PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

OCTOBER 2020 • VOLUME 146 • NUMBER 4

www.pediatrics.org

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN®

90 Years of Caring for Children—1930–2020

CONNECT THE DOTS:

There are about 7,000 rare diseases, which by definition each affect fewer than 200,000 people. Due to the uncommonality of these diseases, they often go undetected.[1] So how do we best hunt for a diagnosis of a rare disease?

Hunter syndrome (also known as MPS II) is a rare, inherited lysosomal storage disorder which mainly affects boys.[2,3] Symptoms vary, but the majority of patients experience symptoms before the age of 2.[3] However, since the symptoms overlap with common childhood complaints, these patients may visit healthcare professionals multiple times before a diagnosis is suspected.[4]

Hunter syndrome is a progressive and multisystemic disorder, requiring management from a **multidisciplinary team**.[4] Pediatricians may work alongside geneticists, rheumatologists, neurologists, cardiologists, physiotherapists, speech therapists, and many other specialists to diagnose and manage Hunter syndrome patients.[4]

WOULD YOU SUSPECT HUNTER SYNDROME?

As a pediatrician, you might notice progressive symptoms of Hunter syndrome. Some of these symptoms can be seen in the timeline below – this timeline depicts the journey of one patient, Aiden, and his specific route to diagnosis, as described by his mother, Toni-Ann. **It is important to note that the onset of clinical manifestation in Hunter syndrome may vary by individual and may not always present in the same manner.**

AIDEN'S AGE IN MONTHS	KEY SIGNS & SYMPTOMS	WHAT AIDEN'S MOTHER, TONI-ANN, SAID AT THIS TIME	PEDIATRICIAN VISIT LOG
0	No suspicions[3]	Aiden was a beautiful, healthy baby boy	Child appears normal at birth, no indication of any symptoms
4-10	Recurrent ear infections[2,3] Recurrent hernias[2,3]	He had frequent ear infections that we were told were typical	Child has developed an ear infection and has been suffering from a chronic runny nose
18	Respiratory infection[2,4] Enlarged tonsils[2] Developmental delays[4]	Aiden had two sets of tubes put in his ears, his adenoids removed, and he got colds a lot	Child has suffered from a few colds. His parents are growing concerned that he has not yet started teething or crawling
24	Speech delays[3]	When he was about 2 years old I noticed a speech delay, but we thought he would catch up. Aiden had occupational therapy, physiotherapy, and speech therapy for a year	Child returns – his parents are worried that he has not yet started speaking
30	Coarse facial features[2,4]	His pediatrician suggested we see a geneticist because of Aiden's facial features (broad nose, large head); he wanted to have Aiden evaluated	Child returns again – his facial features appear to be coarsening – his nose is broad, his brows are promiment, his tongue is protruding

As a child with Hunter syndrome gets older, they may present with an array of symptoms, including severe **hearing loss, stiff joints**, **claw-like hands, and/or developmental delays**.[2,3,4] With progressively **enlarging tonsils and tongue**, they may be referred for a tonsillectomy and may have already had several other surgeries to address early-onset symptoms, such as **recurrent hernias** – more than half of patients receive surgery before a diagnosis is made.[4]

Clusters of common childhood symptoms could indicate Hunter syndrome. If you see a child with a **recurrent combination of these red flag symptoms, consider Hunter syndrome and refer early**.

THINK HUNTER SYNDROME

Abdominal hernia[2]

+

Otitis media[2]

+

Enlarged tongue and tonsils[2]

Aiden, age 3

Coarse facial features[2]

Stiff joints and claw-like hands[2]

Developmental delays[4]

Aiden, age 5

A rare combination of common childhood complaints could be an indicator for Hunter syndrome (MPS II), a genetic disorder mainly affecting males.[2,4]

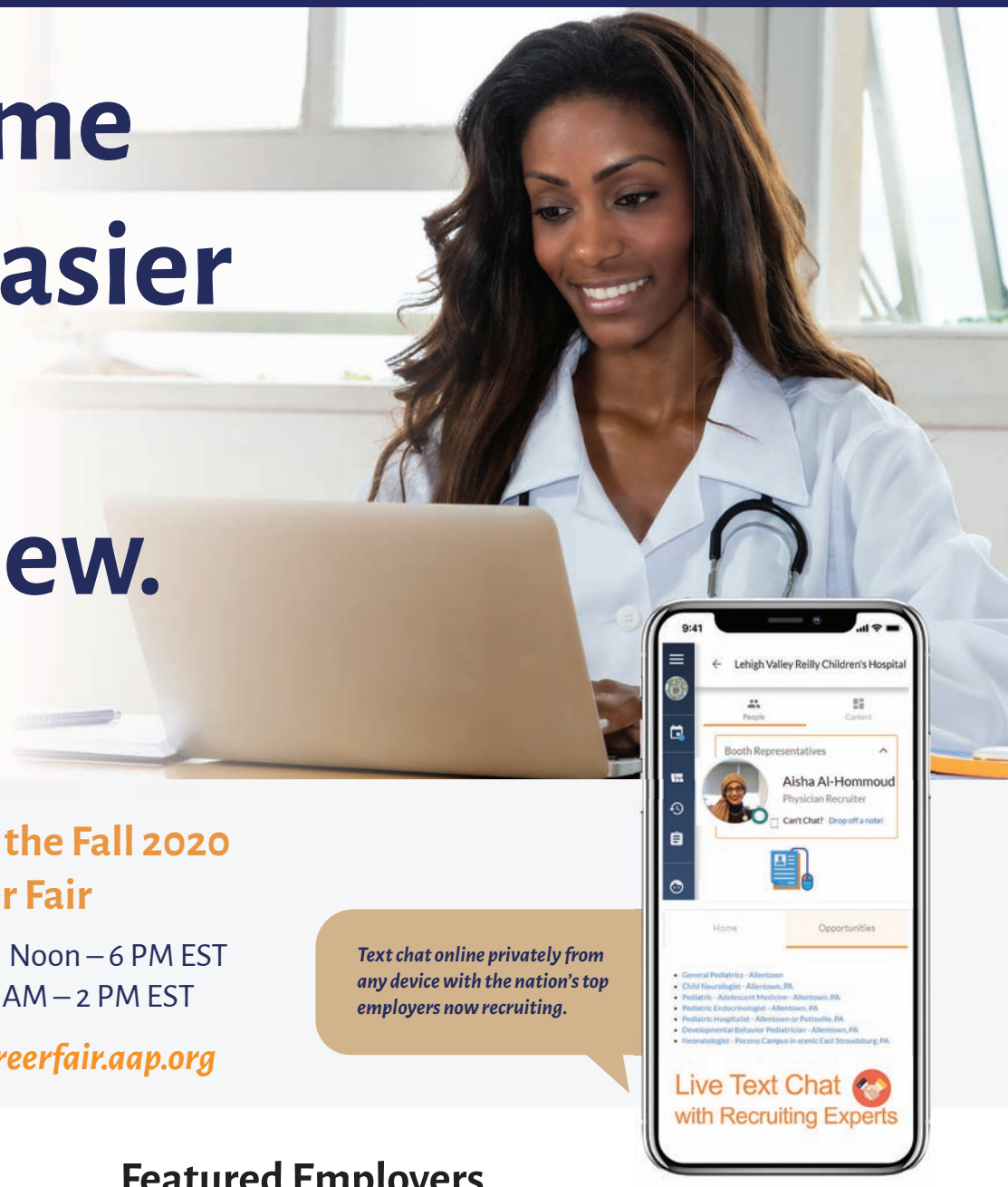
For more information visit: **hunterpatients.com/healthcare-professionals**

1. NIH. 2019. *FAQs About Rare Diseases.* [Accessed 4 September 2019]
2. Wraith JE *et al.* Genet Med. 2008; 10(7): 508-516
3. Martin R *et al.* Pediatrics. 2008; 121(2): e377-e386
4. Burton K *et al.* Eur J Pediatr. 2012; 171(1): 631-639

AAP Career Center
careercenter.aap.org

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN®
90 Years of Caring for Children—1930–2020

Welcome to an easier way to interview.



Register today for the Fall 2020 AAP Virtual Career Fair

Wednesday, October 14 | Noon – 6 PM EST
Thursday, October 15 | 11 AM – 2 PM EST

Job seeker sign up at careerfair.aap.org

Text chat online privately from any device with the nation's top employers now recruiting.

Featured Employers

KAISER PERMANENTE®

PEDIATRIC ASSOCIATES

PEDIATRIC search partners

PennState Health Children's Hospital

NORTON HEALTHCARE

The content of the journal is intended to encompass the needs of the whole child in his physiologic, mental, emotional, and social structure.

The single word, PEDIATRICS, *has been chosen to indicate this catholic intent.*

Hugh McCulloch
PEDIATRICS, January 1948

PEDIATRICS (ISSN 0031 4005) is owned and controlled by the American Academy of Pediatrics. It is published monthly by the American Academy of Pediatrics, 345 Park Blvd, Itasca, IL 60143.

Subscriptions to PEDIATRICS are provided to AAP Members as part of annual membership dues. All others please go to http://shop.aap.org/Pediatrics. To contact customer service, email mcc@aap.org or call (866) 843-2271.

Periodicals postage paid at ARLINGTON HEIGHTS, ILLINOIS, and at additional mailing offices. Printed in USA.

POSTMASTER: Send address changes to: THE AMERICAN ACADEMY OF PEDIATRICS, Attn: Customer Service Center, 345 Park Blvd, Itasca, IL 60143.

Printed on recycled paper. ♻

PEDIATRICS®

OCTOBER 2020 • VOLUME 146 • NUMBER 4

contents

For Author Guidelines please visit www.pediatrics.org

For a Thank You to Our Reviewers please visit www.pediatrics.org/cgi/doi/10.1542/peds.2018Tribute

ARTICLES

icon legend

Most of the articles in *PEDIATRICS* have more content available online at www.pediatrics.org.

= supplement

= data file/supplementary information available online

= podcast available online

= video available online

= funded by NIH

STAY CONNECTED

AAP News & Journals Gateway

Sample citation format: Ralston SL, Garber MD, Rice-Conboy E, et al. A Multicenter Collaborative to Reduce Unnecessary Care in Inpatient Bronchiolitis. *Pediatrics*. 2016;137(1):e20150851.

PEDIATRICS®

OCTOBER 2020 • VOLUME 146 • NUMBER 4

contents

ARTICLES *(continued)*

PEDIATRICS®

OCTOBER 2020 • VOLUME 146 • NUMBER 4

contents

ARTICLES *(continued)*

PEDIATRICS®

OCTOBER 2020 • VOLUME 146 • NUMBER 4

contents

ARTICLES *(continued)*

COMMENTARIES

PEDIATRICS®

OCTOBER 2020 • VOLUME 146 • NUMBER 4

contents

PEDIATRICS®

OCTOBER 2020 • VOLUME 146 • NUMBER 4

contents

PEDIATRICS®

OCTOBER 2020 • VOLUME 146 • NUMBER 4

contents

PEDIATRICS PERSPECTIVES

Addressing Pandemic-Intensified Food Insecurity

Rebecca L. Hetrick, MD,[a] Ovini D. Rodrigo, MD,[a] Claire E. Bocchini, MD[a,b]

As the coronavirus disease 2019 (COVID-19) pandemic progresses, child health advocates must continue to address the pandemic's impact on child health and well-being. School meal programs serve as a critical safety net against food insecurity and malnutrition for vulnerable children worldwide.[1] When the pandemic emerged as a global threat in the early months of 2020, most national governments shuttered schools as part of their efforts to slow viral spread. In total 194 countries, including the United States, closed schools and universities by early April 2020.[2] Overnight, school-aged children lost access to affordable, nutritious meals.[1] This occurred in the setting of pandemic-related economic contraction, job losses, supply chain disruptions, and rising food costs.[3,4] It comes as no surprise that food insecurity has skyrocketed across the United States, especially among families with children.[5–7] Early analyses suggest the prevalence of food insecurity in US households with children at least doubled, if not tripled, from prepandemic levels.[5–7] Furthermore, experts report this rise in food insecurity cannot be explained by unemployment alone, pointing to the loss of school meals as a major contributor.[7]

Even brief spells of food insecurity have detrimental consequences for child health and well-being; students living in households that experience food insecurity during the summer are more likely to lose reading skills, gain excessive weight, and have mental health and behavioral problems compared with peers.[8] As pediatricians, we must call for strong policies to protect school-aged children from pandemic-intensified food insecurity.

BACKGROUND ON SCHOOL-BASED CHILD NUTRITION PROGRAMS

The US Department of Agriculture (USDA) runs several federally funded child nutrition programs, many of which are integrated into our nation's school systems. The 2 largest programs, the National School Lunch Program (NSLP) and School Breakfast Program (SBP), provide free or reduced-price meals to children of low-income families. Approximately 29.6 million children participated in NSLP and 14.8 million participated in SBP daily in 2019.[9] For children receiving both school lunch and breakfast, these programs provide nearly half of the calories they consume in a school day.[10]

The USDA has 2 approaches to address summer food insecurity in students who depend on school meals during the academic year. The

[b]Division of Infectious Diseases, [a]Department of Pediatrics, Baylor College of Medicine and Texas Children's Hospital, Houston, Texas

Drs Hetrick and Rodrigo conceptualized and drafted the initial manuscript and reviewed and revised the manuscript; Dr Bocchini contributed to research and content discussions and provided critical contributions to the revision process; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2020-006924

Accepted for publication Jul 23, 2020

Address correspondence to Ovini D. Rodrigo, MD, Pediatrics Residency Program, One Baylor Plaza, BCM 320, Houston, TX 77030. E-mail: orodrigo@bcm.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

To cite: Hetrick RL, Rodrigo OD, Bocchini CE. Addressing Pandemic-Intensified Food Insecurity. *Pediatrics*. 2020; 146(4):e2020006924

Summer Food Service Program (SFSP) relies on community organizations, such as churches, schools, and recreation centers to plan and manage meal distribution in low-income areas. Unfortunately, the program serves less than one-seventh of the students who qualify.[11] Barriers to use of SFSP include access to transportation, administrative burden, and food distribution.[11] Another program, the Summer Seamless Option, allows schools already serving meals through the NSLP and SBP to continue offering these meals over the summer.[12]

POLICY RECOMMENDATION 1: USDA CHILD NUTRITION PROGRAM WAIVERS

When schools closed in the spring of 2020, the USDA took steps to replace the meals typically supplied by schools and community sites.[13] The USDA implemented a series of waivers that lifted restrictions normally attached to school meal funding. For example, the USDA waivers permitted schools and program sites to distribute meals directly to parents or guardians in the child's absence, outside of traditional mealtimes, and in noncongregate settings. Recognizing the tremendous need, school districts and community sites across the country stepped up, creating meal distribution programs overnight. Initiatives varied from grab-and-go pickup locations to meal delivery by school bus.[14] Some school food authorities partnered with local nonprofit organizations or private businesses to distribute groceries and shelf-stable goods.[15]

Although these Herculean efforts undoubtedly served as a lifeline for millions of children and their families, the USDA child nutrition program waivers have 2 critical limitations. First, the USDA did not mandate schools to provide food during school closures, so many did not. Second, like the SFSP, school districts have struggled with the logistics of physically handing out meals in noncongregate settings.[14] Despite these limitations, the USDA waivers facilitated meal distribution to vulnerable children across the country. Fortunately, the USDA has extended some of the waivers to include the upcoming 2020–2021 school year, anticipating that pandemic-related school closures will continue.[16] We recommend that the USDA should extend all child nutrition program waivers for the entire duration of this public health crisis. Additionally, the USDA should streamline the process by which states apply for the waivers. Currently, states must apply for each waiver individually, which creates significant administrative burden and limits the states' ability to respond quickly. Lastly, the USDA should provide additional logistic guidance and support for school districts to address barriers to reaching vulnerable children.

POLICY RECOMMENDATION 2: ELECTRONIC BENEFITS TRANSFER PROGRAMS

Another potential policy option eliminates the onus for schools and community organizations to distribute meals during school closures. Electronic Benefits Transfer (EBT) programs provide families with debit cards containing funds for grocery purchases. This model has been successfully piloted to address summer food insecurity in children.[17] In 2011, the USDA launched the summer EBT program. Although limited to a select group of states, the summer EBT program reduced food insecurity and improved nutritional intake in participating children, demonstrating the ability of this model to address food insecurity during school closures.[17] The Families First Coronavirus Response Act, signed into law on March 18, 2020, created the Pandemic Electronic Benefits Transfer (P-EBT) program. The legislation allowed states to directly provide funds to households that lost access to the NSLP during pandemic-related school closures. As of June 2020, 46 states and the District of Columbia have been approved to operate a P-EBT program.[18]

Given the efficacy of the EBT model, this type of program should play a critical role in alleviating pandemic-intensified food insecurity. We therefore recommend that the P-EBT program should be continued for the 2020–2021 school year to ensure vulnerable children have uninterrupted access to food in the event of ongoing school disruptions due to COVID-19. Additionally, the previously piloted summer EBT program should be expanded nationwide as a means of supporting families throughout the coming years of economic recovery.

POLICY RECOMMENDATION 3: FOOD DELIVERY PROGRAMS FOR RURAL COMMUNITIES

Food-insecure children living in rural communities represent a particularly vulnerable group during pandemic-related school closures. Rural communities across the country have higher rates of poverty and food insecurity.[11] Families in rural areas may live a considerable distance away from schools, child nutrition program sites, and grocery stores, limiting their ability to benefit from most USDA child nutrition programs. In 2019, the USDA partnered with the Texas Department of Agriculture and Baylor University's Texas Hunger Initiative to pilot a summer meals program targeted at children in rural or remote communities in east and west Texas. The program, called Meals-to-You (MTY), mailed weekly meal boxes to each child eligible for free or reduced-price meals.[19] MTY successfully addressed the transportation barriers that previously kept these families from accessing existing nutritional support programs.[19] This program was expanded to select counties in New

Mexico and Alaska for summer 2020.[20] In March 2020, the USDA announced a public-private partnership based on the MTY pilot and managed by Baylor University's Collaborative on Hunger and Poverty to provide meals to rural children affected by pandemic-related school closures. The Emergency Meals-to-You (eMTY) program mails boxes of shelf-stable goods every 2 weeks to children who typically received lunch through NSLP.[21]

Programs like summer MTY and eMTY provide children in rural and isolated communities with a consistent adjunct to the family's food supply when schools are not in session. With the inevitability of COVID-19–related disruptions to the 2020–2021 school year, we recommend that eMTY programs are extended through the next school year and expanded to serve more remote communities. Additionally, the summer MTY programs should be expanded nationwide to secure reliable access to food during summer months beyond the scope of the COVID-19 pandemic.

TABLE 1 Summary of Proposed Policy Recommendations

Policy	Current State	Ideal State
USDA child nutrition program waivers	Waivers regarding meal patterns, mealtimes, noncongregate feeding, and parent or guardian meal pickup have been extended through August 30, 2021.[16]	Extend all child nutrition program waivers for the duration of the COVID-19 pandemic. Streamline the process by which states apply for the waivers. The USDA should provide logistic guidance and support for school districts to overcome barriers to reaching vulnerable children.
P-EBT programs	Varies by state. Such programs have issued benefits to households of children whose schools were closed for at least 5 consecutive days during emergency designation and who would have received meals through NSLP.[22]	Continue the P-EBT program through the 2020–2021 school year (June 30, 2021). Eliminate the requirement for consecutive days of missed classes given the schedule variations that school districts may use to limit in-person attendance.
Summer EBT programs	In 2020, limited to participating school districts in Michigan and the Chickasaw Nation. Provides ∼$30 per eligible child per month in May, June, and July.[23,24]	Create permanent summer EBT programs nationwide.
Meal delivery programs for rural communities	eMTY shipments will continue until August 18, 2020, in participating school districts. Provides box containing 10 shelf-stable breakfasts and lunches every 2 wk by mail.[20]	Extend eMTY programs through the 2020–2021 school year and expand program to all school districts with children living in rural or isolated communities.
	Summer MTY programs are available in participating school districts in Alaska, New Mexico, and Texas.[20]	Expand summer MTY programs to all school districts with children living in rural or isolated communities.

—, not applicable.

CONCLUSIONS

Although the pandemic has had a multitude of devastating effects, it provides a unique opportunity to create meaningful change by creating sustainable solutions to address food insecurity in school-aged children (see Table 1 for a summary of proposed policy recommendations). In the coming months, the policies we develop in response to the current crisis have the potential to greatly strengthen the safety net protecting our children from hunger and poor nutrition.

As pediatricians, we are in a prime position to identify and address food insecurity. We urge all pediatric providers to incorporate sensitive food insecurity screening into all outpatient clinic appointments and emergency department visits and at least once during each inpatient admission. The American Academy of Pediatrics recommends the Hunger Vital Sign, a well-regarded 2-question screening tool.[8] For families who screen positive, pediatric practices should refer families to local food banks and food distribution sites as well as provide information about evidence-based programs that ameliorate food insecurity such as the Supplemental Nutrition Assistance Program (SNAP) and the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC).[25] As the COVID-19 pandemic continues to unfold, food insecurity in children will remain in flux. It is our privilege and responsibility as pediatricians to strive to alleviate the burden of food insecurity on children.

ACKNOWLEDGMENTS

We applaud the efforts of school districts, food banks, nonprofit organizations, private donors, and volunteers in striving to provide meals for vulnerable children during these unprecedented times.

ABBREVIATIONS

COVID-19: coronavirus disease 2019
EBT: Electronic Benefits Transfer
eMTY: Emergency Meals-to-You
MTY: Meals-to-You
NSLP: National School Lunch Program
P-EBT: Pandemic Electronic Benefits Transfer
SBP: School Breakfast Program
SFSP: Summer Food Service Program
USDA: US Department of Agriculture

REFERENCES

1. World Food Programme. *State of School Feeding Worldwide 2013*. Rome, Italy: World Food Programme; 2013. Available at: https://documents.wfp.org/stellent/groups/public/documents/communications/wfp257481.pdf?_ga=2.219157404.487657597.1593463062-2047298266.1593110854. Accessed July 7, 2020
2. United Nations Educational, Scientific and Cultural Organization. Education: from disruption to recovery. 2020. Available at: https://en.unesco.org/covid19/educationresponse. Accessed July 7, 2020
3. US Bureau of Labor Statistics. Consumer Price Index news release. 2020. Available at: https://www.bls.gov/news.release/archives/cpi_06102020.htm. Accessed July 7, 2020
4. Macias CJ. Is the food supply strong enough to weather the COVID-19 pandemic? Feeding a growing nation. 2020. Available at: https://www.ucdavis.edu/food/news/is-food-supply-strong-enough-to-weather-covid-19-pandemic/. Accessed July 7, 2020
5. Bauer L; The Hamilton Project. The COVID-19 crisis has already left too many children hungry in America. 2020. Available at: https://www.hamiltonproject.org/blog/the_covid_19_crisis_has_already_left_too_many_children_hungry_in_america. Accessed May 11, 2020
6. Schanzenbach DW, Pitts A; Institute for Policy Research. Food insecurity in the Census Household Pulse Survey data tables. 2020. Available at: https://www.ipr.northwestern.edu/documents/reports/ipr-rapid-research-reports-pulse-hh-data-1-june-2020.pdf. Accessed July 7, 2020
7. Bitler MP, Hoynes HW, Schanzenbach DW. The social safety net in the wake of COVID-19. 2020. Available at: https://www.brookings.edu/wp-content/uploads/2020/06/Bitler-et-al-conference-draft.pdf. Accessed July 7, 2020
8. Council on Community Pediatrics; Committee on Nutrition. Promoting food security for all children. *Pediatrics*. 2015;136(5). Available at: www.pediatrics.org/cgi/content/full/136/5/e1431
9. US Department of Agriculture Food and Nutrition Service. Child nutrition tables. 2020. Available at: https://www.fns.usda.gov/pd/child-nutrition-tables. Accessed May 24, 2020
10. Cullen KW, Chen T-A. The contribution of the USDA school breakfast and lunch program meals to student daily dietary intake. *Prev Med Rep*. 2016;5:82–85
11. Food Research & Action Center. Hunger doesn't take a vacation: summer nutrition status report. 2019. Available at: https://frac.org/wp-content/uploads/frac-summer-nutrition-report-2019.pdf. Accessed May 10, 2020
12. US Department of Agriculture Food and Nutrition Service. An opportunity for schools. 2020. Available at: https://www.fns.usda.gov/school-meals/opportunity-schools. Accessed July 5, 2020
13. US Department of Agriculture Food and Nutrition Service. FNS responds to COVID-19. 2020. Available at: https://www.fns.usda.gov/disaster/pandemic/covid-19. Accessed June 30, 2020
14. Sugar R. The scramble to feed the kids left hungry by the coronavirus crisis. *Vox*. April 17, 2020. Available at: https://www.vox.com/the-goods/2020/4/17/21220016/school-lunch-coronavirus-meal-programs. Accessed May 11, 2020
15. Abad-Santos A. How US schools are (and aren't) providing meals to children in the Covid-19 crisis. *Vox*. March 28, 2020. Available at: https://www.vox.com/2020/3/28/21197965/coronavirus-school-shutdown-free-meals. Accessed July 16, 2020
16. US Department of Agriculture. USDA provides flexibilities to ensure kids receive meals this fall. 2020. Available at: https://www.usda.gov/media/press-releases/2020/06/25/usda-provides-flexibilities-ensure-kids-receive-meals-fall. Accessed June 30, 2020
17. Collins AM, Klerman JA, Briefel R, et al. A summer nutrition benefit pilot program and low-income children's food security. *Pediatrics*. 2018;141(4):e20171657
18. US Department of Agriculture Food and Nutrition Service. State guidance on coronavirus Pandemic EBT (P-EBT). 2020. Available at: https://www.fns.usda.gov/snap/state-guidance-coronavirus-pandemic-ebt-pebt. Accessed July 5, 2020
19. US Department of Agriculture. Innovation and collaboration bring summer meals to children in rural Texas. 2020. Available at: https://www.usda.gov/media/blog/2019/08/15/innovation-and-collaboration-bring-summer-meals-children-rural-texas. Accessed July 5, 2020
20. Meals-to-You. Meals-to-you. 2020. Available at: https://mealstoyou.org. Accessed July 5, 2020
21. Baylor University Media and Public Relations. Baylor University receives $75,000 gift from H-E-B to combat food insecurity during COVID-19 pandemic. 2020. Available at: https://www.baylor.edu/mediacommunications/news.php?action=story&story=219073. Accessed May 22, 2020
22. US Department of Agriculture Food and Nutrition Service. Child nutrition programs: COVID-19 waivers by state. 2020. Available at: https://www.fns.usda.gov/disaster/pandemic/covid-19/cn-waivers-flexibilities. Accessed July 5, 2020
23. Summer EBT for Children. Welcome to summer EBT for children. 2020. Available at: www.sebtc-mi.com. Accessed July 5, 2020
24. The Chickasaw Nation. Summer EBT for children program. 2020. Available at: https://chickasaw.net/summerebt. Accessed July 5, 2020
25. Keith-Jennings B, Llobrera J, Dean S. Links of the Supplemental Nutrition Assistance Program with food insecurity, poverty, and health: evidence and potential. *Am J Public Health*. 2019;109(12):1636–1640

PEDIATRICS PERSPECTIVES

An Equity Lens for Identifying and Addressing Social Needs Within Pediatric Value-Based Care

Alon Peltz, MD, MBA, MHS,[a,b] Stephen Rogers, BS,[c] Arvin Garg, MD, MPH[c]

Socioeconomic disparities in health outcomes have proven to be persistent in the United States. For example, the mortality rate for Black infants is twice as high as it is for white infants, and low-income children are more likely to experience developmental delays as compared with their peers.[1] Emerging data reveal striking racial and socioeconomic inequities in coronavirus disease 2019 outcomes. Healthy People, the national framework for population health, has identified reduction of health disparities and achievement of health equity as crucial goals. However, despite substantial investments, the nation is no closer to achieving these key societal aims, with alarming evidence of widening health disparities in recent years.[2]

Over the past decade, the US health care delivery system has undertaken a large-scale transformation aligned with achieving the triple aim (improving quality, reducing costs, and enhancing experience of care).[3] Pediatricians have made important investments in quality improvement, medical home certification, primary care redesign, and electronic health record adoption to advance these aims. The financing of pediatric care has also evolved with a rapid movement toward value-based care (VBC), whereby pediatricians receive incentives for lowering costs and improving quality. In 2016, approximately half of pediatricians participated in VBC, and that amount has likely increased in recent years.[4] Pediatric VBC programs are often focused on addressing the social determinants of health (SDOHs) that strongly correlate with adverse physical, emotional, and developmental outcomes in children. Examples include incentives for conducting universal SDOH screenings, referrals to community-based organizations, and administration of social supports. VBC aims to enable more proactive care delivery by helping pediatricians make up-front investments in SDOH services and supports, which are sustained with downstream savings from reductions in costs. The intersection of VBC and SDOHs represents an important new paradigm for pediatricians with vast potential for improving health for socioeconomically disadvantaged children. However, if access to these new services is unequal, there becomes an inherent risk of unintentionally exacerbating existing inequities. In this article, we outline core constructs that are essential to identifying and addressing SDOHs in VBC programs, those of surveillance, referral, and supports, and examine how applying an equity lens can help

[a]*Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Harvard University, Boston, Massachusetts;* [b]*Division of General Pediatrics, Boston Children's Hospital, Boston, Massachusetts; and* [c]*School of Medicine, Boston University and Boston Medical Center, Boston, Massachusetts*

Dr Peltz drafted the initial manuscript; Mr Rogers and Dr Garg helped conceptualize the initial manuscript; and all authors reviewed and revised the manuscript, approved the final manuscript as submitted, and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2020-0320

Accepted for publication Jul 7, 2020

Address correspondence to Alon Peltz, MD, MBA, MHS, Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Harvard University, 401 Park Dr, Suite 401 East, Boston, MA 02215. E-mail: alon_peltz@harvardpilgrim.org

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: Dr Peltz discloses consulting services to the Yale New Haven Hospital and the Centers for Medicare and Medicaid Services in development of methods for evaluating disparities in Medicare quality. This work is not related to the article, and these entities were not involved in any aspect of this article; and Mr Rogers and Dr Garg have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

To cite: Peltz A, Rogers S, Garg A. An Equity Lens for Identifying and Addressing Social Needs Within Pediatric Value-Based Care. *Pediatrics.* 2020;146(4):e20200320

advance child health at the population level.

SDOH SURVEILLANCE AND REFERRAL

Pediatricians regularly assess the psychosocial needs of children as part of routine care. Some insurers, as part of VBC, have started to financially incentivize practitioners to conduct universal screening for SDOHs by using structured screening tools. Although well intended and likely to benefit many children, the current approach risks contributing to unequal recognition of basic needs across the population. First, most VBC initiatives are unique to a single insurer, often Medicaid,[5] with little regional collaboration with private insurers. Although publicly insured children often experience higher levels of unmet needs, this approach risks missing many low- and middle-income privately insured families who also experience unmet social needs. This is particularly relevant during the coronavirus disease 2019 pandemic when many working families have experienced economic adversity. Defining screening interventions by insurance status also creates a challenging dilemma for practitioners who are left deciding between incurring the added costs of nonreimbursed population-wide screening, which can be time and resource intensive, or limiting access to screening on the basis of insurance status, neither of which is ideal. Second, not all screening tools used to identify SDOHs are well validated in highly diverse populations.[6] This may contribute to under-recognition of SDOHs in families from cultural groups not included in the initial design and testing of the screening tool. Third, the availability of community-based supports for referrals is often unequal on the basis of geography, transportation, and language, leading to unequal access to services as well as hesitance by some pediatricians to participate in screenings.[7] For example, pediatricians in rural communities, where the availability of community-based supports can be more limited than in metropolitan areas, may find universal screening mandates more challenging to implement ethically. Pediatricians can apply an equity lens by identifying screening instruments that meet the linguistic and cultural needs of their populations, working to build strong and respectful community-based partnerships with organizations serving people of diverse backgrounds, and advocating with local insurers and policy makers about the importance of regional approaches to SDOH screening and referral.

SDOH SUPPORTS

In recent years, pediatric practices, delivery systems, and hospitals participating in VBC have started investing in food, cell phones, transit passes, and even housing assistance to administer to patients. Ensuring equitable allocation of these limited (and expensive) supports is a new frontier for many practitioners. Few evidence-based protocols exist to guide enrollment, dose, and duration for social supports, especially when contrasted with more established medical interventions. For example, in caring for a homeless infant with chronic lung disease, a pediatrician will find more direction for monoclonal antibody treatment as compared to temporary housing assistance, although both are expensive and impactful therapies for preventing bronchiolitis. Absent evidence-based protocols for SDOH services, clinicians may make these decisions on the basis of best clinical judgement or employ decision-making heuristics that can be susceptible to unconscious implicit bias, inadvertently contributing to inequitable distribution of services. Some VBC programs use data algorithms to identify children with high costs and preferentially administer SDOH supports to them in an effort to reduce health costs. However, this highly efficient approach risks misclassifying children whose unmet basic needs do not immediately manifest in high health costs. In addition, adult studies reveal that racial bias exists in some data algorithms used to identify high-cost patients, although it is unclear if this also occurs in children.[8] Moving beyond high cost as a means for identifying service recipients and instead focusing on shared polysocial risk scores may support more equitable access.[9] Pediatricians can also apply an equity lens by closely tracking which patients receive supports and proactively identifying inequities in allocation of investments.

FUTURE DIRECTIONS

The model of VBC provides opportunities for more coordinated activity among pediatricians, insurers, and policy makers to better identify and address SDOHs. Pediatricians are encouraged to monitor their own performance in an attempt to ensure that all children can equally access and benefit from new SDOH services. Policy makers are encouraged to allocate funding to support pediatricians in collecting more accurate and wider-ranging SDOH data, similar to programs that have been historically successfully in increasing electronic health record and medical home rates. Insurers are encouraged to regionally collaborate on VBC and SDOH screening initiatives, such as those occurring in some areas of the country as part of the Medicare Comprehensive Primary Care Initiative.[10] Regional partnerships should set the reduction of health disparities as an explicit goal, with financial incentives given to pediatricians who both improve quality overall and reduce disparities. Ultimately, employers and governments will bear the initial costs of these up-front investments. However, reducing disparities in

chronic illness incidence and severity has the potential to lower health expenditures over the long run while providing a positive societal return on investment through improved social equity at the population level.[11]

CONCLUSIONS

VBC is at the forefront of pediatric health care delivery with vast potential for improving health outcomes for socioeconomically disadvantaged children. However, if disparities exist in access to SDOH screening, referral, and supports, there is a risk of widening certain health inequities. Placing a health equity lens on the design and implementation of VBC initiatives aimed at ameliorating unmet basic needs will help ensure that all children can benefit equally.

ABBREVIATIONS

SDOH: social determinant of health
VBC: value-based care

REFERENCES

1. Ely DM, Driscoll AK. Infant mortality in the United States, 2017: data from the period linked birth/infant death file. *Natl Vital Stat Rep*. 2019;68(10):1–20
2. Bor J, Cohen GH, Galea S. Population health in an era of rising income inequality: USA, 1980-2015. *Lancet*. 2017; 389(10077):1475–1490
3. Berwick DM, Nolan TW, Whittington J. The triple aim: care, health, and cost. *Health Aff (Millwood)*. 2008;27(3):759–769
4. Tieder JS, Sisk B, Hudak M, Richerson JE, Perrin JM. General pediatricians and value-based payments. *Pediatrics*. 2018;142(4):e20180502
5. Crumley D, Lloyd J, Pucciarello M, Stapelfeld S; Center for Health Care Strategies. Addressing social determinants of health via Medicaid managed care contracts and Section 1115 demonstrations. Available at: https://www.chcs.org/media/Addressing-SDOH-Medicaid-Contracts-1115-Demonstrations-121118.pdf. Accessed April 14, 2020
6. Sokol R, Austin A, Chandler C, et al. Screening children for social determinants of health: a systematic review. *Pediatrics*. 2019;144(4): e20191622
7. Garg A, Cull W, Olson L, et al. Screening and referral for low-income families' social determinants of health by US pediatricians. *Acad Pediatr*. 2019;19(8): 875–883
8. Obermeyer Z, Powers B, Vogeli C, Mullainathan S. Dissecting racial bias in an algorithm used to manage the health of populations. *Science*. 2019;366(6464): 447–453
9. Figueroa JF, Frakt AB, Jha AK. Addressing social determinants of health: time for a polysocial risk score. *JAMA*. 2020;323(16): 1553–1554
10. Centers for Medicare and Medicaid Services. Comprehensive Primary Care Plus. Available at: https://innovation.cms.gov/innovation-models/comprehensive-primary-care-plus. Accessed June 9, 2020
11. LaVeist TA, Gaskin D, Richard P. Estimating the economic burden of racial health inequalities in the United States. *Int J Health Serv*. 2011;41(2): 231–238

PEDIATRICS® PERSPECTIVES

Magical Thinking: How Learning to Act Like a Magician Can Make You a Better Physician

Michael B. Pitt, MD

Department of Pediatrics, M Health Fairview University of Minnesota Masonic Children's Hospital, Minneapolis, Minnesota

DOI: https://doi.org/10.1542/peds.2020-0420

Accepted for publication Mar 9, 2020

Address correspondence to Michael B. Pitt, MD, 2450 Riverside Ave, M653, Minneapolis, MN 55454. E-mail: mbpitt@umn.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

To cite: Pitt MB. Magical Thinking: How Learning to Act Like a Magician Can Make You a Better Physician. *Pediatrics*. 2020;146(4):e20200420

For most of history, the line between magic and medicine was blurred. Before there was a pathophysiologic understanding of disease, there was little distinction between a magician and a physician. Both may wave their hands, utter some Latin-sounding words, produce a potion, and promise to make something (a coin or an ailment) disappear. Still today, providers who have successfully reduced a nursemaid's elbow or who have made vertigo vanish with a canalith repositioning maneuver have borne witness to the healing power of medical sleight of hand.

Recently, the use of magic at the bedside has seen a renaissance of sorts. In a 2017 review, Lam et al[1] described many ways providers are incorporating magic in medicine, ranging from teaching patients magic tricks for physical therapy[2] to its use as humor therapy as a prophylactic anxiolytic for patients.[3,4] As a professional magician and a pediatrician, I have seen how magic and medicine intersect. Whereas I occasionally use a trick to calm an anxious child before an examination, I use the skills of how a magician approaches an audience in every patient encounter. Over the last decade, I have taught over 3000 providers how learning to think and act like a magician, even without doing a magic trick, can improve their ability to connect with patients. In this perspectives article, I will summarize how health care providers can implement 3 skills long used by magicians, those of misdirection, patter, and force, to build rapport and ultimately increase their ability to perform an examination.

HAVE MISDIRECTION UP YOUR SLEEVE

Nearly the whole art of sleight of hand depends on the art of misdirection.

Harlan Tarbell[5]

Chabris and Simmons[6] demonstrated in their landmark invisible gorilla studies that when participants were asked to complete a task (counting how many times basketballs were passed between 6 people in a circle in a video), half failed to notice that someone in a gorilla suit walked into the circle and beat their chest while basketballs whizzed past. Participants were so focused on the task that they missed the literal gorilla in the room. The authors called this failure to notice an unexpected stimulus in one's

field of view when focused on a task "inattentional blindness." Magicians call it misdirection.

Magicians rely on misdirection or the intentional focusing of an audience's attention on one thing to distract its attention from another. Whether using a wave of a wand or a well-timed word, magicians are masters at redirecting eyes to what they want them to look at so they can get away with something they do not want them to see (ie, a secret sleight). Health care providers leverage misdirection as well. The Jendrassik maneuver, or having a patient pull on their interlocked fingers while attempting to elicit reflexes, is misdirection at its core. Pediatricians are taught to use the stethoscope to apply pressure to the right lower quadrant under the guise of listening to differentiate acute appendicitis from other less ominous causes of abdominal pain where a patient might still wince throughout the hand palpation but will not during auscultation. We also often use sounds and imaginative play to allow us to gain access to an ear for an examination ("Is there a birdie in there?"). Touch, sound, movement, eye contact, and distraction with objects (eg, stethoscopes, tongue depressors) by handing them to patients are all misdirection strategies commonly used by magicians and physicians alike.

PATTER MATTERS

Like magic, medicine is a performance art. Daniel Sokol[7] makes the comparison that magicians and physicians both aim to use clear communication that is memorable for their audience while balancing the projection of competence (authority) with the relatability of partnering with the audience (likeability). One of the ways magicians do this is through the use of patter, the story that accompanies a magic trick to elevate it from a mere puzzle to a performance. They are masters at using language (verbal and nonverbal) to guide an audience's attention toward a desired area of focus (ie, misdirection). Additionally, magicians are among the first empathy experts, relying on interpreting reactions from their audience in real-time to alter their approach. Magicians meticulously practice not only their sleight of hand but also spend hours honing the clarity and rhythm of their phrasing that goes with each trick, including when to pause and how to adjust on the basis of reading the tension of their audience.

Like actors and magicians, whether we realize it or not, we too are playing a role for our patients. Before we even set foot on the stage at the examination table, we enter with our patients already having a set of expectations for our performance. We have lines our "audience" is expecting to hear, and failing to respond to the appropriate cue can leave our patients at best dissatisfied and at worse less healthy. Research has revealed that outcomes are better for patients whose providers simply use (even canned) empathic statements in response to common cues during the encounter.[8–10] This can be helpful for those of us who do not consider ourselves to be naturally empathic because we can learn to recognize cues and have responses ready much like magicians who prepare for apparent spontaneity by having patter prepared for common audience

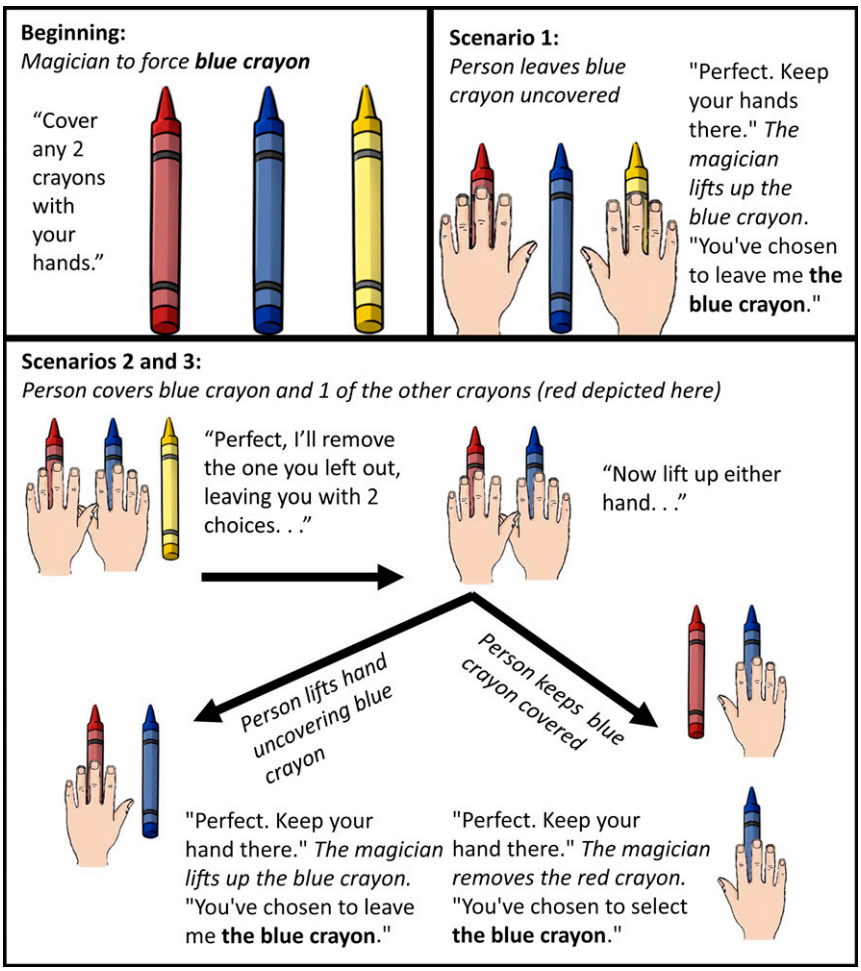


FIGURE 1
Example of magician's choice force.

reactions. For example, when an audience member asks the magician "How'd you do that?" a prepared magician often responds, "Very well."

USE THE FORCE

Many magic tricks hinge on the magician's ability to convince an audience member that they had a free choice (of a playing card for instance) when they actually did not. Magicians call this false freedom, a "force." A specific type of force, known as the "magician's choice" or equivocation, uses a verbal technique in which the magician guides the audience member through a series of choices to the predetermined desired outcome. For example, Fig 1 illustrates how, by a series of questions and seemingly free choices, a magician can force a particular choice of a crayon.

Providers can use the magician's choice force effectively when they need to give the perception of choice toward a relatively fixed outcome. Instead of simply asking a child "Can I look in your ears now?" reframing this question to "Which ear should I look in first?" allows for choice to guide what could be a difficult examination. When an anxious child is hesitant to let you listen to their heart, starting by placing the stethoscope on the toe to listen, then the knee, on so on, making a confused face as you don't hear heart sounds often leads to the patient pointing to their heart or even grabbing the stethoscope to move it there. The same child who, moments before, was hesitant now invites the examination under the guise of choosing to help. I have also had success with a seemingly more extreme use of magician's choice. Whenever a patient asks me if they need a shot, I respond clearly, "Yes, but you have a choice of having it in your arm or your eyeball." Without fail, the child looks to their parent and then back to me and says something like, "My arm please! Phew, that could have been worse!"

It is important to note the distinction between using these magical techniques as strategies to improve communication and put patients at ease during an examination as opposed to leveraging frank deception. Shared decision-making, informed consent, and clear communication remain at the forefront of effective patient-provider relationships. Misdirection in medicine is not about manipulation but rather intentional redirection to maintain a patient's comfort. These are methods skilled pediatricians already employ regularly when we maintain eye contact and keep conversation going about interests while performing an abdominal examination (misdirection and patter) or ask patients which ear they would prefer we look in first (magician's choice). Being aware of the framework underlying these approaches, however, allows us to embrace that the art of medicine is in fact a performance art similar to the art of magic. Recognizing the overlap of these skills with those used by magicians for centuries provides a framework that can help us intentionally hone and practice this art. Moreover, although the era when magicians and medical providers were one and the same has passed, our pediatric patients still often see us through this lens as they put hope in us to make their symptoms disappear.

REFERENCES

1. Lam MT, Lam HR, Chawla L. Application of magic in healthcare: a scoping review. *Complement Ther Clin Pract*. 2017;26:5–11
2. Hines A, Bundy AC, Haertsch M, Wallen M. A magic-themed upper limb intervention for children with unilateral cerebral palsy: the perspectives of parents. *Dev Neurorehabil*. 2019;22(2): 104–110
3. Elkin DJ, Pravder HD. Bridging magic and medicine. *Lancet*. 2018;391(10127): 1254–1255
4. Hart R, Walton M. Magic as a therapeutic intervention to promote coping in hospitalized pediatric patients. *Pediatr Nurs*. 2010;36(1): 11–16; quiz 17
5. Tarbell H. *Tarbell Course in Magic*, vol. 1. New York: Louis Tannen; 1953:59
6. Chabris C, Simons D. *The Invisible Gorilla: How Our Intuitions Deceive Us*. New York, NY: Crown Publishing Group; 2009
7. Sokol DK. Medicine as performance: what can magicians teach doctors? *J R Soc Med*. 2008;101(9):443–446
8. Rakel DP, Hoeft TJ, Barrett BP, Chewning BA, Craig BM, Niu M. Practitioner empathy and the duration of the common cold. *Fam Med*. 2009;41(7): 494–501
9. Dambha-Miller H, Feldman AL, Kinmonth AL, Griffin SJ. Association between primary care practitioner empathy and risk of cardiovascular events and all-cause mortality among patients with type 2 diabetes: a population-based prospective cohort study. *Ann Fam Med*. 2019; 17(4):311–318
10. Derksen F, Bensing J, Lagro-Janssen A. Effectiveness of empathy in general practice: a systematic review. *Br J Gen Pract*. 2013;63(606):e76–e84

Community-Informed Peer Support for Parents of Gender-Diverse Youth

Caitlin Thornburgh, MSW, LSW,[a] Kacie M. Kidd, MD,[a,b] Johanna D. Burnett, PhD,[c] Gina M. Sequeira, MD, MS[a,b]

Gender identity refers to an individual's innate sense of self in the context of gender and may not correspond with their sex assigned at birth. Gender-diverse or transgender individuals are those who experience any discordance between their gender identity and sex assigned at birth. According to the 2017 Youth Risk Behavior Survey, gender-diverse identities are more prevalent than previously recognized, with 1.8% of high school–aged students identifying as transgender.[1] Gender-diverse youth (GDY) experience high rates of discrimination and victimization as well as mental health disparities including increased depression, anxiety, and suicidality.[1,2] Previous studies suggest that family support and acceptance have the potential to mitigate existing health disparities.[2,3] Some parents experience anxiety or fear in response to learning their child's gender identity.[4] They may lack understanding of gender-diverse experiences and knowledge of resources available, which can make it difficult for parents to affirm their child's identity.[3] Parental support is beneficial for all young people and, given the health disparities that GDY experience, strategies to empower parents to better support their gender-diverse children should be explored.[4,5]

Peer support programs have been implemented to help parents of other pediatric patient populations increase their ability to navigate challenges when caring for their children,[6,7] but this has not been well documented in parents of GDY. After reviewing peer support literature and consulting with parents of GDY, we conceptualized a theoretical framework (Fig 1) that identifies factors promoting parent support surrounding a list of strategies employed to facilitate this for families in our clinic.

