Food and Drug Administration has granted full approval for a third COVID-19 vaccine in the United States: the mRNA vaccine BNT162b2 (Pfizer-BioNTech COVID-19 vaccine).

MY ROLE IN UC'S COVID-19 VACCINATION POLICY TO PROTECT STUDENTS, STAFF, AND FACULTY THROUGHOUT THE UC

SYSTEM

12. I joined UC in 2019 as Executive Vice President, UCH, and a Professor of Pediatric Infectious Diseases at the University of California, San Francisco.

13. Since January 1, 2020, I have been collaborating with UC leadership and its campus and hospital leaders regarding UC's emergency response to what we now recognize as the SARS-CoV2 pandemic. Our goal has been to prioritize the health and safety of our students, staff, and faculty at UC and the patients in its health system. I have also served on numerous COVID-19 advisory groups for the State of California.

14. Beginning on March 18, 2020, I have chaired a subcommittee of the UC Office of the President (**UCOP**) Management Response Team (**MRT**) named the UC Health Coordinating Committee (**UC-HCC**) to advise the UC system, including the six academic health centers and 20 health professional schools that comprise UC Health, the 10 UC campuses, the 3 National Laboratories, and UCDC in a system-wide response to the pandemic. Among other things, I, as Chair of the UC-HHC, have been offering UC Health leaders, the Council of UC Chancellors, the UC President, and the UC Board of Regents, my expert advice through the UC-HCC and the incident command structure at each UC Health location, collaborating with internal stakeholders, and coordinating with various federal and state public health officials, other health systems, and relevant professional organizations. A narrative of many of the activities related to the UC-HCC COVID-19 response is found in published guidance available at: https://www.ucop.edu/uc-health/reports-resources/uch-coordinating-committee-guidance/index.html and in my written updates to the UC Board of Regents available at: https://www.ucop.edu/uc-health/staff/bios/carrie_byington.html.

15. In my role as the leader of the UC-HCC, I interact with the UCOP MRT. In that context, over a period of many months beginning in Fall 2020, when

it was clear one or more COVID-19 vaccines would be available by EUA, I brought the recommendations of our UC subject matter experts that the University should require the COVID-19 vaccine for students, faculty, and employees to be vaccinated before the start of the fall 2021 academic year, unless a person has been approved for a medical exemption. Those recommendations were then shared with the Council of Chancellors and the President.

16. After months of preparation and planning with many subject matter experts, in April 2021 the University of California announced a proposed policy for review that would require all UC faculty, staff, academic appointees and students who will be present on university premises to be vaccinated against COVID-19, subject to exceptions for medical exemption, disability, and religious objection.

17. The UC Office of the President invited comments on the proposed COVID-19 vaccine policy through the end of the comment period of May 31, 2021.

18. On or about July 15, 2021, the final UC COVID-19 Vaccine Policy was issued.

IN ORDER TO HELP COMBAT COVID-19 RISKS AND PROTECT STUDENTS, STAFF, AND FACULTY THROUGHOUT THE UC SYSTEM, I SUPPORT UC'S COVID-19 VACCINE POLICY

19. I was involved in developing the UC campus recommendations to address the threat of COVID-19 and support the science underlying the recommendation of the COVID-19 vaccine as an important tool to protect human life during the pandemic, which is reflected in the UC COVID-19 Vaccine Policy.

20. By way of background, case numbers, hospitalizations and daily death rates have declined significantly since our peak in January 2021 because of vaccination efforts. However, COVID-19 continues to present very real public health risks, including the rise of the delta variant discussed below. Hospitalized cases in the UCH system are once again increasing and have reached levels that exceed the Summer 2020 surge. Given that new variants of the virus are rapidly

emerging and some people are hesitant to take the vaccine, this combination presents serious and potentially deadly public health risks and threatens the likelihood of herd immunity on a large scale.

21. Nearly all COVID-19-related hospitalizations and deaths in the U.S. and in California now are in people who have not been vaccinated, according to an Associated Press analysis of data from the CDC (https://apnews.com/article/coronavirus-pandemic-health-941fcf43d9731c76c16e7354f5d5e187). Vaccination is the key to immunity from severe COVID-19 disease.

22. In addition, viruses, of course, evolve, and the strain of greatest concern today is the delta variant. The World Health Organization reports the delta variant has been detected in at least 130 countries and is the most transmissible of the variants thus far. Fortunately, the vaccines approved for use in the U.S. by the FDA continue to be effective, especially against hospitalization and death, but wherever there are pockets of unvaccinated people, there will be outbreaks. Outbreaks represent ongoing viral replication and transmission and offer further opportunities for the emergence of new variants, which could be more transmissible, more deadly, or in the worst-case, allow the emergence of variants that escape vaccine immunity altogether, essentially bringing us back to the start of the pandemic.

23. In my capacity as an infectious diseases physician and Executive Vice President of UCH, I have expressed support for the UC COVID-19 Vaccine Policy, which I helped to develop. See my July 2, 2021 COVID-19 update for the Regents published days before the UC COVID-19 Vaccine Policy issued (COVID-19 Update to UC Regents 7-2-2021 (ucop.edu), attached as **Exhibit D**.

24. Based on my training and experience and analysis of data shared by the vaccine manufacturers, the CDC, and the U.S. Food and Drug Administration, as well as investigators throughout the world, the COVID-19 vaccines under EUA

or full licensure in the U.S. are safe and effective. These vaccines reduce the health risks posed by the SARS-CoV2 virus and provide protection above and beyond non-pharmaceutical interventions (**NPIs**) including face coverings, masking, physical distancing, and hand-washing. In addition, COVID-19 vaccines have been shown to be safe and effective for individuals previously infected with COVID-19, and are recommended for that population as an added layer of protection against reinfection and disease spread. The vaccines and high vaccination rates provide a pathway to avoid further lockdowns and to more safely reopen campuses, including congregate living and learning spaces, such as classrooms, laboratories, and residence halls. The vaccines and high vaccination rates also protect the capacity of the hospitals to provide care for those with COVID-19 and importantly, for those who have other medical or surgical conditions. The UC COVID-19 Vaccine Policy reflects a prudent step towards health protection for students, staff, faculty, and others in the UC community who are in close physical proximity to one another. The vaccine mandate also protects the communities in which UC campuses are located by decreasing the risk that UC sites will serve as accelerants for the pandemic, as other colleges and universities have done. See https://www.wpr.org/sites/default/files/medrxlacrosse.pdf and https://www.cdc.gov/mmwr/volumes/70/wr/mm7001a4.htm?s_cid=mm7001a4_w, attached as attached as **Exhibits E, F**.

25. I have reviewed the submissions of Plaintiff in this case, including the declarations of Plaintiff Dr. Aaron Kheriaty, Dr. Peter McCullough, and the joint declaration of Dr. Joseph Ladapo, Dr. John Whelan, Dr. Laszlo Boros, Dr. Carole Browner, Dr. Aditi Bhargava, and Dr. Gabriel Vorobiof.

26. None of these materials change my opinions set forth above.

27. The UC COVID-19 Vaccine Policy is evidence based. It was developed in consultation with UC infectious disease and public health experts in addition to campus administrators and experts in campus operations. The policy is

the product of ongoing regular review of scientific evidence from medical studies and evidence generated by UC campuses concerning the dangers of COVID-19 and emerging variants of concern, as well as the safety and effectiveness of the vaccines and other measures for preventing infection, hospitalizations, and deaths from COVID-19, and for reducing the spread of this deadly disease.

28. I understand the declarants take the position that, as of today, any individual previously infected with COVID-19 who has recovered possesses long-term natural immunity to COVID-19 that is superior to immunity conferred by one of the three COVID-19 vaccines the U.S. Food and Drug Administration has approved for use in the United States. I further understand the declarants suggest it is well-settled that the rate of transmission of COVID-19 by previously infected individuals is significantly lower than for vaccinated individuals who experience a breakthrough COVID-19 infection. As of today, these positions are not well-accepted in the medical and scientific community nor endorsed by the U.S. Food and Drug Administration or the CDC.

29. New studies and information about the transmission of COVID-19, variants including delta, and immunity achieved either through vaccination or prior infection are published on a daily basis. This fast pace for emerging research shows no signs of slowing down any time soon. As more research and underlying data become publicly available and are subject to peer-review, the body of evidence regarding COVID-19 will continue to mature and inform what is generally known and well-accepted in the medical and scientific community about this highly contagious and deadly disease. In turn, federal government agencies such as the U.S. FDA and CDC, including the Advisory Committee on Immunization Practices (ACIP), may issue updated public health recommendations and guidance in time. But it is important recognize the broader context and what is known today when making definitive statements about immunity to and transmission of COVID-19.

30. I am in support of the UC COVID-19 Vaccine Policy and believe that

it should apply to individuals who have previously been diagnosed with COVID-19 but are no longer receiving treatment and no longer test positive for the disease. Today, COVID-19 infection rates in California have entered the fourth surge, due to the highly contagious delta variant, with unvaccinated individuals being at particularly high-risk. The research and underlying data as of today regarding natural immunity for individuals who had COVID-19 previously, particularly in light of the new and highly transmissible delta variant, is not sufficiently mature to justify permitting individuals in this group to unilaterally opt out of the UC COVID-19 Vaccine Policy and doing so would put the greater UC community at risk.

31. I disagree with the suggestion offered by the declarants that the three COVID-19 vaccines currently available in the United States are unsafe or not effective, particularly for individuals who previously had or currently have COVID-19. There are numerous publications demonstrating excellent immune response following vaccination in individuals who have been infected with COVID-19. These individuals (infected and vaccinated) may experience the greatest protection from COVID-19.

32. In support of this suggestion, the joint declaration of Dr. Ladapo, et al. cites to a preprint article that has not been peer reviewed.[1] The cited article demonstrated greater transient side effects with the first vaccination shot for people who have had COVID-19. This is well-known, and the side effects are transient fever, fatigue, and lymph node swelling. These are not permanent and do not cause severe harm or death, as Plaintiff suggests. The same side effects are seen in people who have not had COVID-19 infection when they receive the second vaccination shot of the MRNA vaccination series.

33. I also disagree with the suggestion that a correlation exists between

[1] Paragraph 23 of the Joint Declaration of Dr. Ladapo, et al., citing Raw, et al., entitled "Previous COVID-19 infection but not Long-COVID is associated with increased adverse events following BNT162b2/Pfizer vaccination," medRxiv preprint, posted April 22, 2021.

COVID-19 vaccines and increased health risks.[2] For example, with respect to the example of myocarditis, the CDC held a meeting of the Advisory Committee on Immunization Practices (ACIP) and the risk was deemed low for vaccination and myocarditis. Cases were limited and rarely required treatment. ACIP recommended continuing vaccination as the risk of COVID-19 was significantly greater than the risk of myocarditis after vaccination and the benefits of vaccination greatly outweighed the potential for harm. See CDC Morbidity and Mortality Weekly Report (MMWR), July 9, 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", attached as **Exhibit G**. Another recent publication has demonstrated that the risk for myocarditis is much greater following natural infection than following COVID vaccination. See https://www.nejm.org/doi/full/10.1056/NEJMoa2110475, attached as **Exhibit H**. In this study in a nationwide mass vaccination setting, the BNT162b2 vaccine was not associated with an elevated risk of most of the adverse events examined. The vaccine was associated with an excess risk of myocarditis (1 to 5 events per 100,000 persons). The risk of this potentially serious adverse event and of many other serious adverse events was substantially greater after SARS-CoV-2 infection than after vaccination.

34. I similarly disagree with the suggestion that the Vaccine Adverse Event Reporting System (VAERS) data prove, either directly or based on an assumption of underreporting, that COVID-19 vaccines currently administered in the United States are not safe or effective.

35. Established in 1990, the Vaccine Adverse Event Reporting System (VAERS) is a national early warning system to detect possible safety problems in U.S.-licensed vaccines.[3] VAERS is co-managed by the Centers for Disease Control

[2] Id., Paragraph 26.
[3] https://vaers.hhs.gov/about.html

and Prevention (CDC) and the U.S. Food and Drug Administration (FDA). VAERS accepts and analyzes reports of adverse events after a person has received a vaccination. Anyone can report an adverse event to VAERS. Healthcare professionals are required to report certain adverse events and vaccine manufacturers are required to report all adverse events that come to their attention.

36. The VAERS website states that VAERS is not designed to determine if a vaccine caused a health problem. Instead, VAERS is useful for detecting unusual or unexpected patterns of adverse event reporting that might indicate a possible safety problem with a vaccine. This way, VAERS can provide CDC and FDA with valuable information that additional work and evaluation is necessary to further assess a possible safety concern. Adjudication of VAERS reports by experienced clinicians and epidemiologists is required when analyzing a potential adverse event.

37. VAERS has limitations, that are also identified on its website[4]; namely that (1) it is generally not possible to find out from VAERS data if a vaccine caused the adverse event; (2) reports submitted to VAERS often lack details and sometimes contains errors and in some cases intentional falsehoods; (3) serious adverse events are more likely to be reported than non-serious events; (4) numbers of reports may increase in response to media attention and increased public awareness; and (5) VAERS data cannot be used to determine rates of adverse events.

38. Importantly, a report to VAERS alone does not support an apparent link to vaccination.

39. Last, I understand the declaration of Plaintiff Dr. Kheriaty suggests the UC COVID-19 Vaccine Policy medical exemption is too narrow.[5] I disagree with that characterization.

40. The UC COVID-19 Vaccine Policy permits a medical exemption due

[4] https://vaers.hhs.gov/faq.html
[5] Paragraphs 27-28 of the Declaration of Dr. Kheriaty.

to a contraindication or precaution to COVID-19 vaccination recognized by CDC or by the vaccines' manufacturers.[6]

41. Contraindications (conditions in a recipient that increases the risk for a serious adverse reaction) to vaccination are conditions under which vaccines should not be administered.[7] A precaution is a condition in a recipient that might increase the risk for a serious adverse reaction, might cause diagnostic confusion, or might compromise the ability of the vaccine to produce immunity.[8]

42. Based on my experience and in my professional opinion, following CDC and vaccine manufacturers' guidance regarding a contraindication or precaution to COVID-19 vaccination is an evidence-based and responsible approach to define the scope of medical exemptions to the UC COVID-19 Vaccine Policy.

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct to the best of my knowledge.

Executed in Oakland, California, on this 2nd day of September, 2021.

DocuSigned by:
Carrie Byington
DA0AB8BA41B7429...

Carrie L. Byington, M.D.

[6] https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html#Contraindications
[7] https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/contraindications.html
[8] Id.

EXHIBIT A

CURRICULUM VITAE

CARRIE LYNN BYINGTON, M.D.
September 22, 2020

I. PERSONAL DATA

Birth Date-Place:

Citizenship:

Languages: English and Spanish

II. EDUCATION

Undergraduate:
Texas A&M University 1981-1985
College Station, TX
B.S. Biology *cum laude*

Graduate:
Baylor College of Medicine 1985-1989
Houston, TX
M.D. with Honors

University of Utah
Salt Lake City, UT
Graduate Certificate
Conflict Mediation 2010-2011

Training:

Internship:
Baylor College of Medicine
Houston, TX
Pediatrics 1989-1990

Residency:
Baylor College of Medicine
Houston, TX
Pediatrics 1990-1992
Neonatal Chief Resident 1992

Fellowship:
University of California, San Francisco
San Francisco, CA
Pediatric Infectious Diseases 1993-1995

Board Certification/Licenses:

American Board of Pediatrics 1992
Recertification #048487 1999-2006
Recertification #048487 2007-2013
Recertification 2011-2016
Recertification 2016-2026
American Board of Pediatrics
Pediatric Infectious Diseases
525 1997

Recertification	2004-2011
Recertification	2011-2015
Recertification	2014-2024
Texas # H7592	1990 (Active)
California # A052113	1993 (inactive)
Utah # 95-2950011205	1995 (Active)
Nevada # 7831	1996 (inactive)

III. PROFESSIONAL EXPERIENCE

Administrative and Faculty Positions:

Professor, Step VI
University of California San Francisco
Department of Pediatrics 2020

Executive Vice President
University of California Health 2019

The Jean and Thomas McMullin Professor and Dean
College of Medicine
Senior Vice President for Health Sciences
Texas A&M University 2017-2019

Vice Chancellor for Health Services
Texas A&M System 2017-2019

Distinguished Service Professor
University of Utah 2015

Director and Principal Investigator,
Utah Center for Clinical and Translational Science
Salt Lake City, UT 2015-2016

Associate Vice President,
Faculty and Academic Affairs
University of Utah Health Sciences Center
Salt Lake City, UT 2013-2016

Co-Director and Principal Investigator,
Utah Center for Clinical and Translational Science
Salt Lake City, UT 2013-2016

Vice Dean for Academic Affairs and Faculty Development

University of Utah School of Medicine
Salt Lake City, UT 2012-2016

HA and Edna Benning
Presidential Professor of Pediatrics
University of Utah Health Sciences Center
Salt Lake City, UT 2010-2016

Vice Chair (Oversight Research Enterprise)
Department of Pediatrics
University of Utah Health Sciences Center
Salt Lake City, UT 2009-2013

Associate Director,
University of Utah
Center for Clinical and Translational Science
Salt Lake City, UT 2008-2013

Associate Chair for Clinical Research
Department of Pediatrics
University of Utah Health Sciences Center
Salt Lake City, UT 2007-2009

Professor of Pediatrics
Division of General Pediatrics
and Division of Pediatric Infectious Diseases
University of Utah Health Sciences Center
Salt Lake City, UT July1, 2006

Lowell Bennion Public Service Professor
University of Utah 2001-2002

Associate Professor
Division of General Pediatrics
and Division of Pediatric Infectious Diseases
University of Utah Health Sciences Center
Salt Lake City, UT 2000-2006
Tenure Awarded July 1, 2003

Assistant Professor
Division of General Pediatrics
and Division of Pediatric Infectious Diseases
University of Utah Health Sciences Center

Salt Lake City, UT 1995-2000

Assistant Professor
Division of Ambulatory Pediatrics
Baylor College of Medicine
Houston, TX 1992-1993

Additional Research Experience:

Compucyte Corporation
Cambridge, MA 1998-1999

Consumer Health Interactive
San Francisco, CA 1999

BabyCenter.com
San Francisco, CA 2000

Intermountain Healthcare
Chair, Pediatric Research Council 2009-17

US Olympic Committee
Chair, Infectious Diseases Advisory Group
Responsible for protecting Team USA athletes and staff from Zika Virus during the 2016 Olympic Games in Brazil
2016-2017

Scientific Advisory Board
IDbyDNA 2017

Houston Methodist Research Institute
Full Member-Affiliate TAMU 2018

External Advisory Board
TL1 and KL2 Training Program
University of Utah
Center for Clinical and Translational Science 2020

Editorial Experience:

<u>*Editorial Board:*</u>

Pediatric Infectious Disease Journal 2009-2016
Academic Medicine 2018-

<u>*Ad Hoc* Reviewer:</u>

Pediatric Infectious Diseases Journal 1996-
Pediatrics 1999-

Clinical Infectious Diseases	2001-
The Journal of Pediatrics	2002-
European Journal of Clinical Microbiology and Infectious Diseases	2006-
JAMA Pediatrics	2007-
Pediatric Pulmonology	2009-
Journal of Public Health Management and Practice	2010-
Effective Health Care	2010-
Academic Pediatrics	2011-
Journal of Pediatric Infectious Diseases (JPIDS)	*2012-*
Academic Emergency Medicine	*2013-*
JAMA	*2014-*
PLOS One	*2015-*

Research Awards:

Pediatric Scientist Development Program	
Training Grant	$50,000
Molecular Parasitology	1994-1995
Division of General Pediatrics	
Research Award	$4,000
Foster Care Clinic	1996
Roche Molecular Systems	
Research Award (in kind)	$75,000
Enteroviral PCR Project	1996
Primary Children's Medical Center Foundation	
Research Award	$25,000
Enteroviral PCR Project	1997
Pediatric Primary Care Grant	$50,000
Salary Support	1997-99
Division of General Pediatrics	
Research Award	$3,000
Orthotic Bracing for Pectus	1997-98
Robert Wood Johnson Generalist Physician Faculty Scholar Award	$240,000
Viral Diagnostics in the Febrile Infant	1998-2003
Reach Out and Read	
National Literacy Project	
Book credit (2000 volumes)	1998

First Book Foundation Literacy Project (3000 volumes)	1998
Compucyte Corp CD11b in Infants	$10,000 1998
Starbucks Opportunity Award Reach Out and Read	$5,000 1999
University of Utah General Clinical Research Center Rapid Diagnostics for the Evaluation of the Febrile Infant	$45,000 1999-2002
NIAID and CASG Pleconaril Clinical Trial	$2,000 1999
Division of General Pediatrics Research Award Viral Respiratory PCR	$4,100 1999
AAP Resident Research Award Empyema in Utah (LaShonda Spencer)	$2,500 1999
PCMC Foundation Reach Out and Read	$3, 500 2000
Travis Gurr Endowment Awarded for Research at South Main	$6,500 1999-2000
I Am Your Child Foundation Literacy Project (300 volumes)	2000
Chemicon, Inc. HHV-6 in Infants	$2,000 2000
Reach Out and Read Sustainability Award	$1,500 2000
Leah L. Hartshorn Estate Reach Out and Read	$2,500 2000
Castle Foundation	$4,000

Reach Out and Read	2001
Wyeth-Lederle	$5,000
Pneumococcal Serotype Analysis	2001
Lowell Bennion Professorship	$5,000
Reach Out and Read	2001
Reach Out and Read	$2,200
Sustainability Award	2001
University of Utah Research Foundation	
Technology Commercialization Project	
Decision Support Software for	$50,000
Evaluation of the Febrile Infant	2003-2004
The Castle Foundation	$5,000
Reach Out and Read	2002-2003
Reach Out and Read	$1,400
Sustainability Award	2002
National Medical Fellowship	$6,000
(Mentor for Miguel Knochel)	2003-2004
Anemia in US Born Children of Mexican Women	
Target Foundation	$3,000
Literacy Support	2003
Reach Out and Read	$900
Sustainability Award	2003
Reach Out and Read	$1,400
Sustainability Award	2004
Katherine Gilbert Foundation	$50,000
Reach Out and Read	2004
Target Foundation	$2,250
Literacy Support	2004
Reach Out and Read	$920
Sustainability Award	2005

U01-A1061611-01 (PI-Poritz)

NIH/NIAID $4,000,000
PCR Identification of Respiratory Viruses including SARS
Role-Co-Investigator 2005-2009

K24- HD047249-01A1 (PI Byington)
NIH/NICHD $626,591
Decision Support for Evaluation of the Febrile Infant
Role: Principal Investigator 2005-2010

2R24HSO11826 (PI Young)
AHRQ $190,000
Intermountain Child Health Services Research Consortium

Role: Mentor 2005-2006

5D14HP00115 (PI Magill)
HRSA $275,634
Faculty Development in Primary Care
Role: Mentor 2005-2007

5D12HP00122 (PI Magill)
HRSA $275,634
Grants for Academic Administrative Units in Primary Care

Role: Mentor 2005-2008

Reach Out and Read $1,626
Sustainability Award April 2005

Reach Out and Read $1,551
Sustainability Award October 2005

Target Foundation $1,000
Reach Out and Read December 2005

Michael Foundation $5,000
Reach Out and Read December 2005

Reach Out and Read $2, 325
Sustainability Award 2006

Travis Gurr Memorial $12,750
Reach Out and Read July 2006

Target Foundation $5,000

Reach Out and Read October 2006

1 PO1 CD000284-01 (PI Samore)
CDC
Center of Excellence
in Public Health Informatics $4,500,000
Role: Co-Investigator and
PI INTERACT Project (R-01) 2006-2009

1 U01 AI074419-01 (PI Poritz)
NIH/NIAID $8,900,000
FilmArray for Diagnosis of Influenza
Role: Co-Investigator 2007-2012

Wyeth (PI-Byington)
Multilocus Sequence Typing of *$75,000*
Pneumococcal Empyema
Role: PI 2007-2008

Wyeth (Site PI-Byington)
Clinical Trials of PCV-13 Infants 2007-2010

Wyeth (Site PI-Byington)
Clinical Trials of PCV-13 Children 2008-2010

Reach Out and Read National (PI Byington)
Impact of ROR on School Readiness
of Hispanic Children $30,000
Role: PI 2008-2009

1UL1RR025764 (PI McClain, D)
NIH/NCRR $22,000,000
CTSA 2008-2013
Roles: Associate Program Director - Pediatrics, Participant Interaction Core
Director, Minority Outreach
Director K12, MSCI

1U01AI082482-01 (PI Byington, Dobrowolski, Kriesel)
NIH/NIAID 2009-2013
$2,000,000
STI and Respiratory Pathogen Testing in Non-Traditional Settings.

1R18HS018034-01 (PI Byington)
AHRQ 2009-2012

$900,000
Evaluation of an Evidence-Based Care Process Model (EB-CPM) for Febrile Infants
Role: PI

1U01 CDC (PI Ampofo)
CDC 2009-2013
$1,500,000
Diagnostic Evaluation of Pneumonia in Children
Role: Co-I/Mentor

AARA/ CIO7-70404 (PI Rolfs, UDOH)
CDC 2009-2013
$112,924
Effect of PCV-13 on Invasive Pneumococcal Disease in Utah
Role: Consultant

5K12HD001410-08 (PI Clark)
NIH/NICHD 2003-2013
$4,320,000
Genetic and Developmental Mechanisms of Pediatric Disease
Role: Program Director

1KM1CA156723 (PI Byington)
NIH/NCI 2010-2013
$2,500,000
Mentored Scholars Program for Translational Comparative Effectiveness Research
Role: PI

1R25HL108828 (PI Byington)
NIH/NHLBI 2011-2016
$336,000
Native American Short-Term Research Education Program in Children's Health
Role: PI

1R25MD00678 (PI Byington)
NIH/NIMHD 2011-2016
$1,250,000
Native American Summer Research Internship in Maternal and Child Health
Role PI

5 U50CI000866 (PI Dimond)
CDC 8/1/11-7/31/14
$1,602, 358
Epidemiology and Laboratory Capacity for Infectious Diseases: Vaccine Effectiveness-PCV13
Role: Consultant

1R43 AI098197 (**PI Welch**)
NIH/NIAID 2012-2018
$1,000,000
Protease-resistant D-peptide inhibitors of RSV entry
Role: Consultant

1 P20MD008777 (PI Byington and Freund)
NIH/NIMHD 2013-2014
$192, 132
Clinical and Translational Science National Research Mentoring Network Furthering a Diverse Biomedical Workforce
Role: Contact PI

1 KL2TR001065 (PI McClain and Byington)
1 TL1TR001066 (PI McClain and Byington)
1UL1TR001067 (PI McClain and Byington)
NIH/NCATS 2013-2015
$8,800,000
Utah Center for Clinical and Translational Science and associated TL1 and KL2 Training Programs
Role: Multi-PI

1 KL2TR001065 (PI Byington and Dere)
1 TL1TR001066 (PI Byington and Dere)
1UL1TR001067 (PI Byington and Dere)
NIH/NCATS 2015-2018
$13,200,000
Utah Center for Clinical and Translational Science and associated TL1 and KL2 Training Programs
Role: Contact-PI

3UL1TR001067-02S1 (PI T. Shanley-Michigan)
NIH/NCATS 2014-2015
$7,000,000 (All Sites)
$111,735 (Utah)
Enhancing Clinical Research Professionals Training and Qualifications

Role: Site PI

1K12HD085816 (PI Peterson, C, Matthew)
NIH/NICHD 2015-2020
$1,701,00
Utah Women's Reproductive Health Research Career Development Award
Role: Director-Mentorship

1K12HD085852 (PI Varner, M)
NIH/NICHD 2015-2020
$1,890,000
Utah Building Interdisciplinary Research Careers in Women's Health Career Development Program
Role: Director-Mentorship

1R21HD090955 (PI Byington, CL)
NIH/NICHD 2016-2018
$275,00
Novel Testing to Elucidate Reproductive Outcomes of ZIKV Infection—Olympics 2016
Role: PI

Blue Cross/Blue Shield of Texas Foundation
(PIs Brown, Byington, Dickey)
A Rural Health Moonshot 2018
Role: Multi-PI $10,000,000

Patents:
US Patent **7,461,046** entitled:
Method for Creating and Using a Treatment Protocol for the Evaluation of the Febrile Infant
Awarded December 2, 2008

Licensed Intellectual Property to
Idaho Technology/Biofire Diagnostics/bioMerieux
Clinical Applications of the FilmArray and Rapid Typing of Bacteria
January 29, 2009

FilmArray FDA cleared panels
Respiratory Panel 2011
Blood Culture Panel 2013
Gastrointestinal Panel 2014

Meningitis/Encephalitis	2015
Pneumonia	2018
Respiratory Panel 2 +COVID	2020

IV. HONORS and AWARDS

National Merit Scholar	1981-1985
Dean's List Texas A&M University	1981-1985
Lechner Undergraduate Research Fellow	1985
Alpha Omega Alpha	1988
Lange Medical Publications Award	1989
Janet M. Glasgow Memorial Achievement Citation of the American Medical Women's Association	1989
Outstanding Resident Award, Houston Pediatric Society	1992
Pediatric Scientist Development Award	1994-1995
Robert Wood Johnson Generalist Physician Faculty Scholar Nominee/Finalist, University of Utah	1996, 1997
Excellence in Teaching Award-Pediatric Housestaff	1997-1998
Nomination: Early Career Teaching Award	1999
Nomination: Leon W. Jarcho Distinguished Teaching Award	2000, 2005
Selected for *Best Doctors in America* (General Pediatrics and Pediatric Infectious Diseases)	2002-2017
The University of Utah Golden Anniversary Prize for Distinguished Clinical Investigation	2004
Doris Duke Charitable Foundation: Distinguished Clinical Scientist Award Semi-Finalist	2006
Gary C. Schoenwolf Mentorship Award-Department of Pediatrics	2011
Department of Pediatrics Grand Rounds MVP	2011
Beacon of Excellence Award—Native American Summer Internship University of Utah	2012

Linda Amos Award for Service to Women-University of Utah	2012
Beacon of Excellence Award—Academic Associates Program University of Utah	2013
AAMC Building Bridges and Spanning Boundaries Award for Innovation in Research and Research Education Academic Associates Program	2014
American Academy of Pediatrics Unsung Hero Award In recognition of work of the Committee on Infectious Diseases	2015
Distinguished Service Professor University of Utah	2015
AAMC Group on Women in Medicine and Science Leadership Award for Individuals	2015
36th Annual Mossell Lectureship on Health Equity	2017
Barbara Stark Baxter Medical Volunteer of the Year	2017
Election—National Academy of Medicine	**2017**
Election—National Academy of Inventors	**2017**
Texas A&M College of Science Academy of Distinguished Former Students	2018
Marion Spencer Fay Award—Drexel University Institute for Women's Health and Leadership	2019
AAMC Innovation in Research and Research Education Award for the VPCAT Program (University of Utah)	2019

V. ADMINISTRATIVE EXPERIENCE

Director-Pediatric Telemedicine Clinic	1996-1998
Core Faculty-Primary Care Track Residency Program	1995-2000
Medical Director-Reach out and Read	

South Main Clinic	1997-2009
Chair-PCMC Committee: Management of the Febrile Infant	1998-2000
Research Committee, Department of Pediatrics	2004-present
Co-Director of the Pediatric Honors Research Program	2004-2006
Division of General Pediatrics Executive Committee	2005-2009
Director of the Mentored Program in Pediatric Research	2006-present
Associate Director of the Huntsman General Clinical Research Center-Pediatrics	2006-2008
Member Internal Advisory Committee for the General Clinical Research Center/ CTSA Clinical Services Core	2006-2012
Primary Care Research Center Steering Committee	2006-present
Associate Chair for Clinical Research Department of Pediatrics	2007-2009
Director of the Pediatric Clinical and Translational (PCAT) Research Scholars Program	2007-2012
University of Utah Center for Clinical and Translational Science Associate Director of the University of Utah	2008-2012
University of Utah Center for Clinical and Translational Science Director of Research with Minority and Vulnerable Populations Director K12 program Director MSCI Clinical Services Core Advisory Committee	2008-2012
University of Utah Center for Clinical and Translational Science Associate Director and Executive Steering Committee	2009-12
Vice Chair-Research Enterprise Department of Pediatrics	2009-13
Director of Graduate Studies-MSCI Program Utah CCTS	2010-13

Director-Children's Health Research Career Development Award Department of Pediatrics	2010-14
Executive Steering Committee T-32 Training Program in Microbial Pathogenesis	2010-17
Internal Advisory Board Huntsman Center for Children's Cancer Research	2010-12
PI/Program Director Training Program in Translational Comparative Effectiveness (T-CER)	2010-13
Member- University of Utah Research Advisory Committee	2011-17
Co-Chair-Search Committee Utah Center for Health Delivery and Implementation Research	2012-13
Benning Society/SOM Lecture Series Planning Committee	2012-2015
Director, Vice President's Clinical and Translational Scholar Program	2012-
Co-Director Utah Center for Clinical and Translational Science	2012-2015
School of Medicine Executive Committee	2012-17
University Community Physicians Executive Committee	2013-17
Health Care Executive Committee	2014-17
Health Sciences Executive Committee	2014-17
SOM Academic Executive Committee	2014-17
Director, Utah Center for Clinical and Translational Science	2015-17
Dean, SVP Health Sciences Texas A&M University	2017-2019
Vice Chancellor for Health Services, Texas A&M University System	2017-2019
Executive Vice President, University of California Health System	2019-

VI. PROFESSIONAL ACTIVITIES (Current)

AAMC Council of Teaching Hospitals (**COTH**) **Administrative Board**	2020
Co-Chair—Health Evolution Work Group on Leveraging Data to Improve Health Equity	2020-
Presidential Council—Association of Academic Health Centers • Focus on Academic Health Plans	2020-
Board Member—ROCS for Health Care	2020
Board Member—The Commonwealth Fund	2020-
Board Member—Houston Methodist Research Institute	2017-19
The Cancer Prevention and Research Institute of Texas University Advisory Committee	2017-19
NIH/NIAID—Microbiology and Infectious Diseases (MID) Career Development Study Section	2017-19
External Advisory Board Georgetown and Howard Universities Center for Clinical and Translational Science	2016-18
AAMC Annual Meeting Advisory Committee	2015-16
NIH Clinical and Translational Awards (CTSA) National Steering Committee	2015-16
NIH Clinical and Translational Awards Lead Team-Workforce Development	2015-16
AAP Liaison to the Canadian Pediatric Society Infectious Diseases and Immunization Committee	2014-18
US Centers for Disease Control and Prevention Expert Consultant Panel on Parental Presence During the Evaluation of a Child with Suspected or Confirmed	

Ebola Virus Disease	2014-15
Society of Pediatric Research Young Investigator Coaching Program	2014-16
Chair: American Academy of Pediatrics Committee on Infectious Diseases (Red Book)	2014-2018
Robert Wood Johnson-Harold Amos- Career Development Award National Advisory Committee	2014-
Mountain West Research Consortium: Alaska, Hawaii, Idaho, Montana, Nevada, New Mexico, and Wyoming (IDeA Institutions) Study Section	2013-17
NIH Infectious Diseases, Reproductive Health, and Pulmonary (IRAP) Study Section	2012-15
Association of Medical School Pediatric Department Chairs Pediatric Leadership Development Program	2012-13
National CTSA Consortium-Child Health Oversight Committee (**elected office**)	2011-13
American Academy of Pediatrics Subcommittee on Fever in Infants Younger than 3 months	2010-18
SPR Mentorship Committee	2010-14
Vice Chair: AAP Committee on Infectious Diseases (Red Book)	2010-2014
2011 International Meeting Planning Committee, European Society of Pediatric Infectious Diseases	2010
2010 23rd Annual Infectious Diseases in Children Symposium National Program Committee	2010
Federation of Pediatric Organizations (FOPO) Task Force On Women in Pediatrics (SPR Representative)	2010-12
National Medical Advisory Board Amigos de las Americas	2010-12

2010 National Meeting Planning Committee-Infectious Disease Society

of America	2009-10
Pediatric Infectious Diseases Society Awards and Nomination Committee (**Elected position**)	2009-12
Centers for Disease Control and Prevention Pediatric Infectious Diseases Technical Expert and Liaison for American Academy of Pediatrics for Guideline Committee for Prevention of Early Onset GBS	2009-2010
Infectious Disease Society of America **Co-Chair** Guideline Committee for Pediatric Community Acquired Pneumonia	2009-2011
Director, Intermountain Healthcare, University of Utah, and Intermountain Pediatric Society (AAP), American Board of Pediatrics (ABP) Maintenance of Certification Process, An Evidence Based Care Process Model for the Febrile Infant. Approved by ABP January 1, 2009.	2009-13
Thrasher Research Foundation Scientific Advisory Board	2009-10
Chair Scientific Advisory Board	2010-13
Intermountain Healthcare Research Guidance Council	2008-17
International Working Group on Pediatric Empyema, (Representation from US, Canada, Europe, Asia, Latin America) **Founding Chair**	2007-12
AHRQ/AAP Technical Expert Panel on the Management Of Febrile Infants	2007-2011
National Advisory Board for Leyendo Juntos, a Reach Out and Read Initiative to improve literacy in Spanish-speaking Families	2007-2010
American Academy of Pediatrics, Executive Committee of the Committee on Infectious Diseases (**Red Book Committee**)	2007-2010
Executive Leadership in Academic Medicine (ELAM)	2007-2008
IHC Pediatric Subspecialty Guidance Council	
Director of Pediatric Infectious Disease Committee	2005-present

Utah Department of Health Vaccine Advisory Committee	2005-present
PCMC Foundation Innovative Research Grant Review Panel	2004-present
Chair	2009
CDC National Respiratory and Enteric Virus Surveillance System	
PCMC Laboratory Representative	2004-present
US Pediatric Multicenter Meningococcal Surveillance Group	2001-13
Subspecialty abstract reviewer-PAS annual meeting	2001-15
IDSA-Emerging Infections Network	1998-present
NIAID Collaborative Antiviral Study Group	
Enteroviruses	1998-present
American Academy of Pediatrics	
Section on Infectious Diseases	1996-present

Professional Activities (Past)

Moderator, Infectious Diseases and Immunology, National Institute of Child Health and Human Development (NICHD) Children's Health Research Center Annual Retreat	2006
Invited Reviewer for Proposals to the Michael Smith Foundation For Health Services Research British Columbia, Canada	2005
Poster Facilitator, Infectious Diseases, PAS 2005 Annual Meeting	2005
Utah Department of Health Perinatal GBS Work Group	2003
SPR Student Research and House Officer Award Committee	2003-2006
Moderator: Underserved Populations Platform	
PAS Annual Meeting	2002
The Migrant Head Start Health Advisory Committee	2000-2007
Utah State Task Force on Child Care	
Early Childhood Literacy Committee	1998-2000
Utah State Health Care Advisory Board-	
Task Force on Foster Care-	
Executive Committee	1997-2000

American Board of Pediatrics
Question Writer for ID Exam 1998-2000

Moderator: Pediatric and Neonatal Infections
WSPR annual meeting 1998

American Academy of Pediatrics-
Section on Community Pediatrics 1996-1999
American Academy of Pediatrics-
Section on Child Abuse and Neglect 1996-1999
American Academy of Pediatrics-
Section on International Child Health 1996-2000

VII. UNIVERSITY COMMUNITY ACTIVITIES

Volunteer, Migrant Health Care Clinic 1996
Volunteer, Women in Medicine 1996, 1997
Pediatric Grand Rounds Advisory Committee 1996-1999
Promotion, Retention, Tenure Subcommittee 1997
Medical Student Core Curriculum Committee 1997
University of Utah Diversity Committee 1999
Retention, Promotion, Tenure Pediatric Ad-Hoc Committee 1999-2007
Research Enterprise Committee 2003-present
University Academic Senate 2004-2007
Senate Executive Committee **2005-2007**
Center of Excellence in Women's Health
Leadership Committee 2006-2010
Presidential Committee for the Status of Women 2006-2010
Personalized Health Care Pilot Project Review Committee 2011-2015
Council of Academic Deans 2012-
Academic Senate Ex-Officio 2012-
BIRCWH and WRHR Selection and Oversight 2015-

VIII. PROFESSIONAL SOCIETIES

American Medical Association 1985-present
American Academy of Pediatrics 1989-present
Fellow 1998
Pediatric Infectious Diseases Society 1993-present
Infectious Diseases Society of America 1993-present
Fellow 2014
American Academy of Pediatrics, Utah Chapter &
Intermountain Pediatric Society 1996-present
Ambulatory Pediatric Association 1996-present
Western Society for Pediatric Research 1998-present
National Association for the Education of Young Children 1998-present
Utah Association for the Education of Young Children 1999-2016
American Society of Microbiology 1999-present

Pan American Society for Clinical Virology	1999-present
Association for Academic Minority Physicians	1999-present
National Hispanic Medical Association	2001-present
Society for Pediatric Research	2003-present
American Pediatric Society	2009-present
Association for Academic Minority Physicians	2014-present

IX. TEACHING RESPONSIBILITIES

Mentoring Junior Faculty

Pediatric Clinical and Translational Scholars

1) Mandy Allison, MD General Pediatrics	2007-2009
2) Krow Ampofo, MD Pediatric Infectious Diseases	2007-2009
3) Cammon Arrington, MD, PHD Pediatric Cardiology	2007-2009
4) Anne Blaschke, MD, PhD Pediatric Infectious Diseases	2007-2009
5) Kristine Campbell, MD, MSPH Safe and Healthy Families	2007-2009
6) Per Gesteland, MD, MS Inpatient Medicine	2007-2009
7) Maija Holsti, MD Emergency Medicine	2007-2009
8) Nicole Mihalopoulos, MD General Pediatricss/Adolescent Medicine	2007-2009
9) Tess Saarel, MD Pediatric Cardiology	2007-2009
10) Tamara Simon, MD, MPH Inpatient Medicine	2007-2009
11) Kimberly Statler, MD Critical Care	2007-2009
12) Kathleen Ventre, MD Critical Care	2007-2009

13) Andrew Zeft, MD, MS Pediatric Immunology and Rheumatology	2007-2009
14) AK Kaza, MD Pediatric CV Surgery	2008-2010
15) Nelangi Pinto, MD, MSCI Pediatric Cardiology	2008-2010
16) Julie Shakib, MD, MPH, MSCI General Pediatrics	2008-2010
17) Marcia Feldkamp, PhD Medical Genetics	2009-2011
18) Ellie Hirshberg, MD Intermountain Healthcare/Critical Care	2009-2011
19) Laurie Linder, PhD Pediatric Oncology/School of Nursing	2009-2011
20) Shajii Menon, MD Pediatric Cardiology	2009-2011
21) Joshua Schiffman, MD Pediatric Hematology/Oncology	2009-2011
22) Susan Benedict, MD Pediatric Neurology	2010-2012
23) Pamela Clarkson-Freeman, PhD, MSW Social Research Institute	2010-2012
24) Mark Fluchel, MD Pediatric Hematology/Oncology	2010-2012
25) Jerry Jou, MD Pediatric Cardiology	2010-2012
26) Tracy Manuk, MD Department of Obstetrics/Gynecology	2010-2012
27) Ryan Metzgar, PhD Pediatric Surgery	2010-2012

Child Health Research Career Development Scholars

1) Camille Fung, MD, PhD
Neonatology 2010

2) Jeff Ekstrand, MD, PhD
Pediatric Neurology 2010-2011

3) Michelle Schoeber, MD
Neonatology 2010-2012

4) Karin Chen, MD
Pediatric Rheumatology 2010-2012

CCTS KL2 Scholars

1) Matthew Rondina, MD
Internal Medicine 2008-2009

2) Kristine Campbell, MD, MSPH
Pediatric Safe and Healthy Families 2008-2010

3) Per Gesteland
Pediatric Inpatient Medicine 2008-2010

4) Curry Koenig, MD
Internal Medicine 2009-2010

5) Julie Shakib, DO, MSCI
General Pediatrics 2009-2011

6) Aga Lewalt, MD
Pediatric Physical Medicine and Rehabilitation 2010-2012

7) Lance Davidson, PhD 2011-2013
Medicine/Cardiology

8) Siam Oottamasathien, MD 2011-2013
Pediatric Urology

8) Tracy Manuk ,MD 2011-2013
Obstetrics and Gynecology

9) Tracy Frech, MD 2012-2014
Medicine/Rhuematology

10) Nicholas Johnson, MD 2013-2014
Neurology

11) Adam Hersh, MD Pediatric Infectious Diseases	2013-2014
12) Deanna Kepka, PhD Nursing	2013-2015
13) Adam Spivak, MD Internal Medicine-Infectious Diseases	2013-2015
14) Robert Schlaberg, MD Pathology	2014-2016
15) Noah Kolb, MD Neurology	2014-2015
16) Kailah Davis, PhD Utah Department of Health	2014-2016
17) Adam deHavenon Neurology	2015-
18) Adam Bress, PhD Pharmacology	2015-

Translational-Comparative Effectiveness Research Scholars

1) Tellen Bennett, MD Pediatric Critical Care	2010-12
2) Mark Fluchel, MD Pediatric Hematology/Oncology	2010-12
3) Nelangi, Pinto, MD, MSCI Pediatric Cardiology	2010-12
4) Lance Davidson, PhD Cardiovascular Genetics	2010-12
5) Jennifer Majersick, MD, MSPH Neurology	2010-12
6) Richard Nelson, PhD Internal Medicine, Epidemiology	2010-12
7) Kalani Raphael, MD Internal Medicine, Nephrology	2010-12
8) Nazem Akoum, MD Internal Medicine	2011-13
9) Kristina Callis-Duffin, MD Dermatology	2011-13

10) Jaewhan Kim, PhD
Family and Preventive Medicine 2011-13
11) Carrie McAdam-Mark
Pharmacotherapy 2011-13
12) Christian Niedzwecki, MD
Pediatrics/PM&R 2011-13
13) Bryan Stone, MD, PhD
Pediatric Inpatient Medicine 2011-13
14) Emily Thorell, MD
Pediatric Infectious Diseases 2011-13
15) Ashley Warnock, MD
Pediatric Genetics 2011-13

Vice President's Clinical and Translational (VPCAT) Scholars

1) Richard Gurgel, MD
Otolaryngology 2013-2015
2) Gang Luo, PhD Biomedical
Informatics 2013-2015
3) Heather Major, MD
Maternal Fetal Medicine 2013-2015
4) Jeremy Meier, MD
Pediatric Otolaryngology 2013-2015
5) Jewel Samadder, MD
Medicine/Gatroenterology 2013-2015
6) Robert Schmidt, MD, PhD
Pathology 2013-2015
7) Emily Sydnor, MD
Medicine/Infectious Diseases 2013-2015
8) Jessica Walsh, MD
Medicine/Rhuematology 2013-2015
9) Theresa Werner, MD
Medicine/Oncology 2013-2015
10) Robert Bollo, MD
Neurosurgery 2014-2016
11) Benjamin Brooke, MD, PhD
Vascular Surgery 2014-2016
12) Melissa Cheng, MD, MOH, MSPH
Occupational Medicine 2014-2016
13) Jane Dyer, CNM, FNP, MBA, PhD
College of Nursing 2014-2016
14) Summer Gibson, MD
Neurology 2014-2016
15) Skyler Jennings, PhD, AuD
College of Health 2014-2016
16) Sujee Jeyapalina, PhD

Orthopaedics/Bioengineering	2014-2016
17) Giavonni Lewis, MD	
Surgery	2014-2016
18) Catherine Loc-Carillo, PhD	
Orthopaedics	2014-2016
19) William Lowrance, MD	
Urology	2014-2016
20) Scott McNally	
Radiology	2014-2016
21) Jose Nativi-Nicolau	
Cardiology	2014-2016
22) Quynh Nguyen, PhD	
College of Health	2014-2016
23) Robert Schlaberg, MD	
Pathology	2014-2016
24) Adam Spivak, MD	
Infectious Diseases	2014-2016
25) Gail Towsley, PhD	
College of Nursing	2014-2016
26) Yelena Wu, PhD	
Family and Preventive Medicine	2014-2016
27) Vanessa Stevens, PhD	
College of Pharmacy-Pharmacotherapy	2014-2016
28) Deanna Kepka, PhD	
College of Nursing	2014-2016
29) Nancy Allen, PhD	
College of Nursing	2015-2017
30) Jeremiah Alt, PhD	
Otolaryngology	2015-2017
31) Adam Bress, MS, PharmD	
Pharmacotherapy	2015-2017
32) Mignan Chen, PhD	
Pharmaceutical Chemistry	2015-2017
33) Lori Gawron, MD, MPH	
Obstetrics and Gynecology	2015-2017
34) Andrew Gawron, MD, PhD	
Gastroenterology	2015-2017
35) Heidi Hanson, PhD	
Ramily and Preventive Medicine	2015-2017
36) Noah Kolb, MD	
Neurology	2015-2017
37) Stephen McKellar, MD, MSc	
Cardiovascular Surgery	2015-2017
38) Mateo Paz-Soldan, MD, PhD	
Neurology	2015-2017
39) Ana Sanchez-Birkhead, PhD	

College of Nursing 2015-2017
40) Deborah Stephens, DO
Hematology/Bone Marrow Transplant 2015-2017
41) Alexandra Terrill, PhD
Occupational Therapy 2015-2017
42) Anandh Velayutham, PhD
College of Health 2015-2017

Building Interdisciplinary Research Careers In Women's Health (BIRCWH) Scholars

1) Heidi Hanson, PhD 2015-2017
Department of Family and Preventive Medicine
2) Cindy Matsen, MD 2015-2017
Department of Surgery

Women's Reproductive Health Research Scholars

1) Laurie Gawron, MD 2015-2017
2) Karen Gibbens, MD 2015-2017

Other Academic Institutions

1) Derek Williams, MD
Pediatric Community Acquired Pneumonia
Associate Professor of Pediatrics
Vanderbilt University
Memphis, TN 2010-2017
(**K12 awarded July 2011 and K23 awarded Jan 2013**)

2) Margaret Rosenfeld, MD
Mentoring of Junior Faculty and K-24
Associate Professor of Pediatrics
University of Washington
Seattle, WA 2010-2012

3) Pui-Ying Iroh Tam
Pneumococcal Epidemiology and Vaccine Selective Pressure
SPR Young Investigator
Assistant Professor of Pediatrics
University of Minnesota 2014-2017

4) Richelle Charles, MD
Cholera vaccine development
Assistant Professor, Internal Medicine
Harvard Medical School
Harold Amos Scholar 2014-2018

5) Florence Momplaisir, MD
HIV perinatal treatment
Assistant Professor, Obstetrics and Gynecology
Drexel University College of Medicine
Harold Amos Scholar 2015-2019

Mentoring of Post-Graduate Fellows
Nicole Pershing, MD
Fellow Pediatric Infectious Diseases
Pneumococcal Empyema 2019-

Eric Glissmeyer, MD
Fellow Pediatric Emergency Medicine
UTI Diagnostics in Febrile Infants and
HSV Infection in Infants 2013-14

Brian Kendall, MD
Fellow Adult Infectious Diseases
Epidemiology *S.pneumoniae* Adults 2010-2012

Elizabeth Justice, MD
Fellow Pediatric Infectious Diseases
Molecular Epidemiology of *S. pneumoniae*
Molecular Diagnostics of Respiratory Viruses 2009-2013

Jeffrey Bender, MD
Fellow Infectious Diseases
Influenza and *Streptococcus pneumoniae* 2006-2009

Laurie Pulver, MD
Fellow General Pediatrics
GBS in the Era of Prophylaxis
Probiotics and Maternal/Infant Flora 2006-2009

Julie Shakib, MD
Fellow General Pediatrics
Maternal/Infant Pertussis Immunity
Optimizing Pertussis Immunization 2006-2009

Amy Herbener, MD
Infectious Diseases Fellow
PCR Analysis of DFA negative Respiratory Illness 2005-2008

Anne Blaschke, MD
Fellow Pediatric Infectious Diseases

Molecular Diagnosis of CNS Infections	2004-2006
Alison C. Rentz, MD Fellow, Neonatology Early Onset Sepsis in the Term Infant HHV-6 Infections in the NICU ECHO 7 Infection in the Neonate University of Utah (PCMCF Award)	2002-2005
Gregory Harlan, MD Fellow General Pediatrics Monoarticular arthritis in Rheumatic Fever	2004-2005
Michael Mallory, MD Fellow Pediatric Emergency Medicine Evaluation of Health Literacy in Spanish-Speaking Families (PCMCF Award)	2004
Maija Holsti, MD Fellow Pediatric Emergency Medicine Evaluation of a Model to Predict SBI in Febrile Infants	2004-2005
Christian Rochell, MD Pediatric Chief Resident Adenoviral Infections in Immune Competent Children University of Utah	2002-2003
Lonnie Miner, MD Fellow, Neonatology Understanding Bacterial Culture-Negative “Sepsis” in the NICU University of Utah	2002-2003
Sherrie Butler, MD Fellow Critical Care Understanding Bacterial Culture-Negative “Sepsis” in the PICU University of Utah (PCMCF Award)	2002-2003
Paul Bryan, MD Fellow Pediatric Emergency Medicine Evaluation of an Early Discharge Protocol for the Febrile Infant	2001-2003
Scholarship Oversight Committee Laurie Pulver, MD Fellow General Pediatrics	2006-2009
Julie Shakib, MD Fellow General Pediatrics	2006-2009

Jeffery Bender, MD
Fellow Pediatric ID 2006-2009

Anne Blaschke, MD
Fellow Pediatric ID 2005-2006

Wyc Cheatam, MD 2005-2006
Fellow Neonatology

Alison Rentz, MD
Fellow Neonatology 2002-2005

Thesis Committee

Dana Seif, MS
Diagnosis of Parechovirus Infections in Children 2009-2010

Audrey Stevenson, MSN, MPH 2006-2007
Barriers to Immunization in an Insured Population
PhD Thesis

Ann Marie Hannon, RN- The Development and Implementation of an HIV Prevention Program for Adolescents in Foster Care
Masters Thesis CPNP-Degree awarded 6/13/97 1996-97

Undergraduate Research
Rachel Korth
HHV-6 Infection in Febrile Infants 1-90 days of age 2003

Maria Arce-Larreta
Impact of a Clinic-Based Literacy Support Program on the Academic Achievement of Children Living in Poverty 2002

David Glover
Serotype Analysis of Invasive Pneumococcal Isolates 2002

Dawn Ngo
Genetic Susceptibility to Pneumococcal Infections 2001

Graduate Research
Heidi Castillo, MD
DFA testing in Hospitalized Children and
The Changing Epidemiology of Bacterial Infections in Infants 2001-2002

Richard Tuohy, MBA Cost-Effectiveness of Rapid Diagnostics in the Evaluation of the Febrile Infant	1999-2000

Resident Research

Rebecca Partridge, MD and Colleen Druzgal, MD DFA testing for Respiratory Viruses Using a Gargle Technique (AAP Resident Research Award)	2004-2006
Allison Keller, MD Adenovirus as a Mimic of Kawasaki Disease	2004-2005
Jasmine Low, MD Comparison of CSF Results from Bactec vs. Conventional Media	2004-2005
Noemi Adame, MD Radiographic Imaging in Pediatric Brain Abscess (IPS AAP Service to Children Award)	2003-2004
Bryan Upham, MD Parainfluenza Infection and the Risk for SBI	2003-2004
Mandy Allison, MD Risk Factors for Anemia in US-Born Children of Foreign-Born Mothers	2002-2003
Joshua Bonkowsky, MD, PhD Metamizole Use by Latino Immigrants	2001-2002
Peter Lindgren, M.D., Pediatrics An Analysis of the Cost and Length of Stay for Latino vs. Non-Latino Febrile Infants	1999
LaShonda Spencer, M.D., Medicine/Pediatrics An Epidemiologic Evaluation of Pulmonary Empyema in Pediatric Patients from Utah (AAP Resident Research Award)	1999-2001
Robin Nemer, M.D., Pediatrics Evaluation of a Developmental Screening Tool in English and Non-English Speaking Patients	1999-2000
Susan Wiet, M.D., Psychiatry Screening Adolescents in Foster Care for Depression and Suicidal Ideation in a Primary Care Setting	1997-1998

Margaret Kluthe, M.D., Pediatrics
Orthotic Bracing for Pectus Carinatum 1997-1999

Medical Student Research
Research Elective
Analysis of the Rochester Criteria in Infants with Confirmed Viral Infection
Sean Biggs, MS III 1999

Analysis of the Rochester Criteria in Infants with Confirmed Viral Infection
Jon Bowman, MS III 1999

PCR for the Identification of Enteroviral Infection in Febrile Infants
Nicole Priest, MS IV 1997

NIH-funded Summer Research
HHV-6 in the Febrile Infant
Mindy McCurry, MS I 2004

Anemia in US-Born Children of Foreign-Born Mothers
Miguel Knochel MS IV 2003

An Evaluation of Compliance with the Rochester Criteria
In a Children's Hospital: Consequences of Variation
Neal Davis, MS I 2000

The Role of HHV-6 in Fever in Infants Under 90 Days
Neal Davis, MS I 2000

An Epidemiologic Evaluation of Pulmonary Empyema
in Pediatric Patients from Utah
Tim Johnson, MS I 1999

Senior Pediatric Honors Research
The Impact of the Sepsis Evaluation on Families
Richard Paxton, MS IV 1998-99

Comparison of Bacterial PCR to Blood Culture
Michelle Burnside, MS IV 1998-99

Analysis of the Rochester Criteria in Infants with Confirmed Viral Infection
Sean Biggs, MS IV 1999-2000

Impact of Respiratory Viral DFA on Patient Management
Heidi Castillo, MS IV 2000-2001

Anemia in US-Born Children of Foreign-Born Mothers
Miguel Knochel MS IV
(National Medical Foundation Award) 2002-2003

Epidemiology of Invasive Pneumococcal Infections in Children
Jasmine Jensen, MS II 2003

An Analysis of Bronchiolitis by Virus Type
Jose Mendoza, MS IV 2004

Normal CSF Values in the Febrile Infant
Jeremy Kendrick, MS IV 2004

Economic Impact of Antibiotic Resistant Infections in Pediatric Settings
Jasmin Jensen MS IV 2005

Group B Streptococcal Infections in the Era of Prophylaxis
Mindy McCurry, MS IV 2006

Courses/ Electives:

Management Essentials for Principal Investigators 2012-
2-year course for all VPCAT and other Career Development Scholars

Team Communication and Collaboration 2011-
Masters of Science in Clinical Investigation
Semester course

Clinical Research Methods and Practice 2009-
Undergraduate Health Science Majors
Semester long course (3 sessions/yr with 30 students per session)

Mentored Program in Pediatric Research 2007-
4th Year Medical Students
Year long course

Graduate Students and Fellows
Case Studies in Research Ethics
Biomedical Sciences Fall 2004
Social and Behavioral Sciences Spring 2005

Primary Care Essentials (12 Primary Care Residents)
Topics: Delivery of Health Care to the Underserved, Cultural Diversity, Alternative Medicine, Foster Care, Antibiotic Use 1996-1998

Freshman Medical Students
Longitudinal Patient in the Community 1997-2002
The Social Aspects of Care in the Community 2003-2005

Sophomore Medical Students
Medical Microbiology: Virology Study Group (13 students)1997

Pediatrics Organ System Course
The Infant and Illness 1999-2005

Third Year Medical Students
Pediatric Core Lectures
Immunizations (q 6 weeks) 1999-2000

Senior Medical Students
Clinical Elective
The Practice of Pediatrics in Underserved Communities.
Ben Stevens MS IV 1996

Resident Supervision:
Continuity Clinic
Pediatric Residents at the University South Main Community Health Center (1995-present) with more than 100 residents trained
Infectious Diseases Inpatient Attending – 12-26 weeks per year (1995-200

X. PUBLICATIONS (0000-0002-7350-9495)

Other Peer- Reviewed Educational Materials:

1) Leyendo Juntos (Reading Together: Spanish Language Literacy Promotion for Primary Care Providers. Glusman, M (Chair) and Aristy, C, Arauz-Boudreau, A, Augustyn, M, Betances, JA, **Byington, CL**, et al. Reach Out and Read. 2009.
2) Management of the Febrile Infant and Child. PREP Audio Issue #70, American Academy of Pediatrics. October 2011.

Other Publications
1) Use of Regional Epidemiologic Data May Help Determine Timing of RSV Immunoprophylaxis. **Carrie L. Byington, MD** and H. Cody Meissner, MD. AAP News 2007. 28:14.
2) CDC updates guidelines on prevention of perinatal GBS. **Carrie L. Byington, MD** and Carol Baker, MD. AAP News December 2010. 31:1

3) Evidence-based guidelines for pediatric CAP offer diagnosis, treatment recommendations. **Carrie L. Byington, MD**. AAP News October 2011. 32:30
4) Be ready to respond to traveler's questions about novel viruses. **Carrie L. Byington, MD**. AAP News. 2013. 34:8
5) Study: Number of antigens in vaccines unrelated to neuropsychological outcomes. **Carrie L. Byington, MD**. AAP News. November 2013: 34:1
6) Ebola and Children: Identifying and meeting the needs. **Carrie L. Byington, MD**. AAP News. 2014.
7) Ebola virus epidemic: global picture and impact on children. H. Dele Davies, MD and **Carrie L. Byington, MD.** AAP News. February 2015.
8) Updated AAP guidance will help you prepare for 2015-16 flu season. Henry H. Berstein, DO and **Carrie L. Byington, MD**. AAP News September 2015.

Original Peer-Reviewed Articles and Policy Statements Published:

196) Lypson, M, Ross, P, **Byington, CL** et al. Learning from the Past and Working in the present to create an anti-racist future for academic medicine. Academic Medicine October 2020.

195) Hobson, WL, Olson, LM, Hopf, HW, Winters, LC, **Byington, CL**. The adjunct faculty are our lifeblood: An institution's response to deliver value to volunteer community faculty. Family Medicine. 2020 (in press).

194) Holsti, M, Keenan, H, Clark, E, Fischer, S, Hawkins, S, Just, S, Lee, J, Napia, E, Taylor, F, Rodriguez, J, White, R, Willie, S, and **Byington CL**. Lessons Learned from the First Decade of the Native American Summer Internship at the University of Utah. Academic Medicine October 2020.

193) Cooper DM, Guay-Woodford L, Blazar BR, Bowman S, **Byington CL**, Dome J, Forthal D, Konstan MW, Kuppermann N, Liem RI, Ochoa ER Jr, Pollock BH, Price OA, Ramsey BW, Ross LF, Sokol RJ, Wright RJ. Re-Opening Schools Safely: The Case for Collaboration, Constructive Disruption of Pre-COVID Expectations, and Creative Solutions. J Pediatrics. 2020 May. S0022-3476.

192) Gladstone RA, Lo SW, Goater R, Yeats C, Taylor B, Hadfield J, Lees JA, Croucher NJ, van Tonder AJ, Bentley LJ, Quah FX, Blaschke AJ, Pershing NL, **Byington CL**, Balaji V, Hryniewicz W, Sigauque B, Ravikumar KL, Almeida SCG, Ochoa TJ, Ho PL, du Plessis M, Ndlangisa KM, Cornick JE, Kwambana-Adams B, Benisty R, Nzenze SA, Madhi SA, Hawkins PA, Pollard AJ, Everett DB, Antonio M, Dagan R, Klugman KP, von Gottberg A, Metcalf BJ, Li Y, Beall BW, McGee L, Breiman RF, Aanensen DM, Bentley SD, The Global Pneumococcal Sequencing Consortium. Visualizing variation within Global Pneumococcal Sequence Clusters (**GPSCs**) and country oopulation snapshots to contextualize pneumococcal isolates. Microb Genom 2020. May 6 (5).

191) Fink, AK, Graff, G, **Byington, CL**, Loeffler, DR, Rosenfeld, M, Saiman, L. Association of Palivizumab and Longitudinal Outcomes in Children with Cystic Fibrosis. *Pediatrics.* **2019**: 144:e20183495.

190) Krah, NM, Bardsley, T, Nelson, R, Esquibel, L, **Byington, CL**, Pavia, AT, Hersh, AL. Economic Burden of Home Antimicrobial Therapy: OPAT vs. Oral Antibiotic Therapy. *Hospital Pediatrics*. **2019**. 9:4: 234-240.

189) Choo, EK, Byington, CL, Jagsi, R, Lubin-Johnson, N. From #MeToo to #TimesUp: the clock has run out on fundamental change in the culture of inequity and harassment in science, medicine, and global health. *Lancet*. **2019.** 393:499-502.

188) Puopolo, KM, Benitz, WE, Zaoutis, TE, Committee on Fetus and Newborn, **Committee on Infectious Diseases**. Management of neonates born at ≤ 34 6/7 weeks' gestation with suspected or proven early-onset bacterial sepsis. *Pediatrics*. **2018**. 142: e e20182896

187) Puopolo, KM, Benitz, WE, Zaoutis, TE, Committee on Fetus and Newborn, **Committee on Infectious Diseases**. Management of neonates born at ≥ 35 0/7 weeks' gestation with suspected or proven early-onset bacterial sepsis. *Pediatrics*. **2018**. 142: e20182894

186) Fairchild, AL, Holyfield, LJ, Byington, CL. National Academies of Science, Engineering, and Medicine Report on Sexual Harassment: Making the Case for Fundamental Institutional Change. *JAMA*. **2018**. 320: 873-74.

185) Adler, FR, Stockmann, C, Ampofo, K, Pavia, AT, **Byington, CL**. Transmission of Rhinoviruses in Utah BIG-LoVE Families: Consequences of Age and Household Structure. PLOS One. 2018. 13: e0199388.

184) **Committee on Infectious Diseases**. Recommended Childhood and Adolescent Immunization Schedule: United States, 2018. *Pediatrics*. **2018**. 141: e20180083

183) Rothwell, E, Botkin, J, Cheek-O'Donnel, S, Wong, B, Case, G, Johnson, E, Matheson, T, Wilson, A, Robinson, NR, Rawlings, J, Horejsi, B, Lopez, AM, **Byington, CL**. Assessing the Impact of a Theatrical Performance on Audience Attitudes and Behavior Intentions toward Research: An Empirical Study of a Reading of Deborah Zoe Laufer's drama *Informed Consent*. *AJOB Empirical Bioethics*. **2018.** 7: 1-23.

182) Blaschke, AJ, Korgenski, EK, Wilkes, J, Presson, AP, Thorrell, EA, Pavia, AT, Knackstedt, ED, Reynolds, C, Shunck, JE, Daly, JA, **Byington, CL**. Rhinovirus detection in well-appearing febrile infants: Risk of concomitant bacterial infection. Pediatrics. **2018**.141: e20172384.

181) Rathore, MH and Jackson, MA, **Committee on Infectious Diseases**. Infection Prevention and Control in Pediatric Ambulatory Settings. Pediatrics. **2017**. 140:e20172857.

180) Davies, HD, Jackson, MA, Rice, SG, **Committee of Infectious Diseases** and Council on Sports Medicine and Fitness. Infectious Diseases Associated with Organized Sports and Outbreak Control. Pediatrics. **2017**: 140: e20172477.

179) O'Leary, ST, Maldonado, YA, **Byington, CL**. Update from the Advisory Committee on Immunization Practices. J Pediatric Infectious Diseases Society. **2017**: 6: 215-18.

178) Kim, L Rha, B, Abramson, JA, Anderson, LJ, **Byington, CL** et al. Identifying Gaps in Respiratory Syncytial Virus Disease Epidemiology in the United States prior to the Introduction of Vaccines. Clinical Infectious Diseases. **2017**: 65: 1020-5.

177) **Committee on Infectious Diseases**. Recommendation for Prevention and Control of Influenza in Children 2017-2018. *Pediatrics*. **2017**: 140: e20172550

176) **Committee on Infectious Diseases** and Committee on Fetus and Newborn. Elimination of Perinatal Hepatitis B: Providing the First Vaccine within 24 Hours of Birth. *Pediatrics*. **2017**. 140:1870.

175) **Byington, CL**, Rothwell, E, Matheson, T, Childs, R, Wachs, E, Rocha, R, Murtaugh, Turok, D, Letsou, Shakib, J, Hess, R, Dere, W. Developing Sustainable Research Career for KL2 Scholars: The Importance of an Inclusive Environment and Mentorship. Journal of *Clinical and Translational Science*. **2017**.

174) Bernstein, HH, Bocchini, JA, Jr. and the **Committee of Infectious Diseases**. Practical Approaches to Optimize Adolescent Immunization. Pediatrics. **2017**. e20164187

173) Bernstein, HH, Bocchini, JA, Jr. and the **Committee of Infectious Diseases**. The Need to Optimize Adolescent Immunization. Pediatrics. **2017**. e20164186

172) Maldonado, YA, Read, J and the **Committee on Infectious Diseases**. Technical Report: Diagnosis, Prevention, and Treatment of Congenital Toxoplasmosis in the United States. *Pediatrics*. **2017** (in press).

171) Stockmann, C, **Byington, CL**, Pavia, AT, Ampofo, K, Wilkes, J, Korgenski, EK, Hersh, AL. Limited and variable use of antivirals for children hospitalized with influenza. *JAMA Pediatrics*. **2017**. Jan 23 (epub ahead of print).

170) Jackson, MA, Schutze, G, and the **Committee on Infectious Diseases**. The use of systemic and topical Fluoroquinolones. **2016**. Pediatrics. 138:5 e20162706.

169) **Committee on Infectious Diseases**. Recommendations for the Prevention and Control of Influenza Infection in Children 2016-2017. **2016**. *Pediatrics*. 138:4 e20162527.

168) Committee on Practice and Ambulatory Medicine, **Committee on Infectious Diseases**, Committee on State Government Affairs, Council on School Health, Section on Administration

Practice and Management. Medical versus Non-Medical Exemptions for Child Care and School Attendance. **2016**. *Pediatrics*; 138: 3 e20162145.

167) Edwards, K, Hackell, J and **Committee on Infectious Diseases.** Countering Vaccine Hesitancy. **2016**. *Pediatrics*. 138: 3 e20162146.

166) Davies, D, **Byington, CL**, and the Committee on Infectious Diseases. Parental Presence during Treatment of Ebola or Other Highly Consequential Infection. **2016**. *Pediatrics*: 138:3 e20161891.

165) **Committee on Infectious Diseases**. Recommendations for Serogroup B Meningococcal Vaccine for Persons 10 Years and Older. **2016**. *Pediatrics*; 138:3 e20161890

164) **Byington, CL** and Munoz, FM. Palivizumab Prophylaxis for Healthy Preterm Infants: More Data Supporting American Academy of Pediatrics Guidelines. 2016. Pediatrics. 138:2. E20161494.

163) H. Dele Davies and the **Committee on Infectious Diseases**. Infectious Complications with Use of Biologic Response Modifiers in Infants and Children. **2016**. *Pediatrics*. 138:2 e20161209.

162) Stockmann, C, Ampofo, K, Pavia, AT, Mason, EO, Presson, AP, Forney, LJ, **Byington, CL**. Clinical and Epidemiological Evidence of the Red Queen Hypothesis in Pneumococcal Serotype Dynamics. *Clinical Infectious Diseases*. **2016**. 63: 5; 619-26.

161) Flygare, S, Simmon, K, Miller, C, Qiao, Y, Kennedy, B, Di Sera, T, Graf, EH, Tardif, KD, Kapusta, A, Rynearson, S, Stockmann, C, Queen, K, Tong, S, Voelkerding, KV, Blaschke, A, **Byington, CL**, Jani, S, Pavia, AT, Ampofo, K, Eilbeck, K, Marth, G, Yandell, M, Schlaberg, R. Taxonemer: an interactive metagenomics analysis portal for universal pathogen detection and host mRNA expression profiling. **2016**. *Genome Biology*. 17 (1) 111.

160) Sawyer, M, Simon, G, **Byington, CL**. Vaccines and Febrile Seizures: Quantifying the Risk. **2016**. *Pediatrics*. 138: 1 e20152360.

159) Shakib, J, Korgenski, K, Presson, AP, Sheng, X, Varner, MW, Pavia, AT, **Byington, CL.** Influenza in Infants Born to Women Vaccinated During Pregnancy. **2016**. *Pediatrics* 137:e2015-2360.

158) Curfman, A, Glissmeyer, EW, Ahmad, FA, Korgenski, K, Blaschke, AJ, **Byington, CL**, Miller, AS. Initial Presentation of Neonatal Herpes Infection. **2016**. *J Pediatrics*. 172: 121-126.

157) Byington, CL, Wright Clayton, E, Edwards, KE. Childhood Vaccine Exemptions—A Broader Perspective is Required. *Pediatrics*. **2016.** 137 (4) e20160189.

156) **Byington, CL** and Maldonado, Y. Rotavirus Vaccines—OK to Mix and Match. *Pediatrics*. **2016** (epub ahead of print Jan 28, 2016). doi: 10.1542/peds.2008-1536

155) Kendall, BA, Dascomb, KK, Mehta, RR, Stockmann, C, Mason, EO, Ampofo, K, Pavia, AT, **Byington, CL**. Early Streptococcus pneumonia serotype changes in Utah adults after the introduction of PCV13 in children. *Vaccine*. *2016*. 34: 474-8.

154) Paulsen, JA, Zaoutis, T, and the **Committee on Infectious Diseases**. Non-therapeutic use of antimicrobial agents in animal agriculture: Implications for pediatrics. *Pediatrics*. **2015**. 136: e 1670-77.

153) **Committee on Infectious Diseases.** Policy Statement: Recommendations for the Prevention and Control of Influenza in Children 2015-2016. **2015**. *Pediatrics*. 136: 4; 792-808.

152) **Committee on Infectious Diseases.** Policy Statement: Influenza Immunization for all Health Care Personnel: Keep if Mandatory. *Pediatrics*. 136: 4 809-818.

151) **Byington, CL**, Lee, V. Addressing Disparities in Academic Medicine: Moving Forward. *JAMA*. 2015. 314: 1139-41.

150) Biondi, E and **Byington, CL**. Evaluation and Management of the Febrile Well Appearing Infant. *Infectious Diseases Clinics of North America*. **2015**. 3: 575-85

149) Stockmann, C, Ampofo, K, Pavia, AT, **Byington, CL**, Sheng, X, Greene, TH, Korgenski, K, Hersh, AL. Comparative Effectiveness of Oral vs. Outpatient Parenteral Antibiotic Therapy for Empyema. **2015**. *J Pediatric Infectious Diseases* 5: 605-12.

148) Davis, CR, Stockmann, C, Pavia, AT, **Byington, CL**, Blaschke, AJ, Hersh, AL, Thorell, EA, Korgenski, K, Daly, J, Ampofo, K. Incidence, Morbidity, and Costs of Human Metapneumovirus Infection in Hospitalized Children. *Journal of the Pediatric Infectious Diseases Society*. **2016**. 5 (3) 303-11.

147) Hester, G, Hersh, AL, Mundorff, M, Korgenski, K, Wilkes, J, Stoddard, G, **Byington, CL**, Srivastava, R. Outcomes following Skin and Soft Tissue Infection in Infants 90 Days Old or Younger. *Hospital Pediatrics*. **2015**. 11: 580-5.

146) **Byington, CL**, Keenan, H, Phillips, J, Childs, R, Wachs, E, Berzins, MA, Clark, K, Torres, MK, Abramson, J, Lee, V, Clark, EB. A Matrix Mentoring Model Effectively Supports Clinical and Translational Scientists and Increases Inclusion in Biomedical Research. *Academic Medicine*. **2016**. 91(4) 497-502.

145) **Byington, CL**, Ampofo, K, Stockmann, C, Adler, F, Herbener, A, Miller, T, Sheng, X, Blaschke, AJ, Crisp, R, Pavia, AT. Community Surveillance of Respiratory Viruses among Families in Utah: Better Identification of Germs: Longitudinal Viral Epidemiology (BIG-LoVE) Study. *Clinical Infectious Diseases*. **2015**. 61(8) 1217-24.

144) **Committee on Infectious Diseases**. Head Lice. *Pediatrics*. **2015**. 135 (5) e1355-65.

143) Stockmann, C, Ampofo, K, Pavia, AT, Byington, CL, Blaschke, AJ, Sherwin, CM, Spigarelli, M, Hersh, AL. National trends in incidence, outcomes, and charges of pediatric osteoarticular infections 1997-2012. **2015**. *Pediatric Infectious Diseases Journal*. 34:672-4.

142) Jain, S, Williams, DJ, Arnold, SR, Ampofo, K, et al for the **CDC EPIC Study Team**. Community-Acquired Pneumonia requiring Hospitalization among US Children. **2015**. *New England Journal of Medicine*. 372: 835-45.

141) Stockmann, C and **Byington, CL**. PCV13 in the US; Early Successes and Potential Challenges. **2015**. *Lancet Infectious Diseases*. 15: 254-6.

140) Ornstein, W and the Committee on Infectious Diseases. Eradicating Polio: How the World's Pediatricians can help stop this Crippling Disease Forever. 2015. Pediatrics. 135; 196-202.

139) **Byington, CL**, Wilkes, J, Korgenski, K, Sheng, X. Respiratory Syncytial Virus Associated Mortality in Hospitalized US Infants and Young Children. **2015**. *Pediatrics*. 135: e24-31.

138) Holsti, M, Hawkins, S, Bloom, K, White, R, Clark, EB, **Byington, CL**. Increasing the Diversity of the Biomedical Workforce through Community Engagement: The University of Utah Native American Summer Research Internship. *Clinical and Translational Science*. **2015**. 8 (2) 87-90.

137) Starke, JR, **Committee on Infectious Diseases**. Interferon-γ Release Assays for Diagnosis of Tuberculosis Infection and Disease in Children. 2014. Pediatrics. 134; e1763-1773.

136) **Committee on Infectious Diseases.** Immunization for Streptococcus pneumoniae Infection in High-Risk Children**. 2014.** *Pediatrics.* 134: 1230-3**.**

135) **Committee on Infectious Diseases**. Recommendations on the Prevention and Control of Influenza 2014-2015. **2014**. *Pediatrics*. 13: 1503-19.

134) **Committee on Infectious Diseases**. Updated Recommendations on the use of Meningococcal Vaccines. **2014**. *Pediatric*s; 134: 400-403.

133) **Byington, CL**. Can Transparency Increase Confidence and Reduce Hesitancy? **2014**. *Pediatrics* 134: 377-9.

132) **Committee on Infectious Diseases**. Updated guidance for palivizumab prophylaxis among infants and young children at increased risk of hospitalization for respiratory syncytial virus infection. **2014**. *Pediatrics*: 134: e620-38.

131) Stockmann, C, Pavia, AT, Hersh, A, Spigarelli, M, Castle, B, Korgenski, K,

Byington, CL, Ampofo, K. Age Specific Patterns of Influenza Activity in Utah: Do Older School Children Drive the Epidemic? *J Pediatric Infectious Diseases*. **2014**. 3: 163-67.

130) Blaschke, AJ; Shapiro, D; Pavia, AT; **Byington, CL**; Ampofo, K; Stockmann, C; Hersh, A. A National Study of the Impact of Rapid Influenza Testing on Clinical Care in the Emergency Department. 2014. *JPIDS*. 3: 112-118.

129) Glissmeyer, EW, Korgenski, EK, Wilkes, J, Schunk, J, Sheng, X, Blaschke, AJ, Byington, CL. Dipstick screening for urinary tract infections in febrile infants. **2014**. *Pediatrics*; 133: 1121-7.

128) Bradley, JS, Peacock, G, Krug, SE, Bower, WA, Cohen, AC, Meaney-Delman, D, Pavia, AT, **Committee on Infectious Diseases**. Pediatric Anthrax Clinical Management. 2014. Pediatrics: 133: e1411-36.

127) Committee on Infectious Diseases. Recommended Childhood and Adolescent Immunization Schedule-United States 2014. **2014**. *Pediatrics*. 133: 357-63.

126) **Committee on Infectious Diseases.** Recommendations for Prevention and Control of Influenza in Children 2013-2014. **2014**. *Pediatrics.* 134: e1503-19.

125) Committee on Infectious Diseases and Committee on Nutrition. Consumption of Raw or Unpasteurized Milk and Milk Products by Pregnant Women and Children. **2014**. *Pediatrics*. 133: 175-9.

124) **Byington, CL**, Higgins, S, Kaskel, FJ, Purucker, M, Davis, JM, Smoyer, WE. The CTSA Mentored Career Development Program: Supporting the Careers of Child Health Investigators. **2013**. *Clinical and Translational Science*. 7: 44-7.

123) Feikin, D, Kagucia, EW, Loo, JD, Link-Gelles, R, Puhan, MA, Cherian, T, Levine, OS, Whitney, CG, O'Brien, KL, Moore, MR, Adegbola, RA, Agocs, M, Ampofo, K, Andrews, N, Barton, T, Benito, J, Broome, CV, Bruce, MG, Bulko, LR, **Byington, CL**. et al. Serotype-specific Changes in Invasive Pneumococcal Disease after Pneumococcal Conjugate Vaccine Introduction: A Pooled Analysis of Multiple Surveillance Sites. **2013.** *PLOS Medicine.* 10: e1001517.

122) Shakib, J, Korgenski, K, Sheng, X, **Byington. CL**. Pertussis Immunization during Pregnancy. **2013**. *J Pediatrics*.

121) Stockmann, C, Ampofo, K, **Byington, CL**, Filloux, F, Hersh, A, Blaschke, AJ, Cowan, P, Korgenski, K, Mason, EO, Pavia, AT. Pneumococcal Meningitis in Children; Epidemiology, Serotypes, and Outcomes 1997-2010 in Utah. **2013**. *Pediatrics*.

120) Demissie, DE, Kaplan, SL, Romero, JR, Leake, JAD, Barson, WJ, Halasa, NB, **Byington CL**, Avinash, KS, Tan, TQ, Hoffman, JA, Lin, PL, Edwards, KE, Mason, EO, Cooperstock, MS. Altered Neutrophil Counts at Diagnosis of Invasive Meningococcal Infection in Children. **2013**. *PIDJ*.

119) Stockmann, C, Sherwin, C, Ampofo, K, Hersh AL, Pavia, AT, **Byington, CL**, Ward, RM, Spigarelli, MG. Characteristics of Antimicrobial Studies Registered in the United States through ClinicalTrials.gov. *International J of Antimicrobial Agents*. **2013**.

118) Stockman, C, Ampofo, K, Filloux, F, Hersh, AL, **Byington, CL,** Pavia, AT. Pneumococcal Meningitis in Children: Epidemiology, Serotypes and Sequelae in Utah 1996-2010. *Pediatrics*. **2013**. (in press)

117) Olarte, L, Ampofo, K, Stockmann, C, Mason, EO, Pavia, AT, **Byington, CL**. Invasive Pneumococcal Disease in Infants 1-90 DaysBefore and After Introduction of the Pneumococcal Conjugate Vaccine. *Pediatrics*. **2013**.

116) **Committee on Infectious Diseases**. Recommended Childhood and Adolescent Immunization Schedule—United States 2013. *Pediatrics*. **2013**. 131:397-398.

115) Alexxan, SS, **Byington, CL**. Finklestein, JI, Tarini, BA. Blindness in Walnut Grove: How did Mary Ingalls Lose Her Sight. *Pediatrics*. **2013**. 131:404-6.

114) Schutze, GE, Willoughby, R, and the **Committee on Infectious Diseases**. Clostridium dificile infections in Infants and Children. *Pediatrics*. January **2013**: 196-200.

113) Doby, EJ, Stockmann, C, Korgenski, K, Blaschke, AJ, and **Byington, CL**. Cerebrospinal Fluid Pleocytosis in Febrile Infants 1-90 Days: Can the Cause be Identified? **2013**. PIDJ (April 11 epub ahead of print)

111) Kimberlin, D, Bally, J and the **Committee on Infectious Diseases** and the Committee on Fetus and Newborn. Guidance on the Management of Asymptomatic Neonates Born to Women with Active Genital Herpes Lesions. *Pediatrics* **2013**. 131: 383-386.

110) Holsti, M, Adelgais, KM, Willis, L, Jacobsen, K, Clark, EB, **Byington, CL**. Developing Future Clinician Scientists while Supporting a Research Infrastructure. *Clinical Translational Science*. 2013. 6: 94-97.

109) Blaschke AJ, **Byington CL,** Ampofo K, Pavia AT, Heyrend C, Rankin SC, McGowan KL, Harris MC, Shah SS. Species-specific PCR improves detection of bacterial

pathogens in parapneumonic empyema compared to 16S PCR and conventional culture. *Pediatric Infectious Disease Journal* **2013**. 32:302-303.

108) Stockman, C, Ampofo, K, Hersh, A, Blaschke, AJ, Bennett, T, Korgenski, K, Andrews, S, **Byington, CL**, Pavia, AT. Local Health Department Influenza Surveillance Estimates and Projections of Peak Pediatric Intensive Care Unit Occupancy during the 2009 H1N1 Influenza Pandemic. *JPIDS*. **2013**. 2: 405-6.

107) Stockmann, C, Ampofo, A, Hersh, A, Carleton, ST, Korgenski, K, Sheng, X, Pavia, AT, Byington, C. Seasonality of Acute Otitis Media and the Role of Respiratory Viral Activity in Children. *Pediatric Infectious Disease Journal*. **2013**. 2: 314-19.

106) **Committee on Infectious Diseases**. Recommendations for Prevention and Control of Influenza Infection in Children 2012-2013. **2012**. *Pediatrics*. 130: 780-92.

105) Allexan, SS, **Byington, CL**, Finklestein, JI, Tarini, BA. Blindness in Walnut Grove: How did Mary Ingalls lose her sight? **2013**. *Pediatrics*. 131: 404-6.

104) Blaschke, AJ, Heyrend, C, **Byington, CL**, Fisher, MA, Barker, E, Garrone, NF, Thatcher, SA, Pavia, AT, Barney, T, Alger, GD, Daly, JA, Ririe, KM, Ota, I, Poritz, MA. Rapid Identification of Pathogens from Positive Blood Culture by Multiplex PCR using the FilmArray System. **2012.** *Diagnostic Microbiology and Infectious Diseases.*

103) **Byington, CL**, Savitz, L, Varner, M, McClain, D. The Utah Center for Clinical and Translational Science: Transformation through Collaboration. 2012. *Clinical and Translational Science*. 5: 377-78.

102) Polin, RA, Denson, S, Brady, MT, Committee on Fetus and Newborn, **Committee on Infectious Diseases**. Strategies for Prevention of Health Care Associated Infections in the NICU. 2012. *Pediatrics*. 129: E1085-93.

101) Polin, RA, Denson, S, Brady, MT, Committee on Fetus and Newborn, **Committee on Infectious Diseases**. Epidemiology and Diagnosis of Health Care Associated Infections in the NICU. 2012. Pediatrics. 129:E1104-1109.

100) **Committee on Infectious Diseases.** HPV Vaccine Recommendations. 2012. Pediatrics; 129:602-5.

99) Herrera Guerra, A, Stockman, C, Pavia, AT, Hersh, AL, Thorell, EA, Weng, HY, Korgenski, K, **Byington, CL**, Ampofo, A. Laboratory-Confirmed Rotavirus Disease in Utah Children: Clinical and Economic Impact of Rotavirus Vaccination. **2012**. *J Pediatric Infectious Diseases*. 1: 268-77.

98) **Byington, CL**, Reynolds, CC, Korgenski, K, Sheng, X, Valentine, KJ, Nelson, RE, Daly JA, Osguthorpe, RJ, James, B, Savitz, L, Pavia, AT, Clark, EB. Costs and Infant Outcomes After Implementation of a Care Process Model for Febrile Infants. *Pediatrics*. **2012**.130:E16-24

97) Diener, M, Hobson-Rohrer, W, and **Byington, CL**. Kindergarten Readiness and Performance of Latino Children Participating in Reach Out and Read. *Journal of Community Medicine and Health Education*. **2012;** 2:133.

96) Stockman, C, Ampofo, K, Hersh, AL, Blaschke, AJ, Kendall, BA, Korgenski, K, Daly, J, Hill, HR, **Byington, CL**, Pavia, AT. Evolving Epidemiology of Invasive Group A Streptococcal Disease in Utah 2002-2010. *Clinical Infectious Diseases*. **2012**. 55: 479-87.

95) Lessin, HR, Edwards, KM, Committee on Practice and Ambulatory Medicine, **Committee on Infectious Diseases.** Immunizing Parents and Other Close Family Contacts in the Pediatric Office Setting. *Pediatrics*. 2012. 129: e247-53.

94) **Committee on Infectious Diseases.** Meningococcal conjugate vaccine policy update: booster dose recommendations. *Pediatrics*. **2011**. 128: 1213-18.

93) Frenck R Jr, Thompson A, Yeh SH, London A, Sidhu MS, Patterson S, Gruber WC, Emini EA, Scott DA, Gurtman A; 3011 Study Group. Immunogenicity and safety of 13-valent pneumococcal conjugate vaccine in children previously immunized with 7-valent vaccine. *PIDJ*. **2011**. 30:1086-91.

92) Ampofo, K, Pavia, AT, Stockman, C, Hersh, A, Bender, JM, Blaschke, AJ, Weng, HYC, Korgenski, K, Daly, J, Mason, EO, **Byington, CL**. The Changing Epidemiology of Invasive Pneumococcal Disease at a Tertiary Children's Hospital through the PCV-7 Era: A Case for Continuous Surveillance. **2012**. *PIDJ*. 31: 228-34.

91) **American Academy of Pediatrics, Committee on Infectious Diseases**. Prevention of Varicella: Update of Recommendations for use of Quadrivalent and Monovalent Varicella Vaccines in Children. **2011**. *Pediatrics*. 128: 630-2.

90) Kendall, BA, Dascomb, KK, Mehta, RR, Mason, EO, Pombo, DJ, Pavia, AT, **Byington, CL**. *Streptococcus pneumoniae* serotypes in Utah Adults with Invasive Pneumococcal Disease at the end of the PCV7 Era. *Vaccine* **2011**. 29:9123-26.

89) Poritz, M, Blaschke, AJ, **Byington, CL**, Myers, L, Nilsson, C, Jones, DE, Thatcher, SA, Robbins, T, Lingenfelter, B, Amiott, E, Herbener, A, Daly, J, Dobrowolski, S, Teng, DH, Ririe, KM. FilmArray, an automated, nested multiplex pcr

diagnostic system for multi-pathogen detection: Development and application to respiratory tract infection. *PLoS One* **2011**. 6: e26047.

88) Blaschke, A, Allison, M, Meyers. L, Rogatcheva, M, Heyrend, C, Mallin, Carter, M, LaFleur, B, Barney, T, Poritz, MA, Daly, J, **Byington, CL.** Non-Invasive Sample Collection for Respiratory Virus Testing by Multiplex PCR. **2011**. *J Clinical Virology*.52: 210-4.

87) **American Academy of Pediatrics, Committee on Infectious Diseases.** Recommendations for prevention and control of influenza in children 2011-2012. *Pediatrics* **2011**. 128:813-25.

86) **American Academy of Pediatrics, Committee on Infectious Diseases.** Updated recommendations for poliovirus vaccine. *Pediatrics* **2011.** 128:805-8.

85) **American Academy of Pediatrics, Committee on Infectious Diseases.** The use of systemic fluoroquinolones. *Pediatrics* **2011**.128: e1034-45.

84) **American Academy of Pediatrics, Committee on Infectious Diseases.** Recommendations for Tdap Vaccine. *Pediatrics* **2011**. 128:809-12.

83) Ampofo, K, Pavia, AT, Bender, JM, Blaschke, AJ, Weng, C, Korgenski, EK, Daly, J, Mason, EO, **Byington, CL.** Evolution of the Epidemiology of Invasive Pneumococcal Disease Among Utah Children through the PCV7 Era. *PIDJ* **2011**. 30:1100-3.

82) **American Academy of Pediatrics, Committee on Infectious Diseases.** Updated Recommendations for Hepatitis A Vaccine to Households and Other Close Contacts of Arriving International Adoptees. **2011**. *Pediatrics* 128:813-25.

81) Bradley, J, Byington, CL, Shah SS, Alverson, B, Carter, ER, Harrison, C, Kaplan, SL, Mace, S, McCracken, G, Moore, M, St. Peter, S, Stockwell, J, Swanson, JT. Executive Summary-The Management of Community-Acquired Pneumonia (CAP) in Infants and Children Older than 3 Months: Clinical Practice Guidelines by the Pediatric Infectious Diseases Society (PIDS) and the Infectious Diseases Society of America (IDSA). **2011**. *Clinical Infectious Diseases*. 53: 7:617-30.

80) Bradley, JS, **Byington, CL***, Shah, SS, Alverson, B, Carter, ER, Harrison, C, Kaplan, SL, Mace, S, McCracken, G, Moore, M, St. Peter, S, Stockwell, J, Swanson, JT. The Management of Community-Acquired Pneumonia (CAP) in Infants and Children Older than 3 Months: Clinical Practice Guidelines by the Pediatric Infectious Diseases Society (PIDS) and the Infectious Diseases Society of America (IDSA). **2011**. *Clinical Infectious Diseases*. 53: 7:e25-76. ***multiple first author**

79) Javeri, R, **Byington, CL**, Klein, J, Shapiro, E. Management of the Acutely Febrile Infant and Young Child: A 21st Century Approach. **2011**. *J Pediatrics*. 159: 181-185.

78) **American Academy of Pediatrics, Committee on Infectious Diseases.** Policy Statement-Recommended Childhood and Adolescent Immunization Schedules-United States, 2011. **2011**. *Pediatrics*. 127: 387-8.

77) **American Academy of Pediatrics, Committee on Infectious Diseases**. Additional Recommendations for use of Tetanus Toxoid, Reduced Content Diphtheria Toxoid, and Acellular Pertussis Vaccine (Tdap). 2011. *Pediatrics*. 128: 809-12.

76) **American Academy of Pediatrics, Committee on Infectious Disease**. Rabies Prevention Policy Update: New Reduced Dose Schedule. **2011**. *Pediatrics*. 127:785-787.

75) Baker, C and **Byington, CL** and American Academy of Pediatrics, Committee on Infectious Disease and Committee on Fetus and Newborn. Recommendation for the Prevention of Perinatal Group B Streptococcal Disease. **2011**. *Pediatrics*.

74) Leecaster, M, Gesteland, P, Greene, T, Walton, N, Gundlapalli, A, Rolfs, R, **Byington, CL**, Samore, M. Modeling the Variation in Pediatric Respiratory Syncytial Virus Outbreaks. *BMC Infectious Diseases*. **2011**.11:105.

73) Blaschke, A, Heyrend, **C, Byington**, CL, Obando, I, Vasquez-Barba, I, Doby, E, Korgenski, EK, Sheng, X, Poritz, MA, Daly, JA, Mason, EO, Pavia, AT, Ampofo, K. Molecular Analysis Improves Pathogen Identification and Epidemiologic Study of Pediatric Parapneumonic Empyema. *PIDJ*. 2011.

72) Staes, C, Wuthrich A, Gesteland, P, Allison, M, Leecaster, M, Shakib, J, Carter, M, Mallin, B, Mottice, S, Rolfs, R, Pavia, AT, Wallace, B, Risk, I, Gundlapalli, A, Samore, M, **Byington, CL**. Public health communication with frontline clinicians during the first wave of the 2009 pandemic influenza outbreak. **2011**. *Journal of Public Health Manangement and Practice*. 17:36-44.

71) **Byington, CL**, Kendrick, J, Sheng, X. Normative Cerebrospinal Fluid Profiles in Febrile Infants. **2011**. *J Peds*. 158:33-37.

70) **American Academy of Pediatrics, Committee on Infectious Diseases**. Policy Statement-recommendations for prevention and control of influenza in children, 2010-2011. **2010**. *Pediatrics*. 126: 816-26.

69) Bernstein, HH, Starke, JR, **American Academy of Pediatrics Committee on Infectious Diseases**. Policy Statement- recommendation for mandatory influenza for all healthcare personnel. **2010**. *Pediatrics*. 126: 809-15.

68) Frankowski BL, Bocchini JA Jr; Council on School Health and **Committee on Infectious Diseases.** Head Lice. **2010**. *Pediatrics*. 126: 392-403.

67) Rubin, LG, Papsin, B, and the **Committee on Infectious Diseases** and Section on Otolaryngology (AAP). Pediatrics. Cochlear Implants in Children: surgical site infections and prevention and treatment of acute otitis media and meningitis. **2010.** *Pediatrics*. 126:381-391.

66) **American Academy of Pediatrics, Committee on Infectious Diseases**. Recommendations for the prevention of *Streptococcus pneumoniae* infections in children: use of the 13-valent pneumococcal conjugate vaccine (PCV13) and pneumococcal polysaccheride vaccine (PPSV23). **2010**. *Pediatrics*. 126: 186-90.

65) Allison, MA, Guest-Warnick, G, Nelson, D, Pavia, AT, Srivastava, R, Gesteland, P, Rolfs, RT, Anderson, S, Calame, L, Young, PC, **Byington, CL**. Feasability of Elementary School Children's Use of Hand Gel and Face Masks During Influenza Season. **2010**. *Influenza and Other Respiratory Viruses*. 44:223-9.

64) Bender, J, Ampofo, K, **Byington, CL**, Grinsell, M, Korgenski, K, Daly, JA, Mason, EO, Pavia, AT. Epidemiology of *Streptococcus pneumoniae* induced Hemolytic Uremic Syndrome in Utah Children. **2010.** *PIDJ* . 29: 712-16.

63) Ampofo, K, Herbener, A, Blaschke, AJ, Heyrend, C, Poritz, P, Korgenski, K, Rolfs, R, Jain, S, Carvahlo, M, Pimenta, FC, Daly, J, Mason, EO, **Byington, CL**, Pavia, AT. Association of 2009 Pandemic Influenza A (H1N1) Infection and Increased Hospitalization with Parapneumonic Empyema in Children in Utah. **2010**. *PIDJ*. 29: 905-909.

62) Allison, M, Reyes, M, Young, PC, Calame, L, Sheng, X, Weng, HC, **Byington, CL**. Parental Attitudes about School Based Immunization. **2010**. *PIDJ* . 29: 751-755.

61) Policy statement--Recommended childhood and adolescent immunization schedules--United States, 2010. Committee on Infectious Diseases. Pediatrics. **2010** Jan;125(1):195-6.

60) Blaschke, AJ, Pulver, LS, Korgenski, EK, Savitz, LA, Daly, JA, **Byington, CL.** Clindamycin-Resistant Group B *Streptococcus* and Failure of Intrapartum Prophylaxis to Prevent Early Onset Disease**. 2010**. *J Peds*. 156: 501-503.

59) **Byington, CL,** Hulten, K, Ampofo, K, Sheng, X, Pavia, AT, Pettigrew, M, Korgenski, K, Daly, J, Mason, EO. Molecular Epidemiology of Pediatric Empyema in Utah 2001-2007. **2010**. *J Clin Micro*. 48: 520-525.

58) Shakib, J, Ralston, S, Raissey, HH, Stoddard, GJ, Edwards, KE, **Byington, CL**. Pertussis Antibodies in Post-partum Women and Their Newborns. **2010**. *J Perinatology*. 30: 93-97.

57) Bender, J, Ampofo, K, Korgenski, K, Daly, J, Pavia, AT, **Byington, CL.** Influenza infection in Infants 1-90 Days. **2010**. *Pediatric Infectious Disease Journal*. 29: 6-9.

56) **American Academy of Pediatrics, Committee on Infectious Diseases**. Policy statement- modified recommendations for use of Palivizumab for prevention of respiratory syncytial virus infections. **2009**. *Pediatrics*. 124: 1694-1701.

55) **American Academy of Pediatrics, Committee on Infectious Diseases.** Policy statement--recommendations for the prevention and treatment of influenza in children, 2009 -2010. Committee on Infectious Diseases. *Pediatrics*. 2009 Oct;124(4):1216-26.

54) Rogan, WJ, Brady, MT, Committee on Environmental Health; **Committee on Infectious Diseases.** Drinking water from private wells and risks to children. 2009. Pediatrics. 123:e1072-1077.

53) Committee on Environmental Health; **Committee on Infectious Diseases**, Rogan WJ, Brady MT. Drinking water from private wells and risks to children. *Pediatrics*. **2009** Jun;123(6):1599-605.

52) The American Academy of Pediatrics Committee on Infectious Diseases. Prevention of Rotavirus Disease: Updated Guidelines for the Use of Rotavirus Vaccine. **2009**. *Pediatrics*. 123: 1412-20.

51) Staes, CJ, Gesteland, P, Allison, M, Mottice, S, Shakib, J, Rubin, M, Boulton, R, Wuthrich, A, Carter, M, Samore, M, **Byington, CL**. Urgent Care Physician's Knowledge and Attitude about Public Health Reporting and Pertussis Control Measures: Implications for Decision Support. **2009**. *Journal of Public Health Management and Practice*. Focus Issue: Child Health Information Systems; 15: 471-478.

50) Shakib, JH, Wyman, L., Gesteland, PH, Bennion, DW, **Byington, CL**. Should the pertussis definition for public health reporting be refined? **2009**. *Journal of Public Health Management and Practice*. Focus Issue: Child Health Information Systems; 15: 479-484.

49) Pulver, L, Guest-Warnick, G, Stoddard, G, **Byington, CL**, Yong, PC. Weight for Gestational Age Affects the Mortality of Late Preterm Infants. **2009.** *Pediatrics*. 123: e1072-1077.

48) Blaschke, A, Korgenski, K, Daly, J, Pavia, AT, **Byington, CL**. Emergence of Extended-Spectrum b-Lactamase Producing Pathogens in a Children's Hospital: Rates, Incidence and Factors Associated with Infection or Colonization. **2009**. *American Journal of Infection Control*.

47) Bender, J, Ampofo, K, Gesteland, P, Stoddard, GJ, **Byington, CL**, Pavia, AT, Srivastava, R. Development and Validation of a Risk Score for Predicting Hospitalization in Children with Influenza Virus Infection. **2009**. *Pediatric Emergency Care*.

46) The American Academy of Pediatrics Committee on Infectious Diseases. Recommended Childhood and Adolescent Immunization Schedule-United States 2009. **2009**. **Pediatrics**. 123: 189-90.

45) Bender, J, Ampofo, K, Sheng, X., Pavia, AT, Cannon-Albright, L, **Byington, CL**. Analysis of a Century of Parapneumonic Empyema Deaths in Utah: Implications for Influenza Pandemic Preparedness. **2009**. *Emerging Infectious Diseases.* 15: 44-48

44) Pickering, LM, Marano, N, Bocchini, JA, Angulo, F and the **Committee on Infectious Diseases**. Exposure to nontraditional pets at home and to animals in public settings. **2008**. *Pediatrics.* 122: 876-886.

43) American Academy of Pediatrics Committee on Infectious Diseases. Prevention of Influenza: Recommendations fro influenza immunization of children, 2008-2009. **2008**. *Pediatrics.* 122: 1135-41.

42) Pulver, LS, McCurry, M, Young, PC, Stoddard, G, **Byington, CL**. Causes of Continued Early Onset Group B Streptococcal Infections in the Era of Intrapartum Antibiotic Prophylaxis. **2008**. *J Perinatology.* 29: 20-25.

41) Gesteland, PH, Allison, M, Staes, CJ, Samore, MH, Rubin, MA, Carter, ME, Wuthrich, A, Kinney, AY, Mottice, S, **Byington, CL**. Clinician Use and Acceptance of Population-Based Data about Respiratory Pathogens: Implications for Enhancing Population-Based Clinical Practice. **2008**. *JAMIA*.

40) Ampofo, K, Bender, J, Sheng, X, Korgenski, K, Daly, J, Pavia, AT, **Byington, CL**. Seasonal Invasive Pneumococcal Disease in Children: The Role of Preceding Viral Infection. **2008**. *Pediatrics.* 122: 229-237.

39) Byington, CL, Hobson, WL, Torres, G, Winter, K, Ortiz, K, Buchi, KF. The Good Habit of Reading (El Buen Habito de la Lectura): Parental Reactions to an Enhanced Reach Out and Read Program in a Clinic for the Underserved. **2008**. *The Journal of Health Care for the Poor and Underserved*. 19: 363-368.

38) Bender, J, Ampofo, K, Korgenski, K, Daly, J, Pavia, AT, Mason, EO, **Byington, CL**. Pneumococcal Necrotizing Pneumonia: Does Serotype Matter? **2008.** Clin Infect Dis J 46: 1346-52.

37) American Academy of Pediatrics Committee on Infectious Diseases. Prevention of influenza: recommendations for influenza immunization of children, 2007-2008. **2008**. Pediatrics. 121:e1016-31.

36) Haddad, M, Porucznik, CA, Joyce, KE, De, AK, Pavia, AT, Rolfs, RT, **Byington, CL**. Risk Factors for Pediatric Invasive Pneumococcal Disease in the Intermountain West, 1996-2002. **2008**. *Annals of Epidemiology*. 18: 139-146.

35) Gesteland, PH, Samore, MH, Pavia, AT, Srivastava, R, Korgenski, K, Gerber, K, Daly, JA, Mundorff, M, Rolfs, RT, James, BC, **Byington, CL**. Informing the Front Line about Common Respiratory Viral Epidemics. **2007**. Annual American Medical Informatics Association Symposium Proceedings. 2007: 274-278.

34) Boulton, RB, Alder, SC, Mottice, S, Catinella, AP, **Byington, CL**. The Epidemiology of Invasive Meningococcal Disease in Utah: 1995-2005. **2007**. *Emerging Infectious Diseases* . 13: 1225-1227.

33) Blaschke, A, Bender, J, **Byington, CL**, Korgenski, K, Daly, J, Petti, CA, Pavia, A, Ampofo, K. Gordonia species: Emerging Pathogens in Pediatric Patients Identified by 16S rRNA Gene Sequencing. **2007**. *Clinical Infectious Diseases*. 45: 483-486.

32) Glasgow, TS, Speakman, M, Firth, S, James, B, **Byington, CL**, Young, PC. Outcomes for Term Infants in the Era of Increasing Peripartum Antibiotic Use. *Paediatric and Perinatal Epidemiology*. **2007**. 21: 338-346.

31) Hobson, W, Knochel, ML, **Byington, CL**, Young, PC, Hoff, CJ, Buchi, KF. Prevalence of Bottled, Filtered, and Tap Water Use in Latino and Non-Latino Children. *Archives of Pediatrics and Adolescent Medicine*. **2007**. 161: 457-61.

30) Rentz, AC, Taggart, EW, Stevenson, J, Hymas, W, Hillyard, D, **Byington, CL**. Human Herpesvirus 6 Infection in the Newborn Intensive Care Unit. *European Journal of Clinical Microbiology and Infectious Diseases.***2007.** 26: 297-299.

29) Ampofo, K**,** Gesteland, P, Bender, J, Mills, M, Daly, J, Samore, M, **Byington, CL**, Pavia, AT, Srivastava, R. Epidemiology, Complications, and Cost of Hospitalization in Children with Laboratory-Confirmed Influenza. *Pediatrics*. **2006**. 118: 2409-2417.

28) Kaplan, SL, Schutze, GE, Leake, J, Barson, WJ, Halaasa, NB, **Byington, CL**, Woods, CR, Tan, TQ, Hoffman, JA, Wald, ER, Edwards, KM, Mason, EO.

Multicenter Surveillance of Meningococcal Infections in children . *Pediatrics*. **2006**. 118: e979-984.

27) Harlan, G, Tani, L, **Byington, CL.** Monoarticular arthritis presenting as rheumatic fever. *Pediatric Infectious Diseases Journal*. **2006.** 25: 743-746.

26) Byington, CL, Korgenski, K, Daly, J, Ampofo, K, Pavia, A, Mason, EO. Pediatric Pneumococcal Parapneumonic Empyema: Impact of the Pneumococcal Conjugate Vaccine. *Pediatric Infectious Diseases Journal*. **2006.** 25: 250-254.

25) Rentz, AC, Libbey, JE, Fujinami, RS, Whitby, FG, **Byington, CL**. Investigation of Treatment Failure in Neonatal Echovirus 7 Infection. *Pediatric Infectious Disease Journal*. **2006.** 25: 259-62.

24) Adame, N, Hedlund, G, **Byington, CL**. Diagnosis of Sinogenic Intracranial Empyema in Children. *Pediatrics*. **2005.** 116: e461-467.

23) Glasgow, T, Young, PC, **Byington, CL**. The Impact of Intrapartum Antibiotics on Late Onset Sepsis in Infants 1-90 Days of Age. *Pediatrics.* **2005**. 116:696-702.

22) Byington, CL, Samore, MH, Stoddard, GJ, Barlow, S, Daly, J, Korgenski, K, Glover, D, Jensen, J, Shutt, C, Mason, EO, Pavia, AT. Temporal Trends for Invasive Disease due to Streptococcus pneumoniae in Children in the Intermountain West: Emergence of Non-Vaccine Serogroups. *Clinical Infectious Diseases*. **2005**. 41: 21-29.

21) Rittichier, KK, Bassett, KE, Bryan, PA, Taggart, EW, Hillyard, DR, **Byington, CL**. Diagnosis and Outcomes of Enterovirus Infections in Young Infants. *Pediatric Infectious Diseases Journal.* **2005.** 24: 546-550.

20) Rentz, A, Samore, M, Stoddard, G, Faix, R, **Byington, CL**. Early Onset Infection in Neonates in the Age of Group B Streptococcus Prophylaxis: Risk Factors For Antibiotic Resistant Infection. *Archives of Pediatrics and Adolescent Medicine*. **2004**. 158: 556-560.

19) Byington, CL, Enriquez, FR**,** Hoff, C, Tuohy, R, Taggart, EW, Hillyard, DR, Carroll, K, Christenson, JC. Serious bacterial Infection in Febrile Infants 1- 90 Days With and Without Viral Infections. *Pediatrics* **2004**: 113: 1662-1666.

18) Rocholl, C, Gerber, K, Daly, J, Pavia, AT, **Byington, CL**. Adenoviral Infections in Children: The Impact of Rapid Diagnosis. *Pediatrics*. **2004.** 113: e51-56.

17) Deiner, M, Wright, C, Julian, J, **Byington, CL**. Home Literacy Experiences Among Low Socioeconomic, Culturally Diverse Families: A Pediatric Literacy Intervention Program. *J Research in Childhood Educaton*. **2003**. 18: 148-158.

16) Byington, CL, Rittichier, KK, Bassett, KE, Castillo, H, Glasgow, TS, Daly, J, Pavia, AT. Serious Bacterial Infection in Febrile Infants Younger Than 90 Days of Age: The Importance of Ampicillin-Resistant Pathogens. *Pediatrics*. **2003**. 111: 964-968.

15) Byington, CL, Castillo, H, Gerber, K, Daly, J, Christenson, JC, Pavia, AT. The Impact of Rapid Viral Diagnostic Testing on Antibiotic Use in a Children's Hospital. *Archives of Pediatrics and Adolescent Medicine*. **2002.** 156: 1230-34.

14) Byington, CL, Zerr, DM, Taggart, EW, Long, N, Hillyard, D, Carroll, K, Corey, L. Human Herpesvirus-6 Infection in Febrile Infants 90 Days and Younger. *Pediatric Infectious Diseases Journal*. **2002.** 21: 996-99.

13) Taggart, EW, Carroll, KC, **Byington, CL**, Crist, GA, Hillyard, DR. Use of Heat Labile UNG in an RT-PCR Assay for Enterovirus Detection. *J of Virologic Methods* **2002**. 105: 57-65.

12) Bonkowsky, JL, Frazer, JK, Buchi, KF, **Byington, CL**. Metamizole Use by Latino Immigrants: A Common and Potentially Harmful Home Remedy. *Pediatrics* **2002.** 109: e98

11) Byington, CL, Spencer, LY, Johnson, TA, Pavia, AT, Allen, D, Mason, EO, Kaplan, SL, Carroll, KC, Daly, JA, Christenson, JC, Samore, MH. An Epidemiologic Investigation of a Sustained High Rate of Pediatric Parapneumonic Empyema: Risk Factors and Microbiologic Association. *Clinical Infectious Diseases* **2002.** 34: 434-40.

10) Paxton, R and **Byington, CL**. An Examination of the Unintended Consequences of the Rule Out Sepsis Evaluation: A Parental Perspective. *Clinical Pediatrics.* **2001.** 40: 71-77.

9) Adderson, EE, **Byington, CL**, Spencer, L, Kimball, A, Hindiyeh, M, Carroll, K, Mottice, S, Korgenski,K, Christenson, JC, Pavia, AT. Emergence of invasive serotype a *Haemophilus influenzae* infections with a virulence genotype resembling *H. influenzae* type b: A possible emerging pathogen in the vaccine era. *Pediatrics* **2001**. 108: e17.

8) Carroll, KC, Taggart, EW, Robinson, J, **Byington, CL,** Hillyard, DR. Evaluation of the Roche AMPLICOR Enterovirus PCR Assay in the Diagnosis of Enteroviral Central Nervous System Infections. *J Clinical Virology* . **2000**. 19: 149-156.

7) Christenson, JC, **Byington, CL**, Pavia, AT, Korgenski, EK, Adderson, EA, Bruggers, C, Adams, R, Jenkins, E, Hohmann, S, Carroll, K, Daly, J. A Psuedo-Outbreak of Bacillus cereus Infections Among Oncology Patients at a Children's Hospital. *Journal of Infection Control* . **1999**. 27:543-6.

6) Byington, CL, Taggart, EW, Carroll, KC, Hillyard, DR. A PCR-Based Epidemiologic Investigation of the Incidence of Non-Polio Enteroviral Infections in Febrile and Afebrile Infants Under 90 Days of Age. *Pediatrics.* **1999.** 103: e 27.

5) Taggart, EW, **Byington, CL**, Hillyard, DR, Robinson, JE, Carroll, KC. Enhancement of the AMPLICOR Enterovirus PCR Test with a Co-precipitant. *Journal of Clinical Microbiology* . **1998**. 36(11):3408-9.

4) Antonow, JA, Hansen, K, McKinstry, CA, **Byington, CL**, Comparison of Outcomes: Sepsis Evaluations in Hospitalized Infants with Bronchiolitis. *Pediatric Infectious Diseases Journal* . **1998**. 17(3):231-36.

3) Byington, CL, Dunbrack, RL, Jr., Cohen, FE, Agabian, N, *Entamoeba histolytica*: Computer-Assisted Modeling of Phosphofructokinase for the Prediction of Broad Spectrum Antiparasitic Agents. *Experimental Parasitology* . **1997.** 87(3):194-202.

2) Byington, CL, Dunbrack, RL, Jr., Cohen, FE, Agabian, N, Molecular Modeling of Phosphofructokinase from *Entamoeba histolytica* for the Prediction of New Antiparasitic Agents. *Archives of Medical Research* . **1996**. 28:86-9.

1) Matson, DO, **Byington, CL**, Albrecht, P, Feigin, RD, Investigation of a Measles Outbreak in a Fully Immunized School Population, *Pediatric Infectious Disease Journal*, **1993**. 12(4):292-9.

Reviews/Case Reports:

8) **Byington, CL.**, Bender, J, Ampofo, K, Pavia, AT, Korgenski, K, Daly, J, Christenson, JC, Adderson, E. Tularemia with Vesicular Skin Lesions May be Mistaken for Herpesvirus Infection. **2008**. *CID*. 47: e4-6.

7) Keller, M, Pavia, AT, **Byington, CL**. Intrafamilial Transmission of Toxacara Causing Eosinophilic Meningitis in an Infant. **2008**. *Pediatric Infectious Disease Journal*.

6) Ampofo, K and **Byington, CL**. Management of Parapneumonic Empyema. *Pediatric Infectious Disease Journal*,. **2007**. 26: 445-446.

5) Bonkowsky, JL, Filloux, F, **Byington, CL**. Herpes Simplex Virus CNS Relapse During Treatment of Infantile Spasms with ACTH. *Pediatrics*. **2006**. 117: e1045-1048**.**

4) Herron, MD, Vanderhooft, SL, **Byington, CL**, King, JD. Aspergillosis in a 24 week newborn. *Journal of Perinatology*. **2003**. 23: 257-60.

3) Tuohy, AMM, O'Gorman, M, **Byington, CL,** Reid, B, Jackson, WD. *Yersinia enterocolitica* Mimicking Crohn's Disease in a Toddler. *Pediatrics* , **1999**. 104: (3). e 36.

2) Byington, CL, The Diagnosis and Management of Otitis Media with Effusion (OME). *Pediatric Annals*, **1998**. 27(2):96-100.

1) Byington, CL, An Encephalitic Syndrome in a Seven Year Old. *Pediatric Infectious Disease Journal*, **1995**. 14(6):550-5.

Book Chapters/Books:

2018 American Academy of Pediatrics Report of the Committee on Infectious Diseases (**Red Book**). I reviewed and edited the entire document and served as Chair of the Committee during preparation.

Byington, CL and Ampofo, K**.** *Streptococcus pneumoniae* (Chapter 123) in Principles and Practice of Pediatric Infectious Diseases Fourth Edition. Edited by Long, S, Pickering, L, and Prober, C. **2017**.

2015 American Academy of Pediatrics Report of the Committee on Infectious Diseases (**Red Book**). I reviewed and edited the entire document and served as Chair of the Committee during preparation.

Byington, CL and Ampofo, K**.** *Streptococcus pneumoniae* (Chapter 123) in Principles and Practice of Pediatric Infectious Diseases Fourth Edition. Edited by Long, S, Pickering, L, and Prober, C. 2015.

2012 American Academy of Pediatrics Report of the Committee on Infectious Diseases (Red Book). I reviewed and edited the entire document and served as Vice Chair of the Committee during preparation.

Byington, CL and Ampofo, K**.** *Streptococcus pneumoniae* (Chapter 123) in Principles and Practice of Pediatric Infectious Diseases Fourth Edition. Edited by Long, S, Pickering, L, and Prober, C. 2012.

2009 American Academy of Pediatrics Report of the Committee on Infectious Diseases (Red Book). I reviewed and edited the entire document and drafted a new chapter: *Fusobacterium* Infections (including Lemierre Disease).

Byington, CL. *Enteroviruses,* Current Pediatric Therapy, 18th edition, eds. Burg/Ingelfinger/Polin/Gershon, **2005**

Byington, CL, Basow R.D., *Streptobacillus moniliformis*, The Textbook of Pediatric Infectious Diseases, eds. Ralph D. Feigin & James Cherry, 5th ed., **2003**.

Byington, CL, Basow R.D., *Spirillum minus*, The Textbook of Pediatric Infectious Diseases, eds. Ralph D. Feigin & James Cherry, 5th ed., **2003**.

Byington,CL, *Evaluation of Immigrant Children; International Adoptees, Refugees, and Migrants*, Textbook of Pediatric Travel Medicine, editors John C. Christenson and Phillip Fischer, 1st edition, **2002**.

Byington, CL, Basow R.D., *Streptobacillus moniliformis*, The Textbook of Pediatric Infectious Diseases, eds. Ralph D. Feigin & James Cherry, 4th ed., **1997**.

Byington, CL, Basow R.D., *Spirillum minus*, The Textbook of Pediatric Infectious Diseases, eds. Ralph D. Feigin & James Cherry, 4th ed., **1997**.
Feigin, R. D., **Byington, CL**, *Pneumococcal Infections*; Nelson's Textbook of Pediatrics, ed. Richard Berhman, 14th ed., **1992**.
Byington, CL, Basow, R. D., *Rat Bite Fever*; The Textbook of Pediatric Infectious Diseases, eds. Ralph D. Feigin & James Cherry, 3rd ed., **1992**.

Letters to the Editor

Byington, CL, Ampofo, K, Korgenski, K, Daly, J, Pavia, AT. Empyema and Viral Illness in UT. *PIDJ*. **2006**. 25: 854.

Glasgow, T, Young, PC, **Byington, CL.** Impact of Peripartum Antibiotics on Risk for Late Onset Infection. *Pediatrics*. **2006**. 117: 256-257.

Byington, CL, Korgenski, K, Daly, J, Samore, M, Pavia, AT. Invasive pneumococcal disease in children: changing serotypes and clinical expressions of disease (reply). *Clinical Infectious Diseases.* **2005.** 41:1822-23.

Byington, CL. Diagnostic Testing for Enteroviral Infections. *Pediatrics in Review.* **2005.**

Antonow, JA, **Byington, CL**. Use of RSV Elisa May Decrease Need For Sepsis Evaluations in Certain Febrile Infants. *Arch Pediatr Adolesc Med*, **1999**. 153: 1310.

Antonow, JA, **Byington, CL**. Sepsis Evaluations in Hospitalized Infants with Bronchiolitis. *Pediatric Infectious Disease Journal*, **1998**. 17:938-9.

Abstracts: * Indicates Pediatric Academic Societies presentation-103 abstracts presented through 2016

209) Pershing, NL, Kapusta, A, Nielsen, S, Crandall, H, Korgenski, K, Byington, CL, Ampofo, K, Blaschke, AJ. The capsule and beyond: genetic determinants of pediatric *Streptococcus pneumoniae* empyema. ID Week 2020. October 21-25 2020.

208) Ory, MG, Alonzo, JP, Lee, S, Waer, A, Pulliam, CL, Ellis, ML, Williams, M, and **Byington, CL**. Interprofessional Education: Opiod Education and Training. 5th Annual Interprofessional Education and Research Symposium. Bryan, TX October 23, 2019.

207) Blaschke, A, Korgenski, EK, and **Byington , CL**. Meningitis in Well-Appearing Febrile Infants aged 1-90 Day. ID Week 2017. San Francisco, CA. October 7, 2018

206) **Byington, CL**, Ampofo, K, Lewis, T, Mathie, T. Nanayakkara, D, Pavia, AT, Hanson, K, Couturier, M, Moreau, B. Arboviral Infections Following the 2016 Olympic and Paralympic Games in a Cohort of US Athletes and Support Staff. ID Week 2017. San Diego, CA. October 7, 2017

205) Korgenski, EK, **Byington, CL.** Et al. Provider Compliance with Rapid Influenza Detection Testing Guidelines During the 2016-2017 Influenza Season. ID Week 2017. San Diego, CA. October 7, 2017

204) Blaschke, AJ, Korgenski, EK, Wilkes, J, Presson, AP, Thorell, E, Stockmann, C, Pavia, AT, Knackstedt, ED, Reynolds, C, Schunk, JE, Daly, JA, **Byington, CL.** Human Rhinovirus Detection by PCR in Febrile Infants and Risk of Concomitant Bacterial Infection. ID Week 2017. San Diego, CA. October 7, 2017

203) **Rothwell, E.,** Case, G., Cheek-O'Donnell, S., Wong, B., Johnson, E.J., Matheson, T., Wilson, A., Robinson, N.R., Rawlings, J., Horesjsi, B., Botkin, J.R., & Byington, C. (2017). Empirical Assessment of a Theatrical Performance on Attitudes and Behavior Intentions Toward Research: The Informed Consent Play. Translational Science, Association for Clinical and Translational Science, Washington, DC, April 19-21, 2017.

202) Chow, C, Olson, L, Lopez, AM, **Byington, CL**. An exploratory study of how physician identities inform clinical research practice. Translational Science 2017. Washington DC.

201) Hernandez, EJ, Kapusta, A, Flygare, S, Crandall, H, Blaschke, AJ, Byington, CL, Schlaberg, R, andYandell, M. Ultra-fast sequence classification with Taxonomer—a case study of Staphylococcus aureus. The Biology of Genomes Conference. Cold Spring Harbor. May 2017.

200) Association of Palivizumab use in CF Infants with Longitudinal Outcomes. Fink, AK, Graff, GR, Rosenfeld, M, Byington, CL, and Saiman, L. North American CF Meeting. Orlando, FL. October 2016.

199) Assessment of Adjunct Faculty Experience: Results and Actions. Hopf, H, Hobson-Rohr, W, Carcelli, L. Olson, L, Akimseu, P, Byington, CL. AAMC Group on Faculty Affairs Professional Development Conference. Vancouver, BC, Canada. July 15, 2016.

198) Initial Presentation of Neonatal Herpes Simplex Virus Infection. Curfman, AL, Glissmeyer, EW, Ahmad, FA, KOrgenski, EK, Blaschke, AJ, **Byington, CL**, Miller, AS. Pediatric Academic Societies Annual Meeting. Baltimore, MD. April 30, 2016.

197) A Syndromic Evidence-Based Antibiotic Prescribing Tool to Improve Antibiotic Therapy for Febrile Infants 1-90 Days. Korgenski, EK, Stockmann, C, Pavia, AT, Gesteland, PH, Thorell, EA, Stenehjem, E, Hersh, AL, Olson, J, **Byington, CL**. ID Week 2015. San Diego, CA October 7-11, 2015.

196) Shared Genetic Variants among Empyema Causing Isolates of Streptococcus pneumoniae. Osborne, EJ, Blaschke, AJ, Crandall, H, Pavia, AT, Killpack, J,

Stockmann, C, Ampofo, K, Eilbeck, K, Farrell, AP, Schlaberg, R, Fischer, K, Yandell, M, **Byington, CL**. ID Week 2015. San Diego, CA October 7-11, 2015.

195) Initial Presentation of Herpes Simplex Virus Infection in Infants 0-60 Days. Miller, A, Curfman, C, Ahmad, F, Glissmeyer, E, **Byington, CL**, Blaschke, AJ, Korgenski, EK. ID Week 2015. San Diego, CA October 7-11, 2015.

194) Changing Trends in Parapneumonic Empyema (PPE) in the United States during the Pneumococcal Conjugate Vaccine Era. Ampofo, K, Pavia, AT, Hersh, AL, Thorell, EA, Stockmann, C, Blaschke, AJ, Rosen, P, Korgenski, EK, Daly, J, **Byington, CL**. ID Week 2015. San Diego, CA October 7-11, 2015.

193) Changing Etiology of Parapneumonic Empyema through the Pneumococcal Conjugate Vaccine Era in Utah. Sanderson, SK, Ampofo, K, Stockmann, C, Pavia, AT, Mason, EO, Daly, J, Blaschke, AJ, Rosen, P, Korgenski, EK, **Byington, CL**. ID Week 2015. San Diego, CA October 7-11, 2015.

192) Limited and Variable Use of Antivirals for Children Hospitalized with Influenza, 2009-2014. Stockmann, C, **Byington, CL**, Pavia, AT, Ampofo, K, Wilkes, J, Korgenski, EK, Hersh, AL. ID Week 2015. San Diego, CA October 7-11, 2015.

191)* Invasive Bacterial Infection Associated with Skin and Soft Tissue Infections in Infants. Hester, GZ, Hersh, A, Mundorff, MB, Wilkes, JF, Korgenski, K, Byington, CL, Srivastava, R. Pediatric Academic Societies Annual Meeting. Vancouver, Canada. May 4, 2014

190)* National Trends in Pediatric Pyogenic Arthritis and Osteomyelitis, 1997-2009. Stockmann, C, Hersh, AL, Pavia, AT, Byington, Cl. Blaschke, AJ, Sherwin, CMT, Spigarelli, MG, Ampofo, K. Pediatric Academic Societies Annual Meeting. Vancouver, Canada. May 5, 2014.

189) Does monthly palivizumab prevent nosocomial Respiratory Syncytial Virus (RSV) in high-risk infants in Newborn Intensive Care (NICU)? Olson, J, **Byington, CL**, Hersh, AL, Pavia, AT, Ampofo, KK, Faix, R, Thorell, EA. ID Week 2013. San Francisco, CA. October 5, 2013.

188) Probability of Serious Bacterial Infection (SBI) in 1-90 Day old Febrile Infants with Laboratory Viral Testing Performed. Korgenski, EK, Wilkes, J, Reynolds, C, Sheng, X, **Byington, CL**. ID Week 2013. San Francisco, CA. October 5, 2013.

187) Polymerase Chain Reaction (PCR) Improves Pathogen Identification from Pleural Fluid of Children and Adults hospitalized with Community Acquired Pneumonia (CAP): Preliminary Results from the Etiology of Pneumonia in the Community (EPIC) Study. Ampofo, KK, Stockmann, C, Blaschke, AJ, Carvahlo, MG, Bramley, AM, Williams, DJ, Self, WH, Edwards, KE, Grijalva, CJ, Zhu, Y, Anderson, EJ, Wunderink, RG, Courtney, DM, Qi, C, Arnold, SR, McCullers, J,

Hicks, LA, Erdman, D, Hersh, AL, **Byington, CL**, Jain, S, Pavia, AT. ID Week 2013. San Francisco, CA. October 4, 2013.

187) Stockmann, C, Ampofo, K, Hersh, A. Blaschke, AJ, **Byington, CL**, Korgenski, K, Pavia, AT. Age-Specific Patterns of Human Metapneumovirus and Respiratory Syncytial Virus Activity. ID Week 2013. San Francisco, CA. October 3, 2013.

186) The Clinical Epidemiology of Human Coronavirus Infections among Hospitalized Children. Sanderson, S, Stockmann, C, Pavia, AT, **Byington, CL**, Blaschke, AJ, Thorell, E, Hersh, AL, Herbener, A, Cowan, P, Korgenski, K, Daly, J, Ampofo, K. ID Week 2013. San Francisco, CA. October 3, 2013.

185) Comparison of Nasopharyngeal and Anterior Nare Swabs for PCR Detection of Respiratory Viruses in Children. **Byington, CL**., Hobson-Rorher, Hersh, AL, Blaschke, AJ. ID Week 2013. San Francisco, CA. October 3, 2013.

184)* Respiratory Syncytial Virus Associated Mortality in Hospitalized US Infants and Children Younger than 2 Years. Wilkes, J, Korgenski, KK, Sheng, X, **Byington, CL**. Pediatric Academic Societies Annual Meeting. Washington, DC. May 5, 2013.

183)* Analysis of Serious Bacterial Infection in Febrile Infants 1-90 Days by Week of Age. **Byington, CL**, Korgenski, KK, Sheng, X. Pediatric Academic Societies Annual Meeting. Washington, DC. May 5, 2013.

182)* Evidence for Red Queen Dynamics in Invasive *Streptococcus pneumoniae* Serotypes following Vaccine Introduction. **Byington, CL**, Stockmann, C, Ampofo, K, Pavia, AT, Mason, EO, Forney, L. Pediatric Academic Societies Annual Meeting. Washington, DC. May 4, 2013.

181) Community Engagement: A Novel Method for Development of American Indians in the Biomedical Workforce. Holsti, M, White, R, Bloom, K, **Byington, CL**. 2012 NIH/NIMHD Science of Eliminating Health Disparities, National Harbor, MD. November 2, 2012.

180) A Comparison of the Incidence, Outcomes, and Cost of Human Metapneumovirus, RSV, and Influenza among Hospitalized Children. Davis, C, Stockman, C, Ampofo, K, Korgenski, K, **Byington, CL**, Pavia, AT. ID Week 2012. San Diego, CA, October 20, 2012.