In this article, we describe our experiences partnering with local parents of GDY to better support our patients and families. Our authorship team includes a social worker (C.T.) and 2 physicians (K.M.K. and G.M.S.) as well as the mother of a gender-diverse child (J.D.B.). Two authors (C.T. and G.M.S.) identify as members of the lesbian, gay, bisexual, transgender, queer or questioning (LGBTQ) community.

When my son first came out as transgender, I did not know how to best take care of him because I did not understand what being transgender meant. My husband and I felt alone and isolated from friends, family, and the community we once knew. My family and I first experienced a sense of comfort, acceptance, and community at a parent-run potluck dinner. This potluck has now become a regular event hosted by the Pittsburgh Chapter of PFLAG (Parents, Families, and Friends of Lesbians and Gays), an organization that has played an important role in the development of our parent support programs. This partnership began in April of 2018 when a provider from the gender clinic was invited to attend the potluck. She intended to discuss the details of the clinic but was willing to listen to our perspectives instead. We needed space to talk about our experiences parenting gender-diverse children and how we could better support families in the future.

J.D.B.

[a]*University of Pittsburgh Medical Center Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania;* [b]*Department of Pediatrics, University of Pittsburgh, Pittsburgh, Pennsylvania; and* [c]*Department of Chemistry and Biochemistry, Duquesne University, Pittsburgh, Pennsylvania*

Ms Thornburgh and Drs Kidd and Sequeira conceptualized, designed, and drafted the manuscript; Dr Burnett (parent author) conceptualized, designed, and drafted the manuscript and provided numerous quotes for incorporation into the final manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2020-0571

Accepted for publication Jul 1, 2020

Address correspondence to Kacie M. Kidd, MD, Center for Adolescent and Young Adult Health, University of Pittsburgh Medical Center Children's Hospital of Pittsburgh, 120 Lytton Ave, Mezzanine Floor, Suite M060, Pittsburgh, PA 15213. E-mail: kacie.kidd2@chp.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Funded by the following grants: T32 HD71834-5 (PI: Terence Dermody, MD) T32 HD087162 (PI: Elizabeth Miller, MD, PhD), TL1TR001858 (PI: Wishwa N. Kapoor, MD, MPH) from the National Institutes of Health. Funded by the National Institutes of Health (NIH).

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

To cite: Thornburgh C, Kidd KM, Burnett JD, et al. Community-Informed Peer Support for Parents of Gender-Diverse Youth. *Pediatrics.* 2020;146(4): e20200571

COMMUNITY ADVISORY BOARD

Through this meeting, we learned that we needed to find a way to embed parents into the infrastructure of our rapidly expanding gender program. A smaller group of dedicated parents stayed late, exchanged contact information, and scheduled an additional time to meet. This group of parents, along with GDY and gender-diverse adults, formed a community advisory board (CAB) and began meeting with providers from our gender clinic monthly at a local coffee shop. This partnership has profoundly changed the way we provide care to youth in our gender clinic.

CARE DELIVERY MODEL

The CAB expressed the importance of providing parents with the opportunity to speak openly about their concerns during the first visit to our gender clinic. In response, we now begin and end visits collaboratively, and a behavioral health provider meets with parents while the medical provider speaks to the patient alone. During this time, parents often verbalize fears and share questions they hesitate to ask in front of their child. This also allows our team to validate parental concerns, engage in problem-solving, and offer education, resources, and support.

THE PARENT OUTREACH PROGRAM

We learned that one of the most critical pieces in parenting a gender-diverse child is connecting with other parents of GDY. Our partnership with parents of GDY in the CAB allowed us to facilitate these connections by creating the Parent Outreach Program (POP). The POP matches interested parents of gender-diverse children with a CAB parent for individualized peer support. Parents of new patients are given the option to connect via phone, e-mail, or in person and can do so as little or as much as they want.

Within the first few months of implementing the POP, we heard

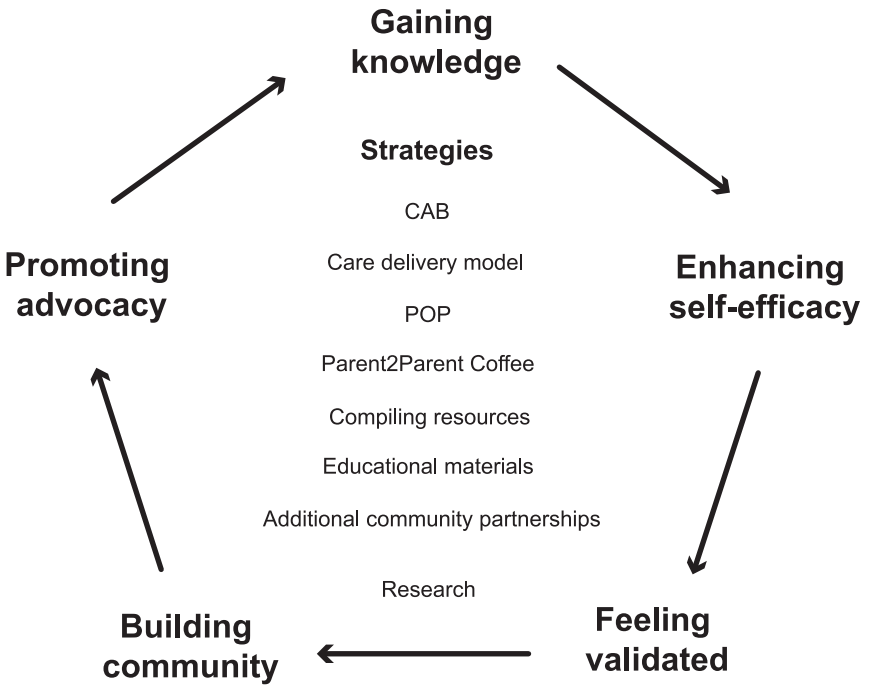


FIGURE 1
Community-informed parent support framework.

from patients, parents, and the CAB that this program was extremely beneficial. CAB parents described witnessing parents learn and grow by changing the words they used with their child and the thoughts and feelings they had about medical interventions. Gender-diverse patients described seeing an increase in their parents' comfort talking about their identity and experiences. Parents returned to our clinic more apt to advocate for their child's needs. One parent expressed that this connection "was the pivotal point in our son's health and it was through our friendship that we were able to walk this journey with him."

"B" is a patient we met during his first visit to our gender clinic, and it was clear that he was nervous. He explained that his parents were struggling with his gender identity and he doubted they would ever see him for who he truly was. B's parents were connected with J.D.B through the POP that day.

I met B's mom through the POP. During our first conversation, she shared that she was angry, frustrated, sad, and frightened after their initial visit to the gender clinic. She was so afraid of making the wrong decisions and did not want to rush into a treatment plan. Her child was suicidal and she was terrified. Her child's sibling was using affirming pronouns, and it upset her, because she was not ready to do that. I shared my journey with my own transgender son. I told her about the challenges I faced with my faith, as this was something we shared. Our families met, and her husband told mine that he was so grateful that he no longer felt alone in this journey.

J.D.B.

When B and his family returned to clinic a few months later, he was a different person, and so were his parents. They came into the visit using B's affirmed name and pronouns and asking questions about medical options and how they could better support their son. While speaking with him alone, we asked him what changed. He said that his mom met another mom and "it changed everything." A year later, B is no longer suicidal, and his

parents describe feeling like they got their child back and are so proud of the young man he is becoming. Additionally, his mother is now a valued member of our CAB and has begun to support other parents in our community.

OUR PROCESS

New parents frequently ask the same questions. "Am I doing the right thing? " "How will society, family, friends, faith-based groups, and educational institutions treat my child when they transition?" "Can my child survive this?" Early on, CAB parents expressed the importance of having space to gain self-efficacy in affirming their children rather than being explicitly told how to do so. Therefore, they both advocate for GDY and provide validation to parents who are struggling to accept their child's identity. To facilitate this process, CAB parents often share their own story and answer questions when providing peer support. This approach can be emotionally taxing and is not something all parents can do. We consider new parents for the CAB after they have demonstrated this ability during monthly PFLAG meetings. We have also developed opportunities for parent volunteers to receive their own support from medical and mental health providers within the CAB and prioritize time during our monthly meetings to process challenging interactions. The CAB parents also lean on one another after difficult conversations and are encouraged to contact on-call providers for guidance.

CHALLENGES AND LIMITATIONS

Despite its success, we faced some logistic challenges regarding matching parents during clinical encounters and trying to expand the POP to other local clinics supporting GDY. We shifted the POP from being a clinic-based program to one that was community based and housed within PFLAG. The CAB parents' connection to our local PFLAG chapter enabled us to create a parent support phone number and e-mail address that are easily disseminated throughout our community. We also realized that talking with another parent through the POP may be intimidating for some parents, and large PFLAG meetings may be overwhelming as well. In response, a CAB parent (J.D.B.) volunteered her personal time to create and host "Parent2Parent Coffee." These are monthly meetings at a local coffee shop or library where a small group of parents of gender-diverse children could connect with CAB members to ask questions, cry, laugh, or just listen.

A limitation of our group is a lack of diversity. The CAB is predominantly white identifying with a limited number of religious affiliations and socioeconomic backgrounds. This is likely associated with a lack of racial diversity among patients receiving care in our clinic,[8] which has also been noted in other gender clinics across the United States.[9,10] We hope to include more people of color as well as different faith practices and diverse experiences in the future to improve the care we provide and better understand how intersecting identities impact the barriers families may face. The CAB is actively seeking opportunities to connect with community-based organizations that primarily serve people of color and with leaders of various religious communities to fill this gap.

FUTURE DIRECTIONS

The CAB has sought additional opportunities to support local gender-diverse young people and their families. We created educational brochures about gender-diverse identities that include testimonials from parents of GDY. CAB parents also suggested that families initiating care could benefit from speaking with a parent of a gender-diverse young person after their visit and have begun working with a community-led initiative partnering trained volunteers with patients to help them navigate the medical system. This partnership has allowed CAB members to meet with parents in the clinic and connect them to resources and community support immediately. Because of the coronavirus disease 2019 pandemic, our meetings have temporarily moved online, which has allowed us to reach parents who experience transportation barriers. We plan to continue both online and in-person meetings moving forward and have encouraged parents without Internet access to connect with their POP match via phone.

The CAB has aided in conceptualization and conduct of research to better understand the parent and family experience of supporting gender-diverse young people. The CAB has helped to create and test a scale measuring empowerment among caregivers of GDY, and members are currently sharing their stories as a part of a qualitative research study. CAB members are also working on helping us share research findings through online groups and local and national speaking engagements. Given the dearth of research that is focused on the experiences of this population, partnerships like this have the potential to impact GDY, their families, and the providers who care for them. Ultimately, the CAB plans to continue to support parents of GDY through this work and has begun to expand from our local community to neighboring states and across the country.

GDY are healthier when they are supported by their family.[2,5] Our work suggests families are best able to affirm the young people in their lives when they are supported by their community and able to engage with parents who have shared experiences. Parent-led peer support programming and advising is

a promising component of pediatric gender care. We hope that by sharing the programming our clinic developed in partnership with a dedicated group of parents, other clinics may consider similar interventions and further study the impact of this work.

ACKNOWLEDGMENTS

We thank the amazing group of parents and community members who have been integral to this program. We specifically thank Rosie Benford, Joel Burnett, Oliver Burnett, Kelly Dembiczak, Kyle Dembiczak, Jamie Mullin, January Furer, Alexandra Lynn, Katia Nascimento, Alicyn Simpson, Dave West, and Michele West.

ABBREVIATIONS

CAB: community advisory board
GDY: gender-diverse youth
PFLAG: Parents, Families, and Friends of Lesbians and Gays
POP: Parent Outreach Program

REFERENCES

1. Johns MM, Lowry R, Andrzejewski J, et al. Transgender identity and experiences of violence victimization, substance use, suicide risk, and sexual risk behaviors among high school students - 19 states and large urban school districts, 2017. *MMWR Morb Mortal Wkly Rep.* 2019;68(3):67–71
2. Olson KR, Durwood L, DeMeules M, McLaughlin KA. Mental health of transgender children who are supported in their identities. *Pediatrics.* 2016;137(3):e20153223
3. Katz-Wise SL, Budge SL, Orovecz JJ, Nguyen B, Nava-Coulter B, Thomson K. Imagining the future: perspectives among youth and caregivers in the trans youth family study. *J Couns Psychol.* 2017;64(1):26–40
4. Hillier A, Torg E. Parent participation in a support group for families with transgender and gender-nonconforming children: "Being in the company of others who do not question the reality of our experience". *Transgend Health.* 2019;4(1):168–175
5. Simons L, Schrager SM, Clark LF, Belzer M, Olson J. Parental support and mental health among transgender adolescents. *J Adolesc Health.* 2013; 53(6):791–793
6. Chernoff RG, Ireys HT, DeVet KA, Kim YJ. A randomized, controlled trial of a community-based support program for families of children with chronic illness: pediatric outcomes. *Arch Pediatr Adolesc Med.* 2002;156(6): 533–539
7. Shor R, Birnbaum M. Meeting unmet needs of families of persons with mental illness: evaluation of a family peer support helpline. *Community Ment Health J.* 2012;48(4):482–488
8. Sequeira GM, Ray KN, Miller E, Coulter RWS. Transgender youth's disclosure of gender identity to providers outside of specialized gender centers. *J Adolesc Health.* 2020;66(6):691–698
9. Olson J, Schrager SM, Belzer M, Simons LK, Clark LF. Baseline physiologic and psychosocial characteristics of transgender youth seeking care for gender dysphoria. *J Adolesc Health.* 2015;57(4):374–380
10. Chen M, Fuqua J, Eugster EA. Characteristics of referrals for gender dysphoria over a 13-year period. *J Adolesc Health.* 2016;58(3): 369–371

Protecting Youth From Tobacco Around the Globe: Evidence to Practice

Indu B. Ahluwalia, PhD, MPH,[a] Karen Wilson, MD, MPH, FAAP,[b] Julie Gorzkowski, MSW[c]

Tobacco use and secondhand smoke (SHS) exposure are harmful to development and have significant health risks across the life span, including asthma, respiratory infections, cardiovascular disease, and cancer.[1] Most adults begin smoking during adolescence, highlighting the importance of clinical and public health interventions to prevent tobacco use and encourage youth cessation. Data from the US Centers for Disease Control and Prevention (CDC) Global Youth Tobacco Surveys (GYTS) from 61 countries reveal that a substantial number of youth report current cigarette smoking (mean prevalence: 10.7%, range: 1.7%–35%), and >50% of young smokers wish to quit.[2] Globally, GYTS data indicate that youth who have never used tobacco products are susceptible to begin using them (Fig 1). In the United States, 5.8% of high schoolers currently smoke cigarettes, 58% of young smokers want to quit, and nearly half are susceptible to using cigarettes or electronic cigarettes (e-cigarettes).[3] Thus, global efforts to protect youth against such vulnerabilities are critical to ensure future tobacco-free generations. In this report, we describe a partnership between CDC and the American Academy of Pediatrics (AAP) that highlights how strategic relationships can foster change.

Interventions are also important to protect youth from SHS. Researchers from 21 countries indicate that half a billion youth are exposed to SHS at home.[4] Youth are also exposed to thirdhand smoke (THS), which is defined as residue from smoke that accumulates on surfaces and is re-emitted into the air. Youth can be exposed to THS through inhalation, touching, or ingestion, putting them at risk for negative health effects.[5] SHS and THS expose youth to nicotine and toxic pollutants, which directly impact health. Pediatric tobacco exposures are associated with asthma, bronchiolitis, respiratory infections, and increased risk of sudden unexplained infant death.[1] In addition, youth exposed to SHS have lower scores on cognitive tests and experience behavioral and development issues.[1] Youth with preexisting conditions or comorbidities are at higher risk for increased morbidity and mortality from tobacco.[1,4,6]

In addition to preventing use of smoked tobacco products, it is critical to prevent youth use of emerging tobacco products, such as e-cigarettes and heated tobacco products. These products are changing the global landscape of youth tobacco use. Emerging products are designed to appeal to youth, with sleek designs, youth-friendly flavors, and targeted marketing strategies designed to reach young users. Youth e-cigarette use has become an epidemic in the United States, with 27.5% of high schoolers reporting current use.[7] Emerging tobacco products are renormalizing tobacco

[a]*Office on Smoking and Health, Centers for Disease Control and Prevention, Atlanta, Georgia;* [b]*Jack and Lucy Clark Department of Pediatrics, Icahn School of Medicine at Mount Sinai, New York, New York; and* [c]*American Academy of Pediatrics, Itasca, Illinois*

The opinions expressed by authors contributing to this report do not necessarily reflect the opinions of the US Department of Health and Human Services, the Centers for Disease Control and Prevention, or the authors' affiliated institutions.

Dr Ahluwalia participated in the described global tobacco program, conceptualized the article, and drafted the initial manuscript; Dr Wilson participated in the described global tobacco program and conceptualized the article; Ms Gorzkowski participated in the described global tobacco program; and all authors reviewed and revised the manuscript and approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2020-1585

Accepted for publication Jul 7, 2020

Address correspondence to Julie Gorzkowski, MSW, Director, Adolescent Health Promotion, American Academy of Pediatrics, 345 Park Blvd, Itasca, IL 60143. E-mail: jgorzkowski@aap.org

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: The global tobacco collaboration described in the final paragraph of this article is funded by a Cooperative Agreement from the US Centers for Disease Control and Prevention to the American Academy of Pediatrics (AAP); grant 5 NU38Ot000282-02-00. In addition, AAP receives funding from the Flight Attendant Medical Research Institute to support the tobacco control activities of the AAP Julius B. Richmond Center of Excellence (grant 052302_CoE).

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

To cite: Ahluwalia IB, Wilson K, Gorzkowski J. Protecting Youth From Tobacco Around the Globe: Evidence to Practice. *Pediatrics.* 2020;146(4):e20201585

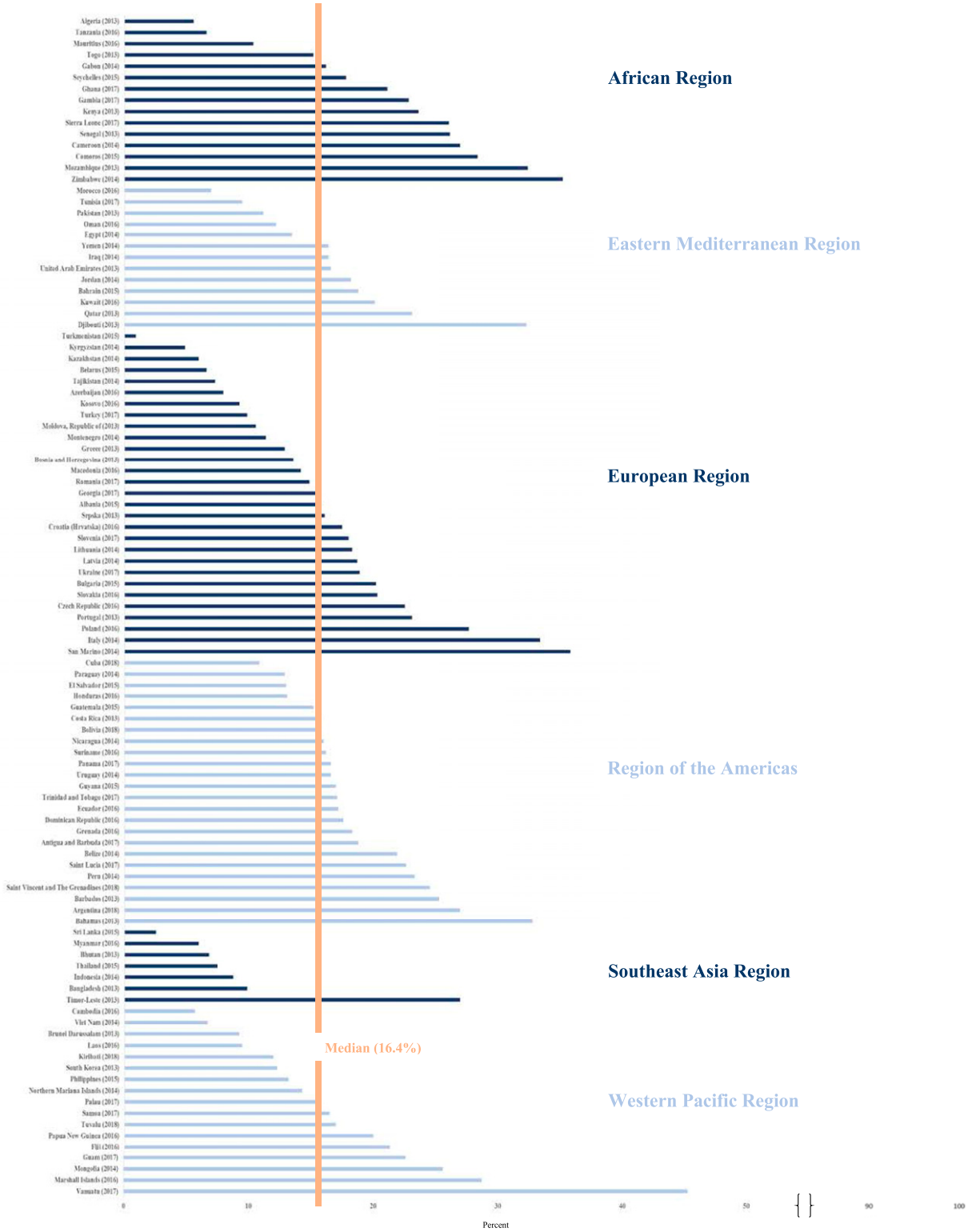


FIGURE 1
Prevalence of susceptibility to tobacco use among never tobacco users aged 13–15 years, GYTS, 2012–2018. Percentage of never tobacco users who are susceptible to using tobacco in the future by answering (1) "definitely yes," "probably yes," or "probably not" to using tobacco if one of their best friends offered it to them or (2) "definitely yes," "probably yes," or "probably not" to using tobacco during the next 12 months.

TABLE 1 Overview of Tobacco Control Work Performed by National Pediatric Societies in 13 Countries, 2016–2019

Country	Description of the Activities Undertaken by the Pediatric Society
Bangladesh	Created a subcommittee to address tobacco use and vaping and promoting awareness among youth.
	Created a partnership with the Bangladesh Heart Foundation and Tobacco-Free Kids to address youth tobacco use and secondhand tobacco exposure as part of building a coalition with stakeholders.
Ethiopia	Hosted a train the trainer workshop for 20 high school students to serve as peer advisors and develop a school-based tobacco awareness campaign.
	Held a stakeholder meeting with representatives from the Education Bureau, Drug and Medicine Authority, and tobacco control nongovernment organizations.
India	The Public Health Foundation of India conducted a seminar on tobacco cessation with leadership from the Indian Academy of Pediatrics.
	A white paper to guide future tobacco cessation strategies in partnership with the government is in development.
Indonesia	Hosted a media conference for 2018 WNTD and held a successful infographic and meme competition promoting tobacco control and reduction of SHS exposure.
	Translated the CDC *Treatment and Beyond* module into Indonesian and identified an expert group of pediatricians to develop guidelines and tools promoting tobacco control and reduction of SHS exposure for Pediatric Society members.
Kenya	Facilitated a continuing medical education session for 75 pediatric health providers on the topic of youth tobacco control and prevention and reduction of SHS exposure.
	Completed a workshop on tobacco control advocacy for 50 pediatric and mental health providers, Hosted a tobacco exposure in children webinar reaching 500+ learners.
	The association also held a tobacco control workshop at the 2019 the Kenya International Scientific Lung Conference.
Mexico	Developed 3 educational videos on the dangers of tobacco use and exposure for 3 audiences: children and youth, physicians, and parents. During the society's annual conference, the campaign materials and videos were launched.
Nigeria	Recognized WNTD 2019 with a press conference and public lecture to introduce the society's new tobacco-free school initiative, which works to prevent tobacco use and exposure of students.
	The society held a 2-day advocacy and capacity development workshop for key stakeholders in the Nigerian school system and the Pediatric Society leadership to promote the tobacco-free school initiative.
Pakistan	Pediatric Pulmonary Group of the Pakistan Pediatric Association conducted a tobacco control advocacy workshop for 25 senior pediatricians and consultants focused on tobacco-free hospitals.
	A press conference was held to raise public awareness of dangers of tobacco use and exposure to SHS in children.
	A seminar on tobacco-free hospitals and schools with 85 participants.
Philippines	The Philippines Pediatric Society (PPS) hosted a tobacco control advocacy workshop for 50 pediatricians from across the country, which addressed strategies for preventing youth tobacco use and decreasing secondhand and thirdhand tobacco exposure of children.
	Convened a stakeholders meeting with representatives from the pediatric society, departments of health and education, World Health Organization Country Office, and multiple specialty societies.
	Developed a PPS-led *Pinoy Kids for Smoke-Free Philippines* campaign, targeting select private and public schools. This campaign reached almost 6300 students and 100 schools with educational information about preventing youth tobacco use and reducing secondhand tobacco exposure.
Romania	Hosted an interactive workshop on tobacco use and exposure in children during the Society's Summer Schools educational events for 70 pediatrician participants.
	Hosted a second workshop with 60 attendees, which focused on targeted counseling of children and families who use tobacco, to promote cessation and reduce SHS exposure.
Sri Lanka	Conducted an advocacy workshop on tobacco control and prevention, including SHS prevention, for 30 pediatricians representing 9 provinces and facilitated 4 regional scientific conferences on tobacco use and exposure, reaching 500 physicians.

use while addicting a new generation of youth to nicotine.[7] Marketing of these products globally remains a cause for concern, and it is important for existing global tobacco control strategies and policies to be mobilized and enforced to ensure that the marketing, distribution, and use of e-cigarettes and other novel tobacco products are monitored closely and adequate protections are in place for preventing and reducing youth use.

Efforts are warranted to protect youth from tobacco use and exposure, as well as from tobacco advertising and marketing. The 1989 United Nations Convention on the Rights of the Child (CRC) and the World Health Organization Framework Convention on Tobacco Control provide strong blueprints for action on behalf of children. The CRC, which is a legally binding treaty with 196 country signatories, notes that children have a basic human right to breathe clean air.[8] The CRC treaty contains several articles relevant to a child's right to be protected from tobacco use and exposure, including Article 3, "*in all actions concerning children… the best interests of the child shall be a primary consideration*"; Article 19, "*Parties shall take all appropriate legislative, administrative, social and educational measures to protect the child from all forms of physical or mental violence, injury or abuse, neglect or negligent treatment, maltreatment or exploitation*"; and Article 24, "*Parties recognize the right of the child to the enjoyment of the highest attainable standard of health*."[8] To protect people, including youth, from tobacco, the World Health Organization Framework Convention on Tobacco Control has outlined key measures called the "MPOWER" demand reduction strategies: monitor tobacco use and prevention policies; protect people from tobacco smoke; offer help to quit tobacco use; warn about the dangers of tobacco; enforce bans on tobacco advertising, promotion,

TABLE 1 Continued

Country	Description of the Activities Undertaken by the Pediatric Society
Tanzania	Conducted a training of trainers for pediatricians and pediatric health care providers on tobacco control and effects of exposure to SHS. These participants then led a workshop on tobacco control and exposure to SHS for providers. Conducted a workshop for media focused on the long-term effects of exposure to SHS.
Uganda	The Uganda Pediatric Association facilitated a sensitization meeting for pediatricians across multiple regions followed by a 1-day stakeholders meeting to engage all local stakeholders on the current status and implementation of a national tobacco control act.

and sponsorship; and raise taxes on tobacco (For more information: https://www.who.int/fctc/en/). These strategies serve as guidelines for communities and nations working to protect youth from tobacco use and exposure, and to promote optimal health for all youth. The rights of youth to be free from tobacco could be fully realized with effective implementation and enforcement of the MPOWER evidence-based strategies.

CRITICAL PARTNERSHIPS WITH PEDIATRICIANS CAN PROTECT YOUTH

To augment children's voices and ensure that effective partnerships are in alignment, it is important to forge a meaningful dialogue between those generating evidence, such as CDC's Global Tobacco Control Program, and providers serving youth and families, such as pediatricians and national medical societies. For example, from 2016 to 2020, the CDC in partnership with AAP implemented a multiyear project to use data and evidence-based interventions to encourage global efforts to protect youth from tobacco. As part of this project, CDC and AAP have partnered with national pediatric societies in 13 countries to develop and implement strategic plans to reduce youth tobacco use and exposure. These partnerships build on the Academy's long history of global child health interventions[9] and use country-level data from the CDC Global Adult Tobacco Surveys and GYTS. Using training from AAP subject-matter experts and peer leaders, these national pediatric societies have built strategic partnerships and educational programs designed to combat youth tobacco use and exposure (Table 1). The activities undertaken by national pediatric societies expand the role of health care providers in tobacco control and connect them with government and nongovernment institutions and stakeholders for mobilizing a wider circle of stakeholders who may interact with youth, their families, and community and may be in positions to protect youth from tobacco. Although it is too early to determine the long-term success of these efforts, participating societies have implemented strategies for sustainability, including forging relationships with multisectoral partners, establishing pediatrician workgroups devoted to tobacco prevention, and advocating for the prioritization of pediatric tobacco prevention in national pediatric societies' strategic planning efforts. In addition, CDC and AAP have worked to encourage sustainability of societal efforts by engaging past participants as program faculty, developing a peer-mentorship network, and issuing sustainability grants to past participants.

Pediatricians and other pediatric health providers are critical partners for promoting well-being of youth. Each year on May 31, the public health community recognizes World No Tobacco Day (WNTD). The 2020 theme was "protecting youth from industry manipulation and preventing them from tobacco and nicotine use." In honor of WNTD, it is important for pediatric health providers to work to prevent and eliminate youth tobacco use and exposure. Such efforts could include raising the tobacco sales age to 21 years, prohibiting flavored tobacco product sales, raising the price of tobacco products, prohibiting the marketing of tobacco products to youth, prohibiting tobacco imagery in media that is viewed by children, comprehensive smoke-free policies in public places, and provision of comprehensive tobacco cessation services to help users quit. WNTD is a critical opportunity for pediatric health providers to partner with national pediatric societies, public health organizations, and governmental health ministries to promote a tobacco-free world for youth.

ACKNOWLEDGMENTS

We thank Mr Edward Rainey for creating the figure and Ms Kyung Ah Lee for creating the data file for the figure.

ABBREVIATIONS

AAP: American Academy of Pediatrics
CDC: US Centers for Disease Control and Prevention
CRC: Convention on the Rights of the Child
e-cigarette: electronic cigarette
GYTS: Global Youth Tobacco Survey
SHS: secondhand smoke
THS: thirdhand smoke
WNTD: World No Tobacco Day

REFERENCES

1. US Department of Health and Human Services. The Health Consequences of Smoking: 50 Years of Progress. A Report of the Surgeon General. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center

for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2014

2. Arrazola RA, Ahluwalia IB, Pun E, Garcia de Quevedo I, Babb S, Armour BS. Current tobacco smoking and desire to quit smoking among students aged 13–15 years - global youth tobacco survey, 61 countries, 2012–2015. *MMWR Morb Mortal Wkly Rep*. 2017;66(20): 533–537
3. Wang TW, Gentzke AS, Creamer MR, et al. Tobacco product use and associated factors among middle and high school students - United States, 2019. *MMWR Surveill Summ*. 2019; 68(12):1–22
4. Mbulo L, Palipudi KM, Andes L, et al; GATS Collaborative Group. Secondhand smoke exposure at home among one billion children in 21 countries: findings from the Global Adult Tobacco Survey (GATS). *Tob Control*. 2016;25(e2): e95–e100
5. Northrup TF, Jacob P III, Benowitz NL, et al. Thirdhand smoke: state of the science and a call for policy expansion. *Public Health Rep*. 2016; 131(2):233–238
6. Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19): people who are at higher risk for severe illness. 2020. Available at: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-at-higher-risk.html. Accessed March 27, 2020
7. Centers for Disease Control and Prevention. Smoking and tobacco use: electronic cigarettes. 2020. Available at: https://www.cdc.gov/tobacco/basic_information/e-cigarettes/index.htm. Accessed March 31, 2020
8. United Nations. The United Nations convention on the rights of the child. 1989. Available at: https://downloads.unicef.org.uk/wp-content/uploads/2010/05/UNCRC_PRESS200910web.pdf?_ga=2.160099513.588977858.1585247111-683003612.1585247111. Accessed March 31, 2020
9. David AM, Mercado SP, Klein JD, Kaundan MSK, Koong HN, Garcia E. Protecting children and families from tobacco and tobacco-related NCDs in the Western Pacific: good practice examples from Malaysia, Philippines and Singapore. *Child Care Health Dev*. 2017;43(5): 774–778

A Seat at the Table: Centering the Voices of Gun Violence Survivors

Kamaal A. Jones, MD

The following is the winning submission from the Fourth Annual Section on Pediatric Trainees Essay Competition. This year's competition was informed by the 2019–2020 Section on Pediatric Trainees Advocacy Campaign: Protect Kids – Trainees for Firearm Safety. We asked writers to share their experiences as pediatric trainee advocates for gun violence prevention and were impressed by the breadth of entries we received from around the country. The winning essay by Dr Kamaal Jones was focused on amplifying the voice of gun violence survivors. Dr Jones eloquently implores us to offer gun violence survivors "A Seat at the Table," so that our policies may be shaped by survivors' lived experiences and calls for change. This inspiring piece reminds us that listening to the community is a critical first step in our advocacy efforts and that doing so can empower us to make the greatest impact. Names and minor identifying details have been altered to protect the privacy of group members.

Stanford Children's Health, Lucile Packard Children's Hospital Stanford, Palo Alto, California; and Department of Pediatrics, Stanford Medicine, Stanford University, Palo Alto, California

DOI: https://doi.org/10.1542/peds.2020-015974

Accepted for publication Jul 21, 2020

Address correspondence to Kamaal A. Jones, MD, Stanford Pediatrics Residency Program, Department of Pediatrics, Stanford Medicine, Stanford University, 725 Welch Rd, Palo Alto, CA 94305-5906. E-mail: kjones17@stanford.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The author has indicated he has no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The author has indicated he has no potential conflicts of interest to disclose.

To cite: Jones KA. A Seat at the Table: Centering the Voices of Gun Violence Survivors. *Pediatrics*. 2020;146(4):e2020015974

Derrick turned the door handle to enter our small conference room with his usual measure of caution, his dexterity still impaired from being shot in the hand several weeks before. Typically drifting between relaxed and jovial, his energy was different today. His face displayed a mix of awe and disbelief, like how one might feel after slipping on an icy step and somehow landing on their feet unscathed. We went around the table to do our customary introductions: your name, how you are feeling, something good from the week, something challenging from the week, and what you hope to learn. When we got to him, Derrick took a breath and explained that while walking home from school with classmates today, someone started shooting at them from across the street. He and the crowd ducked and hid behind nearby cars, and after a few moments, it was over. Fortunately, no one was hurt. He wasn't sure who shot at them or why they did it, although he suspected it was likely because of some sort of dispute between the shooter and someone in the crowd. Regardless, he was just happy to have made it home. I was relieved too, disturbed by how close he had once again come to tragedy.

As a medical student, I spent nearly 2 years helping to facilitate a support group for teenage survivors of gun violence in Chicago. Each week for 12-week blocks of time, 2 social workers and I met with the same group of 8 or so young men, all of whom had been shot on Chicago's South or

West sides.[1] We guided conversation and activities under a Safety, Emotions, Loss, Future (S.E.L.F.) curriculum, with the goal being to create a community in which these young men could find healing, and in so doing, to disrupt the cycle of violence.[2] The stories that I learned were incredible and deeply inform how I think about trauma now as a pediatrics resident. But as I spent time with these young men week after week, it dawned on me that part of the reason their narratives were so striking was that their voices had largely been missing from the mainstream conversation.[3] I began to understand that our nation was trying to create policy around gun violence while simultaneously leaving some of the most critical experts out of the discussion.

According to the Brady Campaign, every day, 313 people are shot in the United States.[4] Among those, 103 people die of their injury.[4] Approximately 60% of those deaths are from suicides and 37% are from homicides, of which Black young people like the ones with whom I worked bear a disproportionate amount of loss. [5–8] The remaining 3% of gun deaths are from additional causes, including accidents, police shootings, and other unknown reasons.[5,6] We also know that each day, ~210 people go on to survive their gun injuries; that's >76 000 survivors every year.[4] So often when we talk about gun violence, we talk in terms of those lives that we have lost. This is natural given the profound and permanent impact such loss has on our communities. Seldomly though do we give thought to the tens of thousands of survivors every year. This attention to survivors is not only critical in terms of their own healing, but also in terms of their wealth of lived experience, which could play a pivotal role in bringing about solutions.

There were so many lessons to be learned in the stories of these young men from our support group. Some spoke of being shot while playing basketball or going to the grocery store. Others had a history of gang-related activity and had at points been the perpetrators of violence themselves. One spoke of the rage he had to let go. Another spoke of his profound struggle to comprehend why he had been to 6 funerals in a calendar year. They spoke of a culture of fear, which often dictated decisions, and a currency of respect that kept them alive. I watched as we rescheduled a barbecue per their request because it was too hot out, not because the temperature itself was dangerous, but because they understood that there was a higher likelihood for a shooting to occur when the weather was warm. They also spoke of deep joy and belly laughs. Of video games with friends. Of hip-hop and poetry. Of college. Of entrepreneurship. One spoke of plans to dye the tips of his dreaded hair bright red to match his tuxedo for the senior prom. Each of their textured narratives represented another perspective on the spaces in which life and violence intersect, and through that, a better understanding of what we can do about it.

Whether as trainees, or as seasoned pediatricians, we have the privilege of engaging with these same young people and their families in our clinics, in our hospitals, and in our communities. As we advocate for gun safety, whether at a local level or through broad policy, it is important to keep their voices at the center. Here are a few key steps that we can take to accomplish this:

1. Prepare our trainees and clinicians to be comfortable with trauma-informed care[9]: Our priority as caregivers must be to establish an environment that makes safety, healing, and empowerment paramount and avoids retraumatizing the patients we are here to serve. Learning these skills should be part of the clinical training for all pediatricians. As a starting point, the American Academy of Pediatrics has a rich trauma toolbox with resources for how to incorporate an understanding of trauma into our work.[10]
2. Listen to and amplify the stories of survivors: Data are crucial but can only get us so far. We rely on storytelling to humanize statistics.[11] With appropriate permission and protection of sensitive information, sharing these critical narratives can help the general public and policy makers to understand the complex realities that many of our patients live in. Ultimately, if survivors are willing and feel safe, creating opportunities for them to speak for themselves in public forums and conferences can be a powerful catalyst for systemic and community-level transformation.
3. Work directly with survivors to design policy changes and counseling methods: Survivors need a seat at the table when it comes to creating gun safety legislation. It is important that we lean on their experience and work with them directly when making policy recommendations. On a local level, through methods such as individual interviews, focus groups, and other qualitative modalities, our hospitals and clinics can partner with survivors to learn how to better support and counsel young people who have been shot or are at elevated risk for gun violence.

Ultimately, survivors like Derrick are our experts. Our job is to foster a safe environment, to help amplify their stories, to make room for them to be leaders in the policy-making process, and to fiercely advocate for the change that they have called for.

REFERENCES

1. Stroger JH Jr; American Hospital Association. Healing hurt people—Chicago seeks to save lives by offering support beyond the hospital. 2018. Available at: https://www.aha.org/system/files/2018-03/healing-hurt-people-stroger.pdf. Accessed April 19, 2020
2. Bloom SL, Foderaro JF, Ryan R. *S.E.L.F.: A Trauma-Informed, Psychoeducational Group Curriculum*. Philadelphia, PA: Community Works; 2006
3. Beckett L. How the gun control debate ignores black lives. *ProPublica*. November 24, 2015. Available at: https://www.propublica.org/article/how-the-gun-control-debate-ignores-black-lives. Accessed April 19, 2020
4. Brady Campaign to Prevent Gun Violence. Key statistics. 2020. Available at: https://www.bradyunited.org/key-statistics. Accessed April 19, 2020
5. Gramlich J. What the data says about gun deaths in the US. 2020. Available at: https://www.pewresearch.org/fact-tank/2019/08/16/what-the-data-says-about-gun-deaths-in-the-u-s/. Accessed April 19, 2020
6. Kochanek KD, Murphy SL, Xu JQ, Arias E; National Vital Statistics Reports. *Deaths: Final Data for 2017*, vol. 68. Hyattsville, MD: National Center for Health Statistics; 2019
7. Giffords Law Center to Prevent Gun Violence. Gun violence statistics. 2020. Available at: https://lawcenter.giffords.org/facts/gun-violence-statistics. Accessed April 19, 2020
8. Dowd MD, Sege RD; Council on Injury, Violence, and Poison Prevention Executive Committee; American Academy of Pediatrics. Firearm-related injuries affecting the pediatric population. *Pediatrics*. 2012;130(5). Available at: www.pediatrics.org/cgi/content/full/130/5/e1416
9. The Institute on Trauma and Trauma-Informed Care; University at Buffalo. What is trauma-informed care? 2020. Available at: http://socialwork.buffalo.edu/social-research/institutes-centers/institute-on-trauma-and-trauma-informed-care/what-is-trauma-informed-care.html. Accessed May 23, 2020
10. American Academy of Pediatrics. Trauma toolbox for primary care. 2020. Available at: https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/healthy-foster-care-america/Pages/Trauma-Guide.aspx#trauma. Accessed May 24, 2020
11. The Health Foundation. The power of storytelling. 2020. Available at: https://www.health.org.uk/newsletter-feature/power-of-storytelling. Accessed May 24, 2020

Social Distancing for COVID-19 and Diagnoses of Other Infectious Diseases in Children

Jonathan Hatoun, MD, MPH, MS,[a,b] Emily Trudell Correa, MPH, MS,[a] Sara Mary Alice Donahue, DrPH, MPH,[c] Louis Vernacchio, MD, MSc[a,b]

Social distancing (SD) during the coronavirus disease 2019 (COVID-19) pandemic has largely removed children from school, day care, and other contact with peers. In addition to reducing transmission of severe acute respiratory syndrome coronavirus 2, these changes would be expected to reduce the transmission of other infectious diseases among children. We sought to determine the effect of SD on 12 infectious diseases commonly diagnosed in pediatric primary care that are contagious to various extents: acute otitis media (AOM), bronchiolitis, common cold, croup, gastroenteritis, influenza, nonstreptococcal pharyngitis, pneumonia, sinusitis, skin and soft tissue infections (SSTIs), streptococcal pharyngitis, and urinary tract infection (UTI).

METHODS

Using electronic health record data from a large Massachusetts pediatric primary care network that cares for ~375 000 children, we analyzed the weekly incidence of each diagnosis from weekday in-person and telemedicine encounters (excluding holidays) for children age 0 to 17 years of age for the same calendar period in 2019 and 2020 starting from January 1. We defined the pre-SD period as calendar weeks 1 to 9 of each respective year; allowed for a 3-week implementation period as SD was enacted in 2020 (statewide state of emergency declared in week 10, school and nonessential businesses closed in week 11, and stay-at-home advisory issued in week 12); and defined the post-SD period as calendar weeks 13 to 18, the most recent data available for analysis. To

TABLE 1 Rates of Diagnosis of Common Pediatric Infectious Diseases in 2019 and 2020 and Difference-in-Differences Between 2019 and 2020

Diagnosis	2019		2020		Difference-in-Differences, 2020 vs 2019 (95% CI)
	Pre-SD	Post-SD	Pre-SD	Post-SD	
AOM	113.4	96.2	113.4	11.5	−85.1 (−86.8 to −83.5)
Bronchiolitis	17.5	8.4	20.1	0.6	−10.4 (−11.0 to −9.8)
Common cold	106.6	79.9	107.1	5.4	−75.4 (−76.9 to −73.8)
Croup	12.0	11.3	11.8	0.4	−10.7 (−11.2 to −10.2)
Gastroenteritis	18.4	15.0	14.9	1.8	−9.8 (−10.5 to −9.2)
Influenza	41.4	19.0	94.4	0.1	−71.7 (−72.8 to −70.6)
Nonstreptococcal pharyngitis	114.7	100.6	126.7	12.4	−100.6 (−102.3 to −98.9)
Pneumonia	22.3	15.0	22.6	1.4	−14.0 (−14.7 to −13.3)
Sinusitis	22.2	15.3	20.6	2.7	−11.1 (−11.8 to −10.4)
SSTI	17.6	17.9	17.8	11.6	−6.6 (−7.4 to −5.9)
Streptococcal pharyngitis	46.4	39.9	41.2	3.8	−31.1 (−32.1 to −30.0)
UTI	3.3	3.7	3.4	2.4	−1.5 (−1.8 to −1.1)

Rates are expressed as diagnoses per 100 000 patients per day. CI, confidence interval.

[a]*Pediatric Physicians' Organization at Children's, Brookline, Massachusetts;* [b]*Department of Pediatrics, Harvard Medical School, Harvard University, Boston, Massachusetts; and* [c]*Department of Accountable Care and Clinical Integration, Boston Children's Hospital, Boston, Massachusetts*

Dr Hatoun drafted the initial manuscript; Ms Correa performed the analysis; and all authors conceptualized and designed the study, reviewed and revised the manuscript, and approved the final manuscript as submitted.

DOI: https://doi.org/10.1542/peds.2020-006460

Accepted for publication Jun 12, 2020

Address correspondence to Louis Vernacchio, MD, MSc, Pediatric Physicians' Organization at Children's, 77 Pond Ave, Suite 205c, Brookline, MA 02445. E-mail: louis.vernacchio@childrens.harvard.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest relevant to this article to disclose.

To cite: Hatoun J, Correa ET, Donahue SMA, et al. Social Distancing for COVID-19 and Diagnoses of Other Infectious Diseases in Children. *Pediatrics.* 2020;146(4):e2020006460

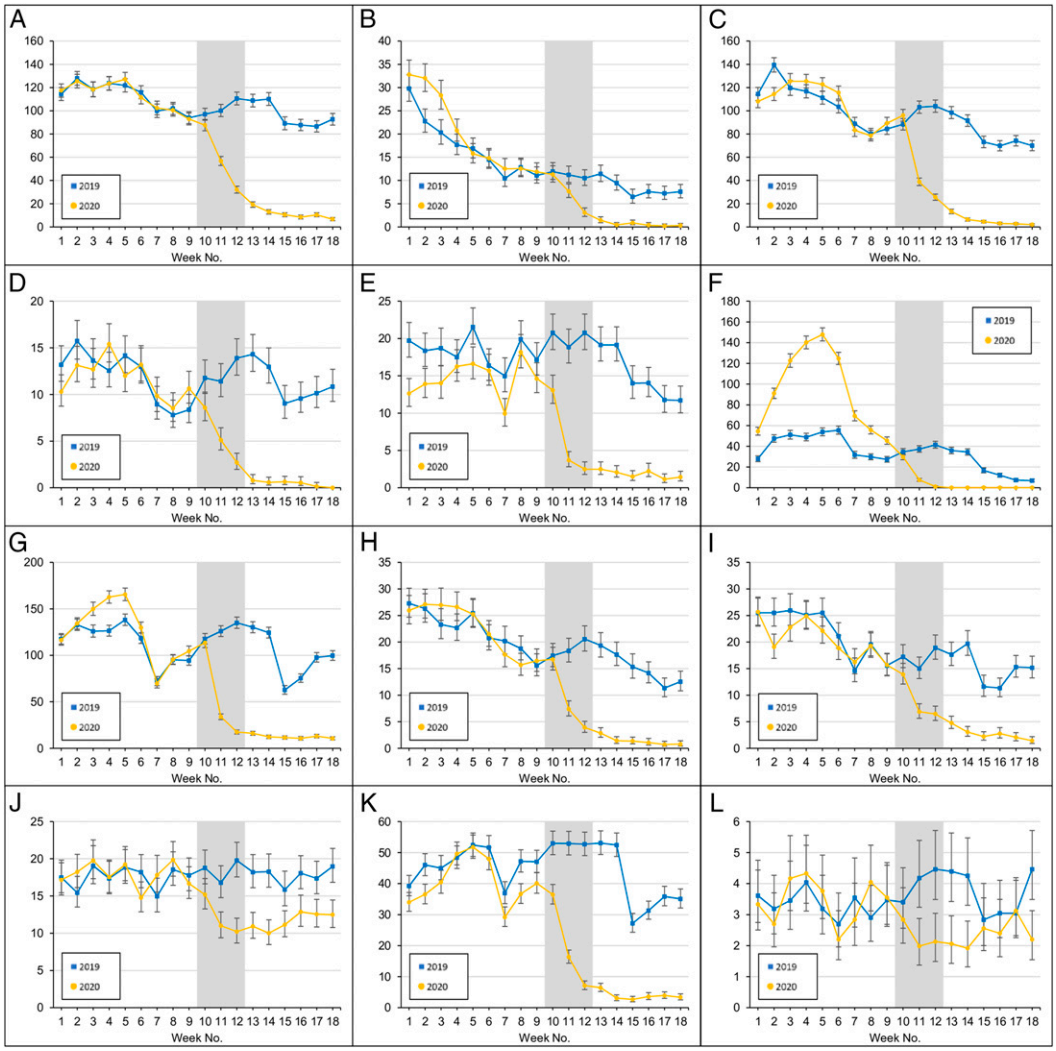


FIGURE 1

Weekly rates with 95% confidence intervals of diagnosis of common pediatric infectious diseases in 2019 and 2020. Rates are expressed as diagnoses per 100 000 patients per day. The shaded area represents period of SD implementation in 2020. A, AOM. B, Bronchiolitis. C, Common cold. D, Croup. E, Gastroenteritis. F, Influenza. G, Nonstreptococcal pharyngitis. H, Pneumonia. I, Sinusitis. J, SSTI. K, Streptococcal pharyngitis. L, UTI.

isolate the effect of SD, we performed a difference-in-differences regression analysis[1] using a multivariable Poisson regression model with diagnosis count as a function of calendar year, time period (pre-SD versus post-SD), and the interaction between the two.