179) Quantification of Human Rhinovirus Load and Disease Severity among Hospitalized Children with Pneumonia Enrolled in the CDC Etiology of Pneumonia in the Community (EPIC) Study. Stockman, C, Pavia, AT, Hymas, W, London, H, Myer, T, Hillyard, D, **Byington, CL**, Liu, X, Erdman, D, Jain, S, Ampofo, K and the Centers fro Disease Control and Prevention (CDC) Etiology

of Pneumonia in the Community (EPIC) Study Team. ID Week 2012. San Diego, CA, October 20, 2012.

178) Community Surveillance of Respiratory Viruses among Families in the Utah Better Identification of Germs-Longitudinal Viral Epidemiology (BIG-LoVE) Study. Ampofo, K, Stockman, C, Pavia, AT, Blaschke, AJ, Miller, T, Crisp, R, **Byington, CL**. ID Week 2012. San Diego, CA, October 20, 2012.

177) Human Coronavirus (HCoV) Shedding and Association with Illness among Families in a Longitudinal Cohort Study: The Utah Better Identification of Germs-Longitudinal Viral Epidemiology (BIG-LoVE) Study. Ampofo, K, Stockman, C, Pavia, AT, Blaschke, AJ, Miller, T, Crisp, R, **Byington, CL**. ID Week 2012. San Diego, CA, October 20, 2012.

176) Quantification of Human Metapneumovirus Load and Disease Severity among Hospitalized Children with Pneumonia Enrolled in the CDC Etiology of Pneumonia in the Community (EPIC) Study. Stockman, C, Pavia, AT, Hymas, W, London, H, Myer, T, Hillyard, D, **Byington, CL**, Liu, X, Erdman, D, Jain, S, Ampofo, K and the Centers fro Disease Control and Prevention (CDC) Etiology of Pneumonia in the Community (EPIC) Study Team. ID Week 2012. San Diego, CA, October 18, 2012.

175) Symptoms Associated with Molecular Viral Detection in the Utah Better Identification of Germs-Longitudinal Viral Epidemiology (BIG-LoVE) Study. **Byington, CL**, Ampofo, KK, Herbener, A, Miller, T, Stockman, C, Sheng, X, Pavia, AT, Crisp, R. 112th General Meeting, American Society of Microbiology. San Francisco, CA. June 17, 2012.

174) * Seasonal Acute Otitis Media and the Role of Respiratory Viral Activity in Children. Stockman, C, Ampofo, K, Hersh, A, Carleton, S, Sheng, X, Weng, HYC, Korgenski, K, Pavia, AT, Byington, CL. Pediatric Academic Societies Annual Meeting. Boston, MA, April 28, 2012

173) * A Care Process Model for Febrile Infants Increases Evidence-Based Care, Improves Outcomes, and Reduces Costs. Byington, CL, Reynolds, C, Korgenski, K, Sheng, X, Valentine, K, Nelson, R, Daly, J, Osguthorpe, R, James, B, Savitz, L, Pavia, AT, Clark, EB. Pediatric Academic Societies Annual Meeting. Boston, MA, April 29, 2012.

172) * Neutrophil Profile at Diagnosis of Invasive Meningococcal Infection in Children. Demisse, DE, Kaplan, SL, Romero, J, Leake, J, Barson, W, Halasa, N, Byington, CL, Peters, T, Tan, T, Hoffman, J, Lin, P, Edwards, KM, Mason, EO, Cooperstock, M. Pediatric Academic Societies Annual Meeting. Boston, MA, April 29, 2012.

171) * Population-Based Incidence and Costs of Hospitalization of Children with Human Metapneumovirus Infection. Davis, C, Stockman, C, Korgenski, K, Daly, J, **Byington, CL**, Pavia, AT, Ampofo, K. Pediatric Academic Societies Annual Meeting. Boston, MA, April 30, 2012.

170) * Performance of Urinaysis Tests to Detect Urinary Tract Infection in 1-90 day old Febrile Infants. Korgenski, K, Sheng, X, Valentine, K, Reynolds, C, Wilkes, J, Byington, CL. Pediatric Academic Societies Annual Meeting. Boston, MA, April 29, 2012.

169)* Cerebrospinal Fluid Pleocytosis in Febrile Infants 1-90 Days with Urinary Tract Infection; Can a Cause be Identified? Doby, E, Korgenski, K, **Byington, CL**. Pediatric Academic Societies Annual Meeting. Boston, MA, April 29, 2012.

168)* Invasive Pneumococcal Disease in Infants 1-90 Days Before and After Introduction of Pneumococcal Conjugate Vaccine. Olarte, L, Ampofo, K, Stockman, C, Korgenski, K, Mason, EO, **Byington, CL**. Pediatric Academic Societies Annual Meeting. Boston, MA, May 1, 2012.

167) Expansion of Serotypes Causing Invasive Pneumococcal Disease among Utah Children through the PCV7 Era. 8th International Symposium on Pneumococci and Pneumococcal Diseases. Ampofo, K, Stockman, C, Korgenski, K, Mason, EO, **Byington CL**. Iguacu, Brazil. March 11-15, 2012.

166) Invasive Pneumococcal Disease in Infants 90 Days and Younger. 8th International Symposium on Pneumococci and Pneumococcal Diseases. Iguacu, Brazil. Ampofo, K, Stockman, C, Olarte, L, Korgenski, K, Mason, EO, **Byington, CL**. March 11-15, 2012.

165) Once a Year and Every Other Friday: Peer Mentoring for Academic Women. Bar-On, M, **Byington, CL**, Cosgrove, E, Gordon, L, Joad, J, Kutner, J, Lopez, AM, Wren, S. AAMC Annual Meeting, Denver, CO. November 6, 2011.

164) Financial Impact of an Imported Measles Outbreak on Public and Private Sectors. Leniek, K, Pavia, AT, Abouzelof, R, Ampofo, K, Byington, CL, Vernon, V, Risk, I, Vitek, D, Hill, M. 49th Annual Meeting of the Infectious Disease Society of America. Boston, MA. October 21, 2011.

163) *Streptococcus pneumoniae* serotypes in Utah Adults with Invasive Pneumococcal Disease at the End of the PCV7 Era. Kendall, B, Dascombe, K, Mehta, RR, Mason, EO, Pombo, DJ, Pavia, AT, **Byington, CL**. 49th Annual Meeting of the Infectious Disease Society of America. Boston, MA. October 21, 2011.

162) Serious Bacterial Infections in Infants 1-90 Days: Pathogen Incidence and *in-vitro* Susceptibility. Korgenski, EK, Hersh, AL, Thorell, EA, Valentine, KJ, Reynolds, C, Clark, EB, **Byington, CL**. 49th Annual Meeting of the Infectious Disease Society of America. Boston, MA. October 21, 2011.

161) Molecular Evaluation and Pathogen Identification from Pleural Fluid in Pediatric Parapneumonic Empyema: Preliminary Data from the CDC Etiology of Pneumonia in the Community (EPIC) Study. Ampofo, K, Stockman, C, Blaschke, A, **Byington, CL**, Heyrend, C, Williams, DJ, Edwards, KE, Arnold, S, McCullers, JA, Hicks, L, Carvahlo, M, Jain, S, Pavia, AT. 49th Annual Meeting of the Infectious Disease Society of America. Boston, MA. October 21, 2011.

160) Influenza Immunization During Pregnancy and Infant Antibody at 4 Months. Shakib, JH, Suarez, CM, Pavia, AT, Varner, MW, Rock, MT, Edwards, KM, **Byington, CL**. 49th Annual Meeting of the Infectious Disease Society of America. Boston, MA. October 21, 2011.

159) Impact of Rapid Influenza Testing on Specificity of Clinical Care in the Emergency Department. Blaschke, AJ, Hersh, AL, Shapiro, DJ, **Byington, CL**, Pavia, AT. 49th Annual Meeting of the Infectious Disease Society of America. Boston, MA. October 21, 2011.

158) Teaching Future Clinician Scientists and Supporting the Research Infrastructure of an Academic Medical Center. Holsti, M, Adelgais, K, Jacobson, K, Willis, L, Clark, E, **Byington, CL**. Pediatric Educational Excellence Across the Continuum. 2nd Biannual Conference. Arlington, VA. September 9, 2011.

157)* Clinical Features and Risk Factors for Severe Influenza. Stockmann C, Ampofo K, Willis L, Bender JM, Korgenski K, **Byington CL,** Pavia AT.. Pediatric Academic Societies Annual Meeting. Denver CO. April 30, 2011.

156)* Characteristics of Severe 2009 H1N1 vs. Seasonal Influenza -- Which is More Severe? Stockmann C, Ampofo K, Willis L, Bender JM, Korgenski K, **Byington CL,** Pavia AT. Pediatric Academic Societies Annual Meeting. Denver CO. April 30, 2011.

155)* Development of a Viral Respiratory Activity Information Dashboard: Supporting Outbreak Response and Clinical Decision Making through Information Visualization. Gesteland, P, Korgenski, K, Pavia, AT, **Byington, CL**. Platform Presentation. Pediatric Academic Societies Annual Meeting. Denver, CO April 30-May 3, 2011.

154)* The Accuracy of Detecting ILI (Influenza-Like Illness) Using Electronic Surveillance in the Intermountain West. Korgenski, EK, Gesteland, P, Byington,

CL. Poster Presentation. Pediatric Academic Societies Annual Meeting. Denver, CO April 30-May 3, 2011.

152)* Detection of Rhinovirus does not Decrease the Liklihood of Serious Bacterial Infection in Febrile Infants Younger than 90 Days of Age. Doby, B, Korgenski, K, Reynolds, C, **Byington, CL**. Poster Presentation. Pediatric Academic Societies Annual Meeting. Denver, CO April 30-May 3, 2011.

151)* Rapid Implementation of Viral Testing for Pandemic Influenza in a Hospital Setting. Valentine, K, Ballard, J, Korgenski, EK, Osguthorpe, RJ, Nygaard, M, Brenneman, A, Garner, NK, Christensen, A, Sharp, M, Cartwright, CD, Young, A, Petersen, GL, Reynolds, CC, Clark, EB, **Byington, CL**. Platform Presentation. Pediatric Academic Societies Annual Meeting. Denver, CO. April 30-May 3, 2011.

150)* Respiratory Viruses are Common in Children Attending School. Allison, MA, Carter, M, Mallin, B, Taylor, K, LaFluer, B, Pavia, AT, Young, PC, **Byington, CL**. Pediatric Academic Societies Annual Meeting. Denver, CO. April 30-May 3, 2011.

149) Rapid Molecular Identification of Pathogens from Positive Blood Cultures. Herend, C, Poritz, M, Ota, I, **Byington, CL**, Pavia, AT,48th Daly, JA, Blaschke, A. 48th Annual Infectious Disease Society of America Meeting. October 23, 2010. Vancouver, British Columbia, Canada.

148) Changes in the Clinical Syndromes of Invasive Group A Streptococcus in Utah. Stockman, C, Ampofo, K, Korgenski, EK, Weng, HY, **Byington, CL**, Pavia, AT. 48th Annual Infectious Disease Society of America Meeting. October 23, 2010. Vancouver, British Columbia, Canada.

147) Characteristics of Secondary Attack Rates of H1N1 in Families. Herbener, A, Ampofo, K, Miller, T, Weng, HY, Crisp, RJ, **Byington, CL**. 48th Annual Infectious Disease Society of America Meeting. October 22, 2010. Vancouver, British Columbia, Canada.

146) High Rates of Invasive Methicillin Susceptible Staphylococcus aureus in a Pediatric Population with Little USA300. Blaschke, A, Thorell, EA, Korgenski, EK, **Byington, CL**, Pavia, AT, Daly, JA, Hulten, K. 48th Annual Infectious Disease Society of America Meeting. October 22, 2010. Vancouver, British Columbia, Canada.

145) School Characteristics Associated with Decreased Absenteeism: Implications for Infection Control Practices. Allison, M, LeFleur, B, Young, PC, Byington, CL. American Academy of Pediatrics National Conference and Exhibition. October 3, 2010.

144)* Modeling the Variation in Pediatric Seasonal RSV Epidemics. Leecaster, M, Gesteland, P, Greene, T, Walton, N, Gundlapalli, A, Rolfs, R, Byington, CL, Samore, M. Pediatric Academic Societies Annual Meeting. Vancouver, CA. May 2, 2010.

143)* Comparison of Children Hospitalized with 2009 Influenza A (H1N1) Infection during the First Wave to Seasonal Influenza; Is It More Severe? Herbener, A, Ampofo, K, Bender, J, Pavia, AT, Korgenski, K, Byington, C. Pediatric Academic Societies Annual Meeting. Vancouver, CA. May 2, 2010.

142)* A Comparison of 2009 Influenza A (H1N1) to Seasonal Influenza in Hospitalized Infants 1-90 Days of Age. Herbener, A, Ampofo, K, Bender, J, Pavia, AT, Korgenski, K, Byington, C. Pediatric Academic Societies Annual Meeting. Vancouver, CA. May 2, 2010.

141)* Non-Invasive Sample Collection for Respiratory Virus Testing by Multiplex PCR. M Allison, A. Blaschke, B. LaFleur, M. Portiz, T. Barney, J. Daly, L. Meyers, C. Heyrend, **CL. Byington**. Pediatric Academic Societies Annual Meeting. Vancouver, CA. May 2, 2010.

140)* Elementary Schools' Infection Control Policies and Practices Improved after the Spring 2009 H1N1 Influenza A Outbreak. K. Whittemore, MD; M. Allison, MD, MSPH; M. Carter, MSPH; B. Mallin, MA, MPH; **CL. Byington**, MD. Pediatric Academic Societies Annual Meeting. Vancouver, CA. May 2, 2010.

139)* Molecular Diagnostics Improve Pathogen Identification in Culture Negative Pediatric Parapneumonic Empyema. Ampofo, K, Blaschke, AJ, Pavia, AT, Heyrand, C, Poritz, M, Teng, D, Justice, EH, Korgenski, K, Daly, J, **Byington, CL.** Pediatric Academic Societies Annual Meeting. Vancouver, CA. May 2, 2010.

138)* Detection of Polymicrobial Parapneumonic Empyema using Molecular Methods. Doby, EH, Blaschke, AJ, Pavia, AT, Heyrand, C, Poritz, M, Teng, D, Korgenski, K, Daly, J, **Byington, CL**, Ampofo, K. Pediatric Academic Societies Annual Meeting. Vancouver, CA. May 2, 2010.

137)* Inability of a Rapid Test and Direct Fluorescent Antibody Stain To Detect 2009 Pandemic Influenza A/H1N1 in a Pediatric Population in the Intermountain West. Korgenskli, K, Sheng, X, **Byington, CL**. Pediatric Academic Societies Annual Meeting. Vancouver, CA. May 2, 2010.

136)* Pertussis Immunization During Pregnancy. Shakib, J, Korgenski, K, Sheng, X, Pavia, AT, **Byington, CL**. Pediatric Academic Societies Annual Meeting. Vancouver, CA. May 2, 2010.

135)* Pregnancy Outcomes in Women with Group B *Streptococcus* (GBS) Bacteriuria. Weng, C, Korgenski, K, Sheng, X, **Byington, CL**. Pediatric Academic Societies Annual Meeting. Vancouver, CA. May 2, 2010.

134)* Kindergarten Performance in Latino Children Participating in Reach Out and Read. **Byington, CL**, Hobson, W, Buchi, K, Allison, M, Campbell, K, Deiner, M. Pediatric Academic Societies Annual Meeting. Vancouver, CA. May 1, 2010.

133) Vancomycin Use in the Neonatal ICU: Limited Impact of Negative Culture. Blaschke, A, Korgenski, K, Thorell, E, Weng, Hsin-Yi, Byington, CL. 47th Annual Meeting of the Infectious Diseases Society of America. Philadelphia, PA. October 31, 2009.

132) Serious Bacterial Infection in Febrile Infants with Viral Disease. Korgenski, K, Sheng, X, Valentine, KL, Reynolds, C, **Byington, CL**. 47th Annual Meeting of the Infectious Diseases Society of America. Philadelphia, PA. October 31, 2009.

131) Pertussis Immunization During Pregnancy. Shakib, J, Korgenski, K, Sheng, X, Pavia, AT, **Byington, CL**. 47th Annual Meeting of the Infectious Diseases Society of America. Philadelphia, PA. October 31, 2009.

130) Pediatric Invasive Group A Streptococcus Infections in Utah. Bender, J, Ampofo, K, Osguthorpe, RJ, Korgenski, K, Daly, J, Hill, HR, **Byington, CL**, Pavia, AT. 47th Annual Meeting of the Infectious Diseases Society of America. Philadelphia, PA. October 31, 2009.

129) Influenza Virus Infection in Infants Younger than Three Months. Bender, J, Gesteland, P, Sheng, X, Korgenski, K, Daly, JA, Valentine, K, Srivatatava, R, Pavia, AT, **Byington, CL.** 47th Annual Meeting of the Infectious Diseases Society of America. Philadelphia, PA. October 31, 2009. **(Fellow Award for Best Poster to J Bender)**

128) Impact of Rotavirus Vaccination in Two Utah Hospitals. Herrera-Guerra, A, Thorell, E, Ampofo, K, Korgenski, K, **Byington, CL**, Pavia, AT. 47th Annual Meeting of the Infectious Diseases Society of America. Philadelphia, PA. October 31, 2009.

127) Comparison of Blood and CSF PCR to Identify Herpes Simplex Virus in Febrile Infants. Osguthorpe, RJ, Bender, J, Korgenski, K, Daly, JA, Pavia, AT, **Byington, CL**. 47th Annual Meeting of the Infectious Diseases Society of America. Philadelphia, PA. October 31, 2009.

126) Automated Nested Multiplex PCR Detects a Large Spectrum of Known Viral Variants. Myers, L, Blaschke, A, Poritz, M, Ririe, K, **Byington, CL.** Association for American Pathology 2009 Annual Meeting.

125) Enhancing Population-Based Practice and Clinical Care of Acute Respiratory Tract Infections through Data Visualization and Decision Support. Gesteland, PH, Staes, CJ, Samore, MH, Pavia, AT, Korgenski, K, Savitz, L, James, BC, **Byington, CL**. 2009 AMIA Spring Conference. May 28, 2009. Orlando, FL.

124)* Improvement in Laboratory Testing of Febrile Infants Using an Evidence Based Care Process Model. **Byington, CL**, Valentine, K, Reynolds, C, Conway, T, Clark, E. Pediatric Academic Societies Annual Meeting. May 4, 2009. Baltimore, MD.

123)* *S. pneumoniae*: Serotype 7F, the New Contender**.** Ampofo, K, Sheng, X, Korgenski, K, Mason, EO, Daly, J, Pavia, AT, **Byington, CL**. Pediatric Academic Societies Annual Meeting. May 4, 2009. Baltimore, MD.

122)* The Changing Age and Serotype Distribution of Invasive Pneumococcal Disease in the PCV-7 Era; Implications for New Pneumococcal Vaccines. Ampofo, K, Sheng, X, Korgenski, K, Mason, EO, Daly, J, Pavia, AT, **Byington, CL**. Pediatric Academic Societies Annual Meeting. May 4, 2009. Baltimore, MD.

121)* Factors Associated with Parental Acceptance of School Based Influenza Vaccination. Reyes, M, Calame, L, Young, PC, **Byington, CL**, Allison, M. Pediatric Academic Societies Annual Meeting. May 3, 2009. Baltimore, MD.

120) Clinician Use and Acceptance of Population-Based Data about Respiratory Pathogens: Implications for Enhancing Population-Based Clinical Practice. Gesteland, PH, Allison, M, Staes, CJ, Samore, MH, Rubin, MA, Carter, ME, Wuthrich, A, Kinney, AY, Mottice, S, **Byington, CL**. American Medical Informatics Association Annual Meeting. Washington, DC November 8, 2008.

119) Predominant Clone of Methicillin-Susceptible *Staphylococcus aureus* Causing Severe Disease. Blaschke, A, Thorell, EA, Jackson, MA, Korgenski, K, Daly J, Pavia, AT, **Byington, CL**, Mason, EO, Hulten, K. 48th Annual ICCAC/46th Annual Infectious Disease Society of America Meeting. Washington, DC. October 25-28, 2008.

118) Clinical and cost analysis of children hospitalized due to Human Parainfluenza virus infection. Thorell, E, Ampofo, KK, Blaschke, AJ, Korgenski, K, Daly, J, **Byington, CL**, Pavia, AT. 48th Annual ICCAC/46th Annual Infectious Disease Society of America Meeting. Washington, DC. October 25-28, 2008.

117) Human Metapneumovirus infection in Children; Comparison with other Common Respiratory Viruses. Ampofo, K, **Byington, CL**, Bender, J, Blaschke, A, Pavia,

AT. 48th Annual ICCAC/46th Annual Infectious Disease Society of America Meeting. Washington, DC. October 25-28, 2008.

116) Pneumococcal Meningitis in Utah Children; Evolution of Serotypes (1996- 2008). Ampofo, K, Osguthorpe, R, Mason, EO, Pavia, AT**, Byington, CL**. 48th Annual ICCAC/46th Annual Infectious Disease Society of America Meeting. Washington, DC. October 25-28, 2008.

115) *Streptococcus pneumoniae* Hemolytic Uremic Syndrome in Utah Children. Bender, J, Ampofo, K, **Byington, CL**, Grinsell, M, Korgenski, K, Daly, J, Mason, EO, Pavia, AT. 48th Annual ICCAC/46th Annual Infectious Disease Society of America Meeting. Washington, DC. October 25-28, 2008.

114) Molecular Epidemiology of Pediatric Pneumococcal Empyema in Utah 2001-2007. **Byington, CL**, Mason, EO, Korgenski, K, Daly, J, Hulten, K. 6th International Symposium on Pneumococci and Pneumococcal Diseases. Reykjavik, Iceland. June 8-12, 2008.

113) Pediatric Parapneumonic Empyema and Complicated Pneumonia after Introduction of 7-Valent Pneumococcal Conjugate Vaccine. **Byington, CL**, Pirez, MC, Hsieh, YC, Huang, LM, Kellner, J, Obando, I, Fletcher, M, Spencer, D. 6th International Symposium on Pneumococci and Pneumococcal Diseases. Reykjavik, Iceland. June 8-12, 2008.

112) Rapid Molecular Diagnostics for Serious Bacterial Infection. Blaschke, A, **Byington, CL**, Bawden, AJ, Thopmpson, J, Myers, L, Teng, D, Pavia, AT, Daly, JA, Poritz, MA. American Society for Microbiology. 108th Annual Meeting. Boston, MA. June 2, 2008.

111)* Missed Serious Bacterial Infection in Febrile Infants Managed as Outpatients. Glissmeyer, E, Valentine, K, Reynolds, C, Korgenski, K, Vayo, T. **Byington, CL**. Pediatric Academic Societies Annual Meeting. Honolulu, HI. May 5, 2008.

110)* Emerging Respiratory Viruses, Especially Rhinoviruses, Are Common in Children Evaluated for Respiratory Illness. Herbener, A, Poritz, M, Meyers, L, Korgenski, K, Daly, J, **Byington, CL**. Pediatric Academic Societies Annual Meeting. Honolulu, HI. May 4, 2008.

109)* Influenza Antibodies in Post-partum Women and Newborns. Shakib, J, Edwards, K, **Byington, CL**. Pediatric Academic Societies Annual Meeting. Honolulu, HI. May 4, 2008.

108)* Pediatric Parapneumonic Empyema and Complicated Pneumonia Before and After the Introduction of Pneumococcal Conjugate Vaccine. **Byington, CL.,** Hsieh, Y-C, Huang, L-M, Kellner, J, Obando, I, Fletcher, M, Spencer, D. Pediatric Academic Societies Annual Meeting. Honolulu, HI. May 4, 2008.

107)* The Role of Frontier Physicians in Utah in the Recognition of Human Tularemia. **Byington, CL** and Bender, J. Historical Perspectives. Pediatric Academic Societies Annual Meeting. Honolulu, HI. May 3, 2008.

106) Pediatric Parapneumonic Empyema and Complicated PneumoniaBefore and After the Introduction of Pneumococcal Conjugate Vaccine. Hsieh, Y-C, Huang, L-M, **Byington, CL**., Kellner, J, Obando, I, Fletcher, M, Spencer, D. World Society for Pediatric Infectious Diseases. Bangkok, Thailand. November 15, 2007.

105) Informing the Front Line about Common Respiratory Viral Epidemics. Gesteland, PH, Samore, M, Pavia, AT, Srivastava, R, Korgenski, K, Gerber, K, Daly, JA, Mundorff, MB, Rolfs, RT, James, BC, **Byington, CL**. American Medical Informatics Association Annual Meeting. Chicago, IL November 10, 2007.

104) Population Analysis of Routine Viral Diagnostic Testing ad a Novel, Useful Paradigm for Public Health Surveillance. Wyman, L, Gesteland, P, Samore, M, **Byington, CL**. Public Health Information Networks Conference. August 27-29, 2007. Atlanta, GA.

103) Analysis of a Century of Empyema Deaths: Implications for Pandemic Influenza Preparedness. Bender, J, Ampofo, K, Sheng, X, Pavia, AT, Cannon-Albright, L, **Byington, CL**. Infectious Disease Society of America 45rd Annual Meeting. San Diego, CA . October 7, 2007.

102) Carbapenem-Resistant *Pseudomonas aeruginosa* in Pediatrics. Blaschke, AJ, Korgenski, K, Daly, J, Pavia, AT, **Byington, CL**. Infectious Disease Society of America 45rd Annual Meeting. San Diego, CA . October 7, 2007.

101) Polymerase Chain Reaction and the Clinical Diagnosis of Pertussis. Shakib, JH, Wyman, L, Gesteland, PH, Wuthrich-Reggio, A, **Byington, CL**. Infectious Disease Society of America 45rd Annual Meeting. San Diego, CA . October 7, 2007.

100) An Automated, Nested Multiplex PCR System to Detect 16 Respiratory Viruses. Myers, L, Rink, C, Daly, J, Poritz, M, **Byington, CL**. European Respiratory Society Annual Congress. September 18, 2007. Stockholm Sweden.

99) Population Analysis of Routine Viral Diagnostic Testing as a Novel, Useful Paradigm for Public Health Surveillance. **Byington, CL**, Wyman, L, Gesteland, PH, Gundlapalli, A, Rolfs, RT, Samore, M. CDC Public Health Information Network Conference. Atlanta, GA. August 27, 2007.

98)* Nasopharyngeal Carriage of Common and Emerging Respiratory Viruses in Pediatric Health Care Workers. Gundlapalli, A, **Byington, CL**, Greenberg, R, Poritz, M, Mayer, L, Korgenski, K, Benuzillo, J, Carter, M, Wuthrich-Reggio, A,

Petty, W, Fejlstad, M, Jacketta, C, Stoddard, G, Daly, J, Pavia, AT, Samore, M. Pediatric Academic Societies Annual Meeting, Toronto, Ontario, Canada. May 5, 2007.

97)* Feasibility of Elementary School Children's Use of Hand Gel and Face Masks During Influenza Season. Allison, MA, Guest-Warnick, G, Gesteland, PH, Srivastava, R, Nelson, D, Pavia, AT, Rolfs, RT, Calame, L, **Byington, CL**. Pediatric Academic Societies Annual Meeting, Toronto, Ontario, Canada. May 5, 2007.

96)* Extended Spectrum β-Lactamases: A Problem in Pediatrics? Blaschke, A, Korgenski, K, Daly, JA, **Byington, CL**. Pediatric Academic Societies Annual Meeting, Toronto, Ontario, Canada. May 8, 2007.

95)* Early Onset Group B Streptococcus Infection in the Era of Intrapartum Prophylaxis. Pulver, L, McCurry, M, Young, PC, Stoddard, G, **Byington, CL**. Pediatric Academic Societies Annual Meeting, Toronto, Ontario, Canada. May 8, 2007.

94)* Pertussis Diagnosis by PCR. Shakib, JH, Gesteland PH, **Byington, CL**. Pediatric Academic Societies Annual Meeting, Toronto, Ontario, Canada. May 7, 2007.

93)* Viral Diagnostic Testing in Febrile Infants. **Byington, CL**, Valentine, K, Korgenski, K, Reynolds, C, Daly, J, Raines, B, Gesteland, P. Pediatric Academic Societies Annual Meeting, Toronto, Ontario, Canada. May 7, 2007.

92)* Compliance with Recommended Laboratory Testing for Febrile Infants. **Byington, CL**, Valentine, K, Korgenski, K, Reynolds, C, Daly, J, Raines, B, Gesteland, P. Pediatric Academic Societies Annual Meeting, Toronto, Ontario, Canada. May 7, 2007.

91)* Pertussis Antibodies in Postpartum Women and Newborns. Shakib, JH, Ralston, S, Raissy, HH, Stoddard, G, Byington, CL. Pediatric Academic Societies Annual Meeting, Toronto, Ontario, Canada. May 6, 2007.

90)* Pediatric Pneumococcal Meningitis in the Post-Vaccine Era: The Emergence of Serogroup 22F. **Byington, CL**, Korgenski, K, Daly, JA, Mason, EO. Pediatric Academic Societies Annual Meeting, Toronto, Ontario, Canada. May 6, 2007.

89) Naso-Pharyngeal Carriage of Common and Emerging Respiratory Viruses in Health Care Workers. Gundlapalli, A, **Byington, CL**, Greenberg, R, et al. Society for Healthcare Epidemiology of America. Baltimore, MD. April 16, 2007.

88) Pneumococcal Necrotizing Pneumonia in Utah: Does Serotype Matter? Bender, J, Ampofo, K, Pavia, AT, Daly, J, **Byington, CL**. Infectious Diseases Society of America, 44th Annual Meeting. Toronto, Ontario, Canada. October 13, 2006. (Travel Award- Dr. Bender)

87) Broad-Range Bacterial PCR of CSF in Infants Evaluated for Meningitis. Blaschke, A, Voelkerding, K, Zurcher, BA, Daly, J, **Byington, CL**, Hillyard, D, Petti, C. Infectious Diseases Society of America, 44th Annual Meeting. Toronto, Ontario, Canada. October 13, 2006. (Travel Award- Dr. Blaschke)

86) Pediatric Invasive Pneumococcal Disease in Utah 2005. **Byington, CL**, Mottice, S, Ampofo, K, Pavia, AT, Mason, EO, Rolfs, R. Infectious Diseases Society of America, 44th Annual Meeting. Toronto, Ontario, Canada. October 13, 2006.

85)* Outcomes of Influenza Infection in Infants 1-90 Days of Age. **Byington, CL**, Ampofo, K, Korgenski, K, Raines, B, Daly, J, Srivastava, R, Bender, J, Pavia, AT, Gesteland, P. Pediatric Academic Societies Annual Meeting, San Francisco, CA. May 2, 2006.

84)* Risk Factors and Costs of Respiratory Failure in Children with Hospitalized Influenza. Gesteland, P, Ampofo, K, Pavia, AT, **Byington, CL**, Bender, J, James, B, Srivastava, R. Pediatric Academic Societies Annual Meeting, San Francisco, CA. May 2, 2006.

83)* Differentiating Between Hospitalized and Non-Hospitalized Children with Proven Influenza Infection. Bender, J, Ampofo, K, Gesteland, P, Pavia, AT, **Byington, CL**, Srivastava, R. Pediatric Academic Societies Annual Meeting, San Francisco, CA. May 2, 2006.

82)* Impact of Rapid Viral Testing and Virus-Specific Cohorting on the Rate of Nosocomial RSV infection at a Tertiary Children's Hospital. Gesteland, P, Jenkins, E, Shunk, A, Daly, J, Pavia, AT, Sheng, X, **Byington, CL**. Pediatric Academic Societies Annual Meeting, San Francisco, CA. May 2, 2006.

81)* Predictors of Need for Salvage Therapy with VATS after Chest Tube and Fibinolysis in the Management of Parapneumonic Effusion. Ampofo, K, **Byington, CL**, Myers, R, Feola, P, Gesteland, P, Bender, J, Srivastava, R, Pavia, AT. Pediatric Academic Societies Annual Meeting, San Francisco, CA. April 30, 2006.

80)* Association of Parapneumonic Effusions, Hospitalization, and Streptococcus Empyema with Viral Respiratory Tract Infections in Children in Utah. Ampofo, K, **Byington, CL**, Daly, J, Sheng, X, Gesteland, P, Bender, J, Srivastava, R, Pavia, AT. Pediatric Academic Societies Annual Meeting, San Francisco, CA. April 30, 2006.

79)* Comparison of Bacteremia Due to Antibiotic Susceptible and Resistant *Staphylococcus aureus* and *Streptococcus pneumoniae*. Jensen, J, Korgenski, K, Daly, JA, Gesteland, P, **Byington, CL**. Pediatric Academic Societies Annual Meeting, San Francisco, CA. April 30, 2006.

78)* Impact of Age and Viral Status on Rochester Criteria and Risk of Serious Bacterial Infection in Febrile Infants. **Byington, CL**, Cutler, C, Sheng, X, Enriquez, FR, Pavia, AT. Pediatric Academic Societies Annual Meeting, San Francisco, CA. April 29, 2006.

77) Differences between Hospitalized and Non-Hospitalized Children with Proven Influenza. Bender, J, Ampofo, K, Gesteland, P, Thompson, M, Pavia, AT, Srivatava, R, **Byington, CL**. Infectious Disease Society of America 43rd Annual Meeting. San Francisco, CA . October 8, 2005.

76) Pediatric Pneumococcal Empyema: Increasing Rates and Emerging Serotypes. **Byington, CL**, Korgenski, K, Ampofo, K, Daly, JA, Pavia, AT, Mason, EO. Infectious Disease Society of America 43rd Annual Meeting. San Francisco, CA . October 7, 2005.

75) Impact of Rapid Viral Testing and Virus Specific Cohorting on the Rate of Nosocomial RSV Infections in a Children's Hospital. Gesteland, P, Jenkins, E, Schunk, A, Daly, JA, Pavia, AT, Sheng, X, **Byington, CL**. Infectious Disease Society of America 43rd Annual Meeting. San Francisco, CA . October 7, 2005.

74)* Diagnosis of Sinogenic Intracranial Empyema in Children. Adame, N, Hedlund, G, **Byington, CL**. Pediatric Academic Societies Annual Meeting, Washington, DC, May 16, 2005.

73)* Literacy of Hispanic Caregivers in a Pediatric Emergency Department. Mallory, M, Tapia-Guzman, J, **Byington, CL**, Dudley, N. Pediatric Academic Societies Annual Meeting, Washington, DC, May 16, 2005.

72)* Evolution of Caries in Latino Preschool Children. Ortiz, K, Buchi, K, Watson, D, Johnson, J, **Byington, CL**. Pediatric Academic Societies Annual Meeting, Washington, DC, May 15, 2005.

71)* Use of Bactec Blood Culture System for Culture of Cerebrospinal Fluid. Low, JI, Korgenski, K, Daly, J, **Byington, CL**. Pediatric Academic Societies Annual Meeting, Washington, DC, May 15, 2005.

70)* Cerebrospinal Fluid Profiles in Febrile Infants 1-90 Days of Age without Evidence of Bacterial or Enteroviral Infection. Kendrick, J, Sheng, X, **Byington, CL**. Pediatric Academic Societies Annual Meeting, Washington, DC, May 15, 2005.

69)* Monoarticular Arthritis Differentiating Septic Arthritis from Rheumatic Fever. Harlan, G, Tani, L, **Byington, CL**. Pediatric Academic Societies Annual Meeting, Washington, DC, May 15, 2005.

68)* Epidemiology of Persistent Coagulase Negative Staphylococcal Bacteremia in Newborn Intensive Care Infants. Anderson-Berry, A, Stoddard, G, Britton, B, Samore, M, **Byington, CL**, Faix, R. Pediatric Academic Societies Annual Meeting, Washington, DC, May 14, 2005.

67)* Human Herpesvirus 6 Infections in Febrile Infants. McCurry, M, Taggart, EW, Stevenson, JB, Hymas, W, Hillyard, D, **Byington, CL**. Pediatric Academic Societies Annual Meeting, Washington, DC, May 14, 2005.

66)* Bacteremia in Infants and Children with Bronchiolitis: Impact of Virus Type. Mendoza, J, Raines, WM, Ballard, J, Korgenski, K, Bennion, K, Daly, J, Gerber, K, **Byington, CL**. Pediatric Academic Societies Annual Meeting, Washington, DC, May 14, 2005.

65) Epidemiology of Meningococcal Disease Among Adolescents in 10 Children's Hospitals in the United States 2001-2003. Kaplan, SL and the US Pediatric Meningococcal Surveillance Group. Infectious Disease Society of America 42nd Annual Meeting. Boston, MA. October 2, 2004.

64) Human Herpes Virus 6 Infections in the Neonatal Intensive Care Unit. Rentz, A, Taggart, EW, Stevenson, J, Hillyard, D, **Byington, CL**. Infectious Disease Society of America 42nd Annual Meeting. Boston, MA. October 2, 2004.

63) Temporal Trends in Pediatric Pneumococcal Disease in the Intermountain West. **Byington, CL**, Stoddard, G, Barlow, S, Korgenski, K, Daly, J, Mason, EO, Jensen, J, Pavia, AT. Infectious Disease Society of America 42nd Annual Meeting. Boston, MA. October 2, 2004.

62)* Temporal Trends for Invasive Disease due to *Streptococcus pneumoniae* in Children in the Intermountain West: Increasing Importance of Non-Vaccine Serogroups. **Byington, CL**, Samore, M, Glover, D, Jensen, J, Daly, J, Korgenski, K, Mason, EO, Pavia, AT. Pediatric Academic Societies Annual Meeting, San Francisco, CA. May 3, 2004.

61)* Multicenter Pediatric Surveillance of Invasive Meningococcal Infection. Kaplan, SL, Mason, EO, Shutze, G, Edwards, K, Barson, WJ, **Byington, CL**, et al. Pediatric Academic Societies Annual Meeting, San Francisco, CA. May 2, 2004.

60)* Prevalence and Comparison of Bottled, Filtered and Tap Water Use between Latino and Caucasian Children. Wendy L. Hobson, Miguel Knochel, **Carrie Byington**, Charles Hoff, Karen Buchi. Pediatric Academic Societies Annual Meeting, San Francisco, CA. May 2, 2004.

59)* Iron Deficiency Anemia in Children of Foreign Born Mothers. Mandy Allison, **Carrie Byington ,** Karen Buchi. Pediatric Academic Societies Annual Meeting, San Francisco, CA. May 2, 2004.

58)* 16s Ribosomal PCR in Pediatrics. Sherri Butler, Carl Wittwer, Robert Pryor, **Carrie Byington.** Pediatric Academic Societies Annual Meeting, San Francisco, CA. May 2, 2004.

57)* Occurrence of Bacterial and Viral Infections in Febrile Infants 1-90 days Old Based on Age. **Carrie Byington**, F. Rene Enriquez, Sean Firth. Pediatric Academic Societies Annual Meeting, San Francisco, CA. May 2, 2004.

56)* Parainfluenza and Secondary Bacterial Infections in Children. Bryan Upham, Kris Gerber, Judy Daly, **Carrie Byington.** Pediatric Academic Societies Annual Meeting, San Francisco, CA. May 2, 2004.

55)* Parental Perceptions of a Reach Out and Read Program: La Sabiduria esta en la Lectura. **Carrie Byington,** Wendy Hobson, Kim Winter, Gloria Torres, Karen F. Buchi. Pediatric Academic Societies Annual Meeting, San Francisco, CA. May 2, 2004.

54)* Risks for Iron Deficiency in Pregnant Mexican Women Living in the United States. Miquel Knochel, Karen Buchi, Reta Van Orden, Nica Clark, Laurie Moyer-Mileur, Mandy Allison, **Carrie Byington.** Pediatric Academic Societies Annual Meeting, San Francisco, CA. May 2, 2004.

53)* Dental Health and Habits of Hispanic Two-Year Olds in an Urban Clinic. Karen Ortiz, Jared Johnson, Karen F. Buchi, **Carrie Byington.** Pediatric Academic Societies Annual Meeting, San Francisco, CA. May 2, 2004.

52)* Impact of Health Supervision Visit Forms with Oral Health Prompts on Physician and Patient Behaviors. Karen Ortiz, Jonathan Castillo, Dustin Watson, Karen F. Buchi, Charles J. Hoff, **Carrie Byington.** Pediatric Academic Societies Annual Meeting, San Francisco, CA. May 2, 2004.

51)* Broad Spectrum Intrapartum Antibiotics Associated With Late-Onset Serious Bacterial Infection in Term Infants. Tiffany Glasgow, Paul Young, Carolyn Kwok, Sean Firth, Matthew Samore, **Carrie Byington**. Pediatric Academic Societies Annual Meeting, San Francisco, CA. May 2, 2004.

50)* Human herpes Virus 6: Infections in a Neonatal Intensive Care Unit. A C Rentz, E W Taggart, J B Stevenson, D R Hillyard, **C L Byington**. Pediatric Academic Societies Annual Meeting, San Francisco, CA. May 1, 2004.

49) Temporal Trends in Pediatric Pneumococcal Serogroup Distribution **C. L. BYINGTON**, K. CARROLL, S. ALDER, J. DALY, A. T. PAVIA, M. SANDE, and M. SAMORE. Infectious Diseases Society of America Annual Meeting, San Diego, CA, October 2003.

48) ECHOVirus 7 Infection in a Neonate: A Discussion of Potential Therapies. Rentz, AC, Miles, R, Fujinami, RS, Pevear, DC, **Byington, CL**. AAP District VIII Section on Perinatal Pediatrics. 28th Annual Conference, Hawaii. June 26, 2003 (Presented by Dr. Rentz)

47) Epidemiology of Early Onset Sepsis in Infants > 1500 grams in the Era of Group B Streptococcus Prophylaxis. Rentz, AC, Samore, M, Faix, R, **Byington, CL**. AAP District VIII Section on Perinatal Pediatrics. 28th Annual Conference, Hawaii. June 26, 2003 (Presented by Dr. Rentz, awarded Best Poster of the Meeting)

46)* Oral Health Habits of Toddlers in an Urban Clinic. Ortiz, KA, Castillo, J, Buchi, KF, Hoff, C, **Byington, CL**. Pediatric Academic Societies Annual Meeting, Seattle, WA. May 3, 2003.

45)* The Impact of Intrapartum Antibiotics on Late-Onset Serious Bacterial Infection in Term Infants. Glasgow, TS, Young, PC, Samore, M, **Byington, CL**. Pediatric Academic Societies Annual Meeting, Seattle, WA. May 5, 2003.

44)* Epidemiology of Early Onset Sepsis in Infants > 1500 grams in the Era of Group B Streptococcus Prophylaxis. Rentz, AC, Samore, M, Faix, R, **Byington, CL**. Pediatric Academic Societies Annual Meeting, Seattle, WA. May 3, 2003.

43)* Serious Bacterial Infection in Febrile Infants 1-90 Days of Age with Viral Illness. **Byington, CL**, Enriquez, R, Taggart, EW, Hillyard, D, Carroll, K, Hoff, C. Pediatric Academic Societies Annual Meeting, Seattle, WA. May 5, 2003.

42)* Reassessment of the Rochester Criteria in Febrile Infants 1-90 Days of Age. **Byington, CL**, Hoff, C, Enriquez, R, Pavia, AT, Christenson, JC. Pediatric Academic Societies Annual Meeting, Seattle, WA. May 3, 2003.

41)* Enteroviral Infections in Infants Younger than 90 Days of Age. Rittichier, KK, Bryan, P, Bassett, KE, Enriquez, R, **Byington, CL**. Pediatric Academic Societies Annual Meeting, Seattle, WA. May 4, 2003.

40)* Serious Bacterial Infections in Febrile Infants Younger than 90 Days of Age with Respiratory Syncytial Virus Infection. Bassett, KE, Rittichier, KK, Enriquez, R, **Byington, CL**. Pediatric Academic Societies Annual Meeting, Seattle, WA. May 3, 2003.

39)* Adenovirus Infections in Children. Rocholl, C, Gerber, K, Daly, J, Pavia, AT, **Byington, CL**. Pediatric Academic Societies Annual Meeting, Seattle, WA. May 3, 2003.

38) Invasive Isolates of *Streptococcus pneumoniae* from Children in the Intermountain West: The Importance of Non-Vaccine Serotypes. **C L Byington**, D Glover, J

Daly, K Korgenski, E O Mason, S Murala, A T Pavia. Infectious Diseases Society of America Annual Meeting. October 26, 2002. Chicago, IL.

37)*Metamizole Use: An Under-Recognized Health Threat in Latino Immigrants. Bonkowsky, JL, Frazer, JK, Buchi, KJ, **Byington, CL**. Pediatric Academic Societies Annual Meeting, Baltimore, MD. May 7, 2002. (Presented by J. Bonkowsky).

36)* Evaluation of a Protocol for Early Discharge of Hospitalized Febrile Infants 1-90 Days of Age. **Byington, CL**, Bryan, PA, Castillo, H, Riley, N, Miescer, M, Zebrack, M, Omura, T, Bassett, KE, Rittichier, K. Pediatric Academic Societies Annual Meeting, Baltimore, MD. May 7, 2002.

35)* Human Herpes Virus-6 in Febrile Infants 1-90 Days of Age. **Byington, CL**, Zerr, D. Taggart, EW, Hillyard, DR, Carroll, K. Pediatric Academic Societies Annual Meeting, Baltimore, MD. May 5, 2002.

34)* Serious Bacterial Infections in Febrile Infants 1-90 Days of Age: The Importance of Ampicicllin Resistant Gram-Negative Pathogens. **Byington, CL**, Castillo, H, Rittichier, KK, Bassett, KE, Daly, J, Pavia, AT. Pediatric Academic Societies Annual Meeting, Baltimore, MD. May 5, 2002.

33) The Accuracy of Rapid Respiratory Viral Direct Fluorescent Testing Compared to Viral Culture in Pediatric Patients. Gerber, K, Castillo, H, **Byington, CL**, Daly, J. American Society for Microbiology Annual Meeting. Salt Lake City, UT May 20, 2002

32) Invasive Isolates of *Streptococcus pneumoniae* from Children in the Intermountain West. **Byington, CL**, Daly, J, Korgenski, K, Glover, D, Mason, EO, Pavia AT, Hausdorff, WP. American Society for Microbiology Annual Meeting. Salt Lake City, UT May 23, 2002

31) Evaluation of a Protocol for Early Discharge of Hospitalized Febrile Infants 1-90 Days of Age. **Byington, CL**, Bryan, PA, Castillo, H, Riley, N, Miescer, M, Zebrack, M, Omura, T, Bassett, KE, Rittichier, K. Western Ambulatory Pediatric Association Meeting, Carmel, CA. February 10, 2002 (presented by Paul Bryan).

30) Impact of Respiratory Viral DFA Testing on Antibiotic Use in a Children's Hospital. **Byington, CL**, Castillo, H, Daly, J, Gerber, K, Brimley, L. Adams, S, Christenson, JC. Infectious Diseases Society of America Annual Meeting. San Francisco, CA. October 27,2001.

29)* Compliance with Rochester Guidelines in High-Risk Infants. **Byington, CL**. And Davis, RN. Pediatric Academic Societies Annual Meeting, Baltimore, MD. May 1, 2001.

28) Compliance with Rochester Guidelines in High-Risk Infants. Davis, RN, **Byington, CL**. Western Ambulatory Pediatric Association Meeting, Carmel, CA. February 11, 2001 (presented by Neal Davis).

27)* The Longitudinal Behavior and Development Rotation of the Innovative Track of the University of Utah Pediatric Residency. Parker-Cohen, NY, Buchi, K, **Byington, CL**, Young, PC. Pediatric Academic Societies and American Academy of Pediatrics Joint Meeting. Boston, MA. May 12, 2000.

26)* Invasive Disease due to Haemophilus influenza type a (Hia): An Emerging Pathogen of the Post-Vaccine Era? Adderson, EA, Spencer, LY, Kimball, A, Hindiye,M, Carroll, K, Mottice, S, Korgenski, K, **Byington, CL**, Christenson,J, Pavia, AT. Pediatric Academic Societies and American Academy of Pediatrics Joint Meeting. Boston, MA. May 13, 2000.

25)* Sleeping Patterns and Behavioral Concerns of Latino and Non-Latino Parents. Nemer, RB, Parker-Cohen, NY, Young, PC, Terashima, R, **Byington, CL**. Pediatric Academic Societies and American Academy of Pediatrics Joint Meeting. Boston, MA. May 12, 2000.

24)* An Epidemiologic Investigation of Pediatric Empyema in Utah. Spencer, LY, Johnson, T, Samore, MH, **Byington, CL**. Pediatric Academic Societies and American Academy of Pediatrics Joint Meeting. Boston, MA. May 13, 2000.

23)* An Analysis of Time to Positive Culture for Blood, Urine, and Cerebrospinal Fluid from Febrile Infants. **Byington, CL**, Tuohy, RP, Enriquez, FR, Pavia, AT, Christenson, JC. Pediatric Academic Societies and American Academy of Pediatrics Joint Meeting. Boston, MA. May 13, 2000.

22)* Analysis of the Rochester Criteria in Febrile Infants Under 90 Days of Age with Viral Infections. **Byington, CL**, Biggs, S, Bowman, J, Antonow, JA, Taggart, EW, Hindiyey, M, Hillyard, DR, Carroll, K. Pediatric Academic Societies and American Academy of Pediatrics Joint Meeting. Boston, MA. May 13, 2000.

21) Historical, Physical Examination, and Laboratory Findings in Patients with Enteroviral Meningitis. Kadish, H, Peterson, D, **Byington, CL**, Bolte, R. Western Ambulatory Pediatric Association Meeting, Carmel, CA. February 13, 2000.

20) Analysis of the Rochester Criteria in Febrile Infants Under 90 Days of Age with Viral Infections. **Byington, CL**, Biggs, S, Bowman, J, Antonow, JA, Taggart, EW, Hindiyey, M, Hillyard, DR, Carroll, K. Western Ambulatory Pediatric Association Meeting, Carmel, CA. February 13, 2000.

19) An Analysis of Time to Positive Culture for Blood, Urine, and Cerebrospinal Fluid from Febrile Infants. **Byington, CL**, Tuohy, RP, Enriquez, FR, Pavia, AT,

Christenson, JC. Western Ambulatory Pediatric Association Meeting, Carmel, CA. February 12, 2000.

18) A Comparison of Bacterial PCR of Whole Blood to Bacterial Culture for the Detection of Bacteremia in the Febrile Infant. **Byington, CL**, Burnside, M, Nelson, L, Kaddish, H, Ward, K. AAP Annual Meeting, October, 1999. Washington, D.C.

17) A Comparison of Bacterial PCR of Whole Blood to Bacterial Culture for the Detection of Bacteremia in the Febrile Infant. **Byington, CL**, Burnside, M, Nelson, L, Kaddish, H, Ward, K. 39th Interscience Conference on Antimicrobial Agents and Chemotherapy. San Francisco, CA. September, 1999.

16)* An Examination of the Unintended Consequences of the Rule Out Sepsis Evaluation: A Parental Perspective. **Byington, CL**, Paxton, RD. Ambulatory Pediatric Association Annual Meeting, San Francisco, CA, May 4, 1999.

15) Screening Adolescents in Foster Care for Depression and Suicidal Ideation in a Primary Care Setting. Beall, S.A., Wiet, S.M., Buchi, K.F., **Byington, CL**, National Association of Nurse Practitioners Annual Meeting, San Antonio, TX. April 16, 1999.

14) Rapid Detection of Bacteremia in Febrile Infants Using Polymerase Chain Reaction. **Byington, CL**, Burnside, M, Nelson, L, Ward, K. American Medical Student's Association Annual Meeting, Chicago, IL , March 13, 1999. (Presented by Dr. Burnside and voted top ten abstract for meeting).

13) Parental Perceptions of the Consequences of the Rule Out Sepsis Evaluation. Paxton, RD, **Byington, CL**, Western Ambulatory Pediatric Association Annual Meeting, Carmel, CA. January 30, 1999.

12) Reach Out and Read: A Pediatric Early Literacy Program. Wright, C, Deiner, M., **Byington, CL**, National Association for the Education of Young Children Annual Meeting, Toronto, Ontario, Canada, November, 1998.

11) Collaboration Between a Public Health Department and an Academic Residency Program to Improve Pediatric Training: The Innovative Track of the Pediatric Residency Program at the University of Utah. Buchi, K.F, **Byington, CL**, Norlin, E.C., and Young, P.C., Education for the 21st Century-National Initiatives, Baltimore, MD, September, 1998.

10)* Screening Adolescents in Foster Care for Depression and Suicidal Ideation in a PrimaryCare Setting. Beall, S.A., Wiet, S.M., Buchi, K.F., **Byington, CL**, Ambulatory Pediatric Association Annual Meeting, New Orleans, LA. May, 1998.

9)* The Use of PCR for the Identification of Enteroviral Infection in Febrile and Afebrile Infants under 90 days of age. **Byington, CL**, Taggart, EW, Carroll, K., Hillyard, D., Society for Pediatric Research Annual Meeting, New Orleans, LA. May, 1998.

8) Enterovirus Detection in Cerebrospinal Fluid by Spin Amplified Shell Vial Culture and Polymerase Chain Reaction. Taggart, EW, Hillyard, D, **Byington, CL**, Robinson, J, Carroll, K. 14th Annual Pan-American Society for Clinical Virology Symposium and Meeting, Clear Water, FL. April 26-29, 1998.

7) The Use of PCR for the Identification of Enteroviral Infection in Febrile Infants under 90 days of age. **Byington, CL**, Taggart, EW, Carroll, K, Hillyard, D, Western Society for Pediatric Research Annual Meeting, Carmel, CA February 6, 1998.

6) The Use of Telemedicine in a Pediatric Primary Care Residency Program. **Byington, CL**: MEDNET 97, World Congress of the Internet in Medicine, Brighton, England. November 4, 1997.

5) The Identification of Enteroviral Infection in Febrile Infants During Non-Summer Months. **Byington, CL**, Taggart, EW, Carroll, K, Hillyard, D, Infectious Diseases Society of America Annual Meeting. San Francisco, CA September 14, 1997.

4)* Comparison of Outcomes: The Sepsis Work-up in Hospitalized Infants with Bronchiolitis. Antonow, JA, Hansen, K, McKinstry, CA, **Byington, CL**, National Ambulatory Pediatric Association Meeting, Plenary Session, Washington, D.C., May 1997.

3) Comparison of Outcomes: The Sepsis Work-up in Hospitalized Infants with Bronchiolitis. Antonow, J.A., Hansen, K., McKinstry, C.A., **Byington, CL**, Western Ambulatory Pediatric Association Meeting, Carmel CA, February 1997.

2)* Molecular Modeling of PFK from *Entamoeba histolytica* for the Prediction of New Antiparasitic Agents. **Byington, C.L.**, Dunbrack, R.L., Cohen, F.E., and Agabian, N. Presented at the Society for Pediatric Research Annual Meeting, ID Platform, Washington, D.C., May 1996. Published in *Pediatric Research* 39(2): 1996.

1) Molecular Modeling of Phosphofructokinase from *Entamoeba histolytica* for the Prediction of New Antiparasitic Agents. **Byington, C.L.**, Dunbrack, R.L., Cohen, F.E., and Agabian, N., Presented at the Infectious Diseases Society of America Annual Meeting, San Francisco, CA September 17, 1995. Published in *Clinical Infectious Diseases* 21(3): 781 1995.

XI. INVITED PRESENTATIONS

International:

Working Together—Through Academic Health Centers. Association of Academic Health Centers International (**AAHCI**) European Roundtable - COVID-19 Epicenters: Lessons Learned, Impact, and Next Steps. Virtual Round Table Berlin, Germany. June 22, 2020.

Remaining Challenges in Treatment of Pneumococcal Pneumonia. 10th International Symposium on Pneumococci and Pneumococcal Diseases. Glasgow, Scotland. June 26-30, 2016. (**Voted best presentation of the meeting**)

Tackling the Problem of Antibiotic Resistance in *Streptococcus pneumoniae*. 17th Annual Meeting of the Hong Kong Society of Pediatric Research and 6th Annual Meeting of the Asian Pediatric Respirology Forum. Hong Kong SAR, People's Republic of China. October 19, 2014.

Key Note: Changing Epidemiology of Pneumococcal Diseases and Serotype Replacement in the US and Utah after a Decade of Pneumococcal Conjugate Vaccine. 17th Annual Meeting of the Hong Kong Society of Pediatric Research and 6th Annual Meeting of the Asian Pediatric Respirology Forum. Hong Kong SAR, People's Republic of China. October 19, 2014.

Workshop (Core Curriculum for Pediatric Academic Societies): Navigating Career Development Awards: Lessons from the CTSA Sites. PAS Annual Meeting. May 14, 2014 (Session 2474; 3 hours; 40 attendees). Vancouver, British Columbia, Canada. Role Leader

An Evidence-Based Care Process Model for the Evalaution of the Febrile Infant 1-90 Days and Bacterial and Viral Diagnostics in the Febrile Infant. 10th Annual China Pediatric World Window. August 10-13, 2013. Beijung, Shanghai, and Guangzhou China.

Pinnacles of Infectious Diseases: Red Book 2012. University of Miami 47th Annual Perspectives in Pediatrics. Miami, FL (webcast and translated for audience in Latin America). February 13, 2012.

Meet the Red Book Committee. Infectious Disease Society of America. Annual Meeting. Vancouver, Canada. October 25, 2010.

Topic Symposium: Management of the Febrile Child-A 21st Century Approach? The Role Inflammatory Markers and Viral Diagnostics. Pediatric Academic Societies Annual Meeting. Vancouver, Canada, May 3, 2010.

Pediatric Empyema in Utah: Molecular Epidemiology, MLST and Vaccine Implications. **Visiting Professor**: Taipei University, Taipei, Taiwan. March 24-25, 2008.

Empyema in Children in the USA: The Possible Impact of Introduction of Routine Pneumococcal Immunization. European Respiratory Society Annual Congress. Stockholm, Sweden. September 18, 2007

Complicated Pediatric Pneumococcal Pneumonia in Utah. North American Pneumococcal Advisory Board. Montreal, Quebec. Canada. September 14, 2006.

The Importance of Rapid Viral Diagnostic Testing in Pediatrics. Sino-American Medical Science Exchange, "Best Pediatric Seminar China 2006". Web-based presentation. Beijing Pediatric Hospital. Beijing, China. August 28, 2006.

Rapid Viral Diagnostics in the Evaluation of the Febrile Infant and The Impact of Rapid Respiratory Viral Testing on Antibiotic Use in a Children's Hospital: **Visiting Professor:** Hospital Pediatrico de Sinaloa, Culiacan, Mexico, Annual Meeting of the Mexican Academy of Pediatrics. November 6-8, 2003.

Reach Out and Read: A Pediatric Early Literacy Program. National Association for the Education of Young Children Annual Meeting, Toronto, Ontario, Canada, November 18, 1998.

The Use of Telemedicine in a Pediatric Primary Care Residency Program. MEDNET 97, World Congress of the Internet in Medicine, Brighton, England. November 4, 1997.

The Use of Single Mode DOCK for the Prediction of Clinically Useful Inhibitors of PFK from *Entamoeba histolytica*. XIII Seminario International Sobre Amibiasis-**Bernardo Sepulveda Memorial Lecture: Molecular Frontiers in Amibiasis** Mexico City, Mexico. January 29,1997

National:

Advances in Measuring Disparities Across the University of California Health. Annual Meeting Association of Academic Health Centers (virtual). October 15, 2020.

Panelist: COVID-19 and Higher Education—Returning to University Campuses. JP Morgan Higher Education Webinar. October 6, 2020.

Keynote: Leadership Lessons for Pediatricians. American Academy of Pediatrics Young Physician Leadership Academy at the National Conference and Exhibition (via ZOOM). October 2, 2020.

Panelist representing University of California Health: NIH Government-University Dialogue on COVID-19 Testing and Surveillance. July 24, 2020. Moderated by Dr. Francis Collins.

Keynote: Leadership Lessons: Learning Crossing Borders. Focus on Health and Leadership for Women. University of Pennsylvania Perlman School of Medicine. October 18, 2019.

Elizabeth Blackwell Visiting Professor. Leadership Lessons: Learning from Crossing Borders. Mayo Clinic. September 11, 2019.

Keynote: Times Up: Organizational Changes that Support Gender Equity in Academic Health Centers. AAMC CFAS and WIMS Annual Meeting. Chicago, Il. July 11, 2019

Keynote: Engineering Medicine: Developing Physicianeers to Shape the Future of Healthcare through Innovation. ASAIO 65th Annual Conference. San Francisco, CA. June 26, 2019.

Effective Educational Partnerships Workshop (presented 4 times with Co-presenter Dr. Joy Alonzo). AAMC National Workshop to Advance Medical Education to Combat Opioid Misuse: Working Together Across the Continuum. May 9-10, 2019

Plugging in to Rural Healthcare Solutions. **South by Southwest (SXSW)** March 12, 2019. Austin, TX.

Disrupting Traditional Healthcare with Innovation and Technology. **South by Southwest (SXSW)** March 13, 2018. Austin, TX

Theodore Panos Visiting Professor—University of Arkansas January 28-30, 2018
Matrix Mentoring for KL2 Scholars
Pneumococcal Pneumonia—Epidemiology to Entrepreneurship
A 21st Century Approach to the Febrile Infant (**Panos Lecture**)

Nathan Frances Mossell Visiting Professor—Perelman School of Medicine, University of Pennsylvania. October 3-4-2017

Meet the Red Book. American Academy of Pediatrics National Conference and Exhibit. San Francisco, CA. September 18, 2017.

Meet the Red Book. American Academy of Pediatrics National Conference and Exhibit. San Francisco, CA. October 25, 2016.

Meet the Red Book. ID Week 2015. New Orleans, LA. October 28, 2016.

Vaccine Success and Addressing Vaccine Hesitancy and 21st Century Vaccine Challenges. Alaska Maternal Child Health & Immunization Conference. Anchorage, AK. September 27-28, 2016.

2016 Visiting Scholar, One Academic Journey: Lessons from Many Mentors. Vanderbilt University Medical Center Faculty Research Scholars Program. Nashville, TN. July 2016.

Institutional Support for Physician Scientists: The Return on a Mentoring Investment. AAMC Annual Meeting. Baltimore, MD. November 9, 2015.

Meet the Red Book. American Academy of Pediatrics National Conference and Exhibit. Washington, DC. October 25, 2015.

Meet the Red Book. ID Week 2015. San Diego, CA. October 9, 2015.

Key Note*: Streptococcus pneumoniae* from Epidemiology to Evolution: My Adventures with the Captain of the Men of Death. Symposium of the Statewide Ohio Infectious Diseases Consortium. Visiting Professor The Nationwide Children's Hospital. Columbus, OH. November 19-21, 2014.

Structured Mentoring in Preserving Science in Medical Schools: Sustaining Funding, Aligning Investigation, and Valuing Teaching. AAMC Annual Meeting. Chicago, Il. November 9, 2014.

The Evidence-Based Management of the Febrile Infant. American Academy of Pediatrics Annual Meeting. San Diego, CA. October 13, 2014.

Meet the Red Book: National Influenza Guidelines and Ebola Virus Disease. American Academy of Pediatrics Annual Meeting. San Diego, CA. October 13, 2014.

Using Data to Drive Policies that can Address Salary Equity at US Medical Schools. AAMC Group on Faculty Affairs Annual Meeting. Boston, MA June 19, 2014.

Navigating Career Development Awards: Best Practices from the CTSA Child Health Oversight Committee. Byington, CL, Kaskel, R, and Purucker, M. Workshop. Pediatric Academic Societies Annual Meeting. Vancouver, Canada. May 4, 2014.

Pediatric Pneumococcal Empyema: Translating Epidemiology and Evolution into Clinical Care. 13th Annual St. Jude/PIDS Pediatric Infectious Diseases Research Conference. St. Jude Research Institute. Memphis, TN February 21, 2014.

Getting Started: A Career in Pediatric Infectious Diseases. Meet the Professor. Pediatric Academic Societies Annual Meeting. Washington, DC. May 4, 2013.

Use of an Evidence-Based Care Process Model for the Management of the Febrile Infant. Pediatric Academic Societies Annual Meeting. Washington, DC. May 5, 2013.

Survey of K12/KL2 Programs: The Importance of the CTSA Consortium in Supporting Child Health Investigators. CTSA Consortium-Child Health Oversight Committee Annual Meeting. Boston, MA. April 26, 2012.

The Evidence-Based Care of the Febrile Infant, Management of Pediatric Community Acquired Pneumonia, Periodic Fever Syndromes, and Challenging Pediatric Infectious Disease Cases. **William L. Bradford Visiting Professor** at the 44th Annual Clinical Advances in Pediatrics Symposium. Children's Mercy Hospital. Kansas City, MO. November 16-18, 2011.

Evidence-Based Care of the Febrile Infant. **Visiting Professor and Pediatric Grand Rounds**. University of Alabama, Birmingham. Birmingham, AL. June 2, 2010.

Advances in Diagnostic Testing that Improve the Care of the Febrile Infant. **Carl Smith Visiting Professor in Laboratory Medicine.** Washington University and St. Louis Children's Hospital. St. Louis, MO. February 18, 2011.

Public Health Communication with Physicians During the 2009 Influenza Pandemic. American Academy of Pediatrics and Centers for Disease Control and Prevention Enhancing Pediatric Partnerships to Promote Pandemic Preparedness. Chicago, Il. February 4, 2011.

Meet the Red Book Committee, 2010-2011 Influenza Guidelines and Immunization for the Healthcare Worker. Infectious Disease Society of America Annual Meeting. Vancouver, BC, Canada. October 22 and 23, 2010.

Diagnosis and Management of Pediatric Community Acquired Pneumonia. American Academy of Pediatrics National Conference and Exhibit. Washington, DC. October 10, 2010.

Improving Care of the Febrile Infant: Lessons Learned from the AHRQ Implementation Science Awards. Agency for Health Care Quality and Research Annual Meeting. Bethesda, MD, September 28, 2010.

Challenging Cases in Pediatric Infectious Diseases. Infectious Disease Society Annual Meeting. Philadelphia, PA. October 29, 2009.

The Evaluation of Periodic and Persistent Fever Syndromes. American Academy of Pediatrics National Conference and Exhibit. Washington, DC. October 17, 2009.

The Changing Epidemiology of Invasive Pneumococcal Disease. Infectious Diseases Grand Rounds. Long Island Jewish Schneider Children's Hospital. New York, New York. May 1, 2009.

Evidence Based Care of the Febrile Infant. Pediatric Grand Rounds. Long Island Jewish Schneider Children's Hospital. New York, New York. May 1, 2009.

Evidence Based Care of the Febrile Infant. Medical University of South Carolina 11th Annual Pediatric Review Charleston, SC. December 6, 2008.

Evidence Based Care of the Febrile Infant. Pediatric Grand Rounds. Long Island Jewish Health System and Schneider Children's Hospital. New Hyde Park, NY. December 5, 2008.

Meet the Red Book. American Academy of Pediatrics National Conference and Exhibition. Boston, MA. October 13, 2008.

Diagnostic Testing and the Care of the Febrile Infant, Children's Health research Evaluation Unit (CHEAR), University of Michigan. Ann Arbor, MI. August 28, 2007.

Translational Research in Public Health Informatics: Linking Healthcare, Communities, and Public Health: Centers for Disease Control and Prevention National Center for Public Health Informatics Webinar. May 30, 2007.

Neonatal Intestinal Microbiota: The Rights and Wrongs of Succession. American Society for Microbiology Symposium: Human Microbial Communities and the Immune System. Toronto, Canada. May 24, 2007.

Impact of Age and Viral Status on Rochester Criteria and Risk of Serious Bacterial Infection in Febrile Infants. Pediatric Academic Societies Annual Meeting, San Francisco, CA. April 29, 2006.

The Management of the Febrile Infant: Importance of Viral Diagnostic Testing. Medical University of South Carolina 7th Annual Pediatric Review Charleston, SC. December 3, 2004

Herpes Virus Infections in the Young Infant. Medical University of South Carolina 7th Annual Pediatric Review Charleston, SC. December 3, 2004

Temporal Trends for Invasive Disease due to *Streptococcus pneumoniae* in Children in the Intermountain West: Increasing Importance of Non-Vaccine Serogroups. Pediatric Academic Societies Annual Meeting, San Francisco, CA. May 3, 2004

Parental Perceptions of a Reach Out and Read Program: *La Sabiduria esta en la Lectura*. Fifth Annual National Reach Out and Read Conference. San Francisco, CA May 1, 2004.

The Impact of Intrapartum Antibiotics on Late-Onset Serious Bacterial Infection in Term Infants. Pediatric Academic Societies Annual Meeting. Seattle, WA. May 5, 2003. (Presented by Tiffany Glasgow, MD)

Reassessment of the Rochester Criteria in Febrile Infants 1-90 Days of Age. Pediatric Academic Societies Annual Meeting. Seattle, WA. May 3, 2003.

Serious Bacterial Infections in Febrile Infants Younger than 90 Days of Age with Respiratory Syncytial Virus Infection. Pediatric Academic Societies Annual Meeting. Seattle, WA. May 3, 2003. (Presented by Kathlene Bassett, MD)

Adenovirus Infections in Children. Pediatric Academic Societies Annual Meeting. Seattle, WA. May 3, 2003. (Presented by Christian Rocholl, MD)

Evaluation of a Protocol for Early Discharge of Hospitalized Febrile Infants 1-90 Days of Age. Pediatric Academic Societies Annual Meeting, Baltimore, MD. May 7, 2002.

The Management of the Febrile Infant: An Evidence-Based Approach. Annual Meeting of the Robert Wood Johnson General Physician Scholars Program. La Costa, CA. December 6, 2001.

Impact of Respiratory Viral DFA Testing on Antibiotic Use in a Children's Hospital. Infectious Diseases Society of America Annual Meeting. San Francisco, CA. October 27,2001.

An Evaluation of the Clinical Utility and Cost-Effectiveness of Rapid Diagnostics in the Management of Febrile Infants at Low, Moderate, and High-Risk for Bacterial Infection. Annual Meeting of the Robert Wood Johnson General Physician Scholars Program. La Costa, CA. December 6, 2000.

An Analysis of Time to Positive Culture for Blood, Urine, and Cerebrospinal Fluid from Febrile Infants. Pediatric Academic Societies and American Academy of

Pediatrics Joint Meeting. General Pediatrics: Infectious Diseases Platform, Boston, MA. May 13, 2000.

Analysis of the Rochester Criteria in Febrile Infants Under 90 Days of Age with Viral Infections. Pediatric Academic Societies and American Academy of Pediatrics Joint Meeting. General Pediatrics: Infectious Diseases Platform, Boston, MA. May 13, 2000.

Pediatric Early Literacy in Residency Training. The First Reach Out and Read National Conference: Pediatrics and Early Literacy, March 4, 2000. Cambridge, MA.

A Comparison of Bacterial PCR of Whole Blood to Bacterial Culture for the Detection of Bacteremia in the Febrile Infant. AAP Annual Meeting, Section on Emergency Medicine, October 8, 1999. Washington, D.C.

Comparison of Outcomes: Sepsis Evaluations in Hospitalized Infants with Bronchiolitis. Ambulatory Pediatric Association Annual Meeting Plenary Session. Washington, D.C. May 4, 1997 (presented by Juli Antonow, M.D.)

Molecular Modeling of PFK from *Entamoeba histolytica* for the Prediction of New Antiparasitic Agents. Society for Pediatric Research Annual Meeting. Infectious Diseases Platform Session Washington, D.C. May 9, 1996

Regional:

Culture Inside the Hospital: The Impact and Innovation Within**.** National Healthcare South. Houston, TX. February 27, 2018.

Grand Rounds—A 21st Century Approach to the Febrile Infant. Dell Children's Hospital. Austin, TX. January 19, 2018.

Adventures with the Captain (Pediatric Pneumococcal Empyema). Texas Branch of the American Society of Microbiology. **Keynote** address. October 20, 2017.

Red Book 2015: An Update from the AAP Committee on Infectious Diseases. University of Utah Department of Pediatrics Grand Rounds. December 10, 2015.

An Evidence-Based Approach to the Management of the Febrile Infant. 33rd Annual Conference on Pediatric Infectious Diseases. Vail, CO. August 1-3, 2015.

Meet the Red Book. Common Problems in Pediatrics. June 1, 2015. Salt Lake City, UT.

The Prevention and Management of RSV Bronchiolitis: Update of the AAP Guidelines. University of Utah Department of Pediatrics Grand Rounds. September 2012.

Career Development in the Pediatric Research Enterprise. University of Utah Department of Surgery Grand Rounds. July 12, 2011. Salt Lake City, Utah

Management of Pediatric Community Acquired Pneumonia. Common Problems in Pediatrics. June 8, 2011. Salt Lake City, UT.

Understanding the 2011 IDSA/PIDS Guidelines for the Management of Pediatric Community Acquired Pneumonia. Intermountain Medical Center Clinical Learning Days. May 20, 2011. Salt Lake City, UT.

Understanding the 2011 IDSA/PIDS Guidelines for the Management of Pediatric Community Acquired Pneumonia. Logan Regional Medical Center May 6, 2011. Logan, UT.

2010 Guidelines for the Prevention of Perinatal Group B Streptococcal (GBS) Disease. Logan Regional Medical Center Grand Rounds. Salt Lake City, UT. May 6, 2011. Logan, UT

2010 Guidelines for the Prevention of Perinatal Group B Streptococcal (GBS) Disease. University of Utah Obstetrics and Gynecology Grand Rounds. Salt Lake City, UT. April 14, 2011.

Evidence-Based Care of the Febrile Infant. Intermountain 8th Annual Research Summit. Implementation Science: Finding What Works. March 11, 2011. Salt Lake City, UT.

The Febrile Infant: A Model for Team Science. Benning Society Seminar Series. January 25, 2011. Salt Lake City, UT.

2010 Guidelines for the Prevention of Perinatal Group B Streptococcal (GBS) Disease. PCMC Grand Rounds. Salt Lake City, UT. December 2, 2010.

Management of Community Acquired Pneumonia. Annual CME Conference. Kid's Care. Sundance, UT. June 12, 2010.

The Health Professions and Latino Values. Latino Medical Student Association, Utah Chapter. Annual Meeting. **Keynote Speaker**. University of Utah, Salt Lake City, UT April 24, 2010.

Evidence Based Care of the Febrile Infant: Analysis of the New Care Process Model. Pediatrics in the Wasatch. Intermountain Clinical Learning Days, Salt Lake City, UT. October 10, 2009.

Bad Bugs, MRSA and Drug-Resistant Pneumococci. University of Utah Alumni Association. Salt Lake City, UT. September 26, 2009.

Molecular Diagnostics in Pediatrics. University of Utah Alumni Association. Salt Lake City, UT. September 25, 2009.

Evidence Based Care of the Febrile Infant: Analysis of the New CPM. Pediatric Grand Rounds, McKay Dee Regional Medical Center, Ogden, UT. June 3, 2009.

Persistently Challenging: Periodic Fever Syndromes. 31st Annual Common Problems in Pediatrics. Salt Lake City, UT June 1, 2009.

Evidence Based Care of the Febrile Infant: Analysis of the New CPM. Urban Central Learning Days. Intermountain Healthcare. Intermountain Medical Center, Salt Lake City, UT. May 15, 2009.

Evidence Based Care of the Febrile Infant: Analysis of the New CPM. Ogden Medical and Surgical Society Annual Meeting, Ogden, UT. May 14, 2009.

Evidence Based Care of the Febrile Infant: Analysis of the New CPM. Utah Northern Region Learning Days. Intermountain Healthcare. The Canyons, UT. September 12, 2008.

Evidence Based Care of the Febrile Infant. Intermountain Pediatric Society Regional Meeting. Dixie Regional Medical Center, St. George, UT February 15, 2008.

How Doctor's Think: Simple Strategies to Avoid Medical Errors. Morbidity and Mortality Report. Primary Children's Medical Center. January 29, 2008.

The Diagnostic Evaluation of the Febrile Infant. CHILD Dx Annual Conference. University of Utah. November 15, 2007.

How to Choose a Mentor. University of Utah 1st Annual Mentoring U Workshop, March 1, 2007.

Building Your CV. University of Utah. Women in Medicine. February 13, 2007.

Infectious Diseases in Infants and Children. University of Utah GCRC Skills Day. January 29, 2007.

How to Write a Manuscript Reporting Clinical Science. Women's Research Caucus. University of Utah. December 13, 2006.

Care of the Febrile Infant: The Utah Experience. Pediatric Grand Rounds. PCMC May 25, 2006.

Computerized Decision Support and Advanced Diagnostic Technology for the Evaluation of the Febrile Infant. Combined Noon Conference/RIP. PCMC May 9, 2006.

Outcomes of Influenza in Infants 1-90 Days of Age. Utah Health Services Research Conference. Salt Lake City. February 24, 2006.

Understanding the New Recommendations for Acellular Pertussis Vaccine. Association of College Health Providers. Salt Lake City, UT August 12, 2005.

Reducing the Risk of Meningococcal Disease in College Students. Association of College Health Providers. Salt Lake City, UT August 12, 2005.

Future Methods of Identifying Neonatal Infection. American Academy of Pediatrics, District VIII Perinatal section Meeting. Homestead, UT June 24, 2005

Temporal Trends in Invasive Pneumococcal Disease in the Intermountain West. Epidemiology in Action, Utah Department of Health and the Centers for Disease Control and Prevention. Salt Lake City, UT December 10, 2004

Temporal Trends in Invasive Pneumococcal Disease in the Intermountain West. Pediatric Grand Rounds, Primary Children's Medical Center, Salt Lake City, UT December 9, 2004.

Temporal Trends in Invasive Pneumococcal Disease in the Intermountain West. Utah Chapter of the National Association of Pediatric Nurse Associates and Practitioners. Salt Lake City, UT September 23, 2004.

Update on Meningococcal Disease Including Strategies for Prevention. Salt Lake County Health Department Lunch and Learn. Salt Lake City, UT September 22, 2004.

The Management of the Febrile Infant: An Evidence Based Approach. IHC Clinical Learning Days. Park City, UT September 18, 2004.

Herpes Simplex Infections in Neonates and Young Infants**.** Pediatric Grand Rounds, LDS Hospital, Salt Lake City, UT. March 12, 2004.

Pneumococcal Infections in Children. University of Utah Nurse Practitioner Training. March 1, 2004, Salt Lake City, UT (Webcast to 5 rural areas in UT).

The Management of the Febrile Infant: An Evidence Based Approach. Pediatric Grand Rounds, St. Marks Hospital, Salt Lake City, UT, January 19, 2004.

The Management of the Febrile Infant: An Evidence Based Approach. Pediatric Grand Rounds, Cottonwood Hospital, Salt Lake City, UT, January 14, 2004.

The Management of the Febrile Infant: An Evidence Based Approach. Pediatric Grand Rounds, IHC Kids Care and InstaCare Grand Rounds, Salt Lake City, UT January 8, 2004.

The Management of the Febrile Infant: An Evidence Based Approach. Pediatric Grand Rounds, Utah Valley Regional Medical Center, Ogden, UT, November 11, 2003.

The Management of the Febrile Infant: An Evidence Based Approach. Pediatric Grand Rounds, McKay Dee Hospital Provo, UT, November 11, 2003

Health Issues in Refugee Children**.** University of Utah and the Utah Department of Health Refugee Health Conference. Salt Lake City, UT. September 20, 2003.

The Management of the Febrile Infant: An Evidence Based Approach. Common Problems in Pediatrics. Salt Lake City, UT, June 11, 2003.

Streptococcus pneumoniae: An Update: University of Utah College of Nursing Graduate Nurse Practitioner Pediatric Primary Care Course (N6041). April 7, 2003.

Viral Diagnostics and the Management of Febrile Infants and Children. ARUP Infectious Diseases Conference. March 26, 2003.

Update on Viral Pathogens, Diagnostics, and Treatment: University of Utah Neonatology. March 17, 2003.

Covering the Uninsured: A Robert Wood Johnson Panel Discussion. University of Utah School of Medicine. March 11, 2003.

Herpes Virus Infections in the Young Infant: Pediatric Grand Rounds Wee Care Pediatrics. Layton, UT February 6, 2003.

Bugs and Drugs: An Antibiotic Update. Utah Chapter of the National Association of Pediatric Nurse Associates and Practitioners. Salt Lake City, UT October 24, 2002.

The Management of the Febrile Infant: An Evidence Based Approach. Issues in Pediatric Care. Primary Children's Medical Center, Salt Lake City, UT October 18, 2002.

The Management of the Febrile Infant: An Evidence Based Approach. Colorado Academy of Family Physicians Annual Meeting. Breckenridge, CO. September 19, 2002.

The Management of the Febrile Infant: An Evidence Based Approach. Pediatric Grand Rounds, Utah Valley Medical Center, Provo, UT. July 23, 2002.

The Management of the Febrile Infant: An Evidence Based Approach. Pediatric Grand Rounds, Primary Children's Medical Center, Salt Lake City, UT. April 18, 2002.

Reaching Every Patient: Health Care for Diverse Communities. Martin Luther King Memorial Panel Discussion. University of Utah. January 15, 2002.

The Evaluation and Treatment of the Febrile Infant. Utah Annual Meeting of the National Association of Pediatric Nurse Practitioners. Park City, UT. September 7, 2001.

Pediatric Pneumococcal Empyema in Utah: Unraveling a Mystery. Children's Hospital of Oakland Research Institute. Oakland, CA. September 6, 2001.

The Evaluation of the Internationally Adopted Child or Refugee. Common Problems in Pediatrics. Salt Lake City, UT. June 2001.

The Evaluation of the Febrile Infant in 2001. Common Problems in Pediatrics. Salt Lake City, UT. June 2001.

The Role of Viral Diagnostics in the Evaluation of the Febrile Infant. National Children's Health Improvement Through Laboratory Diagnostics Project. Associated and Regional University Pathologists. Salt Lake City, UT. June 7, 2001.

Cultural Competence. Food and Nutrition 1620: Cultural Aspects of Food. University of Utah. April 9, 2001.

The Evaluation of the Febrile Infant in 2001. Key Note Speaker. 30th Annual University of Utah Family Practice Refresher Course. Salt Lake City, UT. March 20, 2001.

Compliance with Rochester Guidelines in High-Risk Infants. Western Ambulatory Pediatric Association Meeting, Carmel, CA. February 11, 2001 (presented by Neal Davis).

Rule Out Sepsis: What Have We Learned at PCMC? Family Medicine Grand Rounds, Salt Lake Regional Medical Center, October 25, 2000

Rule Out Sepsis: What Have We Learned at PCMC? Pediatric Grand Rounds, Primary Children's Medical Center, September 28, 2000

Management of Rochester High-Risk Febrile Infants: Analysis of Variation. The Sixth Annual Frank Tyler Fall Medical Student Research Symposium. Deer Valley, UT. September 14, 2000. (Presented by R. Neal Davis, MS I)

A Description of a Previously Unknown Human Bunyavirus Responsible for Severe Encephalitis in a Child. The Annual Interim Meeting of the Rocky Mountain Infectious Diseases Society, Salt Lake City, UT, March 11, 2000.

Historical, Physical Examination, and Laboratory Findings in Patients with Enteroviral Meningitis. Western Ambulatory Pediatric Association Meeting, Carmel, CA. February 13, 2000. (Presented by H. Kadish)

Analysis of the Rochester Criteria in Febrile Infants Under 90 Days of Age with Viral Infections. Western Ambulatory Pediatric Association Meeting, Carmel, CA. February 13, 2000. (Presented by Sean Biggs, MS IV)

An Analysis of Time to Positive Culture for Blood, Urine, and Cerebrospinal Fluid from Febrile Infants. Western Ambulatory Pediatric Association Meeting, Carmel, CA. February 12, 2000.

Reading Right: A Documentary on Early Literacy. Family Now, KSL Channel 5 Production. Aired in Salt Lake City, UT January 25, 2000.

An Epidemiologic Investigation of Empyema in Pediatric Patients from Utah. The Fifth Annual Frank Tyler Fall Medical Student Research Symposium. Deer Valley, UT. September 9, 1999. (Presented by Tim Johnson, MS I)

Alternative Therapies and Culturally Competent Medicine for the Pediatric Patient. Critical Issues In Children and Adolescents. Salt Lake City, UT. September 2, 1999.

Strategies for Increasing Literacy for Children Living in Poverty. Bonneville Exchange Club. Salt Lake City, UT. August 18, 1999.

Strategies for Increasing Literacy for Children Living in Poverty. Sugarhouse Rotary Annual Meeting. Salt Lake City, UT. April 22, 1999.

Hepatitis A, B, and C Considerations During Pregnancy and the Peripartum Period. The University of Utah Pregnancy Risk Line Group, March 17, 1999.

The Pediatrician's Role in Identifying Adolescent Depression. First Annual Eric Moerer Memorial Lecture Series. University of Utah. November 7, 1998.

A Pediatric Model for Improving Early Childhood Literacy in a Latino Population. The Utah Coalition of La Raza. Salt Lake City, UT. November 5, 1998.

What am I? An Interactive Presentation of Infectious Rashes. Primary Children's Medical Center IX Annual Pediatric Update Conference, Sun Valley, ID. September 13, 1998

Enteroviral Infections in Infancy. Primary Children's Medical Center IX Annual Pediatric Update Conference, Sun Valley, ID. September 13, 1998

Principles of Judicious Antibiotic Use. Primary Children's Medical Center IX Annual Pediatric Update Conference, Sun Valley, ID. September 13, 1998

Potential for the Rapid Diagnosis of Fever in Infants. Compucyte Corporation, Cambridge, MA, August 31, 1998.

Enteroviral Infections in Infancy. Pediatric Grand Rounds, Primary Children's Medical Center. April 30, 1998.

Neonatal Enteroviral Infections. Neonatal Fellows Conference, University of Utah. March 9, 1998.

Persistent Pneumonia , Fever, and Elevated LDH. Audio Case Conference, Primary Children's Medical Center. February 23, 1998.

The Use of PCR for the Identification of Enteroviral Infection in Febrile Infants under 90 days of age. Western Society for Pediatric Research Annual Meeting, Infectious Diseases Platform Session, Carmel, CA February 6, 1998.

Purulent Rhinitis: Is it Sinusitis or the Common Cold? Common Problems in Pediatrics Nineteenth Annual Conference. Salt Lake City, UT June 16,1997

Pediatric Immunizations: An Update. University of Utah-Division of Family Medicine Grand Rounds, Salt Lake Regional Medical Center. March 12, 1997.

Pediatric Immunizations: An Update. Wyoming Academy of Family Physicians Annual Meeting. Jackson, WY. February 25, 1997.

Pharyngitis. Wyoming Academy of Family Physicians Annual Meeting Jackson, WY. February 25, 1997

Comparison of Outcomes: Sepsis Evaluations in Hospitalized Infants with Bronchiolitis. Western Section of the Ambulatory Pediatric Association Annual Meeting. Carmel, CA. February 8, 1997 (presented by Kim Hansen, M.D.)

Penicillin Resistant *Streptococcus pneumoniae*. Medical Advisory Committee, Salt Lake City-County Health Department. October, 1995.

PPi-PFK in *Entamoeba histolytica* . Audio-conference: Research in Glycolytic Enzymes. California State University-Northridge, Department of Cell Biology, September, 1995.

EXHIBIT B

COVID-19 Pandemic Planning Scenarios

Updated Mar. 19, 2021 Print

Summary of Recent Changes

Updates as of March 19, 2021:

- The Infection Fatality Ratio (IFR) parameter has been updated to reflect recently published estimates. This parameter is now presented as the number of deaths per 1,000,000 infections for ease of interpretation.
- The healthcare utilization statistics in Table 2 have been updated to include a 0–17-years-old age group.
- This will be the final update to the COVID-19 Pandemic Planning Scenarios, as there is now a substantial body of published literature that modelers can draw on to inform parameter estimates and assumptions for their models for the general population and for sub-populations of interest. In addition, CDC has several sources that will continue to update COVID-19-related data over time, including COVID Data Tracker, COVID-19 Case Surveillance Public Use Data, and COVID-19-Associated Hospitalization Surveillance Network (COVID-NET).

CDC and the Office of the Assistant Secretary for Preparedness and Response (**ASPR**) have developed five COVID-19 Pandemic Planning Scenarios that are designed to advance public health preparedness and planning and help inform decisions by public health officials who use mathematical modeling and by mathematical modelers throughout the federal government. Models developed using the data provided in the Planning Scenario tables can help evaluate the potential effects of different community mitigation strategies (e.g., social distancing). The Planning Scenarios may also be useful to hospital administrators in assessing resource needs and can be used in conjunction with the COVID-19 Surge Tool.

Each Planning Scenario is based on a set of numerical values for the biological and epidemiological characteristics of COVID-19 illness, which is caused by the SARS-CoV-2 virus. These values—called *parameter values*—can be used in models to estimate the possible effects of COVID-19 in U.S. states and localities. This document was first posted on May 20, 2020, with the understanding that the parameter values in each Scenario would be updated and augmented over time as we learn more about the epidemiology of COVID-19. This will be the final update of the COVID-19 Pandemic Planning Scenarios, as there is now a substantial body of published literature that modelers can draw on to inform parameter estimates and assumptions for their models. In addition, CDC has several sources that will continue to update COVID-19-related data over time, including:

- COVID Data Tracker is the repository for CDC's COVID-19 data. COVID Data Tracker combines data from across the response and provides summary statistics by category (e.g., cases and deaths, testing, and vaccinations). These data are updated daily.
- COVID-19 Case Surveillance Public Use Data are deidentified line-level data from COVID-19 cases reported to CDC. This includes data on demographics and clinical information (e.g., symptom-onset date and hospital status) and is updated monthly. In addition, a restricted-use version of these data, which includes county and state information, is available to users who complete a registration process, sign a data use agreement, and obtain approval from CDC.
- COVID-NET is a population-based surveillance system that collects data on laboratory-confirmed COVID-19-associated hospitalizations through a network of more than 250 acute care hospitals in 14 states. COVID-NET provides information on age-specific clinical outcomes as well as age- and location-specific COVID-19 hospitalization rates and are updated weekly.

In this final update, the age-specific estimates of Infection Fatality Ratios (IFRs) have been updated to reflect recently published estimates of IFRs from a systematic review and meta-analysis.[1] These updated estimates have a wider uncertainty range to better reflect the potential variation in IFR geographically and over time. These values are intended to capture the national-level burden of COVID-19 deaths; however, national-level estimates may not reflect region-specific IFRs. Therefore, caution should be used when applying suggested IFR values to specific states, counties, and cities. This update also includes parameter values for healthcare utilization in individuals aged 0–17-years-old.

New data on COVID-19 are available daily, yet information about the biological aspects of SARS-CoV-2 and epidemiological characteristics of COVID-19 remain limited, and uncertainty remains around nearly all parameter values. For example, current estimates of IFRs do not account for time-varying changes in hospital capacity (e.g., bed capacity, ventilator capacity, or workforce capacity) or for differences in case ascertainment in congregate and community settings or in rates of underlying health conditions that may contribute to a higher frequency of severe illness in those settings. A nursing home, for example, may have a high incidence of infection (because of close contacts among many individuals) and severe disease (because of a high rate of underlying conditions) that does not reflect the frequency or severity of disease in the broader population of older adults. In addition, the practices for testing nursing home residents for SARS-CoV-2 upon identification of a positive resident may be different than testing practices for contacts of confirmed cases in the community. Observed parameter values may also change over time. For example, the percentage of transmission occurring before symptom onset will be influenced by how quickly and effectively both symptomatic people and the contacts of known individuals with COVID-19 (cases) are quarantined. In addition, observed parameter values may be influenced by the recent emergence of novel SARS-CoV-2 variants.

The parameters in the Planning Scenarios:

- Are estimates intended to support public health preparedness and planning;
- Are **not** predictions of the expected effects of COVID-19;
- Do **not** reflect the impact of any behavioral changes, social distancing, or other interventions; and
- Do **not** reflect the impact of the emergence of novel SARS-CoV-2 variants.

The Five Scenarios

The five COVID-19 Pandemic Planning Scenarios (Box 1) represent a range of possible parameters for COVID-19 in the United States. All parameter values are based on current COVID-19 surveillance data and scientific knowledge.

- Scenarios 1 through 4 are based on parameter values that represent the lower and upper bounds of disease severity and viral transmissibility. The parameter values used in these Pandemic Planning Scenarios are likely to change as we obtain additional data about the upper and lower bounds of disease severity and the transmissibility of SARS-CoV-2, the virus that causes COVID-19.
- Scenario 5 represents a current best estimate about viral transmission and disease severity in the United States, with the same caveat: the parameter values will change as more data become available.

Parameter values that vary among the Pandemic Planning Scenarios are listed in Table 1, while parameter values common to all five scenarios are listed in Table 2. Definitions of the parameters are provided below, and the source for each parameter value is indicated in the Tables.

The Parameter Values: Definitions

Parameter values that vary across the five COVID-19 Pandemic Planning Scenarios (Table 1) include measures of viral transmissibility, disease severity, and pre-symptomatic and asymptomatic disease transmission. Age-stratified estimates are provided, where sufficient data are available.

Viral Transmissibility

- **Basic reproduction number (R_0):** The average number of people that one person with SARS-CoV-2 is likely to infect in a population without any immunity (from previous infection) or any interventions. R_0 is an estimate of the average transmissibility in a completely naïve population. R_0 estimates vary across populations and are a function of the duration of contagiousness, the likelihood of infection per contact between a susceptible person and an infectious person, and the contact rate.[2,3] A separate but related parameter is the effective or time-varying

reproduction number (R_e or R_t), which estimates the average transmission in a population with mitigation measures and immunity.

Disease Severity

- **Infection Fatality Ratio (IFR):** The number of individuals who **die** of the disease among all infected individuals (symptomatic and asymptomatic). This parameter is not necessarily equivalent to the number of reported deaths per reported case because many cases and deaths are never confirmed to be COVID-19 and there is a lag in time between when people are infected and when they die. This parameter also reflects the existing standard of care, which might vary by location or hospital and could be affected by the introduction of new therapeutics. The IFR values presented in Table 1 are intended to capture the national-level burden of COVID-19 deaths; however, these values may not reflect IFR in specific states, counties, or cities in the United States.

Presymptomatic and Asymptomatic Contribution to Disease Transmission

A **presymptomatic case** of COVID-19 is an individual infected with SARS-CoV-2 who has not yet exhibited symptoms at the time of testing but who later exhibits symptoms during the course of the infection. An **asymptomatic case** is an individual infected with SARS-CoV-2 who does not exhibit symptoms at any time during the course of infection. Parameter values that measure the presymptomatic and asymptomatic contribution to disease transmission include:

- **Percentage of infections that are asymptomatic:** The percentage of persons who are infected with SARS-CoV-2 but never show symptoms of the disease. Asymptomatic cases are challenging to identify because individuals do not know they are infected unless they are tested over the course of their infection, which is typically done systematically only as a part of a scientific study.
- **Infectiousness of asymptomatic individuals relative to symptomatic individuals:** The contribution to transmission of SARS-CoV-2 from asymptomatic individuals compared to the contribution to transmission of SARS-CoV-2 from symptomatic individuals. For example, a parameter value of 50% means that an asymptomatic individual is half as infectious as a symptomatic individual, whereas a parameter value of 100% means that an asymptomatic individual is just as likely to transmit infection as a symptomatic individual.
- **Percentage of transmission occurring before symptom onset:** Among symptomatic cases, the percentage of new cases of COVID-19 due to transmission from a person with COVID-19 who infects others before exhibiting symptoms (presymptomatic).

Parameter values that do not vary across the five Pandemic Planning Scenarios (Table 2) are:

- **Level of pre-existing immunity to COVID-19 in the community:** The percentage of the U.S. population with existing immunity to COVID-19 before the start of the pandemic, which began in late 2019.
- **Ratio of estimated infections to reported case counts:** The estimated number of infections divided by the number of reported cases. The level of case detection likely varies by the age distribution of cases, location, and over time.
- **Time from exposure to symptom onset:** The number of days from the time a person has contact with an infected person that results in COVID-19 infection and the first appearance of symptoms.
- **Time from symptom onset in an individual and symptom onset of a second person infected by that individual:** The number of days from the time a person becomes symptomatic and when the person who they infect becomes symptomatic.

Additional parameter values common to the five COVID-19 Pandemic Planning Scenarios are these 10 measures of healthcare usage:

- Median number of days from symptom onset to SARS-CoV-2 test among SARS-CoV-2–positive patients
- Median number of days from symptom onset to hospitalization
- Median number of days of hospitalization among those not admitted to the intensive care unit (ICU)
- Median number of days of hospitalization among those admitted to the ICU
- Percentage of patients admitted to the ICU among those hospitalized
- Percentage of patients on mechanical ventilation among those hospitalized (includes both non-ICU and ICU admissions)
- Percentage of patients who die among those hospitalized (includes both non-ICU and ICU admissions)
- Median number of days on mechanical ventilation
- Median number of days from symptom onset to death (for patients who die)

- Median number of days from death to reporting of that death

These healthcare-related parameters (Table 2) assist in the assessment of resource needs as the pandemic progresses.

Box 1 Description of the Five COVID-19 Pandemic Planning Scenarios

For each Pandemic Planning Scenario:

- Parameter value for **viral transmissibility** is the Basic Reproduction Number (R_0)
- Parameter value for **disease severity** is the Infection Fatality Ratio (IFR)
- Parameter values for the **presymptomatic and asymptomatic contribution** to disease transmission are:
  - Percentage of transmission occurring before the symptom onset (from presymptomatic individuals)
  - Percentage of infections that are asymptomatic
  - Infectiousness of asymptomatic individuals relative to symptomatic individuals

For Pandemic Scenarios 1-4:

- These Scenarios are based on parameter values that represent the lower and upper bounds of disease severity and viral transmissibility. The parameter values used in these Scenarios are likely to change as we obtain additional data about the upper and lower bounds of disease severity and viral transmissibility of COVID-19.

For Pandemic Scenario 5:

- This Scenario represents a current best estimate about viral transmission and disease severity in the United States, with the same caveat: The parameter values will change as more data become available.

Scenario 1:

- Lower-bound values for virus transmissibility and disease severity
- Lower percentage of transmission before the onset of symptoms
- Lower percentage of infections that never have symptoms and lower contribution of those cases to transmission

Scenario 2:

- Lower-bound values for virus transmissibility and disease severity
- Higher percentage of transmission before the onset of symptoms
- Higher percentage of infections that never have symptoms and higher contribution of those cases to transmission

Scenario 3:

- Upper-bound values for virus transmissibility and disease severity
- Lower percentage of transmission before the onset of symptoms
- Lower percentage of infections that never have symptoms and lower contribution of those cases to transmission

Scenario 4:

- Upper-bound values for virus transmissibility and disease severity
- Higher percentage of transmission before the onset of symptoms
- Higher percentage of infections that never have symptoms and higher contribution of those cases to transmission

Scenario 5:

- Parameter values for disease severity, viral transmissibility, and presymptomatic and asymptomatic disease transmission that represent the best estimate, based on the latest surveillance data and scientific knowledge.

Table 1. Parameter Values that vary among the five COVID-19 Pandemic Planning Scenarios. The scenarios are intended to advance public health preparedness and planning. They are **not** predictions or estimates of the expected impact of COVID-19.

Parameter	Scenario 1	Scenario 2	Scenario 3	Scenario 4	Scenario 5: Current Best Estimate
R_0*	2.0		4.0		2.5
Infection fatality ratio (Estimated number of deaths per 1,000,000 infections)†	0–17 years old: 6 18–49 years old: 150 50–64 years old: 1,800 65+ years old: 26,000		0–17 years old: 80 18–49 years old: 1,700 50–64 years old: 20,000 65+ years old: 270,000		0–17 years old: 20 18–49 years old: 500 50–64 years old: 6,000 65+ years old: 90,000
Percent of infections that are asymptomatic§	15%	70%	15%	70%	30%
Infectiousness of asymptomatic individuals relative to symptomatic^	25%	100%	25%	100%	75%
Percentage of transmission occurring prior to symptom onset**	30%	70%	30%	70%	50%

* The best estimate representative of the point estimates of R0 from the following sources:

- Chinazzi M, Davis JT, Ajelli M, *et al.* The effect of travel restrictions on the spread of the 2019 novel coronavirus (COVID-19) outbreak. *Science*. 2020;368(6489):395–400; Imai N, Cori A, Dorigatti I, *et al.* (2020). Report 3: Transmissibility of 2019-nCoV. *Online report*
- Li Q, Guan X, Wu P, *et al.* Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med*. 2020;382(13):1199–1207.
- Munayco CV, Tariq A, Rothenberg R, *et al.* Early transmission dynamics of COVID-19 in a southern hemisphere setting: Lima-Peru: February 29th-March 30th, 2020. *Infect Dis Model*. 2020;5:338–345.
- Salje H, Tran Kiem C, Lefrancq N, *et al.* Estimating the burden of SARS-CoV-2 in France *Science* 2020;81(5):816-846.

The range of estimates for Scenarios 1–4 represent the upper and lower bound of the widest confidence interval estimates reported in: Li Q, Guan X, Wu P, *et al.* Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med*. 2020;382(13):1199–1207.

Substantial uncertainty remains around the R0 estimate. Notably, Sanche S, Lin YT, Xu C, *et al.* High contagiousness and rapid spread of severe acute respiratory syndrome coronavirus 2. *Emerg Infect Dis*. 2020;26(7):1470–1477. This study estimated a median R0 value of 5.7 in Wuhan, China. In an analysis of eight European countries and the United States, the same group estimated R0 of between 4.0 and 7.1 in the preprint manuscript: Ke R, Sanche S, Romero-Severson E, Hengartner N. (2020). Fast spread of COVID-19 in Europe and the United States suggests the necessity of early, strong, and comprehensive interventions. *medRxiv*.

† These estimates are based on age-specific estimates of infection fatality ratios from Levin AT, Hanage WP, Owusu-Boaitey N, *et al.* Assessing the age specificity of infection fatality rates for COVID-19: Systematic review, meta-analysis, and public policy implications. *Euro J Epidemiol*. 2020;35(12):1123–1135.

public policy implications. *Euro J Epidemiol*. 2020;35(12):1123–1138.

Using a meta regression of data from England, France, Ireland, Italy, Netherlands, Portugal, Spain, Geneva (Switzerland), Belgium, Sweden, Ontario (Canada), and 12 U.S. locations (Atlanta, Georgia; Connecticut; Indiana; Louisiana; Miami;, Minneapolis, Minnesota; Missouri; New York; Philadelphia, Pennsylvania; Salt Lake City, Utah; San Francisco, California; and Seattle, Washington), Levin *et al.* produced estimates of IFR and associated 95% confidence intervals for 0.5–year age bands from 1 to 96 years old. To obtain the estimated values for each scenario, the IFR estimates by age were averaged to broader age groups, using weights based on the age distribution of cases from COVID-19 Case Surveillance Data reported by February 14, 2021 (public use version of data: https://data.cdc.gov/Case-Surveillance/COVID-19-Case-Surveillance-Public-Use-Data/vbim-akqf).

§ The percent of cases that are asymptomatic (i.e., never experience symptoms) remains uncertain. Longitudinal testing of individuals is required to accurately detect the absence of symptoms for the full period of infectiousness. Current peer-reviewed and preprint studies vary widely in follow-up times for re-testing, or do not include re-testing of cases. Additionally, studies vary in the definition of a symptomatic case, which makes it difficult to make direct comparisons between estimates. Furthermore, the percent of cases that are asymptomatic may vary by age, and the age groups reported in the studies can vary.

Given these limitations, the range of estimates for Scenarios 1–4 is wide. The lower-bound estimate approximates the lower 95% confidence interval bound estimated from: Byambasuren O, Cardona M, Bell K, Clark J, McLaws ML, Glasziou P. Estimating the extent of asymptomatic COVID-19 and its potential for community transmission: Systematic review and meta-analysis. *Official Journal of the Association of Medical Microbiology and Infectious Disease Canada* 2020;5(4):223–234. The upper-bound estimate approximates the upper 95% confidence interval bound estimated from: Poletti P, Tirani M, Cereda D, *et al.* (2020). Probability of symptoms and critical disease after SARS-CoV-2 infection. *arXiv preprint arXiv:2006.08471*. The best estimate aligns with estimates from:

- Oran DP, Topol EJ. Prevalence of asymptomatic SARS-CoV-2 infection: A narrative review. *Ann Intern Med*. 2020;173(5):362–367.
- Oran DP, Topol EJ. The proportion of SARS-CoV-2 infections that are asymptomatic: A systematic review. [published online ahead of print, 2021 January 22] *Ann Intern Med*.
- Buitrago-Garcia D, Egli-Gany D, Counotte MJ, *et al.* Occurrence and transmission potential of asymptomatic and presymptomatic SARS-CoV-2 infections: A living systematic review and meta-analysis. *PLoS medicine*, 2020;17(9):e1003346.
- Ravindra K, Malik VS, Padhi BK, Goel S, and Gupta M. (2020) Consideration for the asymptomatic transmission of COVID-19: Systematic review and meta-analysis. *medRxiv*.
- Beale S, Hayward A, Shallcross L, Aldridge RW, and Fragaszy E. (2020) A rapid review of the asymptomatic proportion of PCR-confirmed SARS-CoV-2 infections in community settings. *medRxiv*.

^ The current best estimate is based on multiple assumptions. The relative infectiousness of asymptomatic cases to symptomatic cases remains highly uncertain, as asymptomatic cases are difficult to identify and transmission is difficult to observe and quantify. The estimates for relative infectiousness are assumptions based on studies of viral shedding dynamics. The upper bound of this estimate reflects studies that have shown similar durations and amounts of viral shedding between symptomatic and asymptomatic cases:

- Lee S, Kim T, Lee E, *et al.* Clinical course and molecular viral shedding among asymptomatic and symptomatic patients with SARS-CoV-2 infection in a community treatment center in the Republic of Korea. *JAMA Intern Med.* 2020;180(11):1–6.
- Zou L, Ruan F, Huang M, *et al.* SARS-CoV-2 viral load in upper respiratory specimens of infected patients. *N Engl J Med*. 2020;382(12):1177–1179.
- Zhou R, Li F, Chen F, *et al.* Viral dynamics in asymptomatic patients with COVID-19. *Int J Infect Dis*. 2020;96:288–290.

The lower bound of this estimate reflects data indicating that viral loads are higher in severe cases relative to mild cases (Liu Y, Yan LM, Wan L, *et al.* Viral dynamics in mild and severe cases of COVID-19. *Lancet Infect Dis*. 2020;20(6):656–657) and data showing that viral loads and shedding durations are higher among symptomatic cases relative to asymptomatic cases (Noh JY, Yoon JG, Seong H, *et al.* Asymptomatic infection and atypical manifestations of COVID-19: Comparison of viral shedding duration. *J Infect*. 2020;81(5):816–846.

** The lower bound of this parameter is approximated from the lower 95% confidence interval bound from: He X, Lau EH, Wu P, *et al*. Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nature Med*. 2020;26(5):672–675. The upper bound of this parameter is approximated from the higher estimates of individual studies included in: Casey M, Griffin J, McAloon CG, *et al*. (2020). Estimating presymptomatic transmission of COVID-19: A secondary analysis using published data. *medRxiv*. The best estimate is the geometric mean of the point estimates from these two studies and aligns with estimates from:

- Moghadas SM, Fitzpatrick MC, Sah P, *et al*. The implications of silent transmission for the control of COVID-19 outbreaks. *Proc Natl Acad Sci USA*. 2020;117(30):17513–17515.
- Johansson MA, Quandelacy TM, Kada S, *et al*. 2021. SARS-CoV-2 transmission from people without COVID-19 symptoms. *JAMA Network Open* 2021;4(1):e2035057-e2035057.

Table 2. Parameter Values Common to the Five COVID-19 Pandemic Planning Scenarios. The parameter values are likely to change as we obtain additional data about disease severity and viral transmissibility of COVID-19.

Parameter values are based on data received by CDC between December 31, 2020, and February 14, 2021, including COVID-19 Case Surveillance Data (public use version of data: https://data.cdc.gov/Case-Surveillance/COVID-19-Case-Surveillance-Public-Use-Data/vbim-akqf); data from the Hospitalization Surveillance Network (COVID-NET) (through December 31, 2020); and data from Human and Health Services Protect (*HHS Protect*) (through February 14, 2020).

Pre-existing immunity **Assumption, ASPR and CDC**	No pre-existing immunity before the pandemic began in 2019. It is assumed that all members of the U.S. population were susceptible to infection prior to the pandemic.
Time from exposure to symptom onset*	~6 days (mean)
Time from symptom onset in an individual and symptom onset of a second person infected by that individual†	~6 days (mean)
Mean ratio of estimated infections to reported case counts, overall (range)§	11 (6, 24)
Parameter Values Related to Healthcare Usage	
Median number of days from symptom onset to SARS-CoV-2 test among SARS-CoV-2 positive patients (interquartile range)^	Overall: 2 (0, 4) days
Median number of days from symptom onset to hospitalization (interquartile range)**	0–17 years old: 2 (0, 7) days 18–49 years old: 6 (2, 10) days 50–64 years old: 6 (2, 10) days ≥65 years old: 4 (1, 9) days
Median number of days of hospitalization among those not admitted to ICU (interquartile range) ††	0–17 years old: 2 (1, 4) days 18–49 years old: 3 (2, 6) days 50–64 years old: 4 (2, 7) days ≥65 years old: 5 (3, 9) days
Median number of days of hospitalization among those admitted to the ICU (interquartile range)††,§§	0–17 years old: 5 (2, 10.5) days 18–49 years old: 10 (6, 20) days 50–64 years old: 14 (8, 25) days ≥65 years old: 13 (7, 22) days

Percent admitted to the ICU among those hospitalized††	0–17 years old: 27.5% 18–49 years old: 18.9% 50–64 years old: 27.1% ≥65 years old: 26.9%
Percent on mechanical ventilation among those hospitalized. Includes both non-ICU and ICU admissions††	0–17 years old: 5.8% 18–49 years old: 9.0% 50–64 years old: 15.1% ≥65 years old: 15.6%
Percent that die among those hospitalized. Includes both non-ICU and ICU admissions††	0–17 years old: 0.7% 18–49 years old: 2.1% 50–64 years old: 7.9% ≥65 years old: 18.8%
Median number of days of mechanical ventilation (interquartile range)**	Overall: 5 (2, 11) days
Median number of days from symptom onset to death (interquartile range)**	0–17 years old: 10 (4, 31) days 18–49 years old: 17 (10, 30) days 50–64 years old: 19 (11, 30) days ≥65 years old: 16 (9, 25) days
Median number of days from death to reporting (interquartile range)^^	0–17 years old: 8 (3, 33) days 18–49 years old: 26 (5, 63) days 50–64 years old: 28 (5, 64) days ≥65 years old: 23 (4, 59) days

* McAloon C, Collins Á, Hunt K, *et al*. Incubation period of COVID-19: A rapid systematic review and meta-analysis of observational research. *BMJ Open*. 2020;10(8):e039652; Ma S, Zhang J, Zeng M, *et al*. Epidemiological parameters of COVID-19: Case series study. *J Med Internet Res.* 2020;22(10):e19994.

† He X, Lau EH, Wu P, *et al*. Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nat Med.* 2020;26(5):672–675; Saurabh S, Verma MK, Gautam V, *et al*. Transmission dynamics of the COVID-19 epidemic at the district level in India: Prospective observational study. *JMIR Public Health Surveill*. 2020;6(4):e22678.

§ The point estimate is the geometric mean of the location-specific point estimates of the ratio of estimated infections to reported cases, from Havers FP, Reed C, Lim T, *et al*. Seroprevalence of antibodies to SARS-CoV-2 in 10 sites in the United States, March 23-May 12, 2020. *JAMA Intern Med*. 2020 Jul 12. doi: 10.1001/jamainternmed.2020.4130. The lower and upper bounds for this parameter estimate are the lowest and highest point estimates of the ratio of estimated infections to reported cases, respectively.

^ Estimates only include symptom onset dates during March 1, 2020 – January 31, 2021, to ensure cases have had sufficient time to obtain SARS-CoV-2 tests. Estimates represent time to obtain SARS-CoV-2 tests among cases who tested positive for SARS-CoV-2. Estimates are based on line-level case surveillance data reported to CDC.

** Estimates only include symptom onset dates during March 1, 2020 – January 31, 2021, to ensure cases have had sufficient time to observe the outcome (hospital discharge or death).

†† Based on data reported to COVID-NET by December 31, 2020. https://gis.cdc.gov/grasp/COVIDNet/COVID19_5.html

§§ Cumulative length of stay for persons admitted to the ICU, inclusive of both ICU and non-ICU days.

^^ Estimates only include death dates between March 1, 2020 – January 31, 2021, to ensure sufficient time for reporting.

References

1. Levin AT, Hanage WP, Owusu-Boaitey N, *et al*. Ass ssing he ag sp cificity of inf c ion fatality rates for COVID- 9: Systematic review, meta-analysis, and public policy implications. *Euro J Epidemiol*. 2020;35(12):1123–1138
2. Dietz K. The estimation of the basic reproduction number for infectious diseases. *Stat Methods Med Res*. 993;2:23–41
3. Delamater PL, Street EJ, Lesli TF, *et al*. Complexity of the basic reproduction number (R0). *Emerg Infect Dis* 2019;25(1):1

Archive

COVID-19 Pandemic Planning Scenarios – May 20, 2020 [7 pag s]

COVID-19 Pandemic Planning Scenarios – July 10, 2020 [9 pages]

COVID-19 Pandemic Planning Scenarios – September 10, 2020 [9 Pages]

Last Upda ed Mar. 19, 2021

/

EXHIBIT C

REVIEW SUMMARY

CORONAVIRUS

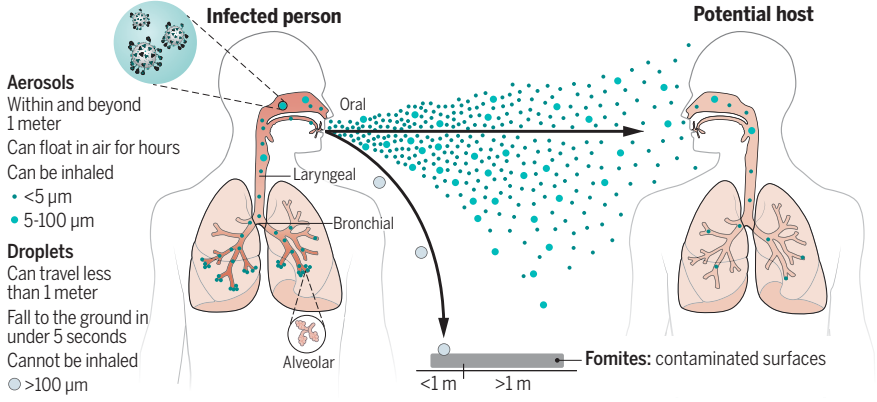
Airborne transmission of respiratory viruses

Chia C. Wang*, Kimberly A. Prather*, Josué Sznitman, Jose L. Jimenez, Seema S. Lakdawala, Zeynep Tufekci, Linsey C. Marr

BACKGROUND: Exposure to droplets produced in the coughs and sneezes of infected individuals or contact with droplet-contaminated surfaces (fomites) have been widely perceived as the dominant transmission modes for respiratory pathogens. Airborne transmission is traditionally defined as involving the inhalation of infectious aerosols or "droplet nuclei" smaller than 5 μm and mainly at a distance of >1 to 2 m away from the infected individual, and such transmission has been thought to be relevant only for "unusual" diseases. However, there is robust evidence supporting the airborne transmission of many respiratory viruses, including severe acute respiratory syndrome coronavirus (SARS-CoV), Middle East respiratory syndrome (MERS)–CoV, influenza virus, human rhinovirus, and respiratory syncytial virus (RSV). The limitations of traditional views of droplet, fomite, and airborne transmission were illuminated during the COVID-19 pandemic. Droplet and fomite transmission of SARS-CoV-2 alone cannot account for the numerous superspreading events and differences in transmission between indoor and outdoor environments observed during the COVID-19 pandemic. Controversy surrounding how COVID-19 is transmitted and what interventions are needed to control the pandemic has revealed a critical need to better understand the airborne transmission pathway of respiratory viruses, which will allow for better-informed strategies to mitigate the transmission of respiratory infections.

ADVANCES: Respiratory droplets and aerosols can be generated by various expiratory activities. Advances in aerosol measurement techniques, such as aerodynamic and scanning mobility particle sizing, have shown that the majority of exhaled aerosols are smaller than 5 μm, and a large fraction are <1 μm for most respiratory activities, including those produced during breathing, talking, and coughing. Exhaled aerosols occur in multiple size modes that are associated with different generation sites and production mechanisms in the respiratory tract. Although 5 μm has been used historically to distinguish aerosols from droplets, the size distinction between aerosols and droplets should be 100 μm, which represents the largest particle size that can remain suspended in still air for more than 5 s from a height of 1.5 m, typically reach a distance of 1 to 2 m from the emitter (depending on the velocity of airflow carrying the aerosols), and can be inhaled. Aerosols produced by an infected individual may contain infectious viruses, and studies have shown that viruses are enriched in small aerosols (<5 μm). The transport of virus-laden aerosols is affected by the physicochemical properties of aerosols themselves and environmental factors, including temperature, relative humidity, ultraviolet radiation, airflow, and ventilation. Once inhaled, virus-laden aerosols can deposit in different parts of the respiratory tract. Larger aerosols tend to be deposited in the upper airway; however, smaller aerosols, although they can also be deposited there, can penetrate deep into the alveolar region of the lungs. The strong effect of ventilation on transmission, the distinct difference between indoor and outdoor transmission, well-documented long-range transmission, the observed transmission of SARS-CoV-2 despite the use of masks and eye protection, the high frequency of indoor superspreading events of SARS-CoV-2, animal experiments, and airflow simulations provide strong and unequivocal evidence for airborne transmission. Fomite transmission of SARS-CoV-2 has been found to be far less efficient, and droplets are only dominant when individuals are within 0.2 m of each other when talking. Although both aerosols and droplets can be produced by infected individuals during expiratory activities, droplets fall quickly to the ground or surfaces within seconds, leaving an enrichment of aerosols over droplets. The airborne pathway likely contributes to the spread of other respiratory viruses whose transmission was previously characterized as droplet driven. The World Health Organization (WHO) and the US Centers for Disease Control and Prevention (CDC) have officially acknowledged the inhalation of virus-laden aerosols as a main transmission mode in spreading COVID-19 at both short and long ranges in 2021.

OUTLOOK: Airborne transmission of pathogens has been vastly underappreciated, mostly because of an insufficient understanding about the airborne behavior of aerosols and at least partially because of the misattribution of anecdotal observations. Given the lack of evidence for droplet and fomite transmission and the increasingly strong evidence for aerosols in transmitting numerous respiratory viruses, we must acknowledge that airborne transmission is much more prevalent than previously recognized. Given all that we have learned about SARS-CoV-2 infection, the aerosol transmission pathway needs to be reevaluated for all respiratory infectious diseases. Additional precautionary measures must be implemented for mitigating aerosol transmission at both short and long ranges, with particular attention to ventilation, airflows, air filtration, UV disinfection, and mask fit. These interventions are critical tools for ending the current pandemic and preventing future outbreaks. ■



CREDIT: N. CARY/*SCIENCE*

Phases involved in airborne transmission of respiratory viruses. Virus-laden aerosols (<100 μm) are first generated by an infected individual through expiratory activities, through which they are exhaled and transported in the environment. They may be inhaled by a potential host to initiate a new infection, provided that they remain infectious. In contrast to droplets (>100 μm), aerosols can linger in air for hours and travel beyond 1 to 2 m from the infected individual who exhales them, causing new infections at both short and long ranges.

The list of author affiliations is available in the full article online.
*Corresponding author. Email: chiawang@mail.nsysu.edu.tw (C.C.W.); kprather@ucsd.edu (K.A.P.)

Cite this article as C. C. Wang *et al.*, *Science* **373**, eabd9149 (2021). DOI: 10.1126/science.abd9149

READ THE FULL ARTICLE AT
https://doi.org/10.1126/science.abd9149

REVIEW

CORONAVIRUS

Airborne transmission of respiratory viruses

Chia C. Wang[1,2]*, Kimberly A. Prather[3]*, Josué Sznitman[4], Jose L. Jimenez[5], Seema S. Lakdawala[6], Zeynep Tufekci[7], Linsey C. Marr[8]

The COVID-19 pandemic has revealed critical knowledge gaps in our understanding of and a need to update the traditional view of transmission pathways for respiratory viruses. The long-standing definitions of droplet and airborne transmission do not account for the mechanisms by which virus-laden respiratory droplets and aerosols travel through the air and lead to infection. In this Review, we discuss current evidence regarding the transmission of respiratory viruses by aerosols—how they are generated, transported, and deposited, as well as the factors affecting the relative contributions of droplet-spray deposition versus aerosol inhalation as modes of transmission. Improved understanding of aerosol transmission brought about by studies of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection requires a reevaluation of the major transmission pathways for other respiratory viruses, which will allow better-informed controls to reduce airborne transmission.

Over the past century, respiratory viruses were thought to be spread mainly through large respiratory droplets, produced in the coughs and sneezes of infected individuals that deposit on the mucous membranes of the eyes, nose, or mouth of potential hosts (droplet transmission) or that deposit on surfaces that are then touched by potential hosts and transferred to mucous membranes (fomite transmission). Such droplets are thought to fall to the ground within 1 to 2 m of the infectious person—a key assumption used by most public health agencies in recommending a safe distance from people infected with respiratory viruses. Thought to be less common, airborne transmission refers to the inhalation of infectious aerosols or "droplet nuclei" (droplets that evaporate in the air), often defined to be smaller than 5 μm and traveling distances of >1 to 2 m away from the infected individual. Aerosols are microscopic liquid, solid, or semisolid particles that are so small that they remain suspended in air. Respiratory aerosols are produced during all expiratory activities, including breathing, talking, singing, shouting, coughing, and sneezing from both healthy individuals and those with respiratory infections (*1*–*4*).

[1]Aerosol Science Research Center, National Sun Yat-sen University, Kaohsiung, Taiwan 804, Republic of China. [2]Department of Chemistry, National Sun Yat-sen University, Kaohsiung, Taiwan 804, Republic of China. [3]Scripps Institution of Oceanography, University of California San Diego, La Jolla, CA 92037, USA. [4]Department of Biomedical Engineering, Israel Institute of Technology, Haifa 32000, Israel. [5]Department of Chemistry and CIRES, University of Colorado, Boulder, CO 80309, USA. [6]Department of Microbiology and Molecular Genetics, University of Pittsburgh School of Medicine, Pittsburgh, PA 15219, USA. [7]School of Information and Department of Sociology, University of North Carolina, Chapel Hill, NC 27599, USA. [8]Department of Civil and Environmental Engineering, Virginia Tech, Blacksburg, VA 24061, USA.
*Corresponding author. Email: chiawang@mail.nsysu.edu.tw (C.C.W.); kprather@ucsd.edu (K.A.P.)

The historical definition of airborne transmission ignores the possibility that aerosols can also be inhaled at close range to an infected person, where exposure is more likely because exhaled aerosols are more concentrated closer to the person emitting them. Moreover, rather than the conventional definition of 5 μm, it has recently been suggested that the size distinction between aerosols and droplets should be updated to 100 μm, as this distinguishes between the two on the basis of their aerodynamic behavior (*5*–*7*). Specifically, 100 μm represents the largest particles that remain suspended in still air for >5 s (from a height of 1.5 m), travel beyond 1 m from the infectious person, and can be inhaled. Although droplets produced by an infectious individual through coughing or sneezing may convey infection at short distances (<0.5 m), the number and viral load of aerosols produced through speaking and other expiratory activities are much higher than those of droplets (*8*–*10*). Aerosols are small enough to linger in air, accumulate in poorly ventilated spaces, and be inhaled at both short and long ranges, calling for an urgent need to include aerosol precautions in current respiratory disease control protocols. During the COVID-19 pandemic, controls have focused mainly on protecting against droplet and fomite transmission, whereas the airborne route has required much more evidence before controls can be added to protect against it.

Debates surrounding the relative importance of different transmission modes in spreading respiratory disease have spanned centuries. Before the 20th century, infectious respiratory diseases were thought to spread by "pestilential particles" released by infected individuals (*11*, *12*). This view of airborne transmission was dismissed in the early 1900s by Charles Chapin, who claimed that contact was the chief route for respiratory disease transmission, with spray-borne (droplet) transmission being an extension of contact transmission (*13*). Chapin was concerned that mentioning transmission by air would scare people into inaction and displace hygiene practices. Chapin erroneously equated infections at close range with droplet transmission—neglecting the fact that aerosol transmission also occurs at short distances. This unsupported assumption became widespread in epidemiological studies (*14*), and mitigation strategies for controlling respiratory virus transmission have since focused on limiting droplet and fomite transmission (*15*). Some of these strategies are also partially effective for limiting aerosol transmission, leading to the erroneous conclusion that their efficacy proved droplet transmission.

Despite the assumed dominance of droplet transmission, there is robust evidence supporting the airborne transmission of many respiratory viruses, including measles virus (*16*–*18*), influenza virus (*19*–*24*), respiratory syncytial virus (RSV) (*25*), human rhinovirus (hRV) (*9*, *26*–*28*), adenovirus, enterovirus (*29*), severe acute respiratory syndrome coronavirus (SARS-CoV) (*30*, *31*), Middle East respiratory syndrome coronavirus (MERS-CoV) (*32*), and SARS-CoV-2 (*33*–*36*) (Table 1). Airborne transmission has been estimated to account for approximately half of the transmission of influenza A virus in one study of a household setting (*20*). A human challenge study on rhinovirus transmission concluded that aerosols were likely the dominant transmission mode (*26*). SARS-CoV-2 infection of hamsters and ferrets has been shown to transmit through air in experimental configurations designed to exclude contributions from direct contact and droplet transmission (*33*, *37*, *38*). Analysis of respiratory emissions during infection with influenza virus, parainfluenza virus, RSV, human metapneumovirus, and hRV has revealed the presence of viral genomes in a variety of aerosol sizes, with the highest amount detected in aerosols <5 μm rather than in larger aerosols (*39*). SARS-CoV-2 RNA has been detected and infectious virus has been recovered in aerosols ranging from 0.25 to >4 μm (*34*, *35*, *40*–*44*). Influenza virus RNA has also been detected in both fine (≤5 μm) and coarse (>5 μm) aerosols exhaled from infected individuals, with more viral RNA contained in the fine aerosol particles (*23*). Laboratory studies have found that aerosolized SARS-CoV-2 has a half-life of ~1 to 3 hours (*45*–*47*). The World Health Organization (WHO) and the US Centers for Disease Control and Prevention (CDC) officially acknowledged inhalation of virus-laden aerosols as a main mode in spreading SARS-CoV-2 at both short and long ranges in April and May of 2021, respectively (*48*, *49*).

Mathematical modeling of exposure to respiratory pathogens supports that transmission

Table 1. Airborne transmission of respiratory viruses. Representative evidence of airborne transmission for various respiratory viruses and their basic reproduction number. Cells with dashes indicate not applicable.

Virus name	Scope of studies and/or approaches							Basic reproduction number (R_0)
	Air sampling and PCR	Air sampling and cell culture	Animal models	Laboratory or clinical studies	Epidemiological analysis	Simulation and modeling	Size-resolved information	
SARS-CoV	(*31*)	(*31*)	–	(*30*)	(*30*)	(*30*)	–	2.0–3.0 (*197*)
MERS-CoV	(*32*)	(*32*, *103*)	(*103*, *198*)	(*32*)	–	–	–	0.50–0.92 (*197*)
SARS-CoV-2	(*41*–*44*)	(*34*, *35*, *40*)	(*33*, *37*, *199*)	(*34*, *45*, *107*)	(*36*, *64*, *71*, *72*, *186*)	(*36*, *50*)	(*34*, *41*, *43*)	1.4–8.9 (*57*, *58*)
Influenza virus	(*22*, *23*, *98*, *102*, *106*)	(*23*, *98*, *101*)	(*24*, *137*, *200*, *201*)	(*24*, *138*, *202*, *203*)	(*20*)	(*20*, *114*, *204*)	(*23*, *105*, *106*)	1.0–21 (*205*)
Rhinovirus	(*9*, *27*)	(*26*, *28*)	–	(*26*–*28*)	–	(*27*)	(*9*)	1.2–2.7 (*205*)
Measles virus	(*16*)	(*16*)	–	–	(*17*)	(*17*)	(*16*)	12–18 (*206*)
Respiratory syncytial virus (RSV)	(*102*)	(*25*)	–	(*25*)	–	–	(*25*)	0.9–21.9 (*205*)

is dominated by short-range aerosol inhalation at most distances within 2 m of the infectious person, and droplets are only dominant when individuals are within 0.2 m when talking or 0.5 m when coughing (*50*). Anecdotal observations of measles virus (*16*–*18*) and *Mycobacterium tuberculosis* (*51*, *52*) infection in close proximity, previously attributed solely to droplets, include transmission by aerosols at short range. Further studies are warranted for respiratory diseases whose transmission has previously been characterized as droplet driven because it is plausible that airborne transmission is important or even dominant for most of them.

Early in the COVID-19 pandemic, it was assumed that droplets and fomites were the main transmission routes on the basis of the relatively low basic reproduction number (R_0) compared with that of measles (*53*–*55*) (Table 1). R_0 is the average number of secondary infections caused by a primary infected individual in a homogeneously susceptible population. This argument was built on a long-standing belief that all airborne diseases must be highly contagious. However, there is no scientific basis for such an assumption because airborne diseases exhibit a range of R_0 values that cannot be well represented by a single average value, which depends on numerous factors. For example, tuberculosis (R_0, 0.26 to 4.3) is an obligate airborne bacterial infection (*56*), but it is less transmissible than COVID-19 (R_0, 1.4 to 8.9) (*57*–*59*). The factors affecting airborne transmission include viral load in different-sized respiratory particles, the stability of the virus in aerosols, and the dose-response relationship for each virus (the probability of infection given exposure to a certain number of virions through a particular exposure route). Moreover, R_0 is an average, and COVID-19 is greatly overdispersed, meaning that, under certain conditions, it can be highly contagious. Epidemiological studies have found that 10 to 20% of infected individuals account for 80 to 90% of subsequent infections for SARS-CoV-2, highlighting the heterogeneity in secondary attack rates (the proportion of exposed individuals who become infected) (*60*–*63*).