RESULTS

The diagnosis rates per 100 000 patients for each time period and the difference-in-differences analysis for 2020 vs 2019 are displayed in Table 1 and Fig 1. The prevalence of each condition was significantly lower in the 2020 post-SD period than would be expected for all conditions analyzed ($P < .001$ for all diagnoses).

DISCUSSION

SD policies enacted in Massachusetts to mitigate the COVID-19 pandemic resulted in a profound decrease in the diagnosis of common infectious diseases among children. This reduction could be due to 1, or both, of 2 factors: a decline in the prevalence of the conditions or a choice not to seek care when the conditions occurred.[2] The smaller decrease in diagnoses for UTI, an infectious but not generally not contagious disease, suggests that changes in care-seeking behavior had a relatively modest effect on the other observed declines.

Although it is not surprising that the transmission of infectious diseases decreased with SD, these data demonstrate the extent to which transmission of common pediatric infections can be altered when close contact with other children is eliminated. Notably, 3 of the studied diseases, namely, influenza, croup, and bronchiolitis, essentially disappeared with SD.

The trajectory of influenza is especially interesting. Diagnoses in 2020 exceeded those in 2019 as expected from national surveillance data,[3] but the spread of influenza appears to have ended abruptly with SD. This finding differs somewhat from a recent report from Japan revealing a significant but not as dramatic decline in influenza cases coincident with SD in that country.[4] The differing results may relate to the timing of SD within the influenza season, different approaches to SD in the 2 locations, or the fact that the Japanese study included patients of all ages, whereas ours is focused only on children.

The infectious disease risks of contact with others have always been implicitly weighed against the benefits of social interaction. The current natural experiment of abrupt, widespread SD during the COVID-19 pandemic has allowed for a more explicit appreciation of the magnitude of these risks in children and may inform strategies for infectious disease risk mitigation as social interaction increases in the future.

ABBREVIATIONS

AOM: acute otitis media
COVID-19: coronavirus disease 2019
SD: social distancing
SSTI: skin and soft tissue infections
UTI: urinary tract infection

REFERENCES

1. Wing C, Simon K, Bello-Gomez RA. Designing difference in difference studies: best practices for public health policy research. *Annu Rev Public Health*. 2018;39:453–469
2. Isba R, Edge R, Jenner R, Broughton E, Francis N, Butler J. Where have all the children gone? Decreases in paediatric emergency department attendances at the start of the COVID-19 pandemic of 2020. *Arch Dis Child*. 2020;105(7):704
3. Centers for Disease Control and Prevention. Weekly US influenza surveillance report. Available at: https://www.cdc.gov/flu/weekly/#ILINet. Accessed May 7, 2020
4. Sakamoto H, Ishikane M, Ueda P. Seasonal influenza activity during the SARS-CoV-2 outbreak in Japan. *JAMA*. 2020;323(19):1969–1971

COVID-19 and the Law of Unforeseen Consequences

David W. Kimberlin, MD, Erica C. Bjornstad, MD, PhD, MPH

Divisions of Pediatric Infectious Diseases and Pediatric Nephrology, Department of Pediatrics, School of Medicine, The University of Alabama at Birmingham, Birmingham, Alabama

DOI: https://doi.org/10.1542/peds.2020-019232

Accepted for publication Jul 14, 2020

Address correspondence to David W. Kimberlin, MD, Division of Pediatric Infectious Diseases, Department of Pediatrics, School of Medicine, The University of Alabama at Birmingham, 1600 Seventh Ave South, CHB 303, Birmingham, AL 35233. E-mail: dkimberlin@peds.uab.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

COMPANION PAPER: A companion to this article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-006460.

To cite: Kimberlin DW and Bjornstad EC. COVID-19 and the Law of Unforeseen Consequences. *Pediatrics.* 2020;146(4):e2020019232

On January 29, 1964, Stanley Kubrick released to the world one of his most brilliant films, *Dr Strangelove or: How I Learned to Stop Worrying and Love the Bomb.* America was at the height of the Cold War. Children were sheltering under school desks in drills preparing for nuclear annihilation. The last influenza pandemic was 7 years in the rearview mirror, and the next one to come was 4 years in the future. The film viciously satirized world leaders and foretold an era of dark pessimism that defines the world and America to this day.

On January 29, 2020, Peter Navarro, trade advisor to President Donald Trump, wrote an internal memo warning of the threat to the United States of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreak that had been recognized in China in late December. On that day, the World Health Organization reported that there were 6065 confirmed cases worldwide, 68 of which were in 15 countries outside of China.[1] According to the *New York Times*, Mr Navarro wrote that, "The lack of immune protection or an existing cure or vaccine would leave Americans defenseless in the case of a full-blown coronavirus outbreak on U.S. soil…This lack of protection elevates the risk of the coronavirus evolving into a full-blown pandemic, imperiling the lives of millions of Americans."[2] A worst-case scenario of more than half a million American deaths was cited in the memo.

By June 29, 2020, Mr Navarro's prediction was well on its way to fulfillment, with >133 000 Americans dead from coronavirus disease 2019 (COVID-19). Although Americans constitute only 4% of the world's population, we account for ~25% of global SARS-CoV-2 infections and COVID-19 deaths.[3,4] With a vaccine months or years away, if even possible, we are left with limited options for slowing the spread of the virus. Chief among these is social distancing.[5] A century ago, social distancing played a key role in limiting the 1918 influenza pandemic. The principle is simple. If someone is infected with a respiratory virus, they are less likely to spread it to others if they are not in close proximity to them. Significant challenges remain in the embrace by average Americans of the need for social distancing, based on its limited success thus far.

In this month's issue of *Pediatrics*, Vernacchio and co-workers[6] provide a short but provocative report of diagnoses of common pediatric infectious diseases across a large Massachusetts pediatric primary care network and the changes between 2019 and 2020. Each disease evaluated was dramatically less likely to occur during the initial weeks of enforced social distancing compared to the same time period the previous year. Before social distancing measures, the diseases of 2019 and 2020 followed similar trajectories, suggesting that had social distancing not occurred, this year's infections would have continued on a similar path as 2019. The difference-in-difference approach is key for analyzing these data, as is the diversity of infections reported (including

urinary tract infections, which are not considered contagious). By analyzing the data within the same primary care network, on a population level, the people included are roughly the same; comparing each week keeps the seasons the same from 2019 to 2020, leaving key societal events as the primary differences. In this case, the key differences in the analyzed time periods (pre–week 10 and post–week 12; 2019 and 2020) are social isolation and perhaps decreased medical care seeking both due to reactions to COVID-19.

As the authors note, it is not as clear as to which factor is driving the significant drop in common pediatric infections. If it is decreasing access to medical care, this would be an unforeseen consequence of our social distancing efforts, and our response requires improved outreach and communication with families on seeking appropriate medical care throughout the remainder of the pandemic. On the other hand, if the decrease in pediatric infections is the direct consequence of social distancing, then it would be a rare positive development in the health of Americans during the pandemic.

Similar observations of infections dropping during periods of isolation have been made in Seattle.[7] Between February 3 and 11, 2019, a record snowstorm covered Seattle, Washington. Seattle does not have dedicated snowplows, and the city's steep topography is especially challenging during snow and ice storms. Most public schools in the region were closed, and highway traffic in the region decreased by one-third during those few weeks. The Seattle Flu Study that had started a few months before to evaluate the transmission of influenza and other respiratory viruses was well positioned to assess the impact that this social disruption caused on these infections.[8] The Seattle Flu Study researchers calculated that the percentage of infections averted during the period of weather-imposed isolation ranged from 3.0% (95% confidence interval, 2.0%–3.7%) for human metapneumovirus to 9.2% (95% confidence interval, 6.2%–10.3%) for respiratory syncytial virus B.[7] In other modeling studies, researchers likewise have predicted that social distancing measures initiated early in the course of a pandemic can reduce viral spread.[9–12] Taken together, these reports would suggest that the decline in other infectious diseases reported by Vernacchio and co-workers[6] is indeed real.

However, we also now know that immunization rates for American children have plummeted since the onset of the SARS-CoV-2 pandemic.[13] The cause of this is a dramatic decrease in use of health care during the first months of the pandemic. This raises real possibility that the travesty of a measles epidemic occurring on top of the coronavirus pandemic could happen. Viewed through this lens, the report of Vernacchio and co-workers[6] could be due not to a true decrease in infections but simply a lack of recognition because the infections are going undiagnosed and untreated. It goes without saying that the health and well-being of children would be significantly and detrimentally impacted if this is the case.

What do we make of all of this? First, we simply must socially distance. The immediate threat is the coronavirus pandemic. We must also employ all other public health measures we have at our disposal: wearing masks, practicing excellent hand hygiene, avoiding gathering in crowds, and being mindful of surfaces. Until there is a treatment or a vaccine, we must settle in for the long haul with SARS-CoV-2 as part of our daily lives. We must find a way to live with it, much as in decades past we had to learn to live with the threat of the bomb. This includes going to all pediatric well visits and seeking timely medical attention when sick. Ultimately, the verdict remains out as to whether the observations of Vernacchio and co-workers[6] are an unforeseen good consequence of a bad situation or yet another blow in an increasingly long struggle.

ABBREVIATIONS

COVID-19: coronavirus disease 2019

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

REFERENCES

1. World Health Organization. Novel coronavirus (2019-nCoV) situation report – 9. Available at: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200129-sitrep-9-ncov-v2.pdf?sfvrsn=e2c8915_2. Accessed July 11, 2020
2. Haberman M. Trade adviser warned white house in January of risks of pandemic. New York Times. April 6, 2020. Available at: https://www.nytimes.com/2020/04/06/us/politics/navarro-warning-trump-coronavirus.html. Accessed July 11, 2020
3. US Census Bureau. U.S. Census Bureau current population. Available at: https://www.census.gov/popclock/print.php?component=counter. Accessed July 13, 2020
4. Johns Hopkins University and Medicine. COVID-19 dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University. Available at: https://coronavirus.jhu.edu/map.html. Accessed July 13, 2020
5. Nussbaumer-Streit B, Mayr V, Dobrescu AI, et al. Quarantine alone or in combination with other public health measures to control COVID-19: a rapid review. *Cochrane Database Syst Rev.* 2020;(4):CD013574
6. Hatoun J, Correa ET, Donahue SMA, Vernacchio L. Social distancing for COVID-19 and diagnoses of other infectious diseases in children. *Pediatrics.* 2020;146(3):e2020006460

7. Jackson ML, Hart GR, McCulloch DJ, et al. Effects of weather-related social distancing on city-scale transmission of respiratory viruses [published online ahead of print March 3, 2020]. doi: 10.1101/2020.03.02.20027599
8. Chu HY, Boeckh M, Englund JA, et al. LB21. The Seattle Flu Study: a community-based study of influenza. *Open Forum Infect Dis*. 2019;6(suppl 2):S1002
9. Ferguson NM, Cummings DAT, Fraser C, Cajka JC, Cooley PC, Burke DS. Strategies for mitigating an influenza pandemic. *Nature*. 2006;442(7101): 448–452
10. Halloran ME, Ferguson NM, Eubank S, et al. Modeling targeted layered containment of an influenza pandemic in the United States. *Proc Natl Acad Sci USA*. 2008;105(12): 4639–4644
11. Germann TC, Kadau K, Longini IM Jr., Macken CA. Mitigation strategies for pandemic influenza in the United States. *Proc Natl Acad Sci USA*. 2006; 103(15):5935–5940
12. Glass RJ, Glass LM, Beyeler WE, Min HJ. Targeted social distancing design for pandemic influenza. *Emerg Infect Dis*. 2006;12(11):1671–1681
13. Santoli JM, Lindley MC, DeSilva MB, et al. Effects of the COVID-19 pandemic on routine pediatric vaccine ordering and administration - United States, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(19):591–593

Tracking Potential COVID-19 Outbreaks With Influenzalike Symptoms Urgent Care Visits

Brian Muchmore, BS,[a,b,c] Patrick Muchmore, MA, MS, PhD,[a] Chi Wing Lee, BS,[a] Marta E. Alarcón-Riquelme, MD, PhD,[b,d] Andrew Muchmore, MD[a]

The 2019–2020 influenza season has had elevated influenza-confirmed hospitalization rates.[1] Simultaneously, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has infected millions worldwide.[2] There are open questions about coronavirus disease 2019 (COVID-19) related to its prevalence[3] and seasonality.[4] Many individuals who develop COVID-19 present with influenzalike illness (ILI) symptoms, including fever, cough, or sore throat.[5] This symptom overlap makes it difficult to differentiate COVID-19 from influenza or other related illnesses without testing, which has limited availability in the United States.[6] Understanding the degree to which ILI in a community is not due to influenza could help clinicians estimate the risk of COVID-19. The proportion of local current cases of ILI that are influenza-negative could inform clinical care and provide epidemiological insight into the ongoing pandemic.

METHODS

CodoniX is an electronic health record that captures data from ∼3000 patients daily from >100 urgent care clinics in 15 states. We evaluated data for patients ≤21 years seen during the months of January, February, and March from 2018 to 2020. We also evaluated COVID-19 data from the same period; however, because there were fewer recorded cases, all ages were used.

We evaluated *International Classification of Diseases, 10th Revision* (ICD-10) codes for discharge diagnoses of fever, cough, sore throat, influenza, streptococcal pharyngitis, COVID-19, mononucleosis, and respiratory syncytial virus, and we evaluated Logical Observation Identifiers Names and Codes (LOINC) for positive test results. The diagnosis of influenza was based on either a positive test result or the discharge diagnosis. There is no ICD-10 code for ILI, so it was defined as an *ICD-10* diagnosis of fever with cough and/or sore throat without another known cause, such as mononucleosis or respiratory syncytial virus. The distribution of these diagnoses by age range is presented in Supplemental Table 1.

To validate the CodoniX data findings, publicly available ILI, influenza, and COVID-19 data from the Centers for Disease Control and Prevention (CDC) were collected. ILI diagnoses were collected from the CDC's Outpatient Influenzalike Illness Surveillance Network, and CDC COVID-19 data were acquired from the Johns Hopkins University Center for Systems Science and Engineering coronavirus repository. For both of these data sets, all ages were used for analysis. However, influenza data collected from public health laboratories that report as World Health Organization Collaborating Centres and Essential Regulatory Laboratories are stratified by age, so only ages 0 to 4 and 5 to 24 years were used in the analysis.

RESULTS

In both the CodoniX and CDC data, an increase in the ratio of ILI diagnoses to

[a]*CodoniX, Inc, Potomac, Maryland;* [b]*Medical Genomics, Pfizer–University of Granada–Junta de Andalucía Centre for Genomics and Oncological Research, Granada, Spain;* [c]*The Robert Larner College of Medicine, The University of Vermont, Burlington, Vermont; and* [d]*Unit of Chronic Inflammatory Diseases, Karolinska Institutet, Solna, Sweden*

Mr Muchmore conceptualized and designed the study, collected data, conducted initial and final analyses, and drafted the initial manuscript; Dr P. Muchmore, Mr Lee, and Dr Alarcón-Riquelme conducted the initial analyses and collected data; Dr A. Muchmore designed the data collection platform and coordinated and supervised data collection; and all authors reviewed and revised the manuscript and approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2020-1798

Accepted for publication Jul 9, 2020

Address correspondence to Brian Muchmore, BS, Data Intelligence Division, CodoniX, Inc, 390 Colchester Ave, Burlington, VT 05401. E-mail: brian.muchmore@med.uvm.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Partially supported by the Innovative Medicines Initiative Joint Undertaking funded by the European Union's Seventh Framework Programme (FP7/2007-2013) and European Federation of Pharmaceutical Industries and Associations companies' in kind contributions (grant 115565).

To cite: Muchmore B, Muchmore P, Lee CW, et al. Tracking Potential COVID-19 Outbreaks With Influenzalike Symptoms Urgent Care Visits. *Pediatrics*. 2020;146(4):e20201798

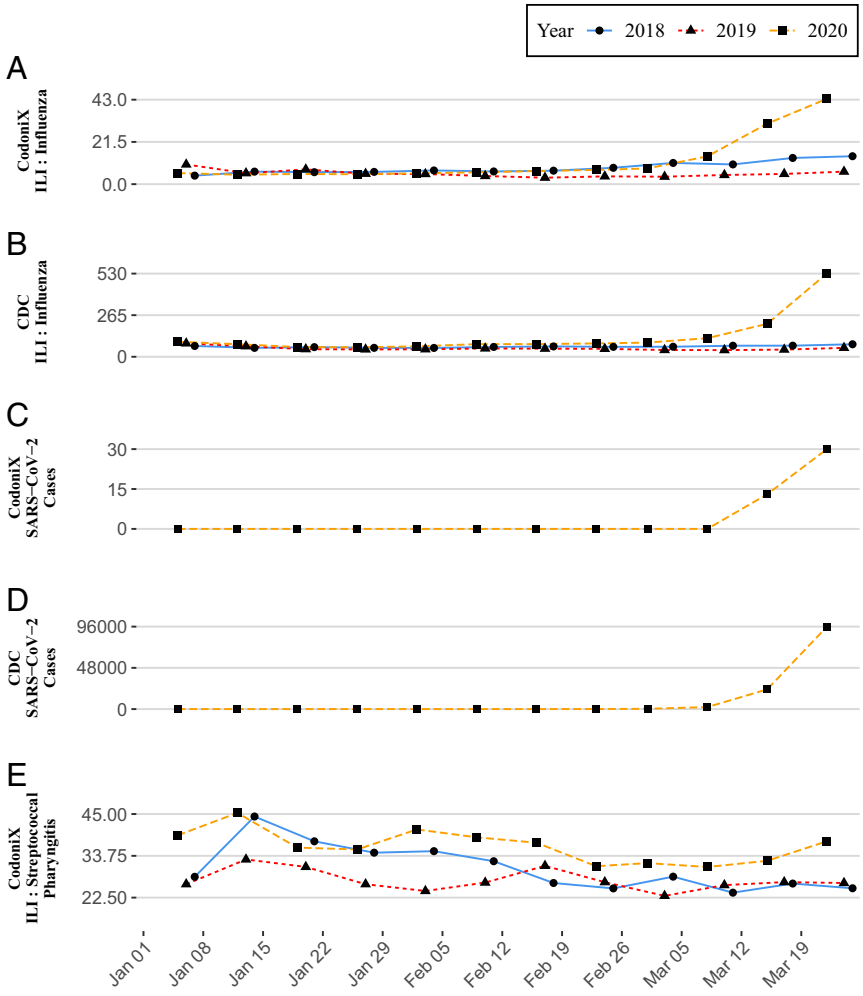


FIGURE 1

Time series of disease ratios along with weekly SARS-CoV-2 positive test results. A, The ratio of weekly CodoniX ILI cases to influenza cases. B, The ratio of weekly CDC ILI cases to CDC influenza-confirmed hospitalizations. C, Weekly CodoniX positive SARS-CoV-2 test results. D, Weekly CDC positive SARS-CoV-2 test results. E, The ratio of weekly CodoniX ILI cases to streptococcal pharyngitis cases.

confirmed influenza cases was observed in late February and early March 2020, which was not evident during the same period in 2018 or 2019. Figures 1 A–D illustrate, for each year, the ILI to influenza ratio and number of COVID-19 cases. Figures 1 A and B suggest an increasing trend in March 2020 that was absent in March of 2018 and 2019, and these temporal patterns match the absolute weekly COVID-19 case incidence seen in both the CodoniX (Fig 1C) and CDC COVID-19 data (Fig 1D). In 2020, the ILI to influenza ratio rose in February, and, with Buishand U test, a change point during the last week of February (P = .01) was indicated. By using an adjusted Mann-Kendall trend test for the same time series, a statistically significant trend ($P < .001$) was indicated (Supplemental Table 2). Figure 1E shows the ratio of ILI cases to streptococcal pharyngitis cases, and Supplemental Fig 2 illustrates a heat map and the clustering of these time series based on a statistical measure of similarity.

DISCUSSION

Our results indicate that, beginning in February 2020, a significant number of patients receiving ILI diagnoses were infected with a virus other than influenza. This suggests that monitoring the ratio of influenza-negative ILI cases to influenza-positive cases could potentially be used as an early warning system for influenza-negative viral syndromes with features of ILI.

A limitation of our study is that many diseases, including COVID-19, do not always present as ILI. For example, although influenza patients typically present with ILI symptoms, streptococcal pharyngitis patients often do not, so we would not expect the ratio between the two to contain a discernible pattern, which is supported by Fig 1E. However, although describing the clinical presentation of COVID-19 is an ongoing topic of study, recent data indicate it may often present as ILI.[7] Additionally, although the CDC and CodoniX data exhibit similar patterns, neither constitute a random sample of US residents, and the extent to which they are representative of the entire population is unknown.

ACKNOWLEDGMENTS

We thank Dr James D. Michelson, Dr Jacob Shaw, and Kristen Koeller for their feedback and support throughout the project.

ABBREVIATIONS

CDC: Centers for Disease Control and Prevention
COVID-19: coronavirus disease 2019
ICD-10: *International Classification of Diseases, 10th Revision*
ILI: influenzalike illness
LOINC: Logical Observation Identifiers Names and Codes
SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

POTENTIAL CONFLICT OF INTEREST: Dr A. Muchmore is founder and CEO of CodoniX, Inc. Mr Lee is a CodoniX employee. Mr Muchmore and Dr P. Muchmore consult for CodoniX. Drs A. Muchmore and P. Muchmore own stock in CodoniX, Inc.

REFERENCES

1. Dawood FS, Chung JR, Kim SS, et al. Interim estimates of 2019–20 seasonal influenza vaccine effectiveness - United States, February 2020. [published correction appears in *MMWR Morb Mortal Wkly Rep*. 2020;69(12):358]. *MMWR Morb Mortal Wkly Rep*. 2020; 69(7):177–182
2. Centers for Disease Control and Prevention COVID-19 Response Team. Preliminary estimates of the prevalence of selected underlying health conditions among patients with coronavirus disease 2019 - United States, February 12–March 28, 2020. *MMWR Morb Mortal Wkly Rep*. 2020; 69(13):382–386
3. Kissler SM, Tedijanto C, Goldstein E, Grad YH, Lipsitch M. Projecting the transmission dynamics of SARS-CoV-2 through the postpandemic period. *Science*. 2020;368(6493):860–868
4. Monto AS, DeJonge PM, Callear AP, et al. Coronavirus occurrence and transmission over 8 years in the HIVE cohort of households in Michigan. *J Infect Dis*. 2020;222(1):9–16
5. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020;395(10223):507–513
6. Cheng MP, Papenburg J, Desjardins M, et al. Diagnostic testing for severe acute respiratory syndrome-related coronavirus 2: a narrative review. *Ann Intern Med*. 2020;172(11): 726–734
7. Guan W-J, Ni Z-Y, Hu Y, et al; China Medical Treatment Expert Group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. 2020;382(18): 1708–1720

Routine Intubation in Newborns With Congenital Diaphragmatic Hernia

Suzan C.M. Cochius-den Otter, MD,[a] Emily J.J. Horn-Oudshoorn, MD,[b] Karel Allegaert, MD, PhD,[b,c] Philip L.J. DeKoninck, MD, PhD,[d] Nina C.J. Peters, MD,[d] Titia E. Cohen-Overbeek, MD, PhD,[d] Irwin K.M. Reiss, MD, PhD,[b] Dick Tibboel, MD, PhD[a]

[b]Division of Neonatology, Department of Pediatrics and [d]Division of Obstetrics and Fetal Medicine, Department of Obstetrics and Gynaecology and [a]Intensive Care and Department of Pediatric Surgery, Erasmus University Medical Center, Rotterdam, Netherlands; and [c]Departments of Development and Regeneration and Pharmaceutical and Pharmacological Sciences, Katholieke Universiteit Leuven, Leuven, Belgium

Dr Cochius-den Otter conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript; Dr Horn-Oudshoorn collected data, drafted the initial manuscript, and reviewed and revised the manuscript; Prof Tibboel, Prof Allegaert, Dr DeKoninck, and Prof Reiss conceptualized and designed the study and critically reviewed the manuscript for important intellectual content; Drs Peters and Cohen-Overbeek coordinated and supervised data collection and revised the manuscript critically; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2020-1258

Accepted for publication Jul 29, 2020

Address correspondence to Suzan C.M. Cochius-den Otter, MD, Erasmus University Medical Center, Wytemaweg 80, 3015 CN, Rotterdam, Netherlands. E-mail: s.denotter@erasmusmc.nl

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Supported by the Friends of Sophia Hospital Foundation.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

To cite: Cochius-den Otter SCM, Horn-Oudshoorn EJJ, Allegaert K, et al. Routine Intubation in Newborns With Congenital Diaphragmatic Hernia. *Pediatrics*. 2020;146(4):e20201258

Congenital diaphragmatic hernia (CDH) is a rare developmental defect of the diaphragm and lungs, resulting in pulmonary hypoplasia and pulmonary hypertension (PH). With improved prenatal diagnostics, lung hypoplasia severity in CDH can be classified more accurately.[1,2] Infants with isolated left-sided CDH, observed-to-expected lung-to-head ratio (O/E LHR) ≥50%, and intraabdominal liver position are categorized as "mild lung hypoplasia" because their survival rate exceeds 95%.[1,3] All international guidelines advise routine intubation at birth for neonates with CDH to establish adequate oxygenation and cardiovascular stability.[4–7] However, in mild CDH, this potentially results in overtreatment and disturbance of physiologic perinatal transition.[8] Our aim with this study was to evaluate a spontaneous breathing approach (SBA) in the treatment algorithm of infants with mild CDH.

METHODS

After study approval by the local institutional review board (MEC2019-714) and waived informed consent, we performed a retrospective study in newborns with CDH born at Erasmus University Medical Center Rotterdam, a national and level 3 referral center with extracorporeal membrane oxygenation.

Our local protocol is based on the CDH EURO Consortium guidelines. Accordingly, we modified our protocol in December 2014, allowing planned SBA in patients with mild CDH born >35 weeks' gestation.[4] We used the O/E LHR measured between 24 and 38 weeks' gestational age.[1] Congenital anomalies were defined as anatomic anomalies on prenatal ultrasound or genetic mutations (microarray). We included all patients with mild CDH born between December 2014 and July 2019. The SBA was classified as failed if the infant required intubation any time before elective intubation for surgery. Surgery was planned electively with an experienced CDH operating team.

In our center, a perinatal treatment plan is made for all patients with CDH in a multidisciplinary team meeting at ~32 weeks' gestation, attended by obstetricians, fetal medicine specialists, neonatologists, pediatric intensivists, and surgeons. The treatment strategies are subsequently discussed with the parents, including an SBA if applicable. Postnatal resuscitation is executed according to CDH guidelines.[4] The newborn is positioned on the resuscitation table and a Replogle tube (10F catheter) is inserted for continuous stomach decompression. In the case of planned SBA, the infant is supported with oxygen if necessary (Neopuff infant T-piece resuscitator; Fisher & Paykel Healthcare, Ltd, Auckland, New Zealand), aiming for preductal saturations >85%.[4] Continuous positive airway pressure is allowed. The infant is intubated if insufflation breaths or ventilation are needed because positive pressure ventilation via mask increases the air in the digestive tract, subsequently compressing the lungs, resulting in hypoxia and PH.

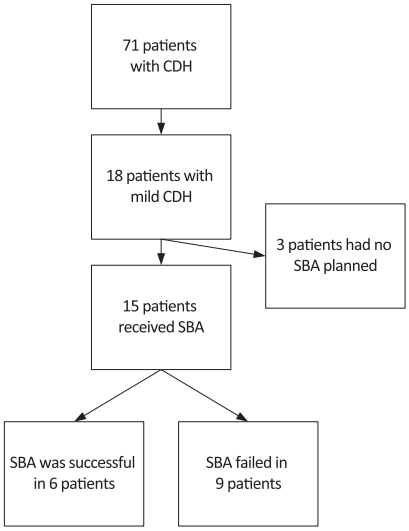


FIGURE 1
Patient flowchart. Flowchart of patient selection for the case series.

Patient characteristics and outcome parameters were described as numbers or percentages for categorical data or median (interquartile range [IQR]) for continuous data. The Mann–Whitney *U* test was used to compare patients with successful and failed SBA.

RESULTS

During the study period, 71 newborns with CDH were treated in our referral center, and 18 (25%) fulfilled the SBA criteria. However, in 3 patients, SBA was not prenatally planned and thus not performed (Fig 1). SBA was successful in 6 of 15 patients (40%); 3 required continuous positive airway pressure for several minutes, and 5 were transferred to the unit with binasal cannulae (Intersurgical, Inc, Syracuse, NY) with 1 to 2 L flow and 30% to 40% of inspired oxygen. All were electively intubated for surgery. In total, 9 of 15 patients required intubation after birth (7 at birth and 2 several hours after birth). Only 1 patient (O/E LHR 57%) developed PH and was treated with inhaled nitric oxide for 4 days and oxygen supplement therapy for 28 days. Apart from the anticipated difference in ventilation days and duration of oxygen therapy, there were no clinical differences between patients with successful and failed SBA (Table 1). The overall survival was 100%.

TABLE 1 Patients With and Without Successful SBA

	Successful SBA (n = 6)	Failed SBA (n = 9)	P
Male sex, %	50	78	—
Birth wt, kg, median (IQR)	2.78 (2.38–3.22)	3.0 (2.85–3.20)	.24
Apgar score 1 min, median (IQR)	7.5 (5.8–8)	6.5 (4.3–7.8)	.41
Apgar score 5 min, median (IQR)	8 (8–9.3)	7 (7–8.8)	.18
Gestational age at birth, wk, median (IQR)	37.8 (37.0–38.5)	38.3 (37.9–38.6)	.37
O/E LHR, %, median (IQR)	66 (49.8–82.3)	55 (52–64.5)	.56
Peak ventilator pressure,[a] cm H_2O, median (IQR)	23.5 (21.5–27)	23 (19.5–25)	.37
VIS score,[a] median (IQR)	0 (0–18.8)	4.6 (0–15.5)	.57
Days on ventilator, median (IQR)	1 (1–2.5)	7 (4–10)	<.05
Day of surgery, median (IQR)	3 (2–4)	3 (2–5)	.90
Defect type, *n* (%)			.89
A	0 (0)	2 (22)	—
B	2 (33)	5 (56)	—
C	1 (17)	0 (0)	—
D	0 (0)	0 (0)	—
Missing	3 (50)	2 (22)	—
Patch repair, *n* (%)	2 (33)	5 (56)	.53
Days on ventilator after surgery, median (IQR)	1 (1–2.5)	4 (2–5.5)	.05
Total oxygen therapy, d, median (IQR)	4.5 (2.5–7)	15 (5–17)	<.05
Discharge from ICU in d, median (IQR)	6 (5–10.75)	18 (7.5–25)	<.05
Discharge from the hospital in d, median (IQR)	18 (9–31.5)	28 (13.5–45)	.44
Medical support at discharge,[b] *n* (%)			
None	4 (66)	4 (44)	.7
G-tube feeding	2 (33)	5 (56)	—

G-tube, nasogastric tube; VIS, vasoactive inotropic support; —, not applicable.
[a] Recorded continuously during ICU admission.
[b] Defined as ventilatory, oxygen, pharmaceutical, G-tube feeding.

DISCUSSION

In the group of patients with mild CDH, a prenatally planned SBA is feasible. We consider it safe, and it avoids overtreatment with potential adverse side effects. Although numbers are low, and data are collected retrospectively in a single center, this suggests that individualized care in patients with CDH should be considered. By allowing SBA, iatrogenic complications due to prompt intubation and ventilation could be minimized. In addition, stress, pain, and the need for sedation is reduced in these infants; consequently, postnatal parent-infant interaction is improved. Delayed intubation did not seem to negatively affect outcomes. However, a larger prospective trial is needed to ensure that SBA is safe. Furthermore, we believe that this approach should only be done in expertise centers that have a multidisciplinary team of specialists caring for infants with CDH.

ABBREVIATIONS

CDH: congenital diaphragmatic hernia
IQR: interquartile range
O/E LHR: observed-to-expected lung-to-head ratio
PH: pulmonary hypertension
SBA: spontaneous breathing approach

REFERENCES

1. Snoek KG, Peters NCJ, van Rosmalen J, et al. The validity of the observed-to-expected lung-to-head ratio in congenital diaphragmatic hernia in an era of standardized neonatal treatment; a multicenter study. *Prenat Diagn*. 2017; 37(7):658–665

2. Oluyomi-Obi T, Kuret V, Puligandla P, et al. Antenatal predictors of outcome in prenatally diagnosed congenital diaphragmatic hernia (CDH). *J Pediatr Surg*. 2017;52(5):881–888
3. Russo FM, Cordier AG, De Catte L, Saada J, Benachi A, Deprest J; Workstream Prenatal Management, ERNICA European reference network. Proposal for standardized prenatal ultrasound assessment of the fetus with congenital diaphragmatic hernia by the European Reference Network on Rare Inherited and Congenital Anomalies (ERNICA). *Prenat Diagn*. 2018;38(9):629–637
4. Snoek KG, Reiss IK, Greenough A, et al; CDH EURO Consortium. Standardized postnatal management of infants with congenital diaphragmatic hernia in Europe: the CDH EURO Consortium consensus - 2015 update. *Neonatology*. 2016;110(1):66–74
5. Storme L, Boubnova J, Mur S, et al. Review shows that implementing a nationwide protocol for congenital diaphragmatic hernia was a key factor in reducing mortality and morbidity. *Acta Paediatr*. 2018;107(7): 1131–1139
6. Puligandla PS, Skarsgard ED, Offringa M, et al; Canadian Congenital Diaphragmatic Hernia Collaborative. Diagnosis and management of congenital diaphragmatic hernia: a clinical practice guideline. *CMAJ*. 2018;190(4):E103–E112
7. Jancelewicz T, Brindle ME, Guner YS, Lally PA, Lally KP, Harting MT; Congenital Diaphragmatic Hernia Study Group (CDHSG); Pediatric Surgery Research Collaborative (PedSRC). Toward standardized management of congenital diaphragmatic hernia: an analysis of practice guidelines. *J Surg Res*. 2019;243: 229–235
8. Dumpa V, Bhandari V. Surfactant, steroids and non-invasive ventilation in the prevention of BPD. *Semin Perinatol*. 2018;42(7):444–452

Well-Child Visits While in State Care

Rebeccah L. Sokol, PhD,[a] Alison L. Miller, PhD,[b] Joseph P. Ryan, PhD[c]

Given the rapid nature of development in early life (and the ability for developmental screenings to improve health trajectories), the American Academy of Pediatrics recommends that children attend regular well-child care visits (WCV) frequently between ages 0 and 5 years.[1,2] Children involved in the child welfare system are more likely to have developmental delays compared with their peers.[3–5] Thus, it is important for these children to attend recommended WCVs on time. National estimates suggest that 89% of children between ages 0 and 5 years attended a WCV in the past year.[6] Yet we do not have comparable estimates for children involved in the child welfare system. Using state-level administrative data, we undertook the current study to identify the proportion of young children (aged 0–5 years) in state care who attended (1) all recommended WCVs on time (question 1) and (2) at least 1 WCV in the past year (question 2). We further explored correlates of WCV attendance.

METHODS

The University of Michigan Institutional Review Board approved this research. We obtained child welfare administrative records for all substantiated referrals of child maltreatment in a midwestern state where the child entered state care between January 2017 and December 2019 (N = 12 824). Caseworkers enter information pertaining to their cases into the state administrative data system, and the study team extracted data pertinent to the current study from this system.

To address question 1, we excluded children who were older than 5 years (n = 7425), were in state custody for $<$1 month (n = 383), or had incomplete information on covariates (n = 1358), leaving an analytic sample of 3658.

To address question 2 and identify the proportion of children in care who attended a WCV in the past year (January 1, 2019, to –December 31, 2019), we further restricted our analytic sample to children who were in care for $\geq$1 year as of December 31, 2019, and who were still in care at this date (n = 2054).

State policy mandates that children in state care attend WCVs at 2, 4, 6, 9, 12, 15, and 18 months and at 2, 3, 4, and 5 years. Our question 1 outcome was a dichotomous variable indicating if a child attended all recommended WCVs while in care. For example, if a child was in care between ages 10 and 20 months, this child would have attended all WCVs if they had a 12-, 15-, and 18-month WCV. Our question 2 outcome was a dichotomous variable indicating if a child had attended any WCV within the 2019 calendar year. Covariates included child age, sex (male or female), race (Black or non-Black), duration of care, foster placement (kinship or nonkinship), and agency type (county or private).

To identify correlates of WCV attendance, we estimated multivariate logistic regressions and generated robust SEs clustered at the child welfare agency level.

RESULTS

Descriptive statistics stratified by race are provided in Table 1. Only 66% of

[a]School of Social Work, Wayne State University, Detroit, Michigan; and [b]Department of Health Behavior and Health Education, School of Public Health and [c]School of Social Work, University of Michigan, Ann Arbor, Michigan

Dr Sokol conceptualized and designed the study, conducted the initial analyses, drafted the initial manuscript, and reviewed and revised the manuscript; Drs Miller and Ryan supported the conceptualization of the study, reviewed and revised the analytic plan, and critically reviewed and revised the manuscript for important intellectual content; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2020-1539

Accepted for publication Jul 2, 2020

Address correspondence to Rebeccah L. Sokol, PhD, School of Social Work, Wayne State University, 5447 Woodward Ave, Detroit, MI 48202. E-mail: rlsokol@wayne.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Funded by a postdoctoral award through the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (F32HD100021-01). Funded by the National Institutes of Health (NIH).

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

To cite: Sokol RL, Miller AL, Ryan JP. Well-Child Visits While in State Care. *Pediatrics*. 2020; 146(4):e20201539

children attended all age-appropriate WCVs, but 95% attended at least 1 WCV in 2019 while in state care. Bivariate analyses illustrate significant differences in the primary outcomes between Black and non-Black children. Namely, a lower proportion of Black children attended any WCV in the past year compared with non-Black children (P = .04), and a lower proportion of Black children attended all WCVs while in state care (P = .04). Additionally, a higher proportion of Black children were in kinship placements compared with non-Black children; however, this difference only reached significance within the question 1 analytic sample.

Results of logistic regressions are provided in Table 2. Of note, Black children had lower odds of attending all WCVs while in state care compared with non-Black children (odds ratio [OR]: 0.78; 95% confidence interval [CI]: 0.64–0.94), and Black children also had lower odds of attending a WCV in the past year while in care (OR: 0.60; 95% CI: 0.38–0.94). Children placed with a relative had lower odds of attending all WCVs compared with children in nonkinship placements (OR: 0.87; 95% CI: 0.76–0.99).

TABLE 1 Descriptive Statistics of the Analytic Samples, Stratified by Race

	Question 1: Attending All WCVs			Question 2: Attending Any WCV in 2019		
	Black	Non-Black	Total	Black	Non-Black	Total
Attend all WCVs, % (*n*)	62 (719)[a]	68 (1702)[a]	66 (2421)[a]	—	—	—
Attend ≥1 WCV in 2019, % (*n*)	—	—	—	94 (748)[a]	96 (1202)[a]	95 (1950)[a]
Age, y, mean (SD)	1.57 (1.6)	1.50 (1.5)	1.55 (1.5)	2.89 (1.1)	2.89 (1.1)	2.89 (1.1)
Months in care, mean (SD)	15.1 (7.4)[a]	15.7 (7.5)[a]	15.5 (7.5)[a]	23.4 (9.2)[a]	21.4 (7.8)[a]	22.2 (8.4)[a]
Agency type, % (*n*)						
County	54 (627)	54 (1361)	54 (1988)	25 (201)	29 (363)	28 (564)
Private	46 (531)	46 (1139)	46 (1670)	75 (598)	71 (892)	73 (1490)
Sex, % (*n*)						
Male	53 (617)	52 (1302)	52 (1919)	54 (432)	52 (658)	53 (1090)
Female	47 (541)	48 (1198)	48 (1739)	46 (367)	48 (597)	47 (964)
Placement type, % (*n*)						
Kinship	57 (665)[a]	53 (1335)[a]	45 (1658)[a]	47 (376)	38 (608)	48 (984)
Nonkinship	43 (493)[a]	47 (1165)[a]	55 (2000)[a]	53 (423)	52 (647)	52 (1070)
Total	1158	2500	3658	799	1255	2054

—, not applicable.

[a] Significant difference in percentages or means between Black and non-Black children at α = .05 according to Pearson's χ^2 test (proportions) or the t test (means).

DISCUSSION

Although it is mandated that children entering state care attend all American Academy of Pediatrics–recommended WCVs, only 66% of 0- to 5-year-old children met this requirement. The percentage of young children in state care attending any WCV in the past year, however, was 95%, higher than both national (89%) and state (92%) levels.[6] This proportion was also higher than that of other subgroups of children. Nationally, 82% of children with >1 adverse childhood experience (eg, parent or guardian served time in jail) and 76% of children living in poverty attended a WCV in the past year.[6] Thus, being in state care may engage some children in WCVs who otherwise would not have received preventive care. A limitation of the current study, however, is that data only included information on WCVs while a child was in state care. Thus, we were unable to compare WCVs attended for children who were not in state care.

Children placed in kinship care were less likely to attend all WCVs while in care, and we posit that this is due to less caseworker involvement in kinship care cases compared with nonrelative foster care. Children in kinship placements experience fewer behavioral problems and mental health disorders, better well-being, and less placement disruption.[7,8] Given time and resource constraints, we hypothesize that caseworkers might bias their efforts toward

TABLE 2 ORs and Corresponding CIs for Children Aged 0–5 Years Attending (1) All WCVs (Versus Not Attending All Visits) and (2) at Least 1 WCV in the 2019 Calendar Year (Versus No Visits) While in State Custody

Variable	Question 1: Attending All WCVs While in State Care	Question 2: Attending Any WCV in 2019
Private agency (reference: county), OR (95% CI)	1.31 (1.01–1.70)*	1.34 (0.86–2.08)
Months in care, OR (95% CI)	1.03 (1.02–1.04)***	1.02 (0.99–1.05)
Black (reference: non-Black), OR (95% CI)	0.78 (0.64–0.94)*	0.60 (0.38–0.94)*
Age (y), OR (95% CI)	0.96 (0.89–1.03)	0.50 (0.44–0.58)***
Male sex (reference: female), OR (95% CI)	0.90 (0.79–1.03)	1.21 (0.80–1.83)
Kinship placement (reference: nonkinship), OR (95% CI)	0.87 (0.76–0.99)*	1.31 (0.84–2.03)
Total	3649	2054

In the analysis, clustered robust SEs were used for generating CIs at the agency level.

* $P < .05$.

** $P < .01$.

*** $P < .001$.

nonrelative foster care cases, including ensuring that these cases are adhering to state policy (eg, WCV attendance). Additionally, there are likely caseworker reporting errors within the administrative data system. These errors may be systematic (eg, caseworkers might be less likely to collect data from kinship placements compared with nonkinship placements); however, we do not know the exact nature of such biases.

Although more children in a midwestern state's care attended WCVs compared with children in the general or other high-risk populations, Black children were less likely to attend WCVs. Not only are Black children more likely to become involved in the child welfare system,[9] but our analyses also suggest that Black children do not receive equal treatment within the system. As described above, this may be due to caseworkers focusing more on certain cases at the expense of others. Indeed, we found a higher proportion of Black children in kinship placements compared with non-Black children, and kinship placements may not receive equal caseworker effort compared with nonkinship placements. Yet significant racial disparities in WCV attendance remained even after controlling for placement type. Given systematic biases and the overrepresentation of Black children within the child welfare system, this finding may be an artifact of caseworker overload in counties with a higher proportion of Black individuals as a percentage of the total population. In future work, researchers should consider how primary care providers and caseworkers can support Black children in state care to encourage on-time WCVs.

CONCLUSIONS

Children within state care attend WCVs at higher rates compared with children in the general population and other at-risk groups. Racial disparities in WCVs, however, perpetuate within the child welfare system.

ABBREVIATIONS

CI: confidence interval
OR: odds ratio
WCV: well-child care visit

REFERENCES

1. Noritz GH, Murphy NA; Neuromotor Screening Expert Panel. Motor delays: early identification and evaluation [published correction appears in *Pediatrics*. 2017;140(3):e20172081]. *Pediatrics*. 2013;131(6). Available at: www.pediatrics.org/cgi/content/full/131/6/e2016
2. Lipkin PH, Macias MM; Council on Children With Disabilities; Section on Developmental and Behavioral Pediatrics. Promoting optimal development: identifying infants and young children with developmental disorders through developmental surveillance and screening. *Pediatrics*. 2020;145(1):e20193449
3. Lightfoot E, Hill K, LaLiberte T. Prevalence of children with disabilities in the child welfare system and out of home placement: an examination of administrative records. *Child Youth Serv Rev*. 2011;33(11):2069–2075
4. Slayter E. Youth with disabilities in the United States child welfare system. *Child Youth Serv Rev*. 2016;64:155–165
5. Nanni V, Uher R, Danese A. Childhood maltreatment predicts unfavorable course of illness and treatment outcome in depression: a meta-analysis. *Am J Psychiatry*. 2012;169(2):141–151
6. Child and Adolescent Health Measurement Initiative. *2017 National Survey of Children's Health (NSCH) Data Query*. Rockville, MD: Maternal and Child Health Bureau, Health Resources and Services Administration, US Department of Health and Human Services
7. Winokur MA, Holtan A, Batchelder KE. Systematic review of kinship care effects on safety, permanency, and well-being outcomes. *Res Soc Work Pract*. 2018;28(1):19–32
8. Ariyo E, Mortelmans D, Wouters E. The African child in kinship care: a systematic review. *Child Youth Serv Rev*. 2019;98:178–187
9. US Department of Health and Human Services; Administration for Children and Families; Administration on Children, Youth and Families; Children's Bureau. Child maltreatment 2018. 2020. Available at: https://www.acf.hhs.gov/sites/default/files/cb/cm2018.pdf. Accessed February 6, 2020

Racial and/or Ethnic and Socioeconomic Disparities of SARS-CoV-2 Infection Among Children

Monika K. Goyal, MD, MSCE,[a,b] Joelle N. Simpson, MD, MPH,[a,b] Meleah D. Boyle, MPH,[a] Gia M. Badolato, MPH,[a] Meghan Delaney, DO, MPH,[a,b,c] Robert McCarter, ScD,[a,b] Denice Cora-Bramble, MD, MBA[a,b]

abstract

OBJECTIVES: To evaluate racial and/or ethnic and socioeconomic differences in rates of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection among children.

METHODS: We performed a cross-sectional study of children tested for SARS-CoV-2 at an exclusively pediatric drive-through and walk-up SARS-CoV-2 testing site from March 21, 2020, to April 28, 2020. We performed bivariable and multivariable logistic regression to measure the association of patient race and/or ethnicity and estimated median family income (based on census block group estimates) with (1) SARS-CoV-2 infection and (2) reported exposure to SARS-CoV-2.

RESULTS: Of 1000 children tested for SARS-CoV-2 infection, 20.7% tested positive for SARS-CoV-2. In comparison with non-Hispanic white children (7.3%), minority children had higher rates of infection (non-Hispanic Black: 30.0%, adjusted odds ratio [aOR] 2.3 [95% confidence interval (CI) 1.2–4.4]; Hispanic: 46.4%, aOR 6.3 [95% CI 3.3–11.9]). In comparison with children in the highest median family income quartile (8.7%), infection rates were higher among children in quartile 3 (23.7%; aOR 2.6 [95% CI 1.4–4.9]), quartile 2 (27.1%; aOR 2.3 [95% CI 1.2–4.3]), and quartile 1 (37.7%; aOR 2.4 [95% CI 1.3–4.6]). Rates of reported exposure to SARS-CoV-2 also differed by race and/or ethnicity and socioeconomic status.

CONCLUSIONS: In this large cohort of children tested for SARS-CoV-2 through a community-based testing site, racial and/or ethnic minorities and socioeconomically disadvantaged children carry the highest burden of infection. Understanding and addressing the causes of these differences are needed to mitigate disparities and limit the spread of infection.

WHAT'S KNOWN ON THIS SUBJECT: Racial and/or ethnic and socioeconomic disparities in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection have been reported among adults but are understudied in relation to infection risk in children.

WHAT THIS STUDY ADDS: In this cross-sectional study of a large cohort of children tested in the United States for SARS-CoV-2 through an exclusively pediatric drive-through and walk-up testing site, rates of SARS-CoV-2 infection were disproportionately higher among minority and socioeconomically disadvantaged youth.

To cite: Goyal MK, Simpson JN, Boyle MD, et al. Racial and/or Ethnic and Socioeconomic Disparities of SARS-CoV-2 Infection Among Children. *Pediatrics*. 2020;146(4): e2020009951

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-009951

[a]Children's National Hospital, Washington, District of Columbia; and [b]Departments of Pediatrics and [c]Pathology, The George Washington University, Washington, District of Columbia

Dr Goyal conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript; Dr Simpson conceptualized and designed the study, designed the data collection instruments, coordinated and supervised data collection, and reviewed and revised the manuscript; Ms Boyle and Ms Badolato collected data, conducted the initial analyses, and reviewed and revised the manuscript; Dr Delaney coordinated and supervised data collection and reviewed and revised the manuscript; Dr McCarter supervised and conducted the analyses and reviewed and revised the manuscript; Dr Cora Bramble conceptualized and designed the study and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2020-009951

Accepted for publication Jul 30, 2020

Outcomes of Maternal-Newborn Dyads After Maternal SARS-CoV-2

Sourabh Verma, MD,[a,e] Chanda Bradshaw, MD,[a,e] N.S. Freda Auyeung, MD, MPH,[a] Rishi Lumba, MD,[a] Jonathan S. Farkas, MD,[a,e] Nicole B. Sweeney, DO,[d] Elena V. Wachtel, MD, MPH,[a,e] Sean M. Bailey, MD,[a,e] Asif Noor, MD,[d] Bgee Kunjumon, MD,[a] Erin Cicalese, MD,[a,e] Rahul Hate, MD,[a] Jennifer L. Lighter, MD,[a,e] Samantha Alessi, MSN, AACNS-N,[a] William E. Schweizer, MD, MPH,[b] Nazeeh Hanna, MD,[d] Ashley S. Roman, MD, MPH,[c] Benard Dreyer, MD,[a,e] Pradeep V. Mally, MD[a,e]

abstract

BACKGROUND AND OBJECTIVES: Infection with a novel coronavirus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become a global pandemic. There are limited data describing the impact of SARS-CoV-2 infection on pregnant mothers and their newborns. The objective of this study is to describe characteristics and outcomes of maternal-newborn dyads with confirmed maternal SARS-CoV-2.