A growing body of research on COVID-19 provides abundant evidence for the predominance of airborne transmission of SARS-CoV-2. This route dominates under certain environmental conditions, particularly indoor environments that are poorly ventilated (*6*, *34*, *35*, *41*, *42*, *45*, *50*, *64*–*68*), an observation that implicates solely aerosols because only aerosols—and not large droplets or surfaces—are affected by ventilation. Moreover, the marked difference between rates of indoor and outdoor transmission can only be explained by airborne transmission, because large droplets, whose trajectories are affected by gravitational settling but not ventilation, behave identically in both settings (*69*). Various combinations of epidemiological analyses; airflow model simulations; tracer experiments; and analysis and modeling of superspreading events in restaurants (*36*), in meatpacking plants (*70*), on a cruise ship (*71*), during singing at a choir rehearsal (*64*), and the long-distance transmission at a church (*72*) all implicate aerosols as the most likely mode of transmission over fomites and droplets. It is highly unlikely that most people at any of these events all touch the same contaminated surface or are exposed to droplets produced from the cough or sneeze of an infectious person at close range and encounter sufficient virus load to cause infection. However, the one common factor for all people at these indoor events is the shared air they inhale in the same room. Commonalities among superspreading events include indoor settings, crowds, exposure durations of 1 hour or more, poor ventilation, vocalization, and lack of properly worn masks (*36*). Given that droplet transmission dominates only when individuals are within 0.2 m when talking (*50*) and that transmission of SARS-CoV-2 through contaminated surfaces is less likely (*73*–*75*), superspreading events can only be explained by including aerosols as a mode of transmission.

To establish effective guidance and policies for protecting against airborne transmission of respiratory viruses, it is important to better understand the mechanisms involved. For airborne transmission to occur, aerosols must be generated, transported through air, inhaled by a susceptible host, and deposited in the respiratory tract to initiate infection. The virus must retain its infectivity throughout these processes. In this Review, we discuss the processes involved in the generation, transport, and deposition of virus-laden aerosols, as well as the important parameters that influence these processes, which are critical to informing effective infection control measures (Fig. 1).

Generation of virus-laden aerosols

Expiratory activities produce aerosols from different sites in the respiratory tract through distinct mechanisms. Aerosols produced by activities such as breathing, speaking, and coughing exhibit different aerosol size distributions and airflow velocities (*76*, *77*), which in turn govern the types and loads of viruses that each aerosol particle may carry, the residence time in air, the distance traveled, and ultimately the deposition sites in the respiratory tract of a person who inhales them (*78*). Aerosols released by an infected individual may contain viruses (*39*, *79*–*81*) as well as electrolytes, proteins, surfactants, and other components in the fluid that lines respiratory surfaces (*82*, *83*) (Fig. 2).

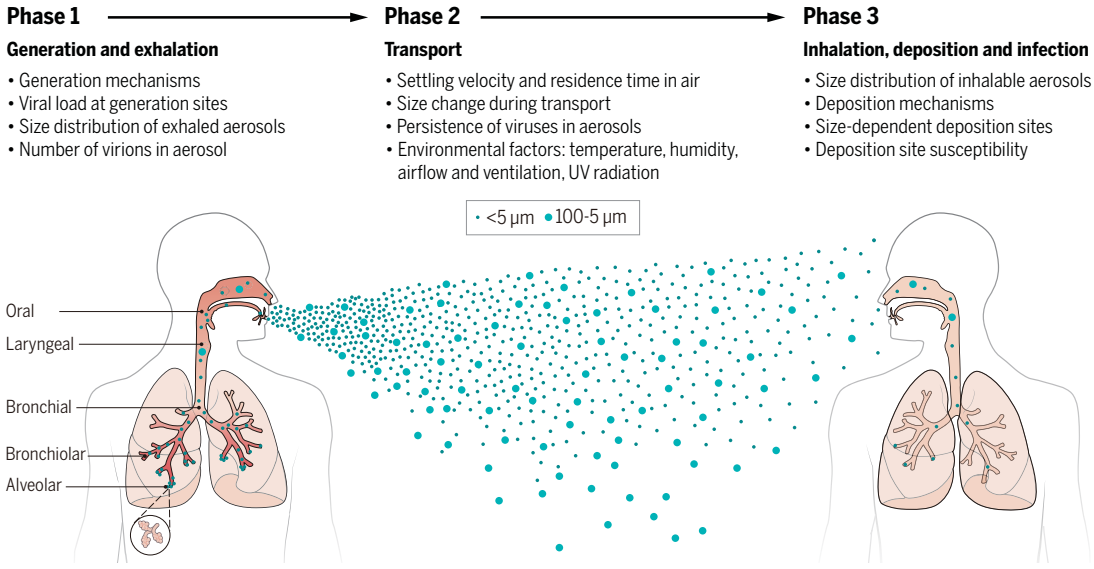


Fig. 1. Airborne transmission of respiratory viruses. Phases involved in the airborne transmission of virus-laden aerosols include (i) generation and exhalation; (ii) transport; and (iii) inhalation, deposition, and infection. Each phase is influenced by a combination of aerodynamic, anatomical, and environmental factors. (The sizes of virus-containing aerosols are not to scale.)

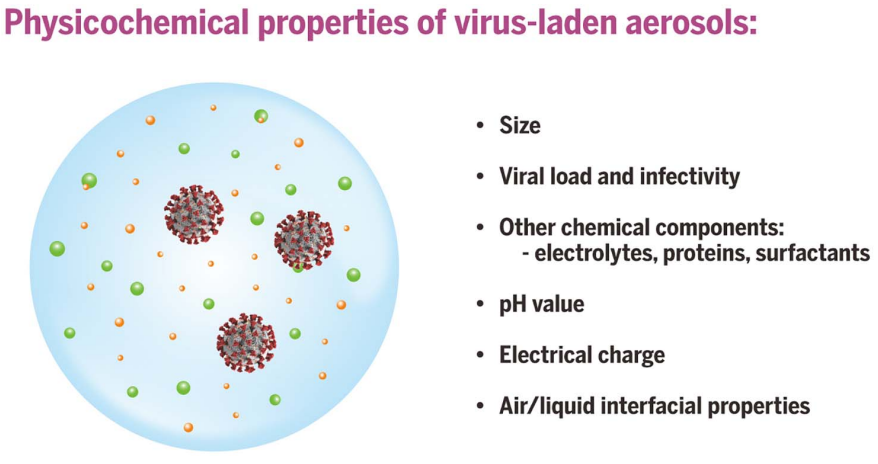


Fig. 2. Physicochemical properties of virus-laden aerosols. The behavior and fate of virus-laden aerosols are inherently governed by their characteristic properties, including physical size, viral load, infectivity, other chemical components in the aerosol, electrostatic charge, pH, and the air-liquid interfacial properties.

Sites of aerosol formation

Respiratory aerosols can be classified into alveolar, bronchiolar, bronchial, laryngeal, and oral aerosols, according to the sites where they are produced (*3*, *84*, *85*). Bronchiolar aerosols are formed during normal breathing (*3*). During exhalation, the liquid film lining the lumenal surfaces of the bronchioles ruptures to produce small aerosols. Such aerosols are generated by shear forces that destabilize the air-liquid or air-mucous interface. Respiratory airflows are often turbulent under high airflow velocities, particularly in the large lumens of the upper airways, which transition to laminar flow in the bronchi and bronchioles (*76*, *86*–*88*). Laryngeal aerosols are generated through vocal fold vibrations during vocalization (*3*). The apposition of vocal folds forms liquid bridges, which burst into aerosols during exhalation. By contrast, droplets (>100 μm) are primarily produced from saliva in the oral cavity (*3*). Aerosol emission rates increase with airflow velocity and speech volume during activities such as singing and shouting (*9*, *89*, *90*).

Number and size distributions

The size of exhaled aerosols is one of the most influential properties governing their fate, because size not only determines their aerodynamic characteristics but also their deposition dynamics and the site of infection. Size distributions of respiratory aerosols have been investigated since the 1890s using various approaches, including optical microscopy, high-speed photography, and, more recently, laser-based detection techniques (*1*, *2*, *91*). Early studies used measuring techniques and analytical methods that were unable to detect aerosols <5 μm (*1*, *92*), but current instruments, such as aerodynamic and scanning mobility particle sizing systems, have enabled the detection of smaller aerosols. Respiratory aerosols produce a multimodal size distribution, with peaks around 0.1 μm, 0.2 to 0.8 μm, 1.5 to 1.8 μm, and 3.5 to 5.0 μm, each representing a different generation site, production process, and expiratory activity (*2*, *8*, *9*, *85*, *91*, *93*). The smaller the modal size, the deeper the aerosols originate in the respiratory tract. A larger mode centered at 145 μm for talking and 123 μm for coughing originates mainly from the oral cavity and lips (*3*). In terms of number, the majority of exhaled aerosols are <5 μm, and a large fraction are <1 μm for most respiratory activities, including those produced during breathing, talking, and coughing (*8*, *9*). Overall, speech produces 100 to 1000 times the number of aerosols <100 μm in size for every droplet that is >100 μm (*3*).

Normal breathing has been shown to release up to 7200 aerosol particles per liter of exhaled air (*9*, *93*). The number of virus-laden aerosols expelled by individuals while breathing varies widely between individuals and depends on disease stage, age, body mass index,

and preexisting health conditions (*94*, *95*). Children generally produce fewer virus-laden aerosols than adults because their lungs are still developing and have fewer bronchioles and alveoli in which aerosols can form (*96*). The processes involved in aerosol formation, particularly the properties of fluid lining the airways that affect its propensity to break up to form aerosols, plays a crucial role in the number of aerosols exhaled (*94*). One study showed that 1 min of speaking may produce at least 1000 aerosols (*97*). Although coughing can produce more aerosols in a short period of time, it is much more sporadic than continuous breathing and speaking, especially for infected individuals who display no clinical symptoms. Therefore, breathing, speaking, and other continuous vocalization by infected individuals will likely release more total virus-laden aerosols overall than less-frequent coughing.

Viral content of aerosols

The viral load of aerosols is a key factor in determining the relative contribution of airborne transmission. However, sampling and detecting airborne viruses is challenging because of their low concentrations in air and susceptibility to destruction and inactivation during sampling. Air samples are often analyzed for the presence of viral genomes by quantitative polymerase chain reaction (qPCR) or quantitative reverse transcription PCR (qRT-PCR) methods, which are highly sensitive. Nevertheless, the presence of genetic material alone does not indicate whether the virus is infectious. The viability of viruses depends on the integrity and function of their genomic material, nucleoprotein, capsid, and/or envelope. Although some studies have tried and failed to culture viruses from air, the use of more gentle methods, such as a liquid condensation collection device, has enabled the detection of numerous viable respiratory viruses, including influenza viruses and SARS-CoV-2 in aerosols (*35*, *40*, *98*).

Many viruses have been isolated from breath and indoor air samples, including adenovirus (*29*, *99*), coxsackievirus (*100*), influenza viruses (*22*, *23*, *98*, *101*), rhinovirus (*9*, *26*–*28*), measles virus (*16*, *17*), RSV (*25*, *102*), SARS-CoV (*31*), MERS-CoV (*32*, *103*), and SARS-CoV-2 (*34*, *35*, *40*–*44*) (Table 1). The concentration of SARS-CoV-2 in the air of a hospital room with two COVID-19 patients was between 6 and 74 $TCID_{50}$ per liter (median tissue culture infectious dose per liter) (*35*). The distribution of virions across different sizes of aerosol particles is related to their site of generation, the production mechanism, and the severity of infection at the generation site, which varies among different viruses (*104*). It is commonly assumed that viral concentrations in clinical samples (e.g., sputum or saliva) translate directly to the concentration in droplets and aerosols generated from respiratory fluid—i.e., that viral load scales with the initial volume of droplets and aerosols (*50*, *55*, *71*). However, size-segregated samples of aerosols collected in the exhaled breath of individuals infected with influenza A or B viruses, parainfluenza virus, coronaviruses, hRV, or RSV and air collected in various settings show that viruses are enriched in smaller aerosols (*10*). In samples collected from influenza patients while breathing, talking, and/or coughing, more than half of the viral RNA was found in aerosols <4 to 5 μm (*23*, *104*, *105*). A study of several respiratory viruses found viral RNA more commonly in small (<5 μm) than in large aerosols (*39*). The distribution of influenza virus and RSV in ambient aerosols measured in a medical clinic revealed that 42% of influenza A virus RNA, but only 9% of RSV RNA, was in aerosols ≤4 μm (*102*). In a study that collected aerosols in a health clinic, childcare center, and airplanes, more than half of influenza A virus RNA was found in aerosols <2.5 μm (*106*). A study found that a subset of COVID-19 patients release up to 10^5 to 10^7 SARS-CoV-2 genome copies per hour in exhaled breath, whereas others do not exhale detectable virus (*107*). Large interpersonal variability in both the number of aerosols produced and their viral load may contribute to overdispersion in COVID-19 transmission, a crucial component in superspreading events (*108*).

Although infectious viruses are enriched in small aerosols, the dose-response relationship that governs the probability of infection given exposure to a certain number of virions, remains to be determined. In a susceptible host, the minimum infectious dose varies on the basis of virus type and deposition site within the respiratory tract, such that the inhalation of smaller aerosols that deposit deeper in the lungs could require less virus to initiate infection. Studies on influenza virus have shown that the dose required to initiate infection in humans, in terms of plaque-forming units (PFU), is, for the inhalation of aerosols, about a hundredth the size of the dose for intranasal inoculation (*101*). Improved characterization of the viral load and distribution of infectious virions in individual aerosols as a function of particle size, for different people and stages of disease, will greatly contribute to our understanding of airborne transmission of respiratory viruses.

Virus-laden aerosols in the environment

The physical characteristics of aerosols affect their transport in air. The initial velocity of respiratory aerosols depends on how they are generated within and released from the respiratory tract; for example, coughing produces droplets and aerosols released at higher velocities than speaking (*109*). Aerosol transport is controlled by a combination of airflow and environmental properties and by the physical characteristics of the aerosols themselves. Aerosols may diverge from streamlines as a result of inertia, Brownian motion, and external

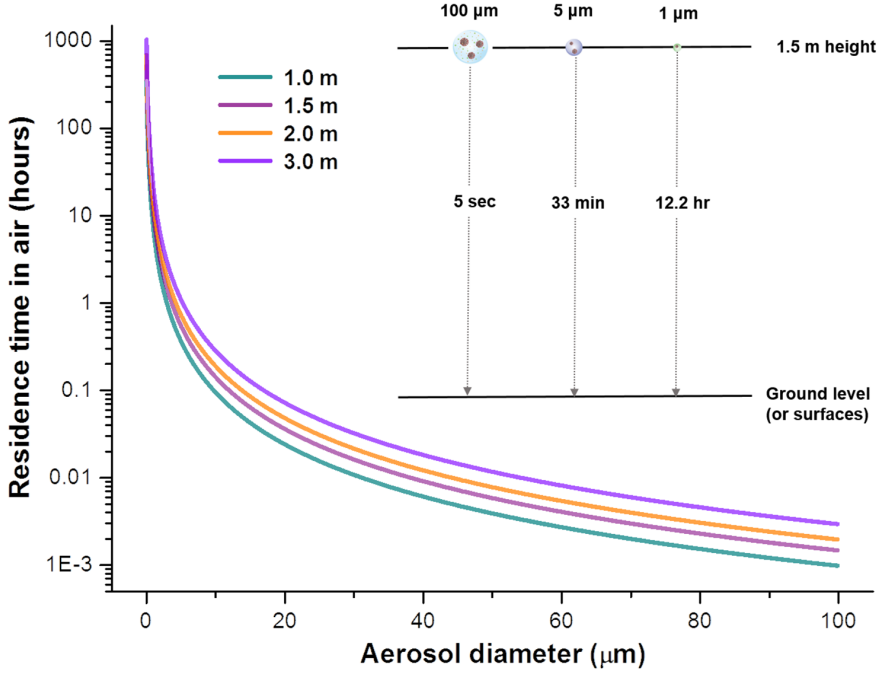


Fig. 3. How long can aerosols linger in air? Residence time of aerosols of varying size in still air can be estimated from Stokes' law for spherical particles (*116*). For example, the time required for an aerosol of 100, 5, or 1 μm to fall to the ground (or surfaces) from a height of 1.5 m is 5 s, 33 min, or 12.2 hours, respectively.

forces including gravitational, electrophoretic, and thermophoretic forces. Such motions can also lead to removal from air by deposition on surfaces. The lifetime of viruses in air is a function of physical transport and biological inactivation, which are affected by environmental factors, such as temperature, humidity, and ultraviolet (UV) radiation.

The sizes of exhaled aerosols that remain airborne evolve over time as a result of evaporation, coagulation, and/or deposition. Evaporation of water from aqueous aerosols is normally described by the Hertz-Knudsen equation (*110*). However, because respiratory aerosols contain nonvolatile components including proteins, electrolytes, and other biological species, the evaporation rate is slower than that of pure water (*111*). During evaporation, aerosols are subject to changes in phase, morphology, viscosity, and pH, all of which have been studied in simulated but not actual respiratory aerosols (*83*, *112*). Changes in physical characteristics of aerosols will affect the transport and fate of any viruses they contain, and associated changes in chemical characteristics of aerosols can affect virus viability (*113*). The overall size distributions of virus-laden aerosols in air also evolve over time because larger aerosols are preferentially removed by sedimentation to the ground or other surfaces, causing the median of the distribution to shift toward smaller sizes (*114*).

The residence time of virus-laden aerosols in air is crucial in determining their range of spread. In the absence of other forces, the residence time of an aerosol of a specific size is related to its terminal settling velocity, u_p, resulting from a balance between the viscous drag force and the gravitational force, as described by Stokes' law for small particles subject to laminar flow (*115*, *116*)

$$u_p = \frac{d_p^2 g \rho_p C_c}{18\eta}$$

where d_p is the diameter of the aerosol particle, g is gravitational acceleration, ρ_p is the density of the aerosol particle, C_c is the Cunningham slip correction factor accounting for the reduced air resistance caused by slippage when the particle size becomes comparable to the mean free path of gas molecules, and η is the dynamic viscosity of air.

The settling time for aerosols of a specific size to reach the ground can thus be estimated on the basis of an assumption that the surrounding air is at rest (Fig. 3). In still air, a 5-μm aerosol takes 33 min to settle to the ground from a height of 1.5 m, whereas a 1-μm aerosol can remain suspended in air for >12 hours (*116*). However, in most realistic environments, the velocity of the surrounding airflow should be taken into consideration. Additionally, when respiratory aerosols are exhaled, these particles are contained in an exhaled humid plume with its own speed and trajectory, which also play a role in determining the final reachable distance and direction (*86*). The distance that virus-laden aerosols travel depends on aerosol size, initial velocity of the flow carrying them, and other environmental conditions, such as outdoor wind speed or indoor air currents induced by natural ventilation or heating, ventilation, and air conditioning (HVAC) systems (*117*, *118*). The concentration of exhaled aerosols is highest close to the source (i.e., the infectious individual) and decreases with distance as the respiratory plume mixes with ambient air (*50*, *119*).

The trajectory and evaporation of exhaled aerosols generated during coughing and speaking have been studied with computational modeling (*117*, *120*). Large droplets tend to reach their maximum horizontal distances quickly and fall to the ground or surfaces within a few meters, whereas aerosols can remain suspended for many seconds to hours, travel long distances, and accumulate in air in poorly ventilated spaces (*117*). The multiphase nature of virus-laden aerosol flows greatly affects flow dynamics and how far aerosols travel, especially for exhalations with higher airflow velocities, such as in a cough (*121*).

Environmental factors that affect aerosol transmission

Survival of viruses in aerosols, also known as persistence, stability, or retention of infectivity, is commonly determined experimentally using a rotating drum, which allows the aerosols to remain suspended longer than in a stationary chamber. The decay of the virus can be described by first-order kinetics

$$C = C_o \times e^{-kt}$$

where C is the concentration of infectious viruses at time t, C_o is the initial concentration of infectious viruses, and k is the inactivation rate constant (*122*). The inactivation rate constant differs by virus and depends on a number of factors, including temperature, humidity, UV radiation, and chemical composition of the fluid from which the virus was aerosolized (*45*, *46*, *123*). This dependence, especially on respiratory fluid composition, makes it challenging to compare results across different studies. The time needed to reach 99.99% inactivation varies from hours to months (*124*). The decay rate can be quantified in terms of the half-life, which is ~1 to 3 hours for SARS-CoV and SARS-CoV-2 in laboratory-generated aerosols (*125*–*127*).

Temperature

Temperature is critical in mediating the survival and transmission of viruses in aerosols (*125*, *128*, *129*), likely by affecting the stability of the proteins, lipids, and genetic material that make up the virus. The upper respiratory tract is maintained at a few degrees cooler than the lungs (*130*), suggesting an enhanced replication capacity in the upper respiratory tract (*131*). SARS-CoV (*132*), SARS-CoV-2 (*133*), and influenza virus (*134*) are more stable at lower temperatures, possibly because of slower decay rates (as governed by the Arrhenius equation) and stronger ordering of phospholipids for enveloped viruses. Epidemiological evidence and animal studies suggest that the transmission of respiratory viruses known to infect the upper airways is favored at lower temperatures (*128*, *135*).

Relative humidity

By modulating the evaporation rate and equilibrium size of aerosols, relative humidity (RH) affects their transport and the viability of viruses they contain (*113*, *114*, *129*). Respiratory aerosols undergo evaporation upon release from the respiratory tract into ambient air as they transition from a saturated environment to lower RH. The evaporation process is expected to take seconds (*114*, *136*). At lower ambient RH, evaporation occurs more quickly and equilibrates at a smaller equilibrium size (*136*). At RH below ~80%, respiratory aerosols reach a final diameter that is 20 to 40% of the original size (*129*).

The seasonality of cases of influenza virus, human coronaviruses that cause common colds, RSV, and others has been at least partially attributed to RH (*134*). The sensitivity of a virus to RH may be influenced by RH-related effects on virus persistence in the environment and/or immune defenses. Mucociliary clearance is not as efficient at low RH (*134*). Animal studies have shown that influenza virus transmission is favored at low RH (*135*, *137*); however, a study of the 2009 pandemic influenza A virus (H1N1) in more physiologically realistic medium reported that the virus remained highly stable and infectious over a broad RH range between 20 and 100% (*138*). A study investigated the sensitivity of 11 airborne viruses to RH and found that although some RNA viruses survived best at low RH, other viruses survived better at high RH (*139*). The relationship between RH and virus viability in droplets and aerosols is characteristic to the virus, modulated by both the intrinsic physicochemical properties of the virus and its surrounding environment (*113*, *129*, *139*) (Fig. 2).

UV radiation

Irradiation with UV light has long been established as an effective approach to inactivate airborne viruses, including influenza virus (*127*, *140*), SARS-CoV, and other human coronaviruses (*141*). UV radiation rapidly inactivates SARS-CoV-2 in bulk culture medium (*142*) and in aerosols (*47*) at wavelengths found in ground-level sunlight. UV radiation damages genetic

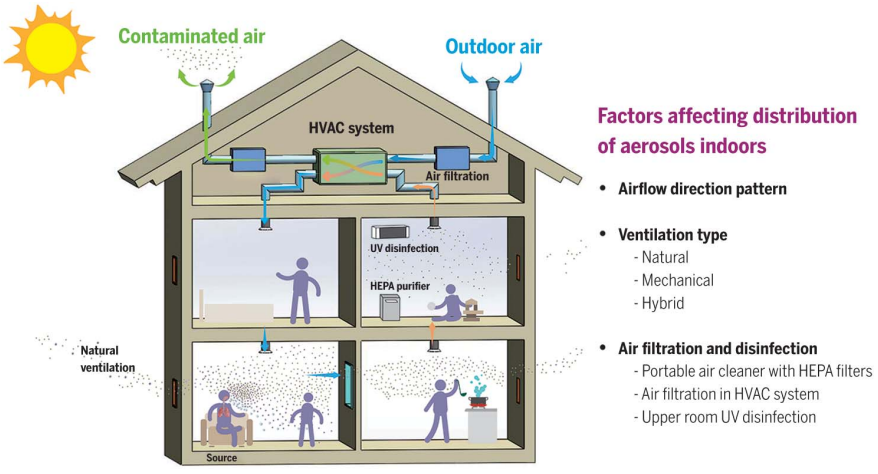


Fig. 4. Factors affecting indoor airborne transmission. Whereas the motion of large droplets is predominantly governed by gravity, the movement of aerosols is more strongly influenced by airflow direction and pattern, type of ventilation, and air filtration and disinfection.

material, leading to inactivation of the virus (*143*). Nevertheless, caution must be taken during operation of UV disinfection lamps to avoid direct eye and skin contact.

Airflow, ventilation, and filtration

Airflow strongly influences the transport of virus-laden aerosols (*81*) in contrast to droplets, which are rapidly deposited because of gravity. Aerosols in exhaled air tend to rise because the exhaled air is warmer than the environment (*50*), and their trajectories can also be influenced by the body's thermal plume (*81*). Greater airflow outdoors contributes to greater dispersion, whereas indoors the airflow is restricted by the surrounding walls and ceiling. Ventilation rate and airflow patterns play an important role in airborne transmission of viruses in indoor environments (*144*–*146*). A study of rhinovirus transmission showed that a low ventilation rate increases the risk of exposure to virus-laden aerosols indoors (*27*, *28*). An outbreak of COVID-19 in a high-rise apartment building occurred along vertically aligned units that were connected by a single air duct, demonstrating the risk of airborne transmission associated with shared air (*147*). Improving ventilation rates to reduce the carbon dioxide levels in under-ventilated buildings from 3200 parts per million (ppm) to 600 ppm (corresponding to an estimated increase of ventilation rate from 1.7 liters per second per person to 24 liters per second per person) has been shown to reduce the secondary attack rate of tuberculosis to zero (*146*).

The airflow in indoor environments is mediated by the design and operational status of ventilation systems, including the type of ventilation system (whether natural with open windows and doors, mechanical with blowers, or a hybrid of these), airflow patterns, air change rate, and supplementary systems such as air filtration (*145*, *148*) (Fig. 4). The WHO has recently recommended a ventilation rate of 10 liters per second per person (*149*). Proper placement of portable high-efficiency particulate air (HEPA) purifiers, which are capable of removing ≥99.97% of aerosol particles ≥0.3 μm, is also effective in reducing exposure of infectious aerosols, especially when combined with ventilation and universal masking (*150*–*152*). Although ventilation and filtration help to remove virus-laden aerosols, they must be implemented correctly to reduce the spread and risk of aerosol inhalation (*93*, *151*). A study quantitatively assessed the risk of airborne transmission of COVID-19 by asymptomatic individuals in elevator, classroom, and supermarket settings by combining in situ measurements and computational fluid dynamics (CFD) simulations, showing that inappropriate ventilation may create hotspots with risks much higher than in other room locations (*93*). Additionally, the physical plexiglass barriers designed to block droplet spray from coughs and sneezes in indoor spaces can impede the airflow and even trap higher concentrations of aerosols in the breathing zone and has been shown to increase transmission of SARS-CoV-2 (*153*).

The risk of airborne infection and correlation with ventilation rate can be assessed by a box model of virus transport and the Wells-Riley infection model (*17*, *64*)

$$P = \frac{N}{S} = 1 - e^{-Iqpt/Q}$$

where P is the probability of infection, N is the number of confirmed infection cases, S is the number of susceptible cases, I is number of infectors, q is the quanta (infectious dose) generation rate (quanta per hour), p is the pulmonary ventilation rate of susceptible individual (cubic meters per second), t is the exposure time (hours), and Q is the room ventilation rate (cubic meters per second). A model using the Wells-Riley method was applied to a large community outbreak of COVID-19 in a choir practice with one index case known to be symptomatic that led to 53 cases among 61 members in attendance (87% secondary attack rate), which concluded that poor ventilation along with a crowded venue, loud vocalization, and long duration all contributed to the high secondary attack rate (*64*). The choir practice had limited face-to-face interaction and strong attention on hand disinfection, which allowed major contributions from fomite or droplet transmission to be ruled out (*64*). Research is needed to establish minimum acceptable ventilation rates under different conditions and the effect of ventilation type on the risk of transmission.

Deposition of virus-laden aerosols

Once inhaled, virus-laden aerosols may deposit in the respiratory tract of a potential host. The size of aerosols is again central to determining the deposition site, although numerous anatomical, physiological, and aerodynamic factors (including the airway anatomical structure, breathing patterns, aerosol transport aerodynamics in the respiratory tract, and the physicochemical properties of inhaled aerosols) also affect the deposition pattern. Infection may be initiated at the deposition site if the virus remains infectious and appropriate receptors are present.

Aerosols up to 100 μm can be inhaled. Depending on their size, they deposit in different regions of the respiratory tract, based on one of several key mechanisms, including inertial impaction, gravitational sedimentation, Brownian diffusion, electrostatic precipitation, and interception (*154*, *155*) (Fig. 5A). Upon inhalation, the size of inhaled aerosols may increase as a result of hygroscopic growth in the nearly saturated respiratory tract (*156*). The International Committee for Radiological Protection (ICRP) has developed a model, based on human lung architecture, that quantifies deposition efficiency as a function of aerosol size (*157*) (Fig. 5B). Aerosols >5 μm deposit primarily in the nasopharyngeal region (87 to 95%), mainly through inertial impaction and gravitational sedimentation (*115*); although aerosols <5 μm also deposit there, they also may penetrate more deeply into the lungs and deposit in the alveolar lumen (*115*, *157*, *158*). Brownian diffusion is the dominant deposition mechanism of inhaled particles <0.1 μm in the bronchiolar and alveolar regions (*78*, *116*, *159*). Aerosols that carry natural electrostatic charge may be attracted to the airway walls (*160*). Provided a cellular receptor is present at the deposition site, infection may be initiated. The infection efficiency is further governed by

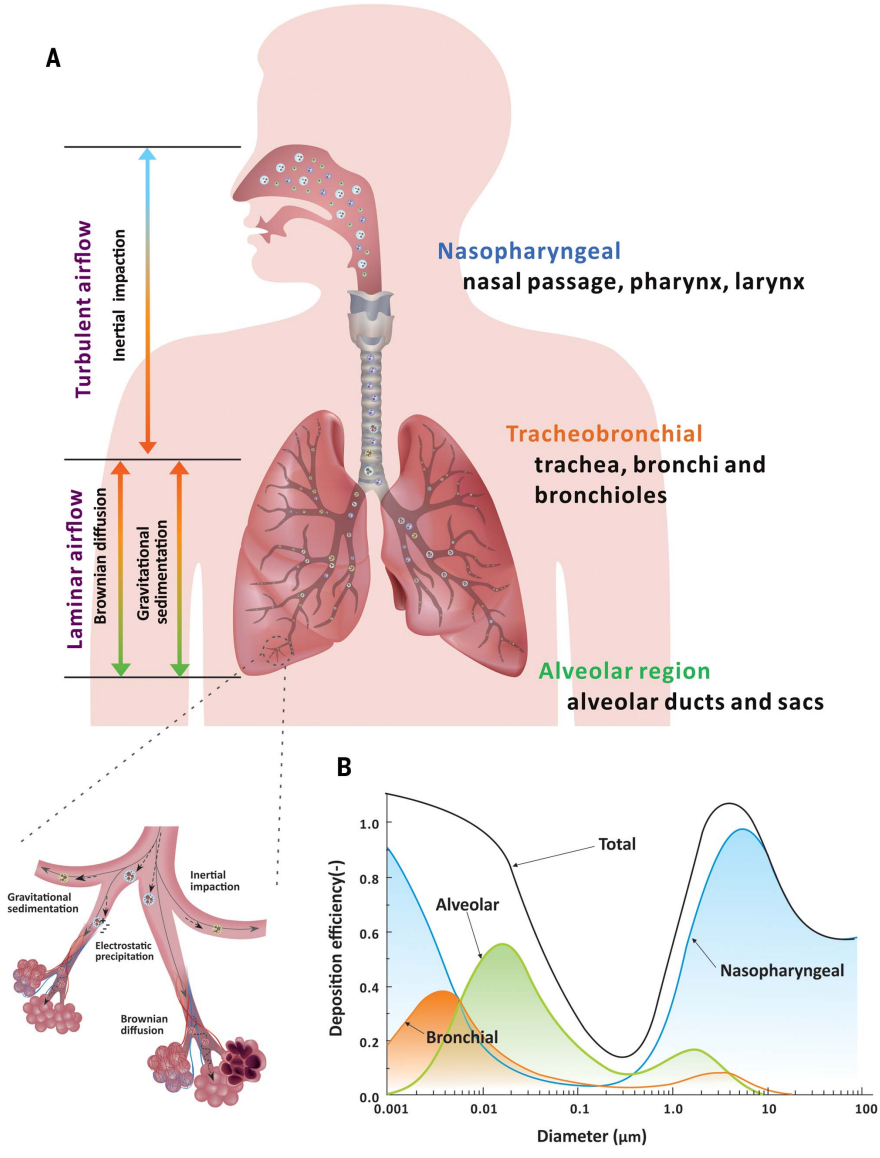


Fig. 5. Size-dependent aerosol deposition mechanisms to sites in the respiratory tract. (**A**) Main deposition mechanisms and corresponding airflow regimes in different regions of the human respiratory tract. Large aerosols tend to deposit in the nasopharyngeal region as a result of inertial impaction, whereas small aerosols tend to deposit in the tracheobronchial and alveolar regions on the basis of gravitational sedimentation and Brownian diffusion. An enlarged view of tracheobronchial and alveolar regions illustrates the deposition mechanism. (**B**) The deposition efficiency of aerosols at different regions of the respiratory tract as a function of aerosol diameter based on the ICRP lung deposition model is shown (*116*). The majority of large aerosols deposit in the nasopharyngeal region; only aerosols that are sufficiently small can reach and deposit in the alveolar region.

the distribution of cellular receptors along the respiratory tract and the virus-host interaction.

Deposition of aerosols in diseased lungs may differ from that in normal lungs because of airway surface structure changes and obstruction by mucous (*161*). Changes in the surface properties of the respiratory epithelium in asthmatic airways and airway narrowing as a result of chronic obstructive pulmonary disease (COPD) alter the airflow and aerodynamic behaviors of inhaled aerosols, thus modifying their deposition dynamics and sites (*162*, *163*). Deposition is generally higher in patients with COPD than in healthy individuals; bronchial deposition is higher in patients with asthma and chronic bronchitis (*154*).

Because viruses are enriched in small aerosols (<5 μm), they can travel deeper into and be deposited in the lower respiratory tract. The viral load of SARS-CoV-2 has been reported to be higher and the virus persists longer in the lower respiratory tract compared with the upper respiratory tract (*164*, *165*). Initiation of an infection in the lower respiratory tract adds technical challenges in diagnosing patients because current screening commonly collects samples from the nasopharyngeal or oral cavity using swabs.

Discussion

Airborne transmission has long been an underappreciated route for contributing to the transmission of respiratory viral diseases, largely because of an insufficient understanding of the generation and transport processes of virus-laden aerosols as well as misattribution of anecdotal observations. The epidemiological evidence for the dominance of airborne spread of SARS-CoV-2 has increased over time and has become especially strong. First, the distinct difference between indoor and outdoor transmission cannot be explained by droplet transmission because gravity-driven droplets behave identically indoors and outdoors. The high frequency of indoor superspreading events relative to those outdoors points to the importance of airborne transmission (*63*). The demonstrated role of poor ventilation in transmission and superspreading clusters indoors is also only compatible with aerosols, because droplets and fomite transmission are not affected by ventilation. Long-range airborne transmission of SARS-CoV-2 has been observed in hotel quarantines in countries with very low transmission (*166*) and in a large church (*72*).

During the emergence of novel respiratory viruses, a more holistic approach that acknowledges all modes of transmission (airborne, droplet, and fomite) is needed to successfully mitigate risk and prevent spread. The requirement for direct evidence of infectiousness of sampled aerosols before acknowledging and adding controls to address airborne transmission leaves people at potential risk (*69*). When unburdened by conventional definitions of transmission routes, the available evidence for SARS-CoV-2, influenza virus, and other respiratory viruses is much more consistent with transmission by aerosols <100 μm rather than by rare, large droplets sprayed onto mucous membranes of people in very close proximity. Recent acknowledgement of airborne transmission of SARS-CoV-2 by the WHO (*48*) and US CDC (*49*) reinforces the necessity to implement protection against this transmission route at both short and long ranges.

Once the mechanisms leading to airborne transmission are fully understood—acknowledging that transmission by aerosols is largest at close range—it becomes clear there is an overlap in precautions and mitigation measures for both droplets and aerosols (such as distancing and masks), but extra considerations must be taken into account for mitigating aerosol transmission at both short and long ranges. These

include attention to ventilation, airflows, mask fit and type, air filtration, and UV disinfection, as well as distinguishing measures between indoor and outdoor environments. Although our knowledge is still increasing, enough is already known to add protective measures to better protect against airborne transmission of respiratory viruses, noting that "droplet precautions" are not replaced but instead expanded.

A high proportion of individuals infected with SARS-CoV-2 have no symptoms at the time of testing (*167*, *168*). About 20 to 45% of individuals infected with SARS-CoV-2 remained asymptomatic throughout the course of infection, whereas some infected individuals experienced a presymptomatic phase and began to develop symptoms several days after infection (*168*, *169*). The infectiousness of SARS-CoV-2 peaks two days before and extends to one day after symptom onset (*170*). High asymptomatic infection rates have also been reported for influenza virus and other respiratory virus infections (*171*–*173*). Although some studies suggest that airborne transmission is not an efficient route, particularly for asymptomatic and mildly symptomatic individuals who likely have low viral loads in their saliva (*55*), the viral load in presymptomatic individuals is comparable to that of symptomatic patients (*174*, *175*). It is important to implement controls that protect against exposure of infectious virus-laden aerosols produced when infected individuals without any symptoms speak, sing, or simply breathe. Because these individuals do not know they are infected, they generally continue to be involved in social activities, leading to airborne transmission.

Universal masking is an effective and economical way to block virus-laden aerosols (*67*). Model simulations show that masks effectively prevent asymptomatic transmission and reduce the total number of infected individuals as well as mortalities as a result of COVID-19 (*176*). It is crucial to optimize the allocation of masks (*177*). Surgical masks have been shown to reduce the release of influenza virus, seasonal human coronaviruses, and rhinovirus in aerosols <5 μm into the air by infected individuals by up to 100% (*104*, *178*), although for some individuals there was no reduction; and masks are more effective for limiting droplets (*179*). Masks made of combinations of different fabrics and/or multiple layers, when worn properly with no leaks, can block up to 90% of particles between 0.5 and 10 μm (*179*). Small gaps between the mask material and skin can lead to substantial decreases in the overall filtration efficiency. For aerosols <2.5 μm, filtration efficiency decreases by 50% for a relative leak area of 1% (*180*). A study compared the viral filtration efficiency of N95, surgical, and fabric masks using a model virus and found that the efficiency of N95 and some surgical masks exceeded 99%; all fabric masks tested were at least 50% efficient (*181*). The effectiveness of N95, surgical, and cotton masks in blocking SARS-CoV-2–containing aerosols has been investigated using manikins placed face-to-face. N95 respirators demonstrated the highest efficiency in blocking infectious SARS-CoV-2 (*182*). Almost all masks offer at least some protection, but they are not 100% effective. Transmission of SARS-CoV-2 has occurred in health care settings despite medical masks (designed for droplets not aerosols) and eye protection (*183*–*185*), which illustrates the need for proper personal protective equipment (PPE) and layering multiple interventions against airborne transmission, especially in high-risk indoor settings.

Health care facilities are more likely to accommodate patients infected with respiratory viruses. Thus, health care personnel should be provided with proper PPE to reduce airborne exposure. People occupying indoor spaces have increased potential to be exposed to high concentrations of virus-laden aerosols, especially in poorly ventilated and/or crowded indoor settings where virus-laden aerosols can readily accumulate (*93*). Preventive measures should be implemented at all times when traveling in airplanes, trains, buses, ships, and cruise ships, which have relatively small and enclosed air spaces where the ventilation may not always be optimal. Many studies indicate that the risk of airborne transmission in outdoor environments is substantially lower than indoor environments (*186*); however, the risk of transmission outdoors exists in close proximity situations, especially if talking, singing, or shouting over time. The risk of outdoor transmission may rise with increased lifetime and transmissibility of viruses, such as certain variants of SARS-CoV-2 (*187*, *188*). Aerosolization of virus-containing wastewater and hospital fecal discharges also poses potential outdoor exposure risks, which should not be underestimated (*189*).

Implementing effective ventilation systems reduces airborne transmission of infectious virus-laden aerosols. Strategies such as ensuring sufficient ventilation rates and avoiding recirculation are advised (*190*, *191*). Carbon dioxide sensors can be used as indicators of the build-up of exhaled air and serve as a simple way to monitor and optimize ventilation (*192*, *193*). Aerosol sensors can also be used to assess HEPA and HVAC aerosol filtration efficiencies, which are key to lowering infections caused by virus-laden aerosols. Assuring a minimum ventilation rate of 4 to 6 air changes per hour (ACH) and maintaining carbon dioxide levels below 700 to 800 ppm have been advised, although the ventilation type and airflow direction and pattern should also be taken into account (*148*, *194*). Increasing the efficiency of air filtration in HVAC systems, stand-alone HEPA purifiers, or implementing upper room UV disinfection systems can further reduce the concentrations of virus-laden aerosols (*47*, *127*, *140*, *141*, *195*).

Physical distancing, a mitigation put in place to address droplet transmission, is also effective in reducing the chances of aerosol inhalation because aerosol concentrations are much higher in close proximity to an infected individual (*50*). The WHO and many national public health agencies recommend maintaining physical distances of either 1 or 2 m. However, this distance is not sufficient to protect against aerosols that travel beyond this range. If large droplets dominated transmission, distancing alone would have effectively suppressed the transmission of SARS-CoV-2. As has been repeatedly shown in superspreading events, airborne transmission occurs in poorly ventilated rooms when occupants inhale infectious room air (*18*, *36*, *62*, *64*, *71*). Additionally, although distancing helps by moving people away from the most concentrated parts of respiratory plumes, distancing alone does not stop transmission and is not sufficient without accounting for other measures, such as ventilation and filtration, the number of people emitting infectious aerosols, and the amount of time spent in enclosed spaces (*196*). The unknown number of asymptomatic (including presymptomatic) infected individuals present in specific environmental settings is an additional challenge in respiratory disease control. Engineering measures to reduce aerosol concentrations through ventilation, filtration, and upper room UV disinfection remain critical strategies for reducing airborne transmission risks.

Despite the emerging recognition of airborne transmission of respiratory viruses, numerous issues require further exploration. For example, direct measurements are needed of the concentration of virus in aerosols and droplets as a function of size and their potential to initiate a new infection. The lifetime of viruses in aerosols of varying size requires systematic investigation. More studies are needed to quantify the relationship between viral dose delivered by aerosols and droplets and severity of infection; this relationship likely varies considerably for different viruses. It is also important to investigate whether the severity of disease correlates with the size and number of aerosols and the location in which they are deposited in the respiratory tract. Although more studies are needed, unequivocal evidence indicates that airborne transmission is a major pathway for the spread of SARS-CoV-2 and many other respiratory viruses. Additional precautionary measures must be implemented for mitigating aerosol transmission at both short and long ranges, with a major focus on ventilation, airflows, air filtration, UV disinfection, and mask fit. These interventions are critical strategies for helping end the current pandemic and preventing future outbreaks. It is

important to note that these proposed measures to improve indoor air quality will lead to long overdue improvements that have health benefits extending well beyond the COVID-19 pandemic.

REFERENCES AND NOTES

1. J. P. Duguid, The size and the duration of air-carriage of respiratory droplets and droplet-nuclei. *Epidemiol. Infect.* **44**, 471–479 (1946). doi: 10.1017/S0022172400019288; pmid: 20475760
2. L. Morawska *et al.*, Size distribution and sites of origin of droplets expelled from the human respiratory tract during expiratory activities. *J. Aerosol Sci.* **40**, 256–269 (2009). doi: 10.1016/j.jaerosci.2008.11.002
3. G. R. Johnson *et al.*, Modality of human expired aerosol size distributions. *J. Aerosol Sci.* **42**, 839–851 (2011). doi: 10.1016/j.jaerosci.2011.07.009
4. G. Scheuch, Breathing is enough: For the spread of influenza virus and SARS-CoV-2 by breathing only. *J. Aerosol Med. Pulm. Drug Deliv.* **33**, 230–234 (2020). doi: 10.1089/jamp.2020.1616; pmid: 32552296
5. W. F. Wells, On air-borne infection: Study II. Droplets and droplet nuclei. *Am. J. Epidemiol.* **20**, 611–618 (1934). doi: 10.1093/oxfordjournals.aje.a118097
6. The National Academies of Sciences, Engineering, and Medicine (NASEM), "Airborne transmission of SARS-CoV-2: A virtual workshop, 26 to 27 August 2020" (NASEM, 2020); www.nationalacademies.org/event/08-26-2020/airborne-transmission-of-sars-cov-2-a-virtual-workshop.
7. K. A. Prather *et al.*, Airborne transmission of SARS-CoV-2. *Science* **370**, 303–304 (2020). doi: 10.1126/science.abf0521; pmid: 33020250
8. G. Zayas *et al.*, Cough aerosol in healthy participants: Fundamental knowledge to optimize droplet-spread infectious respiratory disease management. *BMC Pulm. Med.* **12**, 11 (2012). doi: 10.1186/1471-2466-12-11; pmid: 22436202
9. P. Fabian, J. Brain, E. A. Houseman, J. Gern, D. K. Milton, Origin of exhaled breath particles from healthy and human rhinovirus-infected subjects. *J. Aerosol Med. Pulm. Drug Deliv.* **24**, 137–147 (2011). doi: 10.1089/jamp.2010.0815; pmid: 21361786
10. K. P. Fennelly, Particle sizes of infectious aerosols: Implications for infection control. *Lancet Respir. Med.* **8**, 914–924 (2020). doi: 10.1016/S2213-2600(20)30323-4; pmid: 32717211
11. C. A. E. Winslow, *Conquest of Epidemic Disease* (Princeton Univ. Press, 1943).
12. B. Rush, *The Works of Thomas Sydenham, M.D., On Acute and Chronic Diseases: With Their Histories and Modes of Cure* (Benjamin & Thomas Kite, 1809).
13. C. V. Chapin, *The Sources and Modes of Infection* (Wiley, 1910).
14. K. Han *et al.*, Lack of airborne transmission during outbreak of pandemic (H1N1) 2009 among tour group members, China, June 2009. *Emerg. Infect. Dis.* **15**, 1578–1581 (2009). doi: 10.3201/eid1510.091013; pmid: 19861048
15. A. Bak *et al.*, SARS-CoV-2 routes of transmission and recommendations for preventing acquisition: Joint British Infection Association (BIA), Healthcare Infection Society (HIS), Infection Prevention Society (IPS) and Royal College of Pathologists (RCPath) guidance. *J. Hosp. Infect.* **114**, 79–103 (2021). doi: 10.1016/j.jhin.2021.04.027; pmid: 33940093
16. W. E. Bischoff *et al.*, Detection of measles virus RNA in air and surface specimens in a hospital setting. *J. Infect. Dis.* **213**, 600–603 (2016). doi: 10.1093/infdis/jiv465; pmid: 26386428
17. E. C. Riley, G. Murphy, R. L. Riley, Airborne spread of measles in a suburban elementary school. *Am. J. Epidemiol.* **107**, 421–432 (1978). doi: 10.1093/oxfordjournals.aje.a112560; pmid: 665658
18. A. B. Bloch *et al.*, Measles outbreak in a pediatric practice: Airborne transmission in an office setting. *Pediatrics* **75**, 676–683 (1985). pmid: 3982900
19. R. Tellier, Review of aerosol transmission of influenza A virus. *Emerg. Infect. Dis.* **12**, 1657–1662 (2006). doi: 10.3201/eid1211.060426; pmid: 17283614
20. B. J. Cowling *et al.*, Aerosol transmission is an important mode of influenza A virus spread. *Nat. Commun.* **4**, 1935 (2013). doi: 10.1038/ncomms2922; pmid: 23736803
21. R. Tellier, Aerosol transmission of influenza A virus: A review of new studies. *J. R. Soc. Interface* **6**, S783–S790 (2009). doi: 10.1098/rsif.2009.0302.focus; pmid: 19773292
22. W. E. Bischoff, K. Swett, I. Leng, T. R. Peters, Exposure to influenza virus aerosols during routine patient care. *J. Infect. Dis.* **207**, 1037–1046 (2013). doi: 10.1093/infdis/jis773; pmid: 23372182
23. J. Yan *et al.*, Infectious virus in exhaled breath of symptomatic seasonal influenza cases from a college community. *Proc. Natl. Acad. Sci. U.S.A.* **115**, 1081–1086 (2018). doi: 10.1073/pnas.1716561115; pmid: 29348203
24. F. Koster *et al.*, Exhaled aerosol transmission of pandemic and seasonal H1N1 influenza viruses in the ferret. *PLOS ONE* **7**, e33118 (2012). doi: 10.1371/journal.pone.0033118; pmid: 22509254
25. H. Kulkarni *et al.*, Evidence of respiratory syncytial virus spread by aerosol. Time to revisit infection control strategies? *Am. J. Respir. Crit. Care Med.* **194**, 308–316 (2016). doi: 10.1164/rccm.201509-18330C; pmid: 26890617
26. E. C. Dick, L. C. Jennings, K. A. Mink, C. D. Wartgow, S. L. Inhorn, Aerosol transmission of rhinovirus colds. *J. Infect. Dis.* **156**, 442–448 (1987). doi: 10.1093/infdis/156.3.442; pmid: 3039011
27. T. A. Myatt *et al.*, Detection of airborne rhinovirus and its relation to outdoor air supply in office environments. *Am. J. Respir. Crit. Care Med.* **169**, 1187–1190 (2004). doi: 10.1164/rccm.200306-760OC; pmid: 14754759
28. T. A. Myatt, S. L. Johnston, S. Rudnick, D. K. Milton, Airborne rhinovirus detection and effect of ultraviolet irradiation on detection by a semi-nested RT-PCR assay. *BMC Public Health* **3**, 5 (2003). doi: 10.1186/1471-2458-3-5; pmid: 12525263
29. C.-C. Tseng, L.-Y. Chang, C.-S. Li, Detection of airborne viruses in a pediatrics department measured using real-time qPCR coupled to an air-sampling filter method. *J. Environ. Health* **73**, 22–28 (2010). pmid: 21133312
30. I. T. S. Yu *et al.*, Evidence of airborne transmission of the severe acute respiratory syndrome virus. *N. Engl. J. Med.* **350**, 1731–1739 (2004). doi: 10.1056/NEJMoa032867; pmid: 15102999
31. T. F. Booth *et al.*, Detection of airborne severe acute respiratory syndrome (SARS) coronavirus and environmental contamination in SARS outbreak units. *J. Infect. Dis.* **191**, 1472–1477 (2005). doi: 10.1086/429634; pmid: 15809906
32. S. H. Kim *et al.*, Extensive viable Middle East respiratory syndrome (MERS) coronavirus contamination in air and surrounding environment in MERS isolation wards. *Clin. Infect. Dis.* **63**, 363–369 (2016). doi: 10.1093/cid/ciw239; pmid: 27090992
33. J. S. Kutter *et al.*, SARS-CoV and SARS-CoV-2 are transmitted through the air between ferrets over more than one meter distance. *Nat. Commun.* **12**, 1653 (2021). doi: 10.1038/s41467-021-21918-6; pmid: 33712573
34. J. L. Santarpia *et al.*, The Infectious Nature of Patient-Generated SARS-CoV-2 Aerosol. medRxiv 2020.07.13.20041632 [Preprint] (2020). doi: 10.1101/2020.07.13.20041632
35. J. A. Lednicky *et al.*, Viable SARS-CoV-2 in the air of a hospital room with COVID-19 patients. *Int. J. Infect. Dis.* **100**, 476–482 (2020). doi: 10.1016/j.ijid.2020.09.025; pmid: 32949774
36. Y. Li *et al.*, Probable airborne transmission of SARS-CoV-2 in a poorly ventilated restaurant. *Build. Environ.* **196**, 107788 (2021). doi: 10.1016/j.buildenv.2021.107788; pmid: 33746341
37. S. F. Sia *et al.*, Pathogenesis and transmission of SARS-CoV-2 in golden hamsters. *Nature* **583**, 834–838 (2020). doi: 10.1038/s41586-020-2342-5; pmid: 32408338
38. J. Shi *et al.*, Susceptibility of ferrets, cats, dogs, and other domesticated animals to SARS-coronavirus 2. *Science* **368**, 1016–1020 (2020). doi: 10.1126/science.abb7015; pmid: 32269068
39. J. Gralton, E. R. Tovey, M.-L. McLaws, W. D. Rawlinson, Respiratory virus RNA is detectable in airborne and droplet particles. *J. Med. Virol.* **85**, 2151–2159 (2013). doi: 10.1002/jmv.23698; pmid: 23959825
40. J. A. Lednicky *et al.*, Isolation of SARS-CoV-2 from the air in a car driven by a COVID patient with mild illness. *Int. J. Infect. Dis.* **108**, 212–216 (2021). doi: 10.1016/j.ijid.2021.04.063; pmid: 33901650
41. Y. Liu *et al.*, Aerodynamic analysis of SARS-CoV-2 in two Wuhan hospitals. *Nature* **582**, 557–560 (2020). doi: 10.1038/s41586-020-2271-3; pmid: 32340022
42. Z.-D. Guo *et al.*, Aerosol and surface distribution of severe acute respiratory syndrome coronavirus 2 in hospital wards, Wuhan, China, 2020. *Emerg. Infect. Dis.* **26**, 1583–1591 (2020). doi: 10.3201/eid2607.200885; pmid: 32275497
43. P. Y. Chia *et al.*, Detection of air and surface contamination by SARS-CoV-2 in hospital rooms of infected patients. *Nat. Commun.* **11**, 2800 (2020). doi: 10.1038/s41467-020-16670-2; pmid: 32472043
44. J. L. Santarpia *et al.*, Aerosol and surface contamination of SARS-CoV-2 observed in quarantine and isolation care. *Sci. Rep.* **10**, 12732 (2020). doi: 10.1038/s41598-020-69286-3; pmid: 32728118
45. N. van Doremalen *et al.*, Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. *N. Engl. J. Med.* **382**, 1564–1567 (2020). doi: 10.1056/NEJMc2004973; pmid: 32182409
46. S. J. Smither, L. S. Eastaugh, J. S. Findlay, M. S. Lever, Experimental aerosol survival of SARS-CoV-2 in artificial saliva and tissue culture media at medium and high humidity. *Emerg. Microbes Infect.* **9**, 1415–1417 (2020). doi: 10.1080/22221751.2020.1777906; pmid: 32496967
47. M. Schuit *et al.*, Airborne SARS-CoV-2 is rapidly inactivated by simulated sunlight. *J. Infect. Dis.* **222**, 564–571 (2020). doi: 10.1093/infdis/jiaa334; pmid: 32525979
48. World Health Organization (WHO), "Coronavirus disease (COVID-19): How is it transmitted?" (2021); www.who.int/news-room/q-a-detail/coronavirus-disease-covid-19-how-is-it-transmitted.
49. U.S. Centers for Disease Control and Prevention (CDC), "Scientific brief: SARS-CoV-2 transmission" (2021); www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/sars-cov-2-transmission.html.
50. W. Chen, N. Zhang, J. Wei, H.-L. Yen, Y. Li, Short-range airborne route dominates exposure of respiratory infection during close contact. *Build. Environ.* **176**, 106859 (2020). doi: 10.1016/j.buildenv.2020.106859
51. R. L. Riley *et al.*, Aerial dissemination of pulmonary tuberculosis a two-year study of contagion in a tuberculosis ward1. *Am. J. Epidemiol.* **70**, 185–196 (1959). doi: 10.1093/oxfordjournals.aje.a120069
52. E. A. Nardell, Transmission and institutional infection control of tuberculosis. *Cold Spring Harb. Perspect. Med.* **6**, a018192 (2015). doi: 10.1101/cshperspect.a018192; pmid: 26292985
53. M. Klompas, M. A. Baker, C. Rhee, Airborne transmission of SARS-CoV-2: Theoretical considerations and available evidence. *JAMA* **324**, 441–442 (2020). doi: 10.1001/jama.2020.12458; pmid: 32749495
54. J. Conly *et al.*, Use of medical face masks versus particulate respirators as a component of personal protective equipment for health care workers in the context of the COVID-19 pandemic. *Antimicrob. Resist. Infect. Control* **9**, 126 (2020). doi: 10.1186/s13756-020-00779-6; pmid: 32762735
55. S. H. Smith *et al.*, Aerosol persistence in relation to possible transmission of SARS-CoV-2. *Phys. Fluids* **32**, 107108 (2020). doi: 10.1063/5.0027844; pmid: 33154612
56. Y. Ma, C. R. Horsburgh Jr., L. F. White, H. E. Jenkins, Quantifying TB transmission: A systematic review of reproduction number and serial interval estimates for tuberculosis. *Epidemiol. Infect.* **146**, 1478–1494 (2018). doi: 10.1017/S0950268818001760; pmid: 29970199
57. Y. Liu, A. A. Gayle, A. Wilder-Smith, J. Rocklöv, The reproductive number of COVID-19 is higher compared to SARS coronavirus. *J. Travel Med.* **27**, taaa021 (2020). doi: 10.1093/jtm/taaa021; pmid: 32052846
58. S. Sanche *et al.*, High contagiousness and rapid spread of severe acute respiratory syndrome coronavirus 2. *Emerg. Infect. Dis.* **26**, 1470–1477 (2020). doi: 10.3201/eid2607.200282; pmid: 32255761
59. C. R. MacIntyre, M. R. Ananda-Rajah, Scientific evidence supports aerosol transmission of SARS-COV-2. *Antimicrob. Resist. Infect. Control* **9**, 202 (2020). doi: 10.1186/s13756-020-00868-6; pmid: 33339522
60. R. Laxminarayan *et al.*, Epidemiology and transmission dynamics of COVID-19 in two Indian states. *Science* **370**, 691–697 (2020). doi: 10.1126/science.abd7672; pmid: 33154136
61. K. Sun *et al.*, Transmission heterogeneities, kinetics, and controllability of SARS-CoV-2. *Science* **371**, eabe2424 (2021). doi: 10.1126/science.abe2424; pmid: 33234698
62. D. C. Adam *et al.*, Clustering and superspreading potential of SARS-CoV-2 infections in Hong Kong. *Nat. Med.* **26**,