METHODS: This was a multicenter, observational, descriptive cohort study with data collection from charts of maternal-newborn dyads who delivered at 4 major New York City metropolitan area hospitals between March 1 and May 10, 2020, with maternal SARS-CoV-2 infection.

RESULTS: There were a total of 149 mothers with SARS-CoV-2 infection and 149 newborns analyzed (3 sets of twins; 3 stillbirths). Forty percent of these mothers were asymptomatic. Approximately 15% of symptomatic mothers required some form of respiratory support, and 8% required intubation. Eighteen newborns (12%) were admitted to the ICU. Fifteen (10%) were born preterm, and 5 (3%) required mechanical ventilation. Symptomatic mothers had more premature deliveries (16% vs 3%, $P = .02$), and their newborns were more likely to require intensive care (19% vs 2%, $P = .001$) than asymptomatic mothers. One newborn tested positive for SARS-CoV-2, which was considered a case of horizontal postnatal transmission.

CONCLUSIONS: Although there was no distinct evidence of vertical transmission from mothers with SARS-CoV-2 to their newborns, we did observe perinatal morbidities among both mothers and newborns. Symptomatic mothers were more likely to experience premature delivery and their newborns to require intensive care.

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-005637

Departments of [a]Pediatrics and [b]Obstetrics and Gynecology, and [c]Division of Maternal Fetal Medicine, New York University Grossman School of Medicine, New York, New York; [d]Department of Pediatrics, New York University Long Island School of Medicine, New York University, New York, New York; and [e]Department of Pediatrics, Bellevue Hospital Center, New York, New York

Drs Verma, Bradshaw, Lumba, and Mally conceptualized and designed the study, did acquisition of data, helped in analysis and interpretation of data, and drafted the initial manuscript; Drs Auyeung, Hate, Farkas, Kunjumon, Sweeney, and Dr Noor, Ms Alessi, and Dr Cicalese provided substantial contribution to acquisition of data; Drs Wachtel, Bailey, Roman, Dreyer, Schweizer, Hanna, and Lighter provided substantial contribution to analysis and interpretation of data; and all authors critically reviewed and revised the manuscript and approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2020-005637

Accepted for publication Jul 29, 2020

WHAT'S KNOWN ON THIS SUBJECT: Pregnant mothers appear to be at similar risk of getting infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as other healthy adults.

WHAT THIS STUDY ADDS: Vertical transmission from pregnant mothers with SARS-CoV-2 to newborns seems less likely, but there can be significant perinatal morbidities among mothers and newborns. Symptomatic mothers with SARS-CoV-2 were more likely to experience premature delivery and their newborns requiring intensive care.

To cite: Verma S, Bradshaw C, Auyeung NSF, et al. Outcomes of Maternal-Newborn Dyads After Maternal SARS-CoV-2. *Pediatrics.* 2020;146(4):e2020005637

Well-being of Parents and Children During the COVID-19 Pandemic: A National Survey

Stephen W. Patrick, MD, MPH, MS,[a,b,c,d] Laura E. Henkhaus, PhD,[a,c,e] Joseph S. Zickafoose, MD, MS,[a,b,f] Kim Lovell, MPH, MBA,[a,c] Alese Halvorson, MS,[g] Sarah Loch, MPH,[a] Mia Letterie, BA,[a] Matthew M. Davis, MD, MAPP[h,i]

abstract

BACKGROUND: As the coronavirus disease pandemic spread across the United States and protective measures to mitigate its impact were enacted, parents and children experienced widespread disruptions in daily life. Our objective with this national survey was to determine how the pandemic and mitigation efforts affected the physical and emotional well-being of parents and children in the United States through early June 2020.

METHODS: In June 2020, we conducted a national survey of parents with children age <18 to measure changes in health status, insurance status, food security, use of public food assistance resources, child care, and use of health care services since the pandemic began.

RESULTS: Since March 2020, 27% of parents reported worsening mental health for themselves, and 14% reported worsening behavioral health for their children. The proportion of families with moderate or severe food insecurity increased from 6% before March 2020 to 8% after, employer-sponsored insurance coverage of children decreased from 63% to 60%, and 24% of parents reported a loss of regular child care. Worsening mental health for parents occurred alongside worsening behavioral health for children in nearly 1 in 10 families, among whom 48% reported loss of regular child care, 16% reported change in insurance status, and 11% reported worsening food security.

CONCLUSIONS: The coronavirus disease pandemic has had a substantial tandem impact on parents and children in the United States. As policy makers consider additional measures to mitigate the health and economic effects of the pandemic, they should consider the unique needs of families with children.

WHAT'S KNOWN ON THIS SUBJECT: The coronavirus disease 2019 (COVID-19) pandemic and protective measures associated with it created widespread disruptions in daily life of US parents and children. Families with children disproportionately live in poverty, potentially increasing their risk to COVID-19–related economic distress and difficulties sustaining basic needs.

WHAT THIS STUDY ADDS: COVID-19 has had a substantial impact on the well-being of parents and children. As policy makers consider additional measures to mitigate the health and economic effects of the pandemic, they should consider the unique needs of families with children.

To cite: Patrick SW, Henkhaus LE, Zickafoose JS, et al. Well-being of Parents and Children During the COVID-19 Pandemic: A National Survey. *Pediatrics.* 2020;146(4):e2020016824

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-016824

[a]Vanderbilt Center for Child Health Policy and [b]Departments of Pediatrics, [c]Health Policy, and [g]Biostatistics, Vanderbilt University Medical Center, Nashville, Tennessee; [d]Mildred Stahlman Division of Neonatology and [e]Data Science Institute, Vanderbilt University, Nashville, Tennessee; [f]Mathematica, Nashville, Tennessee; [h]Mary Ann & J. Milburn Smith Child Health Research, Outreach, and Advocacy Center, Stanley Manne Children's Research Institute, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, Illinois; and [i]Departments of Pediatrics, Medicine, Medical Social Sciences, and Preventive Medicine, Feinberg School of Medicine, Northwestern University, Chicago, Illinois

Dr Patrick conceptualized the study, was involved in conducting the analysis and in interpretation of the results, drafted the initial manuscript, and approved the final manuscript as submitted; Dr Davis conceptualized the study, was involved in conducting the analysis and in interpretation of the results, and approved the final manuscript as submitted; Ms Halvorson conducted the analysis, was involved in interpretation of the results, and revised and approved the manuscript as written; Drs Henkhaus and Zickafoose and Ms Lovell, Ms Letterie, and Ms Loch were involved in the analytic plan and interpretation of the results and revised and approved the manuscript as written; (Continued)

COVID-19 and the Well-being of Children and Families

Ryan J. Coller, MD, MPH, Sarah Webber, MD

No one is immune to the effects of coronavirus disease 2019 (COVID-19). Although the United States has >4 million confirmed cases and >144 000 deaths at the time of this writing,[1] COVID-19's effects on individuals and communities extend far beyond hospitalizations and mortality. Pandemics disturb individual and community well-being through direct effects of the illness and through emotional isolation, economic loss, work and school closure, and inadequate distribution of needed resources, among others.[2] Previous research highlights consequences of pandemic mitigation efforts (such as quarantine) on stress, depression, fear, anger, boredom, stigma, and other negative states.[3] Adults already report worse psychological well-being now as compared to before COVID-19.[4] Because data suggest that children might less frequently transmit[5] or become severely ill from the virus,[6,7] the unique consequences that COVID-19 exerts on children risk being overlooked. Data on child and family well-being during COVID-19 are sparse, yet recent reports of increased family violence are ominous.[8] Given the body of knowledge of the damaging effects of toxic stress and adverse childhood experiences on developing brains and lifelong health,[9] a clearer representation of how the pandemic is affecting children and families is urgently needed.

Addressing this critical issue in this month's *Pediatrics*, Patrick et al[10] report findings from a cross-sectional survey inquiring how COVID-19 has affected the physical and emotional health of US parents and children. By leveraging an existing panel, the research team rapidly deployed a novel online survey to parents (N = 1011) of children aged <18 years, generating nationally representative estimates of changes in well-being between March and June. Patrick et al[10] observed that more than one-quarter of parents reported worse mental health and that 14% reported worse behavioral health in their children. Results were most striking for single parents and parents of the youngest children, of whom approximately one-third reported worse mental health. Nearly 1 in 4 lost regular child care, and modest changes in food insecurity and employer-sponsored insurance coverage were observed.

These findings are foreboding even if some expected higher rates of worsening well-being. The effects of stress during crises are cumulative, and we should expect well-being outcomes to worsen with time. Consequences of isolation and quarantine are perpetuated by longer duration, financial loss, and preexisting mental health challenges, and they can persist beyond the quarantine period.[3] Data from the severe acute respiratory syndrome coronavirus 1 epidemic in 2003 suggest that members of the general public impacted by the epidemic (ie, quarantined) had psychiatric symptoms months after the epidemic's control.[11] Additionally, common survey limitations, including cross-sectional rather than longitudinal data collection, social desirability bias,

Department of Pediatrics, School of Medicine and Public Health, University of Wisconsin–Madison, Madison, Wisconsin

DOI: https://doi.org/10.1542/peds.2020-022079

Accepted for publication Jul 27, 2020

Address correspondence to Ryan J. Coller, MD, MPH, Department of Pediatrics, School of Medicine and Public Health, University of Wisconsin–Madison, 600 Highland Ave, Madison, WI 53792. E-mail: rcoller@pediatrics.wisc.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

COMPANION PAPER: A companion to this article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-016824.

To cite: Coller RJ and Webber S. COVID-19 and the Well-being of Children and Families. *Pediatrics*. 2020;146(4):e2020022079

or unintended selection bias due to COVID-19 itself, could skew the results toward more neutral findings.

Families' experiences of the pandemic are not uniform. Baseline physical and mental health, local and state policy decisions,[12] race and/or ethnicity,[13,14] economic stability,[15] individual and community resources,[13] immigration status,[16] and geography[17] all influence the relationship between COVID-19 and well-being. In the study by Patrick et al,[10] although some parents reported worse child physical health, even more reported better physical health. Exploring what drove some parents to report improvements in child and/or parent mental or physical health could inspire novel interventions to bolster resilience during the pandemic. Longitudinal analyses may reveal COVID-19's dynamic relationship with well-being. Future studies quantifying variation in well-being metrics within communities and over time could reveal best- and worst-case scenarios for children and families, expose critical inequities, and help uncover novel risk and protective factors to guide policy.

The pandemic has wide-reaching ramifications, and responses must account for its impact on children and families. With their findings, Patrick et al[10] reiterate the need for clinicians to address these concepts during routine encounters. Researchers can build on this study by expanding the conceptualization of well-being to integrate resilience, positive social connection, purpose, autonomy, etc[18] in observational and interventional studies. Policy makers should address several immediate challenges on the horizon facing families. Although the Families First Coronavirus Response Act[19] and the Coronavirus Aid, Relief, and Economic Securities Act[20] may have temporized well-being consequences, unemployment subsidies and eviction moratoria expire at the end of July, eroding safeguards against homelessness, hunger, and poverty.[21–23] Schools are unlikely to open for most children next year, despite providing vital access to food for >30 million children[24] as well as health and therapeutic services.[25] Online school may be more challenging for children with special health care needs.[26] Limited child care will strain working parents, especially mothers. Racial and/or ethnic disparities in COVID-19 infection and consequences[27,28] are inexcusable and should be addressed directly. A full recovery from COVID-19 will require care for the well-being of our populations. The study by Patrick et al[10] is a valuable step toward that recovery.

ABBREVIATION

COVID-19: coronavirus disease 2019

REFERENCES

1. Johns Hopkins University of Medicine Coronavirus Resource Center. COVID-19 dashboard by the Center for Systems Science and Engineering at Johns Hopkins University. Available at: https://coronavirus.jhu.edu/map.html. Accessed July, 24, 2020
2. Pfefferbaum B, North CS. Mental health and the Covid-19 pandemic. *N Engl J Med*. 2020;383(6):510–512
3. Brooks SK, Webster RK, Smith LE, et al. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. *Lancet*. 2020;395(10227):912–920
4. Vindegaard N, Benros ME. COVID-19 pandemic and mental health consequences: systematic review of the current evidence. Brain Behav Immun. 2020:S0889-1591(20):30954-5
5. Posfay-Barbe KM, Wagner N, Gauthey M, et al. COVID-19 in children and the dynamics of infection in families. *Pediatrics*. 2020;146(2):e20201576
6. Castagnoli R, Votto M, Licari A, et al. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children and adolescents: a systematic review [published online ahead of print April 22, 2020]. *JAMA Pediatr*. doi:10.1001/jamapediatrics.2020.1467
7. Shekerdemian LS, Mahmood NR, Wolfe KK, et al; International COVID-19 PICU Collaborative. Characteristics and outcomes of children with Coronavirus disease 2019 (COVID-19) infection admitted to US and Canadian pediatric intensive care units [published online ahead of print May 11, 2020]. *JAMA Pediatr*. doi:10.1001/jamapediatrics.2020.1948
8. Kofman YB, Garfin DR. Home is not always a haven: the domestic violence crisis amid the COVID-19 pandemic. *Psychol Trauma*. 2020;12(S1):S199–S201
9. Shonkoff JP, Garner AS; Committee on Psychosocial Aspects of Child and Family Health; Committee on Early Childhood, Adoption, and Dependent Care; Section on Developmental and Behavioral Pediatrics. The lifelong effects of early childhood adversity and toxic stress. *Pediatrics*. 2012;129(1). Available at: www.pediatrics.org/cgi/content/full/129/1/e232
10. Patrick SW, Henkhaus LE, Zickafoose JS, et al. Well-being of parents and children during the COVID-19 pandemic: a national survey. *Pediatrics*. 2020;146(4):e2020016824
11. Peng EYC, Lee MB, Tsai ST, et al. Population-based post-crisis psychological distress: an example from the SARS outbreak in Taiwan. *J Formosa Med Assoc*. 2010;109(7):524–532
12. Hsiang S, Allen D, Annan-Phan S, et al. The effect of large-scale anti-contagion policies on the COVID-19 pandemic [published online ahead of print June 8, 2020]. *Nature*. doi:10.1038/s41586-020-2404-8
13. Berkowitz SA, Cené CW, Chatterjee A. Covid-19 and health equity - time to think big [published online ahead of print July 22, 2020]. *N Engl J Med*. doi:10.1056/NEJMp2021209
14. van Dorn A, Cooney RE, Sabin ML. COVID-19 exacerbating inequalities in the US. *Lancet*. 2020;395(10232):1243–1244
15. Dooley DG, Bandealy A, Tschudy MM. Low-income children and coronavirus disease 2019 (COVID-19) in the US

[published online ahead of print May 13, 2020]. *JAMA Pediatr*. doi:10.1001/jamapediatrics.2020.2065

16. Wilson FA, Stimpson JP. US policies increase vulnerability of immigrant communities to the COVID-19 pandemic. *Ann Glob Health*. 2020;86(1):57
17. CDC COVID-19 Response Team. Geographic differences in COVID-19 cases, deaths, and incidence - United States, February 12-April 7, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(15):465–471
18. Centers for Disease Control and Prevention. Health-related quality of life (HRQOL): well-being concepts. Available at: https://www.cdc.gov/hrqol/wellbeing.htm#three. Accessed July 24, 2020
19. Families First Coronavirus Response Act, HR 6201, 116th Cong (2019–2020). Available at: https://www.congress.gov/bill/116thcongress/house-bill/6201/text. Accessed July 24, 2020
20. Coronavirus Aid, Relief, and Economic Security Act, S 2548, 116th Cong, 2nd Sess (2019–2020). Available at: https://www.congress.gov/bill/116th-congress/senate-bill/3548/text. Accessed July 24, 2020
21. Consumer Financial Protection Bureau. Protections for renters. Available at: https://www.consumerfinance.gov/coronavirus/mortgage-and-housing-assistance/renter-protections/. Accessed July 24, 2020
22. Merle R. A federal eviction moratorium ends this week, putting 12 million tenants at risk. *Washington Post*. July 21, 2020. Available at: https://www.washingtonpost.com/business/2020/07/21/eviction-moratorium-ending/. Accessed July 21, 2020
23. Casselman B. End of $600 unemployment bonus could push millions past the brink. *New York Times*. July 21, 2020. Available at: https://www.nytimes.com/2020/07/21/business/economy/coronavirus-unemployment-benefits.html. Accessed July 21, 2020
24. US Department of Agriculture. The national school lunch program. Available at: https://fns-prod.azureedge.net/sites/default/files/resource-files/NSLPFactSheet.pdf. Accessed July 24, 2020
25. Gustafson EM. History and overview of school-based health centers in the US. *Nurs Clin North Am*. 2005;40(4):595–606, vii
26. Thompson LA, Ferdig R, Black E. Online schools and children with special health and educational needs: comparison with performance in traditional schools. *J Med Internet Res*. 2012;14(3):e62
27. Millett GA, Jones AT, Benkeser D, et al. Assessing differential impacts of COVID-19 on black communities. *Ann Epidemiol*. 2020;47:37–44
28. Kim EJ, Marrast L, Conigliaro J. COVID-19: magnifying the effect of health disparities [published online ahead of print May 11, 2020]. *J Gen Intern Med*. doi:10.1007/s11606-020-05881-4

COVID-19 and Parent-Child Psychological Well-being

Anna Gassman-Pines, PhD,[a] Elizabeth Oltmans Ananat, PhD,[b] John Fitz-Henley, II, BA[a]

abstract

BACKGROUND AND OBJECTIVES: The outbreak of coronavirus disease 2019 has changed American society in ways that are difficult to capture in a timely manner. With this study, we take advantage of daily survey data collected before and after the crisis started to investigate the hypothesis that the crisis has worsened parents' and children's psychological well-being. We also examine the extent of crisis-related hardships and evaluate the hypothesis that the accumulation of hardships will be associated with parent and child psychological well-being.

METHODS: Daily survey data were collected between February 20 and April 27, 2020, from hourly service workers with a young child (aged 2–7) in a large US city (N = 8222 person-days from 645 individuals). A subsample completed a one-time survey about the effects of the crisis fielded between March 23 and April 26 (subsample n = 561).

RESULTS: Ordered probit models revealed that the frequency of parent-reported daily negative mood increased significantly since the start of the crisis. Many families have experienced hardships during the crisis, including job loss, income loss, caregiving burden, and illness. Both parents' and children's well-being in the postcrisis period was strongly associated with the number of crisis-related hardships that the family experienced.

CONCLUSIONS: Consistent with our hypotheses, in families that have experienced multiple hardships related to the coronavirus disease 2019 crisis, both parents' and children's mental health is worse. As the crisis continues to unfold, pediatricians should screen for mental health, with particular attention to children whose families are especially vulnerable to economic and disease aspects of the crisis.

WHAT'S KNOWN ON THIS SUBJECT: The outbreak of coronavirus disease 2019 has profoundly affected many American families. One major consequence of the crisis has been huge increases in unemployment. However, less is known about the psychological consequences of the crisis for families.

WHAT THIS STUDY ADDS: This study reveals that parent psychological well-being worsened after the restrictions that were put in place in response to the coronavirus outbreak. The more coronavirus disease 2019–related hardships that families experienced, the worse parents' and children's psychological well-being.

To cite: Gassman-Pines A, Ananat EO, Fitz-Henley J. COVID-19 and Parent-Child Psychological Well-being. *Pediatrics*. 2020;146(4):e2020007294

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-007294

[a]*Sanford School of Public Policy, Duke University, Durham, North Carolina; and* [b]*Department of Economics, Barnard College, Columbia University, New York, New York*

Prof Ananat and Prof Gassman-Pines conceptualized and designed the study, designed the data collection instruments, coordinated and supervised data collection, drafted the initial manuscript, and reviewed and revised the manuscript; Mr Fitz-Henley conducted the initial analyses and critically reviewed the manuscript for important intellectual content; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2020-007294

Accepted for publication Jul 30, 2020

Address correspondence to Anna Gassman-Pines, PhD, Sanford School of Public Policy, Duke University, Box 90312, Durham, NC 27708. E-mail: agassman.pines@duke.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

COVID-19 Disease Severity Risk Factors for Pediatric Patients in Italy

Stefania Bellino, PhD,[a,*] Ornella Punzo, MD, PhD,[a,*] Maria Cristina Rota, MD,[a] Martina Del Manso, DStat,[a] Alberto Mateo Urdiales, MD,[a] Xanthi Andrianou, PhD,[a] Massimo Fabiani, DStat,[a] Stefano Boros,[a] Fenicia Vescio, MD, Flavia Riccardo, MD,[a] Antonino Bella, DStat,[a] Antonietta Filia, MD, PhD,[a] Giovanni Rezza, MD,[b] Alberto Villani, MD, PhD,[c] Patrizio Pezzotti, DStat,[a] COVID-19 WORKING GROUP

abstract

OBJECTIVES: To describe the epidemiological and clinical characteristics of coronavirus disease (COVID-19) pediatric patients aged <18 years in Italy.

METHODS: Data from the national case-based surveillance system of confirmed COVID-19 infections until May 8, 2020, were analyzed. Demographic and clinical characteristics of subjects were summarized by age groups (0–1, 2–6, 7–12, 13–18 years), and risk factors for disease severity were evaluated by using a multilevel (clustered by region) multivariable logistic regression model. Furthermore, a comparison among children, adults, and elderly was performed.

RESULTS: Pediatric patients (3836) accounted for 1.8% of total infections (216 305); the median age was 11 years, 51.4% were male, 13.3% were hospitalized, and 5.4% presented underlying medical conditions. The disease was mild in 32.4% of cases and severe in 4.3%, particularly in children ≤6 years old (10.8%); among 511 hospitalized patients, 3.5% were admitted in ICU, and 4 deaths occurred. Lower risk of disease severity was associated with increasing age and calendar time, whereas a higher risk was associated with preexisting underlying medical conditions (odds ratio = 2.80, 95% confidence interval = 1.74–4.48). Hospitalization rate, admission in ICU, disease severity, and days from symptoms onset to recovery significantly increased with age among children, adults and elderly.

CONCLUSIONS: Data suggest that pediatric cases of COVID-19 are less severe than adults; however, age ≤1 year and the presence of underlying conditions represent severity risk factors. A better understanding of the infection in children may give important insights into disease pathogenesis, health care practices, and public health policies.

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-009399

[a]Department of Infectious Diseases, Istituto Superiore di Sanità, Rome, Italy; [b]General Directorate for Prevention, Ministry of Health, Rome, Italy; and [c]General Pediatrics and Infectious Diseases Unit, Pediatric Hospital Bambino Gesù, Rome, Italy [*]Contributed equally as co-first authors

Dr Bellino performed the statistical analyses and drafted the manuscript; Dr Punzo contributed to collect the clinical data and drafted the manuscript; Drs Rota, Filia, Rezza, and Prof Villani critically reviewed the manuscript; Drs Del Manso, Mateo Urdiales, Andrianou, Fabiani, Vescio, and Mr Boros contributed to collect the data and conducted the final database; Dr Riccardo contributed to the coordination of the coronavirus disease national surveillance; Dr Bella coordinated and supervised the surveillance data collection; Dr Pezzotti is the head of the Italian coronavirus disease surveillance system and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2020-009399

Accepted for publication Jul 9, 2020

WHAT'S KNOWN ON THIS SUBJECT: Although coronavirus disease is less frequent and often less severe in children compared with adults, limited data exist on risk factors for disease severity and death in pediatric patients.

WHAT THIS STUDY ADDS: In the current study, we describe pediatric cases (persons aged <18 years) of severe acute respiratory syndrome coronavirus 2 infection in Italy and compare them with adult and elderly patients. Underlying medical conditions and younger age represent risk factors for disease severity among children and adolescents.

To cite: Bellino S, Punzo O, Rota MC, et al. COVID-19 Disease Severity Risk Factors for Pediatric Patients in Italy. *Pediatrics.* 2020;146(4):e2020009399

Early Experience of COVID-19 in a US Children's Hospital

Mundeep K. Kainth, DO, MPH,[a,b,c] Pratichi K. Goenka, MD,[a,b] Kristy A. Williamson, MD,[a,b] Joanna S. Fishbein, MPH,[c] Anupama Subramony, MD, MBA,[a,b] Stephen Barone, MD,[a,b] Joshua A. Belfer, MD,[a] Lance M. Feld, MD,[a] William I. Krief, MD,[a,b] Nancy Palumbo, MD,[a,b] Sujatha Rajan, MD,[a,b] Joshua Rocker, MD,[a,b] Tiffany Scotto, BS,[a] Smiriti Sharma, MD,[a,b] William C. Sokoloff, MD,[a] Charles Schleien, MD, MBA,[a,b] Lorry G. Rubin, MD,[a,b,c] NORTHWELL HEALTH COVID-19 RESEARCH CONSORTIUM

abstract

OBJECTIVES: We aim to describe the demographics, clinical presentation, hospital course, and severity of pediatric inpatients with coronavirus disease 2019 (COVID-19), with an emphasis on healthy, immunocompromised, and chronically ill children.

METHODS: We conducted a single-center retrospective cohort study of hospitalized children aged younger than 22 years with COVID-19 infection at Steven and Alexandra Cohen Children's Medical Center at Northwell Health. Cases were identified from patients with fever and/or respiratory symptoms who underwent a nucleic acid amplification–based test for severe acute respiratory syndrome coronavirus 2.

RESULTS: Sixty-five patients were identified. The median age was 10.3 years (interquartile range, 1.4 months to 16.3 years), with 48% of patients older than 12 years and 29% of patients younger than 60 days of age. Fever was present in 86% of patients, lower respiratory symptoms or signs in 60%, and gastrointestinal symptoms in 62%. Thirty-five percent of patients required ICU care. The white blood cell count was elevated in severe disease (P = .0027), as was the C-reactive protein level (P = .0192), compared with mild and moderate disease. Respiratory support was required in 34% of patients. Severity was lowest in infants younger than 60 days of age and highest in chronically ill children; 79% of immunocompromised children had mild disease. One death was reported.

CONCLUSIONS: Among children who are hospitalized for COVID-19, most are younger than 60 days or older than 12 years of age. Children may have severe infection requiring intensive care support. The clinical course of immunocompromised patients was not more severe than that of other children. Elevated white blood cell count and C-reactive protein level are associated with greater illness severity.

WHAT'S KNOWN ON THIS SUBJECT: Pediatric coronavirus disease 2019 (COVID-19) is less common than adult COVID-19. Reports of COVID-19 in hospitalized children have varied from severe disease in infants and adolescents to disease primarily in children with underlying conditions.

WHAT THIS STUDY ADDS: Among inpatients, COVID-19 was common and mild in infants younger than age 60 days and severe in older, healthy children. Approximately half of all children were chronically ill or immunocompromised. Elevation of white blood cell count and C-reactive protein level correlated with severity.

To cite: Kainth MK, Goenka PK, Williamson KA, et al. Early Experience of COVID-19 in a US Children's Hospital. *Pediatrics.* 2020;146(4):e2020003186

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-003186

[a]*Department of Pediatrics, Cohen Children's Medical Center, Northwell Health, Queens, New York;* [b]*Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Northwell Health, Hempstead, New York; and* [c]*Institute of Molecular Medicine, Feinstein Institutes for Medical Research, Northwell Health, Manhasset, New York*

Drs Kainth, Goenka, Williamson, and Rubin conceptualized and designed the study, designed the data collection instruments, coordinated and supervised data collection, drafted the initial manuscript, and critically reviewed and revised the manuscript for important intellectual content; Ms Fishbein and Dr Subramony conducted the analysis, validated the integrity of data collection, and reviewed and revised the manuscript; Dr Schleien critically reviewed and revised the manuscript for important intellectual content; Drs Barone, Belfer, Feld, Krief, Palumbo, Rajan, Rocker, Sharma, and Sokoloff collected data and reviewed and revised the manuscript; Ms Scotto designed the data collection instruments; and all authors approved the final manuscript as submitted.

Persistent Hypertension in Children and Adolescents: A 6-Year Cohort Study

David C. Kaelber, MD, PhD, MPH,[a,b,c] A. Russell Localio, PhD,[a,d] Michelle Ross, PhD,[a,d] Janeen B. Leon, MS, RDN, LD,[a,b] Wilson D. Pace, MD,[a,e] Richard C. Wasserman, MD, MPH,[a,f,g] Robert W. Grundmeier, MD,[a,f,h,i,j,k] Jennifer Steffes,[a,f] Alexander G. Fiks, MD, MSCE[a,f,h,i,j,k]

abstract

OBJECTIVES: To determine the natural history of pediatric hypertension.

METHODS: We conducted a 72-month retrospective cohort study among 165 primary care sites. Blood pressure measurements from two consecutive 36 month periods were compared.

RESULTS: Among 398 079 primary care pediatric patients ages 3 to 18, 89 347 had ≥3 blood pressure levels recorded during a 36-month period, and 43 825 children had ≥3 blood pressure levels for 2 consecutive 36-month periods. Among these 43 825 children, 4.3% (1881) met criteria for hypertension (3.5% [1515] stage 1, 0.8% [366] stage 2) and 4.9% (2144) met criteria for elevated blood pressure in the first 36 months. During the second 36 months, 50% (933) of hypertensive patients had no abnormal blood pressure levels, 22% (406) had elevated blood pressure levels or <3 hypertensive blood pressure levels, and 29% (542) had ≥3 hypertensive blood pressure levels. Of 2144 patients with elevated blood pressure in the first 36 months, 70% (1492) had no abnormal blood pressure levels, 18% (378) had persistent elevated blood pressure levels, and 13% (274) developed hypertension in the second 36-months. Among the 7775 patients with abnormal blood pressure levels in the first 36-months, only 52% (4025) had ≥3 blood pressure levels recorded during the second 36-months.

CONCLUSIONS: In a primary care cohort, most children initially meeting criteria for hypertension or elevated blood pressure had subsequent normal blood pressure levels or did not receive recommended follow-up measurements. These results highlight the need for more nuanced initial blood pressure assessment and systems to promote follow-up of abnormal results.

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2019-3778

This article has an accompanying video summary.

[a]*Comparative Effectiveness Research through Collaborative Electronic Reporting Consortium Research Team, Elk Grove Village, Illinois;* [b]*Center for Clinical Informatics Research and Education and* [c]*Departments of Internal Medicine, Pediatrics, Population and Quantitative Health Sciences, The MetroHealth System, Case Western Reserve University, Cleveland, Ohio;* [d]*Department of Biostatistics, Epidemiology, and Informatics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania;* [e]*American Academy of Family Physicians, National Research Network, Leawood, Kansas;* [f]*Pediatric Research in Office Settings, American Academy of Pediatrics, Elk Grove Village, Illinois;* [g]*Department of Pediatrics, Larner College of Medicine, University of Vermont, Burlington, Vermont;* [h]*The Pediatric Research Consortium, Philadelphia, Pennsylvania;* [i]*Department of Biomedical and Health Informatics, Philadelphia, Pennsylvania;* [j]*Center for Pediatric Clinical Effectiveness, Philadelphia, Pennsylvania; and* [k]*PolicyLab at The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania*

Dr Kaelber conceptualized and designed the study, assisted in obtaining data, drafted the initial manuscript, and reviewed the manuscript; Dr Localio helped design the study, led and helped conduct data analyses, helped draft the initial manuscript, and reviewed the manuscript; Dr Ross helped design the study, helped conduct data analyses, and reviewed the manuscript; Ms Leon helped design the study, assisted in obtaining data, drafted the initial manuscript, and reviewed the manuscript; Dr Pace helped design the study, assisted in obtaining data, and reviewed the manuscript; Dr Wasserman helped conceptualize and design the study, assisted in obtaining data, and reviewed the manuscript; (Continued)

WHAT'S KNOWN ON THIS SUBJECT: Pediatric hypertension, currently defined as 3 high blood pressure levels, is known to be underdiagnosed. No studies using routine clinical measurements in primary care show the natural history of pediatric hypertension.

WHAT THIS STUDY ADDS: We show that most children and adolescents meeting criteria for hypertension have their abnormal blood pressure levels normalize over several years with repeated measurement. Many children even with stage 2 hypertension do not have routine blood pressure levels measured annually.

To cite: Kaelber DC, Localio AR, Ross M, et al. Persistent Hypertension in Children and Adolescents: A 6-Year Cohort Study. *Pediatrics.* 2020;146(4):e20193778

Stability of Blood Pressure and Diagnosis of Hypertension in Childhood

Joseph T. Flynn, MD, MS

Department of Pediatrics, School of Medicine, University of Washington; and Division of Nephrology, Seattle Children's Hospital, Seattle, Washington

DOI: https://doi.org/10.1542/peds.2020-018481

Accepted for publication Jul 9, 2020

Address correspondence to Joseph T. Flynn, MD, MS, Division of Nephrology, Seattle Children's Hospital, 4800 Sand Point Way NE, M/S OC.9.820, Seattle, WA 98105. E-mail: joseph.flynn@seattlechildrens.org

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: Dr Flynn reports receipt of personal fees from Silvergate Pharmaceuticals, UptoDate, and Springer and grant support from the American Heart Association and National Institute of Diabetes and Digestive and Kidney Diseases, all unrelated to this work.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

COMPANION PAPER: A companion to this article can be found online at www.pediatrics.org/cgi/doi/10.1542/2019-3778.

To cite: Flynn JT. Stability of Blood Pressure and Diagnosis of Hypertension in Childhood. *Pediatrics*. 2020;146(4):e2020018481

Longitudinal tracking studies as well as multiple long-term cohort studies have demonstrated that blood pressure (BP) in childhood tracks into adulthood and that individuals with high BP levels in childhood are more likely to develop intermediate markers of cardiovascular disease by adulthood than those with normal BP.[1] What is less well understood is what happens to childhood BP levels over shorter periods of time: weeks, months, or just a few years? This question is relevant to making a diagnosis of hypertension because the 2017 American Academy of Pediatrics (AAP) Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents (CPG) recommends repeat BP measurements over a period of weeks to months (depending on how high the BP category) before making a diagnosis of hypertension.[2] This recommendation is based on the known lability of childhood BP over short time periods, a point that was established by Ogborn and Crocker over 30 years ago.[3]

In their study reported in this issue of *Pediatrics*, Kaelber et al[4] provide some new insights into this question. Using electronic health record data, they retrospectively examined BP measurements from primary care practices to ascertain the natural history of abnormal childhood BP measurements over 2 consecutive 36-month periods. They found that only 30% of children with BP readings in the elevated category diagnosed over the first 36 months continued to have abnormal BP readings during the second 36 months and that 48% of children meeting criteria for stage 1 hypertension during the first 36 months continued to demonstrate abnormal BP during the second 36 months. An additional finding only briefly mentioned by the authors was that 12% of children with elevated BP progressed to a higher BP category, and 5% of children with stage 1 hypertension progressed to stage 2 hypertension in the second 36 months. Similar findings have been seen in analyses of school BP screening data from the Houston Pediatric and Adolescent Hypertension Program,[5] as well as from analyses of the National High Blood Pressure Education Program childhood hypertension database,[6] which highlights the need for ongoing follow-up of abnormal BP readings in a child or adolescent. Finally, they found that many children with initially elevated or hypertensive BP readings failed to receive follow-up BP readings as recommended in the AAP CPG.

As noted by the authors, these data have notable limitations, especially reliance on BP readings obtained across a wide variety of clinical sites that would no doubt have used a variety of BP measurement devices and protocols. The standardized BP measurement protocol outlined in the AAP CPG,[2] specifically the use of carefully obtained auscultatory BP readings, is designed to minimize variability and, if followed, should result in more reliable data. Standardized BP measurement has also been recommended for diagnosis of hypertension in adults[7] and has been

successfully used in research studies involving children.[8,9] Reliance on office BP measurements alone may also be problematic because some of the children diagnosed with elevated BP and hypertension may have actually had white coat hypertension if 24-hour ambulatory BP monitoring had been performed to confirm the diagnosis.[2]

The issue of failure to follow guidelines in the diagnosis of childhood hypertension has been described by multiple studies dating back to Dr Kaelber's 2007 study demonstrating that only 22% of children who met the criteria from the 2004 National High Blood Pressure Education Program Fourth Report[10] for diagnosis of hypertension were actually diagnosed as having hypertension.[11] Fast-forward to 2020, three years after publication of the AAP CPG; we continue to see papers outlining missed or delayed subspecialty referral for evaluation of hypertension[12] and failure to perform recommended BP screening in young children with underlying conditions known to predispose to the development of hypertension.[13] Unfortunately, failure to adhere to guidelines is not unique to BP measurement and diagnosis of hypertension; even height and weight are frequently not documented at preventive and well-child visits.[14] The current study certainly shines additional light on this problem but does not provide new insights on how to improve guideline adherence.

In this study, Kaelber et al[4] confirm that BP in childhood can vary over time; from a prevention standpoint, the fact that some children's BP falls over time is less important than the fact that a notable percentage progress to higher BP categories. Repeated measures of BP over time by using a standard technique are needed to identify children who may be at risk for developing adult cardiovascular disease.

ABBREVIATIONS

AAP: American Academy of Pediatrics
BP: blood pressure
CPG: Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents

REFERENCES

1. Flynn JT. High blood pressure in the young: why should we care? *Acta Paediatr*. 2018;107(1):14–19
2. Flynn JT, Kaelber DC, Baker-Smith CM, et al; Subcommittee on Screening and Management of High Blood Pressure in Children. Clinical practice guideline for screening and management of high blood pressure in children and adolescents. *Pediatrics*. 2017;140(3): e20171904
3. Ogborn MR, Crocker JF. Investigation of pediatric hypertension. Use of a tailored protocol. *Am J Dis Child*. 1987;141(11):1205–1209
4. Kaelber DC, Localio AR, Leon JB, et al. Persistent hypertension in children and adolescents: a 6-year cohort study. *Pediatrics*. 2020;146(4):e20193778
5. Redwine KM, Acosta AA, Poffenbarger T, Portman RJ, Samuels J. Development of hypertension in adolescents with pre-hypertension. *J Pediatr*. 2012;160(1): 98–103
6. Falkner B, Gidding SS, Portman R, Rosner B. Blood pressure variability and classification of prehypertension and hypertension in adolescence. *Pediatrics*. 2008;122(2):238–242
7. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2018;71(19):2199–2269
8. Mendizábal B, Urbina EM, Becker R, et al. SHIP-AHOY (study of high blood pressure in pediatrics: adult hypertension onset in youth). *Hypertension*. 2018;72(3):625–631
9. Wilson AC, Flynn JT. Blood pressure in children with chronic kidney disease: lessons learned from the Chronic Kidney Disease in Children Cohort Study. *Pediatr Nephrol*. 2020;35(7): 1203–1209
10. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. *Pediatrics*. 2004;114(2, suppl 4th Report):555–576
11. Hansen ML, Gunn PW, Kaelber DC. Underdiagnosis of hypertension in children and adolescents. *JAMA*. 2007; 298(8):874–879
12. Hamby T, Pueringer MR, Noorani S, Khanna A, Barrow J, Razzouk R. Time to referral to a nephrology clinic for pediatric hypertension. *Pediatr Nephrol*. 2020;35(5):907–910
13. Shah L, Hossain J, Xie S, Zaritsky J. Poor adherence to early childhood blood pressure measurement guidelines in a large pediatric healthcare system. *Pediatr Nephrol*. 2019;34(4):697–701
14. Burman NJ, Cabana MD, Maselli JH, Hilton JF, Patel AI. Missing documentation of weight and height at preventive visits for children. *Clin Pediatr (Phila)*. 2012;51(10):933–938

Children's Relative Age and ADHD Medication Use: A Finnish Population-Based Study

Miika Vuori, PhD, RMN,[a] Jaana E. Martikainen, PhD,[b] Anna Koski-Pirilä, PhD,[c] Andre Sourander, MD, PhD,[d,e,f] Anita Puustjärvi, MD,[g] Eeva T. Aronen, MD, PhD,[h,i] Roshan Chudal, MBBS, MPH, PhD,[d,e] Leena K. Saastamoinen, PhD[b]

abstract

OBJECTIVES: The youngest children in a classroom are at increased risk of being medicated for attention-deficit/hyperactivity disorder (ADHD). We examined the association between children's birth month and ADHD medication rates in Finland.

METHODS: Using a population-based study, we analyzed ADHD medication use among children born in 2005 to 2007. Cases (n = 7054) were identified from the first purchase of medication for ADHD. Cox proportional hazard models and hazard ratios (HRs) were examined by birth month and sex. Finnish children start first grade in the year of their seventh birthday. The cutoff date is December 31.

RESULTS: Risk of ADHD medication use increased throughout the year by birth month (ie, January through April to May through August to September through December). Among boys born in September to December, the association remained stable across cohorts (HR: 1.3; 95% confidence interval [CI]: 1.1–1.5). Among girls born in September to December, the HR in the 2005 cohort was 1.4 (95% CI: 1.1–1.8), whereas in the 2007 cohort it was 1.7 (95% CI: 1.3–2.2). In a restricted follow-up, which ended at the end of the year of the children's eighth birthday, the HRs for boys and girls born in September to December 2007 were 1.5 (95% CI: 1.3–1.7) and 2.0 (95% CI: 1.5–2.8), respectively.

CONCLUSIONS: Relative immaturity increases the likelihood of ADHD medication use in Finland. The association was more pronounced during the first school years. Increased awareness of this association is needed among clinicians and teachers.

WHAT'S KNOWN IN THIS SUBJECT: The relative age effect (RAE) in attention-deficit/hyperactivity disorder (ADHD) indicates that ADHD medication use is more common in the relatively youngest children within a school grade. Within-country sex differences in ADHD medication use vary and are among the largest in Finland.

WHAT THIS STUDY ADDS: This population-based study reveals that the RAE in ADHD medication use among children was more pronounced during the first school years (ages 6–8). The RAE in ADHD medication was stable among boys across 3 cohorts but increasing among girls.

To cite: Vuori M, Martikainen JE, Koski-Pirilä A, et al. Children's Relative Age and ADHD Medication Use: A Finnish Population-Based Study. *Pediatrics*. 2020;146(4): e20194046

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2019-4046

[a]Department of Teacher Education, Turku Institute of Advanced Studies, [d]Department of Child Psychiatry, and [f]Invest Flagship, University of Turku, Turku, Finland; [b]Research Unit and [c]Statistical Information Service, The Social Insurance Institution (Kela), Helsinki, Finland; [e]Department of Child Psychiatry, Turku University Hospital, Turku, Finland; [g]Kuopio University Hospital, Kuopio, Finland; and [h]Department of Child Psychiatry and [i]Laboratory of Developmental Psychopathology, Pediatric Research Center, Children's Hospital, University of Helsinki and Helsinki University Hospital, Helsinki, Finland

Mr Vuori conceptualized and designed the study, coordinated data collection, conducted the initial analyses, drafted the initial manuscript, and reviewed and revised the manuscript; Ms Koski-Pirilä conceptualized and designed the study, collected data, and reviewed and revised the manuscript; Ms Martikainen, Ms Saastamoinen, Profs Sourander and Aronen, and Drs Puustjärvi and Chudal conceptualized and designed the study and critically reviewed the manuscript for important intellectual content; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Deidentified individual participant data will not be made available.

DOI: https://doi.org/10.1542/peds.2019-4046

Keeping Relative Age Effects and ADHD Care in Context

Eric M. Butter, PhD

The diagnosis and treatment of attention-deficit/hyperactivity disorder (ADHD) requires discerning clinical judgment and deliberate shared decision-making between parents, teachers, and other engaged caregivers. ADHD is widely accepted as a neurodevelopmental disorder that emerges early in life and has life span implications for many. The functional impairment associated with ADHD is significant, and the available treatments, including medication, can be effective at improving educational, behavioral, and social-emotional functioning. Missing or delaying the diagnosis of ADHD can lead to unnecessary suffering and poor adaptation for children.[1] Similarly, overdiagnosing and overprescribing to children who are misidentified as having ADHD brings many serious adverse consequences, including medication side effects such as sleep disturbance, appetite suppression, and cardiovascular system impacts as well as negative psychosocial sequelae of being misdiagnosed with a behavioral health disorder.

In this issue of *Pediatrics*, Vuori et al,[2] using a national registry from Finland, report on the relative age effect (RAE) associated with ADHD diagnoses in which the youngest children in a classroom are at the higher risk of being diagnosed with ADHD and being prescribed medications compared with older classmates. This study builds on the findings of Sayal et al[3] and others, which document that a younger relative age increases the risk of being diagnosed with ADHD. Support for the RAE has grown in the literature, and a significant body of evidence documents similar observations of 6the RAE worldwide.[4]

Many may interpret the findings of relative age impacts on rates of diagnosis of ADHD and medication use as reflecting teacher biases rather than a true presence of the disorder in some younger children. From this perspective, the finding suggests that teachers are more likely to initiate a diagnostic process for less mature children who may exhibit more problematic behavior in the classroom than slightly older peers. This line of thinking suggests that there is a bias in referring younger children for an evaluation of ADHD symptoms supported by both the teacher's intention to help the identified children and difficulty to manage classroom behavior of relatively immature students. Vuori et al[2] and most others who have reported on RAEs and ADHD recommend a reconsideration of school entry regulations and increased classroom contingency management programs.

This understanding of the association between the RAE and inappropriate ADHD diagnoses and treatment assumes the diagnostic assessment process lacks sufficient internal validity to combat the underlying bias. It further assumes that when an ADHD diagnosis is sought, one will be obtained, sometimes regardless of critical clinical discernment. In addition, the implied impact of the RAE by these authors is that the risk to beginning medication for ADHD is directly related to being diagnosed with ADHD and, thus, is routinely or

Nationwide Children's Hospital and The Ohio State University, Columbus, Ohio

DOI: https://doi.org/10.1542/peds.2020-022798

Accepted for publication Jul 29, 2020

Address correspondence to Eric M. Butter, PhD, Department of Pediatric Psychology and Neuropsychology, Nationwide Children's Hospital, 700 Children's Drive, JWest Building 3rd Floor, Columbus, OH 43205. E-mail: eric.butter@nationwidechildrens.org

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The author has indicated he has no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The author has indicated he has no potential conflicts of interest to disclose.

COMPANION PAPER: A companion to this article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2019-4046.

To cite: Butter EM. Keeping Relative Age Effects and ADHD Care in Context. *Pediatrics*. 2020; 146(4):e2020022798

automatically connected to teacher bias against younger children in their classrooms. This presumed process toward inappropriate prescribing also implies that there are flaws in how decisions are made by physicians to begin ADHD medications with young children. The necessary practice changes recommended by those who understand the RAE this way would be to implore parents or teachers to provide information about ADHD symptoms, keeping the child's relative age in mind as they report to the provider. Presumably, analysis of the child's age in relation to the age for school entry could be used to influence starting medication treatment in a child newly diagnosed with ADHD or even whether medication treatment should be continued for a child or adolescent with a long-standing history of ADHD. Although there is much unproven in this reasoning, the reminder that age matters when considering developmental psychopathology seems like an appropriate and worthy caution.

There are other considerations, however. Vuori et al[2] do offer that their study does not settle whether increased medication use in younger children was due to "misidentification of ADHD or, perhaps, to the fact that relative immaturity aggravates ADHD traits." Indeed, an alternative explanation of the observation that younger children are more likely to be diagnosed with ADHD than older classroom peers is related to school entry being a trigger for ADHD symptoms. Similarly, the possibility also exists that older children among a school-year cohort, because of relative maturity, may be able to mask ADHD symptoms. Within limited and circumscribed contexts like the low academic demands and highly structured social environment of the first grades of schooling, these children's ADHD symptoms could be overlooked until more serious academic impacts, behavioral problems, and social deficits emerge later in childhood. Indeed, Vuori et al[2] and the body of research on the RAE in ADHD has not yet answered the question of the direction, cause, or implication of the effect. It remains to be seen if the RAE is a factor in overdiagnosing and overprescribing or is a signal that school entry could trigger ADHD symptoms in younger children and/or mask symptoms of ADHD in older children.

ADVANTAGES AND LIMITATIONS OF POPULATION-BASED REGISTRY RESEARCH

The research by Vuori et al[2] is another example of the effective use of large population-based registry databases to observe how a disease is manifesting within specific societal parameters or geographies. More, not less, of this kind of population-based research is needed in pediatric behavioral health. In this case, the observation is about ADHD in young children in Finland born ~15 years ago and diagnosed with ADHD before cautions about diagnosing ADHD in the context of relative immaturity were offered. The primary observation in this study is based on prescribing patterns that date back 9 years. The current data do not account for practice changes that may have occurred with cautions made by many organizations about RAE to consider children's symptoms relative to age and other contexts.

Aside from the conclusions being dated and historical, another concern is that the nature of large national registries allow for great variability and large unknowns in what diagnostic processes were used to identify ADHD. Also, the course of treatment is often not well characterized in registry research. That is the case here as well. In this cohort, the main finding is related to children who "received ADHD medication at least once" without regard for how the treatment course may have been adjusted over time. And, actually, the cohort is best defined as those children whose parents made "the first purchase of medication for ADHD." It is inappropriate for anyone to conclude sweeping statements implying biases toward overdiagnosing or overprescribing solely on the basis of the observations made in limited data sets, such as the one used here. At best, Vuori et al[2] and authors of other reports like it offer guidance for the questions yet to be asked and answered. In fact, the authors call for prospective studies to advance this knowledge. The conversation about RAE and ADHD is supported but not greatly advanced by this report, given the limited generalizability of the data set.

WHAT DO WE HAVE AND WHAT IS NEEDED TO RESPOND TO RAE IN ADHD?

There are many known limitations to our diagnostic classification systems for ADHD. Using only the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) as a diagnostic tool, clinicians may not adequately account for environmental contexts, may overly focus on individual functioning, and could struggle with defining the boundaries between subthreshold symptoms and disorder.[5] The questions raised by the RAE in ADHD lay at the center of these limitations of the DSM-5. The understanding of the developmental pathways of ADHD and the interconnections of ADHD diagnoses and treatment decisions with school and age require additional research and then application to practice.

Beyond the DSM-5, we do have best practice guidelines in diagnosing and treating ADHD.[6] The American Academy of Pediatrics "Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents" represents an opportunity to mitigate any negative consequences of the observed RAEs, such as those reported in Vuori et al.[2] This guideline, as well as others available to clinicians,

used in combination with responsible application of the DSM-5 criteria for ADHD, offers protection against inappropriate diagnosing and prescribing. It is widely accepted that to receive a diagnosis of ADHD a child must show a persistent pattern of inattention and/or hyperactivity-impulsivity across multiple settings. Critically, children's ADHD symptoms must be inconsistent with their developmental level, and it is recommended to use norm-referenced rating scales across multiple raters to aide in diagnostic assessment. Finally, a diagnostic impression for ADHD can only be positive if children's symptoms interfere with their everyday functioning. There must be clear impairment in academic, social, and occupational activities. In addition, ADHD diagnoses can be specified by the severity of symptoms. Clinicians can allow treatment to be guided by the level of mild, moderate, or severe presentations and age of the child. Best practice implementation could mitigate the implied bias in the reports of a RAE for ADHD among early school-aged cohorts.

CONCLUSIONS

There is risk that continued reporting on the RAEs on the diagnosis of ADHD and medication prescribing could inadvertently lead to delays in diagnosis of this impairing neurodevelopmental disability. More research is needed on understanding what causes this effect and the implications of it. However, any reminder for clinicians to use best practice guidelines in diagnosing and treating children with ADHD symptoms is welcomed. These guidelines include the recommendation that diagnosing and treating ADHD should be a developmentally sensitive process. The use of norm-referenced standardized rating scales, multiinformant and multidimensional assessment, and careful observation and monitoring of a child's symptoms and functional impairment remain critical foundations of treating ADHD in children. Another report observing that there is a RAE for ADHD diagnoses in young children is a reminder of the carefulness by which pediatricians and other clinical providers must approach this complicated developmental disability.

ABBREVIATIONS

ADHD: attention-deficit/hyperactivity disorder
DSM-5: *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*
RAE: relative age effect

REFERENCES

1. Nigg JT, Barkley RA. Attention-Deficit/Hyperactivity Disorder. In: Mash EJ, Barkley RA, eds. *Child Psychopathology*. New York, NY: The Guilford Press; 2014: 75–144
2. Vuori M, Turun Y, Martikainen J, et al. Children's relative age and ADHD medication use: a Finnish population-based study. *Pediatrics*. 2020;146(4): e20194046
3. Sayal K, Prasad V, Daley D, Ford T, Coghill D. ADHD in children and young people: prevalence, care pathways, and service provision. *Lancet Psychiatry*. 2018;5(2):175–186
4. Holland J, Sayal K. Relative age and ADHD symptoms, diagnosis and medication: a systematic review. *Eur Child Adolesc Psychiatry*. 2019;28(11): 1417–1429
5. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed. Washington, DC: American Psychiatric Association; 2013
6. Wolraich ML, Hagan JF Jr., Allan C, et al; Subcommittee on Children and Adolescents with Attention-Deficit/Hyperactive Disorder. Clinical practice guideline for the diagnosis, evaluation, and treatment of attention-deficit/hyperactivity disorder in children and adolescents. [published correction appears in *Pediatrics*. 2020;145(3): e20193997]. *Pediatrics*. 2019;144(4): e20192528

Trends in Human Papillomavirus Vaccination in Commercially Insured Children in the United States

Szu-Ta Chen, MD, PhD, MPH,[a] Krista F. Huybrechts, MS, PhD,[b] Brian T. Bateman, MD, MSc,[b,c] Sonia Hernández-Díaz, MD, DrPH[a]

abstract

OBJECTIVES: The human papillomavirus (HPV) vaccine was recommended in 2006 for girls and in 2011 for boys. The Healthy People 2020 goal for 2-dose HPV vaccination coverage is 80% by age 15 for girls and boys. We used nationwide population-based data to describe trends in HPV vaccination in children.

METHODS: We conducted a cohort study nested within the MarketScan health care database between January 2003 and December 2017. Children were followed from the year they turned 9 until HPV vaccination, insurance disenrollment, or the end of the year when they turned 17, whichever came first. We estimated the cumulative incidence of at least 1- and 2-dose HPV vaccination, stratified by birth year, sex, and state. In secondary analyses, we evaluated the association between state-level vaccination policies and HPV vaccination coverage.

RESULTS: This study included 7 837 480 children and 19.8 million person-years. The proportion of 15-year-old girls and boys with at least a 1-dose HPV vaccination increased from 38% and 5% in 2011 to 57% and 51% in 2017, respectively; the proportion with at least a 2-dose vaccination went from 30% and 2% in 2011 to 46% and 39% in 2017, respectively. By 2017, 2-dose HPV vaccination coverage varied from 80% in Washington, District of Columbia, among girls to 15% in Mississippi among boys and was positively correlated with legislation for HPV vaccine education and pediatrician availability.

CONCLUSIONS: Despite the increasing trends in uptake, HPV vaccine coverage among commercially insured children in the United States remains behind target levels, with substantial disparities by state.

WHAT'S KNOWN ON THIS SUBJECT: The human papillomavirus (HPV) vaccine has been recommended for girls since 2006 and for boys since 2011. The Healthy People 2020 goal for HPV vaccination coverage is 80% by age 15. There is a lack of nationwide population-based data on HPV vaccination.

WHAT THIS STUDY ADDS: This study revealed that by 2017, the HPV vaccine coverage by age 15 in commercially insured children was still lower than the Healthy People 2020 goal and that the substantial variability in coverage across states correlated with state-level vaccination policies.

To cite: Chen S, Huybrechts KF, Bateman BT, et al. Trends in Human Papillomavirus Vaccination in Commercially Insured Children in the United States. *Pediatrics*. 2020; 146(4):e20193557

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2019-3557

This article has an accompanying video summary.

[a]*Department of Epidemiology, Harvard T.H. Chan School of Public Health, Harvard University, Boston, Massachusetts; and* [b]*Division of Pharmacoepidemiology and Pharmacoeconomics, Departments of Medicine and* [c]*Anesthesiology, Perioperative and Pain Medicine, Brigham and Women's Hospital and Harvard Medical School, Harvard University, Boston, Massachusetts*

Dr Chen designed the study, conducted analyses, and wrote the manuscript; Drs Huybrechts and Bateman conceptualized the study and reviewed and revised the manuscript; Dr Hernández-Díaz conceptualized and designed the study, supervised data analyses, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

DOI: https://doi.org/10.1542/peds.2019-3557

Accepted for publication Jul 24, 2020

Address correspondence to Szu-Ta Chen, MD, PhD, MPH, Department of Epidemiology, Harvard T.H. Chan School of Public Health, Harvard University, 677 Huntington Ave, Boston, MA 02115. E-mail: szutachen@alumni.harvard.edu

Learning More About Ways to Improve Adolescent HPV Coverage

Amanda F. Dempsey, MD, PhD, MPH

Human papillomavirus (HPV) vaccines have been available for use in the United States since 2006 for girls and 2009 for boys.[1] Vaccination uptake levels among adolescents, the preferred age for vaccination, have been examined annually through several different mechanisms and found to be continually well below national goals.[2] The repetition of these findings is now, sadly, "old news." So you may be asking yourself, "Do we need yet another study on adolescent HPV vaccination coverage in the United States?" Based on the findings of the study by Chen et al[3] presented in this issue of *Pediatrics* the answer is a definitive "yes!" In this study, the authors provide some new and valuable insights regarding HPV vaccine uptake in the United States.

Like researchers in many other studies, these researchers used a nationwide, population-based database to examine HPV vaccination initiation and completion by age, sex, and geographic location. With >7 million children included, researchers in the study were well powered to examine differences in vaccination coverage by these and other factors. And, like in many other studies, Chen et al[3] demonstrated increasing vaccination levels over time, with no states reaching national target vaccination coverage levels of 80% series completion by age 15 years, and significant disparities between states in vaccination levels.

Although these data reiterate what has been demonstrated by others, a unique feature of this study is the ability of its researchers to study individuals over time, particularly at a national scope. The database, which represents commercially insured individuals, includes >800 000 children with continuous enrollment and data from age 9 to 17 years. It is from these longitudinal analyses that 2 unique insights arise.

The first comes from a longitudinal examination of vaccination levels among birth cohorts. This analysis shows us that with each subsequent year, we are able to achieve similar vaccination levels more and more quickly. For example, among the birth cohort from the year 2000, representing 17-year-olds at the time data were abstracted for the study, 40% vaccination coverage was achieved when this group was ~14 years old. In contrast, among the birth cohort from the year 2005, representing 12-year-olds at the time of data abstraction, 40% vaccination coverage was reached at the age of 12. So, although we still have not reached national target levels of 80% coverage by age 15 among any birth cohort, we are getting faster at reaching the levels we can currently achieve.

The second insight from these longitudinal analyses comes from using the trends in vaccination over time to model future projections of coverage. Using this approach, the authors estimate that by the year 2022, the 2012 birth cohort will have reached 80% coverage for the first dose in the HPV vaccine series. This would correspond to when this birth cohort is 17 years old. Given that at this age, most individuals will not have been

University of Colorado Denver, Aurora, Colorado

DOI: https://doi.org/10.1542/peds.2020-005454

Accepted for publication May 22, 2020

Address correspondence to Amanda F. Dempsey, MD, PhD, MPH, University of Colorado Denver, 13199 East Montview Blvd, Suite 300, Aurora, CO 80045. E-mail: amanda.dempsey@cuanschutz.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: Dr Dempsey serves on Advisory Boards for Merck, Pfizer, and Sanofi Pasteur. Dr Dempsey does not receive any research funding from these companies, nor did these companies play any role in this manuscript.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The author has indicated she has no potential conflicts of interest to disclose.

COMPANION PAPER: A companion to this article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2019-3557

To cite: Dempsey AF. Learning More About Ways to Improve Adolescent HPV Coverage. *Pediatrics*. 2020;146(4):e2020005454

exposed to most concerning disease-causing HPV types, achieving 80% vaccine coverage would be a major public health victory. This is especially so given that the models also suggest that levels will be equivalently high among both boys and girls. Yet, it is important to remind ourselves that that these models are for a single HPV vaccine dose. Two or 3 doses (depending on the age of initiation) of the HPV vaccine are currently recommended for optimal protection. Ongoing research is examining the benefit of just 1 dose, which may actually be quite substantial.[4]

A final set of interesting conclusions from this study comes from the authors' exploratory analyses examining the association between vaccine coverage levels and various state policies related to vaccination. Somewhat surprisingly, the statistical models presented did not support the hypothesis that the presence of a school requirement for vaccination (ie, a "school mandate") results in higher vaccine coverage levels. This contrasts past data for other vaccines in which it was demonstrated that mandates do have a substantial positive influence on vaccination coverage.[5] However, it is important to note that the number of states included in this category was small (Rhode Island, Virginia, and Washington DC), limiting conclusions on this point. The strongest association with increased vaccination coverage was the presence of "legislation to improve HPV education," associated with a 3% to 14% increase in vaccination, depending on the state. Pediatrician density was the third factor identified, with a ≤2% vaccination coverage increase for every additional pediatrician per 10 000 children available in the state. This last point is especially noteworthy given recent data demonstrating significant disparities among rural teens in HPV vaccine coverage compared with urban ones,[6] presumably due at least in part to lack of providers in rural areas.

As with any study, this study has limitations, the biggest being that it represents only commercially insured children. With ~40% of US children insured by Medicaid, and 5% uninsured,[7] it is not known how broadly the findings from this study can be translated to the US adolescent population as a whole. Despite this fact, there are some encouraging conclusions found in this study related to the ability to achieve national vaccination goals as well as important, and potentially actionable, findings that warrant close consideration by policy makers and the medical community at large regarding vaccination policies and workforce.

REFERENCES

1. Markowitz LE, Gee J, Chesson H, Stokley S. Ten years of human papillomavirus vaccination in the United States. *Acad Pediatr*. 2018;18(2S):S3–S10
2. Walker TY, Elam-Evans LD, Yankey D, et al. National, regional, state, and selected local area vaccination coverage among adolescents aged 13–17 Years - United States, 2018. *MMWR Morb Mortal Wkly Rep*. 2019; 68(33):718–723
3. Chen ST, Huybrechts KF, Bateman B, Hernandez-Diaz S. Trends in human papillomavirus vaccination in commercially insured children in the United States. *Pediatrics*. 2020;146(4): e20193557
4. Markowitz LE, Naleway AL, Klein NP, et al. Human papillomavirus vaccine effectiveness against HPV infection: evaluation of one, two, and three doses. *J Infect Dis*. 2020;221(6):910–918
5. Hinman AR, Orenstein WA, Williamson DE, Darrington D. Childhood immunization: laws that work. *J Law Med Ethics*. 2002;30(3 suppl):122–127
6. Walker TY, Elam-Evans LD, Williams CL, et al. Trends in human papillomavirus (HPV) vaccination initiation among adolescents aged 13–17 by metropolitan statistical area (MSA) status, National Immunization Survey - teen, 2013–2017. *Hum Vaccin Immunother*. 2020;16(3):554–561
7. Kaiser Family Foundation. Health insurance coverage of children 0-18. 2018. Available at: https://www.kff.org/other/state-indicator/children-0-18/?currentTimeframe=0&sortModel=%7B%22colId%22:%22Location%22,%22sort%22:%22asc%22%7D. Accessed June 14, 2009

Delivery and Impact of a Motivational Intervention for Smoking Cessation: A PROS Study

Jonathan D. Klein, MD, MPH,[a,b] Julie Gorzkowski, MSW, LSW,[b] Elissa A. Resnick, MPH,[a] Donna Harris, MA,[c] Kristen Kaseeska, MPH,[b] Lori Pbert, PhD,[d] Alex Prokorov, MD, PhD,[e] Tianxiu Wang, PhD, MS,[g] James Davis, MD,[c] Edward Gotlieb, MD,[c] Richard Wasserman, MD, MPH[c,f]

abstract

OBJECTIVES: We tested a Public Health Service 5As-based clinician-delivered smoking cessation counseling intervention with adolescent smokers in pediatric primary care practice.

METHODS: We enrolled clinicians from 120 practices and recruited youth (age ≥14) from the American Academy of Pediatrics Pediatric Research in Office Settings practice-based research network. Practices were randomly assigned to training in smoking cessation (intervention) or social media counseling (attentional control). Youth recruited during clinical visits completed confidential screening forms. All self-reported smokers and a random sample of nonsmokers were offered enrollment and interviewed by phone at 4 to 6 weeks, 6 months, and 12 months after visits. Measures included adolescents' report of clinicians' delivery of screening and counseling, current tobacco use, and cessation behaviors and intentions. Analysis assessed receipt of screening and counseling, predictors of receiving 5As counseling, and effects of interventions on smoking behaviors and cessation at 6 and 12 months.

RESULTS: Clinicians trained in the 5As intervention delivered more screening ($\beta = 1.0605$, $P < .0001$) and counseling ($\beta = 0.4354$, $P < .0001$). In both arms, clinicians more often screened smokers than nonsmokers. At 6 months, study arm was not significantly associated with successful cessation; however, smokers in the 5As group were more likely to have quit at 12 months. Addicted smokers more often were counseled, regardless of study arm, but were less likely to successfully quit smoking.

CONCLUSIONS: Adolescent smokers whose clinicians were trained in 5As were more likely to receive smoking screening and counseling than controls, but the ability of this intervention to help adolescents quit smoking was limited.

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-0644

[a]Department of Pediatrics, University of Illinois at Chicago, Chicago, Illinois; [b]Julius B. Richmond Center of Excellence, American Academy of Pediatrics, Itasca, Illinois; [c]Primary Care Research, American Academy of Pediatrics, Itasca, Illinois; [d]Department of Population and Quantitative Health Sciences, University of Massachusetts Medical School, Worcester, Massachusetts; [e]MD Anderson Center, Houston, Texas; [f]Department of Pediatrics, Larner College of Medicine, University of Vermont, Burlington, Vermont; and [g]Institute for Health Research and Policy, University of Illinois at Chicago, Chicago, Illinois

Drs Klein conceptualized and designed the study, drafted the initial manuscript, participated in analyses, and reviewed and revised the manuscript; Drs Pbert, Prokorov, Davis, Gotlieb, and Wasserman conceptualized and designed the study and reviewed and revised the manuscript; Ms Gorzkowski, Dr Wang, Ms Resnick, Ms Kaseeska, and Ms Harris participated in data analyses and in drafting, reviewing, and revising the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

WHAT'S KNOWN ON THIS SUBJECT: Tobacco use is a significant health issue for adolescents. Pediatricians have an opportunity to screen and counsel youth about smoking. There is limited evidence that brief cessation counseling for adolescent smokers results in cessation attempts or sustained abstinence.

WHAT THIS STUDY ADDS: In a 5As randomized control trial for adolescent smokers, intervention clinicians provided more screening and counseling than those in the control group; adolescents who received interventions more often tried to quit. Nicotine addiction was the strongest predictor of continued smoking.

To cite: Klein JD, Gorzkowski J, Resnick EA, et al. Delivery and Impact of a Motivational Intervention for Smoking Cessation: A PROS Study. *Pediatrics*. 2020;146(4):e20200644

Addressing Teenage Tobacco Use: Still an Urgent Issue for Pediatricians

Judith Groner, MD,[a] Sophie J. Balk, MD[b]

[a]*Nationwide Children's Hospital, Columbus, Ohio; and*
[b]*Children's Hospital at Montefiore, Bronx, New York*

DOI: https://doi.org/10.1542/peds.2020-010595

Accepted for publication Jun 18, 2020

Address correspondence to Judith Groner, MD, Nationwide Children's Hospital, 700 Children's Dr, Columbus, OH 43205. E-mail: judith.groner@nationwidechildrens.org

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

COMPANION PAPER: A companion to this article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-0644.

To cite: Groner J and Balk SJ. Addressing Teenage Tobacco Use: Still an Urgent Issue for Pediatricians. *Pediatrics.* 2020;146(4):e2020010595

Smoking is a pediatric disease that usually originates during adolescence, with 90% of adult smokers beginning to smoke before age 18.[1] Every day, nearly 200 youth under age 18 become regular cigarette smokers.[2] Adolescents' brains are uniquely susceptible to nicotine addiction, and youth become addicted far more quickly than they realize.[3,4] The US Preventive Services Task Force, which recently reassessed the evidence supporting youth-focused tobacco prevention and cessation efforts, continues to recommend that primary care clinicians provide interventions to prevent initiation of tobacco use among school-aged children and adolescents.[5] However, the Task Force identified key gaps in our knowledge about how to intervene once teenagers have already become smokers.[5] In this issue of *Pediatrics*, Klein et al[6] describe an office-based intervention that could help address this.

The investigators trained 120 clinicians in an intervention for smoking cessation based on the "5As" or in a control intervention (social media counseling). The 5As are the foundation for a brief intervention demonstrated to be effective for adults and include the following components: ask about tobacco use, advise to quit, assess willingness to make a quit attempt, assist those willing to attempt, and arrange follow-up.[7] Almost 11 000 adolescents were enrolled between January 2012 and December 2014, including 936 self-identified smokers. Not surprisingly, clinicians trained in the 5As were more likely to screen for smoking, assess quit readiness, and provide resources to quit.

The results of the trial, however, are somewhat disappointing. At 6 months, receipt of counseling did not affect motivation to quit. Surprisingly, smokers receiving counseling were more likely to report smoking in the past 30 days at this follow-up. Receipt of screening and counseling, regardless of study arm, did not affect motivation to quit. After adjusting for study arm assignment, demographics, receipt of counseling, addiction, and clinician behaviors, the only predictors of successful quitting were a lower addiction score and younger age. At 12 months, the results were similar. Those who received counseling, regardless of study arm, were more likely to have smoked in the past 30 days before the 12-month follow-up. There was, however, at 12 months, the suggestion of a delayed effect of being in the intervention arm. After adjusting for confounders, adolescents whose clinicians were in the intervention arm or who were female were more likely to quit. In addition, adolescents who were more addicted were less likely to quit.

Although this study did not find clear positive results for the 5As intervention, it does suggest a path forward for clinicians. The investigators demonstrated that clinicians can consistently provide screening, counseling, and resources for adolescents to help them quit smoking. Successful clinician training is necessary but not sufficient to reduce adolescent smoking.

This study reinforces the concept that youth who are more addicted to nicotine are less likely to quit smoking. The intervention did not include nicotine replacement therapy. Currently, there is no evidence supporting the effectiveness of using nicotine replacement therapy in teenagers, but studies have been underpowered, perhaps because of difficulties recruiting and retaining adolescents. Since this study was initiated, a more urgent problem has emerged: the explosion of teenage electronic cigarette use and resulting nicotine addiction, with 27.5% of US middle- and high school students reporting past 30-day use.[8] We believe there is a crucial need for research in pharmacologic treatment of nicotine-addicted teenagers.

At the same time, more innovative approaches to promoting tobacco and nicotine cessation within primary care are needed. For example, Web sites or apps that extend the reach of primary care might be helpful. These approaches have been successfully used in skin cancer prevention[9,10] and should be studied within the context of adolescent tobacco cessation.

Accelerating the pace of cessation research becomes an imperative given recently described health issues: electronic cigarette or vaping use-associated lung injury[11] and coronavirus disease (COVID-19). Smokers face a greater risk of COVID-19, in part because of hand–mouth behavior inherent to smoking. Among adult patients with COVID-19, smoking is a risk factor for increased severity of disease.[12]

Amid the tragic COVID-19 pandemic, with >164 000 American deaths as we write, we must also remember that tobacco use kills 480 000 Americans yearly. Teenage smokers who do not quit face morbidity and premature death. Current epidemics suggest that smoking also poses immediate hazards. Pediatricians and other clinicians will continue to care for teenagers, either in person or through telehealth. We must continue to develop and evaluate the best approaches to treating teenage tobacco users to ensure that they enter adulthood free of nicotine addiction.

ABBREVIATION

COVID-19: coronavirus disease

REFERENCES

1. Alberg AJ, Shopland DR, Cummings KM. The 2014 Surgeon General's report: commemorating the 50th Anniversary of the 1964 Report of the Advisory Committee to the US Surgeon General and updating the evidence on the health consequences of cigarette smoking. *Am J Epidemiol*. 2014;179(4):403–412
2. Centers for Disease Control and Prevention. Youth and tobacco use. Available at: https://tools.cdc.gov/medialibrary/index.aspx#/media/id/127046. Accessed June 16, 2020
3. Yuan M, Cross SJ, Loughlin SE, Leslie FM. Nicotine and the adolescent brain. *J Physiol*. 2015;593(16):3397–3412
4. DiFranza JR. Who are you going to believe? Adolescents and nicotine addiction. *J Adolesc Health*. 2011;48(1):1–2
5. Owens DK, Davidson KW, Krist AH, et al; US Preventive Services Task Force. Primary care interventions for prevention and cessation of tobacco use in children and adolescents: US Preventive Services Task Force Recommendation Statement. *JAMA*. 2020;323(16):1590–1598
6. Klein JD, Gorzkowski J, Resnick EA, et al. Delivery and impact of a motivational intervention for smoking cessation: a PROS study. *Pediatrics*. 2020;146(4):e20200644
7. 2008 PHS Guideline Update Panel, Liaisons, and Staff. Treating tobacco use and dependence: 2008 update US Public Health Service Clinical Practice Guideline executive summary. *Respir Care*. 2008;53(9):1217–1222
8. Wang TW, Gentzke A, Sharapova S, Cullen KA, Ambrose BK, Jamal A. Tobacco product use among middle and high school students - United States, 2011–2017. *MMWR Morb Mortal Wkly Rep*. 2018;67(22):629–633
9. Norman GJ, Adams MA, Calfas KJ, et al. A randomized trial of a multicomponent intervention for adolescent sun protection behaviors. *Arch Pediatr Adolesc Med*. 2007;161(2):146–152
10. Falzone AE, Brindis CD, Chren MM, et al. Teens, tweets, and tanning beds: rethinking the use of social media for skin cancer prevention. *Am J Prev Med*. 2017;53(3s1):S86–S94
11. Moritz ED, Zapata LB, Lekiachvili A, et al; Lung Injury Response Epidemiology/Surveillance Group; Lung Injury Response Epidemiology/Surveillance Task Force. Update: characteristics of patients in a national outbreak of e-cigarette, or vaping, product use-associated lung injuries - United States, October 2019. *MMWR Morb Mortal Wkly Rep*. 2019;68(43):985–989
12. Berlin I, Thomas D, Le Faou AL, Cornuz J. COVID-19 and smoking [published online ahead of print April 3, 2020]. *Nicotine Tob Res*. doi:10.1093/ntr/ntaa059

Accuracy of a Modified qSOFA Score for Predicting Critical Care Admission in Febrile Children

Sam T. Romaine, BSc, MBChB,[a] Jessica Potter, BSc,[a,b] Aakash Khanijau, BA, BMBCh,[a] Rachel J. McGalliard, MA, BMBCh,[a] Jemma L. Wright, MBChB,[c] Gerri Sefton, BSc, MSc,[a] Simon Leigh, BSc, MSc,[a] Karl Edwardson, BSc,[d] Philip Johnston, BSc,[d] Anne Kerr, BSc, MBBS, MRCPCH,[e] Luregn J. Schlapbach, MD, PhD,[f] Philip Pallmann, PhD,[g] Enitan D. Carrol, MBChB, MD, FRCPCH[a,c,h]

abstract

BACKGROUND AND OBJECTIVES: The identification of life-threatening infection in febrile children presenting to the emergency department (ED) remains difficult. The quick Sequential Organ Failure Assessment (qSOFA) was only derived for adult populations, implying an urgent need for pediatric scores. We developed and validated a novel, adapted qSOFA score (Liverpool quick Sequential Organ Failure Assessment [LqSOFA]) and compared its performance with qSOFA, Pediatric Early Warning Score (PEWS), and National Institute for Health and Care Excellence (NICE) high-risk criteria in predicting critical care (CC) admission in febrile children presenting to the ED.

METHODS: The LqSOFA (range, 0–4) incorporates age-adjusted heart rate, respiratory rate, capillary refill, and consciousness level on the Alert, Voice, Pain, Unresponsive scale. The primary outcome was CC admission within 48 hours of ED presentation, and the secondary outcome was sepsis-related mortality. LqSOFA, qSOFA, PEWS, and NICE high-risk criteria scores were calculated, and performance characteristics, including area under the receiver operating characteristic curve, were calculated for each score.

RESULTS: In the initial (n = 1121) cohort, 47 CC admissions (4.2%) occurred, and in the validation (n = 12 241) cohort, 135 CC admissions (1.1%) occurred, and there were 5 sepsis-related deaths. In the validation cohort, LqSOFA predicted CC admission with an area under the receiver operating characteristic curve of 0.81 (95% confidence interval [CI], 0.76 to 0.86), versus qSOFA (0.66; 95% CI, 0.60 to 0.71), PEWS (0.93; 95% CI, 0.90 to 0.95), and NICE high-risk criteria (0.81; 95% CI, 0.78 to 0.85). For predicting CC admission, the LqSOFA outperformed the qSOFA, with a net reclassification index of 10.4% (95% CI, 1.0% to 19.9%).

CONCLUSIONS: In this large study, we demonstrate improved performance of the LqSOFA over qSOFA in identifying febrile children at risk for CC admission and sepsis-related mortality. Further validation is required in other settings.

WHAT'S KNOWN ON THIS SUBJECT: The quick Sequential Organ Failure Assessment has been shown to more accurately predict mortality or ICU transfer than systemic inflammatory response syndrome or the quick Pediatric Logistic Organ Dysfunction-2 in an emergency department population, but with only moderate prognostic accuracy.

WHAT THIS STUDY ADDS: In this retrospective study of >12 000 febrile children, the Liverpool quick Sequential Organ Failure Assessment outperforms the quick Sequential Organ Failure Assessment in predicting critical care admission. Liverpool quick Sequential Organ Failure Assessment is a rapid bedside tool that should undergo implementation testing.

To cite: Romaine ST, Potter J, Khanijau A, et al. Accuracy of a Modified qSOFA Score for Predicting Critical Care Admission in Febrile Children. *Pediatrics.* 2020;146(4): e20200782

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-0782

This article has an accompanying video summary.

[a]Institute of Infection and Global Health and [b]School of Medicine, University of Liverpool, Liverpool, United Kingdom; [c]Department of Infectious Diseases, [d]Informatics Department, and [e]Emergency Department, Alder Hey Children's National Health Service Foundation Trust, Liverpool, United Kingdom; [f]Paediatric Critical Care Research Group, Child Health Research Centre, The University of Queensland and Paediatric ICU, Queensland Children's Hospital, South Brisbane, Australia; [g]Centre for Trials Research, College of Biomedical and Life Sciences, Cardiff University, Cardiff, United Kingdom; and [h]Liverpool Health Partners, Liverpool, United Kingdom

Prof Carrol conceptualized and designed the study, analyzed data, reviewed and revised the manuscript, and oversaw all aspects of the study; Dr Romaine drafted the initial manuscript, cleaned data, analyzed data, and reviewed and revised the manuscript; Drs Khanijau, Wright, and McGalliard, Mr Leigh, and Ms Potter collected data, cleaned data, conducted initial analyses, and reviewed and revised the manuscript; (Continued)

The Need for Risk Stratification Tools in the Pediatric Emergency Department

Fran Balamuth, MD, PhD,[a,b] Elizabeth R. Alpern, MD, MSCE,[c] Halden F. Scott, MD, MSCS[d,e]

In this issue of *Pediatrics,* Romaine et al[1] describe the derivation and validation of a novel risk stratification score, the Liverpool quick Sequential Organ Failure Assessment (LqSOFA) score, in predicting critical care admission for febrile children in a single emergency department (ED) in the United Kingdom. The authors aimed to address the long-standing challenge of identifying potentially critically ill children from the sea of well children with fever who present for pediatric emergency care: identifying the proverbial "needle in a haystack." Their team proposed the LqSOFA as a rapid, easily implemented score that can be applied during an ED visit to facilitate recognition of ill children, with a particular interest in identifying children with sepsis.

The elements of the LqSOFA were determined by consensus, and the score gives a point each for poor perfusion, altered mental status (measured by the Awake, Verbal, Pain, Unresponsive scale), and heart rate and respiratory rate above the 99th percentile for age. Overall, the authors report a high specificity and negative predictive value of >99% for an LqSOFA score ≥2 but a negative predictive value of only 85% for scores ≥1. The LqSOFA had low sensitivity (39% for an LqSOFA score ≥2 and 72% for an LqSOFA score ≥1). The balance of sensitivity and specificity is particularly tricky in sepsis, in which the cost is immeasurably high for a missed fatal case, yet these outcomes are rare when the common nature of febrile illnesses in children is considered such that purely maximizing the area under the receiver operating characteristic curve may not always be the true goal. Interestingly, the score with the highest area under the receiver operating characteristic curve in this study, the pediatric early warning score, also demonstrated a better balance of sensitivity (87%) and specificity (89%).

Before implementing the LqSOFA, one must consider whether the environment in which it was derived and validated generalizes to a setting, such as an ED in the United States.[2] As presented, the LqSOFA was studied in a single center in the United Kingdom, with significant differences in comparison with many US children's hospitals. One particularly noteworthy element was that blood pressure measurement was lacking in a large majority of children (missing in >75% in the derivation cohort, which included only children sick enough to have blood work performed). It may be that in settings that routinely measure blood pressure, such as a US ED,[1] the addition of this element would be feasible and would substantially change the characteristics of the score. However, the proposed LqSOFA may be easier to operationalize in a prehospital setting, for example, where obtaining a blood pressure may be more difficult and less common. In addition, lactate was deemed poorly discriminative, yet it was measured in <4% of the study population. Lactate and blood pressure have been crucial elements of pediatric and adult septic shock definitions and are highly associated with mortality.[3–5]

[a]*Department of Pediatrics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania;* [b]*Division of Emergency Medicine and Pediatric Sepsis Program, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania;* [c]*Department of Pediatrics, Feinberg School of Medicine, Northwestern University and Ann and Robert H. Lurie Children's Hospital of Chicago, Chicago, Illinois;* [d]*Department of Pediatrics, School of Medicine, University of Colorado, Aurora, Colorado; and* [e]*Division of Emergency Medicine, Children's Hospital Colorado, Aurora, Colorado*

DOI: https://doi.org/10.1542/peds.2020-022012

Accepted for publication Jul 30, 2020

Address correspondence to Fran Balamuth, MD, PhD, Division of Emergency Medicine, Children's Hospital of Philadelphia, 3501 Civic Center Blvd, Colket Translational Research Building 2nd Floor, Philadelphia, PA 19104. E-mail: balamuthf@email.chop.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

COMPANION PAPER: A companion to this article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-0782.

To cite: Balamuth F, Alpern ER, Scott HF. The Need for Risk Stratification Tools in the Pediatric Emergency Department. *Pediatrics.* 2020;146(4):e2020022012

The predictive accuracy of any new score would benefit from comparison with these elements in data sets with lower rates of missing data before implementation.

There are several challenges in deriving scores that may be surmountable by taking advantage of both emerging machine learning techniques and human factors approaches. These include the ability to identify predictive elements and cutoffs in a data-driven fashion as well as to develop dynamic scores using techniques that collect and incorporate minute-to-minute changes in clinical data elements.[6,7] The context and setting in which a score was derived should be considered and may influence its performance in a different setting. Additionally, the importance of human decision-making in score implementation remains an understudied area. Many sepsis alert systems employed in children's hospitals use a combination of vital signs measurement, physical examination data, and clinician judgment to inform treatment choices.[8] Further exploration of these human factors will also likely inform and augment performance of both this proposed and future predictive scores. Although the LqSOFA adds to our understanding of pediatric risk for critical illness in the ED, more study is required before it is ready for broad implementation.

ABBREVIATIONS

ED: emergency department
LqSOFA: Liverpool quick Sequential Organ Failure Assessment

REFERENCES

1. Romaine ST, Potter J, Khanijau A, et al. Accuracy of a modified qSOFA score for predicting critical care admission in febrile children. *Pediatrics*. 2020;146(4): e20200782
2. Ricke TL, Hendry PL, Kalynych C, Buzaianu EM, Kumar V, Redfield C. Incidence and recognition of elevated triage blood pressure in the pediatric emergency department. *Pediatr Emerg Care*. 2011;27(10):922–927
3. Schlapbach LJ, MacLaren G, Festa M, et al; Australian & New Zealand Intensive Care Society (ANZICS) Centre for Outcomes & Resource Evaluation (CORE) and Australian & New Zealand Intensive Care Society (ANZICS) Paediatric Study Group. Prediction of pediatric sepsis mortality within 1 h of intensive care admission. *Intensive Care Med*. 2017;43(8):1085–1096
4. Scott HF, Brou L, Deakyne SJ, Kempe A, Fairclough DL, Bajaj L. Association between early lactate levels and 30-day mortality in clinically suspected sepsis in children. *JAMA Pediatr*. 2017;171(3): 249–255
5. Singer M, Deutschman CS, Seymour CW, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA*. 2016;315(8): 801–810
6. Bohanon FJ, Mrazek AA, Shabana MT, et al. Heart rate variability analysis is more sensitive at identifying neonatal sepsis than conventional vital signs. *Am J Surg*. 2015;210(4):661–667
7. Wee BYH, Lee JH, Mok YH, Chong SL. A narrative review of heart rate and variability in sepsis. *Ann Transl Med*. 2020;8(12):768
8. Balamuth F, Alpern ER, Abbadessa MK, et al. Improving recognition of pediatric severe sepsis in the emergency department: contributions of a vital sign-based electronic alert and bedside clinician identification. *Ann Emerg Med*. 2017;70(6):759–768.e2

Mental Health and Timing of Gender-Affirming Care

Julia C. Sorbara, MD, MSc,[a,b] Lyne N. Chiniara, MD,[a] Shelby Thompson, MD,[b] Mark R. Palmert, MD, PhD[a,b,c]

abstract

BACKGROUND: Gender-incongruent (GI) youth have high rates of mental health problems. Although gender-affirming medical care (GAMC) provides psychological benefit, some GI youth present to care at older ages. Whether a relationship exists between age of presentation to GAMC and mental health difficulties warrants study.

METHODS: A cross-sectional chart review of patients presenting to GAMC. Subjects were classified a priori as younger presenting youth (YPY) (<15 years of age at presentation) or older presenting youth (OPY) (≥15 years of age). Self-reported rates of mental health problems and medication use were compared between groups. Binary logistic regression analysis was used to identify determinants of mental health problems. Covariates included pubertal stage at presentation, social transition status, and assigned sex.

RESULTS: Of 300 youth, there were 116 YPY and 184 OPY. After presentation, more OPY than YPY reported a diagnosis of depression (46% vs 30%), had self-harmed (40% vs 28%), had considered suicide (52% vs 40%), had attempted suicide (17% vs 9%), and required psychoactive medications (36% vs 23%), with all $P < .05$. After controlling for covariates, late puberty (Tanner stage 4 or 5) was associated with depressive disorders (odds ratio 5.49; 95% confidence interval [CI]: 1.14–26.32) and anxiety disorders (odds ratio 4.18 [95% CI: 1.22–14.49]), whereas older age remained associated only with psychoactive medication use (odd ratio 1.31 [95% CI: 1.05–1.63]).

CONCLUSIONS: Late pubertal stage and older age are associated with worse mental health among GI youth presenting to GAMC, suggesting that this group may be particularly vulnerable and in need of appropriate care.

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2019-3600

[a]*Division of Endocrinology and* [b]*Department of Pediatrics, The Hospital for Sick Children and University of Toronto, Toronto, Ontario, Canada; and* [c]*Department of Physiology, Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada*

Dr Sorbara conceptualized and designed the study, collected data, conducted initial data analyses, drafted the initial manuscript, and reviewed and revised the manuscript; Dr Chiniara designed the initial data collection instruments, collected data, and reviewed the manuscript for important intellectual content; Dr Thompson collected data and drafted the initial manuscript; Dr Palmert conceptualized, designed, and supervised the study and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2019-3600

Accepted for publication May 7, 2020

Address correspondence to Julia C. Sorbara, MD, MSc, Division of Endocrinology, The Hospital for Sick Children, 555 University Ave, Toronto, ON, Canada M5G 1X8. E-mail: julia.sorbara@sickkids.ca

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

WHAT'S KNOWN ON THIS SUBJECT: Mental health problems are prevalent among gender-incongruent youth. Although gender-affirmative treatment provides psychological benefit, some youth present to care later in age and puberty. It is not known if older age at presentation is associated with worse mental health.

WHAT THIS STUDY ADDS: Gender-incongruent youth who present to gender-affirming care later in life have higher rates of psychoactive medication use and mental health problems. We use our findings to suggest that this group is particularly vulnerable and highlight the need for appropriate care.

To cite: Sorbara JC, Chiniara LN, Thompson S, et al. Mental Health and Timing of Gender-Affirming Care. *Pediatrics.* 2020;146(4):e20193600

Challenges in Timing Puberty Suppression for Gender-Nonconforming Adolescents

Annelou L.C. de Vries, MD, PhD

Department of Child and Adolescent Psychiatry, Amsterdam University Medical Centers, Location VUMC, Amsterdam, Netherlands

DOI: https://doi.org/10.1542/peds.2020-010611

Accepted for publication Jul 14, 2020

Address correspondence to Annelou L.C. de Vries, MD, PhD, Department of Child and Adolescent Psychiatry, Amsterdam University Medical Centers, Location VUmc, Room 1y130, PO Box 7057, 1007 MB, Amsterdam, Netherlands. E-mail alc.devries@amsterdamumc.nl

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The author has indicated she has no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The author has indicated she has no potential conflicts of interest to disclose.

COMPANION PAPER: A companion to this article can be found online at www.pediatrics.org/cgi/doi/10.1542/2019-3600.

To cite: de Vries ALC. Challenges in Timing Puberty Suppression for Gender-Nonconforming Adolescents. *Pediatrics*. 2020;146(4):e2020010611

Sorbara et al,[1] in their report "Mental Health and Timing of Gender-Affirming Care" in this issue of *Pediatrics*, focus on the interesting matter of age of clinical presentation for gender-affirming medical interventions and its association with mental health in transgender youth. Because experiencing puberty is often stressful for gender-nonconforming youth, puberty suppression as a reversible medical intervention was introduced in clinical care in the early 2000s by Dutch clinicians Cohen-Kettenis et al.[2] The aim of puberty suppression was to prevent the psychological suffering stemming from undesired physical changes when puberty starts and allowing the adolescent time to make plans regarding further transition or not. Following this rationale, younger age at the time of starting medical-affirming treatment (puberty suppression or hormones) would be expected to correlate with fewer psychological difficulties related to physical changes than older individuals. Sorbara et al[1] confirmed this in their study. Adolescents presenting at younger age (<15 years) reported lower rates of self-reported diagnosed depression, self-harm, suicide thoughts or attempts, and use of psychoactive medication.

One could claim from these findings that gender-affirming medical interventions including puberty suppression should be offered at an early age (age <15 in the Sorbara study). Some caution is warranted, however, as the authors acknowledge in their report. One reason is that, despite the increased availability of gender-affirming medical interventions for younger ages in recent years, there has not been a proportional decline in older presenting youth with gender incongruence (GI), which is the discrepancy between one's birth-assigned sex and experienced gender identity.[3] It is even the case that most transgender people still present as older adolescents, as in the study by Sorbara et al[1], or as adults.[4] Interestingly, this older adolescent group did not only have more mental health difficulties but also a later age of onset of GI. As seen by using medical records, the older presenting youth "simply experienced gender history events at older ages" before attending the clinic.[1]

According to the original Dutch protocol, one of the criteria to start puberty suppression was "a presence of gender dysphoria from early childhood on."[2] Prospective follow-up studies evaluating these Dutch transgender adolescents showed improved psychological functioning.[5] However, authors of case histories and a parent-report study warrant that gender identity development is diverse, and a new developmental pathway is proposed involving youth with postpuberty adolescent-onset transgender histories.[6–8] These youth did not yet participate in the early evaluation studies.[5,9] This raises the question whether the positive

outcomes of early medical interventions also apply to adolescents who more recently present in overwhelming large numbers for transgender care, including those that come at an older age, possibly without a childhood history of GI. It also asks for caution because some case histories illustrate the complexities that may be associated with later-presenting transgender adolescents and describe that some eventually detransition.[9,10]

A study at the Amsterdam transgender clinic, one of the oldest in the world, whose researchers aimed to gain insight in the possible changes of certain key characteristics of earlier compared with recent applicants, revealed no changes in intensity of gender dysphoria, psychological functioning, and age over time between 2000 and 2016.[11] The only yet-unexplained observed change was a shift in sex ratio in favor of assigned female individuals. However, researchers of this time-trend study did not focus on differences between younger and older referred youth nor on the age of onset of gender nonconformity. In future, more-detailed studies like the one by Sorbara et al[1] and the time-trend study by Arnoldussen et al,[11] researchers should investigate whether older transgender adolescents might include individuals who experience later onset of GI, possibly postpuberty, and with more mental health challenges.

So far, researchers of the limited follow-up studies after puberty suppression show that the rate of adolescents that stop the reversible blockers is low (1.4%, 1.9%, and 3.5%).[4,12,13] However, systematic studies on the rate of adolescents who discontinue their transitions after they have started affirming hormones or surgeries with lasting effects are lacking at present. Given these uncertainties, providing early medical treatment to transgender adolescents remains a challenging area to work in. Prospective longer-term follow-up studies of clinical samples like the study of Sorbara et al[1] are needed to inform clinicians so that an individualized approach can be offered that differentiates who will benefit from medical gender affirmation and for whom (additional) mental health support might be more appropriate.

ABBREVIATION

GI: gender incongruence

REFERENCES

1. Sorbara JC, Chiniara LN, Thompson S, Palmert MR. Mental health and timing of gender-affirming care. *Pediatrics*. 2020;146(4):e20193600
2. Cohen-Kettenis PT, Delemarre-van de Waal HA, Gooren LJ. The treatment of adolescent transsexuals: changing insights. *J Sex Med*. 2008;5(8):1892–1897
3. World Health Organization. ICD-11 for mortality and morbidity statistics (ICD-11 MMS) 2018 version. 2019. Available at: https://icd.who.int/browse11/l-m/en. Accessed July 10, 2020
4. Wiepjes CM, Nota NM, de Blok CJM, et al. The Amsterdam cohort of gender dysphoria study (1972-2015): trends in prevalence, treatment, and regrets. *J Sex Med*. 2018;15(4):582–590
5. de Vries AL, McGuire JK, Steensma TD, Wagenaar EC, Doreleijers TA, Cohen-Kettenis PT. Young adult psychological outcome after puberty suppression and gender reassignment. *Pediatrics*. 2014;134(4):696–704
6. Kaltiala-Heino R, Bergman H, Työläjärvi M, Frisén L. Gender dysphoria in adolescence: current perspectives. *Adolesc Health Med Ther*. 2018;9:31–41
7. Littman L. Correction: parent reports of adolescents and young adults perceived to show signs of a rapid onset of gender dysphoria. *PLoS One*. 2019;14(3):e0214157
8. Zucker KJ. Adolescents with gender dysphoria: reflections on some contemporary clinical and research issues. *Arch Sex Behav*. 2019;48(7):1983–1992
9. Sevlever M, Meyer-Bahlburg HFL. Late-onset transgender identity development of adolescents in psychotherapy for mood and anxiety problems: approach to assessment and treatment. *Arch Sex Behav*. 2019;48(7):1993–2001
10. Turban JL, Carswell J, Keuroghlian AS. Understanding pediatric patients who discontinue gender-affirming hormonal interventions. *JAMA Pediatr*. 2018;172(10):903–904
11. Arnoldussen M, Steensma TD, Popma A, van der Miesen AIR, Twisk JWR, de Vries ALC. Re-evaluation of the Dutch approach: are recently referred transgender youth different compared to earlier referrals? *Eur Child Adolesc Psychiatry*. 2020;29(6):803–811
12. Brik T, Vrouenraets LJJJ, de Vries MC, Hannema SE. Trajectories of adolescents treated with gonadotropin-releasing hormone analogues for gender dysphoria [published online ahead of print March 9, 2020]. *Arch Sex Behav*. doi:10.1007/s10508-020-01660-8
13. Kuper LE, Stewart S, Preston S, Lau M, Lopez X. Body dissatisfaction and mental health outcomes of youth on gender-affirming hormone therapy. *Pediatrics*. 2020;145(4):e20193006

Trends in the Use of Noninvasive and Invasive Ventilation for Severe Asthma

Alla Smith, MD,[a] Urbano L. França, PhD,[b] Michael L. McManus, MD, MPH[b]

abstract

OBJECTIVES: To explore and define contemporary trends in the use of invasive mechanical ventilation (IMV) and noninvasive ventilation (NIV) in the treatment of children with asthma.

METHODS: We performed a serial cross-sectional analysis using data from the Pediatric Health Information System. We examined 2014–2018 admission abstracts from patients aged 2 to 17 years who were admitted to member hospitals with a primary diagnosis of asthma. We report temporal trends in IMV use, NIV use, ICU admission, length of stay, and mortality.

RESULTS: Over the study period, 48 hospitals reported 95 204 admissions with a primary diagnosis of asthma. Overall, IMV use remained stable at 0.6% between 2014 and 2018 (interquartile range [IQR]: 0.3%–1.1% and 0.2%–1.3%, respectively), whereas NIV use increased from 1.5% (IQR: 0.3%–3.2%) to 2.1% (IQR: 0.3%–5.6%). There was considerable practice variation among centers, with NIV rates more than doubling within the highest quartile of users (from 4.8% [IQR: 2.8%–7.5%] to 13.2% [IQR: 7.4%–15.2%]; $P < .02$). ICU admission was more common among centers with high NIV use, but centers with high NIV use did not differ from lower-use centers in mortality, IMV use, or overall average length of stay.

CONCLUSIONS: The use of IMV is at historic lows, and NIV has replaced it as the primary mechanical support mode for asthma. However, there is considerable variability in NIV use. Increased NIV use was not associated with a change in IMV rates, which remained stable. Higher NIV use was associated with increased ICU admissions. NIV's precise contribution to the cost and quality of care remains to be determined.

WHAT'S KNOWN ON THIS SUBJECT: Although asthma remains a common chronic disease, there is variation in the management of children admitted with asthma exacerbations. Noninvasive ventilation (NIV) and invasive mechanical ventilation can be used to support these patients, but recent trends in their use are unknown.

WHAT THIS STUDY ADDS: There was significant interhospital variability in the use of NIV over the study period. At centers with high NIV use, we saw no impact on intubation rates or mortality, but we did see markedly increased ICU use.