1714–1719 (2020). doi: 10.1038/s41591-020-1092-0; pmid: 32943787
63. D. Lewis, Superspreading drives the COVID pandemic - and could help to tame it. *Nature* **590**, 544–546 (2021). doi: 10.1038/d41586-021-00460-x; pmid: 33623168
64. S. L. Miller *et al*., Transmission of SARS-CoV-2 by inhalation of respiratory aerosol in the Skagit Valley Chorale superspreading event. *Indoor Air* **31**, 314–323 (2021). doi: 10.1111/ina.12751; pmid: 32979298
65. L. Morawska, D. K. Milton, It is time to address airborne transmission of coronavirus disease 2019 (COVID-19). *Clin. Infect. Dis.* **71**, 2311–2313 (2020). doi: 10.1093/cid/ciaa939; pmid: 32628269
66. E. L. Anderson, P. Turnham, J. R. Griffin, C. C. Clarke, Consideration of the aerosol transmission for COVID-19 and public health. *Risk Anal.* **40**, 902–907 (2020). doi: 10.1111/risa.13500; pmid: 32356927
67. K. A. Prather, C. C. Wang, R. T. Schooley, Reducing transmission of SARS-CoV-2. *Science* **368**, 1422–1424 (2020). doi: 10.1126/science.abc6197; pmid: 32461212
68. L. Morawska, J. Cao, Airborne transmission of SARS-CoV-2: The world should face the reality. *Environ. Int.* **139**, 105730 (2020). doi: 10.1016/j.envint.2020.105730; pmid: 32294574
69. T. Greenhalgh *et al*., Ten scientific reasons in support of airborne transmission of SARS-CoV-2. *Lancet* **397**, 1603–1605 (2021). doi: 10.1016/S0140-6736(21)00869-2; pmid: 33865497
70. J. Middleton, R. Reintjes, H. Lopes, Meat plants-a new front line in the covid-19 pandemic. *BMJ* **370**, m2716 (2020). doi: 10.1136/bmj.m2716; pmid: 32646892
71. P. Azimi, Z. Keshavarz, J. G. Cedeno Laurent, B. Stephens, J. G. Allen, Mechanistic transmission modeling of COVID-19 on the *Diamond Princess* cruise ship demonstrates the importance of aerosol transmission. *Proc. Natl. Acad. Sci. U.S.A.* **118**, e2015482118 (2021). doi: 10.1073/pnas.2015482118; pmid: 33536312
72. A. L. Katelaris *et al*., Epidemiologic evidence for airborne transmission of SARS-CoV-2 during church singing, Australia, 2020. *Emerg. Infect. Dis.* **27**, 1677–1680 (2021). doi: 10.3201/eid2706.210465; pmid: 33818372
73. E. Goldman, Exaggerated risk of transmission of COVID-19 by fomites. *Lancet Infect. Dis.* **20**, 892–893 (2020). doi: 10.1016/S1473-3099(20)30561-2; pmid: 32628907
74. M. U. Mondelli, M. Colaneri, E. M. Seminari, F. Baldanti, R. Bruno, Low risk of SARS-CoV-2 transmission by fomites in real-life conditions. *Lancet Infect. Dis.* **21**, e112 (2021). doi: 10.1016/S1473-3099(20)30678-2; pmid: 33007224
75. A. K. Pitol, T. R. Julian, Community transmission of SARS-CoV-2 by surfaces: Risks and risk reduction strategies. *Environ. Sci. Technol. Lett.* **8**, 263–269 (2021). doi: 10.1021/acs.estlett.0c00966
76. M. Abkarian, S. Mendez, N. Xue, F. Yang, H. A. Stone, Speech can produce jet-like transport relevant to asymptomatic spreading of virus. *Proc. Natl. Acad. Sci. U.S.A.* **117**, 25237–25245 (2020). doi: 10.1073/pnas.2012156117; pmid: 32978297
77. L. Bourouiba, The fluid dynamics of disease transmission. *Annu. Rev. Fluid Mech.* **53**, 473–508 (2021). doi: 10.1146/annurev-fluid-060220-113712
78. R. J. Thomas, Particle size and pathogenicity in the respiratory tract. *Virulence* **4**, 847–858 (2013). doi: 10.4161/viru.27172; pmid: 24225380
79. S. A. Sattar, M. K. Ijaz, C. P. Gerba, Spread of viral infections by aerosols. *Crit. Rev. Environ. Control* **17**, 89–131 (1987). doi: 10.1080/10643388709388331
80. R. M. Jones, L. M. Brosseau, Aerosol transmission of infectious disease. *J. Occup. Environ. Med.* **57**, 501–508 (2015). doi: 10.1097/JOM.0000000000000448; pmid: 25816216
81. J. Wei, Y. Li, Airborne spread of infectious agents in the indoor environment. *Am. J. Infect. Control* **44**, S102–S108 (2016). doi: 10.1016/j.ajic.2016.06.003; pmid: 27590694
82. S. Niazi, R. Groth, K. Spann, G. R. Johnson, The role of respiratory droplet physicochemistry in limiting and promoting the airborne transmission of human coronaviruses: A critical review. *Environ. Pollut.* **276**, 115767 (2021). doi: 10.1016/j.envpol.2020.115767; pmid: 33243541
83. E. P. Vejerano, L. C. Marr, Physico-chemical characteristics of evaporating respiratory fluid droplets. *J. R. Soc. Interface* **15**, 20170939 (2018). doi: 10.1098/rsif.2017.0939; pmid: 29491178
84. B. Patterson, R. Wood, Is cough really necessary for TB transmission? *Tuberculosis* **117**, 31–35 (2019). doi: 10.1016/j.tube.2019.05.003; pmid: 31378265
85. H. Holmgren, E. Ljungström, A.-C. Almstrand, B. Bake, A.-C. Olin, Size distribution of exhaled particles in the range from 0.01 to 2.0 μm. *J. Aerosol Sci.* **41**, 439–446 (2010). doi: 10.1016/j.jaerosci.2010.02.011
86. L. Bourouiba, Turbulent gas clouds and respiratory pathogen emissions: Potential implications for reducing transmission of COVID-19. *JAMA* **323**, 1837–1838 (2020). doi: 10.1001/jama.2020.4756; pmid: 32215590
87. C. Kleinstreuer, Z. Zhang, Airflow and particle transport in the human respiratory system. *Annu. Rev. Fluid Mech.* **42**, 301–334 (2010). doi: 10.1146/annurev-fluid-121108-145453
88. G. R. Johnson, L. Morawska, The mechanism of breath aerosol formation. *J. Aerosol Med. Pulm. Drug Deliv.* **22**, 229–237 (2009). doi: 10.1089/jamp.2008.0720; pmid: 19415984
89. F. Koster, The experimental aerosol transmission of influenza virus. *Future Virol.* **8**, 969–981 (2013). doi: 10.2217/fvl.13.83
90. S. Asadi *et al*., Aerosol emission and superemission during human speech increase with voice loudness. *Sci. Rep.* **9**, 2348 (2019). doi: 10.1038/s41598-019-38808-z; pmid: 30787335
91. R. S. Papineni, F. S. Rosenthal, The size distribution of droplets in the exhaled breath of healthy human subjects. *J. Aerosol Med.* **10**, 105–116 (1997). doi: 10.1089/jam.1997.10.105; pmid: 10168531
92. M. W. Jennison, "Atomizing of Mouth and Nose Secretions into the Air as Revealed by High-Speed Photography" in *Aerobiology* (American Association for the Advancement of Science, ed. 17, 1942), pp. 106–128.
93. S. Shao *et al*., Risk assessment of airborne transmission of COVID-19 by asymptomatic individuals under different practical settings. *J. Aerosol Sci.* **151**, 105661 (2021). doi: 10.1016/j.jaerosci.2020.105661; pmid: 32968325
94. D. A. Edwards *et al*., Exhaled aerosol increases with COVID-19 infection, age, and obesity. *Proc. Natl. Acad. Sci. U.S.A.* **118**, e2021830118 (2021). doi: 10.1073/pnas.2021830118; pmid: 33563754
95. W. G. Lindsley *et al*., Quantity and size distribution of cough-generated aerosol particles produced by influenza patients during and after illness. *J. Occup. Environ. Hyg.* **9**, 443–449 (2012). doi: 10.1080/15459624.2012.684582; pmid: 22651099
96. M. Riediker, L. Morawska, Low exhaled breath droplet formation may explain why children are poor SARS-CoV-2 transmitters. *Aerosol Air Qual. Res.* **20**, 1513–1515 (2020). doi: 10.4209/aaqr.2020.06.0304
97. V. Stadnytskyi, C. E. Bax, A. Bax, P. Anfinrud, The airborne lifetime of small speech droplets and their potential importance in SARS-CoV-2 transmission. *Proc. Natl. Acad. Sci. U.S.A.* **117**, 11875–11877 (2020). doi: 10.1073/pnas.2006874117; pmid: 32404416
98. M. Pan *et al*., Collection of viable aerosolized influenza virus and other respiratory viruses in a student health care center through water-based condensation growth. *MSphere* **2**, e00251-17 (2017). doi: 10.1128/mSphere.00251-17; pmid: 29034325
99. J. Y. Choi *et al*., Aerosol sampling in a hospital emergency room setting: A complementary surveillance method for the detection of respiratory viruses. *Front. Public Health* **6**, 174 (2018). doi: 10.3389/fpubh.2018.00174; pmid: 29963543
100. V. Knight, Viruses as agents of airborne contagion. *Ann. N. Y. Acad. Sci.* **353**, 147–156 (1980). doi: 10.1111/j.1749-6632.1980.tb18917.x; pmid: 6261640
101. W. G. Lindsley *et al*., Viable influenza A virus in airborne particles from human coughs. *J. Occup. Environ. Hyg.* **12**, 107–113 (2015). doi: 10.1080/15459624.2014.973113; pmid: 25523206
102. W. G. Lindsley *et al*., Distribution of airborne influenza virus and respiratory syncytial virus in an urgent care medical clinic. *Clin. Infect. Dis.* **50**, 693–698 (2010). doi: 10.1086/650457; pmid: 20100093
103. A. Totura *et al*., Small particle aerosol exposure of african green monkeys to MERS-CoV as a model for highly pathogenic coronavirus infection. *Emerg. Infect. Dis.* **26**, 2835–2843 (2020). doi: 10.3201/eid2612.201664; pmid: 32744989
104. D. K. Milton, M. P. Fabian, B. J. Cowling, M. L. Grantham, J. J. McDevitt, Influenza virus aerosols in human exhaled breath: Particle size, culturability, and effect of surgical masks. *PLOS Pathog.* **9**, e1003205 (2013). doi: 10.1371/journal.ppat.1003205; pmid: 23505369
105. W. G. Lindsley *et al*., Measurements of airborne influenza virus in aerosol particles from human coughs. *PLOS ONE* **5**, e15100 (2010). doi: 10.1371/journal.pone.0015100; pmid: 21152051
106. W. Yang, S. Elankumaran, L. C. Marr, Concentrations and size distributions of airborne influenza A viruses measured indoors at a health centre, a day-care centre and on aeroplanes. *J. R. Soc. Interface* **8**, 1176–1184 (2011). doi: 10.1098/rsif.2010.0686; pmid: 21300628
107. J. Ma *et al*., Coronavirus disease 2019 patients in earlier stages exhaled millions of severe acute respiratory syndrome coronavirus 2 per hour. *Clin. Infect. Dis.* **72**, e652–e654 (2021). doi: 10.1093/cid/ciaa1283; pmid: 32857833
108. P. Z. Chen *et al*., Heterogeneity in transmissibility and shedding SARS-CoV-2 via droplets and aerosols. *eLife* **10**, e65774 (2021). doi: 10.7554/eLife.65774; pmid: 33861198
109. S. B. Kwon *et al*., Study on the initial velocity distribution of exhaled air from coughing and speaking. *Chemosphere* **87**, 1260–1264 (2012). doi: 10.1016/j.chemosphere.2012.01.032; pmid: 22342283
110. J. D. Smith, C. D. Cappa, W. S. Drisdell, R. C. Cohen, R. J. Saykally, Raman thermometry measurements of free evaporation from liquid water droplets. *J. Am. Chem. Soc.* **128**, 12892–12898 (2006). doi: 10.1021/ja063579v; pmid: 17002384
111. L. Liu, J. Wei, Y. Li, A. Ooi, Evaporation and dispersion of respiratory droplets from coughing. *Indoor Air* **27**, 179–190 (2017). doi: 10.1111/ina.12297; pmid: 26945674
112. H. Wei *et al*., Aerosol microdroplets exhibit a stable pH gradient. *Proc. Natl. Acad. Sci. U.S.A.* **115**, 7272–7277 (2018). doi: 10.1073/pnas.1720488115; pmid: 29941550
113. K. Lin, L. C. Marr, Humidity-dependent decay of viruses, but not bacteria, in aerosols and droplets follows disinfection kinetics. *Environ. Sci. Technol.* **54**, 1024–1032 (2020). doi: 10.1021/acs.est.9b04959; pmid: 31886650
114. W. Yang, L. C. Marr, Dynamics of airborne influenza A viruses indoors and dependence on humidity. *PLOS ONE* **6**, e21481 (2011). doi: 10.1371/journal.pone.0021481; pmid: 21731764
115. J. Sznitman, Respiratory microflows in the pulmonary acinus. *J. Biomech.* **46**, 284–298 (2013). doi: 10.1016/j.jbiomech.2012.10.028; pmid: 23178038
116. W. C. Hinds, *Aerosol Technology: Properties, Behavior, and Measurement of Airborne Particles* (Wiley, ed. 2, 1999).
117. D. Parienta *et al*., Theoretical analysis of the motion and evaporation of exhaled respiratory droplets of mixed composition. *J. Aerosol Sci.* **42**, 1–10 (2011). doi: 10.1016/j.jaerosci.2010.10.005
118. R. Mittal, R. Ni, J.-H. Seo, The flow physics of COVID-19. *J. Fluid Mech.* **894**, F2 (2020). doi: 10.1017/jfm.2020.330
119. V. Vuorinen *et al*., Modelling aerosol transport and virus exposure with numerical simulations in relation to SARS-CoV-2 transmission by inhalation indoors. *Saf. Sci.* **130**, 104866 (2020). doi: 10.1016/j.ssci.2020.104866; pmid: 32834511
120. X. Xie, Y. Li, A. T. Y. Chwang, P. L. Ho, W. H. Seto, How far droplets can move in indoor environments—Revisiting the Wells evaporation-falling curve. *Indoor Air* **17**, 211–225 (2007). doi: 10.1111/j.1600-0668.2007.00469.x; pmid: 17542834
121. L. Bourouiba, E. Dehandschoewercker, J. W. M. Bush, Violent expiratory events: On coughing and sneezing. *J. Fluid Mech.* **745**, 537–563 (2014). doi: 10.1017/jfm.2014.88
122. J. A. Posada, J. Redrow, I. Celik, A mathematical model for predicting the viability of airborne viruses. *J. Virol. Methods* **164**, 88–95 (2010). doi: 10.1016/j.jviromet.2009.12.004; pmid: 20025904
123. P. Dabisch *et al*., The influence of temperature, humidity, and simulated sunlight on the infectivity of SARS-CoV-2 in aerosols. *Aerosol Sci. Technol.* **55**, 142–153 (2021). doi: 10.1080/02786826.2020.1829536
124. E. C. Pirtle, G. W. Beran, Virus survival in the environment. *Rev. Sci. Tech.* **10**, 733–748 (1991). doi: 10.20506/rst.10.3.570; pmid: 1782426
125. J. W. Tang, The effect of environmental parameters on the survival of airborne infectious agents. *J. R. Soc. Interface* **6**, S737–S746 (2009). doi: 10.1098/rsif.2009.0227.focus; pmid: 19773291
126. D. Welch *et al*., Far-UVC light: A new tool to control the spread of airborne-mediated microbial diseases. *Sci. Rep.* **8**, 2752 (2018). doi: 10.1038/s41598-018-21058-w; pmid: 29426899
127. J. J. McDevitt, S. N. Rudnick, L. J. Radonovich, Aerosol susceptibility of influenza virus to UV-C light. *Appl. Environ.*

Microbiol. **78**, 1666–1669 (2012). doi: 10.1128/AEM.06960-11; pmid: 22226954

128. K. Lin, D. Yee-Tak Fong, B. Zhu, J. Karlberg, Environmental factors on the SARS epidemic: Air temperature, passage of time and multiplicative effect of hospital infection. *Epidemiol. Infect.* **134**, 223–230 (2006). doi: 10.1017/S0950268805005054; pmid: 16490124
129. L. C. Marr, J. W. Tang, J. Van Mullekom, S. S. Lakdawala, Mechanistic insights into the effect of humidity on airborne influenza virus survival, transmission and incidence. *J. R. Soc. Interface* **16**, 20180298 (2019). doi: 10.1098/rsif.2018.0298; pmid: 30958176
130. E. R. McFadden Jr *et al*., Thermal mapping of the airways in humans. *J. Appl. Physiol.* **58**, 564–570 (1985). doi: 10.1152/jappl.1985.58.2.564; pmid: 3980358
131. D. A. Tyrrell, R. Parsons, Some virus isolations from common colds. III. Cytopathic effects in tissue cultures. *Lancet* **275**, 239–242 (1960). doi: 10.1016/S0140-6736(60)90168-9; pmid: 13840115
132. K. H. Chan *et al*., The effects of temperature and relative humidity on the viability of the SARS coronavirus. *Adv. Virol.* **2011**, 734690 (2011). doi: 10.1155/2011/734690; pmid: 22312351
133. A. W. H. Chin *et al*., Stability of SARS-CoV-2 in different environmental conditions. *Lancet Microbe* **1**, e10 (2020). doi: 10.1016/S2666-5247(20)30003-3; pmid: 32835322
134. M. Moriyama, W. J. Hugentobler, A. Iwasaki, Seasonality of respiratory viral infections. *Annu. Rev. Virol.* **7**, 83–101 (2020). doi: 10.1146/annurev-virology-012420-022445; pmid: 32196426
135. A. C. Lowen, J. Steel, S. Mubareka, P. Palese, High temperature (30°C) blocks aerosol but not contact transmission of influenza virus. *J. Virol.* **82**, 5650–5652 (2008). doi: 10.1128/JVI.00325-08; pmid: 18367530
136. J. S. Walker *et al*., Accurate representations of the microphysical processes occurring during the transport of exhaled aerosols and droplets. *ACS Cent. Sci.* **7**, 200–209 (2021). doi: 10.1021/acscentsci.0c01522; pmid: 33532579
137. K. M. Gustin *et al*., Environmental conditions affect exhalation of H3N2 seasonal and variant influenza viruses and respiratory droplet transmission in ferrets. *PLOS ONE* **10**, e0125874 (2015). doi: 10.1371/journal.pone.0125874; pmid: 25969995
138. K. A. Kormuth *et al*., Influenza virus infectivity is retained in aerosols and droplets independent of relative humidity. *J. Infect. Dis.* **218**, 739–747 (2018). doi: 10.1093/infdis/jiy221; pmid: 29878137
139. J. R. Songer, Influence of relative humidity on the survival of some airborne viruses. *Appl. Microbiol.* **15**, 35–42 (1967). doi: 10.1128/am.15.1.35-42.1967; pmid: 4291670
140. M. Schuit *et al*., The influence of simulated sunlight on the inactivation of influenza virus in aerosols. *J. Infect. Dis.* **221**, 372–378 (2020). doi: 10.1093/infdis/jiz582; pmid: 31778532
141. M. Buonanno, D. Welch, I. Shuryak, D. J. Brenner, Far-UVC light (222 nm) efficiently and safely inactivates airborne human coronaviruses. *Sci. Rep.* **10**, 10285 (2020). doi: 10.1038/s41598-020-67211-2; pmid: 32581288
142. C. S. Heilingloh *et al*., Susceptibility of SARS-CoV-2 to UV irradiation. *Am. J. Infect. Control* **48**, 1273–1275 (2020). doi: 10.1016/j.ajic.2020.07.031; pmid: 32763344
143. Y. Ye, P. H. Chang, J. Hartert, K. R. Wigginton, Reactivity of enveloped virus genome, proteins, and lipids with free chlorine and UV_{254}. *Environ. Sci. Technol.* **52**, 7698–7708 (2018). doi: 10.1021/acs.est.8b00824; pmid: 29886734
144. Y. Li *et al*., Role of ventilation in airborne transmission of infectious agents in the built environment - a multidisciplinary systematic review. *Indoor Air* **17**, 2–18 (2007). doi: 10.1111/j.1600-0668.2006.00445.x; pmid: 17257148
145. J. W. Tang, Y. Li, I. Eames, P. K. S. Chan, G. L. Ridgway, Factors involved in the aerosol transmission of infection and control of ventilation in healthcare premises. *J. Hosp. Infect.* **64**, 100–114 (2006). doi: 10.1016/j.jhin.2006.05.022; pmid: 16916564
146. C.-R. Du *et al*., Effect of ventilation improvement during a tuberculosis outbreak in underventilated university buildings. *Indoor Air* **30**, 422–432 (2020). doi: 10.1111/ina.12639; pmid: 31883403
147. S. E. Hwang, J. H. Chang, B. Oh, J. Heo, Possible aerosol transmission of COVID-19 associated with an outbreak in an apartment in Seoul, South Korea, 2020. *Int. J. Infect. Dis.* **104**, 73–76 (2021). doi: 10.1016/j.ijid.2020.12.035; pmid: 33346125
148. H. Qian, X. Zheng, Ventilation control for airborne transmission of human exhaled bio-aerosols in buildings. *J. Thorac. Dis.* **10**, S2295–S2304 (2018). doi: 10.21037/jtd.2018.01.24; pmid: 30116608
149. World Health Organization (WHO), "Roadmap to improve and ensure good indoor ventilation in the context of COVID-19" (2021); www.who.int/publications/i/item/9789240021280.
150. W. G. Lindsley *et al*., Efficacy of portable air cleaners and masking for reducing indoor exposure to simulated exhaled SARS-CoV-2 aerosols — United States, 2021. *MMWR Morb. Mortal. Wkly. Rep.* **70**, 972–976 (2021). doi: 10.15585/mmwr.mm7027e1; pmid: 34237047
151. S. R. Narayanan, S. Yang, Airborne transmission of virus-laden aerosols inside a music classroom: Effects of portable purifiers and aerosol injection rates. *Phys. Fluids* **33**, 033307 (2021). doi: 10.1063/5.0042474; pmid: 33746493
152. J. Curtius, M. Granzin, J. Schrod, Testing mobile air purifiers in a school classroom: Reducing the airborne transmission risk for SARS-CoV-2. *Aerosol Sci. Technol.* **55**, 586–599 (2021). doi: 10.1080/02786826.2021.1877257
153. J. Lessler *et al*., Household COVID-19 risk and in-person schooling. *Science* **372**, 1092–1097 (2021). doi: 10.1126/science.abh2939; pmid: 33927057
154. C. Darquenne, Aerosol deposition in health and disease. *J. Aerosol Med. Pulm. Drug Deliv.* **25**, 140–147 (2012). doi: 10.1089/jamp.2011.0916; pmid: 22686623
155. C. Darquenne, Deposition Mechanisms. *J. Aerosol Med. Pulm. Drug Deliv.* **33**, 181–185 (2020). doi: 10.1089/jamp.2020.29029.cd; pmid: 32598200
156. A. E. Haddrell *et al*., Pulmonary aerosol delivery and the importance of growth dynamics. *Ther. Deliv.* **8**, 1051–1061 (2017). doi: 10.4155/tde-2017-0093; pmid: 29125064
157. S. Guha, P. Hariharan, M. R. Myers, Enhancement of ICRP's lung deposition model for pathogenic bioaerosols. *Aerosol Sci. Technol.* **48**, 1226–1235 (2014). doi: 10.1080/02786826.2014.975334
158. D. K. Milton, A rosetta stone for understanding infectious drops and aerosols. *J. Pediatric Infect. Dis. Soc.* **9**, 413–415 (2020). doi: 10.1093/jpids/piaa079; pmid: 32706376
159. P. Hofemeier, K. Koshiyama, S. Wada, J. Sznitman, One (sub-)acinus for all: Fate of inhaled aerosols in heterogeneous pulmonary acinar structures. *Eur. J. Pharm. Sci.* **113**, 53–63 (2018). doi: 10.1016/j.ejps.2017.09.033; pmid: 28954217
160. L. Zhang, Z. Gu, C. Yu, Y. Zhang, Y. Cheng, Surface charges on aerosol particles – accelerating particle growth rate and atmospheric pollution. *Indoor Built Environ.* **25**, 437–440 (2016). doi: 10.1177/1420326X16643799
161. M. S. P. Islam *et al*., A review of respiratory anatomical development, air flow characterization and particle deposition. *Int. J. Environ. Res. Public Health* **17**, 380 (2020). doi: 10.3390/ijerph17020380; pmid: 31935991
162. J. K. Mutuku, W.-C. Hou, W.-H. Chen, Two-phase flow dynamics and $PM_{2.5}$ deposition in healthy and obstructed human airways during inhalation. *Aerosol Air Qual. Res.* **20**, 1091–1110 (2020). doi: 10.4209/aaqr.2020.03.0107
163. W.-H. Chen, K.-H. Lee, J. K. Mutuku, C.-J. Hwang, Flow dynamics and $PM_{2.5}$ deposition in healthy and asthmatic airways at different inhalation statuses. *Aerosol Air Qual. Res.* **18**, 866–883 (2018). doi: 10.4209/aaqr.2018.02.0058
164. E. K. Alidjinou *et al*., Spatial and temporal virus load dynamics of SARS-CoV-2: A single-center cohort study. *Diagnostics* **11**, 427 (2021). doi: 10.3390/diagnostics11030427; pmid: 33802451
165. A. Weiss, M. Jellingsø, M. O. A. Sommer, Spatial and temporal dynamics of SARS-CoV-2 in COVID-19 patients: A systematic review and meta-analysis. *EBioMedicine* **58**, 102916 (2020). doi: 10.1016/j.ebiom.2020.102916; pmid: 32711256
166. N. Eichler *et al*., Transmission of severe acute respiratory syndrome coronavirus 2 during border quarantine and air travel, New Zealand (Aotearoa). *Emerg. Infect. Dis.* **27**, 1274–1278 (2021). doi: 10.3201/eid2705.210514; pmid: 33734063
167. M. M. Arons *et al*., Presymptomatic SARS-CoV-2 infections and transmission in a skilled nursing facility. *N. Engl. J. Med.* **382**, 2081–2090 (2020). doi: 10.1056/NEJMoa2008457; pmid: 32329971
168. M. A. Johansson *et al*., SARS-CoV-2 transmission from people without COVID-19 symptoms. *JAMA Netw. Open* **4**, e2035057 (2021). doi: 10.1001/jamanetworkopen.2020.35057; pmid: 33410879
169. D. P. Oran, E. J. Topol, Prevalence of asymptomatic SARS-CoV-2 infection: A Narrative Review. *Ann. Intern. Med.* **173**, 362–367 (2020). doi: 10.7326/M20-3012; pmid: 32491919
170. X. He *et al*., Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nat. Med.* **26**, 672–675 (2020). doi: 10.1038/s41591-020-0869-5; pmid: 32296168
171. M. Galanti *et al*., Rates of asymptomatic respiratory virus infection across age groups. *Epidemiol. Infect.* **147**, e176 (2019). doi: 10.1017/S0950268819000505; pmid: 31063096
172. N. H. L. Leung, C. Xu, D. K. M. Ip, B. J. Cowling, Review article: The fraction of influenza virus infections that are asymptomatic: A systematic review and meta-analysis. *Epidemiology* **26**, 862–872 (2015). doi: 10.1097/EDE.0000000000000340; pmid: 26133025
173. F. Carrat *et al*., Time lines of infection and disease in human influenza: A review of volunteer challenge studies. *Am. J. Epidemiol.* **167**, 775–785 (2008). doi: 10.1093/aje/kwm375; pmid: 18230677
174. L. Zou *et al*., SARS-CoV-2 viral load in upper respiratory specimens of infected patients. *N. Engl. J. Med.* **382**, 1177–1179 (2020). doi: 10.1056/NEJMc2001737; pmid: 32074444
175. K. A. Walsh *et al*., SARS-CoV-2 detection, viral load and infectivity over the course of an infection. *J. Infect.* **81**, 357–371 (2020). doi: 10.1016/j.jinf.2020.06.067; pmid: 32615199
176. S. E. Eikenberry *et al*., To mask or not to mask: Modeling the potential for face mask use by the general public to curtail the COVID-19 pandemic. *Infect. Dis. Model.* **5**, 293–308 (2020). doi: 10.1016/j.idm.2020.04.001; pmid: 32355904
177. C. J. Worby, H.-H. Chang, Face mask use in the general population and optimal resource allocation during the COVID-19 pandemic. *Nat. Commun.* **11**, 4049 (2020). doi: 10.1038/s41467-020-17922-x; pmid: 32792562
178. N. H. L. Leung *et al*., Respiratory virus shedding in exhaled breath and efficacy of face masks. *Nat. Med.* **26**, 676–680 (2020). doi: 10.1038/s41591-020-0843-2; pmid: 32371934
179. M. Gandhi, L. C. Marr, Uniting infectious disease and physical science principles on the importance of face masks for COVID-19. *Med* **2**, 29–32 (2021). doi: 10.1016/j.medj.2020.12.008; pmid: 33521753
180. F. Drewnick *et al*., Aerosol filtration efficiency of household materials for homemade face masks: Influence of material properties, particle size, particle electrical charge, face velocity, and leaks. *Aerosol Sci. Technol.* **55**, 63–79 (2021). doi: 10.1080/02786826.2020.1817846
181. H. Whiley, T. P. Keerthirathne, M. A. Nisar, M. A. F. White, K. E. Ross, Viral filtration efficiency of fabric masks compared with surgical and N95 masks. *Pathogens* **9**, 762 (2020). doi: 10.3390/pathogens9090762; pmid: 32957638
182. H. Ueki *et al*., Effectiveness of face masks in preventing airborne transmission of SARS-CoV-2. *mSphere* **5**, e00637-20 (2020). doi: 10.1128/mSphere.00637-20; pmid: 33087517
183. M. Klompas *et al*., Transmission of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) From Asymptomatic and Presymptomatic Individuals in Healthcare Settings Despite Medical Masks and Eye Protection. *Clin. Infect. Dis.* 10.1093/cid/ciab218 (2021). doi: 10.1093/cid/ciab218; pmid: 33704451
184. L. Goldberg *et al*., SARS-CoV-2 infection among health care workers despite the use of surgical masks and physical distancing—the role of airborne transmission. *Open Forum Infect. Dis.* **8**, ofab036 (2021). doi: 10.1093/ofid/ofab036; pmid: 33732749
185. M. Klompas *et al*., A SARS-CoV-2 cluster in an acute care hospital. *Ann. Intern. Med.* **174**, 794–802 (2021). doi: 10.7326/M20-7567; pmid: 33556277
186. T. C. Bulfone, M. Malekinejad, G. W. Rutherford, N. Razani, Outdoor transmission of SARS-CoV-2 and other respiratory viruses: A systematic review. *J. Infect. Dis.* **223**, 550–561 (2021). doi: 10.1093/infdis/jiaa742; pmid: 33249484
187. N. R. Faria *et al*., Genomics and epidemiology of the P.1 SARS-CoV-2 lineage in Manaus, Brazil. *Science* **372**, 815–821 (2021). doi: 10.1126/science.abh2644; pmid: 33853970
188. N. G. Davies *et al*., Estimated transmissibility and impact of SARS-CoV-2 lineage B.1.1.7 in England. *Science* **372**, eabg3055 (2021). doi: 10.1126/science.abg3055; pmid: 33658326
189. M. Kang *et al*., Probable evidence of fecal aerosol transmission of SARS-CoV-2 in a high-rise building. *Ann. Intern. Med.* **173**, 974–980 (2020). doi: 10.7326/M20-0928; pmid: 32870707

190. G. A. Somsen, C. van Rijn, S. Kooij, R. A. Bem, D. Bonn, Small droplet aerosols in poorly ventilated spaces and SARS-CoV-2 transmission. *Lancet Respir. Med.* **8**, 658–659 (2020). doi: 10.1016/S2213-2600(20)30245-9; pmid: 32473123

191. L. Morawska *et al.*, How can airborne transmission of COVID-19 indoors be minimised? *Environ. Int.* **142**, 105832 (2020). doi: 10.1016/j.envint.2020.105832; pmid: 32521345

192. S. N. Rudnick, D. K. Milton, Risk of indoor airborne infection transmission estimated from carbon dioxide concentration. *Indoor Air* **13**, 237–245 (2003). doi: 10.1034/j.1600-0668.2003.00189.x; pmid: 12950586

193. Z. Peng, J. L. Jimenez, Exhaled CO_2 as COVID-19 infection risk proxy for different indoor environments and activities. *Environ. Sci. Technol. Lett.* **8**, 392–397 (2021). doi: 10.1021/acs.estlett.1c00183

194. F. Villanueva *et al.*, Assessment of CO_2 and aerosol ($PM_{2.5}$, PM_{10}, UFP) concentrations during the reopening of schools in the COVID-19 pandemic: The case of a metropolitan area in Central-Southern Spain. *Environ. Res.* **197**, 111092 (2021). doi: 10.1016/j.envres.2021.111092; pmid: 33785326

195. C. Chen *et al.*, The effectiveness of an air cleaner in controlling droplet/aerosol particle dispersion emitted from a patient's mouth in the indoor environment of dental clinics. *J. R. Soc. Interface* **7**, 1105–1118 (2010). doi: 10.1098/rsif.2009.0516; pmid: 20031985

196. M. Z. Bazant, J. W. M. Bush, A guideline to limit indoor airborne transmission of COVID-19. *Proc. Natl. Acad. Sci. U.S.A.* **118**, e2018995118 (2021). doi: 10.1073/pnas.2018995118; pmid: 33858987

197. E. Petersen *et al.*, Comparing SARS-CoV-2 with SARS-CoV and influenza pandemics. *Lancet Infect. Dis.* **20**, e238–e244 (2020). doi: 10.1016/S1473-3099(20)30484-9; pmid: 32628905

198. X.-Y. Hao, Q. Lv, F. D. Li, Y. F. Xu, H. Gao, The characteristics of hDPP4 transgenic mice subjected to aerosol MERS coronavirus infection via an animal nose-only exposure device. *Animal Model Exp. Med.* **2**, 269–281 (2019). doi: 10.1002/ame2.12088; pmid: 31942559

199. S. L. Bixler *et al.*, Aerosol Exposure of Cynomolgus Macaques to SARS-CoV-2 Results in More Severe Pathology than Existing Models. bioRxiv 2021.04.27.441510 [Preprint] (2021). doi: 10.1101/2021.04.27.441510

200. S. S. Lakdawala *et al.*, Eurasian-origin gene segments contribute to the transmissibility, aerosol release, and morphology of the 2009 pandemic H1N1 influenza virus. *PLOS Pathog.* **7**, e1002443 (2011). doi: 10.1371/journal.ppat.1002443; pmid: 22241979

201. J. Zhou *et al.*, Defining the sizes of airborne particles that mediate influenza transmission in ferrets. *Proc. Natl. Acad. Sci. U.S.A.* **115**, E2386–E2392 (2018). doi: 10.1073/pnas.1716771115; pmid: 29463703

202. J. S. Nguyen-Van-Tam *et al.*, Minimal transmission in an influenza A (H3N2) human challenge-transmission model within a controlled exposure environment. *PLOS Pathog.* **16**, e1008704 (2020). doi: 10.1371/journal.ppat.1008704; pmid: 32658939

203. K. A. Kormuth *et al.*, Environmental persistence of influenza viruses is dependent upon virus type and host origin. *MSphere* **4**, e00552-19 (2019). doi: 10.1128/mSphere.00552-19; pmid: 31434749

204. P. J. Bueno de Mesquita, C. J. Noakes, D. K. Milton, Quantitative aerobiologic analysis of an influenza human challenge-transmission trial. *Indoor Air* **30**, 1189–1198 (2020). doi: 10.1111/ina.12701; pmid: 32542890

205. N. H. L. Leung, Transmissibility and transmission of respiratory viruses. *Nat. Rev. Microbiol.* **19**, 528–545 (2021). doi: 10.1038/s41579-021-00535-6; pmid: 33753932

206. F. M. Guerra *et al.*, The basic reproduction number (R_0) of measles: A systematic review. *Lancet Infect. Dis.* **17**, e420–e428 (2017). doi: 10.1016/S1473-3099(17)30307-9; pmid: 28757186

ACKNOWLEDGMENTS

C.C.W. thanks D. M. Neumark, K. Liu, I. Gonda, and Y.-Y. Cheng for helpful discussions. **Funding:** C.C.W. is supported by the Ministry of Science and Technology (MOST 109-2113-M-110-011 and MOST 109-2621-110-006) and the Higher Education Sprout Project of the Ministry of Education, Taiwan, ROC. K.A.P. is supported by the US NSF Center for Aerosol Impacts on Chemistry of the Environment, USA. J.L.J. is supported by the US National Science Foundation (AGS-1822664). L.C.M. is supported by the National Institute of Allergy and Infectious Diseases Center of Excellence in Influenza Research and Surveillance (HHSN272201400007C) and the NSF National Nanotechnology Coordinated Infrastructure (ECCS 1542100 and ECCS 2025151). **Competing interests:** L.C.M. has served on Advisory Boards for Crossfit and Phylagen, has served as a paid consultant for The MITRE Corporation and Smiths Detection, and was a paid reviewer for the Alfred P. Sloan Foundation. She is an unpaid member of the National Academies of Sciences, Engineering, and Medicine Board on Environmental Studies and Toxicology and the Committee on Public Health Interventions and Countermeasures for Advancing Pandemic and Seasonal Influenza Preparedness and Response. The authors declare no other competing interests.

10.1126/science.abd9149

Science

Airborne transmission of respiratory viruses

Chia C. WangKimberly A. PratherJosué SznitmanJose L. JimenezSeema S. LakdawalaZeynep TufekciLinsey C. Marr

Science, 373 (6558), eabd9149.

Mechanisms of airborne transmission

The COVID-19 pandemic has highlighted controversies and unknowns about how respiratory pathogens spread between hosts. Traditionally, it was thought that respiratory pathogens spread between people through large droplets produced in coughs and through contact with contaminated surfaces (fomites). However, several respiratory pathogens are known to spread through small respiratory aerosols, which can float and travel in air flows, infecting people who inhale them at short and long distances from the infected person. Wang *et al*. review recent advances in understanding airborne transmission gained from studying the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections and other respiratory pathogens. The authors suggest that airborne transmission may be the dominant form of transmission for several respiratory pathogens, including SARS-CoV-2, and that further understanding of the mechanisms underlying infection from the airborne route will better inform mitigation measures. —GKA

Science (ISSN) is published by the American Association for the Advancement of Science. 1200 New York Avenue NW, Washington, DC 20005. The title *Science* is a registered trademark of AAAS.

EXHIBIT D

UNIVERSITY OF CALIFORNIA
HEALTH

July 2, 2021 Update
COVID-19 AND 'CORONAVIRUS' UPDATES

CARRIE L. BYINGTON, MD
Executive Vice President, University of California Health

THE IMPACT ON OUR HEALTH SYSTEM

This is the 31st update for Regents regarding the SARS-CoV-2 virus pandemic and its impact on the University's health and academic enterprise. This issue will be the last in the series unless circumstances necessitate a resumption.

On Sunday, we will celebrate Independence Day. Two hundred and forty five years ago, our nation's founders signed the Declaration of Independence with this closing message, **"We mutually pledge to each other our lives, our fortunes and our sacred honor."** Those words continue to ring true after the searing events of the past 18 months. A new virus emerged half a world away, swept every continent, disrupted the world's economy and killed more than 600,000 Americans. This shared experience speaks to our interdependence.

Yet through science and perseverance, we developed three new vaccines and administered more than 320 million doses in the United States. Case numbers, hospitalizations and daily death rates have plunged since our peak in January 2021. Nearly all COVID-19 deaths in the U.S. now are in people who have **not** been vaccinated, according to an Associated Press analysis of data from the Centers for Disease Control and Prevention (CDC). Of the hospitalizations that occurred in May, "breakthrough" infections in fully vaccinated people accounted for fewer than 1,200, or 0.1%, of more than 853,000 hospitalizations attributable to COVID-19, and 0.8% of deaths.

The end of the pandemic in this country is within reach. For those who have been vaccinated, this July 4th commemorates our freedom not only as a people but also from overwhelming fear.

The return of joy, however, does not signal a return to normal. Things cannot truly return to normal until more of us are vaccinated. Viruses, of course, evolve, and the strain of greatest concern today is the delta variant.

The World Health Organization reports the delta variant has been detected in at least 96 countries and is the most transmissible of the variants thus far. Fortunately, the vaccines approved for emergency use in the U.S. by the Food and Drug Administration continue to be effective, but wherever there are pockets of unvaccinated people, there will be outbreaks.

THE WHITE HOUSE

Unfortunately, we will not achieve the goal set by the Biden-Harris administration to have 70% of all eligible Americans vaccinated by July 4th.

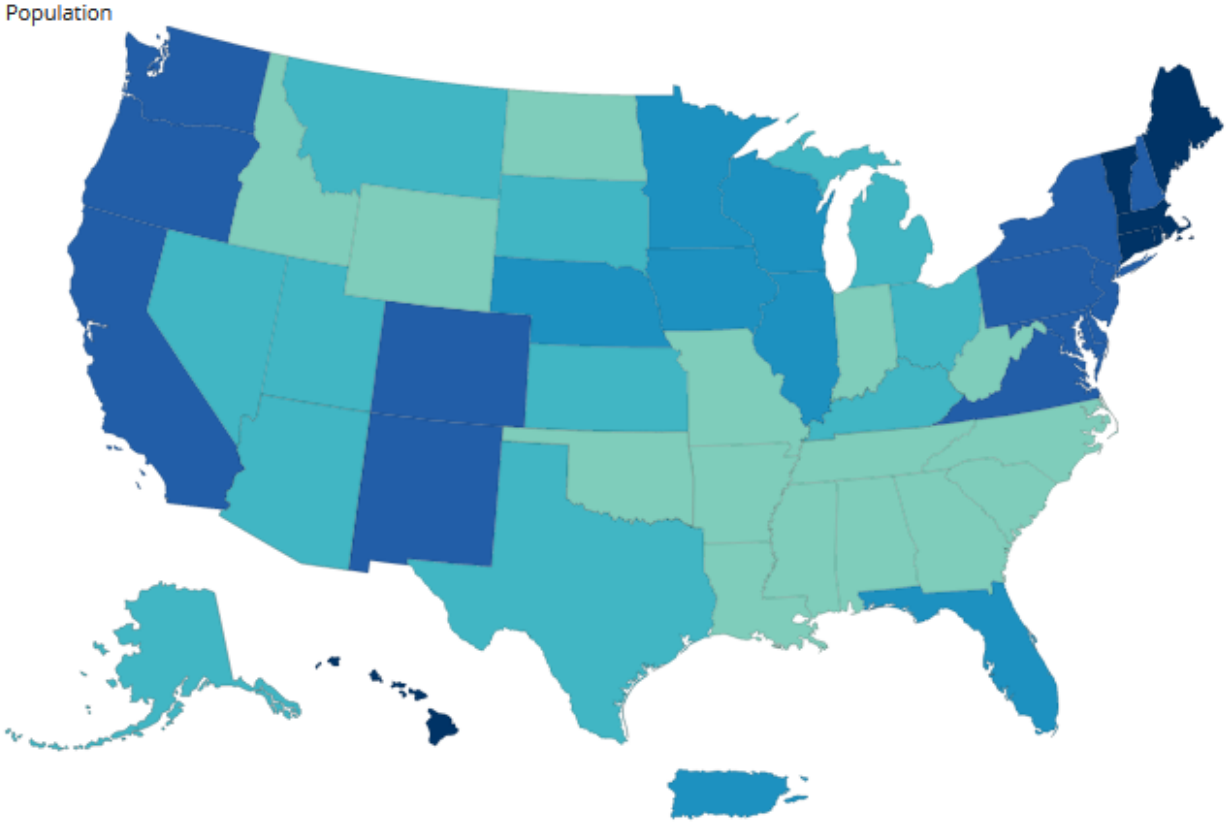
That's why, after a consultative process, the University is finalizing a policy that will require UC students and employees to be vaccinated before the start of the fall 2021 academic year, unless a person has been approved for a medical exemption or religious accommodations. The policy announcement, expected in mid-July will include implementation guidance that campuses can tailor to their needs.

COVID-19 BY THE NUMBERS

As of June 28, California has experienced more than 3.7 million cases of COVID-19 infection, nearly 63,000 deaths and 7-day average test positivity rate that has crept back up to 1.2 percent, according to the California Department of Public Health (CDPH). Fortunately, with more than 41.6 million doses administered, 59.0% of eligible Californians are fully vaccinated and 9.7% are partially vaccinated, as of June 29. A vaccination breakdown by county can be seen here.

Nationally, 54.3% of eligible people have been fully vaccinated and another 9.1% partially vaccinated, according to the CDC, as of June 29 Although those percentages are impressive compared to where we were just a few months ago, vaccination rates vary significantly by location. There's already been an increase in hospitalizations in areas with lower vaccination. The darker the color blue on the map, the higher the vaccination rate.

Total Doses Administered Reported to the CDC by State/Territory and for Select Federal Entities per 100,000 of the Total Population

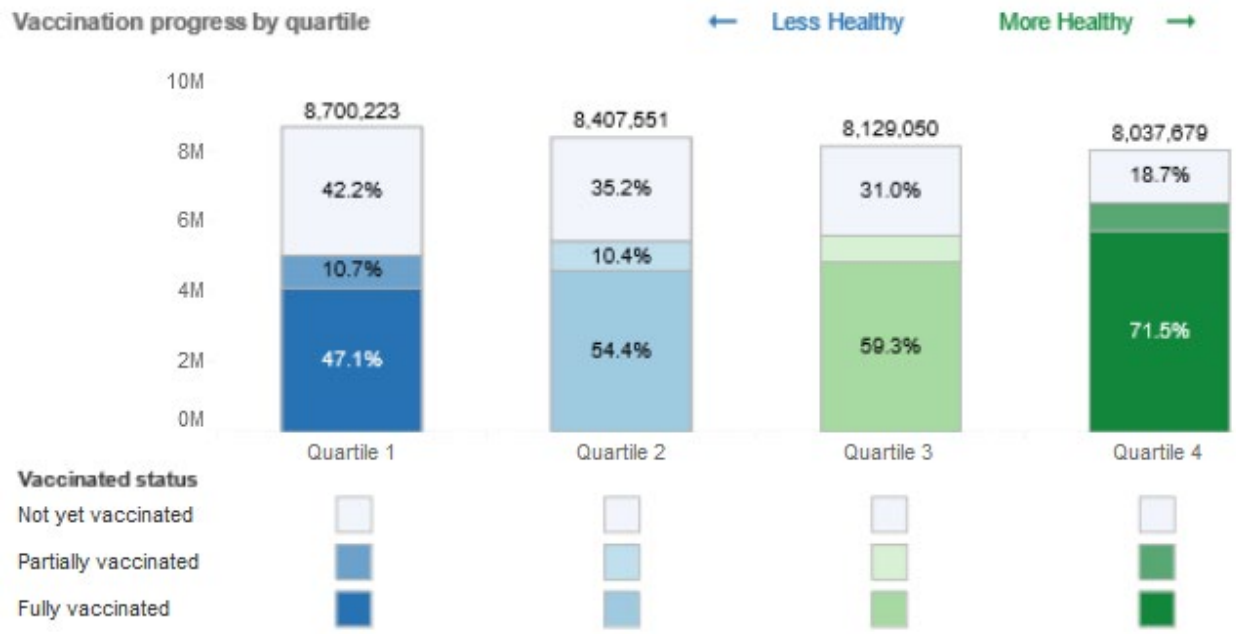


Source: CDC COVID Data Tracker

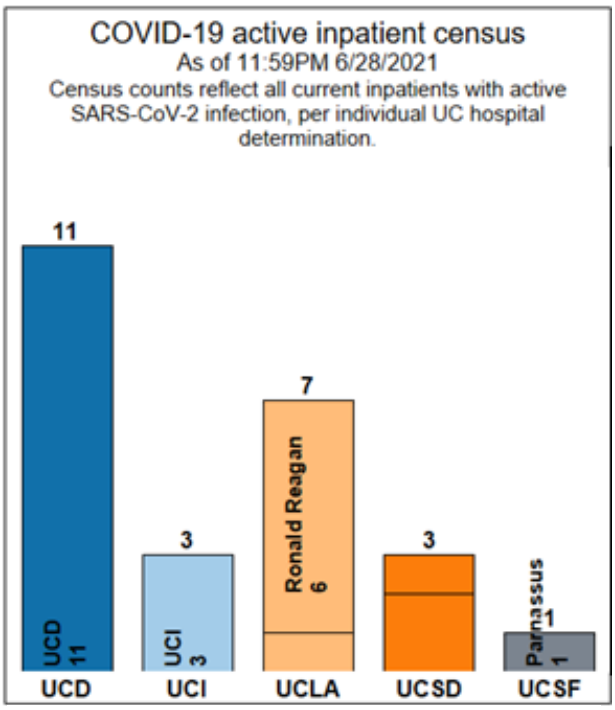
Since we announced our million-dose milestone in April, UC personnel have continued to vaccinate Californians with an emphasis on the most vulnerable populations. As traffic to mass

vaccination sites slows to a trickle, vaccination emphasis pivots to smaller groups, individualized outreach and promotional efforts like lotteries.

As with so many things in the pandemic, significant disparities exist in vaccinations based on socioeconomic and health status. The below chart from CDPH shows vaccinations in four population segments based on health status. Vaccinations are highest among the healthiest segment (71.5% fully vaccinated) while the least healthy segment is 47.1% fully vaccinated.



Source CDPH: The Vaccine Equity Metric (VEM) combines the Healthy Places Index with CDPH-derived scores to create four population quartiles, ranging from less healthy community conditions in Quartile 1 to healthier communities in Quartile 4.



Source: UCH Data Warehouse

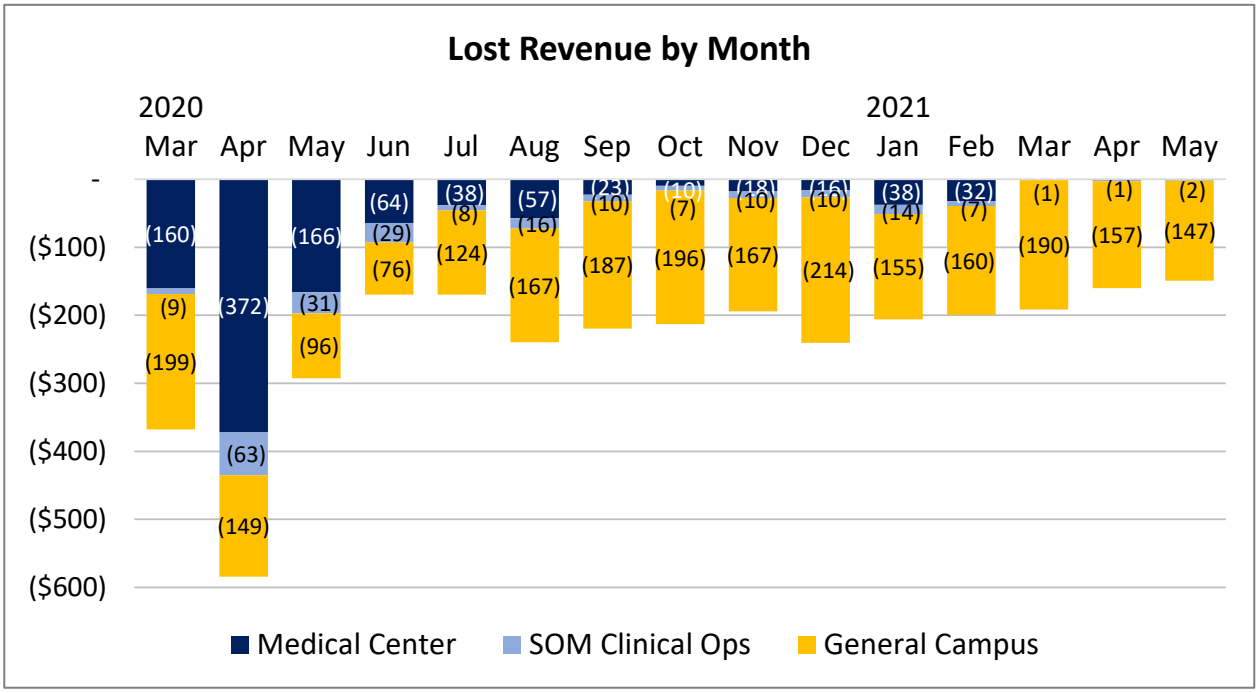
The electronic health records at our academic health centers not only capture an individual's health status but also overlay place of residence with the Healthy Places Index. We will continue leveraging these tools to the fullest of our ability to close the gap among the most vulnerable.

By now, you are very familiar with our inpatient data, which we've tweeted each weekday for more than a year (**left**). I want to thank Dr. Atul Butte and his team at the UCH Center for Data Driven Insights & Innovation (CDI2) for this heavy lift. We are discontinuing external reporting but stand ready to resume if needed.

RECOVERING FROM THE FINANCIAL IMPACT

The human toll is the figure foremost in our minds. The more than 600,000 deaths across the country are accompanied by that many grieving families and many times that of friends and colleagues. Health care workers on the front lines, and those who support them, bear an emotional toll that will take time to process.

Operational costs have been significant. From the earliest days of the pandemic, University of California Health prepared and supported the state's response. The soaring costs and plunging revenues for the health centers have moderated and stabilized.



Lost Revenue due to COVID from March, 2020 to May, 2021. Source: DOF COVID-19 Cost Impact Report, June 11, 2021

A FOURTH VACCINE MAY BE ON ITS WAY IN THE U.S.

There are three COVID-19 vaccines in the U.S. with Emergency Use Authorization (EUA) approval from the Food and Drug Administration. They may soon be joined by a fourth.

Vaccine maker Novavax reported preliminary results of its vaccine from late-stage clinical trials, indicating approximately 90% effectiveness, including against many variants. UC Davis Health participated in its clinical trials.

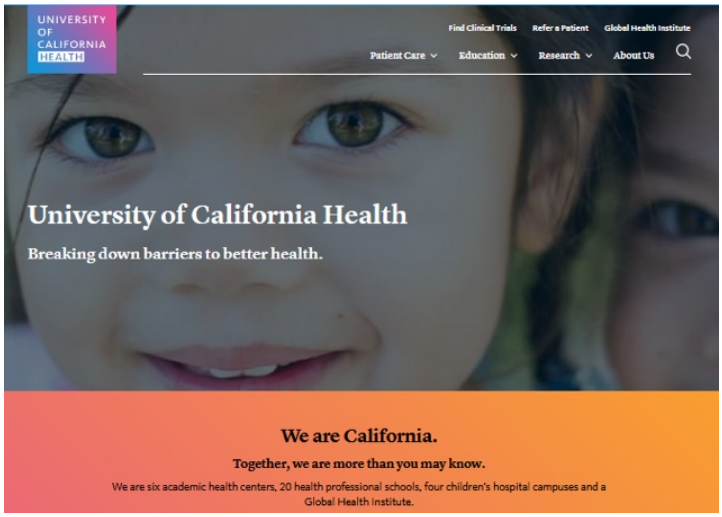
In its June 14 announcement, Novavax said it would seek U.S., European, and other authorizations in the fall with a goal of producing 100 million doses per month. Although vaccines are readily available now in this country, there remains a worldwide shortage of vaccine, especially in countries with the lowest household incomes. Like the Jansen/Johnson & Johnson vaccine, the Novavax product is less temperature sensitive, which increases its ability to be transported and administered in more settings.

I urge all of us to remember that beyond our borders, there are literally billions of people who remain at risk of COVID-19. Ensuring global access to vaccination is not simply ethical and humane, but it is also the only way to stop the widespread circulation of the virus that leads to mutations. I applaud the efforts of the Biden-Harris administration to provide up to 80 million doses of vaccines internationally by the end of June 2021, and remind us that the global population stands at 7.6 billion.

NEWS OTHER THAN COVID-19

We have an extraordinary organization and some of the world's most talented people. Each academic health center, health professional school and the Global Health Institute have earned national and international acclaim. When we work together, amazing things happen.

Our journey toward 'systemness' began long before COVID-19. The experience of working closely in pandemic response brought that strength to the forefront. To us, 'systemness' means we share knowledge and work with colleagues across all locations with a common purpose. By working within each location and across the system, we accelerate the pace of discovery and sharing of best practices for the common good. Thus, systemness does not refer to a top-down structure, but one that is dynamic and naturally drawn to the toughest challenges in health and society.



Source: UniversityofCalifornia.Health website

We now have a platform to express our unique version of systemness – UniversityofCalifornia.Health is a new website that helps tell our story to prospective patients, aspiring health students, elected officials, media and others. It does not replace our other platform, but tells our story from another perspective and links to each entity for the visitor's benefit. I hope you will explore it and share it.

IN CLOSING

Summer has always been my favorite season. I am hopeful that in California, with our excellent vaccine rates, we can enjoy summer 2021. As you enjoy the season, I ask you to remember the sacrifice, work, and miracles of science that have brought us to this moment.

Vaccination is key to maintaining the gains we have made in the US and is key to controlling the pandemic globally. You can help by ensuring that you and your loved ones are vaccinated. Talk with your friends, acquaintances, neighbors, and co-workers to encourage them to be vaccinated. Support efforts in your communities to bring vaccines to those in hard-to-reach areas. Finally consider supporting efforts to bring COVID-19 vaccines to less affluent parts of the world by donating to established non-profits such as UNICEF USA, the GAVI Alliance COVAX program or the charitable organization of your choice.

I will gratefully celebrate another birthday on July 1 and on the same day, across University of California Health we start a new academic year. This is a time both for new beginnings and a time for reflection.

I found this verse in the recently published crowd-sourced poem by Kwame Alexander particularly resonant. I hope you will enjoy the full poem available here.

I WAKE WITH WONDER

We rise
even when our spirits feel deflated
because this too shall be past
because we are made of stardust
I am
A new breath in an older body
with
A future to ponder

Crowd Sourced by Kwame Alexander

I wish you all a happy 4th of July and a joyful and safe summer. At UCH, be assured that we will continue to monitor the trajectory of the pandemic and work to keep our patients and communities healthy and informed. Like each of you, we hope this will be our last COVID-19 newsletter.

Fiat Lux.

Carrie L. Byington, MD
Executive Vice President
University of California Health

EXHIBIT E

SARS-CoV-2 sequencing reveals rapid transmission from college student clusters resulting in morbidity and deaths in vulnerable populations

Craig S. Richmond[1], Arick P. Sabin[2], Dean A. Jobe[3], Steven D. Lovrich[3], Paraic A. Kenny[1,*]

[1]Kabara Cancer Research Institute, Gundersen Medical Foundation, La Crosse, Wisconsin.

[2]Department of Infectious Disease, Gundersen Health System, La Crosse, Wisconsin.

[3]Gundersen Microbiology Research Laboratory, Gundersen Medical Foundation, La Crosse, Wisconsin

*For correspondence: pakenny@gundersenhealth.org

ABSTRACT

College reopening decisions during the SARS-CoV-2 pandemic represent a trade-off between competing risks to students, faculty and staff, and college finances. Additionally, risks taken in reopening colleges can impose significant burdens on individuals living in surrounding communities. Many colleges that reopened for in-person instruction have reported frequent SARS-CoV-2 outbreaks. La Crosse County, Wisconsin experienced a substantial SARS-CoV-2 outbreak (2,002 cases in September 2020) that coincided with the return to in-person instruction at three local academic institutions. Genomic sequencing of SARS-CoV-2 cases in La Crosse during that period found rapid expansion of two viral substrains. Although the majority of cases were among college-age individuals, from a total of 111 genomes sequenced we identified rapid transmission of the virus into more vulnerable populations. Eight sampled genomes represented two independent transmission events into two skilled nursing facilities, resulting in two fatalities. Our study highlights the very significant risks imposed by college administrator reopening decisions, not just on college-associated populations, but on vulnerable individuals in surrounding communities.

INTRODUCTION

The SARS-CoV-2 betacoronavirus is a novel respiratory pathogen which emerged in Wuhan, China in late 2019 (1). Numerous teams around the world have produced a rapidly increasing number of publicly available sequences (116,650 in GISAID on 9/28/20) with obvious sequence diversification as viral replication and spread has continued. These sequence variants, inherited in each cycle of viral replication, allow the generation of phylogenetic trees through which the evolution of the virus can be traced. Individual viruses acquire mutations during replication at an approximate rate of 1-2 sites per month (2). This mutation rate provides good resolution for both global and local tracking of viral substrains. Because viral replication occurs in individuals, tracking these inherited variants acts as a proxy for tracking the spread of the virus through populations of individuals.

Starting in late March 2020, we have monitored the introduction and spread of SARS-CoV-2 to the service area of the Gundersen Health System, an integrated healthcare system headquartered in La Crosse, WI and providing care in 21 counties in southwestern Wisconsin, northeastern Iowa and southeastern Minnesota. We have performed whole viral genome sequencing on 514 positive cases from this region, spanning three states which have adopted mitigation approaches of differing intensity.

In September 2020, La Crosse County (Wisconsin) experienced a rapid increase in cases, strongly driven by infections among the 10-19 and 20-29 age groups. The period coincided with the return of college students to three institutions of higher education in the city of La Crosse: University of Wisconsin La Crosse, Western Technical College and Viterbo University, with total enrollments of 10,558, 4,004 and 2,592, respectively (3). Our regional SARS-CoV-2 surveillance and sequencing program captured many of these genomes, allowing assessment of the substrain contributions to the outbreak and analysis of the speed with which vulnerable non-student populations were affected.

MATERIALS AND METHODS

Specimens

Specimens were nasopharyngeal swabs taken for diagnostic purposes and evaluated for SARS-CoV-2 positivity at the Gundersen Medical Foundation's Molecular Diagnostics Laboratory using the CDC 2019-nCoV Real-Time RT-PCR Diagnostic assay. This study includes positive cases diagnosed between

3/18/2020 and 9/23/2020. Ethical approval was obtained from the Gundersen Health System Institutional Review Board (#2-20-03-008; PI: Kenny) to perform additional next-generation sequencing on remnant specimens after completion of diagnostic testing. Samples for this study include only those testing positive in Gundersen Healthcare System's diagnostic laboratories and, as such, do not include other cases from the region which may have been tested in other healthcare systems and/or public health laboratories.

RNA isolation and cDNA synthesis

Nasopharyngeal swabs were immersed in liquid medium. RNA was isolated using QIAmp Viral RNA Mini kit (Qiagen, Germantown, MD). cDNA was synthesized from 5 µl of purified RNA using ProtoScript II First Strand cDNA Synthesis Kit (New England Biolabs, Ipswich, MA) with random hexamers.

Next Generation sequencing

We used the Ion AmpliSeq SARS-CoV-2 Panel (Thermo-Fisher, Waltham, MA) to sequence 237 viral specific targets encompassing the complete viral genome from cDNA derived from SARS-COV-2-positive clinical specimens. Barcoded multiplexed libraries were prepared in batches of eight on the Ion Chef (Thermo-Fisher) and sequenced on the Ion Torrent S5 (Thermo-Fisher).

Bioinformatics

Demultiplexed Tmap-aligned bam files were produced by the Ion Torrent S5. To overcome difficulties caused by read soft-clipping by this non-splice aware aligner, individual sequence reads were extracted using samtools (4) and re-aligned to the SARS-CoV-2 genome using a splice-aware aligner, hisat2 (5). These bam files were subjected to QC review in IGV. Samples passing QC had a consensus sequence computed according to the method of Cavener (6). Consensus sequences were reported to GISAID (7). For phylogenetic inference (i.e. to determine the hierarchy of case relationships) samples were integrated with associated metadata and aligned on a local implementation of NextStrain (8) using augur and displayed via a web browser using auspice. Choropleth maps were generated using folium.

RESULTS

The cumulative history of SARS-CoV-2 cases, stratified by age, for La Crosse county is shown in Figure 1. Notable events along this timeline include the reopening of bars in Wisconsin (5/14/2020) and the onset

of warm summer weather (first day above 80'F was on Memorial Day Weekend on 5/24/2020) which preceded a rapid rise in cases in early-mid June. Case growth continued at a slower rate for much of the summer before abruptly increasing in the second week of September, coinciding with the return of students to three colleges located in the city of La Crosse. Analysis of cases by census tract showed that the most rapid case growth was occurring the immediate vicinity of the three colleges, an area of high density student housing (Figure 2).

Between 3/18/20 and 9/23/20 we obtained 514 high quality genomes (Figure 3A) from surveillance in a 21-county region of western Wisconsin, southeastern Minnesota and northeastern Iowa. Clades are colored for ease of visualization and include several epidemiologically relevant outbreaks. Significant examples include (i) an outbreak originating in a meatpacking plant in Postville, IA (9) and (ii) a large outbreak associated with a cluster of bars in downtown La Crosse in June/July. Figure 3B highlights newly sequenced genomes in our region in September 2020. The overwhelming majority of case growth in La Crosse county was explained by two clusters, designated "College A" and "College B". The small light-blue cluster at the 11 o'clock position represents a substrain detected in the city of Holmen, which did not involve college students, while the other highlighted clades represented case growth in our region outside of La Crosse county. Here we focus on the analysis of the College A and College B clusters.

During this period, all three academic institutions posted "COVID19 dashboards" on their websites, analysis of which indicated that the majority of cases were associated with the largest institution (University of Wisconsin – La Crosse, "UWL"), followed by Viterbo University and with relatively few cases affecting students enrolled at Western Technical College. UWL ran its own surveillance and diagnostic program for students living in dormitories (approximately 3000 students), but did not deploy resources sufficient to provide any surveillance for its large off-campus student population. Our sequencing program captured all positive tests conducted at the Gundersen Health System molecular diagnostic laboratory, a service availed of by many members of the off-campus population. Accordingly, while we generally lack genomes from the student dorm populations, our considerable coverage of the off-campus population and the presumably large amount of intermixing that occurred between the on and-off campus student populations due to the prevalent "party culture" (10,11) makes it unlikely that a substantial outbreak comprising an unrelated substrain might have occurred in and been restricted to the dorm-dwelling population.

Demographic details of the 111 individuals carrying the College A and B substrains are shown in Table 1. In total, 40.5% of the specimens were obtained from individuals aged between 17 and 24, with a further 16.2% from the 25-29 age group. For the entire cohort, 57.7% of cases affected females, although cases were more evenly distributed between sexes among the 17-29 year old group. 19 cases (17.1%) affected individuals aged over 60, including 4 cases among individuals in their 90s. This pattern of spread from clusters of younger age individuals into more vulnerable age groups is consistent with observations of a time-lag in which cases among older individuals tend to rise after outbreaks among young individuals (12). Although this statistical trend is evident from a nationwide analyses (12), our ability to establish direct genetic links using sequencing between the two age groups provides compelling evidence that risks of rapid spread of SARS-CoV-2 among college-age individuals are not limited to college environs but pose a direct threat to older persons in the surrounding community.

Table 1: Demographics of individuals associated with College A and College B clusters

		College A (n=68)	College B (n=43)	Both Strains (n=111)
Age Group	**0-5**	0 (0%)	1 (2.3%)	1 (0.9%)
	6-16	1 (1.5%)	1 (2.3%)	2 (1.8%)
	17-24	24 (35.3%)	21 (48.8%)	45 (40.5%)
	25-29	15 (22.1%)	3 (7%)	18 (16.2%)
	30-39	6 (8.8%)	4 (9.3%)	10 (9.0%)
	40-49	9 (13.2%)	1 (2.3%)	10 (9.0%)
	50-59	4 (5.9%)	2 (4.7%)	6 (5.4%)
	60-69	4 (5.9%)	3 (7%)	7 (6.3%)
	70-79	3 (4.4%)	1 (2.3%)	4 (3.6%)
	80-89	2 (4.7%)	2 (4.7%)	4 (3.6%)
	90-99	0 (0%)	4 (9.3%)	4 (3.6%)
Sex (All ages)	**Male**	30 (44.1%)	17 (39.5%)	47 (42.3%)
	Female	38 (55/9%)	26 (60.5%)	64 (57.7%)
Sex (Ages 17-29)	**Male**	22 (56.4%)	10 (41.6%)	32 (50.8%)
	Female	17 (43.6%)	14 (58.3%)	31 (49.2%)

Detailed phylogenetic trees for both College A and B clusters are shown in Figure 4. Trees are scaled to show genetic divergence of the virus, such that samples aligned vertically are genetically identical and placement of a sample one increment to the right indicates acquisition of a single new mutation. Within both clusters, we found evidence of subgroups sharing identical viruses which typically reflect individuals infected in quick succession from a common source (e.g. at one or more parties). Groups of cases containing five or more genetically identical genomes are highlighted in orange, and the median age of individuals in these four groups were 20.5, 21, 25 and 29. This pattern is consistent with rapid spread of SARS-CoV-2 among the younger age group. Although both College A and B clusters included older individuals (See Table 1), analysis of the College B cluster indicated that this particular substrain had been transmitted into two skilled nursing facilities. The sequencing data revealed independent clusters affecting three patients in one facility and two staff and five patients in the second facility. Two of these patients died from COVID-19.

DISCUSSION

This study provides an interim yet comprehensive look at a still-ongoing outbreak centered on the neighborhoods surrounding college campuses in a midwestern city, La Crosse, WI. While the 111 genomes sampled represent a fraction of the total cases in La Crosse county in this September outbreak, the data appear sufficient to draw some important conclusions about the nature of the outbreak and early consequences for vulnerable populations, as well as prompting consideration of whether various mitigation strategies adopted elsewhere could have been helpful.

Firstly, this large outbreak was overwhelmingly driven by just two substrains of SARS-CoV-2 which was quite surprising. Restarting of in-person education involved the return of many thousands of students from a wide range of cities and small towns throughout the Midwest at a time when SARS-CoV-2 cases in Midwestern 18-22 year olds were increasing at a rate more than twice the national average for that age group (13). Accordingly, we had expected greater viral diversity consistent with multiple independent viral introductions. In contrast, the major signal detected was for just two substrains which spread very rapidly among an at-risk population which socialized repeatedly at high-density alcohol-fueled indoor and outdoor gatherings. We cannot exclude the possibility that there were additional contemporaneous viral introductions and that these two substrains fortuitously happened to be the earliest to be exposed to large susceptible populations at events favoring rapid SARS-CoV-2 spread such that other potential substrains did not have the opportunity to access such a large susceptible

population. Nevertheless, our data imply that the overwhelming majority of students were SARS-CoV-2-negative upon return to the campus environs and that rapid local spread, rather than imported cases, was the primary cause of the local outbreak.

Nationally, several universities made very considerable financial investments in pre-testing all students before their return to campus, a mitigation strategy that was not attempted in La Crosse. Our data suggest that, had that strategy been employed in La Crosse, it would have had a negligible impact on preventing the outbreak. At best, it might have delayed an inevitable outcome by a few days. Clearly, introduction of just two viral substrains was sufficient to fuel this very significant outbreak. In a setting where students from multiple colleges interact with each other and with other residents of a city with pre-existing SARS-COV-2 cases, student behavior will likely lead to significant outbreaks whether the initial student-imported viral input is large or small.

Testing of symptomatic and asymptomatic students after college opening is likely a more useful intervention, if performed at a sufficient frequency. When modeling multiple scenarios to mitigate SARS-CoV-2 spread during college re-opening for an 80-day fall semester, Paltiel and colleagues estimated that testing the entire student population every two days could limit cumulative infections to 4.9% of students, while weekly testing would result in 37% of students becoming infected (14). Importantly, both estimates involved assumptions of strong adherence to mask-wearing, handwashing, social-distancing, de-densifying classrooms and limiting bathroom sharing. The UWL plan for its 10,500 student body involved asymptomatic testing of its dormitory resident population (3000 students) once every 14 days with no surveillance testing among the much larger off-campus population. Considering that Paltiel estimated that testing 100% of an idealized guideline-adherent student population weekly would still lead to a cumulative infection rate of 37%, it seems likely that testing only 28% of an actual student population at half that frequency would be utterly inadequate to manage inevitable outbreaks. Success in Paltiel's model also required efficiently functioning quarantine and isolation dormitories, a situation at variance with the chaotic situation at UWL where student reporters described individuals quarantined while the results of their tests were pending, partying in the quarantine dorm with COVID19-positive individuals, and then being released when their pre-quarantine test returned negative (15).