To cite: Smith A, França UL, McManus ML. Trends in the Use of Noninvasive and Invasive Ventilation for Severe Asthma. *Pediatrics.* 2020;146(4):e20200534

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-0534

[a]*Division of Medical Critical Care, Department of Medicine and* [b]*Division of Critical Care, Department of Anesthesiology, Critical Care and Pain Medicine, Boston Children's Hospital, Boston, Massachusetts*

All authors participated in the conceptualization and design of the study, drafted the manuscript, conducted the analyses, reviewed and revised the manuscript, approved the final manuscript as submitted and agree to be accountable for all aspects of the work, and had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

DOI: https://doi.org/10.1542/peds.2020-0534

Accepted for publication Jul 1, 2020

Address correspondence to Alla Smith, MD, Division of Medical Critical Care, Boston Children's Hospital, 333 Longwood Ave, Boston, MA 02115. E-mail: alla.smith@childrens.harvard.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

In Search of Evidence for Using Noninvasive Ventilation for Severe Acute Asthma

Michael D. Johnson, MD, MS

Noninvasive ventilation (NIV) is appealing for the treatment of severe asthma because it likely avoids the potential airway and lung trauma of intubation and invasive mechanical ventilation (IMV). In this issue of *Pediatrics*, Smith et al[1] illustrate the compelling appeal of NIV in clinical use, showing that centers with high use of NIV in 2014 doubled their use of NIV in the next 4 years and that NIV is more common as a mode of respiratory support than IMV. Despite widespread increase in use over time, the evidence for NIV is still immature, with no conclusive evidence to reveal its superiority to IMV or to confirm its superiority to asthma treatment with inhaled and intravenous bronchodilators.[2] In this regard, the evidence to guide use of NIV is similar to evidence used to guide most treatments for severe acute pediatric asthma: based on a handful of small randomized trials[3,4] that have not been followed by larger trials for confirmation. A recent overview of Cochrane reviews of secondary interventions for children with asthma highlights that most interventions lack sufficient evidence to guide treatment, including a lack of evidence to conclude if any interventions decrease intensive care admission.[5] Without conclusive evidence to guide treatment, it should come as no surprise that use of NIV was widely variable among the 48 hospitals studied, similar to wide variability previously described in other treatments for severe acute pediatric asthma.[6,7] We could possibly be content that the undesirable variability in care delivery found in this study is balanced with the encouraging simultaneous downward trend in hospitalization and conclude that asthma care overall has improved. However, if our goal is to provide optimal care for children with acute asthma and to provide optimal care equitably regardless of where children seek care, then this study illuminates a pressing need for additional research to guide the care we deliver to children with asthma when they are at their most vulnerable.

ABBREVIATIONS

IMV: invasive mechanical ventilation
NIV: noninvasive ventilation

REFERENCES

1. Smith A, Franca UL, McManus ML. Trends in the use of noninvasive and invasive ventilation for severe asthma. *Pediatrics*. 2020;146(4):e20200534
2. Korang SK, Feinberg J, Wetterslev J, Jakobsen JC. Non-invasive positive pressure ventilation for acute asthma in children. *Cochrane Database Syst Rev*. 2016;(9):CD012067
3. Thill PJ, McGuire JK, Baden HP, Green TP, Checchia PA. Noninvasive positive-pressure ventilation in children with lower airway obstruction. *Pediatr Crit Care Med*. 2004;5(4):337–342
4. Basnet S, Mander G, Andoh J, Klaska H, Verhulst S, Koirala J. Safety, efficacy, and tolerability of early initiation of

Primary Children's Hospital, Salt Lake City, Utah

DOI: https://doi.org/10.1542/peds.2020-022103

Accepted for publication Jul 29, 2020

Address correspondence to Michael D. Johnson, MD, MS, Primary Children's Hospital, 100 N Mario Capecchi Dr, Salt Lake City, UT 84108.
E-mail: mike.johnson@hsc.utah.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The author has indicated he has no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The author has indicated he has no potential conflicts of interest to disclose.

COMPANION PAPER: A companion to this article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-0534.

To cite: Johnson MD. In Search of Evidence for Using Noninvasive Ventilation for Severe Acute Asthma. *Pediatrics*. 2020;146(4):e2020022103

noninvasive positive pressure ventilation in pediatric patients admitted with status asthmaticus: a pilot study. *Pediatr Crit Care Med*. 2012;13(4):393–398

5. Craig SS, Dalziel SR, Graudins A, Babl FE, Lunny C. Interventions for escalation of therapy for acute exacerbations of asthma in children: an overview of Cochrane Reviews. *Cochrane Database of Systematic Reviews*. 2020;8:CD012977
6. Bratton SL, Newth CJ, Zuppa AF, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network. Critical care for pediatric asthma: wide care variability and challenges for study. *Pediatr Crit Care Med*. 2012;13(4):407–414
7. Johnson MD, Zorc JJ, Nelson DS, et al; Pediatric Emergency Care Applied Research Network (PECARN). Intravenous magnesium in asthma pharmacotherapy: variability in use in the PECARN registry. *J Pediatr*. 2020;220:165–174.e2

Longitudinal Changes in Early Nasal Microbiota and the Risk of Childhood Asthma

Laura Toivonen, MD,[a,b] Sinikka Karppinen, MD,[b] Linnea Schuez-Havupalo, MD,[b] Matti Waris, PhD,[c] Qiushui He, MD,[d,e] Kristi L. Hoffman, PhD,[f] Joseph F. Petrosino, PhD,[f] Orianne Dumas, PhD,[g,h] Carlos A. Camargo, Jr, MD,[a] Kohei Hasegawa, MD,[a] Ville Peltola, MD[b]

abstract

OBJECTIVES: Although the airway microbiota is a highly dynamic ecology, the role of longitudinal changes in airway microbiota during early childhood in asthma development is unclear. We aimed to investigate the association of longitudinal changes in early nasal microbiota with the risk of developing asthma.

METHODS: In this prospective, population-based birth cohort study, we followed children from birth to age 7 years. The nasal microbiota was tested by using 16S ribosomal RNA gene sequencing at ages 2, 13, and 24 months. We applied an unsupervised machine learning approach to identify longitudinal nasal microbiota profiles during age 2 to 13 months (the primary exposure) and during age 2 to 24 months (the secondary exposure) and examined the association of these profiles with the risk of physician-diagnosed asthma at age 7 years.

RESULTS: Of the analytic cohort of 704 children, 57 (8%) later developed asthma. We identified 4 distinct longitudinal nasal microbiota profiles during age 2 to 13 months. In the multivariable analysis, compared with the persistent *Moraxella* dominance profile during age 2 to 13 months, the persistent *Moraxella* sparsity profile was associated with a significantly higher risk of asthma (adjusted odds ratio, 2.74; 95% confidence interval, 1.20–6.27). Similar associations were observed between the longitudinal changes in nasal microbiota during age 2 to 24 months and risk of asthma.

CONCLUSIONS: Children with an altered longitudinal pattern in the nasal microbiota during early childhood had a high risk of developing asthma. Our data guide the development of primary prevention strategies (eg, early identification of children at high risk and modification of microbiota) for childhood asthma. These observations present a new avenue for risk modification for asthma (eg, microbiota modification).

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-0421

[a]*Department of Emergency Medicine, Massachusetts General Hospital and Harvard Medical School, Harvard University, Boston, Massachusetts;* [b]*Department of Paediatrics and Adolescent Medicine, Turku University Hospital and University of Turku, Turku, Finland;* [c]*Virology Unit, Institute of Biomedicine and* [d]*Department of Microbiology, Virology and Immunology and Institute of Biomedicine, University of Turku, Turku, Finland;* [e]*Department of Medical Microbiology, Capital Medical University, Beijing, China;* [f]*Alkek Center for Metagenomics and Microbiome Research, Department of Molecular Virology and Microbiology, Baylor College of Medicine, Houston, Texas;* [g]*INSERM U1168, VIMA: Aging and Chronic Diseases, Epidemiological and Public Health Approaches, Villejuif, France; and* [h]*UMR-S 1168, Université de Versailles Saint-Quentin-en-Yvelines, Montigny-le-Bretonneux, France*

Dr Toivonen collected the data, conducted the statistical analysis, and drafted the initial manuscript; Drs Karppinen and Schuez-Havupalo collected the data and critically reviewed and revised the manuscript; Dr Waris contributed to the conception and design of the study, conducted the DNA extractions, and critically reviewed and revised the manuscript; Dr He contributed to the conception and design of the study, conducted the bacterial cultures, and critically reviewed and revised the manuscript; Drs Hoffman and Petrosino generated the microbiome data, conducted the initial statistical analysis, and critically reviewed and revised the manuscript; (Continued)

WHAT'S KNOWN ON THIS SUBJECT: Airway microbiota modulates immune responses in the airways and may contribute to the risk of asthma. Although the airway microbiota is a highly dynamic ecology, the role of longitudinal changes in early airway microbiota in asthma development is unclear.

WHAT THIS STUDY ADDS: In this birth cohort of 704 children, we identified distinct longitudinal nasal microbiota profiles in early life that were associated with differential risks of developing asthma. These observations present a new avenue for risk modification for asthma (eg, microbiota modification).

To cite: Toivonen L, Karppinen S, Schuez-Havupalo L, et al. Longitudinal Changes in Early Nasal Microbiota and the Risk of Childhood Asthma. *Pediatrics*. 2020;146(4): e20200421

Fatty Acid Supplementation and Socioemotional Outcomes: Secondary Analysis of a Randomized Trial

Kelly M. Boone, MA,[a] Andria Parrott, PhD,[a] Joseph Rausch, PhD,[a,b] Keith Owen Yeates, PhD,[c] Mark A. Klebanoff, MD, MPH,[b,d,e,f] Abigail Norris Turner, PhD,[e,g] Sarah A. Keim, MA, MS, PhD[a,b,e]

abstract

BACKGROUND AND OBJECTIVES: Children born preterm experience socioemotional difficulties, including increased risk of autism spectrum disorder (ASD). In this secondary analysis, we tested the effect of combined docosahexaenoic acid (DHA) and arachidonic acid (AA) supplementation during toddlerhood on caregiver-reported socioemotional outcomes of children born preterm. We hypothesized that children randomly assigned to DHA + AA would display better socioemotional outcomes compared with those randomly assigned to a placebo.

METHODS: Omega Tots was a single-site randomized, fully masked, parallel-group, placebo-controlled trial. Children (N = 377) were 10 to 16 months at enrollment, born at <35 weeks' gestation, and assigned to 180 days of daily 200-mg DHA + 200-mg AA supplementation or a placebo (400 mg corn oil). Caregivers completed the Brief Infant-Toddler Social and Emotional Assessment and the Pervasive Developmental Disorders Screening Test–II, Stage 2 at the end of the trial. Liner mixed models and log-binomial regression compared socioemotional outcomes between the DHA + AA and placebo groups.

RESULTS: Outcome data were available for 83% of children ($n_{\text{treatment}}$ = 161; n_{placebo} = 153). Differences between DHA + AA and placebo groups on Brief Infant-Toddler Social and Emotional Assessment scores were of small magnitude (Cohen's $d \leq 0.15$) and not statistically significant. Children randomly assigned to DHA + AA had a decreased risk of scoring at-risk for ASD on the Pervasive Developmental Disorders Screening Test–II, Stage 2 (21% vs 32%; risk ratio = 0.66 [95% confidence interval: 0.45 to 0.97]; risk difference = −0.11 [95% confidence interval: −0.21 to −0.01]) compared with children randomly assigned to a placebo.

CONCLUSIONS: No evidence of benefit of DHA + AA supplementation on caregiver-reported outcomes of broad socioemotional development was observed. Supplementation resulted in decreased risk of clinical concern for ASD. Further exploration in larger samples of preterm children and continued follow-up of children who received DHA + AA supplementation as they approach school age is warranted.

WHAT'S KNOWN ON THIS SUBJECT: Preterm children are at increased risk for socioemotional difficulties, including autism spectrum disorder (ASD). Docosahexaenoic acid (DHA) supplementation may reduce ASD behaviors, but effects on socioemotional development more broadly are less clear.

WHAT THIS STUDY ADDS: Differences between the DHA + arachidonic acid and placebo groups on socioemotional development were not statistically significant, and effects were small. Children randomly assigned to DHA + arachidonic acid had a decreased risk of clinical concern for ASD compared with children randomly assigned to a placebo.

To cite: Boone KM, Parrott A, Rausch J, et al. Fatty Acid Supplementation and Socioemotional Outcomes: Secondary Analysis of a Randomized Trial. *Pediatrics*. 2020;146(4):e20200284

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-0284

[a]Centers for Biobehavioral Health and [d]Perinatal Research, Abigail Wexner Research Institute, Nationwide Children's Hospital, Columbus, Ohio; [e]Division of Epidemiology, College of Public Health, and [g]Departments of Internal Medicine, [b]Pediatrics, and [f]Obstetrics and Gynecology, College of Medicine, The Ohio State University, Columbus, Ohio; and [c]Department of Psychology, Alberta Children's Hospital Research Institute and Hotchkiss Brain Institute, University of Calgary, Calgary, Alberta

Caregiver Perceptions of Fatty Acid Supplementation to Toddlers Born Preterm

Susan S. Baker, MD, PhD,[a] Peter S. Martin, MD, MPH,[b] Robert D. Baker, MD, PhD[a]

For the past several decades, it has been hoped that docosahexaenoic acid (DHA) and arachidonic acid supplementation to the preterm infant would improve cognitive outcomes. In this issue of *Pediatrics,* Boone et al[1] present their findings regarding long-chain polyunsaturated fatty acid supplementation for 6 months to children between 10 and 16 months of age born <35 weeks' gestation. Outcome measures, including caregiver reports of socioemotional development using the Brief Infant-Toddler Social and Emotional Assessment (BITSEA) and the Pervasive Developmental Disorders Screening Test–II, Stage 2 (PDDST-II), revealed no evidence of benefit on broad socioemotional development, although there was a decrease in risk of clinical concern for autism spectrum disorder (ASD) among those who received supplementation. The investigators suggest cautious interpretation of results given the short time frame and the post hoc analysis.

Cell, animal, and postmortem studies[2,3] have shown that rates of DHA incorporation into the brain occur mainly from the last trimester of pregnancy until age 2. The study by Boone et al[1] had only a narrow window of supplementation that did not begin until 10 months, which might have missed the therapeutic window of opportunity.

This study is a secondary analysis.[4] In the report of the main outcomes, the same subjects as included in this study were administered the Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III) to measure developmental functioning. The Bayley-III and the way it was used for the primary outcomes has several advantages over BITSEA and PDDST-II that were used in this study, including the following: (1) results from Bayley-III can be directly compared to other similar trials that used the same instrument[4,5]; (2) Bayley-III is administered by a trained research assistant and consists of a structured clinical assessment to allow for a more objective assessment of functioning; and (3) Bayley-III was administered both at baseline and at study completion versus only at study completion for the BITSEA and PDDST-II, thereby allowing for change to be ascribed to the supplementation. In the previous report,[4] no improvement in cognitive development or early measures of executive function were observed. Disturbingly, in the previous report,[4] supplementation may have resulted in negative effects on language development and effortful control in some subgroups of children. This combination of findings led the investigators to "not support DHA supplementation in the second year of life for children who are born preterm."[4]

The lack of significance in this study offers reason for caution. The only statistically significant results came about on subgroup analyses when looking at sex. The authors here found a statistically significant decreased risk

Departments of [a]Pediatrics and [b]Psychiatry, Jacobs School of Medicine and Biomedical Sciences, University of Buffalo, Buffalo, New York

DOI: https://doi.org/10.1542/peds.2020-016634

Accepted for publication Jul 22, 2020

Address correspondence to Susan S. Baker, MD, PhD, Department of Pediatrics, 39 Irving Place, Buffalo, NY 14201. E-mail: ssbaker@buffalo.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

COMPANION PAPER: A companion to this article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-0284.

To cite: Baker SS, Martin PS, Baker RD. Caregiver Perceptions of Fatty Acid Supplementation to Toddlers Born Preterm. *Pediatrics.* 2020;146(4):e2020016634

of scoring above the cutoff and threshold for ASD-related concerns in girls with the BITSEA and in boys with the PDDST-II. This suggests that there may be some difference in how sex influences the effects of supplementation. However, without further analysis, it is not possible to make any meaningful conclusion beyond that a difference may exist. Previous studies have revealed both positive[5] and negative[6] effects of supplementation on female patients. At this time, it is unclear what relation sex has, if any, with DHA supplementation.

The authors' overall conclusion that DHA supplementation resulted in decreased risk of clinical concern for ASD appears to be a more generous interpretation than the results show. As the authors noted, even with the statistically significant results, the magnitude was small. More accurately, they were able to show that caregivers' perception of risk and/or concern in their child decreased, but it is unclear whether that risk would also be perceived or interpreted in the same way by an objective third party.

There are other concerns with the measures used in this study. For both the BITSEA and PDDST-II, there are concerns about a lack of validity or clinical efficacy in the sample population used in this study.[7–9] For clinicians, neither tool is used extensively in practice settings, leading to caution in direct clinical applicability.

Regretfully, DHA supplementation did not improve developmental outcomes for preterm infants as the authors reveal in this report, in their previous publications,[1,10] and as found in a Cochrane review.[11] There may be small, inconsistent benefit on clinical concerns for ASD; however, there may also be negative consequences to supplementation during the second year of life. Supplementation of preterm infants with DHA and arachidonic acid after the first year of life should be approached with caution.

ABBREVIATIONS

ASD: autism spectrum disorder
Bayley-III: Bayley Scales of Infant and Toddler Development, Third Edition
BITSEA: Brief Infant-Toddler Social and Emotional Assessment
DHA: docosahexaenoic acid
PDDST-II: Pervasive Developmental Disorders Screening Test–II, Stage 2

REFERENCES

1. Boone KM, Parrott A, Rausch J, et al. Fatty acid supplementation and socioemotional outcomes: secondary analysis of a randomized trial. *Pediatrics*. 2020;146(4):e20200284
2. Mallick R, Basak S, Duttaroy AK. Docosahexaenoic acid,22:6n-3: its roles in the structure and function of the brain. *Int J Dev Neurosci*. 2019;79:21–31
3. Lauritzen L, Brambilla P, Mazzocchi A, Harsløf LB, Ciappolino V, Agostoni C. DHA effects in brain development and function. *Nutrients*. 2016;8(1):6
4. Keim SA, Boone KM, Klebanoff MA, et al. Effect of docosahexaenoic acid supplementation vs placebo on developmental outcomes of toddlers born preterm: a randomized clinical trial. [published correction appears in *JAMA Pediatr*. 2019;173(12):1215]. *JAMA Pediatr*. 2018;172(12):1126–1134
5. Fewtrell MS, Abbott RA, Kennedy K, et al. Randomized, double-blind trial of long-chain polyunsaturated fatty acid supplementation with fish oil and borage oil in preterm infants. *J Pediatr*. 2004;144(4):471–479
6. Collins CT, Gibson RA, Anderson PJ, et al. Neurodevelopmental outcomes at 7 years' corrected age in preterm infants who were fed high-dose docosahexaenoic acid to term equivalent: a follow-up of a randomised controlled trial. *BMJ Open*. 2015;5(3):e007314
7. Kruizinga I, Jansen W, Mieloo CL, Carter AS, Raat H. Screening accuracy and clinical application of the Brief Infant-Toddler Social and Emotional Assessment (BITSEA). *PLoS One*. 2013;8(8):e72602
8. Kruizinga I, Jansen W, van Sprang NC, Carter AS, Raat H. The effectiveness of the BITSEA as a tool to early detect psychosocial problems in toddlers, a cluster randomized trial. *PLoS One*. 2015;10(9):e0136488
9. Montgomery JM, Randy Duncan C, Farncis GC. Test review: Siegel, B. (2004). *Pervasive Developmental Disorder Screening Test-II (PDDST-II)*. San Antonio, TX: Harcourt. *J Psychoed Assess*. 2007;25(3):299–306
10. Keim SA, Gracious B, Boone KM, et al. ω-3 and ω-6 fatty acid supplementation may reduce autism symptoms based on parent report in preterm toddlers. *J Nutr*. 2018;148(2):227–235
11. Moon K, Rao SC, Schulzke SM, Patole SK, Simmer K. Longchain polyunsaturated fatty acid supplementation in preterm infants. *Cochrane Database Syst Rev*. 2016;(12):CD000375

Early Neurodevelopmental Trajectories for Autism Spectrum Disorder in Children Born Very Preterm

Li-Wen Chen, MD, MSc,[a,b] Shan-Tair Wang, PhD,[c,d] Lan-Wan Wang, MD, PhD,[e,f,g] Yu-Chia Kao, MD,[a,h] Ching-Lin Chu, PhD,[i] Chin-Chin Wu, PhD,[j,k] Chung-Hsin Chiang, PhD,[i] Chao-Ching Huang, MD[b,f]

abstract

BACKGROUND: Children born preterm are at high risk for autism spectrum disorder (ASD). However, there is still a lack of appropriate developmental markers. In this study, we aim to examine whether early mental performance trajectory is related to ASD outcome in the preterm population.

METHODS: The population-based cohort included 414 very preterm survivors born between 2008 and 2014. After excluding children with severe neurosensory impairment, 319 children with available records of developmental quotients before age 2 years were enrolled. The trajectory of mental performance evaluated by using the Bayley Scales of Infant Development across 6, 12, and 24 months of age was analyzed with group-based trajectory modeling. At 5 years of age, the ASD diagnosis was established by using the Autism Diagnostic Observation Schedule and the Autism Diagnostic Interview–Revised.

RESULTS: There were 29 children with ASD and 290 children without ASD. The mental performances from age 6 to 24 months could be classified into 3 trajectory patterns: low declining, high declining, and high stable, which corresponded to ASD prevalence at age 5 years of 35%, 9%, and 3%, respectively. ASD odds was 15 times higher in the low-declining group than in the high-stable group (odds ratio 15; 95% confidence interval 3.8–59; $P <$ .001). Through the analysis of multinomial logistic regression, we found that male infants with longer exposure to oxygen therapy whose mothers had lower maternal education levels tended to follow the low-declining trajectory.

CONCLUSIONS: The early-life mental trajectory patterns, by using the Bayley Scales of Infant Development, may lead to identification of vulnerable children born preterm for early ASD diagnosis and targeted intervention.

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-0297

This article has an accompanying video summary.

[a]*Graduate Institutes of Clinical Medicine and* [c]*Gerontology, College of Medicine, National Cheng Kung University, Tainan, Taiwan;* [b]*Department of Pediatrics, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan;* [d]*Division of Research, Ditmanson Medical Foundation Chia-Yi Christian Hospital, Chiayi, Taiwan;* [e]*Department of Pediatrics, Chi Mei Medical Center, Tainan, Taiwan;* [f]*Department of Pediatrics, College of Medicine, Taipei Medical University, Taipei, Taiwan;* [g]*Department of Biotechnology and Food Technology, Southern Taiwan University of Science and Technology, Tainan, Taiwan;* [h]*Department of Pediatrics, E-Da Hospital, Kaohsiung, Taiwan;* [i]*Department of Educational Psychology and Counseling, National Pingtung University, Pingtung, Taiwan;* [j]*Department of Psychology, Kaohsiung Medical University, Kaohsiung, Taiwan;* [k]*Department of Medical Research, Kaohsiung Medical University Chung-Ho Memorial Hospital, Kaohsiung, Taiwan; and* [l]*Research Center for Mind, Brain, and Learning and Department of Psychology, National Chengchi University, Taipei, Taiwan*

WHAT'S KNOWN ON THIS SUBJECT: Early developmental trajectory is an indicator for autism spectrum disorder (ASD) in the general population. Preterm infants are at high risk of ASD. However, appropriate developmental markers at toddler age are still lacking.

WHAT THIS STUDY ADDS: In this population-based cohort, using group-based trajectory modeling, we found there are 3 patterns of mental performance trajectory for children born preterm from age 6 to 24 months, which is related to different susceptibility to ASD at age 5 years.

To cite: Chen L, Wang S, Wang L, et al. Early Neurodevelopmental Trajectories for Autism Spectrum Disorder in Children Born Very Preterm. *Pediatrics.* 2020;146(4):e20200297

Predicting Autism Spectrum Disorder in Very Preterm Infants

Janet S. Soul, MDCM, Sarah J. Spence, MD, PhD

Department of Neurology, Harvard Medical School, Harvard University and Boston Children's Hospital, Boston, Massachusetts

DOI: https://doi.org/10.1542/peds.2020-019448

Accepted for publication Jul 15, 2020

Address correspondence to Janet S. Soul, MDCM, Department of Neurology, Boston Children's Hospital, 300 Longwood Ave, Boston, MA 02115.
E-mail: janet.soul@childrens.harvard.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

COMPANION PAPER: A companion to this article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-0297.

To cite: Soul JS and Spence SJ. Predicting Autism Spectrum Disorder in Very Preterm Infants. *Pediatrics*. 2020;146(4):e2020019448

Children born preterm are known to be at higher risk for developing autism spectrum disorder (ASD) compared with their term-born counterparts, with an estimated 7% prevalence of ASD based on a recent large prospective study and a meta-analysis.[1,2] This high prevalence is in contrast to the currently estimated prevalence of ASD in the United States of 1.8% in the general population.[3] ASD has been shown to be associated with a variety of prenatal, perinatal, and neonatal risk factors, including a variety of maternal health risk factors and medications and neonatal risk factors such as seizures, birth asphyxia, and low birth weight.[4] Previously identified perinatal risk factors for ASD specific to preterm infants include factors such as low birth gestational age and birth weight, intracranial hemorrhage, and acute and chronic lung disease (CLD).[5]

The article by Chen et al[6] in this issue of *Pediatrics* provides the first prospectively obtained data regarding whether there is an early developmental trajectory of prematurely born children that predicts who will develop ASD. The authors tested 319 preterm children prospectively with Bayley Scales of Infant Development examinations at 6, 12, and 24 months and used group-based trajectory modeling to assess whether early-life developmental trajectory predicted autism at 5 years of age. The approach of looking at developmental trajectory has been used in other high-risk populations, such as infant siblings of children with ASD[7] or those with a specific genetic disorder (tuberous sclerosis complex) with a high prevalence of ASD.[8]

The authors provide the first data revealing that although a small percentage of preterm infants who develop ASD have a similar early-life trajectory to that of term-born children, with decline in mental development from age 12 to 24 months,[9,10] the highest-risk group was identified as having low cognitive scores at 6 months, with further decline over time, allowing for early identification and intervention. The converse finding that infants with low cognitive scores who improve to >85 and those with stably high cognitive scores are at lower risk of developing ASD enables the clinician to provide reassurance to families.

Their analysis also illuminates risk factors for ASD related to preterm birth by comparing the 29 children who developed ASD with the 290 children without ASD. Notably, their study identified both nonmodifiable (eg, male sex, gestational age, and birth weight) and potentially modifiable risk factors (eg, CLD and duration of oxygen therapy) for the development of ASD. As the authors discussed, CLD is known to be a risk factor for developmental delay and cognitive impairment and/or disability, but it is unclear the extent to which the risk associated with CLD is related to brain injury and altered brain development.

One acknowledged limitation of the study was the lack of neuroimaging data, so it is unknown whether there was a contribution of identifiable brain injury to the development of ASD in their subjects. It is likely that at least

some of the infants in the low cognitive score group had easily detected brain injury, such as large cerebellar injury[11] or cerebral injury and/or impaired brain development,[12–14] both of which are associated with low IQ and are suspected to increase the risk of ASD. Additionally, there were no data regarding genetic risk factors for ASD, which could contribute a "second hit" to risk factors related to prematurity. Numerous genes have now been identified to be associated with ASD and/or intellectual disability and could have contributed to some cases of ASD in this study. Male sex remains a strong risk factor for ASD in both preterm and term-born children, and particularly in preterm children, male sex may contribute to inherent genetic risks related to sex as well as increased vulnerability to complications of preterm birth that also increase the risk of ASD. The importance of neuroimaging and genetic data relates in part to the observation that preterm and term-born children with ASD have been shown to have important phenotypic differences. In one study, boys with ASD born preterm had higher rates of seizures, attention-deficit/hyperactivity disorder, and sleep apnea,[15] suggesting a potentially different neural substrate for ASD than term-born children.

Perhaps most importantly, these findings provide an opportunity for initiating interventions in early life to mitigate ASD before the diagnosis of ASD can be definitively established. Identification of a constellation of prenatal and neonatal risk factors could help clinicians target infants at highest risk, while providing reassurance to parents whose infants are at low risk. Identification of high-risk infants with low cognitive scores at 6 months of age or those with declining scores over time could provide another opportunity to intensify early intervention services aimed at mitigating manifestations and/or symptoms of ASD. Importantly, identification of high-risk infants by neonatal discharge and/or 6 months of age could improve research into novel therapies to mitigate the manifestations of ASD, such as communication and social-emotional deficits or impairments.

ABBREVIATIONS

ASD: autism spectrum disorder
CLD: chronic lung disease

REFERENCES

1. Hirschberger RG, Kuban KCK, O'Shea TM, et al; ELGAN Study Investigators. Co-occurrence and severity of neurodevelopmental burden (cognitive impairment, cerebral palsy, autism spectrum disorder, and epilepsy) at age ten years in children born extremely preterm. *Pediatr Neurol*. 2018;79:45–52
2. Agrawal S, Rao SC, Bulsara MK, Patole SK. Prevalence of autism spectrum disorder in preterm infants: a meta-analysis. *Pediatrics*. 2018;142(3):e20180134
3. Maenner MJ, Shaw KA, Baio J, et al. Prevalence of autism spectrum disorder among children aged 8 years - Autism and Developmental Disabilities Monitoring Network, 11 sites, United States, 2016. *MMWR Surveill Summ*. 2020;69(4):1–12
4. Hisle-Gorman E, Susi A, Stokes T, Gorman G, Erdie-Lalena C, Nylund CM. Prenatal, perinatal, and neonatal risk factors of autism spectrum disorder. *Pediatr Res*. 2018;84(2):190–198
5. Kuzniewicz MW, Wi S, Qian Y, Walsh EM, Armstrong MA, Croen LA. Prevalence and neonatal factors associated with autism spectrum disorders in preterm infants. *J Pediatr*. 2014;164(1):20–25
6. Chen LW, Wang ST, Wang LW, et al. Early neurodevelopmental trajectories for autism spectrum disorder in children born very preterm. *Pediatrics*. 2020;146(4):e20200297
7. Landa RJ, Gross AL, Stuart EA, Faherty A. Developmental trajectories in children with and without autism spectrum disorders: the first 3 years. *Child Dev*. 2013;84(2):429–442
8. Spurling Jeste S, Wu JY, Senturk D, et al. Early developmental trajectories associated with ASD in infants with tuberous sclerosis complex. *Neurology*. 2014;83(2):160–168
9. Nishimura T, Takei N, Tsuchiya KJ. Neurodevelopmental trajectory during infancy and diagnosis of autism spectrum disorder as an outcome at 32 months of age. *Epidemiology*. 2019;30(suppl 1):S9–S14
10. Nishimura T, Takei N, Tsuchiya KJ, Asano R, Mori N. Identification of neurodevelopmental trajectories in infancy and of risk factors affecting deviant development: a longitudinal birth cohort study. *Int J Epidemiol*. 2016;45(2):543–553
11. Limperopoulos C, Bassan H, Gauvreau K, et al. Does cerebellar injury in premature infants contribute to the high prevalence of long-term cognitive, learning, and behavioral disability in survivors? *Pediatrics*. 2007;120(3):584–593
12. Volpe JJ. Brain injury in premature infants: a complex amalgam of destructive and developmental disturbances. *Lancet Neurol*. 2009;8(1):110–124
13. Padilla N, Eklöf E, Mårtensson GE, Bölte S, Lagercrantz H, Ådén U. Poor brain growth in extremely preterm neonates long before the onset of autism spectrum disorder symptoms. *Cereb Cortex*. 2017;27(2):1245–1252
14. Stolp HB, Fleiss B, Arai Y, et al. Interneuron development is disrupted in preterm brains with diffuse white matter injury: observations in mouse and human. *Front Physiol*. 2019;10:955
15. Bowers K, Wink LK, Pottenger A, McDougle CJ, Erickson C. Phenotypic differences in individuals with autism spectrum disorder born preterm and at term gestation. *Autism*. 2015;19(6):758–763

State Insurance Mandates and the Workforce for Children With Autism

Ryan K. McBain, PhD, MPH,[a] Jonathan H. Cantor, PhD, MS,[b] Aaron Kofner, MA,[c] Bradley D. Stein, MD, PhD,[d] Hao Yu, PhD[e]

abstract

BACKGROUND: State mandates have required insurance companies to provide coverage for autism-related child health care services; however, it has not been determined if insurance mandates have improved the supply of child health care providers. We investigate the effect of state insurance mandates on the supply of child psychiatrists, pediatricians, and board-certified behavioral analysts (BCBAs).

METHODS: We used data from the National Conference of State Legislatures and Health Resources and Services Administration's Area Health Resource Files to examine child psychiatrists, pediatricians, and BCBAs in all 50 states from 2003 to 2017. Fixed-effects regression models compared change in workforce density before versus one year after mandate implementation and the effect of mandate generosity across 44 US states implementing mandates between 2003 and 2017.

RESULTS: From 2003 to 2017, child psychiatrists increased from 7.40 to 10.03 per 100 000 children, pediatricians from 62.35 to 68.86, and BCBAs from 1.34 to 29.88. Mandate introduction was associated with an additional increase of 0.77 BCBAs per 100 000 children (95% confidence interval [CI]: 0.18 to 1.42) one year after mandate enactment. Mandate introduction was also associated with a more modest increase among child psychiatrists (95% CI: 0.10 to 0.91) and was not associated with the prevalence of pediatricians (95% CI: −0.76 to 1.13). We also found evidence that more generous mandate benefits were associated with larger effects on workforce supply.

CONCLUSIONS: State insurance mandates were associated with an ~16% increase in BCBAs from 2003 to 2017, but the association with child psychiatrists was smaller and nonsignificant among pediatricians. In these findings, it is suggested that policies are needed that specifically address workforce constraints in the provision of services for children with autism spectrum disorder.

WHAT'S KNOWN ON THIS SUBJECT: State mandates requiring that insurance companies provide coverage for autism-related child health care services have resulted in modest effects on service use and spending.

WHAT THIS STUDY ADDS: In this study, it is indicated that state insurance mandates have had a significant but modest effect on the size of the US workforce for autism-related child health care services, suggesting that other policies may be necessary to address a shortage of care for autism spectrum disorder.

To cite: McBain RK, Cantor JH, Kofner A, et al. State Insurance Mandates and the Workforce for Children With Autism. *Pediatrics.* 2020;146(4):e20200836

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-0836

[a]RAND Corporation, Boston, Massachusetts; [b]RAND Corporation, Santa Monica, California; [c]RAND Corporation, Arlington, Virginia; [d]RAND Corporation, Pittsburgh, Pennsylvania; and [e]Department of Population Medicine, Harvard Medical School, Harvard Pilgrim Health Care Institute, Harvard University, Boston, Massachusetts

Dr McBain conceptualized and designed the study, conducted the initial analyses, and drafted the initial manuscript; Dr Cantor assisted with analyses and drafting of the initial manuscript; Mr Kofner led data gathering and aggregation efforts and helped draft the initial manuscript; Dr Stein conceptualized the study and drafted the initial manuscript; Dr Yu obtained research funding, conceptualized and designed the study, and drafted the initial manuscript; and all authors reviewed and revised the manuscript, approved the final manuscript as submitted, and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2020-0836

Accepted for publication Jun 4, 2020

Simpler Than Possible: Insurance Mandates for Autism Spectrum Disorders

Susan L. Hyman, MD, Suzannah Iadarola, PhD, BCBA-D

The diagnosis and management of autism spectrum disorder (ASD) and co-occurring medical and behavioral health conditions strain both health and educational resources in the United States. State mandates for insurance coverage for ASD-related health care were intended to improve access to indicated services, with inclusion of board-certified behavior analysts (BCBAs) as a newly licensed group of professionals to provide one approach to evidence-based intervention. McBain et al[1] examined the association of the state by state passage of legislation on one indicator of access to services: number of providers who serve this population. Mandated insurance coverage, especially more-generous coverage, was associated with a greater growth in the workforce of BCBAs, a small increase in the number of child psychiatrists, and no change in the number of pediatricians.

The authors acknowledged the associational nature of their study and their inability to explore use or distribution of services. However, when interpreting the impact of insurance mandates that focus primarily on reimbursement for applied behavioral analysis (ABA) as an intervention, there are additional implications that must be considered when examining actual health care provided for individuals with ASD. The insurance mandate did little to improve serious deficits in access to diagnostic services or to address the training needs of existing and available pediatric care providers.[2] Augmenting workforce capacity includes current efforts to enhance pediatricians' ability to contribute to timely ASD diagnosis, thereby promoting earlier entrance to intervention.[3,4] Most interventions provided for children and youth with ASD have not been impacted by the wave of insurance legislation over the past decade but are provided through the legal mandate of the Individuals with Disabilities Education Act through the educational system. Consistent with patterns in specialty behavioral health care, special education and community services are not equitably distributed across a representative population (eg, based on race, ethnicity, age, income, language, and geographic region).[5]

Increases in provider numbers resultant from insurance mandate legislation may imply false equivalence with evidence-based practice. Although behavior analytic services are efficacious for some,[6] there is an increasing evidence base for interventions (eg, naturalistic developmental behavioral interventions[7]) that are not covered by insurance mandates. There is insufficient evidence to assume a single approach is effective for all individuals with ASD. Factors such as child characteristics and family choice become increasingly important drivers of treatment selection as predictors of success and outcome measurement are studied in greater depth. However, insurance legislation that is directly tied to funding ABA and advocated in

Golisano Children's Hospital, University of Rochester, Rochester, New York

DOI: https://doi.org/10.1542/peds.2020-020396

Accepted for publication Jul 28, 2020

Address correspondence to Susan L. Hyman, MD, Division of Developmental and Behavioral Pediatrics, Golisano Children's Hospital, Box 671, 601 Elmwood Ave, Rochester, NY 14642. E-mail: susan_hyman@urmc.rochester.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

COMPANION PAPER: A companion to this article can be found online at www.pediatrics.org/cgi/doi/10.1542/2020-0836.

To cite: Hyman SL and Iadarola S. Simpler Than Possible: Insurance Mandates for Autism Spectrum Disorders. *Pediatrics.* 2020;146(4):e2020020396

parallel to licensure for BCBAs[8] sends a message that ABA is the only effective intervention. This may come at the cost of awareness of and reimbursement for other possibly efficacious interventions, as well as development of comprehensive care plans including both the educational and medical systems.

An additional erroneous assumption is that an increase in number of BCBAs and child psychiatrists leads to increased access to care. Indeed, families who are generally under-represented in service systems on the basis of race, ethnicity, and income level are especially likely to report unmet service needs.[5] Such disparities are exacerbated by Medicaid restrictions for insurance mandates, which may disproportionately affect populations that are already underserved. Second, service quality remains independent from access. Community-based early intervention services, for instance, are delivered with highly variable fidelity, which may affect child outcomes. In addition, despite the general conviction in the field that more intensive intervention yields more positive results, conventions around the minimum recommended number of hours of ABA are not rooted in evidence.[9] Recommendations to steer families toward readily available services should not supplant individualized, evidence-based determinations for intervention selection based on child and family variables and preferences.

McBain et al[1] add support to the evidence that the overall supply of child behavioral health services in the United States is inadequate to address the existing needs of not only children but people with ASD across the life span. We echo the recommendation that policies do need to address the existing behavioral and medical health needs but also suggest the following: (1) in addition to increasing the numbers of psychiatrists and BCBAs, the existing interprofessional workforce needs education and supports to improve quality of care; (2) care coordination must be recognized and funded as a method to improve efficiencies and access across health and educational systems; (3) providers and service systems must prioritize equitable access to services for all families; and (4) innovative research in this area will include the development and evaluation of cost-efficient and effective interventions for all people with ASD. Per Albert Einstein, "Everything should be made as simple as possible, but not simpler." Full consideration of these numerous system complexities is necessary to adequately address the needs of individuals with ASD and their families.

ABBREVIATIONS

ABA: applied behavioral analysis
ASD: autism spectrum disorder
BCBA: board-certified behavior analyst

REFERENCES

1. McBain R, Cantor J, Kofner A, Stein B, Yu H. State insurance mandates and the workforce for children with autism. *Pediatrics*. 2020;146(4):e20200836
2. Chiti G, Warfield ME. Unmet need and problems accessing core health care services for children with Autism spectrum disorder. *Matern Child Health J*. 2012;16(5):1081–1091
3. Mazurek MO, Curran A, Burnette C, Sohl K. ECHO autism STAT: accelerating early access to autism diagnosis. *J Autism Dev Disord*. 2019;49(1):127–137
4. Hyman SL, Levy SE, Myers SM; Council on Children With Disabilities, Section on Developmental and Behavioral Pediatrics. Identification, evaluation, and management of children with autism spectrum disorder. *Pediatrics*. 2020;145(1):e20193447
5. Smith KA, Gehricke JG, Iadarola S, Wolfe A, Kuhlthau KA. Disparities in service use among children with autism: a systematic review. *Pediatrics*. 2020; 145(suppl 1):S35–S46
6. Reichow B, Hume K, Barton EE, Boyd BA. Early intensive behavioral intervention (EIBI) for young children with autism spectrum disorders (ASD). *Cochrane Database Syst Rev*. 2018;(5):CD009260
7. Schreibman L, Dawson G, Stahmer AC, et al. Naturalistic developmental behavioral interventions: empirically validated treatments for autism spectrum disorder. *J Autism Dev Disord*. 2015;45(8):2411–2428
8. Johnston JM, Carr JE, Mellichamp FH. A history of the professional credentialing of applied behavior analysts. *Behav Anal*. 2017;40(2): 523–538
9. Pellecchia M, Iadarola S, Stahmer AC. How meaningful is more? Considerations regarding intensity in early intensive behavioral intervention. *Autism*. 2019;23(5):1075–1078

Pathogenic Yield of Genetic Testing in Autism Spectrum Disorder

Holly K. Harris, MD,[a,b] Georgios D. Sideridis, PhD,[a] William J. Barbaresi, MD,[a] Elizabeth Harstad, MD, MPH[a]

abstract

BACKGROUND AND OBJECTIVES: Genetic testing is recommended for individuals with autism spectrum disorder (ASD). Pathogenic yield varies by clinician and/or patient characteristics. Our objectives were to determine the pathogenic yield of genetic testing, the variability in rate of pathogenic results based on subject characteristics, and the percentage of pathogenic findings resulting in further medical recommendations in toddlers with a *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* diagnosis of ASD.

METHODS: We conducted a retrospective chart review of 500 toddlers, 18 to 36 months, diagnosed with *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* ASD (mean age: 25.8 months, 79% male). Subject demographics, medical and neuropsychological characteristics, and genetic test results were abstracted. Genetic results were divided into negative or normal, variants of unknown significance, and pathogenic. Subject characteristics were compared across results. Manual chart review determined if further recommendations were made after pathogenic results.

RESULTS: Over half of subjects (59.8%, n = 299) completed genetic testing, and of those, 36 (12.0%) had pathogenic findings. There were no significant differences in Bayley Scales of Infant Development cognitive (P = .112), language (P = .898), or motor scores (P = .488) among children with negative or normal findings versus a variant of unknown significance versus pathogenic findings. Medical recommendations in response to the genetic finding were made for 72.2% of those with pathogenic results.

CONCLUSIONS: Our findings reinforce the importance of genetic testing for toddlers diagnosed with ASD given the 12% yield and lack of phenotypic differences between subjects with and without pathogenic findings. The majority of pathogenic results lead to further medical recommendations.

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2019-3211

This article has an accompanying video summary.

[a]*Division of Developmental Medicine, Boston Children's Hospital and Harvard Medical School, Harvard University, Boston, Massachusetts; and* [b]*Department of Pediatrics, Baylor College of Medicine and Meyer Center for Developmental Pediatrics, Texas Children's Hospital, Houston, Texas*

Drs Harris, Barbaresi and Harstad conceptualized and designed the study; Dr Harris designed the data collection instruments, collected data, and drafted the initial manuscript; Dr Sideridis conducted the statistical analyses and reviewed and revised the manuscript; Drs Harris, Sideridis, Barbaresi, and Harstad reviewed and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2019-3211

Accepted for publication Jul 28, 2020

WHAT'S KNOWN ON THIS SUBJECT: Genetic testing (chromosomal microarray and fragile X) is recommended for patients with autism spectrum disorder (ASD). Reported pathogenic yield is 10% for chromosomal microarray and 1to 5% for fragile X. The pathogenic yield in toddlers diagnosed with ASD is unknown.

WHAT THIS STUDY ADDS: In a clinical sample of 500 toddlers with *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* ASD, 299 (59.8%) completed genetic testing, and of those, 36 (12.0%) had pathogenic findings. Pathogenic findings impacted medical decision-making 72.2% of the time.

To cite: Harris HK, Sideridis GD, Barbaresi WJ, et al. Pathogenic Yield of Genetic Testing in Autism Spectrum Disorder. *Pediatrics*. 2020;146(4):e20193211

Medical Use and Misuse of Prescription Opioids in US 12th-Grade Youth: School-Level Correlates

Sean Esteban McCabe, PhD,[a,b,c,d,e] John Schulenberg, PhD,[b,e,f] Vita V. McCabe, MD,[a,g,h] Phil T. Veliz, PhD[a,c,e]

abstract

BACKGROUND AND OBJECTIVES: Opioid misuse and overdose remains a leading US public health concern, and many youth are first exposed to opioids via medical use. In this study, we examine school-level prevalence and correlates of medical use and misuse of prescription opioids among US 12th-grade students.

METHODS: A sample of 228 507 US 12th-graders in 1079 public and private schools from 2002 to 2017 from the Monitoring the Future study was used to identify school-level prevalence and correlates associated with medical use and misuse of prescription opioids.

RESULTS: The past-year prevalence of prescription opioid misuse was 7.6% and ranged from 0% to 73% across US high schools. Lifetime medical use of prescription opioids was 16.9% and ranged from 0% to 85% across US high schools. The odds of prescription opioid misuse were higher at schools with higher proportions of male students, more white students, higher rates of marijuana use, and more medical use of prescription opioids. Students attending schools with the highest rates of medical use of prescription opioids had 57% increased odds of past-year prescription opioid misuse compared with schools with no medical use (adjusted odds ratio = 1.57, 95% confidence interval = 1.35–1.83); this association was found to weaken in recent years.

CONCLUSIONS: Differences exist in the prevalence of prescription opioid misuse among US high schools. The association between greater school-level medical use of prescription opioids and higher prevalence of prescription opioid misuse, although declining, indicates a key risk factor to target for prevention efforts.

WHAT'S KNOWN ON THIS SUBJECT: Prescription opioid misuse remains a major public health concern in the United States. To date, no researchers have assessed the school-level prevalence and correlates associated with medical use and misuse of prescription opioids among US adolescents.

WHAT THIS STUDY ADDS: We show that greater rates of medical use of prescription opioids within schools is directly associated with higher prevalence of prescription opioid misuse among students. School-level assessments should be used to guide prevention efforts to reduce prescription opioid misuse.

To cite: McCabe SE, Schulenberg J, McCabe VV, et al. Medical Use and Misuse of Prescription Opioids in US 12th-Grade Youth: School-Level Correlates. *Pediatrics.* 2020;146(4):e20200387

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-0387

[a]Center for the Study of Drugs, Alcohol, Smoking and Health, School of Nursing, [b]Center for Human Growth and Development, [c]Institutes for Research on Women and Gender, [d]Healthcare Policy and Innovation, and [e]Social Research, and [f]Departments of Psychology, [g]Psychiatry, and [h]Surgery, University of Michigan, Ann Arbor, Michigan

Drs SE McCabe and Schulenberg conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript; Dr Veliz conceptualized and designed the study, conducted all statistical analyses, drafted the initial manuscript, and reviewed and revised the manuscript; Dr VV McCabe provided clinical input, review, and revision of the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2020-0387

Accepted for publication Jul 14, 2020

Address correspondence to Phil T. Veliz, PhD, Research Assistant Professor, University of Michigan Center for the Study of Drugs, Alcohol, Smoking and Health, School of Nursing, University of Michigan, 400 N Ingalls St, Ann Arbor, MI 48109. E-mail: ptveliz@umich.edu

Adolescent Alcohol Use Trajectories: Risk Factors and Adult Outcomes

Wing See Yuen, BPsych(Hons),[a] Gary Chan, PhD,[b] Raimondo Bruno, PhD,[a,c] Philip Clare, MBiostat,[a] Richard Mattick, PhD,[a] Alexandra Aiken, MPH,[a] Veronica Boland, PhD,[a] Nyanda McBride, PhD,[d] Jim McCambridge, PhD,[e] Tim Slade, PhD,[f] Kypros Kypri, PhD,[g] John Horwood, PhD,[h] Delyse Hutchinson, PhD,[a,i,j,k] Jake Najman, PhD,[l] Clara De Torres, BPsych(Hons),[a] Amy Peacock, PhD[a,c]

abstract

OBJECTIVES: Adolescents often display heterogenous trajectories of alcohol use. Initiation and escalation of drinking may be important predictors of later harms, including alcohol use disorder (AUD). Previous conceptualizations of these trajectories lacked adjustment for known confounders of adolescent drinking, which we aimed to address by modeling dynamic changes in drinking throughout adolescence while adjusting for covariates.

METHODS: Survey data from a longitudinal cohort of Australian adolescents (n = 1813) were used to model latent class alcohol use trajectories over 5 annual follow-ups (mean age = 13.9 until 17.8 years). Regression models were used to determine whether child, parent, and peer factors at baseline (mean age = 12.9 years) predicted trajectory membership and whether trajectories predicted self-reported symptoms of AUD at the final follow-up (mean age = 18.8 years).

RESULTS: We identified 4 classes: abstaining (n = 352); late-onset moderate drinking (n = 503); early-onset moderate drinking (n = 663); and early-onset heavy drinking (n = 295). Having more alcohol-specific household rules reduced risk of early-onset heavy drinking compared with late-onset moderate drinking (relative risk ratio: 0.31; 99.5% confidence interval [CI]: 0.11–0.83), whereas having more substance-using peers increased this risk (relative risk ratio: 3.43; 99.5% CI: 2.10–5.62). Early-onset heavy drinking increased odds of meeting criteria for AUD in early adulthood (odds ratio: 7.68; 99.5% CI: 2.41–24.47).

CONCLUSIONS: Our study provides evidence that parenting factors and peer influences in early adolescence should be considered to reduce risk of later alcohol-related harm. Early initiation and heavy alcohol use throughout adolescence are associated with increased risk of alcohol-related harm compared with recommended maximum levels of consumption (late-onset, moderate drinking).

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-0440

This article has an accompanying video summary.

[a]*National Drug and Alcohol Research Centre, University of New South Wales Sydney, Sydney, New South Wales, Australia;* [b]*National Centre for Youth Substance Use Research and* [l]*School of Public Health, The University of Queensland, Brisbane, Queensland, Australia;* [c]*School of Psychological Sciences, University of Tasmania, Hobart, Tasmania, Australia;* [d]*National Drug Research Institute, Curtin University, Perth, Western Australia, Australia;* [e]*Department of Health Sciences, University of York, York, United Kingdom;* [f]*The Matilda Centre for Research in Mental Health and Substance Use, The University of Sydney, Sydney, New South Wales, Australia;* [g]*School of Medicine and Public Health, The University of Newcastle, Newcastle, New South Wales, Australia;* [h]*Department of Psychological Medicine, University of Otago, Christchurch, New Zealand;* [i]*Centre for Social and Early Emotional Development, Deakin University, Geelong, Victoria, Australia;* [j]*Department of Paediatrics, The University of Melbourne, Melbourne, Victoria, Australia; and* [k]*Murdoch Children's Research Institute, Royal Children's Hospital, The University of Melbourne, Victoria, Australia*

WHAT'S KNOWN ON THIS SUBJECT: Adolescent drinking trajectories are often found to be heterogenous. Age at initiation and escalation of drinking may be important predictors of alcohol-related problems in early adulthood. However, no research has conceptualized these trajectories with adjustment for known confounders.

WHAT THIS STUDY ADDS: Parenting factors (alcohol-specific household rules, child monitoring) in early adolescence predicted lower risk of early-onset heavy drinking, whereas peer influences increased risk. Early-onset heavy drinking increased the risk of meeting criteria for alcohol use disorder on the basis of self-reported symptoms.

To cite: Yuen WS, Chan G, Bruno R, et al. Adolescent Alcohol Use Trajectories: Risk Factors and Adult Outcomes. *Pediatrics.* 2020;146(4):e20200440

Early Hypoxic Respiratory Failure in Extreme Prematurity: Mortality and Neurodevelopmental Outcomes

Praveen Chandrasekharan, MD, MS,[a] Satyan Lakshminrusimha, MD,[b] Dhuly Chowdhury, MS, MBA,[c] Krisa Van Meurs, MD,[d] Martin Keszler, MD,[e] Haresh Kirpalani, MD,[f] Abhik Das, PhD,[c] Michele C. Walsh, MD,[g] Elisabeth C. McGowan, MD,[e] Rosemary D. Higgins, MD,[h,i] NRN STEERING COMMITTEE

abstract

OBJECTIVES: To evaluate the survival and neurodevelopmental impairment (NDI) in extremely low birth weight (ELBW) infants at 18 to 26 months with early hypoxemic respiratory failure (HRF). We also assessed whether African American infants with early HRF had improved outcomes after exposure to inhaled nitric oxide (iNO).

METHODS: ELBW infants ≤1000 g and gestational age ≤26 weeks with maximal oxygen ≥60% on either day 1 or day 3 were labeled as "early HRF" and born between 2007 and 2015 in the Neonatal Research Network were included. Using a propensity score regression model, we analyzed outcomes and effects of exposure to iNO overall and separately by race.

RESULTS: Among 7639 ELBW infants born ≤26 weeks, 22.7% had early HRF. Early HRF was associated with a mortality of 51.3%. The incidence of moderate-severe NDI among survivors was 41.2% at 18 to 26 months. Mortality among infants treated with iNO was 59.4%. Female sex (adjusted odds ratio [aOR]: 2.4, 95% confidence interval [CI]: 1.8–3.3), birth weight ≥720 g (aOR: 2.3, 95% CI: 1.7–3.1) and complete course of antenatal steroids (aOR: 1.6, 95% CI: 1.1–2.2) were associated with intact survival. African American infants had a similar incidence of early HRF (21.7% vs 23.3%) but lower exposure to iNO (16.4% vs 21.6%). Among infants with HRF exposed to iNO, intact survival (no death or NDI) was not significantly different between African American and other races (aOR: 1.5, 95% CI: 0.6–3.6).

CONCLUSIONS: Early HRF in infants ≤26 weeks' gestation is associated with high mortality and NDI at 18 to 26 months. Use of iNO did not decrease mortality or NDI. Outcomes following iNO exposure were not different in African American infants.

WHAT'S KNOWN ON THIS SUBJECT: The incidence of early hypoxemic respiratory failure and inhaled nitric oxide therapy are common in preterm infants ≤26 weeks' gestation. There is limited information regarding developmental outcomes and survival at 18 to 26 months by race outside randomized trials.

WHAT THIS STUDY ADDS: In preterm infants ≤26 weeks' gestation, early hypoxemic respiratory failure is associated with high mortality and severe neurodevelopmental impairment among survivors at 18 to 26 months. Therapy with inhaled nitric oxide did not reduce mortality or severe neurodevelopmental impairment in preterm infants of all races.

To cite: Chandrasekharan P, Lakshminrusimha S, Chowdhury D, et al. Early Hypoxic Respiratory Failure in Extreme Prematurity: Mortality and Neurodevelopmental Outcomes. *Pediatrics*. 2020; 146(4):e20193318

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2019-3318

[a]*Division of Neonatology, Department of Pediatrics, UBMD, University at Buffalo, Buffalo, New York;* [b]*Department of Pediatrics, University of California at Davis, Sacramento, California;* [c]*Biostatistics and Epidemiology Division, RTI International, Rockville, Maryland;* [d]*Division of Neonatal and Developmental Medicine, Department of Pediatrics, School of Medicine, Stanford University, Palo Alto, California;* [e]*Department of Neonatology, Brown University, Providence, Rhode Island;* [f]*Children's Hospital of Philadelphia, Philadelphia, Pennsylvania;* [g]*Division of Neonatology, Department of Pediatrics, School of Medicine, Case Western Reserve University, Cleveland, Ohio;* [h]*Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, Maryland; and* [i]*Department of Global and Community Health, George Mason University, Fairfax, Virginia*

Dr Chandrasekharan conceptualized, wrote the manuscript, helped with interpretation of data reviewed, revised, and submitted the final manuscript; Dr Lakshminrusimha conceptualized and wrote the manuscript and helped with interpretation of data, supervision, and critical review; Ms Chowdhury collected data, analyzed data, and wrote part of the manuscript; Drs Van Meurs, Keszler, Kirpalani, Walsh, and Higgins conceptualized and helped with interpretation of data, supervision, and critical review; Dr Das conceptualized the data analysis and helped with interpretation of data, supervision, and critical review; (Continued)

Positive End-Expiratory Pressure in Newborn Resuscitation Around Term: A Randomized Controlled Trial

Kari Holte, MD,[a,b] Hege Ersdal, MD, PhD,[b,c] Joar Eilevstjønn, MSc, PhD,[e] Øystein Gomo, MSc,[e] Claus Klingenberg, MD, PhD,[f,g] Monica Thallinger, MD, PhD,[h] Jørgen Linde, MD, PhD,[b,i] Hein Stigum, PhD,[j] Anita Yeconia, BScN,[k] Hussein Kidanto, MD, PhD,[d,l] Ketil Størdal, MD, PhD[a,j]

abstract

BACKGROUND: International guidelines for resuscitation recommend using positive end-expiratory pressure (PEEP) during ventilation of preterm newborns. Reliable PEEP-valves for self-inflating bags have been lacking, and effects of PEEP during resuscitation of term newborns are insufficiently studied. The objective was to determine if adding a new PEEP valve to the bag-mask during resuscitation of term and near-term newborns could improve heart rate response.

METHODS: This randomized controlled trial was performed at Haydom Lutheran Hospital in Tanzania (September 2016 to June 2018). Helping Babies Breathe–trained midwives performed newborn resuscitation using self-inflating bags with or without a new, integrated PEEP valve. All live-born newborns who received bag-mask ventilation at birth were eligible. Heart rate response measured by ECG was the primary outcome, and clinical outcome and ventilation data were recorded.

RESULTS: Among 417 included newborns (median birth weight 3200 g), 206 were ventilated without and 211 with PEEP. We found no difference in heart rate response. Median (interquartile range) measured PEEP in the PEEP group was 4.7 (2.0–5.6) millibar. The PEEP group received lower tidal volumes (4.9 [1.9–8.2] vs 6.3 [3.9–10.5] mL/kg; P = .02) and had borderline lower expired CO_2 (2.9 [1.5–4.3] vs 3.3 [1.9–5.0] %; P = .05). Twenty four-hour mortality was 9% in both groups.

CONCLUSIONS: We found no evidence for improved heart rate response during bag-mask ventilation with PEEP compared with no PEEP. The PEEP valve delivered a median PEEP within the intended range. The findings do not support routine use of PEEP during resuscitation of newborns around term.

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-0494

[a]Department of Pediatrics and Adolescence Medicine, Østfold Hospital Trust, Grålum, Norway; [b]Faculty of Health Sciences, University of Stavanger, Stavanger, Norway; [c]Departments of Anesthesiology and Intensive Care, [i]Pediatrics and Adolescence Medicine, and [d]Research, Stavanger University Hospital, Stavanger, Norway; [e]Strategic Research Department, Laerdal Medical, Stavanger, Norway; [f]Department of Pediatrics and Adolescence Medicine, University Hospital of North Norway, Tromsø, Norway; [g]Pediatric Research Group, Faculty of Health Sciences, University of Tromsø–Arctic University of Norway, Tromsø, Norway; [h]Department of Anesthesiology and Intensive Care, Vestre Viken Hospital Trust, Bærum, Norway; [j]Norwegian Institute of Public Health, Oslo, Norway; [k]Haydom Lutheran Hospital, Mbulu, Manyara, Tanzania; and [l]Medical College, Agakhan University, Dar es Salaam, Tanzania

Dr Holte conceptualized and designed the study, coordinated and supervised data collection, conducted the analyses, drafted the initial manuscript, and revised the manuscript; Drs Størdal and Ersdal conceptualized and designed the study, coordinated and supervised data collection, helped analyze the data, and thoroughly reviewed and revised the manuscript; (Continued)

WHAT'S KNOWN ON THIS SUBJECT: Positive end-expiratory pressure (PEEP) may facilitate lung liquid clearance and help establish functional residual capacity, and is recommended in international guidelines for resuscitation of preterm newborns. PEEP is also commonly used for newborns around term, but evidence for beneficial effects is sparse.

WHAT THIS STUDY ADDS: Term and near-term newborns who received bag-mask ventilation with PEEP had no better heart rate response or survival than newborns ventilated without PEEP. Adding a PEEP valve to the bag-mask increased leak, and reduced tidal volumes and expired CO_2.

To cite: Holte K, Ersdal H, Eilevstjønn J, et al. Positive End-Expiratory Pressure in Newborn Resuscitation Around Term: A Randomized Controlled Trial. *Pediatrics.* 2020; 146(4):e20200494

Kindergarten Readiness in Children Who Are Deaf or Hard of Hearing Who Received Early Intervention

Jareen Meinzen-Derr, PhD, MPH,[a] Susan Wiley, MD,[b] Wendy Grove, PhD,[c] Mekibib Altaye, PhD,[a] Marcus Gaffney, MPH,[d] Ashley Satterfield-Nash, DrPH, MPH,[e] Alonzo T. Folger, PhD,[a] Georgina Peacock, MD, MPH,[d] Coleen Boyle, PhD, MSHyg[f]

abstract

BACKGROUND: Children who are deaf or hard of hearing (D/HH) have improved language outcomes when enrolled in early intervention (EI) before the age of 6 months. Little is understood about the long-term impact of EI on outcomes of kindergarten readiness (K-readiness). The study objective was to evaluate the impact of EI before the age of 6 months (early) versus after 6 months (later) on K-readiness in children who are D/HH.

METHODS: In this study, we leveraged data from the Ohio Early Hearing Detection and Intervention Data Linkage Project, which linked records of 1746 infants identified with permanent hearing loss born from 2008 to 2014 across 3 Ohio state agencies; 417 had kindergarten records. The Kindergarten Readiness Assessment was used to identify children as ready for kindergarten; 385 had Kindergarten Readiness Assessment scores available. Multiple logistic regression was used to investigate the relationship between K-readiness and early EI entry while controlling for confounders (eg, hearing loss severity and disability status).

RESULTS: Children who were D/HH and entered EI early (n = 222; 57.7% of the cohort) were more likely to demonstrate K-readiness compared with children who entered EI later (33.8% vs 20.9%; P = .005). Children who entered early had similar levels of K-readiness as all Ohio students (39.9%). After controlling for confounders, children who entered EI early were more likely to be ready for kindergarten compared with children who entered later (odds ratio: 2.02; 95% confidence interval 1.18–3.45).

CONCLUSIONS: These findings support the sustained effects of early EI services on early educational outcomes among children who are D/HH. EI entry before the age of 6 months may establish healthy trajectories of early childhood development, reducing the risk for later academic struggles.

WHAT'S KNOWN ON THIS SUBJECT: Enrollment into early intervention (EI) before the age of 6 months is associated with enhanced language, compared with later enrollment ages. Little is understood about the impact of EI on outcomes occurring beyond the EI period (such as early academic outcomes).

WHAT THIS STUDY ADDS: In this study, we include public health and education data across 3 state agencies to provide evidence supporting enrollment into EI before the age of 6 months (versus later ages) for children who are deaf or hard of hearing on the increased likelihood of being kindergarten ready.

To cite: Meinzen-Derr J, Wiley S, Grove W, et al. Kindergarten Readiness in Children Who Are Deaf or Hard of Hearing Who Received Early Intervention. *Pediatrics*. 2020;146(4):e20200557

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-0557

This article has an accompanying video summary.

Divisions of [a]Biostatistics and Epidemiology and [b]Developmental and Behavioral Pediatrics, Department of Pediatrics, Cincinnati Children's Hospital Medical Center and College of Medicine, University of Cincinnati, Cincinnati, Ohio; [c]Office of Early Learning and School Readiness, Ohio Department of Education, Columbus, Ohio; [d]Division of Human Development and Disability and [f]National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, Georgia; and [e]Oak Ridge Institute for Science and Education, Oak Ridge, Tennessee

Dr Meinzen-Derr conceptualized and designed the study, conducted the statistical analyses, drafted the initial manuscript, and reviewed and revised the manuscript; Dr Altaye assisted with the statistical analyses and interpretation of the work and reviewed and critically revised the manuscript; Dr Wiley helped conceptualize the study, assisted with the interpretation of the statistical analyses, drafted the initial manuscript, and edited the manuscript; Dr Folger assisted with the design of the study and interpretation of the statistical analyses and drafted, reviewed, and revised the manuscript; (Continued)

Prenatal and Pediatric Primary Care–Based Child Obesity Prevention Program: A Randomized Trial

Mary Jo Messito, MD,[a] Alan L. Mendelsohn, MD,[b] Michelle W. Katzow, MD, MS,[c] Marc A. Scott, PhD,[d] Sarvenaz Vandyousefi, PhD, MS, RD,[a] Rachel S. Gross, MD, MS[a]

abstract

OBJECTIVES: To determine impact of a primary care–based child obesity prevention intervention beginning during pregnancy on early childhood weight outcomes in low-income Hispanic families.

METHODS: A randomized controlled trial comparing mother–infant pairs receiving either standard care or the Starting Early Program providing prenatal and postpartum nutrition counseling and nutrition parenting support groups targeting key obesity-related feeding practices in low-income groups. Primary outcomes were reduction in weight-for-age *z*-scores (WFAzs) from clinical anthropometric measures, obesity prevalence (weight for age ≥95th percentile), and excess weight gain (WFAz trajectory) from birth to age 3 years. Secondary outcomes included dose effects.

RESULTS: Pregnant women (n = 566) were enrolled in the third trimester; 533 randomized to intervention (n = 266) or control (n = 267). Also, 358 children had their weight measured at age 2 years; 285 children had weight measured at age 3 years. Intervention infants had lower mean WFAz at 18 months (0.49 vs 0.73, P = .04) and 2 years (0.56 vs 0.81, P = .03) but not at 3 years (0.63 vs 0.59, P = .76). No group differences in obesity prevalence were found. When generalized estimating equations were used, significant average treatment effects were detected between 10-26 months (B = −0.19, P = .047), although not through age 3 years. In within group dose analyses at 3 years, obesity rates (26.4%, 22.5%, 8.0%, P = .02) decreased as attendance increased with low, medium, and high attendance.

CONCLUSIONS: Mean WFAz and growth trajectories were lower for the intervention group through age 2 years, but there were no group differences at age 3. Further study is needed to enhance sustainability of effects beyond age 2.

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-0709

Divisions of [a]General Pediatrics and [b]Developmental and Behavioral Pediatrics, Department of Pediatrics, NYU Grossman School of Medicine and [d]Department of Applied Statistics, Social Science, and Humanities, Steinhardt School of Culture, Education, and Human Development, New York University, New York, New York; and [c]Division of General Pediatrics, Department of Pediatrics, Zucker School of Medicine at Hofstra/Northwell, Hempstead, New York

WHAT'S KNOWN ON THIS SUBJECT: Elevated weight in infancy contributes to disparities in later obesity, yet study of primary care–based preventive models during pregnancy and early childhood for high-risk groups is limited.

WHAT THIS STUDY ADDS: In this randomized trial of low-income Hispanic mother–infant pairs, the Starting Early Program led to lower weight trajectories and weight-for-age *z*-scores through age 2 years, although not sustained at age 3 years. Increased intervention exposure was associated with greater impacts.

To cite: Messito MJ, Mendelsohn AL, Katzow MW, et al. Prenatal and Pediatric Primary Care–Based Child Obesity Prevention Program: A Randomized Trial. *Pediatrics*. 2020; 146(4):e20200709

Childhood Adversity and Health After Physical Abuse

Kristine A. Campbell, MD, MSc,[a] Elizabeth Gamarra, MSW, MA,[b] Caren J. Frost, PhD, MPH,[b] Bom Choi, BS,[c] Heather T. Keenan, MDCM, PhD[a]

abstract

BACKGROUND: Involvement with Child Protective Services (CPS) provides an opportunity to recognize those children at risk for ongoing adverse childhood experiences (ACEs). The relationship between ACEs and child health among CPS-involved children and the role of primary care providers (PCPs) in moderating this relationship is unknown.

METHODS: We conducted a convergent mixed-methods study of caregivers of children age 2 to 12 years with a CPS finding of physical abuse, modeling the association between cumulative ACEs and child health-related quality of life (HRQoL) using the PedsQL4.0, a validated 23-item survey of multidimensional health, with and without the moderator of a patient-centered medical home. Interviews elicited descriptions of a child's experience with ACEs, the impact of ACEs on child health, and the role of a PCP in this context.

RESULTS: One hundred seventy-eight surveyed caregivers reported a mean of 5.5 (±3.3) ACE exposures per child. In a fully adjusted model, each ACE resulted in a 1.3-point (95% confidence interval: 0.7–2.0) reduction in HRQoL, a clinically important difference in HRQoL associated with ACE exposures. This association was explained by reduced psychosocial HRQoL and was not moderated by a patient-centered medical home. Twenty-seven interviewed caregivers described the influence of ACEs on a child's health. Many felt that a trusted PCP could support a child's well-being after such experiences.

CONCLUSIONS: Children with CPS involvement have ACE exposures that are associated with reduced HRQoL. Although PCPs are often unaware of CPS involvement or other ACEs, many caregivers welcome the support of a child's PCP in improving child well-being after adversity.

WHAT'S KNOWN ON THIS SUBJECT: An accumulation of childhood adversities is associated with lifelong physical and mental health challenges. The moment of Child Protective Services involvement for abuse is a moment to provide medical and social supports for children with risk for ongoing adverse experiences.

WHAT THIS STUDY ADDS: Children with a Child Protective Services finding of physical abuse carry a high burden of accumulated adversities. These adversities are associated with lower health-related quality of life. Caregivers identify pediatricians as potential support for children struggling with health after adversity.

To cite: Campbell KA, Gamarra E, Frost CJ, et al. Childhood Adversity and Health After Physical Abuse. *Pediatrics.* 2020;146(4):e20200638

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-0638

[a]*Department of Pediatrics and* [b]*College of Social Work,* [c]*University of Utah, Salt Lake City, Utah*

Dr Campbell conceptualized and designed the study, designed the data collection instruments, coordinated and supervised data collection, conducted analyses, drafted the initial manuscript, and reviewed and revised the manuscript; Ms Gamarra designed the data collection instruments, coordinated and collected data, conducted initial analysis, and reviewed and revised the manuscript; Drs Keenan and Frost conceptualized and designed the study and critically reviewed the manuscript for important intellectual content; Ms Choi conducted initial analysis and critically reviewed the manuscript for important intellectual content; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Ms Gamarra's current affiliation is the International Christian University, Tokyo, Japan. Ms Choi's current affiliation is Pennsylvania College of Optometry, Salus University, Elkins Park, Pennsylvania.

DOI: https://doi.org/10.1542/peds.2020-0638

Accepted for publication Jul 27, 2020

Outcomes of Isolated Neutropenia Referred to Pediatric Hematology-Oncology Clinic

Vishnu Nagalapuram, MBBS,[a] David McCall, MD,[b] Prasannalaxmi Palabindela, MBBS,[a] Thomas H. Howard, MD,[a] Christina Bemrich-Stolz, MD, MSPH,[a] Jeffrey Lebensburger, DO, MSPH,[a] Lee Hilliard, MD,[a] Hope P. Wilson, MD[a]

abstract

BACKGROUND: Children with isolated neutropenia (absolute neutrophil count [ANC] <1500/μL) are frequently referred to pediatric hematology and oncology clinics for further diagnostic evaluation. Scant literature exists on interventions and outcomes for isolated neutropenia. We hypothesized that children will have resolution of their neutropenia without the need for intervention(s) by a pediatric hematologist and oncologist.

METHODS: We performed a 5.5-year institutional review board–approved retrospective chart review of children referred to our pediatric hematology and oncology clinics for isolated neutropenia. Neutropenia was categorized as mild (ANC of 1001–1500/μL), moderate (ANC of 500–1000 μL), severe (ANC of 201–500/μL), or very severe (ANC of ≤200/μL).

RESULTS: Among 155 children referred with isolated neutropenia, 45 (29%) had mild neutropenia, 65 (42%) had moderate neutropenia, 30 (19%) had severe neutropenia, and 15 (10%) had very severe neutropenia. Only 29 (19%) children changed to an ANC category lower than their initial referral category. At a median follow-up of 12 months, 101 children had resolution of neutropenia, 40 children had mild neutropenia, 10 children had moderate neutropenia, 3 children had severe neutropenia, and 1 patient had very severe neutropenia. A specific diagnosis was not identified in most (54%) children. The most common etiologies were viral suppression (16%), autoimmune neutropenia (14%), and drug-induced neutropenia (8%). Black children had a 3.5 higher odds of having persistent mild neutropenia. Six (4%) children received granulocyte colony-stimulating factor therapy.

CONCLUSIONS: Most children referred for isolated neutropenia do not progress in severity and do not require subspecialty interventions or hospitalizations.

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2019-3637

[a]*Division of Pediatric Hematology-Oncology, Department of Pediatrics, School of Medicine, The University of Alabama at Birmingham, Birmingham, Alabama; and* [b]*MD Anderson Cancer Center, The University of Texas, Houston, Texas*

Dr Nagalapuram drafted the initial manuscript, collected data, and performed analyses; Drs McCall and Palabindela collected data and performed the initial analysis. Drs Wilson, Hilliard, Howard, and Bemrich-Stolz reviewed and revised the manuscript; Dr Lebensburger designed the study, data collection instruments, and reviewed and revised the manuscript; and all authors have approved the final manuscript as submitted and accept accountability for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2019-3637

Accepted for publication Jul 13, 2020

WHAT'S KNOWN ON THIS SUBJECT: Isolated neutropenia is a common referral to pediatric hematology and oncology clinics.

WHAT THIS STUDY ADDS: Isolated neutropenia most often resolves without intervention from a pediatric hematologist and oncologist. Children referred with isolated neutropenia are not at high risk for hospitalization, bacteremia, or progression to leukemia.

To cite: Nagalapuram V, McCall D, Palabindela P, et al. Outcomes of Isolated Neutropenia Referred to Pediatric Hematology-Oncology Clinic. *Pediatrics.* 2020;146(4):e20193637

Socioeconomic Status and Long-term Outcomes in Single Ventricle Heart Disease

Emily M. Bucholz, MD, PhD, MPH,[a,b] Lynn A. Sleeper, ScD,[a,b] Caren S. Goldberg, MD, MS,[c] Sara K. Pasquali, MD, MPH,[c] Brett R. Anderson, MD, MBA, MS,[d] J. William Gaynor, MD,[e] James F. Cnota, MD,[f] Jane W. Newburger, MD, MPH[a,b]

abstract

BACKGROUND: Low socioeconomic status (SES) has emerged as an important risk factor for higher short-term mortality and neurodevelopmental outcomes in children with hypoplastic left heart syndrome and related anomalies; yet little is known about how SES affects these outcomes over the long-term.

METHODS: We linked data from the Single Ventricle Reconstruction trial to US Census Bureau data to analyze the relationship of neighborhood SES tertiles with mortality and transplantation, neurodevelopment, quality of life, and functional status at 5 and 6 years post–Norwood procedure (N = 525). Cox proportional hazards regression and linear regression were used to assess the association of SES with mortality and neurodevelopmental outcomes, respectively.

RESULTS: Patients in the lowest SES tertile were more likely to be racial minorities, older at stage 2 and Fontan procedures, and to have more complications and fewer cardiac catheterizations over follow-up (all $P < .05$) compared with patients in higher SES tertiles. Unadjusted mortality was highest for patients in the lowest SES tertile and lowest in the highest tertile (41% vs 29%, respectively; log-rank P = .027). Adjustment for patient birth and Norwood factors attenuated these differences slightly (P = .055). Patients in the lowest SES tertile reported lower functional status and lower fine motor, problem-solving, adaptive behavior, and communication skills at 6 years (all $P < .05$). These differences persisted after adjustment for baseline and post-Norwood factors. Quality of life did not differ by SES.

CONCLUSIONS: Among patients with hypoplastic left heart syndrome, those with low SES have worse neurodevelopmental and functional status outcomes at 6 years. These differences were not explained by other patient or clinical characteristics.

WHAT'S KNOWN ON THIS SUBJECT: Low neighborhood socioeconomic status (SES) is associated with worse 1-year survival after the Norwood procedure. Little is known about whether this association persists over the long-term or how SES relates to other measures of well-being.

WHAT THIS STUDY ADDS: Patients with hypoplastic left heart syndrome and low SES have worse neurodevelopmental outcomes (adaptive behavior, problem-solving, fine motor, and communication skills) and functional status outcomes at 6 years post–Norwood procedure compared with patients with higher SES.

To cite: Bucholz EM, Sleeper LA, Goldberg CS, et al. Socioeconomic Status and Long-term Outcomes in Single Ventricle Heart Disease. *Pediatrics*. 2020;146(4):e20201240

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-1240

[a]*Department of Cardiology, Boston Children's Hospital, Boston, Massachusetts;* [b]*Department of Pediatrics, Harvard Medical School, Harvard University, Boston, Massachusetts;* [c]*Department of Pediatrics, University of Michigan and C.S. Mott Children's Hospital, Ann Arbor, Michigan;* [d]*Division of Pediatric Cardiology, Department of Pediatrics, Columbia University Irving Medical Center and NewYork-Presbyterian Morgan Stanley Children's Hospital, New York City, New York;* [e]*Division of Pediatric Cardiac Surgery, Cardiac Center, Children's Hospital of Pennsylvania, Philadelphia, Pennsylvania; and* [f]*Department of Cardiology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio*

Dr Bucholz conceptualized and designed the study, performed and interpreted the data analyses, and drafted and revised the manuscript; Dr Sleeper provided analytic support, interpreted the data analyses, and revised the manuscript; Drs Goldberg, Pasquali, Anderson, Gaynor, and Cnota interpreted the data analyses and revised the manuscript; Dr Newburger conceptualized and designed the study, interpreted the data analyses, and revised the manuscript.

Electromagnetic Versus Blind Guidance of a Postpyloric Feeding Tube in Critically Ill Children

Prashant Jha, MD,[a,b] Lisa Rupp, RN, BSN, CCRN,[c] Lorraine Bonilla, RN,[c] Jonathan Gelfond, MD, PhD,[d] Jay N. Shah, DO, MPH,[c,e] Andrew D. Meyer, MD, MS[c,f]

abstract

BACKGROUND AND OBJECTIVES: Postpyloric feeding tube placement is a time-consuming procedure associated with multiple attempts and radiation exposure. Our objective with this study is to compare the time, attempts, and radiation exposure using the electromagnetic versus blind method to place a postpyloric feeding tube in critically ill children. Our hypothesis is that using electromagnetic guidance decreases the procedure time, number of x-rays, and number of attempts, compared to the blind method.

METHODS: Eleven pediatric nurses participated in a randomized controlled intention-to-treat study at an academic pediatric medical, surgical, and congenital cardiac ICU. University of Texas Health Epidemiology and Biostatistics generated a randomization sequence with sealed envelopes. A standard (2-sided) F-test of association between the electromagnetic and blind method yielded 40 subjects with 86% power. Data were analyzed with Fisher's exact test for categorical variables and the Wilcoxon rank test for continuous variables, with data documented as median (interquartile range [IQR]).

RESULTS: We randomly assigned 52 patients to either the electromagnetic (n = 28) or blind method (n = 24). The number of attempts and radiographs was at a median of 2 (IQR: 1–2.25) using the blind method, compared to the electromagnetic method at a median of 1 (IQR: 1.0–1.0; P = .001). Successful guidance was 96.4% with the electromagnetic method, compared to only 66.7% with the blind technique (P = .008). The total time required was 2.5 minutes (IQR: 2.0–7.25) with the electromagnetic method, compared to 19 minutes (IQR: 9.25–27.0) for the blind method (P = .001).

CONCLUSIONS: Electromagnetic guidance is a superior, faster, and overall safer method to place a postpyloric feeding tube in critically ill children.

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2019-3773

[a]*Division of Critical Care, Department of Pediatrics, Children's Hospital of Nevada at University Medical Center, Las Vegas, Nevada;* [b]*Department of Pediatrics, University of Nevada Las Vegas School of Medicine, Las Vegas, Nevada;* [c]*Pediatric Services, University Health System, San Antonio, Texas; and* [e]*Divisions of Pediatric Gastroenterology and* [f]*Pediatric Critical Care, Department of Pediatrics and* [d]*Department of Epidemiology and Biostatistics, University of Texas Health San Antonio, San Antonio, Texas*

WHAT'S KNOWN ON THIS SUBJECT: Routine placement of a postpyloric feeding tube in a critically ill children using the standard blind technique is time consuming and challenging. This lengthy process can lead to a delay in the initiation of enteral nutritional support.

WHAT THIS STUDY ADDS: This is the first randomized controlled trial in pediatrics documenting that electromagnetic guidance of a postpyloric feeding tube will decrease harm by significantly decreasing radiation exposure, time, and attempts to successful placement.

To cite: Jha P, Rupp L, Bonilla L, et al. Electromagnetic Versus Blind Guidance of a Postpyloric Feeding Tube in Critically Ill Children. *Pediatrics.* 2020;146(4):e20193773

Interferon-γ Release Assays for Tuberculosis Infection Diagnosis in Refugees <5 Years Old

Kristen A. Wendorf, MD, MS,[a] Phil Lowenthal, MPH,[a] Jenna Feraud, BA,[a] Nuny Cabanting, MPH,[b] Christine Murto, PhD[b]

abstract

BACKGROUND: New guidelines support using interferon-γ release assays (IGRAs) in children ≥2 years for diagnosis of latent tuberculosis infection (LTBI). However, lack of experience in young children and concern that IGRAs are less sensitive than tuberculin skin tests (TSTs) limit their use. Our aim was to identify active tuberculosis (TB) cases among high risk children <5 years and tested for LTBI with an IGRA.

METHODS: . Retrospective review of domestic TB screening data from California's Refugee Health Electronic Information System for children <5 years old who resettled in California between October, 2013 and December, 2016. Children were crossmatched with the California TB registry to identify cases of TB disease between October 2013 and December 2018.

RESULTS: A total of 3371 children <5 years were identified; the majority were born in countries with high TB incidence (>150 cases per 100 000). Half received IGRAs (n = 1878; 56%), a quarter received TSTs (n = 811; 24%); 1.4% of children were IGRA-positive (n = 26) and 13% were TST-positive (n = 106). Twenty-two IGRA results were indeterminate (1.2%). Sixteen children had both tests; 9 were discrepant (positive TST with negative IGRA). No cases of TB disease were identified during 10 797 person-years of follow-up.

CONCLUSIONS: IGRA positivity was less than TST positivity in high risk children <5 years old. Despite fewer LTBI diagnoses in the IGRA-tested population, no cases of TB disease among children who tested negative were identified, suggesting IGRA is valuable tool for identifying LTBI in this population.

WHAT'S KNOWN ON THIS SUBJECT: Interferon-γ release assays (IGRAs) are the preferred tests for identification of tuberculosis (TB) infection among non–US-born people because of superior specificity among BCG-vaccinated individuals. Testing and treatment of TB infection in young children limits the severe sequela of TB disease.

WHAT THIS STUDY ADDS: IGRAs are a valuable tool for identifying TB infection among children <5 years old. IGRA identified latent TB infection with greater precision, fewer indeterminates, and without missing children who went on to develop TB disease in subsequent years.

To cite: Wendorf KA, Lowenthal P, Feraud J, et al. Interferon-γ Release Assays for Tuberculosis Infection Diagnosis in Refugees <5 Years Old. *Pediatrics.* 2020; 146(4):e20200715

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-0715

[a]*Tuberculosis Control Branch and* [b]*Office of Refugee Health, California Department of Public Health, Sacramento, California*

Dr Wendorf conceptualized and designed the study and drafted the initial manuscript; Mr Lowenthal conceptualized and designed the study, conducted the initial data analyses, created the figures and the tables, and critically reviewed the draft manuscript and revised critically for important intellectual content and data interpretation; Ms Feraud contributed to the conception and design of the project and assisted with creating figures and tables, review and interpretation of data elements, and overall formatting and other critical edits to the draft manuscript; Ms Cabanting acquired the initial data, assisted with understanding and correct use of the initial data and data analysis, and provided critical revisions of the manuscript to ensure correct interpretation of the data elements and provision of additional literature references in her specialty area; Dr Murto provided interpretation of data analysis and critically reviewed the draft manuscript to ensure correct interpretation of the data elements and analysis; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2020-0715

Accepted for publication Jul 9, 2020

Brief Behavioral Interventions for Substance Use in Adolescents: A Meta-analysis

Dale W. Steele, MD, MS,[a,b,c,d] Sara J. Becker, PhD,[e,f] Kristin J. Danko, PhD,[a,b] Ethan M. Balk, MD, MPH,[a,b] Gaelen P. Adam, MLIS, MPH,[a,b] Ian J. Saldanha, MBBS, MPH, PhD,[a,b] Thomas A. Trikalinos, MD, PhD[a,b]

abstract

CONTEXT: Adolescents with problematic substance use (SU) are at risk for far-reaching adverse outcomes.

OBJECTIVE: Synthesize the evidence regarding the effects of brief behavioral interventions for adolescents (12–20 years) with problematic SU.

DATA SOURCES: We conducted literature searches in Medline, the Cochrane Central Register of Controlled Trials, Embase, Cumulative Index to Nursing and Allied Health Literature, and PsycInfo through October 31, 2019.

STUDY SELECTION: We screened 33 272 records and citations for interventions in adolescents with at least problematic SU, retrieved 1831 articles, and selected 22 randomized controlled trials of brief interventions meeting eligibility criteria for meta-analysis.

DATA EXTRACTION: We followed Agency for Healthcare Research and Quality guidelines. We categorized brief interventions into components, including motivational interviewing (MI), psychoeducation, and treatment as usual. Outcomes included SU (abstinence, days used per month) for alcohol and cannabis, and substance-related problem scales. Strength of evidence (SoE) was assessed.

RESULTS: Both pairwise and network meta-analyses were conducted by using random effects models. Compared to treatment as usual, the use of MI reduces heavy alcohol use days by 0.7 days per month (95% credible interval [CrI]: −1.6 to 0.02; low SoE), alcohol use days by 1.1 days per month (95% CrI −2.2 to −0.3; moderate SoE), and overall substance-related problems by a standardized net mean difference of 0.5 (95% CrI –1.0 to 0; low SoE). The use of MI did not reduce cannabis use days, with a net mean difference of −0.05 days per month (95% CrI: −0.26 to 0.14; moderate SoE).

LIMITATIONS: There was lack of consistently reported outcomes and limited available comparisons.

CONCLUSIONS: The use of MI reduces heavy alcohol use, alcohol use days, and SU-related problems in adolescents but does not reduce cannabis use days.

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-0351

[a]Evidence-based Practice Center, Center for Evidence Synthesis in Health and [b]Departments of Health Services, Policy, and Practice and [e]Behavioral and Social Sciences, School of Public Health and [c]Departments of Emergency Medicine, [d]Pediatrics, and [f]Psychiatry and Human Behavior, Warren Alpert Medical School, Brown University, Providence, Rhode Island

This trial has been registered with PROSPERO (https://www.crd.york.ac.uk/prospero) (identifier CRD42018115388).

To cite: Steele DW, Becker SJ, Danko KJ, et al. Brief Behavioral Interventions for Substance Use in Adolescents: A Meta-analysis. *Pediatrics.* 2020;146(4):e20200351

The Need to Focus Research on Adolescent Cannabis Use Interventions

William P. Adelman, MD

Division of Adolescent Medicine, Children's Mercy Hospital, Kansas City, Missouri; and University of Missouri Kansas City, Kansas City, Missouri

DOI: https://doi.org/10.1542/peds.2020-012336

Accepted for publication Jul 10, 2020

Address correspondence to William P. Adelman, MD, Division of Adolescent Medicine, Children's Mercy Hospital, 3101 Broadway Blvd, Kansas City, MO 64111. E-mail: wpadelman@cmh.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The author has indicated he has no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The author has indicated he has no potential conflicts of interest to disclose.

COMPANION PAPER: A companion to this article can be found online at www.pediatrics.org/cgi/doi/10.1542/2020-0351.

To cite: Adelman WP. The Need to Focus Research on Adolescent Cannabis Use Interventions. *Pediatrics*. 2020;146(4):e2020012336

Nearly one half of all 12th-graders in the United States have used cannabis in their lifetime, with more than one third during the past year, and almost one quarter in the past month.[1] Among individuals who have ever used cannabis, the lifetime risk of developing cannabis use disorder (CUD) is 8% to 12%.[2] With no effective pharmacologic treatment, interventions for adolescents and young adults with CUD rely on psychological modalities. Brief interventions (BIs), defined as "practices that aim to investigate a potential problem and motivate an individual to begin to do something about his substance abuse, either by natural, client-directed means or by seeking additional substance abuse treatment,"[3] including techniques such as motivational interviewing (MI), appear well suited for the pediatrician's office, and is recommended by the American Academy of Pediatrics.[4]

In this issue of *Pediatrics*, Steele et al[5] synthesized 22 trials of BI in adolescents (12–20 years old) with problematic substance use and estimated effects on alcohol use, cannabis use, and substance-related problems. They found that although MI reduced heavy alcohol use, alcohol use-days, and substance use-related problems, MI did not reduce cannabis use-days. The alcohol findings are consistent with those of numerous studies, reviews, and meta-analyses that have shown benefit to 11- to 18-year-old alcohol users who receive BI.[6] In contrast, the cannabis findings are within a range of disparate results from previous studies and highlight 2 important issues regarding the state of research on the role of BIs for adolescent substance users: (1) CUD research among adolescents remains in its infancy with heterogeneity and lack of specificity among intervention trials for adolescent cannabis use, and (2) not all BIs are the same.

During the past decade, the United States increased legalization of cannabis on the state level in the context of shifting public sentiment regarding cannabis use. Various organizations called for research agendas in cannabis, cannabinoids, and their use in adolescents.[7,8] Although descriptive study of adolescent cannabis use is well established, interventions for adolescent cannabis users remains a growing area of research. As a result, few high-quality cannabis-specific intervention studies have been performed, which makes it challenging to draw general conclusions from their results.[9,10] Steele et al[5] point out lack of specificity of cannabis use in studies, because cannabis is conflated with "illicit drug use" or similar terms encompassing marijuana with other drugs.[11–13] Moreover, heterogeneity in setting (primary care, emergency department, school, foster care, homeless, incarcerated), intervention (MI, motivation enhancement therapy, psychoeducation), delivery method (Web, computer, phone, in person, number of sessions) and comparison group (brief advice, information sessions, pamphlets, educational materials, waitlist), all limit the utility of meta-analysis and review to

generalize the role BI may play in treating cannabis users. Further specific research is needed regarding BI and adolescent cannabis use.

Psychosocial interventions are effective for adult cannabis users in reducing frequency of cannabis use, quantity used per occasion, and severity of dependence.[14,15] In adolescents, effectiveness of BI for cannabis use varies. For example, researchers of one randomized trial found that a 2-session BI, when compared with a 3-month delay in treatment, significantly reduced the frequency and quantity of cannabis use and the number of cannabis-dependence symptoms.[16] Another review and meta-analysis indicated that BI targeting non–treatment-seeking adolescents results in significant reductions in symptoms of CUD and an increased likelihood of cannabis abstinence but did not reduce cannabis use compared with passive control.[17] Yet another review noted that numerous individual studies, in a variety of settings, such as schools, pediatric emergency departments, and universities, have found that BIs are effective and feasible when applied by trained counselors to an adolescent and young adult population.[18] This further underscores the need for more uniform and targeted adolescent cannabis research and reminds us that not all BIs are the same.

Drug and alcohol treatment outcomes vary according to which practitioners deliver counseling interventions,[19] what is included in the intervention,[20] and behavior within sessions.[21] Fidelity to MI spirit (collaboration, compassion, evocation, acceptance) and the proportion of complex reflections are independently predictive of cessation outcome for adolescent cannabis users.[22,23] However, fidelity to technique measurement is often absent from BI studies. Similarly, as legalization of recreational and "medical" marijuana increases and perception of harm decreases,[24,25] further research must incorporate individual factors because the adolescent cannabis user may face unique challenges in motivation for change compared with users of alcohol and other substances.

BI remains a promising option for pediatricians who treat adolescent substance users but urgently requires further targeted research. Studies to date are too heterogeneous and nonspecific to cannabis use to reliably draw generalizable conclusions. Clarification of correct BI technique, in appropriate settings, for targeted populations, is necessary to determine best practice for adolescent cannabis use harm reduction.

ABBREVIATIONS

BI: brief intervention
CUD: cannabis use disorder
MI: motivational interviewing

REFERENCES

1. National Institute on Drug Abuse. Monitoring the future. Available at: https://www.drugabuse.gov/drug-topics/trends-statistics/infographics/monitoring-future-2019-survey-results-overall-findings. Accessed August 5, 2020
2. Danovitch I, Gorelick DA. The Treatment of Cannabis Use Disorder. In: Danovitch I, Mooney LJ, eds. *The Assessment and Treatment of Addiction: Best Practices and New Frontiers*. St. Louis, MO: Elsevier; 2019:105–121
3. Center for Substance Abuse Treatment. *Brief Interventions and Brief Therapies for Substance Abuse. Treatment Improvement Protocol (TIP) Series, No. 34. HHS Publication No. (SMA) 12-3952*. Rockville, MD: Substance Abuse and Mental Health Services Administration; 1999
4. Levy SJ, Kokotailo PK; Committee on Substance Abuse. Substance use screening, brief intervention, and referral to treatment for pediatricians. *Pediatrics*. 2011;128(5). Available at: www.pediatrics.org/cgi/content/full/128/5/e1330
5. Steele D, Becker S, Danko K, et al. Brief behavioral interventions for substance use in adolescents: a meta-analysis. *Pediatrics*. 2020;146(4):20200351
6. Tanner-Smith EE, Lipsey MW. Brief alcohol interventions for adolescents and young adults: a systematic review and meta-analysis. *J Subst Abuse Treat*. 2015;51:1–18
7. Ammerman S, Ryan S, Adelman WP; Committee on Substance Abuse, the Committee on Adolescence. The impact of marijuana policies on youth: clinical, research, and legal update. *Pediatrics*. 2015;135(3). Available at: www.pediatrics.org/cgi/content/full/135/3/e769
8. National Academies of Sciences. *Engineering and Medicine. The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research*. Washington, DC: The National Academies Press; 2017
9. Walker E, Hernandez AV, Kattan MW. Meta-analysis: its strengths and limitations. *Cleve Clin J Med*. 2008;75(6):431–439
10. Lee YH. Strengths and limitations of meta-analysis. *Korean J Med*. 2019;94(5):391–395
11. Tanner-Smith EE, Steinka-Fry KT, Hennessy EA, Lipsey MW, Winters KC. Can brief alcohol interventions for youth also address concurrent illicit drug use? results from a meta-analysis. *J Youth Adolesc*. 2015;44(5):1011–1023
12. Li L, Zhu S, Tse N, Tse S, Wong P. Effectiveness of motivational interviewing to reduce illicit drug use in adolescents: a systematic review and meta-analysis. *Addiction*. 2016;111(5):795–805
13. Brown RA, Abrantes AM, Minami H, et al. Motivational Interviewing to reduce substance use in adolescents with psychiatric comorbidity. *J Subst Abuse Treat*. 2015;59:20–29
14. Gates PJ, Sabioni P, Copeland J, Le Foll B, Gowing L. Psychosocial interventions for cannabis use disorder. *Cochrane Database Syst Rev*. 2016;2016(5):CD005336

15. Smedslund G, Berg RC, Hammerstrøm KT, et al. Motivational interviewing for substance abuse. *Cochrane Database Syst Rev*. 2011;(5):CD008063

16. Martin G, Copeland J. The adolescent cannabis check-up: randomized trial of a brief intervention for young cannabis users. *J Subst Abuse Treat*. 2008;34(4): 407–414

17. Halladay J, Scherer J, MacKillop J, et al. Brief interventions for cannabis use in emerging adults: a systematic review, meta-analysis, and evidence map. *Drug Alcohol Depend*. 2019;204:107565

18. Parmar A, Sarkar S. Brief interventions for cannabis use disorders: a review. *Addict Disord Their Treat*. 2017;16(2): 80–93

19. Luborsky L, McLellan AT, Woody GE, O'Brien CP, Auerbach A. Therapist success and its determinants. *Arch Gen Psychiatry*. 1985;42(6):602–611

20. Apodaca TR, Longabaugh R. Mechanisms of change in motivational interviewing: a review and preliminary evaluation of the evidence. *Addiction*. 2009;104(5):705–715

21. Project Match Research Group. Therapist effects in three treatments for alcohol problems. *Psychother Res*. 1998;8(4):455–474

22. McCambridge J, Day M, Thomas BA, Strang J. Fidelity to Motivational Interviewing and subsequent cannabis cessation among adolescents. *Addict Behav*. 2011;36(7):749–754

23. McCambridge J, Slym RL, Strang J. Randomized controlled trial of motivational interviewing compared with drug information and advice for early intervention among young cannabis users. *Addiction*. 2008;103(11): 1809–1818

24. Miech R, Johnston L, O'Malley PM. Prevalence and attitudes regarding marijuana use among adolescents over the past decade. *Pediatrics*. 2017; 140(6):e20170982

25. Committee on Substance Abuse, Committee on Adolescence. The impact of marijuana policies on youth: clinical, research, and legal update. *Pediatrics*. 2015;135(3):584–587

Pediatric Mental Health Boarding

Fiona B. McEnany, MPH,[a,b] Olutosin Ojugbele, MD, MPH,[c] Julie R. Doherty, MA,[a] Jennifer L. McLaren, MD,[a,d] JoAnna K. Leyenaar, MD, PhD, MPH[a,c]

abstract

CONTEXT: The growing prevalence of pediatric mental and behavioral health disorders, coupled with scarce psychiatric resources, has resulted in a substantial increase in the number of youth waiting in emergency departments (EDs) and medical units for inpatient psychiatric care.

OBJECTIVE: To characterize the prevalence of pediatric mental health boarding and identify associated patient and hospital factors.

DATA SOURCES: Medline and PsycINFO.

STUDY SELECTION: All studies describing frequencies, durations, processes, outcomes, and/or risk factors associated with pediatric mental health boarding in youth ≤21 years of age.

DATA EXTRACTION: Publications meeting inclusion criteria were charted by 2 authors and critically appraised for quality.

RESULTS: Eleven studies met inclusion criteria; 10 were retrospective cohort studies and 9 were conducted at single centers. All of the single-center studies were conducted at children's hospitals or pediatric EDs in urban or suburban settings. Study sample sizes ranged from 27 to 44 328. Among youth requiring inpatient psychiatric care, 23% to 58% experienced boarding and 26% to 49% boarded on inpatient medical units. Average boarding durations ranged from 5 to 41 hours in EDs and 2 to 3 days in inpatient units. Risk factors included younger age, suicidal or homicidal ideation, and presentation to a hospital during nonsummer months. Care processes and outcomes were infrequently described. When reported, provision of psychosocial services varied widely.