We detected these student-amplified infection clusters as part of a 21-county surveillance program in the Gundersen Healthcare System's service area. Because this program was not student focused, we were collecting and sequencing other community cases in parallel. This allowed us to quickly detect the overspill from the college-age population in older adults. While these findings were consistent with public health expectations about risk to older population in settings of wide community spread and with epidemiological studies showing a statistical association in which case increases in young adults are typically followed by cases among older adults (12), our ability to genetically link these groups of cases provides direct evidence of transmission between these different age groups. Of particular concern, was the rapid transmission of one of these SARS-CoV-2 substrains into two skilled nursing facilities, causing sustained outbreaks with two fatalities so far. Our first case of what we came to call the "College B" cluster was collected on 8/27/20, a time when cases were slowly but steadily rising (Figure 1). The inflection point on the curve when cases began to rise more rapidly was on 9/10/20 (Figure 1) and the first skilled nursing facility patient specimen associated with this cluster was detected on 9/14/20.

CONCLUSIONS

For college clusters, much concern has focused on higher risks to older faculty/staff as well as less frequent but significant adverse outcomes in younger individuals. In addition, university leaders clearly face a range of concerns including very significant financial pressures. Given the described testing strategy, the highly contagious properties of SARS-CoV-2, news reports of widespread outbreaks in other college communities that had attempted return to in-person instruction at earlier dates (16,17) and the well-understood risk-embracing nature of college students (18), the outbreak that occurred in La Crosse in September 2020 was likely inevitable once the decision to return to in-person instruction was taken. Our study highlights the very significant risks imposed by college administrator reopening decisions, not just on college-associated populations, but on vulnerable individuals in surrounding communities. Although our primary focus has been on using viral genetics to track introduction and spread of these substrains, we note that the adverse effects of college-amplified clusters are not limited to the morbidity and mortality of infected individuals and the substantial associated healthcare costs. Rapid case growth, as experienced in La Crosse, intensifies the magnitude of the multifaceted adverse effects of the pandemic upon communities. These effects include significantly extending the period during which children are unable to attend in-person K-12 schooling (19), further exacerbation of the many psychosocial stresses affecting both individuals and families (20), extending the ongoing unemployment crisis (21), placing more families at risk of losing health insurance (22) and harming small

businesses (23). These factors should all be considered as part of any cost-benefit analysis of reopening colleges and universities.

ACKNOWLEDGEMENTS

This work was supported by the Gundersen Medical Foundation. PK holds the Dr. Jon & Betty Kabara Endowed Chair in Precision Oncology. We thank the members of the Gundersen Medical Foundation's Molecular Diagnostics Laboratory for providing the specimens used in this study.

REFERENCES

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, *et al.* A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med **2020**;382:727-33
2. van Dorp L, Acman M, Richard D, Shaw LP, Ford CE, Ormond L, *et al.* Emergence of genomic diversity and recurrent mutations in SARS-CoV-2. Infect Genet Evol **2020**;83:104351
3. US News and World Report. <https://www.usnews.com/education>.
4. Li H, Handsaker B, Wysoker A, Fennell T, Ruan J, Homer N, *et al.* The Sequence Alignment/Map format and SAMtools. Bioinformatics **2009**;25:2078-9
5. Kim D, Paggi JM, Park C, Bennett C, Salzberg SL. Graph-based genome alignment and genotyping with HISAT2 and HISAT-genotype. Nat Biotechnol **2019**;37:907-15
6. Cavener DR. Comparison of the consensus sequence flanking translational start sites in Drosophila and vertebrates. Nucleic Acids Res **1987**;15:1353-61
7. Shu Y, McCauley J. GISAID: Global initiative on sharing all influenza data - from vision to reality. Euro Surveill **2017**;22
8. Hadfield J, Megill C, Bell SM, Huddleston J, Potter B, Callender C, *et al.* Nextstrain: real-time tracking of pathogen evolution. Bioinformatics **2018**;34:4121-3
9. Richmond CS, Sabin AP, Jobe DA, Lovrich SD, Kenny PA. Interregional SARS-CoV-2 spread from a single introduction outbreak in a meat-packing plant in northeast Iowa. medRxiv **2020**:2020.06.08.20125534
10. Chaudhuri G, Oxley S, Wenzlaff S. Mapping Spatiotemporal Patterns of Liquor Law Violation Citations During Oktoberfest in College Town of La Crosse, Wisconsin. Forensic GIS: Springer; 2014. p 201-20.
11. Swanson DJ, Zegers KM, Zwaska AA. Implementing a social norms approach to reduce alcohol abuse on campus: Lessons learned in the shadow of 'The World's Largest Six-Pack'. The Social Science Journal **2004**;41:621-35
12. Boehmer TK, DeVies J, Caruso E, van Santen KL, Tang S, Black CL, *et al.* Changing Age Distribution of the COVID-19 Pandemic - United States, May-August 2020. MMWR Morb Mortal Wkly Rep **2020**;69:1404-9
13. Salvatore PP, Sula E, Coyle JP, Caruso E, Smith AR, Levine RS, *et al.* Recent Increase in COVID-19 Cases Reported Among Adults Aged 18-22 Years - United States, May 31-September 5, 2020. MMWR Morb Mortal Wkly Rep **2020**;69:1419-24

14. Paltiel AD, Zheng A, Walensky RP. Assessment of SARS-CoV-2 Screening Strategies to Permit the Safe Reopening of College Campuses in the United States. JAMA Netw Open **2020**;3:e2016818
15. Balli J. "I felt like I was in a lot of danger": UWL students tell all on quarantine in Wentz Hall. The Raquet Press 2020;https://theracquet.org/10608/news/i-felt-like-i-was-in-a-lot-of-danger-uwl-students-tell-all-on-quarantine-in-wentz-hall/.
16. Wilson E, Donovan CV, Campbell M, Chai T, Pittman K, Sena AC, *et al.* Multiple COVID-19 Clusters on a University Campus - North Carolina, August 2020. MMWR Morb Mortal Wkly Rep **2020**;69:1416-8
17. Yamey G, Walensky RP. Covid-19: re-opening universities is high risk. BMJ **2020**;370:m3365
18. Willoughby T, Good M, Adachi PJ, Hamza C, Tavernier R. Examining the link between adolescent brain development and risk taking from a social-developmental perspective (reprinted). Brain Cogn **2014**;89:70-8
19. Masonbrink AR, Hurley E. Advocating for Children During the COVID-19 School Closures. Pediatrics **2020**;146
20. Pfefferbaum B, North CS. Mental Health and the Covid-19 Pandemic. N Engl J Med **2020**;383:510-2
21. Blustein DL, Duffy R, Ferreira JA, Cohen-Scali V, Cinamon RG, Allan BA. Unemployment in the time of COVID-19: A research agenda. J Vocat Behav **2020**;119:103436
22. Woolhandler S, Himmelstein DU. Intersecting U.S. Epidemics: COVID-19 and Lack of Health Insurance. Ann Intern Med **2020**;173:63-4
23. Bartik AW, Bertrand M, Cullen Z, Glaeser EL, Luca M, Stanton C. The impact of COVID-19 on small business outcomes and expectations. Proc Natl Acad Sci U S A **2020**;117:17656-66

FIGURES LEGENDS

Figure 1. Cumulative SARS-CoV-2 case incidence in La Crosse County, WI, stratified by age group (March – September 2020).

Figure 2. Choropleth heatmaps showing a weekly assessment of the 7-day rolling average of daily case numbers per 100,000 population in census tracts in the city of La Crosse. Census tract populations were taken from 2010 census data. The locations of University of Wisconsin – La Crosse (UWL), Western Technical College (WTC) and Viterbo University (VIT) are indicated.

Figure 3. Radial time resolved phylogenetic trees containing (A) all 514 high-quality genomes sequenced between 3/18/20 and 9/28/20 and (B) highlighting just those specimens sequenced in September. Sequencing results are from a 21-county region of Wisconsin, Minnesota and Iowa. The case growth in La Crosse County in September was attributed to the College A and College B clusters.

Figure 4. Phylogenetic trees demonstrating the relationships between cases in the College A and College B substrains. Trees are scaled by sequence divergence so that identical genomes are vertically aligned and each further increment to the right represents acquisition a new nucleotide variant. Clade-defining mutations are indicated in both cases. Groups of 5 or more genetically identical cases are highlighted in orange, with the median age of individuals in each group indicated. Transmission chains in two skilled nursing facilities, detected in the College B cluster, are also highlighted.

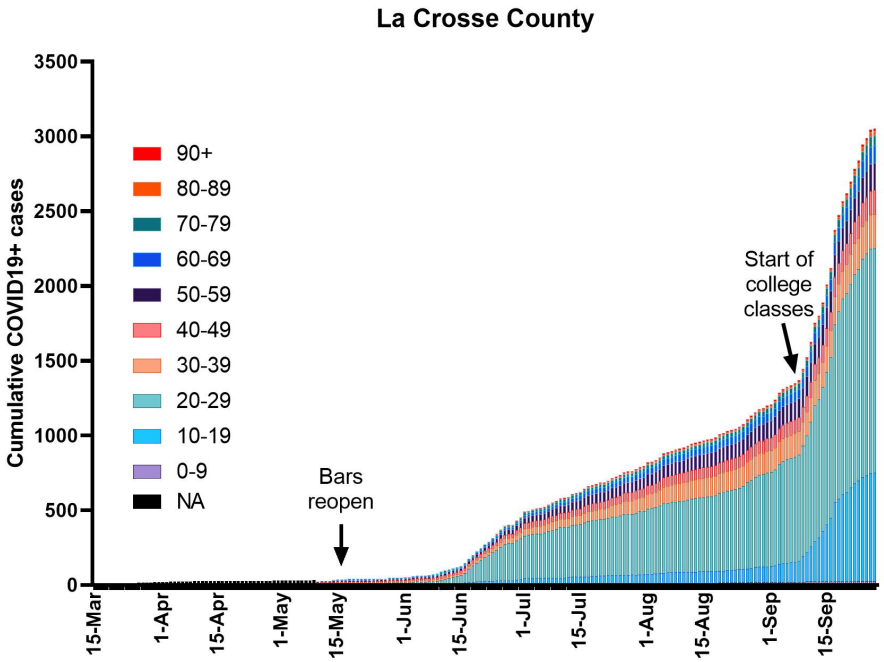

La Crosse County
Cumulative COVID19+ cases
3500
3000
2500
2000
1500
1000
500
0
90+
80-89
70-79
60-69
50-59
40-49
30-39
20-29
10-19
0-9
NA
Bars reopen
Start of college classes
15-Mar
1-Apr
15-Apr
1-May
15-May
1-Jun
15-Jun
1-Jul
15-Jul
1-Aug
15-Aug
1-Sep
15-Sep

Fig 1

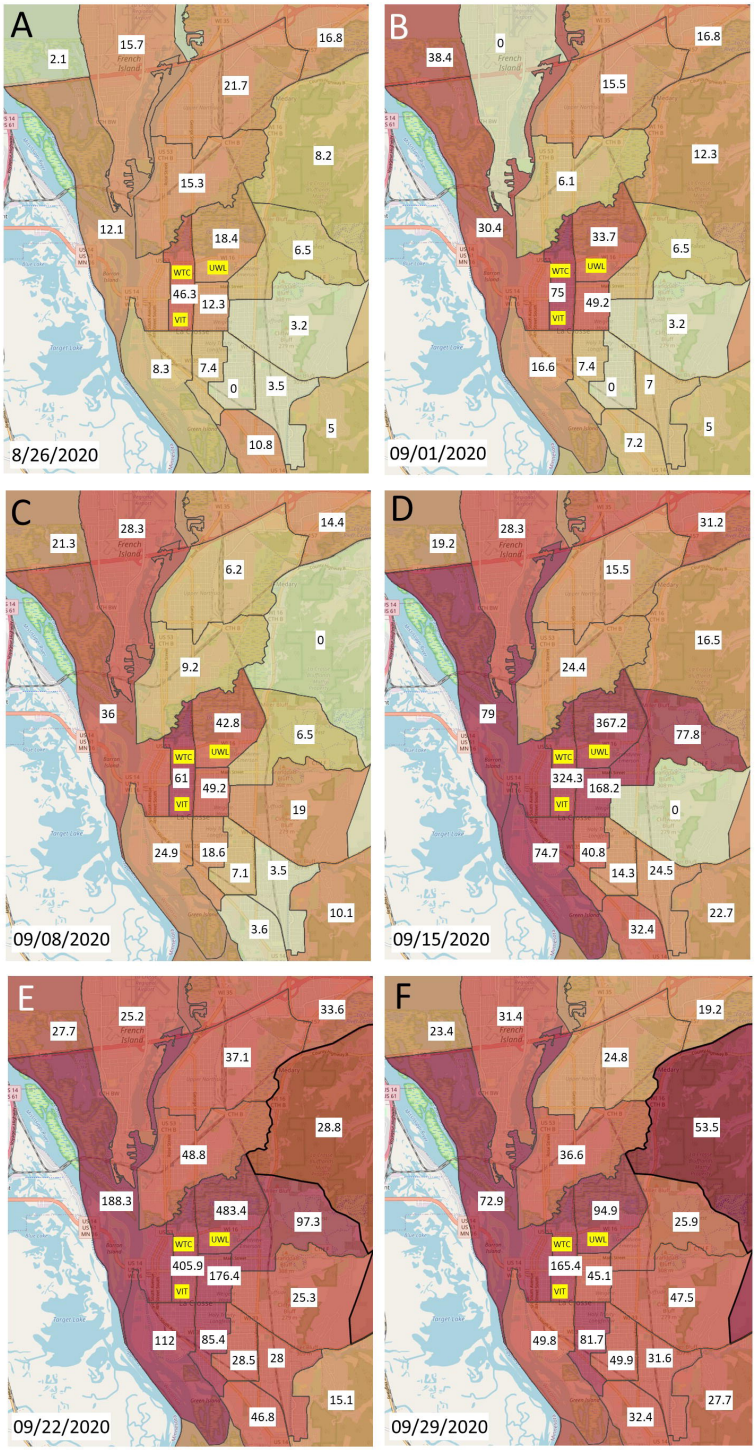

A
8/26/2020
B
09/01/2020
C
09/08/2020
D
09/15/2020
E
09/22/2020
F
09/29/2020
WTC
UWL
VIT

Fig 2

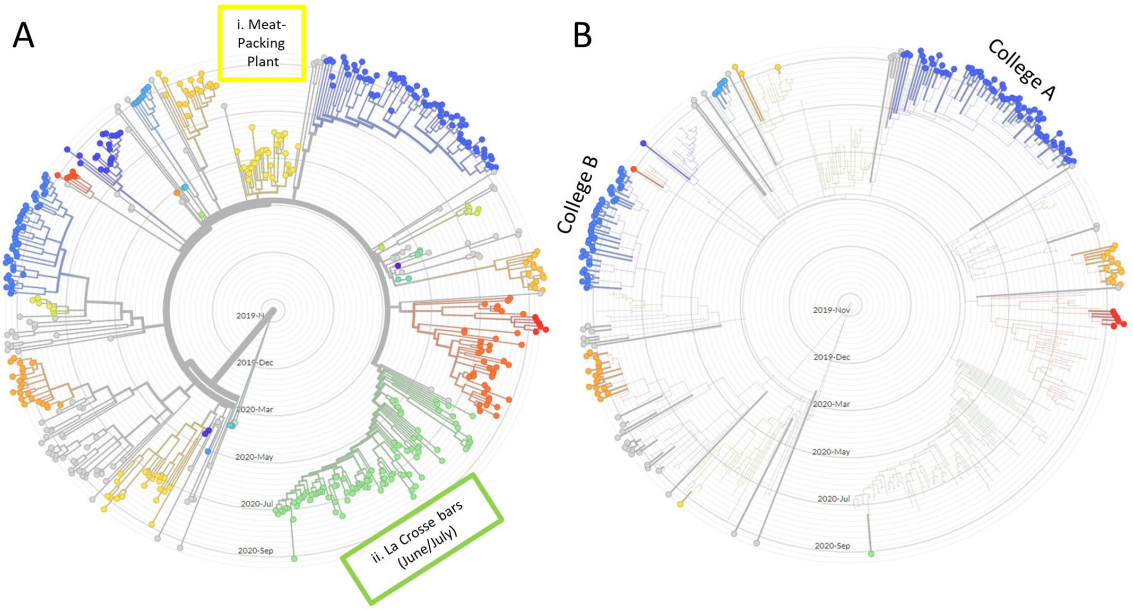

A
i. Meat-Packing Plant
2019-Nov
2019-Dec
2020-Mar
2020-May
2020-Jul
2020-Sep
ii. La Crosse bars (June/July)
B
College A
College B
2019-Nov
2019-Dec
2020-Mar
2020-May
2020-Jul
2020-Sep

Fig 3

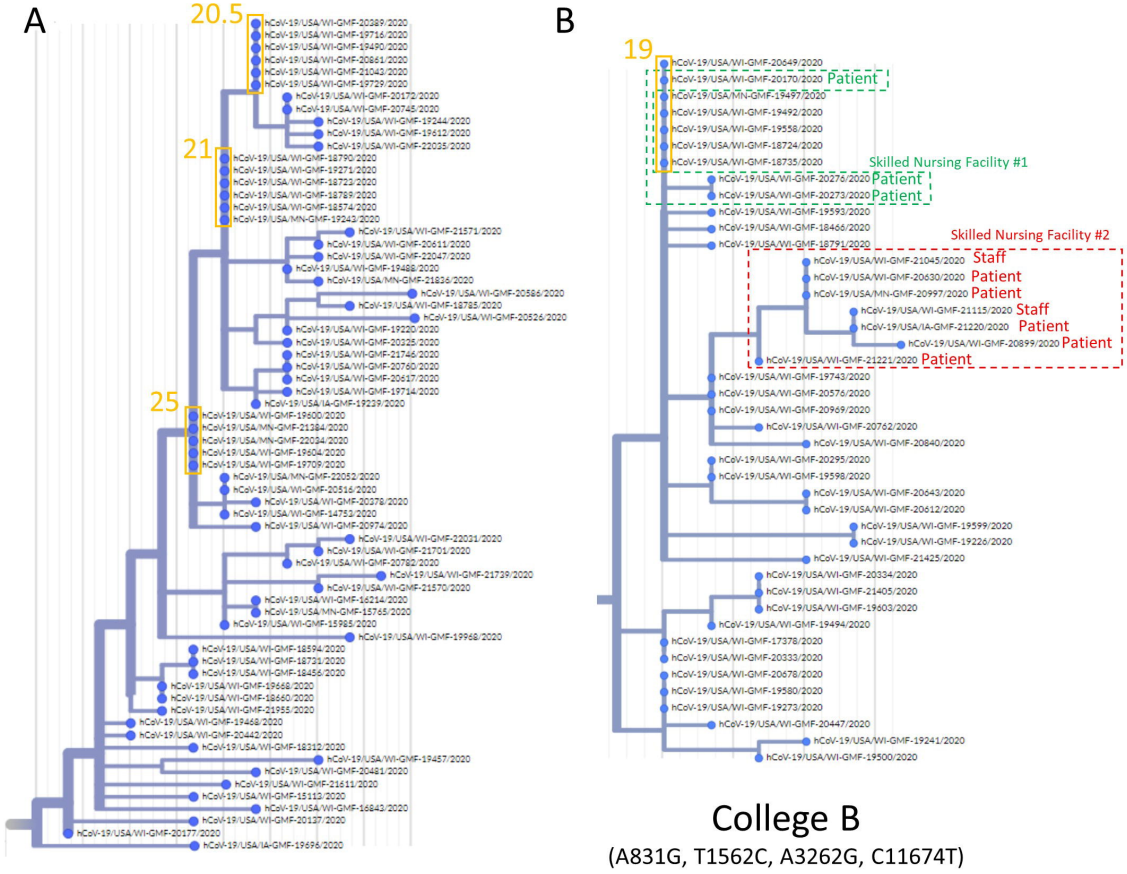

A
20.5
21
25
College A
(C27964T, C28869T)
B
19
Patient
Skilled Nursing Facility #1
Skilled Nursing Facility #2
Staff
Patient
College B
(A831G, T1562C, A3262G, C11674T)

Fig 4

EXHIBIT F

Morbidity and Mortality Weekly Report

Opening of Large Institutions of Higher Education and County-Level COVID-19 Incidence — United States, July 6–September 17, 2020

Andrew J. Leidner, PhD[1]; Vaughn Barry, PhD[1]; Virginia B. Bowen, PhD[1]; Rachel Silver, MPH[1]; Trieste Musial, MS[2]; Gloria J. Kang, PhD[1]; Matthew D. Ritchey, DPT[3]; Kelly Fletcher, MPH[2]; Lisa Barrios, DrPH[1]; Eric Pevzner, PhD[1]

During early August 2020, county-level incidence of coronavirus disease 2019 (COVID-19) generally decreased across the United States, compared with incidence earlier in the summer (*1*); however, among young adults aged 18–22 years, incidence increased (*2*). Increases in incidence among adults aged ≥60 years, who might be more susceptible to severe COVID-19–related illness, have followed increases in younger adults (aged 20–39 years) by an average of 8.7 days (*3*). Institutions of higher education (colleges and universities) have been identified as settings where incidence among young adults increased during August (*4*,*5*). Understanding the extent to which these settings have affected county-level COVID-19 incidence can inform ongoing college and university operations and future planning. To evaluate the effect of large colleges or universities and school instructional format* (remote or in-person) on COVID-19 incidence, start dates and instructional formats for the fall 2020 semester were identified for all not-for-profit large U.S. colleges and universities (≥20,000 total enrolled students). Among counties with large colleges and universities (university counties) included in the analysis, remote-instruction university counties (22) experienced a 17.9% decline in mean COVID-19 incidence during the 21 days before through 21 days after the start of classes (from 17.9 to 14.7 cases per 100,000), and in-person instruction university counties (79) experienced a 56.2% increase in COVID-19 incidence, from 15.3 to 23.9 cases per 100,000. Counties without large colleges and universities (nonuniversity counties) (3,009) experienced a 5.9% decline in COVID-19 incidence, from 15.3 to 14.4 cases per 100,000. Similar findings were observed for percentage of positive test results and hotspot status (i.e., increasing among in-person–instruction university counties). In-person instruction at colleges and universities was associated with increased county-level COVID-19 incidence and percentage test positivity. Implementation of increased mitigation efforts at colleges and universities could minimize on-campus COVID-19 transmission.

The National Center for Educational Statistics' Integrated Postsecondary Education Data System (*6*) was used to identify not-for-profit baccalaureate degree–granting colleges and universities enrolling ≥20,000 full-time and part-time students. Colleges and universities that enrolled <20,000 students or were considered for-profit were excluded. Fall class start dates and instructional formats on the first day of scheduled classes were abstracted from college and university websites during early September 2020. Counties with large colleges and universities were assigned the start date and instructional format of the school. If a county contained multiple large colleges or universities with different start dates, the earliest start date and corresponding instructional format was assigned. If a county contained multiple large schools with the same start date but different instructional formats, then in-person instruction was assigned. Among 133 counties with large colleges and universities (university counties),† the 101 (76%) in which classes started from July 27 to August 28 were included in the analysis (i.e., 32 were excluded because they included institutions that started on or after August 29 and had insufficient data for the 21 days after the start of classes at the time of analysis). County-level mean estimates of COVID-19 incidence,§ testing rates, percentage test positivity,¶ and hotspot status** were compared for university counties with remote-instruction, in-person–instruction, and nonuniversity counties during the 21 days before and after the start of classes.

* Instructional format was assigned based on the advertised method of instruction for the first day of fall 2020 classes. "Remote" format was defined as an instructional format that appeared to minimize in-person classwork on campus. This definition did allow in-person instruction for a very select number of students, including those in laboratory courses, studio courses, or courses for small groups of students with specific instructional needs. In contrast, the "in-person" format was defined for all other colleges and universities that were not considered remote, which included any instructional format that did not appear to minimize in-person classwork on campus. "Hybrid" instructional formats that had reduced, but reoccurring, in-class experiences for many college and university courses (i.e., beyond laboratory and studio courses) were considered "in-person" for this study. The assignment of instructional format was based on the advertised method of instruction and was not based on the college or university policy toward on-campus housing; therefore colleges and universities with remote instruction could have allowed students to stay in on-campus housing.

† A total of 149 large colleges and universities were identified across 133 counties.

§ Incidence was calculated using COVID-19 case counts from state and county health department websites compiled by USAFacts (https://usafacts.org/).

¶ County-level testing rates and rates of percentage positivity represent viral COVID-19 laboratory diagnostic and screening test (RT-PCR) results and exclude antibody and antigen tests. COVID-19 Electronic Laboratory Reporting state health department-reported data are used to describe county-level RT-PCR result totals when information is available on patients' county of residence or health care providers' practice location. HHS Protect laboratory data (provided directly to the federal government from public health laboratories, hospital laboratories, and commercial laboratories) are used otherwise. Total RT-PCR tests reflect the number of tests performed, not the number of persons receiving testing. RT-PCR test positivity rate is the number of positive tests divided by the total number of tests performed and for which results were available.

For all analyses, mean county population size, full-time student enrollment size, urban-rural classifications (large central metro, large fringe metro, medium metro, small metro, micropolitan, and noncore), and COVID-19 outcomes are reported and stratified by county university status and instructional format. The COVID-19 outcomes included incidence and testing rates per 100,000 population, test positivity by SARS-CoV-2 reverse transcription–polymerase chain reaction (RT-PCR) testing, and the percentage of counties identified as hotspots for ≥1 day during the observation periods. COVID-19 outcomes were reported as means for the 21 days before and after the class start date. Absolute differences (i.e., percentage point differences) are described for percentage-based measures (test positivity and hotspot detection) and relative changes described for rate-based measures (testing rate and incidence). Seven-day moving averages for testing rates, percentage test positivity, and incidence are presented as trends over the observation period (day –21 to day +21). In an unmatched analysis, remote-instruction and in-person instruction university counties were compared with nonuniversity counties. Nonuniversity counties were assigned the median start date of university counties. In the matched analysis, in-person–instruction university counties were matched with nonuniversity counties based on geographic proximity and population size. This analysis of 68 matched pairs was conducted to account for differences in population size, urbanicity, and geographic location between university and nonuniversity counties.[††] Nonuniversity counties in the matched sample were assigned the start date of their matched university-county counterpart. In the matched analysis, a regression-based difference-in-difference approach[§§] was used to quantify the impact of in-person instruction on COVID-19 incidence, with and without adjustment for transient student populations,[¶¶] and percentage test positivity. A sensitivity analysis was conducted to explore whether students' early return to campus might affect observed changes using day –7 as the demarcation between before and after periods. Statistical significance was set at $\alpha = 0.05$. Analyses were conducted using R statistical software (version 4.0.2; The R Foundation).

Among 101 university counties (3.2% of all U.S. counties, accounting for 29.4% of the U.S. population), instructional format was remote for 22 (22%) and in-person for 79 (78%). University counties had higher mean population size and were more urban than were nonuniversity counties (Table). Before the start of school, COVID-19 testing rates at the county-level were already higher in university counties than in nonuniversity counties (Figure). Comparing the time from the start of classes through day 21 with the 21 days before classes began, mean daily testing increased 4.2% and 14.1% among remote instruction and in-person instruction university counties, respectively, and decreased 1.0% among nonuniversity counties. Mean test positivity decreased among remote-instruction university counties (absolute change = –1.8%) and nonuniversity counties (–0.6%) but increased among in-person instruction university counties (1.1%). Incidence decreased in nonuniversity counties (–5.9%) and remote-instruction counties (–17.9%), whereas, incidence increased in in-person (56.2%) university counties. The percentage of counties identified at least once as a hotspot

** Hotspot , or rapid riser, counties met all four of the following criteria, relative to the date assessed: 1) >100 new COVID-19 cases in the most recent 7 days; 2) an increase in the most recent 7-day COVID-19 incidence over the preceding 7-day incidence; 3) a decrease of no more than 60% or an increase in the most recent 3-day COVID-19 incidence over the preceding 3-day incidence; and 4) a ratio of 7-day incidence to 30-day incidence exceeding 0.31. In addition, hotspots must have met at least one of the following criteria: 1) >60% change in the most recent 3-day COVID-19 incidence or 2) >60% change in the most recent 7-day incidence. CDC and other federal agencies that are monitoring trends in COVID-19 are collaborating to refine approaches to define and monitor hotspots. As a result, terminology or definitions used in future reports might differ from those used in this report.

†† Matches for each in-person university county were identified by listing all candidate (county) matches without large colleges or universities that had a similar population size (± 30%) and that were located within 500 miles (805 km) of each university county. From these candidate matches, the final match was selected based on closest proximity such that no nonuniversity county was matched more than once. After matching, the average distance between counties in matched in-person university county and nonuniversity county pairs was 114 miles (183 km) with a maximum distance of 471 miles (758 km). Eleven in-person university counties were excluded from the matched analysis because there were no candidate matches meeting population size and proximity specifications. All remote university counties were excluded from the matched analysis because there were an insufficient number of nonuniversity county matches.

§§ Difference-in-difference is a statistical technique that compares the changes in outcomes over time between two groups: those who are part of a control group and those who are part of a treatment or an intervention group. In this analysis, the intervention group was considered to be the counties with colleges and universities that had in-person instruction and the control group was considered to be nonuniversity counties. Difference-in-difference estimates used a regression model with the following specification: $Y_{ct} = \alpha + \beta_1 \cdot \text{In Person}_{ct} + \beta_2 \cdot \text{After}_{ct} + \delta_{IP} \cdot \text{After}_{ct} \cdot \text{In person}_{ct} + \theta_c + \theta_s + \theta_{week} + \theta_{weekday} + \varepsilon_{ct}$, where Y_{ct} is the outcome of interest (i.e., either COVID-19 incidence or percentage test positivity) for each county *c* and each unit of time *t* (days); In Person_{ct} is an indicator equal to 1 if the county has a college or university that started classes in an in-person format; After_{ct} is an indicator equal to 1 for all the days after the county's assigned start date (i.e., an indicator equal to 1 for days 0 to 21, where day 0 is the start date); θ_c and θ_s are county- and state-level fixed effects; θ_{week} and $\theta_{weekday}$ are fixed effects for each calendar week and each weekday; and ε_{ct} is the unobserved error term. The coefficient of interest is δ_{IP}, which captures the difference in outcome before and after the start date among in-person university counties, minus the difference in outcome before and after the assigned start date in nonuniversity counties. Standard errors were clustered at the county level. A placebo test was conducted where the college or university start date used day –21 as the demarcation of before and after periods, and no violation of the parallel trends assumption was found.

¶¶ Because transient student populations might not be included in the population denominator for county incidence estimates, incidence is assessed two ways in the difference-in-difference models: first using county population reported by the U.S. census, then adjusting for student influx by adding full-time student enrollment to each college or university's county population for the period after classes start. The full-time student population was used for this adjustment instead of the total student population, which includes full-time and part-time students.

TABLE. COVID-19 testing, percentage positivity, incidence, and county hotspot status among counties with and without colleges and universities,* by instructional format on the first day of the fall 2020 semester — United States, 2020

Characteristic	Unmatched analysis			Matched analysis†	
	University counties§			University counties	
	Remote instruction	In-person instruction	Nonuniversity counties	In-person instruction	Nonuniversity counties
Total no. of counties	**22**	**79**	**3,009**	**68**	**68**
Mean county population	1,694,739	748,544	69,574	467,187	413,460
Total no. of large colleges/universities	31	84	—	71	—
Mean college/university full-time enrollment in county§	37,769	27,451	—	27,084	—
Mean percentage full-time college/university enrollment of total county population	7.7	11.7	—	13.3	—
Percentage of counties in each urban-rural category¶					
Large central metro	59	27	1	16	9
Large fringe metro	9	13	12	13	32
Medium metro	18	28	11	32	28
Small metro	5	25	11	29	18
Micropolitan	9	8	21	9	9
Noncore	0	0	44	0	4
County COVID-19 testing rate per 100,000 population**					
Mean daily rate from day –21 to day –1††	308	255	209	256	216
Mean daily rate from day 0 to day 21	321	291	207	304	204
Relative change, %§§	4.2	14.1	–1.0	18.8	–5.6
County COVID-19 RT-PCR test percentage positivity**					
Mean from day –21 to day –1	8.1	7.8	8.7	7.5	8.6
Mean from day 0 to day 21	6.4	8.9	8.0	9.1	7.9
Absolute change, %§§	–1.8	1.1	–0.6	1.6	–0.8
County COVID-19 incidence¶¶					
Mean incidence from day –21 to day –1	17.9	15.3	15.3	14.3	16.9
Mean incidence from day 0 to day 21	14.7	23.9	14.4	25.5	13.6
Relative change, %§§	–17.9	56.2	–5.9	78.3	–19.5
County COVID-19 hotspot activity ***					
Percentage detected as a hotspot from day –21 to day –1	9.1	8.9	4.4	8.8	13.2
Percentage detected as a hotspot from day 0 to day 21	18.2	39.2	5.9	42.6	14.7
Absolute change, %§§	9.1	30.4	1.5	33.8	1.5

Abbreviations: COVID-19 = coronavirus disease 2019; RT-PCR = reverse transcription–polymerase chain reaction.

* 133 counties had institutions of higher education (large colleges or universities). Some counties (n = 32; 24%) opened on or after August 29 and were excluded from analysis. University counties are defined as counties with a large college or university. Nonuniversity counties are defined as counties without a large college or university.

† University counties matched to geographically proximate comparison counties with similar population size. Matches for each university county were identified by first listing all candidate (county) matches without large colleges and universities (nonuniversity counties) that had a similar population size (± 30%) and that were located within 500 miles (805 km) of each university county. From these candidate matches the final match was selected based on closest proximity. After matching, the average distance between counties in matched university county and nonuniversity county pairs was 114 miles (183 km) with a maximum distance of 471 miles (758 km).

§ Colleges and universities were included in the analysis if they had ≥20,000 total enrolled students, which included full-time and part-time students. The full-time student enrollments from these included institutions were combined across each university county. The number of full-time student enrollments in the university counties ranged from 11,774 to 192,173.

¶ Urban-rural classifications are from the National Center for Health Statistics' six-level urban-rural classification scheme for U.S. counties (https://www.cdc.gov/nchs/data_access/urban_rural.htm).

** Testing rates and percentage positivity for reverse transcription–polymerase chain reaction tests were obtained from COVID-19 electronic laboratory reporting data submitted by state health departments and from data submitted directly by public health, commercial, and reference laboratories.

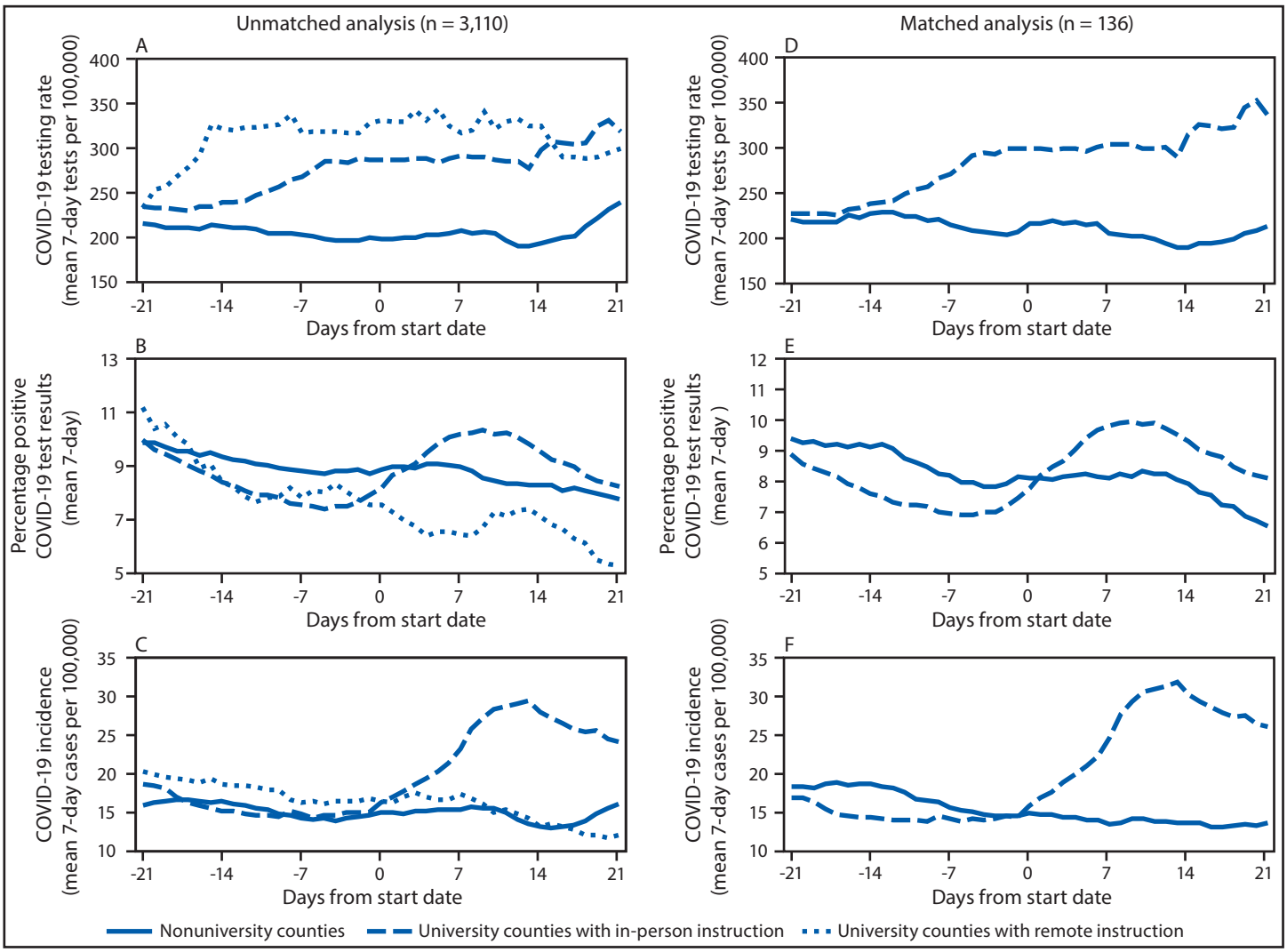
†† Day –21, –1, and 21 are relative to day 0, which indicates the start date of instruction at colleges and universities for the fall 2020 semester. The nonuniversity counties were assigned the median start date in the unmatched analysis and were assigned the start date of their matched university county counterpart in the matched analysis.

§§ Absolute differences are described for percentage-based measures (i.e., test positivity and hotspot detection) and relative changes described for rate-based measures (i.e., testing rate and incidence).

¶¶ Incidence (cases per 100,000) was calculated using daily reported COVID-19 case-counts from state and county health department websites compiled by USAFacts (https://usafacts.org/).

*** Hotspot, or rapid riser, counties met all four of the following criteria, relative to the date assessed: 1) >100 new COVID-19 cases in the most recent 7 days; 2) an increase in the most recent 7-day COVID-19 incidence over the preceding 7-day incidence; 3) a decrease of no more than 60% or an increase in the most recent 3-day COVID-19 incidence over the preceding 3-day incidence; and 4) a ratio of 7-day incidence to 30-day incidence exceeding 0.31. In addition to those four criteria, hotspots met at least one of the following criteria: 1) >60% change in the most recent 3-day COVID-19 incidence or 2) >60% change in the most recent 7-day incidence.

FIGURE. Trends* in COVID-19 testing rates (A, D), percentage test positivity (B, E), and incidence (C, F) for unmatched U.S. counties† and counties matched§ based on population size and geographic proximity, 7-day moving average — United States, 2020



Abbreviation: COVID-19 = coronavirus disease 2019.

* Trends are presented relative to the start date for fall 2020 classes for counties with large colleges and universities (university counties) and the assigned start date for nonuniversity counties.

† University counties with remote (n = 22) and in-person (n = 79) instruction versus nonuniversity (n = 3,009) counties.

§ University counties with in-person instruction versus nonuniversity counties (68 matched pairs). Matches for each in-person university county were identified by listing all candidate (county) matches without large colleges or universities that had a similar population size (± 30%) and that were located within 500 miles (805 km) of each university county. From these candidate matches, the final match was selected based on closest proximity such that no nonuniversity county was matched more than once. After matching, the average distance between counties in matched in-person university county and nonuniversity county pairs was 114 miles (183 km) with a maximum distance of 471 miles (758 km). Eleven in-person university counties were excluded from the matched analysis because there were no candidate matches meeting population size and proximity specifications. All remote university counties were excluded from the matched analysis because there was an insufficient number of nonuniversity county matches.

increased for all three groups, with the highest percentage observed in in-person instruction university counties (30.4% absolute increase), followed by remote-instruction university counties (9.1%) and nonuniversity counties (1.5%).

COVID-19 outcomes were similar in the matched analysis. Compared with nonuniversity counties, in-person instruction university counties experienced a higher relative change in testing rates (18.8% versus –5.6%), a higher absolute change in test positivity (1.6% versus –0.8%), a higher relative change in incidence (78.3% versus –19.5%) (Table) (Figure), and a higher absolute change in the percentage identified as hotspots (33.8% versus 1.5%). Based on the difference-in-difference analysis, university counties with in-person instruction were associated with an increase of 14.4 cases per 100,000 ($p<0.05$) and an increase of 2.4 percent test positivity ($p<0.05$) relative to nonuniversity counties with in-person instruction. When adjusting incidence for the influx of full-time students, in-person instruction university counties were associated with an

increase of 10.6 cases per 100,000 ($p<0.05$) (Supplementary Table, https://stacks.cdc.gov/view/cdc/99533). These results did not change meaningfully in the sensitivity analysis.

Discussion

County-level COVID-19 incidence decreased in much of the United States in late summer 2020. Comparing the 21 days before and after instruction start dates, university counties with in-person instruction experienced a 56% increase in incidence and 30% increase in hotspot occurrence as well as increases in COVID-19-related testing and test percentage positivity. Results from the unmatched analysis were consistent with those from the matched analysis. If percentage positivity had been stable or declining across the observation period, then efforts on the part of many colleges and universities to conduct or require testing before students' return to campus and their ongoing surveillance efforts might explain an increase in case counts, as a result of increased case discovery. However, the concurrent increases in percentage positivity and in incidence in these counties suggest that higher levels of transmission, in addition to increased case discovery, occurred in these communities (*2*).

The findings in this report are subject to at least six limitations. First, data abstraction for schools' instructional formats was conducted in early September and focused on identifying the format used on the first day of classes; some misclassification of instructional format might have occurred because of changes during the first few weeks of instruction. Second, this study did not adjust for mitigation strategies (e.g., mask and social distancing requirements and limits on large crowds and athletic events) implemented at local or state levels or at colleges and universities, which could have affected the association between the institution's opening and county-level incidence. Similarly, whether cases in university counties were college- or university-related (i.e., through contact in classrooms, dormitories, cafeterias, or off-campus activities) or related to community transmission could not be discerned. Third, these results might not be generalizable to counties with smaller colleges and universities. Fourth, U.S. Census 2019 population estimates were used to calculate rates, which do not include all college and university enrollments. County-level rate calculations could be inflated for university counties, especially those for which the enrollment numbers are relatively large compared with the county's population size. Fifth, the longer-term implications for county incidence (i.e., beyond 21 days) were not assessed. Finally, the university counties in the unmatched analysis have larger populations and likely additional characteristics that are different from those of nonuniversity counties. This limitation prompted the decision to conduct the matched analysis, which focused on counties with more similar population levels and geographic proximity. However, broader generalizations based on the matched analysis might not be warranted because 11 university counties with in-person instruction were excluded from the matched analysis because no appropriate matches were available.

Summary

What is already known about this topic?

Increasing COVID-19 incidence was observed among young adults in August 2020, and outbreaks have been reported at institutions of higher education (colleges and universities).

What is added by this report?

U.S. counties with large colleges or universities with remote instruction (n = 22) experienced a 17.9% decrease in incidence and university counties with in-person instruction (n = 79) experienced a 56% increase in incidence, comparing the 21-day periods before and after classes started. Counties without large colleges or universities (n = 3,009) experienced a 6% decrease in incidence during similar time frames.

What are the implications for public health practice?

Additional implementation of effective mitigation activities at colleges and universities with in-person instruction could minimize on-campus COVID-19 transmission and reduce county-level incidence.

COVID-19 incidence, hotspot occurrence, COVID-19-related testing, and test positivity increased in university counties with in-person instruction. Efforts to prevent and mitigate COVID-19 transmission are critical for U.S. colleges and universities. Congregate living settings at colleges and universities were linked to transmissions (*7*). Testing students for COVID-19 when they return to campus and throughout the semester might be an effective strategy to rapidly identify and isolate new cases to interrupt and reduce further transmissions (*8*). Colleges and universities should work to achieve greater adherence to the recommended use of masks, hand hygiene, social distancing, and COVID-19 surveillance among students (*9*), including those who are exposed, symptomatic, and asymptomatic. The increase in testing rates likely reflects local efforts already underway to improve COVID-19 surveillance and response. Increasing testing capacity and engaging in other COVID-19 mitigation strategies might be especially important for colleges and universities in areas where transmission from students into the broader community could exacerbate existing disparities, including access to and utilization of health care, as well as the disproportionate morbidity and mortality of COVID-19 among populations with prevalent underlying conditions associated with more severe outcomes following infection. Some university counties might have one or more concerning factors, such as higher levels of older adult populations, high rates of obesity and cardiovascular disease,

or strained health care resources. These counties might need to consider the implications of in-person instruction on spread of COVID-19 among a student population that might have interactions with persons at higher risk in the community. College and university administrators should work with local decision-makers and public health officials to strengthen community mitigation, in addition to continuing efforts to slow the spread of COVID-19 on college and university campuses.

Acknowledgments

Margaret Honein, Molly Kellum, Rebecca Noe, Diego Arambula, Denise Koo, Kai Hong.

Corresponding author: Andrew J. Leidner, aleidner@cdc.gov.

[1]CDC COVID-19 Response Team; [2]Geospatial Research, Analysis, and Services Program, CDC/ATSDR, Atlanta, Georgia; [3]HHS COVID-19 Joint Coordination Cell.

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflicts of interest were disclosed.

References

1. CDC. Coronavirus disease 2019 (COVID-19): CDC COVID data tracker. Atlanta, GA: US Department of Health and Human Services, CDC; 2020. https://covid.cdc.gov/covid-data-tracker
2. Salvatore PP, Sula E, Coyle JP, et al. Recent increase in COVID-19 cases reported among adults aged 18–22 years—United States, May 31–September 5, 2020. MMWR Morb Mortal Wkly Rep 2020;69:1419–24. PMID:33006586 https://doi.org/10.15585/mmwr.mm6939e4
3. Boehmer TK, DeVies J, Caruso E, et al. Changing age distribution of the COVID-19 pandemic—United States, May–August 2020. MMWR Morb Mortal Wkly Rep 2020;69:1404–9. PMID:33001872 https://doi.org/10.15585/mmwr.mm6939e1
4. Watson S, Hubler S, Ivory D, Gebeloff R. A new front in America's pandemic: college towns. New York Times, September 10, 2020. https://www.nytimes.com/2020/09/06/us/colleges-coronavirus-students.html
5. Wilson E, Donovan CV, Campbell M, et al. Multiple COVID-19 clusters on a university campus—North Carolina, August 2020. MMWR Morb Mortal Wkly Rep 2020;69:1416–8. PMID:33001871 https://doi.org/10.15585/mmwr.mm6939e3
6. US Department of Education. Integrated Postsecondary Education Data System. Washington, DC: US Department of Education, Institute of Education Sciences, National Center for Education Statistics, 2020. https://nces.ed.gov/ipeds/use-the-data
7. Vang KE, Krow-Lucal ER, James AE, et al. Participation in fraternity and sorority activities and the spread of COVID-19 among residential university communities—Arkansas, August 21–September 5, 2020. MMWR Morb Mortal Wkly Rep 2020;70:20–3.
8. Walke HT, Honein MA, Redfield RR. Preventing and responding to COVID-19 on college campuses. JAMA 2020;324:1727–8. PMID:32991681 https://doi.org/10.1001/jama.2020.20027
9. CDC. Coronavirus disease 2019 (COVID-19): considerations for institutions of higher education. Atlanta, GA: US Department of Health and Human Services, CDC; 2020. https://www.cdc.gov/coronavirus/2019-ncov/community/colleges-universities/considerations.html

EXHIBIT G

Morbidity and Mortality Weekly Report

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]

On July 6, 2021 this report was posted as an MMWR *Early Release on the* MMWR *website (https://www.cdc.gov/mmwr).*

In December 2020, the Food and Drug Administration (FDA) issued Emergency Use Authorizations (EUAs) for the Pfizer-BioNTech COVID-19 (BNT162b2) vaccine and the Moderna COVID-19 (mRNA-1273) vaccine,† and the Advisory Committee on Immunization Practices (ACIP) issued interim recommendations for their use in persons aged ≥16 years and ≥18 years, respectively.§ In May 2021, FDA expanded the EUA for the Pfizer-BioNTech COVID-19 vaccine to include adolescents aged 12–15 years; ACIP recommends that all persons aged ≥12 years receive a COVID-19 vaccine. Both Pfizer-BioNTech and Moderna vaccines are mRNA vaccines encoding the stabilized prefusion spike glycoprotein of SARS-CoV-2, the virus that causes COVID-19. Both mRNA vaccines were authorized and recommended as a 2-dose schedule, with second doses administered 21 days (Pfizer-BioNTech) or 28 days (Moderna) after the first dose. After reports of myocarditis and pericarditis in mRNA vaccine recipients,¶ which predominantly occurred in young males after the second dose, an ACIP meeting was rapidly convened to review reported cases of myocarditis and pericarditis and discuss the benefits and risks of mRNA COVID-19 vaccination in the United States. Myocarditis is an inflammation of the heart muscle; if it is accompanied by pericarditis, an inflammation of the thin tissue surrounding the heart (the pericardium), it is referred to as myopericarditis. Hereafter, myocarditis is used to refer to myocarditis, pericarditis, or myopericarditis. On June 23, 2021, after reviewing available evidence including that for risks of myocarditis, ACIP determined that the benefits of using mRNA COVID-19 vaccines under the FDA's EUA clearly outweigh the risks in all populations, including adolescents and young adults. The EUA has been modified to include information on myocarditis after receipt of mRNA COVID-19 vaccines. The EUA fact sheets should be provided before vaccination; in addition, CDC has developed patient and provider education materials about the possibility of myocarditis and symptoms of concern, to ensure prompt recognition and management of myocarditis.

Since June 2020, ACIP has convened 15 public meetings to review data on COVID-19 epidemiology and use of COVID-19 vaccines. The ACIP COVID-19 Vaccines Work Group, comprising experts in infectious diseases, vaccinology, vaccine safety, public health, and ethics, has held weekly meetings since April 2020 to review COVID-19 surveillance data, evidence for vaccine efficacy and safety, and implementation considerations for COVID-19 vaccination programs. After reports of myocarditis, the work group met twice to review clinical trial and postauthorization safety data for myocarditis after receipt of mRNA COVID-19 vaccines. The work group also reviewed a benefit-risk assessment of myocarditis events after receipt of mRNA COVID-19 vaccines, considering recent epidemiology of COVID-19 and sequelae of COVID-19, including myocarditis and multisystem inflammatory syndrome in children (MIS-C).** The ACIP COVID-19 Vaccines Safety Technical (VaST) Work Group, comprising independent vaccine safety expert consultants, had also reviewed safety data on myocarditis after receipt of mRNA COVID-19 vaccines at its weekly meetings. The findings from the VaST and the ACIP COVID-19 Vaccines Work Group assessments, including a summary of the data reviewed, were presented to ACIP during its meeting on June 23, 2021.

Myocarditis typically occurs more commonly in males than in females, and incidence is highest among infants, adolescents, and young adults (*1*,*2*). The clinical presentation and severity of myocarditis vary among patients. Symptoms typically include chest pain, dyspnea, or palpitations, although other symptoms might be present, especially in younger children (*3*). Diagnostic evaluation might reveal an elevated troponin level or abnormal findings on electrocardiogram, echocardiogram, or cardiac magnetic resonance imaging (Table 1). Supportive therapy is

* These authors contributed equally to this work.
† All EUA documents for COVID-19 vaccines, including fact sheets, are available at https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-vaccines.
§ ACIP recommendations for all COVID-19 vaccines are available at https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19.html.
¶ COVID-19 Vaccine Safety Technical Work Group Reports are available at https://www.cdc.gov/vaccines/acip/work-groups-vast/index.html.

** https://www.cdc.gov/mis/hcp/index.html

a mainstay of treatment, with targeted cardiac medications or interventions as needed. Current guidelines from the American Heart Association and American College of Cardiology recommend exercise restriction until the heart recovers.[††]

As of June 11, 2021, approximately 296 million doses of mRNA COVID-19 vaccines had been administered in the United States, with 52 million administered to persons aged 12–29 years; of these, 30 million were first and 22 million were second doses. Within the Vaccine Adverse Event Reporting System (VAERS) (*4*), the national vaccine safety passive monitoring system, 1,226 reports of myocarditis after mRNA vaccination were received during December 29, 2020–June 11, 2021. Among persons with reported myocarditis after mRNA vaccination, the median age was 26 years (range = 12–94 years), with median symptom onset interval of 3 days after vaccination (range = 0–179). Among 1,194 reports for which patient age was known, 687 were among persons aged <30 years and 507 were among persons aged ≥30 years; of 1,212 with sex reported, 923 were male, and 289 were female.[§§] Among 1,094 patients with number of vaccine doses received reported, 76% occurred after receipt of dose 2 of mRNA vaccine; cases were reported after both Pfizer-BioNTech and Moderna vaccines. Informed by early reports, CDC prioritized rapid review of myocarditis in persons aged <30 years reported during May 1–June 11, 2021; the 484 patient records in this subset were evaluated by physicians at CDC, and several reports were also reviewed with Clinical Immunization Safety Assessment Project investigators,[¶¶] including cardiologists. At the time of this report, 323 of these 484 cases were determined to meet criteria in CDC's case definitions for myocarditis, pericarditis, or myopericarditis by provider interview or medical record review (Table 1). The median age of the 323 patients meeting CDC's case definitions was 19 years (range = 12–29 years); 291 were male, and 32 were female. The median interval from vaccination to symptom onset was 2 days (range = 0–40 days); 92% of patients experienced onset of symptoms within 7 days of vaccination. Of the 323 persons meeting CDC's case definitions, 309 (96%) were hospitalized. Acute clinical courses were generally mild; among 304 hospitalized patients with known clinical outcomes, 95% had been discharged at time of review, and none had died. Treatment data in VAERS are preliminary and incomplete; however, many patients have experienced resolution of symptoms with conservative treatment, such as receipt of nonsteroidal antiinflammatory drugs. Follow-up is

TABLE 1. Case definitions of probable and confirmed myocarditis, pericarditis, and myopericarditis

Condition	Definition	
	Probable case	**Confirmed case**
Acute myocarditis	Presence of ≥1 new or worsening of the following clinical symptoms:* • chest pain, pressure, or discomfort • dyspnea, shortness of breath, or pain with breathing • palpitations • syncope OR, infants and children aged <12 years might instead have ≥2 of the following symptoms: • irritability • vomiting • poor feeding • tachypnea • lethargy AND ≥1 new finding of • troponin level above upper limit of normal (any type of troponin) • abnormal electrocardiogram (ECG or EKG) or rhythm monitoring findings consistent with myocarditis[§] • abnormal cardiac function or wall motion abnormalities on echocardiogram • cMRI findings consistent with myocarditis[¶] AND • No other identifiable cause of the symptoms and findings	Presence of ≥1 new or worsening of the following clinical symptoms:* • chest pain, pressure, or discomfort • dyspnea, shortness of breath, or pain with breathing • palpitations • syncope OR, infants and children aged <12 years might instead have ≥2 of the following symptoms: • irritability • vomiting • poor feeding • tachypnea • lethargy AND ≥1 new finding of • Histopathologic confirmation of myocarditis[†] • cMRI findings consistent with myocarditis[¶] in the presence of troponin level above upper limit of normal (any type of troponin) AND • No other identifiable cause of the symptoms and findings
Acute pericarditis**	Presence of ≥2 new or worsening of the following clinical features: • acute chest pain[††] • pericardial rub on exam • new ST-elevation or PR-depression on EKG • new or worsening pericardial effusion on echocardiogram or MRI	
Myopericarditis	This term may be used for patients who meet criteria for both myocarditis and pericarditis.	

Abbreviations: AV = atrioventricular; cMRI = cardiac magnetic resonance imaging; ECG or EKG = electrocardiogram.

* Persons who lack the listed symptoms but who meet other criteria may be classified as subclinical myocarditis (probable or confirmed).

† Using the Dallas criteria (Aretz HT, Billingham ME, Edwards WD, et al. Myocarditis. A histopathologic definition and classification. Am J Cardiovasc Pathol 1987; 1:3–14). Autopsy cases may be classified as confirmed clinical myocarditis on the basis of meeting histopathologic criteria if no other identifiable cause.

§ To meet the ECG or rhythm monitoring criterion, a probable case must include at least one of 1) ST-segment or T-wave abnormalities; 2) Paroxysmal or sustained atrial, supraventricular, or ventricular arrhythmias; or 3) AV nodal conduction delays or intraventricular conduction defects.

¶ Using either the original or the revised Lake Louise criteria. https://www.sciencedirect.com/science/article/pii/S0735109718388430?via%3Dihub

** https://academic.oup.com/eurheartj/article/36/42/2921/2293375

†† Typically described as pain made worse by lying down, deep inspiration, or cough, and relieved by sitting up or leaning forward, although other types of chest pain might occur.

†† https://www.ahajournals.org/doi/10.1161/CIR.0000000000000239?url_ver = Z39.88-2003&rfr_id = ori:rid:crossref.org&rfr_dat = cr_pub%20%200pubmed#d3e785

§§ Age was not reported for 32 patients, and sex was not reported for 14 patients.

¶¶ https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/cisa/index.html

ongoing to identify and understand longer-term outcomes after myocarditis occurring after COVID-19 vaccination.

Using myocarditis cases reported to VAERS with onset within 7 days after dose 2 of an mRNA vaccine, crude reporting rates (i.e., using confirmed and unconfirmed cases) per million second dose recipients were calculated using national COVID-19 vaccine administration data as of June 11, 2021. Myocarditis reporting rates were 40.6 cases per million second doses of mRNA COVID-19 vaccines administered to males aged 12–29 years and 2.4 per million second doses administered to males aged ≥30 years; reporting rates among females in these age groups were 4.2 and 1.0 per million second doses, respectively.*** The highest reporting rates were among males aged 12–17 years and those aged 18–24 years (62.8 and 50.5 reported myocarditis cases per million second doses of mRNA COVID-19 vaccine administered, respectively). Myocarditis rates from Vaccine Safety Datalink (VSD), based on electronic health records, were also evaluated. Although numbers were too small to show rates in all subgroups by age, VSD data indicated increased risk of myocarditis in the 7 days after receipt of dose 1 or dose 2 of an mRNA COVID-19 vaccine compared with the risk 22–42 days after the second dose, particularly among younger males after dose 2 (*5*).

To assess the benefit-risk balance of mRNA vaccines in adolescents and young adults, ACIP reviewed an individual-level assessment that compared the benefits (i.e., COVID-19 infections and severe disease prevented) to the risks (number of cases of myocarditis) of vaccination, using methods similar to those described previously.††† Specifically, the benefits per million second doses administered (i.e., the benefits of being fully vaccinated in accordance with the FDA EUA) were assessed, including 1) COVID-19 cases prevented based on rates the week of May 29, 2021§§§; 2) COVID-19 hospitalizations prevented based on rates the week of May 22, 2021¶¶¶; and 3) COVID-19 intensive care unit (ICU) admissions and deaths prevented based on the proportion of hospitalized patients who were admitted to the ICU or died.**** The risks were assessed as the number of myocarditis patients reported to VAERS that occurred within 7 days of receipt of a second dose of an mRNA COVID-19 vaccine per million second doses administered through the week of June 11, 2021.†††† The benefit-risk assessment was stratified by age group and sex. The analysis assumed 95% vaccine effectiveness§§§§ of 2 doses of a mRNA COVID-19 vaccine in preventing COVID-19 cases and hospitalization and assessed outcomes for a 120-day period. The 120-day period was selected because 1) no alternative vaccine options currently exist for persons aged <18 years or are expected to be available during this period, and 2) inputs regarding community transmission have high uncertainty beyond this period, particularly in the context of circulating variants.¶¶¶¶

The benefits (prevention of COVID-19 disease and associated hospitalizations, ICU admissions, and deaths) outweighed the risks (expected myocarditis cases after vaccination) in all populations for which vaccination has been recommended. However, the balance of benefits and risks varied by age and sex because cases of myocarditis were primarily identified among males aged <30 years, and the risks of poor outcomes related to COVID-19 increase with age. Per million second doses of mRNA COVID-19 vaccine administered to males aged 12–29 years, 11,000 COVID-19 cases, 560 hospitalizations, 138 ICU admissions, and six deaths due to COVID-19 could be prevented, compared with 39–47 expected myocarditis cases after COVID-19 vaccination (Table 2). Among males aged ≥30 years, 15,300 COVID-19 cases, 4,598 hospitalizations, 1,242 ICU admissions, and 700 deaths could be prevented, compared with three to four expected myocarditis cases after COVID-19 vaccination. This analysis did not include the potential benefit of preventing post-COVID-19 conditions, such as prolonged symptoms and MIS-C (*6,7*).

ACIP also reviewed population-level considerations regarding vaccination. No alternatives to mRNA COVID-19 vaccines for adolescents will be available for the foreseeable future, and vaccination of adolescents offers protection against COVID-19 that can be important for returning to educational, social, and extracurricular activities. Higher levels of vaccination coverage can reduce community transmission, which can protect against development and circulation of emerging variants. Regarding health equity considerations, racial and ethnic minority groups have higher rates of COVID-19 and severe disease*****; potential changes in vaccine policy, or anything that would affect vaccination coverage for adolescents or young adults, might disproportionately affect those groups with the highest rates of poor COVID-19 outcomes.

The ACIP discussion concluded that 1) the benefits of vaccinating all recommended age groups with mRNA COVID-19 vaccine clearly outweigh the risks of vaccination, including the risk of myocarditis after vaccination; 2) continuing to monitor

*** Data collection for race/ethnicity of myocarditis cases is ongoing.
††† https://www.cdc.gov/vaccines/covid-19/info-by-product/janssen/risk-benefit-analysis.html
§§§ https://covid.cdc.gov/covid-data-tracker/#demographicsovertime. Data were used for the most recent week not subject to reporting delays prior to the ACIP meeting.
¶¶¶ https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html. Data were used for the most recent week not subject to reporting delays prior to the ACIP meeting.
**** https://gis.cdc.gov/grasp/COVIDNet/COVID19_5.html
†††† Because of uncertainty in the accuracy of myocarditis reporting, given that reviews are ongoing, and some cases might not have been reported yet, myocarditis reporting rates are presented as a range of values, calculated as ±10% of the observed reporting rates.

§§§§ https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html
¶¶¶¶ https://covid.cdc.gov/covid-data-tracker/#variant-proportions
***** https://covid.cdc.gov/covid-data-tracker/#demographics

TABLE 2. Individual-level estimated number of COVID-19 cases and COVID-19–associated hospitalizations, intensive care unit admissions, and deaths prevented after use of 2-dose mRNA COVID-19 vaccine for 120 days and number of myocarditis cases expected per million second mRNA vaccine doses administered, by sex and age group* — United States, 2021

	No. per million vaccine doses administered in each age group (yrs)†				
Sex/Benefits and harms from mRNA vaccination	**12–29**	**12–17**	**18–24**	**25–29**	**≥30**
Male					
Benefit					
COVID-19 cases prevented§	11,000	5,700	12,100	15,200	15,300
Hospitalizations prevented	560	215	530	936	4,598
ICU admissions prevented	138	71	127	215	1,242
Deaths prevented	6	2	3	13	700
Harms					
Myocarditis cases expected¶	39–47	56–69	45–56	15–18	3–4
Female					
Benefit					
COVID-19 cases prevented§	12,500	8,500	14,300	14,700	14,900
Hospitalizations prevented	922	183	1,127	1,459	3,484
ICU admissions prevented	73	38	93	87	707
Deaths prevented	6	1	13	4	347
Harm					
Myocarditis cases expected¶	4–5	8–10	4–5	2	1

Abbreviations: ICU = intensive care unit; VAERS = Vaccine Adverse Event Reporting System.
* This analysis evaluated direct benefits and harms, per million second doses of mRNA COVID-19 vaccine given in each age group, over 120 days. The numbers of events per million persons aged 12–29 years are the averages of numbers per million persons aged 12–17 years, 18–24 years, and 25–29 years.
† Receipt of 2 doses of mRNA COVID-19 vaccine, compared with no vaccination.
§ Case numbers have been rounded to the nearest hundred.
¶ Ranges calculated as ±10% of crude VAERS reporting rates. Estimates include cases of myocarditis, pericarditis, and myopericarditis.

outcomes of myocarditis cases after COVID-19 vaccination is important; and 3) providers and the public should be informed about these myocarditis cases and the use of COVID-19 vaccines. Based on ACIP's conclusion regarding the benefit-risk assessment on June 23, 2021, COVID-19 vaccination continues to be recommended for all persons aged ≥12 years under the FDA's EUA. ACIP emphasized the importance of informing vaccination providers and the public about the benefits and the risks, including the risk for myocarditis after COVID-19 vaccination, particularly for males aged 12–29 years.

CDC has provided guidance regarding evaluation and management of myocarditis after mRNA COVID-19 vaccine (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html), as well as considerations for a second vaccine dose in persons who develop myocarditis after a first dose (https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html). FDA has added information to the Pfizer-BioNTech††††† and Moderna§§§§§ COVID-19 vaccine EUA and fact sheets regarding myocarditis cases that have been reported among vaccine recipients. In addition, CDC has updated patient education and communication materials reflecting this information for the Pfizer-BioNTech¶¶¶¶¶ and Moderna****** COVID-19 vaccines; these are important to ensure that vaccine recipients, especially males aged 12–29 years, are aware of increased risk for myocarditis and to seek care if they develop symptoms of myocarditis. The vaccine product-specific EUA fact sheet should be provided to all vaccine recipients and their caregivers before vaccination with any authorized COVID-19 vaccine.

CDC and FDA will continue to closely monitor reports of myocarditis after receipt of the mRNA COVID-19 vaccines and will bring any additional data to ACIP for consideration. The benefit-risk analysis can be updated as needed to reflect changes in the COVID-19 pandemic and additional information on the risk for and outcomes of myocarditis after COVID-19 vaccination. The ACIP recommendation for use of mRNA COVID-19 vaccines under an EUA is interim and will be updated as additional information becomes available.

Reporting of Vaccine Adverse Events

FDA requires that vaccine providers report to VAERS vaccination administration errors, serious adverse events,†††††† cases of multisystem inflammatory syndrome, and cases of COVID-19 that result in hospitalization or death after

††††† https://www.fda.gov/media/144413/download
§§§§§ https://www.fda.gov/media/144637/download

¶¶¶¶¶ https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/index.html
****** https://www.cdc.gov/vaccines/covid-19/info-by-product/moderna/index.html
†††††† https://vaers.hhs.gov/faq.html

administration of a COVID-19 vaccine under an EUA. CDC also encourages reporting of any additional clinically significant adverse event, even if it is not clear whether a vaccination caused the event. Information on how to submit a report to VAERS is available at https://vaers.hhs.gov/index.html or 1-800-822-7967. In addition, CDC has developed a voluntary smartphone-based online tool (v-safe) that uses text messaging and online surveys to provide near real-time health check-ins after receipt of a COVID-19 vaccine. In cases of v-safe reports that include possible medically attended health events, CDC's v-safe call center follows up with the vaccine recipient to collect additional information for completion of a VAERS report. Information on v-safe is available at https://www.cdc.gov/vsafe.

Summary

What is already known about this topic?

An elevated risk for myocarditis among mRNA COVID-19 vaccinees has been observed, particularly in males aged 12–29 years.

What is added by this report?

On June 23, 2021, the Advisory Committee on Immunization Practices concluded that the benefits of COVID-19 vaccination to individual persons and at the population level clearly outweighed the risks of myocarditis after vaccination.

What are the implications for public health practice?

Continued use of mRNA COVID-19 vaccines in all recommended age groups will prevent morbidity and mortality from COVID-19 that far exceed the number of cases of myocarditis expected. Information regarding the risk for myocarditis with mRNA COVID-19 vaccines should be disseminated to providers to share with vaccine recipients.

Acknowledgments

Mary Chamberland, Thomas Clark, Amanda Cohn, Frank DeStefano, Ruth Gallego, Alice Guh, Theresa Harrington, Fiona P. Havers, Lauri Hicks, Amelia Jazwa, Tara Johnson, Brian Kit, Paige Marquez, Sarah Mbaeyi, Elaine Miller, Hannah Rosenblum, Monica Parise, Kadam Patel, Pragati Prasad, David Shay, Jamila Shields, Christopher A. Taylor, Joshua Wong, CDC COVID-19 Response Team; Clinical Immunization Safety Assessment (CISA) Project; Vaccine Safety Datalink; Center for Biologics Evaluation and Research, Food and Drug Administration; Voting members of the Advisory Committee on Immunization Practices: Kevin A. Ault, University of Kansas Medical Center; Lynn Bahta, Minnesota Department of Health; Henry Bernstein, Zucker School of Medicine at Hofstra/Northwell Cohen Children's Medical Center; Beth Bell, University of Washington, Seattle, Washington; Wilbur Chen, University of Maryland School of Medicine; Sharon E. Frey, Saint Louis University Medical School; Camille Kotton, Harvard Medical School; Sarah Long, Drexel University College of Medicine; Katherine A. Poehling, Wake Forest School of Medicine; Pablo J. Sánchez, The Research Institute at Nationwide Children's Hospital. Members of the Advisory Committee on Immunization Practices COVID-19 Vaccines Work Group: Edward Belongia, Center for Clinical Epidemiology & Population Health, Marshfield Clinic Research Institute; Dayna Bowen Matthew, George Washington University Law School; Oliver Brooks, National Medical Association; Jillian Doss-Walker, Indian Health Service; Marci Drees, Society for Healthcare Epidemiology of America; Jeffrey Duchin, Infectious Diseases Society of America; Kathy Kinlaw, Center for Ethics, Emory University; Doran Fink, Food and Drug Administration; Sandra Fryhofer, American Medical Association; Jason M. Goldman, American College of Physicians; Michael Hogue, American Pharmacists Association; Denise Jamieson, American College of Obstetricians and Gynecologists; Jeffery Kelman, Centers for Medicare & Medicaid Services; David Kim, U.S. Department of Health and Human Services; Susan Lett, Council of State and Territorial Epidemiologists; Kendra McMillan, American Nurses Association; Kathleen Neuzil, Center for Vaccine Development and Global Health, University of Maryland School of Medicine; Sean O'Leary, American Academy of Pediatrics; Christine Oshansky, Biomedical Advanced Research and Development Authority; Stanley Perlman, Department of Microbiology and Immunology, University of Iowa; Marcus Plescia, Association of State and Territorial Health Officials; Chris Roberts, National Institutes of Health; William Schaffner, National Foundation for Infectious Diseases; Kenneth Schmader, American Geriatrics Society; Bryan Schumacher, Department of Defense; Rob Schechter, Association of Immunization Managers; Jonathan Temte, American Academy of Family Physicians; Peter Szilagyi, University of California, Los Angeles; Matthew Tunis, National Advisory Committee on Immunization Secretariat, Public Health Agency of Canada; Thomas Weiser, Indian Health Service; Matt Zahn, National Association of County and City Health Officials; Rachel Zhang, Food and Drug Administration. Members of the Advisory Committee on Immunization Practices COVID-19 Vaccines Safety Technical Work Group: Robert Hopkins, National Vaccine Advisory Committee; Kathryn Edwards, Vanderbilt University School of Medicine; Lisa Jackson, Kaiser Permanente Washington Health Research Institute; Jennifer Nelson: Kaiser Permanente Washington Health Research Institute; Laura Riley, American College of Obstetricians and Gynecologists; Patricia Whitley-Williams, National Medical Association; Tatiana Beresnev, National Institutes of Health; Karen Farizo, Food and Drug Administration; Hui Lee Wong, Food and Drug Administration; Judith Steinberg, U.S. Department of Health and Human Services; Matthew Clark, Indian Health Service; Mary Rubin, Health Resources & Services Administration; Fran Cunningham, Veterans Administration; Limone Collins, Department of Defense.

Corresponding author: Sara E. Oliver, yxo4@cdc.gov.

[1]CDC COVID-19 Response Team; [2]Franny Strong Foundation, West Bloomfield, Michigan; [3]Arkansas Department of Health; [4]Vanderbilt University School of Medicine, Nashville, Tennessee; [5]Stanford University School of Medicine, Stanford, California; [6]Institute for Health Research, Kaiser Permanente Colorado, Denver, Colorado.

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflicts of interest were disclosed.

References

1. Kytö V, Sipilä J, Rautava P. The effects of gender and age on occurrence of clinically suspected myocarditis in adulthood. Heart 2013;99:1681–4. PMID:24064227 https://doi.org/10.1136/heartjnl-2013-304449
2. Vasudeva R, Bhatt P, Lilje C, et al. Trends in acute myocarditis related pediatric hospitalizations in the United States, 2007–2016. Am J Cardiol 2021;149:95–102. PMID:33757784 https://doi.org/10.1016/j.amjcard.2021.03.019
3. Cooper LT Jr. Myocarditis. N Engl J Med 2009;360:1526–38. PMID:19357408 https://doi.org/10.1056/NEJMra0800028
4. Shimabukuro TT, Nguyen M, Martin D, DeStefano F. Safety monitoring in the Vaccine Adverse Event Reporting System (VAERS). Vaccine 2015;33:4398–405. PMID:26209838 https://doi.org/10.1016/j.vaccine.2015.07.035
5. Baggs J, Gee J, Lewis E, et al. The Vaccine Safety Datalink: a model for monitoring immunization safety. Pediatrics 2011;127(Suppl 1):S45–53. PMID:21502240 https://doi.org/10.1542/peds.2010-1722H
6. Buonsenso D, Munblit D, De Rose C, et al. Preliminary evidence on long COVID in children. Acta Paediatr 2021;110:2208–11. PMID:33835507 https://doi.org/10.1111/apa.15870
7. Payne AB, Gilani Z, Godfred-Cato S, et al.; MIS-C Incidence Authorship Group. Incidence of multisystem inflammatory syndrome in children among US persons infected with SARS-CoV-2. JAMA Netw Open 2021;4:e2116420. PMID:34110391 https://doi.org/10.1001/jamanetworkopen.2021.16420

EXHIBIT H

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Safety of the BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting

Noam Barda, M.D., Noa Dagan, M.D., Yatir Ben-Shlomo, B.Sc., Eldad Kepten, Ph.D., Jacob Waxman, M.D., Reut Ohana, M.Sc., Miguel A. Hernán, M.D., Marc Lipsitch, D.Phil., Isaac Kohane, M.D., Doron Netzer, M.D., Ben Y. Reis, Ph.D., and Ran D. Balicer, M.D.

ABSTRACT

BACKGROUND

Preapproval trials showed that messenger RNA (mRNA)–based vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) had a good safety profile, yet these trials were subject to size and patient-mix limitations. An evaluation of the safety of the BNT162b2 mRNA vaccine with respect to a broad range of potential adverse events is needed.

METHODS

We used data from the largest health care organization in Israel to evaluate the safety of the BNT162b2 mRNA vaccine. For each potential adverse event, in a population of persons with no previous diagnosis of that event, we individually matched vaccinated persons to unvaccinated persons according to sociodemographic and clinical variables. Risk ratios and risk differences at 42 days after vaccination were derived with the use of the Kaplan–Meier estimator. To place these results in context, we performed a similar analysis involving SARS-CoV-2–infected persons matched to uninfected persons. The same adverse events were studied in the vaccination and SARS-CoV-2 infection analyses.

RESULTS

In the vaccination analysis, the vaccinated and control groups each included a mean of 884,828 persons. Vaccination was most strongly associated with an elevated risk of myocarditis (risk ratio, 3.24; 95% confidence interval [CI], 1.55 to 12.44; risk difference, 2.7 events per 100,000 persons; 95% CI, 1.0 to 4.6), lymphadenopathy (risk ratio, 2.43; 95% CI, 2.05 to 2.78; risk difference, 78.4 events per 100,000 persons; 95% CI, 64.1 to 89.3), appendicitis (risk ratio, 1.40; 95% CI, 1.02 to 2.01; risk difference, 5.0 events per 100,000 persons; 95% CI, 0.3 to 9.9), and herpes zoster infection (risk ratio, 1.43; 95% CI, 1.20 to 1.73; risk difference, 15.8 events per 100,000 persons; 95% CI, 8.2 to 24.2). SARS-CoV-2 infection was associated with a substantially increased risk of myocarditis (risk ratio, 18.28; 95% CI, 3.95 to 25.12; risk difference, 11.0 events per 100,000 persons; 95% CI, 5.6 to 15.8) and of additional serious adverse events, including pericarditis, arrhythmia, deep-vein thrombosis, pulmonary embolism, myocardial infarction, intracranial hemorrhage, and thrombocytopenia.

CONCLUSIONS

In this study in a nationwide mass vaccination setting, the BNT162b2 vaccine was not associated with an elevated risk of most of the adverse events examined. The vaccine was associated with an excess risk of myocarditis (1 to 5 events per 100,000 persons). The risk of this potentially serious adverse event and of many other serious adverse events was substantially increased after SARS-CoV-2 infection. (Funded by the Ivan and Francesca Berkowitz Family Living Laboratory Collaboration at Harvard Medical School and Clalit Research Institute.)

The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Balicer at the Clalit Research Institute, Innovation Division, Clalit Health Services, 101 Arlozorov St., Tel Aviv, Israel, or at rbalicer@clalit.org.il.

Drs. Barda and Dagan and Drs. Reis and Balicer contributed equally to this article.

This article was published on August 25, 2021, at NEJM.org.

DOI: 10.1056/NEJMoa2110475

More than 1 year into the pandemic of coronavirus disease 2019 (Covid-19), the disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), an unprecedented number of mass vaccination efforts are under way worldwide. Globally, nearly 3.4 billion doses of vaccine have been administered over the 6-month period since the first vaccines were approved.[1]

Phase 3 clinical trials showed that several Covid-19 vaccines were efficacious and had an acceptable safety profile.[2-4] A number of potential adverse events were identified during these trials, including lymphadenopathy and idiopathic facial-nerve (Bell's) palsy.[2,3] Trials of the BNT162b2 vaccine (Pfizer–BioNTech) also showed a mild imbalance between the vaccinated and placebo groups with respect to the number of cases of appendicitis, hypersensitivity reactions, acute myocardial infarction, and cerebrovascular accidents.[5] However, phase 3 trials may have inherent limitations in assessing vaccine safety because of a small number of participants and a healthier-than-average sample population. Hence, they are often underpowered to identify less common adverse events. Postmarketing surveillance is required to monitor the safety of new vaccines in real-world settings.

Much effort is currently focused on characterizing the safety profiles of the recently approved Covid-19 vaccines. Passive surveillance systems such as the Vaccine Adverse Event Reporting System (VAERS)[6] collect information about adverse events that are potentially related to vaccination. This information is voluntarily reported by health care providers and the public. These systems are useful for quickly identifying potential safety signals, which, along with the findings of phase 3 trials, can be translated to lists of adverse events of interest for further exploration (such as that provided by the Safety Platform for Emergency Vaccines [SPEAC]).[7,8] Active surveillance systems such as the Biologics Effectiveness and Safety (BEST) system (part of the Sentinel Initiative)[9] aim to compare the incidence of adverse events of interest in large electronic health record databases with the background historical incidence. Although active surveillance can help highlight suspicious trends, the lack of a rigorously constructed comparable control group limits the ability of such surveillance to identify causal effects of vaccination.

The effectiveness of vaccines against SARS-CoV-2 has been confirmed in real-world studies,[10,11] but high-quality real-world safety data on the messenger RNA (mRNA)–based Covid-19 vaccines remain relatively sparse in the literature. The results of a study based on data reported by more than 600,000 vaccinated persons were recently published[12]; that study mainly assessed common and mild side effects. Two additional studies, which were based on surveys of vaccinated participants, involved small cohorts,[13,14] and another study analyzed adverse events reported in the VAERS database.[15] All these studies lacked controls. One study that did incorporate a control group included 8533 long-term care facility residents who had received the first dose of vaccine.[16] The authors of this study concluded that the mRNA-based vaccines had an acceptable safety profile, and no notable adverse events were reported.

As of May 24, 2021, nearly 5 million people in Israel, comprising more than 55% of the population, had received two doses of the BNT162b2 vaccine.[1] In this study, we used the integrated data repositories of the largest health care organization in Israel to evaluate the safety profile of the BNT162b2 vaccine. We compared the incidence of a broad set of potential short- and medium-term adverse events among vaccinated persons with the incidence among matched unvaccinated persons. Potential adverse events related to medical interventions are best understood in the context of the risks associated with the disease that these interventions aim to prevent or treat, so we also estimated the effects of SARS-CoV-2 infection on this same set of adverse events.

Methods

Study Setting

We analyzed observational data from Clalit Health Services (CHS) in order to emulate a target trial of the effects of the BNT162b2 vaccine on a broad range of potential adverse events in a population without SARS-CoV-2 infection. CHS is the largest of four integrated payer–provider health care organizations that offer mandatory health care coverage in Israel. CHS insures approximately 52% of the population of Israel (>4.7 million of 9.0 million persons), and the CHS-insured population is approximately representative of the Israeli population at large.[17] CHS directly provides out-

patient care, and inpatient care is divided between CHS and out-of-network hospitals. CHS information systems are fully digitized and feed into a central data warehouse. Data regarding Covid-19, including the results of all SARS-CoV-2 polymerase-chain-reaction (PCR) tests, Covid-19 diagnoses and severity, and vaccinations, are collected centrally by the Israeli Ministry of Health and shared with each of the four national health care organizations daily.

This study was approved by the CHS institutional review board. The study was exempt from the requirement for informed consent.

Eligibility Criteria

Eligibility criteria included an age of 16 years or older, continuous membership in the health care organization for a full year, no previous SARS-CoV-2 infection, and no contact with the health care system in the previous 7 days (the latter criterion was included as an indicator of a health event not related to subsequent vaccination that could reduce the probability of receiving the vaccine). Because of difficulties in distinguishing the recoding of previous events from true new events, for each adverse event, persons with a previous diagnosis of that event were excluded.

As in our previous study of the effectiveness of the BNT162b2 vaccine,[10] we also excluded persons from populations in which confounding could not be adequately addressed — long-term care facility residents, persons confined to their homes for medical reasons, health care workers, and persons for whom data on body-mass index or residential area were missing (missing data for these variables are rare in the CHS data). A complete definition of the study variables is included in Table S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org.

Study Design and Oversight

The target trial for this study would assign eligible persons to either vaccination or no vaccination. To emulate this trial, on each day from the beginning of the vaccination campaign in Israel (December 20, 2020) until the end of the study period (May 24, 2021), eligible persons who were vaccinated on that day were matched to eligible controls who had not been previously vaccinated. Since the matching process each day considered only information available on or before that day (and was thus unaffected by later vaccinations or SARS-CoV-2 infections), unvaccinated persons matched on a given day could be vaccinated on a future date, and on that future date they could become newly eligible for inclusion in the study as a vaccinated person.

In an attempt to emulate randomized assignment, vaccinated persons and unvaccinated controls were exactly matched on a set of baseline variables that were deemed to be potential confounders according to domain expertise — namely, variables that were potentially related to vaccination and to a tendency toward the development of a broad set of adverse clinical conditions. These matching criteria included the sociodemographic variables of age (categorized into 2-year age groups), sex (male or female), place of residence (at city- or town-level granularity), socioeconomic status (divided into seven categories), and population sector (general Jewish, Arab, or ultra-Orthodox Jewish). In addition, the matching criteria included clinical factors to account for general clinical condition and disease load, including the number of preexisting chronic conditions (those considered to be risk factors for severe Covid-19 by the Centers for Disease Control and Prevention [CDC] as of December 20, 2020,[18] divided into four categories), the number of diagnoses documented in outpatient visits in the year before the index date (categorized into deciles within each age group), and pregnancy status.

All the authors designed the study and critically reviewed the manuscript. The first three authors collected and analyzed the data. A subgroup of the authors wrote the manuscript. The last author vouches for the accuracy and completeness of the data and for the fidelity of the study to the protocol. There was no commercial funding for this study, and no confidentiality agreements were in place.

Adverse Events of Interest

The set of potential adverse events for the target trial was drawn from several relevant sources, including the VAERS, BEST, and SPEAC frameworks, information provided by the vaccine manufacturer, and relevant scientific publications. We cast a wide net to capture a broad range of clinically meaningful short- and medium-term potential adverse events that would be likely to be documented in the electronic health record. Accordingly, mild adverse events such as fever,

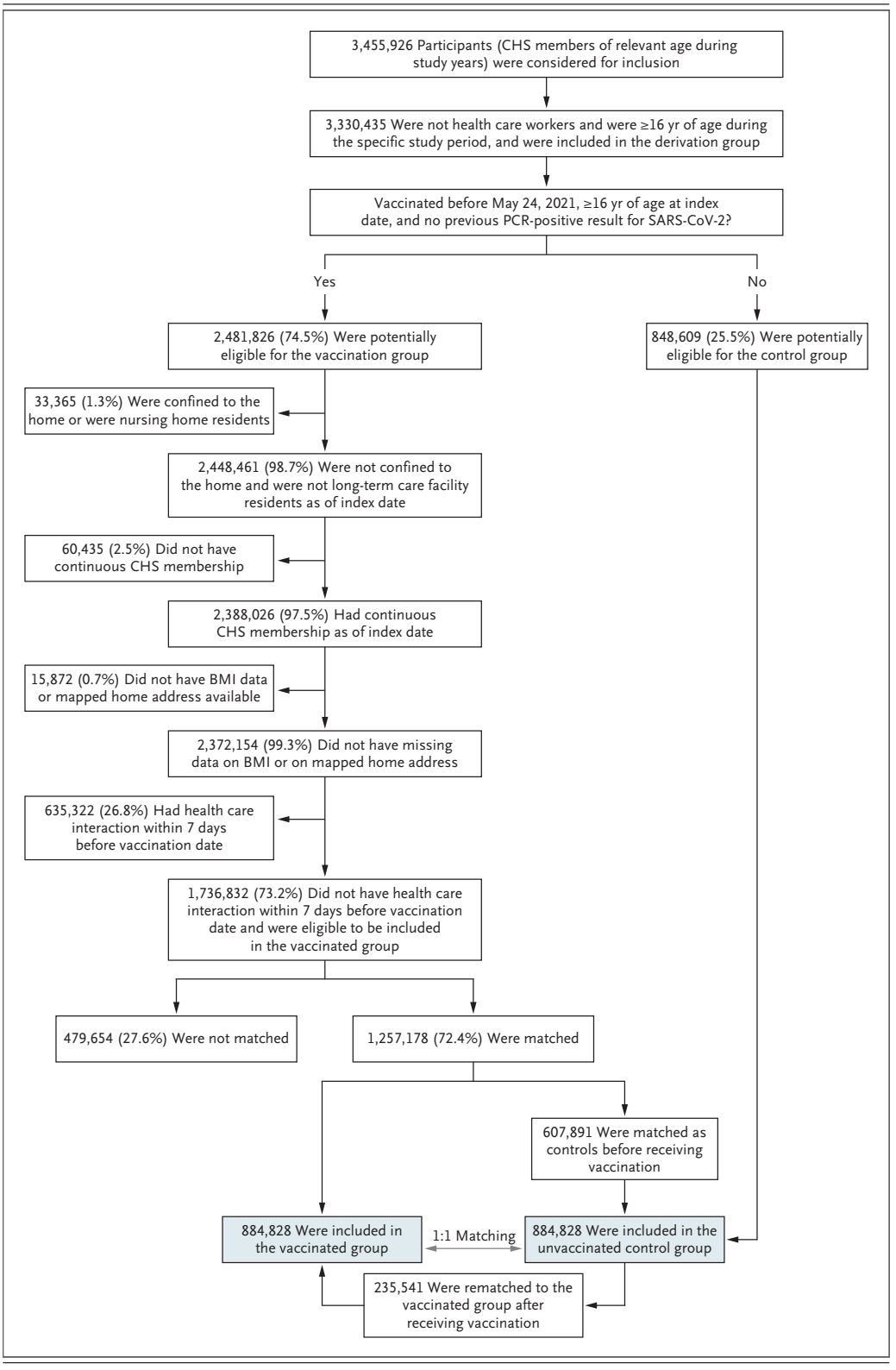


Figure 1 (facing page). Study Population for the Vaccination Analysis.

Absolute numbers and percentage changes are shown for each inclusion and exclusion criterion. The chart focuses on the vaccinated population. The derivation group includes the entire population, including unvaccinated persons. The shaded boxes indicate the two study groups. The same exclusion criteria were applied to the unvaccinated persons for each index date on which they were considered for matching. BMI denotes body-mass index, CHS Clalit Health Services, and PCR polymerase chain reaction.

malaise, and local injection-site reactions were not included in this study. The study included 42 days of follow-up, which provided 21 days of follow-up after each of the first and second vaccine doses. A total of 42 days was deemed to be sufficient for identifying medium-term adverse events, without being so long as to dilute the incidence of short-term adverse events. Similarly, adverse events that could not plausibly be diagnosed within 42 days (e.g., chronic autoimmune disease) were not included.

Adverse events were defined according to diagnostic codes and short free-text phrases that accompany diagnoses in the CHS database. A complete list of the study outcomes (adverse events) and their definitions is provided in Table S2.

For each adverse event, persons were followed from the day of matching (time zero of follow-up) until the earliest of one of the following: documentation of the adverse event, 42 days, the end of the study calendar period, or death. We also ended the follow-up of a matched pair when the unvaccinated control received the first dose of vaccine or when either member of the matched pair received a diagnosis of SARS-CoV-2 infection.

RISKS OF SARS-COV-2 INFECTION

To place the magnitude of the adverse effects of the vaccine in context, we also estimated the effects of SARS-CoV-2 infection on these same adverse events during the 42 days after diagnosis. We used the same design as the one that we used to study the adverse effects of vaccination, except that the analysis period started at the beginning of the Covid-19 pandemic in Israel (March 1, 2020) and persons who had had recent contact with the health care system were not excluded (because such contact may be expected in the days before diagnosis).

Each day in this SARS-CoV-2 analysis, persons with a new diagnosis of SARS-CoV-2 infection were matched to controls who were not previously infected. As in the vaccine safety analysis, persons could become infected with SARS-CoV-2 after they were already matched as controls on a previous day, in which case their data would be censored from the control group (along with their matched SARS-CoV-2–infected person) and they could then be included in the group of SARS-CoV-2–infected persons with a newly matched control. Follow-up of each matched pair started from the date of the positive PCR test result of the infected member and ended in an analogous manner to the main vaccination analysis, this time ending when the control member was infected or when either of the persons in the matched pair was vaccinated.

The effects of vaccination and of SARS-CoV-2 infection were estimated with different cohorts. Thus, they should be treated as separate sets of results rather than directly compared.

STATISTICAL ANALYSIS

Because a large proportion of the unvaccinated controls were vaccinated during the follow-up period, we opted to estimate the observational analogue of the per-protocol effect if all unvaccinated persons had remained unvaccinated during the follow-up. To do so, we censored data on the matched pair if and when the control member was vaccinated. Persons who were first matched as unvaccinated controls and then became vaccinated during the study period could be included again as vaccinated persons with a new matched control. The same procedure was followed in the SARS-CoV-2 infection analysis (i.e., persons who were first matched as uninfected controls and then became infected during the study period could be included again as infected persons with a new matched control).

We used the Kaplan–Meier estimator[19] to construct cumulative incidence curves and to estimate the risk of each adverse event after 42 days in each group. The risks were compared with ratios and differences (per 100,000 persons).

In the vaccination analysis, so as not to attribute complications arising from SARS-CoV-2 infection to the vaccination (or lack thereof), we also censored data on the matched pair if and

Table 1. Baseline Characteristics of the Study Populations According to Vaccination Status and SARS-CoV-2 Infection Status.*

Characteristic	Vaccination Analysis		SARS-CoV-2 Analysis	
	Vaccinated Group (N=884,828)	Control Group (N=884,828)	SARS-CoV-2–Infected Group (N=173,106)	Control Group (N=173,106)
Median age (IQR) — yr	38 (27–53)	38 (27–53)	34 (24–47)	34 (24–47)
Age group — no. (%)				
16–39 yr	472,095 (53)	472,095 (53)	107,046 (62)	107,046 (62)
40–49 yr	160,413 (18)	160,413 (18)	28,738 (17)	28,738 (17)
50–59 yr	93,110 (11)	93,110 (11)	17,851 (10)	17,851 (10)
60–69 yr	87,236 (10)	87,236 (10)	12,100 (7)	12,100 (7)
70–79 yr	51,924 (6)	51,924 (6)	5,371 (3)	5,371 (3)
≥80 yr	20,050 (2)	20,050 (2)	1,999 (1)	1,999 (1)
Sex — no. (%)				
Female	423,238 (48)	423,238 (48)	93,263 (54)	93,263 (54)
Male	461,590 (52)	461,590 (52)	79,843 (46)	79,843 (46)
Population sector — no. (%)				
General Jewish	595,897 (67)	595,897 (67)	90,903 (53)	90,903 (53)
Ultra-Orthodox Jewish	24,343 (3)	24,343 (3)	20,864 (12)	20,864 (12)
Arab	264,588 (30)	264,588 (30)	61,339 (35)	61,339 (35)
No. of risk factors according to CDC criteria — no. (%)				
0	571,604 (65)	571,604 (65)	108,980 (63)	108,980 (63)
1	200,789 (23)	200,789 (23)	41,502 (24)	41,502 (24)
2	61,924 (7)	61,924 (7)	11,976 (7)	11,976 (7)
3	27,175 (3)	27,175 (3)	5,181 (3)	5,181 (3)
≥4	23,335 (3)	23,335 (3)	5,467 (3)	5,467 (3)
CDC “certain” risk criteria — no. (%)				
Cancer	9,957 (1)	10,300 (1)	2,037 (1)	2,308 (1)
Chronic kidney disease	39,837 (4)	40,339 (5)	8,269 (5)	8,141 (5)
Chronic obstructive pulmonary disease	10,121 (1)	11,498 (1)	1,791 (1)	2,212 (1)
Heart disease	31,836 (4)	31,596 (4)	5,653 (3)	5,880 (3)
Solid-organ transplantation	351 (<1)	370 (<1)	148 (<1)	136 (<1)
Obesity: BMI, 30 to 40	129,148 (15)	125,120 (14)	30,558 (18)	28,580 (17)
Severe obesity: BMI, ≥40	11,861 (1)	12,568 (1)	3,478 (2)	3,107 (2)
Pregnancy	6,082 (1)	6,082 (1)	4,959 (3)	4,959 (3)
Sickle cell disease	140 (<1)	182 (<1)	50 (<1)	55 (<1)
Smoking	157,803 (18)	187,822 (21)	18,899 (11)	30,376 (18)
Type 2 diabetes mellitus	61,865 (7)	61,093 (7)	12,448 (7)	12,396 (7)
CDC “possible” risk criteria — no. (%)				
Asthma	46,836 (5)	47,151 (5)	10,079 (6)	10,413 (6)
Cerebrovascular disease	14,296 (2)	14,919 (2)	2,661 (2)	2,738 (2)
Other respiratory disease	1,884 (<1)	1,961 (<1)	322 (<1)	362 (<1)
Hypertension	94,819 (11)	93,357 (11)	15,514 (9)	15,682 (9)
Immunosuppression	15,430 (2)	15,433 (2)	4,346 (2)	4,457 (3)

Table 1. (Continued.)

Characteristic	Vaccination Analysis		SARS-CoV-2 Analysis	
	Vaccinated Group (N=884,828)	Control Group (N=884,828)	SARS-CoV-2–Infected Group (N=173,106)	Control Group (N=173,106)
Neurologic disease	26,340 (3)	28,421 (3)	5,194 (3)	5,455 (3)
Liver disease	10,491 (1)	12,558 (1)	2,391 (1)	2,600 (2)
Overweight: BMI, 25 to 30	284,904 (32)	271,335 (31)	53,374 (31)	50,038 (29)
Thalassemia	5,884 (1)	5,644 (1)	1,599 (1)	1,595 (1)
Type 1 diabetes mellitus	2,797 (<1)	2,648 (<1)	694 (<1)	763 (<1)

* Statistics are based on means and distributions from a pool of all the adverse event–specific cohorts. Characteristics of the various study populations after application of all eligibility criteria and the matching process are listed. BMI denotes body-mass index (the weight in kilograms divided by the square of the height in meters), CDC Centers for Disease Control and Prevention, IQR interquartile range, RT-PCR reverse-transcriptase polymerase chain reaction, and SARS-CoV-2 severe acute respiratory syndrome coronavirus 2.

when either member received a diagnosis of SARS-CoV-2 infection. Similarly, in the SARS-CoV-2 infection analysis, we censored data on the matched pair if and when either member was vaccinated. Additional details are provided in the Supplementary Methods 1 section in the Supplementary Appendix.

We calculated confidence intervals using the nonparametric percentile bootstrap method with 500 repetitions. As is standard practice for studies of safety outcomes, no adjustment for multiple comparisons was performed. Analyses were performed with the use of R software, version 4.0.4.

RESULTS

VACCINATION ANALYSIS

A total of 1,736,832 persons were eligible for inclusion in the vaccination cohort (Fig. 1). The median age in the eligible cohort was 43 years (Table S3). The final size of the study population differed for each studied adverse event because of adverse event–specific exclusion of persons with a history of that event. On average, across the adverse event–specific cohorts, 72.4% of the eligible persons were successfully matched. Table 1 shows the baseline characteristics of the total study population, with the mean distribution of characteristics across the various adverse event–specific cohorts. The characteristics of each adverse event–specific cohort are provided in Table S4. The vaccination cohorts included a mean of 884,828 vaccinated persons, with a median age of 38 years (5 years younger than the median age of the eligible cohort). A total of 48% of the population was female.

The effect of vaccination on the various potential adverse events included in this study is presented in Table 2. The risk was substantially higher on either the multiplicative (risk ratio) or additive (risk difference) scales in the vaccinated group than in the unvaccinated group for myocarditis (risk ratio, 3.24; 95% confidence interval [CI], 1.55 to 12.44; risk difference, 2.7 events per 100,000 persons; 95% CI, 1.0 to 4.6), lymphadenopathy (risk ratio, 2.43; 95% CI, 2.05 to 2.78; risk difference, 78.4 events per 100,000 persons; 95% CI, 64.1 to 89.3), appendicitis (risk ratio, 1.40; 95% CI, 1.02 to 2.01; risk difference, 5.0 events per 100,000 persons; 95% CI, 0.3 to 9.9), and herpes zoster infection (risk ratio, 1.43; 95% CI, 1.20 to 1.73; risk difference, 15.8 events per 100,000 persons; 95% CI, 8.2 to 24.2). Vaccination was substantially protective against adverse events such as anemia, acute kidney injury, intracranial hemorrhage, and lymphopenia.

Figure S1 shows the cumulative incidence (risk) curves for each specific adverse event. Spikes in the incidence of lymphadenopathy were seen after both the first and second doses of vaccine, whereas the incidence of myocarditis spiked mainly after the second dose of vaccine.

SARS-COV-2 INFECTION ANALYSIS

A total of 233,392 persons (median age, 36 years) were eligible to be included in the SARS-CoV-2 infection cohort (Fig. 2). On average, across the adverse event–specific cohorts, 75.8% of the eli-

Table 2. Adverse Events Associated with SARS-CoV-2 Vaccination.*

Event	Adverse-Event Cohort in Each Group	Vaccinated Group	Control Group	Risk Ratio (95% CI)	Risk Difference (95% CI)
	no. of persons	*no. of events*			*no. of events/100,000 persons*
Acute kidney injury	912,019	20	45	0.44 (0.23 to 0.73)	−4.6 (−7.8 to −1.8)
Anemia	709,267	298	378	0.79 (0.67 to 0.93)	−18.7 (−32.1 to −6.1)
Appendicitis	900,289	95	66	1.40 (1.02 to 2.01)	5.0 (0.3 to 9.9)
Arrhythmia	856,152	254	284	0.89 (0.74 to 1.04)	−6.1 (−14.7 to 1.8)
Arthritis or arthropathy	731,340	64	70	0.95 (0.65 to 1.34)	−0.8 (−6.3 to 4.2)
Bell's palsy	923,692	81	59	1.32 (0.92 to 1.86)	3.5 (−1.1 to 7.8)
Cerebrovascular accident	917,598	45	55	0.84 (0.54 to 1.27)	−1.6 (−5.3 to 2.0)
Deep-vein thrombosis	925,380	39	47	0.87 (0.55 to 1.40)	−1.1 (−4.5 to 2.7)
Herpes simplex infection	876,328	219	205	1.13 (0.95 to 1.38)	4.8 (−1.9 to 12.4)
Herpes zoster infection	888,647	283	204	1.43 (1.20 to 1.73)	15.8 (8.2 to 24.2)
Intracranial hemorrhage	933,130	13	30	0.48 (0.20 to 0.89)	−2.9 (−5.6 to −0.5)
Lymphadenopathy	823,006	660	279	2.43 (2.05 to 2.78)	78.4 (64.1 to 89.3)
Lymphopenia	938,939	2	7	0.26 (0.00 to 1.03)	−0.9 (−2.0 to <0.1)
Myocardial infarction	892,785	59	60	1.07 (0.74 to 1.60)	0.8 (−3.3 to 5.2)
Myocarditis	938,812	21	6	3.24 (1.55 to 12.44)	2.7 (1.0 to 4.6)
Neutropenia	919,291	20	22	0.87 (0.46 to 1.66)	−0.5 (−2.8 to 1.8)
Other thrombosis†	932,469	12	22	0.46 (0.19 to 0.91)	−2.2 (−4.6 to −0.3)
Paresthesia	827,478	552	496	1.12 (0.98 to 1.24)	10.8 (−1.8 to 21.4)
Pericarditis	936,197	27	18	1.27 (0.68 to 2.31)	1.0 (−1.6 to 3.4)
Pulmonary embolism	937,116	10	17	0.56 (0.21 to 1.15)	−1.5 (−3.6 to 0.4)
Seizure	913,091	36	35	0.99 (0.62 to 1.64)	−0.4 (−3.0 to 3.1)
Syncope	858,068	326	267	1.12 (0.94 to 1.34)	6.2 (−3.2 to 15.4)
Thrombocytopenia	923,123	56	60	0.94 (0.63 to 1.27)	−0.6 (−4.6 to 2.3)
Uveitis	933,217	26	20	1.27 (0.68 to 2.67)	1.0 (−1.5 to 3.8)
Vertigo	773,263	433	395	1.12 (0.97 to 1.28)	9.3 (−2.5 to 20.0)

* Estimates were calculated with the use of the Kaplan–Meier estimator 42 days after vaccination or SARS-CoV-2 infection. Confidence intervals (CIs) were estimated with the use of the percentile bootstrap method with 500 repetitions.
† The "other thrombosis" category is a composite diagnosis that includes arterial embolism and thrombosis, venous embolism and thrombosis, vascular insufficiency of the intestine, portal-vein thrombosis, or cranial venous sinus thrombosis.

gible persons were successfully matched. Table 1 shows the average distribution of characteristics in these cohorts, across the two study groups (infected and noninfected). The characteristics of each adverse event–specific cohort are provided in Table S5. The cohorts for the analysis of SARS-CoV-2 infection comprised a mean of 173,106 SARS-CoV-2–infected persons (median age, 34 years). A total of 54% of these persons were female.

Table S6 shows the effect of SARS-CoV-2 infection on the incidence of various adverse events. Infection substantially increased the risk of many different adverse events, including myocarditis (risk ratio, 18.28; 95% CI, 3.95 to 25.12; risk difference, 11.0 events per 100,000 persons; 95% CI, 5.6 to 15.8), acute kidney injury (risk ratio, 14.83; 95% CI, 9.24 to 28.75; risk difference, 125.4 events per 100,000 persons; 95% CI, 107.0 to 142.6), pulmonary embolism (risk ratio, 12.14; 95% CI, 6.89 to 29.20; risk difference, 61.7 events per 100,000 persons; 95% CI, 48.5 to 75.4), intracra-

nial hemorrhage (risk ratio, 6.89; 95% CI, 1.90 to 19.16; risk difference, 7.6 events per 100,000 persons; 95% CI, 2.7 to 12.6), pericarditis (risk ratio, 5.39; 95% CI, 2.22 to 23.58; risk difference, 10.9 events per 100,000 persons; 95% CI, 4.9 to 16.9), myocardial infarction (risk ratio, 4.47; 95% CI, 2.47 to 9.95; risk difference, 25.1 events per 100,000 persons; 95% CI, 16.2 to 33.9), deep-vein thrombosis (risk ratio, 3.78; 95% CI, 2.50 to 6.59; risk difference, 43.0 events per 100,000 persons; 95% CI, 29.9 to 56.6), and arrhythmia (risk ratio, 3.83; 95% CI, 3.07 to 4.95; risk difference, 166.1 events per 100,000 persons; 95% CI, 139.6 to 193.2).

Both Analyses

Figure 3 shows estimated risk ratios in both the vaccination and SARS-CoV-2 infection analyses for adverse events in which vaccination or infection substantially increased the risk. Figure 4 shows the absolute risk associated with vaccination, alongside the absolute risk associated with SARS-CoV-2 infection, for the same adverse events.

Discussion

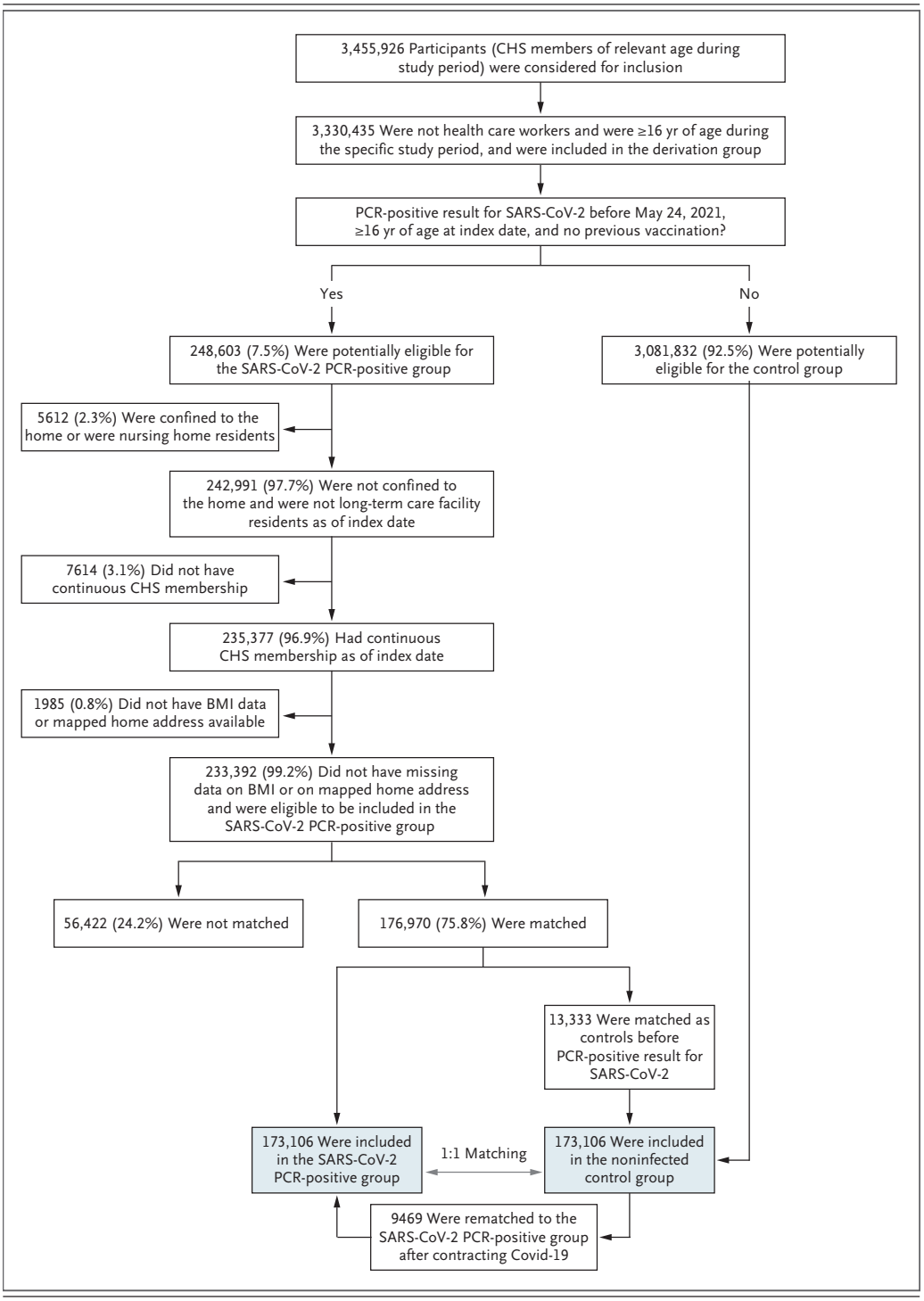
We used a data set involving more than 2.4 million vaccinated persons from an integrated health care organization to evaluate the safety profile of the BNT162b2 mRNA Covid-19 vaccine. The main potential adverse events identified included an excess risk of lymphadenopathy (78.4 events per 100,000 persons), herpes zoster infection (15.8 events), appendicitis (5.0 events), and myocarditis (2.7 events).

To place these risks in context, we also examined data on more than 240,000 infected persons to estimate the effects of a documented SARS-CoV-2 infection on the incidence of the same adverse events. SARS-CoV-2 infection was not estimated to have a meaningful effect on the incidence of lymphadenopathy, herpes zoster infection, or appendicitis, but it was estimated to result in a substantial excess risk of myocarditis (11.0 events per 100,000 persons). SARS-CoV-2 infection was also estimated to substantially increase the risk of several adverse events for which vaccination was not found to increase the risk, including an estimated excess risk of arrhythmia (166.1 events per 100,000 persons), acute kidney injury (125.4 events), pulmonary embolism (61.7 events), deep-vein thrombosis (43.0 events), myocardial infarction (25.1 events), pericarditis (10.9 events), and intracranial hemorrhage (7.6 events).

An association between Covid-19 vaccination and myocarditis has been previously reported.[20] Although no cases of myocarditis were reported in the BNT162b2 (Pfizer–BioNTech),[2] mRNA-1273 (Moderna),[3] or ChAdOx1 nCoV-19 (AstraZeneca)[4] phase 3 clinical trials, multiple cases of myocarditis after Covid-19 vaccination have recently been reported in the literature,[21-25] and both the Israeli Ministry of Health[26] and the CDC have investigated this association.[27] The risk appears to be highest among young men.[26,27] We found that the risk of myocarditis increased by a factor of three after vaccination, which translated to approximately 3 excess events per 100,000 persons; the 95% confidence interval indicated that values between 1 and 5 excess events per 100,000 persons were compatible with our data. Among the 21 persons with myocarditis in the vaccinated group, the median age was 25 years (interquartile range, 20 to 34), and 90.9% were male.

Another vaccine-related adverse event that has recently received attention in the medical literature is Bell's palsy. In a recent article based on publicly available data from the BNT162b2 and mRNA-1273 vaccine trials, Ozonoff et al.[28] suggested a possible association between these vaccines and Bell's palsy and estimated a rate ratio of approximately 7.0. This conclusion differed from the Food and Drug Administration briefing on these vaccines in December 2020; that briefing considered the incidence of Bell's palsy to be similar to the background incidence.[5] A small number of cases of Bell's palsy after Covid-19 vaccination have also been reported in the literature.[29,30] In the current study, the effect estimate was consistent with a potentially mild increase in the risk of Bell's palsy after vaccination, with a risk ratio of 1.32 (95% CI, 0.92 to 1.86). The absolute effect was small, with up to 8 excess events per 100,000 persons being highly compatible with our data according to the 95% confidence interval. Herpes zoster infection, the incidence of which we found to be increased after vaccination, is one of the potential causes of facial-nerve palsy.[31]

Another particularly notable class of adverse events that has been reported in the context of



Covid-19 vaccines is thromboembolic events. These adverse events, which primarily affect young women, have been linked with the ChAdOx1 nCoV-19[32] and Ad26.COV2.S (Johnson & Johnson–Janssen) Covid-19 vaccines,[33] both of which are adenoviral vector vaccines. However, we did not find an association between the BNT162b2 vaccine and various thromboembolic events in this study.

Figure 2 (facing page). Study Population for the SARS-CoV-2 Analysis.

Absolute numbers and percentage changes are shown for each inclusion and exclusion criterion. The chart focuses on the SARS-CoV-2–infected population. The derivation group includes the entire population, including uninfected persons. The shaded boxes indicate the two study groups. The same exclusion criteria were applied to the uninfected persons for each index date on which they were considered for matching. Covid-19 denotes coronavirus disease 2019.

Some initially unexpected effects were seen in the results of the current study. The BNT162b2 vaccine appears to be protective against certain conditions such as anemia and intracranial hemorrhage. These same adverse events are also identified in this study as complications of SARS-CoV-2 infection, so it appears likely that the protective effect of the vaccine is mediated through its protection against undiagnosed SARS-CoV-2 infection, which may be undiagnosed either because of a lack of testing or because of false negative PCR results.

This study has several limitations. First, persons in the study were not randomly assigned according to exposures (vaccinations and SARS-CoV-2 infections); this may have introduced confounding at baseline and selection bias at censoring, especially since a single set of confounders was used for adjustment in the assessment of many disparate adverse events. Second, the matching process that was necessary to attain exchangeability between the study groups resulted in a

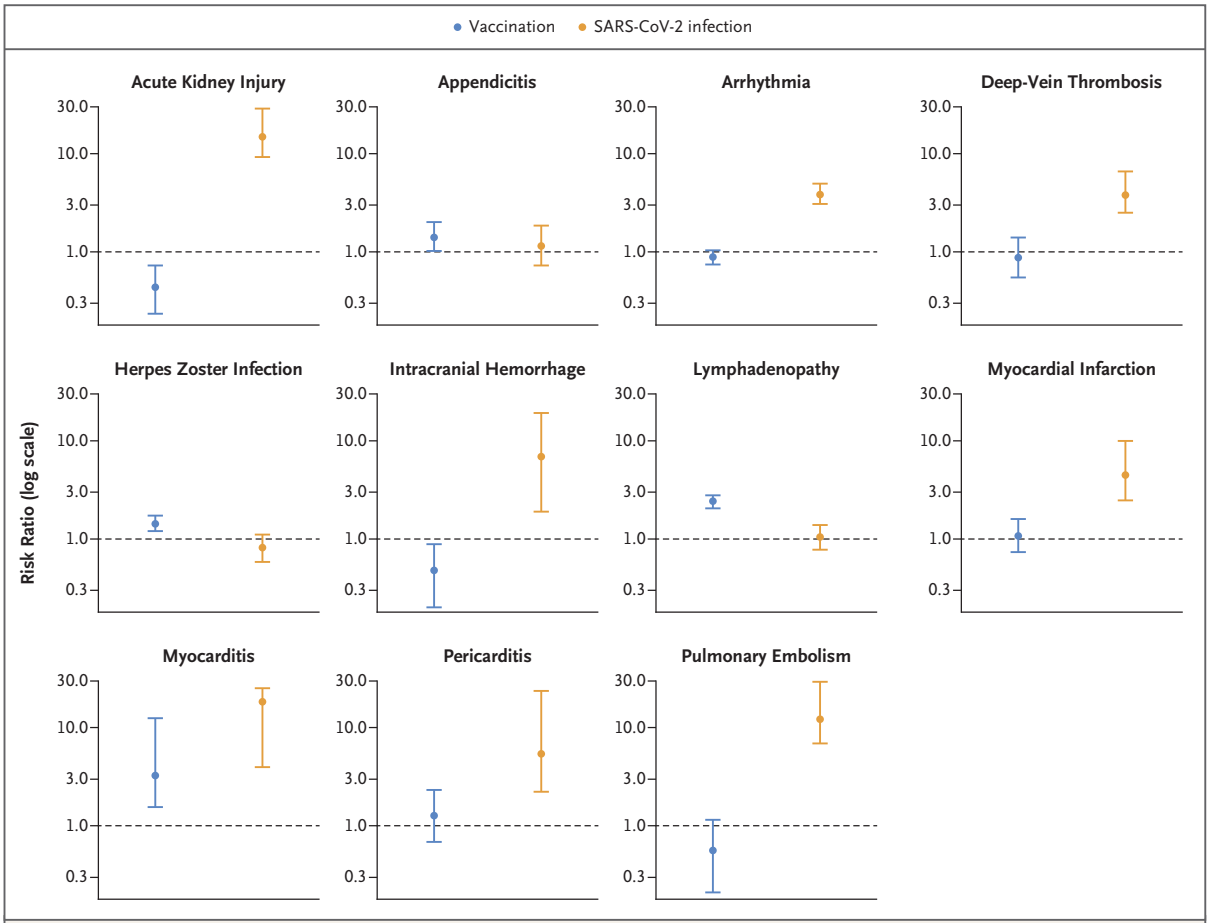


Figure 3. Risk Ratios for Adverse Events after Vaccination or SARS-CoV-2 Infection.

Estimated risk ratios for adverse events after vaccination or SARS-CoV-2 infection are shown. The risk ratio on the y axis is presented on a logarithmic scale to facilitate comparison of both increased and decreased risk. I bars indicate 95% confidence intervals.

study population with a different composition than the eligible population (e.g., median age, 38 years rather than 43 years). Because this different composition changes the population over which the causal effect is being estimated, different estimates might be found for adverse events for which the incidence may differ substantially between subgroups (e.g., myocarditis). Also, we excluded certain populations (such as health care workers and persons residing in long-term care facilities) that could be at particularly high risk for certain adverse events. Both of these issues should be taken into account when considering the generalizability of the findings.

Third, some diagnoses that were recorded in out-of-network hospitals, which were delayed in being reported to the insurer and were not entered by the person's general practitioner from the hospital discharge notes into the outpatient medical record, could have been missed. Fourth, it is possible that persons are more likely to increase their levels of clinical awareness, concern, or both after vaccination or SARS-CoV-2 infection, and thus they may be more likely to report or seek medical care for their symptoms, resulting in a spuriously increased incidence of the various adverse events in the vaccinated or infected groups. Similarly, among persons with SARS-CoV-2 infection, the spike in the incidence of certain adverse events in the first day of follow-up could indicate the initial clinical manifestation of the infection, but it could also be related to active testing for SARS-CoV-2. Fifth, all the effect measures that we presented are based only on a new incidence of the specific adverse event under study; thus, less light was shed on the potential additional risk among persons with a medical history of each of these adverse events. However, this choice was necessary to distinguish between true new diagnoses of a given adverse event and recoding of past diagnoses and to ensure the accuracy of the adverse-event labels.

In this study, we sought to place the increased risk of adverse events caused by the BNT162b2 vaccine in context by contrasting this risk with that of the same adverse events after documented

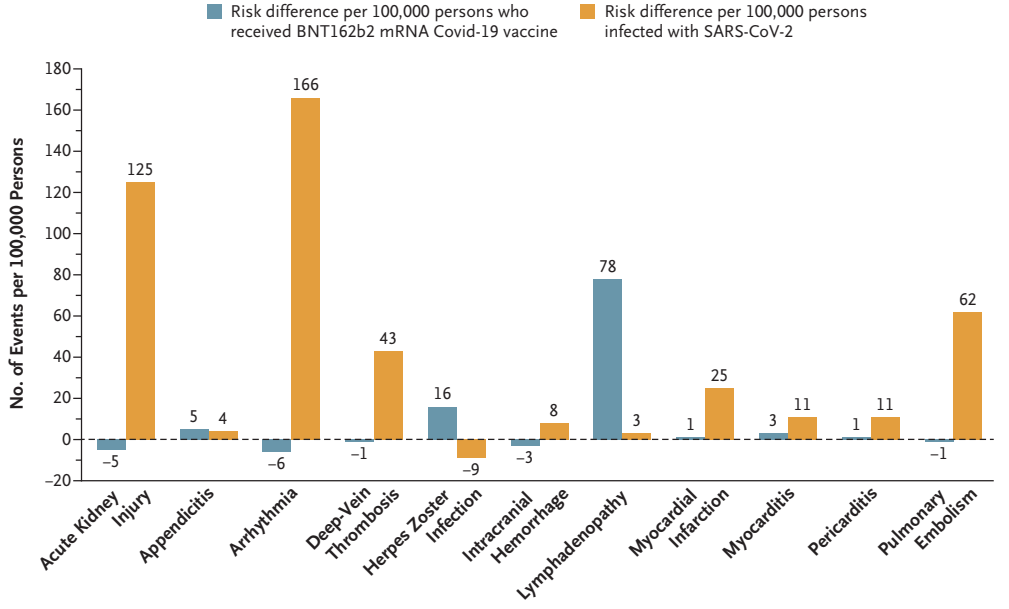


Figure 4. Absolute Excess Risk of Various Adverse Events after Vaccination or SARS-CoV-2 Infection.

Point estimates of the risk differences for selected adverse events are shown. Estimates were derived 42 days after vaccination or SARS-CoV-2 infection with the use of the Kaplan–Meier estimator. Risk differences are shown per 100,000 persons and rounded to the nearest integer. Negative differences (decreased risk) are represented as negative values on the y axis, and positive differences (increased risk) are represented as positive values on the y axis. The abbreviation mRNA denotes messenger RNA.

infection with SARS-CoV-2. We thought that this was necessary because vaccination and its potential risks do not occur in a void but rather in the context of an ongoing pandemic. Although the general risks of hospitalization, severe disease, and death from Covid-19 are widely recognized, secondary complications of infection are less well known. Therefore, in this analysis, we sought to estimate the effects of SARS-CoV-2 infection on the incidence of the same list of adverse events examined in the vaccination analysis. Because the cohorts that we used to study the vaccine and infection effects were different in composition, care should be taken when comparing the resulting risk estimates. In addition, knowledge of these risks alone is insufficient for a complete decision-theoretic analysis. When a person decides to become vaccinated, this choice results in a probability of 100% for the vaccination, whereas the alternative of contracting SARS-CoV-2 infection is an event with uncertain probability that depends on the person, place, and time. Moreover, infection with SARS-CoV-2 has many other adverse effects beyond those considered here, including the risk of transmission to family members and others.

We estimated that the BNT162b2 vaccine resulted in an increased incidence of a few adverse events over a 42-day follow-up period. Although most of these events were mild, some of them, such as myocarditis, could be potentially serious. However, our results indicate that SARS-CoV-2 infection is itself a very strong risk factor for myocarditis, and it also substantially increases the risk of multiple other serious adverse events. These findings help to shed light on the short- and medium-term risks of the vaccine and place them in clinical context. Further studies will be needed to estimate the potential of long-term adverse events.

Because of data privacy regulations, the raw data for this study cannot be shared.

Supported by the Ivan and Francesca Berkowitz Family Living Laboratory Collaboration at Harvard Medical School and Clalit Research Institute. Dr. Lipsitch receives support from the Morris–Singer Foundation.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank Oren Miron for his valuable advice.

Appendix

The authors' affiliations are as follows: the Clalit Research Institute, Innovation Division (N.B., N.D., Y.B.-S., E.K., J.W., R.O., R.D.B.), and the Community Medical Services Division (D.N.), Clalit Health Services, Tel Aviv, and Software and Information Systems Engineering (N.B., N.D.) and the School of Public Health, Faculty of Health Sciences (R.D.B.), Ben-Gurion University of the Negev, Be'er Sheva — both in Israel; the Department of Biomedical Informatics (N.B., N.D., I.K.), and the Ivan and Francesca Berkowitz Family Living Laboratory Collaboration at Harvard Medical School and Clalit Research Institute (N.B., N.D., I.K., B.Y.R., R.D.B.), Harvard Medical School (B.Y.R.), the Departments of Epidemiology and Biostatistics (M.A.H.), CAUSALab (M.A.H.), and the Center for Communicable Disease Dynamics, Departments of Epidemiology and Immunology and Infectious Diseases (M.L.), Harvard T.H. Chan School of Public Health, and the Predictive Medicine Group, Computational Health Informatics Program, Boston Children's Hospital (B.Y.R.) — all in Boston.

References

1. Our World in Data. Coronavirus (COVID-19) vaccinations. Statistics and research (https://ourworldindata.org/covid-vaccinations#source-information-country-by-country).
2. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med 2020;383:2603-15.
3. Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. N Engl J Med 2021;384:403-16.
4. Voysey M, Clemens SAC, Madhi SA, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. Lancet 2021;397:99-111.
5. Food and Drug Administration. Vaccines and Related Biological Products Advisory Committee: December 10, 2020 meeting announcement. December 2020 (https://www.fda.gov/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-december-10-2020-meeting-announcement).
6. Vaccine Adverse Event Reporting System. Report an adverse event to VAERS (https://vaers.hhs.gov/reportevent.html).
7. World Health Organization. Background paper on Covid-19 disease and vaccines: prepared by the Strategic Advisory Group of Experts (SAGE) on immunization working group on COVID-19 vaccines. December 22, 2020 (https://apps.who.int/iris/handle/10665/338095).
8. Law B, Sturkenboom M. SPEAC — Safety Platform for Emergency vACcines D2.3 priority list of adverse events of special interest: COVID-19. May 25, 2020 (https://brightoncollaboration.us/wp-content/uploads/2020/06/SPEAC_D2.3_V2.0_COVID-19_20200525_public.pdf).
9. Biologics Effectiveness and Safety (BEST) Initiative home page (https://www.bestinitiative.org).
10. Dagan N, Barda N, Kepten E, et al. BNT162b2 mRNA Covid-19 vaccine in a nationwide mass vaccination setting. N Engl J Med 2021;384:1412-23.
11. Hall VJ, Foulkes S, Saei A, et al. COVID-19 vaccine coverage in health-care workers in England and effectiveness of BNT162b2 mRNA vaccine against infection (SIREN): a prospective, multicentre, cohort study. Lancet 2021;397:1725-35.
12. Menni C, Klaser K, May A, et al. Vaccine side-effects and SARS-CoV-2 infection after vaccination in users of the COVID Symptom Study app in the UK: a prospec-

tive observational study. Lancet Infect Dis 2021;21:939-49.
13. Mathioudakis AG, Ghrew M, Ustianowski A, et al. Self-reported real-world safety and reactogenicity of COVID-19 vaccines: a vaccine recipient survey. Life (Basel) 2021;11:249.
14. Song JY, Cheong HJ, Kim SR, et al. Early safety monitoring of COVID-19 vaccines in healthcare workers. J Korean Med Sci 2021;36(15):e110.
15. Chen G, Li X, Sun M, et al. COVID-19 mRNA vaccines are generally safe in the short term: a vaccine vigilance real-world study says. Front Immunol 2021;12:669010.
16. Bardenheier BH, Gravenstein S, Blackman C, et al. Adverse events following mRNA SARS-CoV-2 vaccination among U.S. nursing home residents. Vaccine 2021;39:3844-51.
17. Cohen R, Rabin H. National Insurance Institute of Israel. Membership in sick funds 2016. August 2017. (In Hebrew) (https://www.btl.gov.il/Publications/survey/Documents/seker289/seker_289.pdf).
18. Centers for Disease Control and Prevention. People with certain medical conditions. May 2021 (https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html).
19. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. J Am Stat Assoc 1958;53:457-81.
20. Castiello T, Georgiopoulos G, Finocchiaro G, et al. COVID-19 and myocarditis: a systematic review and overview of current challenges. Heart Fail Rev 2021 March 24 (Epub ahead of print).
21. Ammirati E, Cavalotti C, Milazzo A, et al. Temporal relation between second dose BNT162b2 mRNA Covid-19 vaccine and cardiac involvement in a patient with previous SARS-COV-2 infection. Int J Cardiol Heart Vasc 2021;34:100774.
22. Abu Mouch S, Roguin A, Hellou E, et al. Myocarditis following COVID-19 mRNA vaccination. Vaccine 2021;39:3790-3.
23. Marshall M, Ferguson ID, Lewis P, et al. Symptomatic acute myocarditis in seven adolescents following Pfizer-BioNTech COVID-19 vaccination. Pediatrics 2021 June 4 (Epub ahead of print).
24. Albert E, Aurigemma G, Saucedo J, Gerson DS. Myocarditis following COVID-19 vaccination. Radiol Case Rep 2021;16:2142-5.
25. Bautista García J, Peña Ortega P, Bonilla Fernández JA, Cárdenes León A, Ramírez Burgos L, Caballero Dorta E. Acute myocarditis after administration of the BNT162b2 vaccine against COVID-19. Rev Esp Cardiol (Engl Ed) 2021 April 27 (Epub ahead of print).
26. Surveillance of myocarditis (inflammation of the heart muscle) cases between December 2020 and May 2021 (including). Press release of the Israeli Ministry of Health, February 6, 2021 (https://www.gov.il/en/departments/news/01062021-03).
27. Centers for Disease Control and Prevention. Myocarditis and pericarditis following mRNA COVID-19 vaccination. June 23, 2021 (https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/myocarditis.html).
28. Ozonoff A, Nanishi E, Levy O. Bell's palsy and SARS-CoV-2 vaccines. Lancet Infect Dis 2021;21:450-2.
29. Repajic M, Lai XL, Xu P, Liu A. Bell's palsy after second dose of Pfizer COVID-19 vaccination in a patient with history of recurrent Bell's palsy. Brain Behav Immun Health 2021;13:100217.
30. Colella G, Orlandi M, Cirillo N. Bell's palsy following COVID-19 vaccination. J Neurol 2021 February 21 (Epub ahead of print).
31. Peitersen E. Bell's palsy: the spontaneous course of 2,500 peripheral facial nerve palsies of different etiologies. Acta Otolaryngol Suppl 2002;549:4-30.
32. Greinacher A, Thiele T, Warkentin TE, Weisser K, Kyrle PA, Eichinger S. Thrombotic thrombocytopenia after ChAdOx1 nCov-19 vaccination. N Engl J Med 2021;384:2092-101.
33. Centers for Disease Control and Prevention, Health Alert Network. Emergency preparedness and response: cases of cerebral venous sinus thrombosis with thrombocytopenia after receipt of the Johnson & Johnson COVID-19 vaccine. April 13, 2021 (https://emergency.cdc.gov/han/2021/han00442.asp).