LIMITATIONS: Boarding definitions were heterogeneous, study sample sizes were small, and rural regions and general hospitals were underrepresented.

CONCLUSIONS: Pediatric mental health boarding is prevalent and understudied. Additional research representing diverse hospital types and geographic regions is needed to inform clinical interventions and health care policy.

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-1174

This article has an accompanying video summary.

[a]*The Dartmouth Institute for Health Policy and Clinical Practice and* [b]*Department of Biomedical Sciences, Geisel School of Medicine, Dartmouth College, Hanover, New Hampshire; and* [c]*Departments of Pediatrics and* [d]*Psychiatry, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire*

To cite: McEnany FB, Ojugbele O, Doherty JR, et al. Pediatric Mental Health Boarding. *Pediatrics.* 2020;146(4):e20201174

A Call to Action to Address Disparities in Pediatric Mental Health Care

Nicolaus W. Glomb, MD, MPH, Jacqueline Grupp-Phelan, MD, MPH

Department of Emergency Medicine, Benioff Children's Hospital, University of California, San Francisco, San Francisco, California

DOI: https://doi.org/10.1542/peds.2020-018911

Accepted for publication Jul 23, 2020

Address correspondence to Nicolaus W. Glomb, MD, MPH, University of California, 550 16th St #5153, Box 0632, San Francisco, CA 94143.
E-mail: nicolaus.glomb@ucsf.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

COMPANION PAPER: A companion to this article can be found online at www.pediatrics.org/cgi/doi/10.1542/2020-1174.

To cite: Glomb NW and Grupp-Phelan J. A Call to Action to Address Disparities in Pediatric Mental Health Care. *Pediatrics*. 2020;146(4):e2020018911

In this issue of *Pediatrics*, McEnany et al[1] performed a meta-analysis to better understand pediatric mental health boarding in emergency departments and patient and hospital characteristics that increase the likelihood of boarding. Visits to pediatric emergency departments for mental health–related complaints have steadily increased over the past decade,[2,3] resulting in significant delays in care for patients, increased resource use in emergency departments, and significant inpatient costs. McEnany et al[1] highlight the need for additional research, particularly on the national level and in rural and general hospital settings, to inform policy decisions to help address this problem.

A better understanding of the mental health resources available nationally in both rural and urban centers is essential. This includes patient access to hospital-based psychiatric resources, inpatient interventions, community-based psychiatric treatment centers, and psychiatric stabilization units. Significant disparities in mental health services continue to exist, with many communities in the United States lacking regionally coordinated pediatric psychiatric care. The lack of pediatric psychiatric care facilities directly contributes to the increased use of emergency departments for psychiatric care and, consequently, children experience delays in receiving emergent psychiatric assessment and treatment.

Disparities in care have also contributed to the growing problem of pediatric boarding in emergency departments.[4] Children of younger age with mental health problems are found to have a higher likelihood of boarding in emergency departments.[1] In addition, because of the fact that children are disproportionately affected by poverty, with the increased risk for mental health disorders and decreased access to mental health services,[3,4] it becomes clear that there are multifaceted risk factors leading to barriers in accessing mental health care. Those facing challenges in accessing mental health care also have high readmission rates, further stressing hospital systems. Other risk factors, such as identifying as lesbian, gay, bisexual, or transgender; rural residence; and substance abuse, and their association with mental health and boarding need to be further investigated on the national level. More research is needed to investigate the association of sociodemographic and clinical characteristics and mental health.

For regions of the United States that do have access to pediatric psychiatric services, methods for determining prehospital diversion when possible should be developed. Trivedi et al[5] identified that ~10% of adult regional emergency medical service transports were for patients placed on involuntary mental health holds, and with the use of an emergency medical service–directed screening protocol, patients can be safely diverted to an inpatient psychiatric facility and bypass medical clearance in emergency departments. Preliminary data on pediatric patients from the same region of the United

States indicate that diversion of pediatric patients on mental health holds is safe. These upstream efforts can provide potential interventions for expediting assessment, safe diversion, and treatment of these patients.[5]

The need for additional research to understand pediatric mental health boarding and access to care in urban and rural settings throughout the United States is fundamental to creating a mental health system of care that mitigates the need for boarding. McEnany et al[1] lay out the critical information needed to continue to develop proven mechanisms for getting children the care they need in a timely fashion and to continue to explore other potential barriers to care. This in turn can help to fuel the change in pediatric mental health policy and to strive for a more balanced provision of psychosocial services in the United States.

REFERENCES

1. McEnany F, Ojugbele O, Doherty J, McLaren J, Leyenaar J. Pediatric mental health boarding. *Pediatrics*. 2020; 146(4):e20201174
2. Hoffmann JA, Stack AM, Samnaliev M, Monuteaux MC, Lee LK. Trends in visits and costs for mental health emergencies in a pediatric emergency department, 2010–2016. *Acad Pediatr*. 2019;19(4):386–393
3. Lo CB, Bridge JA, Shi J, Ludwig L, Stanley RM. Children's mental health emergency department visits: 2007–2016. *Pediatrics*. 2020;145(6): e20191536
4. Hodgkinson S, Godoy L, Beers LS, Lewin A. Improving mental health access for low-income children and families in the primary care setting. *Pediatrics*. 2017; 139(1):e20151175
5. Trivedi TK, Glenn M, Hern G, Schriger DL, Sporer KA. Emergency medical services use among patients receiving involuntary psychiatric holds and the safety of an out-of-hospital screening protocol to "medically clear" psychiatric emergencies in the field, 2011 to 2016. *Ann Emerg Med*. 2019; 73(1):42–51

The Route, Dose, and Interval of Epinephrine for Neonatal Resuscitation: A Systematic Review

Tetsuya Isayama, MD, MSc, PhD,[a] Lindsay Mildenhall, MBChB, FRACP,[b] Georg M. Schmölzer, MD, PhD,[c,d] Han-Suk Kim, MD, PhD,[e] Yacov Rabi, MD,[f] Carolyn Ziegler, MA, MIS,[g] Helen G. Liley, MBChB, FRACP,[h] INTERNATIONAL LIAISON COMMITTEE ON RESUSCITATION NEWBORN LIFE SUPPORT TASK FORCE

abstract

CONTEXT: Current International Liaison Committee on Resuscitation recommendations on epinephrine administration during neonatal resuscitation were derived in 2010 from indirect evidence in animal or pediatric studies.

OBJECTIVE: Systematic review of human infant and relevant animal studies comparing other doses, routes, and intervals of epinephrine administration in neonatal resuscitation with (currently recommended) administration of 0.01 to 0.03 mg/kg doses given intravenously (IV) every 3 to 5 minutes.

DATA SOURCES: Medline, Embase, Cumulative Index to Nursing and Allied Health Literature, Cochrane Database of Systematic Reviews, and trial registry databases.

STUDY SELECTION: Predefined criteria were used for selection.

DATA EXTRACTION: Risk of bias was assessed by using published tools appropriate for the study type. Certainty of evidence was assessed by using Grading of Recommendations Assessment, Development and Evaluation.

RESULTS: Only 2 of 4 eligible cohort studies among 593 unique retrieved records yielded data allowing comparisons. There were no differences between IV and endotracheal epinephrine for the primary outcome of death at hospital discharge (risk ratio = 1.03 [95% confidence interval 0.62 to 1.71]) or for failure to achieve return of spontaneous circulation, time to return of spontaneous circulation (1 study; 50 infants), or proportion receiving additional epinephrine (2 studies; 97 infants). There were no differences in outcomes between 2 endotracheal doses (1 study). No human infant studies were found in which authors addressed IV dose or dosing interval.

LIMITATIONS: The search yielded sparse human evidence of very low certainty (downgraded for serious risk of bias and imprecision).

CONCLUSIONS: Administration of epinephrine by endotracheal versus IV routes resulted in similar survival and other outcomes. However, in animal studies, researchers continue to suggest benefit of IV administration using currently recommended doses.

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-0586

This article has an accompanying video summary.

[a]National Center for Child Health and Development, Tokyo, Japan; [b]Middlemore Hospital, Otahuhu, Auckland, New Zealand; [c]Centre for the Studies of Asphyxia and Resuscitation, Neonatal Research Unit, Royal Alexandra Hospital, Edmonton, Alberta, Canada; [d]University of Alberta, Edmonton, Alberta, Canada; [e]Department of Pediatrics, Seoul National University College of Medicine, Seoul, Korea; [f]University of Calgary, Calgary, Alberta, Canada; [g]St Michael's Hospital, Toronto, Ontario, Canada; and [h]Mater Research Institute and Mater Clinical School, Faculty of Medicine, The University of Queensland, Brisbane, Queensland, Australia

To cite: Isayama T, Mildenhall L, Schmölzer GM, et al. The Route, Dose, and Interval of Epinephrine for Neonatal Resuscitation: A Systematic Review. *Pediatrics*. 2020; 146(4):e20200586

Epinephrine for Neonatal Resuscitation: The Limits of Knowledge

Mark L. Hudak, MD

Epinephrine (from the Greek epi-nephros, "on top of the kidneys"), known across the Atlantic pond as adrenalin (from the Latin ad-renal, "near the kidneys"), has been an unquestioned staple in the neonatal resuscitation drug toolkit for many decades. First extracted from the adrenal medulla in 1895, purified in 1901, and synthesized in 1904, this drug has proven efficacy for the treatment of a number of acute conditions such as anaphylaxis and glaucoma.

In 2010, the International Liaison Committee on Resuscitation (ILCOR) published recommendations for using epinephrine to resuscitate newborns "derived largely from indirect evidence from pediatric studies of uncertain relevance to neonates or from animal studies."[1] Among newborns in whom effective lung ventilation and chest compressions fail to increase heart rate >60 beats per minute, the guidelines suggested administration of an intravenous dose of epinephrine (0.01–0.03 mg/kg) repeated every 3 to 5 minutes as needed. A higher dose (0.05–0.1 mg/kg) administered through an endotracheal tube was the fallback option in the absence of intravenous access. But what do we really know about the best dose, dosing interval, route of administration, and efficacy of epinephrine in neonatal resuscitation?

In this issue of *Pediatrics*, Isayama et al[1] on the ILCOR Newborn Life Support Task Force present an exhaustive systematic review of the literature to answer this question. Specifically, they asked whether any nonstandard dose, interval, or route of administration of epinephrine administered to term or preterm neonates improved the primary outcome of survival to discharge or some secondary outcomes (eg, rate of achieving return of spontaneous circulation [ROSC], time until ROSC, need for a second dose of epinephrine, absence of major morbidities).[1] They cast a wide net to capture both randomized and nonrandomized controlled studies, interrupted time series studies, controlled before-and-after studies, and observational cohort (but not case series) studies in the published literature that had English abstracts. De rigueur for systematic reviews, the authors assessed each study for risk of bias (using the Risk Of Bias In Non-Randomized Studies of Interventions tool[2]) and certainty of evidence (using the Grading of Recommendation Assessment, Development, and Evaluation methodology that considered risk of bias, inconsistency, and imprecision[3,4]).

Notably, authors of this review documented a striking paucity of evidence that speaks to their question. The authors deemed only 4 of 593 retrieved studies eligible for analysis. All 4 were single-center retrospective cohort studies of delivery room events that in total included 117 infants treated with epinephrine. Researchers of 3 studies reported on different time periods from the same institution. Of the 2 studies in which outcomes in infants treated with endotracheal and/or intravenous epinephrine were

Department of Pediatrics, College of Medicine–Jacksonville, University of Florida, Jacksonville, Florida

DOI: https://doi.org/10.1542/peds.2020-019968

Accepted for publication Jul 15, 2020

Address correspondence to Mark L. Hudak, MD, Department of Pediatrics, University of Florida College of Medicine – Jacksonville, 653-1 W 8th St, Box L-1600, Jacksonville, FL 32209.
E-mail: mark.hudak@jax.ufl.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The author has indicated he has no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The author has indicated he has no potential conflicts of interest to disclose.

COMPANION PAPER: A companion to this article can be found online at www.pediatrics.org/cgi/doi/10.1542/2020-0586.

To cite: Hudak ML. Epinephrine for Neonatal Resuscitation: The Limits of Knowledge. *Pediatrics*. 2020;146(4):e2020019968

described, only 1 pertained to the primary outcome, 2 addressed return to ROSC, 1 assessed time to ROSC, and 1 included data on repeat dosing. Unfortunately, the quality of the studies was suboptimal. All 4 studies were judged to be biased because of confounding or because the threshold for treatment was less stringent than the 2010 ILCOR recommendation. In the end, no analysis found a difference between endotracheal and intravenous epinephrine with respect to the primary or any secondary outcome, but these findings are colored by a low certainty of evidence because of serious imprecision and serious risk of bias.

Having found insufficient guidance in the human literature, the authors turned next to a review of animal studies. Surprisingly, the referenced studies that detail different epinephrine regimens used in models of neonatal asphyxia in 2 animal species do not provide unambiguous assurance that epinephrine improves primary or secondary outcomes.

How should we as clinicians, who "know from experience" that epinephrine is effective, process this systematic review? I would suggest with large doses of honesty and humility! In this systematic review, it is made clear that the body of evidence pertaining to the outcome of infants resuscitated with epinephrine can neither validate nor refute current ILCOR recommendations. But it would be foolhardy to now abandon the use of epinephrine in newborns solely because we lack directly pertinent placebo-controlled trials of efficacy. We must also appreciate that better evidence of good quality is unlikely to emerge soon given that the rare (0.05% of all live births) and unexpected use of epinephrine in newborn infants frustrates the design and execution of controlled studies of sufficient power. The authors note that multicenter cluster-randomized trials might constitute a path forward. One has to question whether optimization of epinephrine administration is truly a priority area for study at the present time. Efforts to improve and maintain competencies in recognizing fetal asphyxia and performing efficient and effective neonatal resuscitation are likely to provide a much greater return on investment.

In the meantime, it seems self-evident to this simple clinician to continue to work to assure an effective team choreography of resuscitation and to administer epinephrine only when indicated via the first route available by using doses recommended by the current ILCOR guidelines.

ABBREVIATIONS

ILCOR: International Liaison Committee on Resuscitation

ROSC: return of spontaneous circulation

REFERENCES

1. Isayama T, Mildenhall L, Schmölzer G, et al. The route, dose, and interval of epinephrine for neonatal resuscitation: a systematic review. *Pediatrics*. 2020; 146(4):e20200586
2. Sterne JA, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ*. 2016;355:i4919
3. Guyatt GH, Oxman AD, Vist GE, et al; GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*. 2008; 336(7650):924–926
4. *GRADEpro GDT*. McMaster University and Evidence Prime, Inc; 2015. Available at: https://gradepro.org/. Accessed July 14, 2020

Trajectories of Lung Function in Infants and Children: Setting a Course for Lifelong Lung Health

Brian K. Jordan, MD, PhD, Cindy T. McEvoy, MD, MCR

For healthy individuals, it is increasingly accepted that lung function follows along an individual percentile established early in life and that the level of maximal function reached as a young adult can affect the subsequent development of lung disease that occurs with the normal aging process. This emphasizes the need to maximize early lung function. The trajectories of lung function are at least partially established by perinatal factors, including prematurity and in utero exposures (tobacco exposure, nutrition, inflammation, etc), although they can also be affected by a variety of additional factors and exposures throughout the life span. Whether lung function trajectories can be impacted or reset if established under suboptimal conditions is an unanswered question, offering new avenues for research. In this review, we will summarize important articles outlining lung function trajectories and linking pediatric lung function tests to adult lung function tests decades later. We will focus on perinatal factors and outline progress and opportunities for further investigation into the potential ability to reset trajectories to impact long-term lung health.

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-0417

abstract

Doernbecher Children's Hospital, Oregon Health & Science University, Portland, Oregon

Drs Jordan and McEvoy conceptualized the review, drafted the initial manuscript, and critically reviewed and revised the manuscript; and both authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2020-0417

Accepted for publication Jun 10, 2020

Address correspondence to Brian K. Jordan, MD, PhD, Division of Neonatology, Department of Pediatrics, Oregon Health & Science University, 2222 CDRC-P, 707 SW Gaines St, Portland, OR 97239. E-mail: jordabr@ohsu.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Supported by the National Center for Advancing Translational Sciences of the National Institutes of Health (NIH) under award number KL2 TR002370 and NIH National Heart, Lung, and Blood Institute under award number K23 HL144918, HL105447, HL129060 and UH3OD023288. The funders had no role in the study design, data collection, analysis, decision to publish, or preparation of the article. Funded by the National Institutes of Health (NIH).

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

To cite: Jordan BK and McEvoy CT. Trajectories of Lung Function in Infants and Children: Setting a Course for Lifelong Lung Health. *Pediatrics*. 2020;146(4):e20200417

Long-term Cognitive, Psychological, and Health Outcomes Associated With Child Abuse and Neglect

Lane Strathearn, MBBS, FRACP, PhD,[a,b] Michele Giannotti, PhD,[c] Ryan Mills, MPH, PhD,[d,e] Steve Kisely, MD, PhD, DMedRes,[f,g,h] Jake Najman, PhD,[d] Amanuel Abajobir, MPH, PhD[d,i]

abstract

Potential long-lasting adverse effects of child maltreatment have been widely reported, although little is known about the distinctive long-term impact of differing types of maltreatment. Our objective for this special article is to integrate findings from the Mater-University of Queensland Study of Pregnancy, a longitudinal prenatal cohort study spanning 2 decades. We compare and contrast the associations of specific types of maltreatment with long-term cognitive, psychological, addiction, sexual health, and physical health outcomes assessed in up to 5200 offspring at 14 and/or 21 years of age. Overall, psychological maltreatment (emotional abuse and/or neglect) was associated with the greatest number of adverse outcomes in almost all areas of assessment. Sexual abuse was associated with early sexual debut and youth pregnancy, attention problems, posttraumatic stress disorder symptoms, and depression, although associations were not specific for sexual abuse. Physical abuse was associated with externalizing behavior problems, delinquency, and drug abuse. Neglect, but not emotional abuse, was associated with having multiple sexual partners, cannabis abuse and/or dependence, and experiencing visual hallucinations. Emotional abuse, but not neglect, revealed increased odds for psychosis, injecting-drug use, experiencing harassment later in life, pregnancy miscarriage, and reporting asthma symptoms. Significant cognitive delays and educational failure were seen for both abuse and neglect during adolescence and adulthood. In conclusion, child maltreatment, particularly emotional abuse and neglect, is associated with a wide range of long-term adverse health and developmental outcomes. A renewed focus on prevention and early intervention strategies, especially related to psychological maltreatment, will be required to address these challenges in the future.

This article has an accompanying video summary.

[a]*Department of Pediatrics, Carver College of Medicine, The University of Iowa, Iowa City, Iowa;* [b]*Center for Disabilities and Development, University of Iowa Stead Family Children's Hospital, Iowa City, Iowa;* [c]*Department of Psychology and Cognitive Science, University of Trento, Trento, Italy;* [d]*School of Public Health, The University of Queensland, Herston, Queensland, Australia;* [e]*Department of Paediatrics, Logan Hospital, Meadowbrook, Queensland, Australia;* [f]*School of Medicine, The University of Queensland and Princess Alexandra Hospital, Woolloongabba, Queensland, Australia;* [g]*Departments of Psychiatry and* [h]*Community Health and Epidemiology, Dalhousie University, Halifax, Nova Scotia, Canada; and* [i]*Maternal and Child Wellbeing Unit, African Population and Health Research Center, Nairobi, Kenya*

Dr Strathearn conceptualized and designed the original study linking the Mater-University of Queensland Study of Pregnancy data set with substantiated reports of child maltreatment, drafted the special article, and reviewed and revised the manuscript; Dr Giannotti assisted in drafting the manuscript and prepared all tables and figures; Drs Mills, Kisely, and Abajobir conceptualized and wrote the original research articles summarized in this article; Dr Najman was the original principal investigator of the Mater-University of Queensland Study of Pregnancy; and all authors critically reviewed the manuscript for important intellectual content and approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2020-0438

Accepted for publication Jul 2, 2020

Address correspondence to Lane Strathearn, MBBS, FRACP, PhD, Stead Family Department of Pediatrics, Carver College of Medicine, The University of Iowa, 100 Hawkins Dr, 213F CDD, Iowa City, IA 52242-1011. E-mail: lane-strathearn@uiowa.edu

To cite: Strathearn L, Giannotti M, Mills R, et al. Long-term Cognitive, Psychological, and Health Outcomes Associated With Child Abuse and Neglect. *Pediatrics.* 2020;146(4):e20200438

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-0438

IDeA States Pediatric Clinical Trials Network for Underserved and Rural Communities

Robert D. Annett, PhD,[a] Sheva Chervinskiy, MD,[b] Thomas H. Chun, MD, MPH,[c] Kelly Cowan, MD,[d] Kristina Foster, MS, RN, APRN-BC, CWOCN,[e] Nathaniel Goodrich, MD,[f] Matthew Hirschfeld, MD, PhD,[g] Daniel S. Hsia, MD,[h] J. Dean Jarvis, BSN, MBA, RN, CCRP,[i] Kurtis Kulbeth, BS,[b] Christi Madden, MPA,[j] Clare Nesmith, MD,[k] Hengameh Raissy, PharmD,[l] Judith Ross, MD,[m] J. Philip Saul, MD,[n] Bruce Shiramizu, MD,[o] Paul Smith, DO, FAAP, FACOP,[p] Janice E. Sullivan, MD, FAAP, FCCM, CPI, CIP,[q] Lauren Tucker, MD,[a] Andrew M. Atz, MD[r]

abstract

The National Institutes of Health's Environmental Influences on Child Health Outcomes (ECHO) program aims to study high-priority and high-impact pediatric conditions. This broad-based health initiative is unique in the National Institutes of Health research portfolio and involves 2 research components: (1) a large group of established centers with pediatric cohorts combining data to support longitudinal studies (ECHO cohorts) and (2) pediatric trials program for institutions within Institutional Development Awards states, known as the ECHO Institutional Development Awards States Pediatric Clinical Trials Network (ISPCTN). In the current presentation, we provide a broad overview of the ISPCTN and, particularly, its importance in enhancing clinical trials capabilities of pediatrician scientists through the support of research infrastructure, while at the same time implementing clinical trials that inform future health care for children. The ISPCTN research mission is aligned with the health priority conditions emphasized in the ECHO program, with a commitment to bringing state-of-the-science trials to children residing in underserved and rural communities. ISPCTN site infrastructure is critical to successful trial implementation and includes research training for pediatric faculty and coordinators. Network sites exist in settings that have historically had limited National Institutes of Health funding success and lacked pediatric research infrastructure, with the initial funding directed to considerable efforts in professional development, implementation of regulatory procedures, and engagement of communities and families. The Network has made considerable headway with these objectives, opening two large research studies during its initial 18 months as well as producing findings that serve as markers of success that will optimize sustainability.

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2020-0290

This article has an accompanying video summary.

[a]*Department of Pediatrics, University of Mississippi Medical Center, Jackson, Mississippi;* [b]*Data Coordinating and Operations Center, University of Arkansas for Medical Sciences, Little Rock, Arkansas;* [c]*Departments of Emergency Medicine and Pediatrics, Brown University, Providence, Rhode Island;* [d]*University of Vermont Medical Center, Burlington, Vermont;* [e]*University of Kansas Medical Center, Kansas City, Kansas;* [f]*University of Nebraska Medical Center, Omaha, Nebraska;* [g]*Alaska Native Medical Center, Anchorage, Alaska;* [h]*Pennington Biomedical Research Center, Baton Rouge, Louisiana;* [i]*Dartmouth-Hitchcock Hospital, Lebanon, New Hampshire;* [j]*The Children's Hospital at University of Oklahoma Medical Center, Oklahoma City, Oklahoma;* [k]*Arkansas Children's Hospital, Little Rock, Arkansas;* [l]*University of New Mexico Health Sciences Center, Albuquerque, New Mexico;* [m]*Nemours/Alfred I. duPont Hospital for Children, Wilmington, Delaware;* [n]*Department of Pediatrics, West Virginia University, Morgantown, West Virginia;* [o]*Departments of Tropical Medicine, Pediatrics, and Medicine, University of Hawai'i, Honolulu, Hawaii;* [p]*Department of Pediatrics, University of Montana, Missoula, Montana;* [q]*Department of Pediatrics, University of Louisville, Louisville, Kentucky; and* [r]*Medical University of South Carolina, Charleston, South Carolina*

Drs Annett and Atz conceptualized and developed the initial manuscript framework and critically reviewed the manuscript for important intellectual content; Drs Chervinskiy, Chun, Cowan, Goodrich, Hirschfeld, Hsia, Nesmith, Raissy, Ross, Saul, Shiramizu, Smith, Sullivan, and Tucker and Ms Jarvis, Mr Kulbeth, Ms Madden, and Ms Foster drafted manuscript sections and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2020-0290

Accepted for publication Jul 16, 2020

To cite: Annett RD, Chervinskiy S, Chun TH, et al. IDeA States Pediatric Clinical Trials Network for Underserved and Rural Communities. *Pediatrics*. 2020;146(4):e20200290

A Complicated Case of Vaccine Refusal

Rebecca Rossi, MD,[a,g] Neil Rellosa, MD,[a,c,g] Robin Miller, MD,[a,b,g] Corinna L. Schultz, MD, MSHP,[a,b,g] Jonathan M. Miller, MD,[a,d,g] Loren Berman, MD, MHS,[a,f] Elissa G. Miller, MD[a,e,g]

abstract

Parents in the United States have a legal right to refuse vaccination for their children. There are, however, special circumstances under which the state may compel vaccination against parental wishes. In this Ethics Rounds article, we present the case of a young boy with sickle cell disease who was partially vaccinated against encapsulated bacteria and the ethics of whether to compel complete vaccination before splenectomy.

[a]*Thomas Jefferson University, Philadelphia, Pennsylvania;* [b]*Nemours Center for Cancer and Blood Disorders and* [c]*Divisions of Infectious Diseases,* [d]*General Pediatrics, and* [e]*Palliative Medicine,* [f]*Departments of Surgery and* [g]*Pediatrics, Nemours/Alfred I. duPont Hospital for Children, Wilmington, Delaware*

Dr Rossi conceived of the manuscript and drafted the case presentation and the ethicist's opinion; Drs R. Miller and Schultz drafted the hematologists' opinion; Dr Rellosa drafted the infectious diseases opinion; Dr Berman drafted the surgeon's opinion; Drs J. M. Miller and E. G. Miller edited the ethicist's opinion as well as the case conclusions; and all authors reviewed and revised the manuscript in its entirety and read and approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2020-0768

Accepted for publication Mar 11, 2020

Address correspondence to Elissa G. Miller, MD, Nemours/Alfred I. duPont Hospital for Children, P.O. Box 269, Wilmington, DE 19899. E-mail: elissa.miller@nemours.org

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose

To cite: Rossi R, Rellosa N, Miller R, et al. A Complicated Case of Vaccine Refusal. *Pediatrics.* 2020;146(4):e20200768

Vaccine hesitancy and refusal are widely discussed topics among pediatricians and ethicists. Parents have the legal right to refuse vaccinations for their children because the immediate benefits of vaccines are not deemed essential. However, in certain medical conditions, children are at much higher risk than the general population for life-threatening complications from vaccine-preventable diseases. In such cases, a stronger argument can be made that vaccines are essential to prevent predictable harm.

A patient who has had a splenectomy is at increased risk of life-threatening infection from encapsulated organisms. Current pediatric guidelines recommend vaccination against these organisms before splenectomy in addition to long-term antibiotic prophylaxis to reduce the risk of overwhelming postsplenectomy infection (OPSI). Children with sickle cell disease (SCD) lack splenic function, so, like splenectomized patients, they are at high risk for sepsis from encapsulated organisms. In this article, we present a case in which splenectomy is indicated for a pediatric patient with SCD but the parents refuse all vaccinations. We ask experts whether performing an elective splenectomy on an unvaccinated child is ethical and whether the medical team is justified in pursuing legal action to override the parents' vaccination refusal in this special circumstance.

THE CASE

A 2-year-old boy, "John," with SCD has been treated by a hematology team since his diagnosis as a newborn. He was hospitalized with dactylitis at 6 weeks old. At age 4 months, John began chronic transfusion therapy because of recurrent episodes of dactylitis. He began experiencing recurrent episodes of splenic sequestration while on chronic transfusion therapy. These worsened just before his second birthday. In light of these dangerous sequestration episodes and the medical risks of remaining on long-term transfusion therapy, John's interdisciplinary medical team strongly recommended splenectomy as his best therapeutic option. They determined that delaying splenectomy would put him at risk for iron overload and even death from a severe sequestration event.

During the early stages of their son's extensive care, John's parents developed a mistrust of vaccines. Although he received vaccinations before his first birthday, his parents refused any subsequent vaccinations, including the vaccinations against Gram-positive encapsulated organisms recommended before splenectomy.

However, they did agree to comply with long-term prophylactic antibiotics.

The care team thoroughly educated John's parents about the gravity of their son's situation and the importance of these vaccines. The parents had also conducted extensive online research of their own. They clearly felt that they were acting in their son's best interest and were appropriate surrogate decision-makers. However, the team was concerned about the safety and ethics of performing a splenectomy in a young patient who would remain partially vaccinated because of his parents' refusal of immunizations. When doctors judge parental preferences to be endangering their child's life, they may seek legal action. Should they do so in this case?

HEMATOLOGIST PERSPECTIVE: DR ROBIN MILLER, DR CORINNA SCHULTZ

Treatment options for patients with SCD remain limited, and preventive care is a critical aspect of care for these patients. Newborn screening, which allows for early initiation of penicillin prophylaxis and prompt initiation of antibiotics for febrile children, together with effective vaccination against *Haemophilus influenza* type b (Hib) and *Streptococcus pneumoniae*, have dramatically reduced the mortality rate for young children with SCD.[1,2] All of these strategies are recommendations in the SCD guidelines published by the National Institutes of Health in 2014. These recommendations have been widely adopted across the country.[3]

Before these preventive therapies, the Cooperative Study of SCD reported an annual incidence of invasive pneumococcal disease (IPD) in children with SCD of 10 per 100 person-years, carrying a 30% risk of mortality.[1] Mortality rates for 1- to 4-year-old children with SCD decreased 41% between 1968 and 1992.[4] Much of this improvement has been attributed to a decreased risk of sepsis related to these important preventive measures.[2] Because most children receive all of these interventions, it is impossible to know the degree to which each of these interventions separately contributes to the reduction in morbidity and mortality. Despite these advancements, we continue to see heartbreaking cases of patients with SCD dying from sepsis despite the medical team and family members providing all of these preventive treatments. The family in this case is the first in our collective years of hematology experience who declined immunizations. Furthermore, we subsequently learned that they had not been filling prophylactic antibiotic prescriptions for several months, despite repeatedly telling us they had been giving the medication daily as prescribed. They subsequently returned to filling prescriptions, but the team had no way of knowing if the medication was being administered.

Trust, or lack thereof, is at the core of all human relationships. Most would agree that, for a successful therapeutic relationship between a patient and a medical provider, the patient must not only trust in that provider's knowledge and expertise but also that the provider is motivated by what they believe is best for the patient. Ideally, the provider not only considers the medical facts but also takes time to understand the values and desires of the individual patient. Less often discussed, but equally important, is the physician's ability to trust that the patient will follow their recommendations and report information truthfully. This is particularly essential in pediatrics, in which the physician must work in partnership with parents and guardians to look out for children who cannot make their own medical decisions.

Pediatric providers are in the precarious position of continually assessing the parent's veracity and adherence to critical medical recommendations. On the basis of those assessments, we sometimes must make a judgment about when nonadherence exposes the child to unacceptable risk.

John's parents were loving and attentive. They never missed a clinic visit, and they clearly felt they were acting in their child's best interest. We had no concerns for his wellbeing outside of this single, medical issue. However, given our concern and our duty as mandatory reporters, we notified Child Protective Services (CPS) of the case and described the parental refusal to give either prophylactic antibiotics or immunizations as life-threatening medical neglect. CPS believed that the only way to authorize immunizations before surgery would be to find John's parents neglectful and to remove him from the home or to obtain a court order to vaccinate against the parents' will. They asked us what we would recommend. Was the risk to his life so significant that CPS should remove John from his otherwise loving home or take his parents to court and risk permanently destroying an already tenuous doctor–parent relationship with this family?

After learning of our referral to CPS, John's family expressed feeling betrayed and angry. With our full support, the family sought a second opinion at another major SCD center a short distance away. Although they were given the same recommendations, John's parents requested to transfer care to that institution. Just as we had lost trust in them, they had lost trust in us. However, the hematologists there recommended against transfer because the family was clearly stating

they would not follow the recommended plan of care. In their opinion, transfer would not be in the child's best interest because the family would have had to travel farther for acute care in the event of a septic episode.

Before responding to the question posed to us by CPS, we sought an ethics consultation to gather the input of our hospital ethics committee.

INFECTIOUS DISEASE PERSPECTIVE: DR NEIL RELLOSA

To understand whether performing an elective splenectomy on an unvaccinated child is ethical or unethical, it is important to attempt to establish the true risk for infection with vaccine-preventable pathogens in such individuals and specifically the risk for the patient in this case. It is well established that children with SCD have increased susceptibility to bacterial infections, especially with encapsulated bacteria such as *S pneumoniae*. Additionally, patients who receive splenectomy for reasons besides SCD are also at risk for OPSI. Although the pathogenesis and pathophysiology of these types of infections may be similar for both situations, the available data regarding absolute risk in pediatric patients in each of these scenarios are limited because of age and prevalence of disease.

Second, the efficacy of prevention strategies such as vaccination and chemoprophylaxis must also be considered. Current recommendations for the prevention of life-threatening infection for patients postsplenectomy or with functional asplenia consist of multiple interventions. Overall, combinations of these interventions have shown significant efficacy in preventing many life-threatening infections; however, the individual contributions of each are more difficult to quantify, especially in scenarios similar to this case. In addition, no one strategy or combination of strategies is 100% effective; infections from bacteria not covered by a vaccine or antibiotic prophylaxis are still a threat to individuals after splenectomy. Issues with parental knowledge, competence, and adherence can also decrease the efficacy of nonvaccination strategies such as administration of prophylactic antibiotics.

Finally, even if we are able to establish that there is a significant risk of life-threatening infection for patients such as John and that vaccination offers a significant amount of protection from these infections, do those risks and benefits supersede the wishes of a family not to vaccinate and justify legal action to facilitate vaccination, in contrast to "routine" vaccine refusal?

In individuals without a spleen, the incidence of infections with encapsulated bacteria (*S pneumoniae, H influenza, and Neisseria meningitides*) has been estimated to be up to 50 times higher than that in normal populations.[5] For individuals with SCD, IPD may be 10 to 100fold times higher than in matched individuals without SCD.[6] Additionally, IPD is a leading cause of mortality in children with SCD, and patients younger than 5 years are at highest risk.

In general, for individuals who are postsplenectomy, life-threatening infections have an estimated incidence of 0.23% to 0.42% per year, with the greatest risk occurring within the first 2 years after splenectomy. The cumulative lifetime risk is estimated at ~5%.[5] Although the incidence of OPSI in splenectomized patients is low, the mortality rate may be as high as 70%.[7] In a recent study of vaccination coverage and mortality after splenectomy, the mortality rate was significantly greater in unvaccinated individuals compared with that in vaccinated individuals, although the statistical significance was lost with adjustment for the cause of splenectomy because of a high burden of solid tumor–related death.[8] Overall, the incidence of life-threatening infections significantly decreases after 5 years postsplenectomy, but late infections have been reported as far as 20 years out.[5] Thus, for John, one could estimate that, if unvaccinated, he had a 5% chance of getting a life-threatening infection and a 3.5% chance of dying from it.

In the late 1980s, clinical trials of oral penicillin for prophylaxis in children with SCD revealed an 84% reduction in the incidence of pneumococcal infection compared with placebo; however, these results were not adjusted for whether individuals received polyvalent pneumococcal polysaccharide vaccine.[1] Antibiotic prophylaxis has also been shown to help prevent postsplenectomy infection and mortality. Jugenburg et al[9] showed that antibiotic prophylaxis with or without immunization decreased incidence of infection by 47% and mortality by 88%.

Although rarer, breakthrough IPD still occurred in children with SCD despite their receiving oral penicillin prophylaxis and pneumococcal polysaccharide vaccine. In 2000, the introduction of the pneumococcal conjugated vaccine additionally helped to decrease the incidence of IPD in children with SCD; in one study, the rate of IPD decreased by 93.4% with pneumococcal conjugated vaccine in children younger than5 years.[10] There is a paucity of data regarding other vaccine-preventable infections such as Hib and *N meningitides* in children with SCD or post splenectomy.

These studies show, unequivocally, that children with SCD or postsplenectomy are at a significantly higher risk for life-threatening infections than are individuals without SCD or with intact spleens.

However, the overall incidence of OPSI is relatively low, and other prevention strategies, such as antibiotic prophylaxis, patient education, and early diagnosis and treatment of these infections, may be quite effective. The individual contribution of each strategy is difficult to discern because of the lack of data.

It is difficult to specify the degree of risk elevation that justifies overriding a parent's vaccination refusal. This child, after a splenectomy, would clearly be at higher-than-average risk for a life-threatening infection. But the absolute risk of such an infection would still be low enough that it is not clear to me that parental refusal of vaccines would be unethical or should be considered illegal.

SURGEON PERSPECTIVE: DR LOREN BERMAN

A critical aspect of surgical decision-making is an appreciation of the risks and benefits of the intervention being considered compared with the alternative of not doing surgery. Decisions to move forward with an invasive procedure should always be based on the conclusion that the benefit of the invasive procedure outweighs the risk. If John's parents refuse vaccines and would not administer antibiotic prophylaxis postoperatively, John would be at increased risk of sepsis. But, in SCD, he is already at increased risk.

For John, the benefit of splenectomy clearly outweighs the risk of leaving the spleen intact because of the morbidity associated with ongoing transfusion requirement as well as the risk of an acute, life-threatening sequestration event. This benefit is so significant that it outweighs risk of splenectomy even in an unvaccinated patient. Our surgical team was of the opinion that the small incremental increased risk of sepsis after spleen removal was not very significant given how high risk he was at baseline considering the severity of SCD and his unvaccinated status. Therefore, we were willing to proceed with surgery.

Shared decision-making is the preferred approach to conversations about treatment decisions.[11] The use of shared decision-making has been shown to improve care and decrease costs.[12] These findings are likely driven by the fact that patients are more likely to comply with the treatment regimen if they are active participants in the choice of treatment path. Alienating parents by taking away their role in medical or surgical decision-making for their child is very likely to have adverse effects on the health of the child.

In pediatrics, the use of shared decision-making is more complex than in adult care. It is not permissible for parents to make choices that are not in the best interests of their child.

Shared decision-making in pediatric surgery can enhance trust in the patient and parent–provider relationship and may increase compliance with treatment regimens after surgery.[13–15] John's parents were always in agreement with the plan for splenectomy and willingly participated in the formulation of this plan despite their resistance to being compliant with other aspects of his care.

ETHICIST PERSPECTIVE: DR REBECCA ROSSI, DR JONATHAN MILLER, DR ELISSA MILLER

The primary ethical question here is, "Does the parental refusal of vaccines in this case justify pursuing state legal action?" To simplify, this case is similar in many ways to the ethical decision primary care physicians face daily when parents refuse vaccination for their currently healthy children. When a child like John is at increased risk for vaccine-preventable disease, how vulnerable must that child be before we consider it unethical to permit vaccine refusal? How can we quantitatively draw that line? An OPSI can be reduced by vaccination against encapsulated organisms, prophylactic antibiotics, and prompt medical attention for fever. John's family was willing to do 2 out of these 3 medically recommended interventions.

We were unable to accurately quantify John's risk if he had a splenectomy and remained only partially immunized, especially because the family still seemed committed to seeking appropriate and immediate care for fever and consistently stated they were giving his antibiotic prophylaxis.

We felt trapped and suspected the family did as well. We remained unsure of how to balance our responsibility to ensure the safety of this child versus the importance of maintaining a supportive medical home for the child and family.

When deciding whether to seek judicial intervention to override parents' medical choices, ethicists consider the patient's best interest, the potential harms, and parental decision-making capacity.[16] Parents and medical professionals often have very different thoughts about what is best for a child. When conflicting yet reasonable ideas of "best interest" coexist, it becomes nearly impossible to objectively overturn a parental decision by claiming a child's best interest is not being pursued.

The harm principle offers a more concrete threshold for deciding when state involvement is justified.[17] By this principle, if refusal of vaccinations places this child at significantly increased risk of serious harm, the care team has ethical grounds to bring this case to the state. In this case, it is very difficult to calculate the added risk reduction from vaccines, as opposed to other strategies to keep John safe and healthy.

When neither the best interest nor the harm principle provides a clear ethically sound course of action, we can consult another ethical framework for guidance. Medical decisions can be classified along a spectrum from "obligatory" (meaning it would be ethically unsound not to do them) down to "impermissible" (meaning they should never be pursued). Between those two extremes are "permissible" decisions ranging from "inadvisable" to "advisable." A decision must fall into the "impermissible" category to justify legal action.

Our view, in this case, is that refusal of vaccination before splenectomy is an inadvisable decision, but it is not "impermissible." There must be a clear burden of harm that outweighs the respect for parental preference to overrule a parent. In the case of John, who had received immunizations during infancy and is partially vaccinated against pneumococcus and Hib, it is quite difficult to estimate how further immunization would affect the burden of harm.

We also considered the importance of maintaining a trusting therapeutic relationship with John's parents. Given the rapid time course of OPSI, it is imperative that parents of young children with asplenia be thoroughly educated in the early signs and symptoms of infections as well as the potentially deadly consequences of delaying medical attention. To effectively communicate this information, maintenance of trust between John's parents and his care team is crucial. If overturning the parents' wishes would plant further seeds of mistrust in the health care system, it may then cancel the benefits of vaccination by discouraging future life-saving action on the part of the parents, because even with vaccination, John would remain at increased risk for OPSI.

John's parents willingly participated in the ethics consult and demonstrated their dedication to responding promptly to signs of infection, indicating to us that there is trust left to salvage. We recommended very close follow-up with John to ensure the proper administration of prophylactic antibiotics and reinforcement of parent education.

OUTCOME OF THE CASE

After consulting with our hospital Ethics Committee, we decided that recommending CPS removal of John from his home or pursuing a court order to compel vaccination against his parents' wishes would both likely be more harmful than splenectomy without additional immunizations.

John underwent splenectomy 18 months ago and no longer requires chronic transfusion therapy. He is doing well, although he remains unvaccinated. His parents report they are giving antibiotic prophylaxis as prescribed. They continue to see our hematology team, and we are working together to rebuild our therapeutic relationship. He has had no hospitalizations for bacteremia or sepsis to date.

JOHN D. LANTOS, MD, COMMENTS

Some ethical dilemmas can only be resolved by careful attention to quantitative data that allow us to calculate risk. In this case, the parents' decision seemed, at first, to be one that would lead to an unacceptably high level of preventable risk for the child. Careful analysis of the attributable risk, however, led to a different conclusion. The thorough and thoughtful analysis by the clinicians and bioethicists illustrates an important generalizable point: ethical principles such as "the harm principle" or "the best interest standard" can only be operationalized after a precise estimate of risk. In this case, the risk associated with the parents' choice to refuse immunizations was estimated to be low enough that their approach was appropriately deemed ethically permissible.

ABBREVIATIONS

CPS: Child Protective Services
Hib: *Haemophilus influenza* type b
IPD: invasive pneumococcal disease
OPSI: overwhelming postsplenectomy infection
SCD: sickle cell disease

REFERENCES

1. Gaston MH, Verter JI, Woods G, et al. Prophylaxis with oral penicillin in children with sickle cell anemia. A randomized trial. *N Engl J Med.* 1986; 314(25):1593–1599
2. Quinn CT, Rogers ZR, McCavit TL, Buchanan GR. Improved survival of children and adolescents with sickle cell disease. *Blood.* 2010;115(17): 3447–3452
3. Yawn BP, Buchanan GR, Afenyi-Annan AN, et al. Management of sickle cell disease: summary of the 2014 evidence-based report by expert panel members [published corrections appear in *JAMA* 2014;312(18):1932 and *JAMA* 2015; 313(7):792]. *JAMA.* 2014;312(10): 1033–1048
4. Davis H, Schoendorf KC, Gergen PJ, Moore RM Jr.. National trends in the mortality of children with sickle cell disease, 1968 through 1992. *Am J Public Health.* 1997;87(8):1317–1322
5. Sumaraju V, Smith LG, Smith SM. Infectious complications in asplenic hosts. *Infect Dis Clin North Am.* 2001; 15(2):551–565
6. Wong WY, Overturf GD, Powars DR. Infection caused by Streptococcus pneumoniae in children with sickle cell disease: epidemiology, immunologic mechanisms, prophylaxis, and vaccination. *Clin Infect Dis.* 1992;14(5): 1124–1136
7. Styrt B. Infection associated with asplenia: risks, mechanisms, and

prevention. *Am J Med*. 1990;88(5N): 33N–42N

8. Di Sabatino A, Lenti MV, Tinozzi FP, et al. Vaccination coverage and mortality after splenectomy: results from an Italian single-centre study. *Intern Emerg Med*. 2017;12(8):1139–1147
9. Jugenburg M, Haddock G, Freedman MH, Ford-Jones L, Ein SH. The morbidity and mortality of pediatric splenectomy: does prophylaxis make a difference? *J Pediatr Surg*. 1999;34(7):1064–1067
10. Halasa NB, Shankar SM, Talbot TR, et al. Incidence of invasive pneumococcal disease among individuals with sickle cell disease before and after the introduction of the pneumococcal conjugate vaccine. *Clin Infect Dis*. 2007; 44(11):1428–1433
11. Braddock CH III. The emerging importance and relevance of shared decision making to clinical practice. *Med Decis Making*. 2010;30(5 suppl):5S–7S
12. Frosch DL, Moulton BW, Wexler RM, Holmes-Rovner M, Volk RJ, Levin CA. Shared decision making in the United States: policy and implementation activity on multiple fronts. *Z Evid Fortbild Qual Gesundhwes*. 2011;105(4): 305–312
13. Carlisle EM, Shinkunas LA, Kaldjian LC. Do surgeons and patients/parents value shared decision-making in pediatric surgery? A systematic review. *J Surg Res*. 2018;231:49–53
14. de Mik SML, Stubenrouch FE, Balm R, Ubbink DT. Systematic review of shared decision-making in surgery. *Br J Surg*. 2018;105(13): 1721–1730
15. Page AE. Safety in surgery: the role of shared decision-making. *Patient Saf Surg*. 2015;9:24
16. Diekema DS. Parental refusals of medical treatment: the harm principle as threshold for state intervention. *Theor Med Bioeth*. 2004; 25(4):243–264
17. McDougall RJ, Notini L. Overriding parents' medical decisions for their children: a systematic review of normative literature. *J Med Ethics*. 2014;40(7):448–452

Catheter-Associated Urinary Tract Infection Reduction in a Pediatric Safety Engagement Network

Charles B. Foster, MD,[a] Kathy Ackerman, PCNS,[a,b] Vera Hupertz, MD,[a] Laurie Mustin, CPNP,[c] Joann Sanders, MD,[d] Patricia Sisson, MS,[c] Rachel E. Wenthe, RN[d]

abstract

BACKGROUND: Catheter-associated urinary tract infections (CAUTIs) are a leading cause of health care–associated infection. Catheter insertion bundles (IBs) and maintenance bundles (MBs) have been developed to prevent CAUTIs but have not been extensively validated for use in pediatric populations. We report the CAUTI prevention efforts of a large network of children's hospitals.

METHODS: Children's hospitals joined the Children's Hospitals' Solutions for Patient Safety engagement network from 2011 to 2017, using an open start time engagement approach, and elected to participate in CAUTI prevention efforts, with 26 submitting data initially and 128 at the end. CAUTI prevention recommendations were first released in May 2012, and IBs and MBs were released in May 2014. Hospitals reported on CAUTIs, patient-days, and urinary catheter-line days and tracked reliability to each bundle. For the network, run charts or control charts were used to plot CAUTI rates, urinary catheter use, and reliability to each bundle component.

RESULTS: After the introduction of the pediatric CAUTI IBs and MBs, CAUTI rates across the network decreased 61.6%, from 2.55 to 0.98 infections per 1000 catheter-line days. Centerline shifts occurred both before and after the 2015 Centers for Disease Control and Prevention CAUTI definition change. Urinary catheter use rates did not decline during the intervention period. Network reliability to the IBs and MBs increased to 95.4% and 86.9%, respectively.

CONCLUSIONS: IBs and MBs aimed at preventing CAUTIs were introduced across a large network of children's hospitals. Across the network, the rate of urinary tract infections among hospitalized children with indwelling urinary catheters decreased 61.6%.

[a]Cleveland Clinic Children's, Cleveland Clinic, Cleveland, Ohio; [b]Memorial Sloan Kettering Cancer Center, New York, New York; [c]Children's Hospitals' Solutions for Patient Safety, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio; and [d]Cook Children's Health Care System, Fort Worth, Texas

Dr Foster contributed to the study design, participated in the catheter-associated urinary tract infection (CAUTI) engagement efforts and interpretation of data, drafted the initial manuscript, and reviewed and revised the manuscript; Ms Ackerman and Ms Wenthe contributed to the study design, participated in the CAUTI engagement efforts and interpretation of data, helped draft the initial manuscript, and reviewed and revised the manuscript; Drs Hupertz and Sanders contributed to the study design, participated in the CAUTI engagement efforts, and reviewed and revised the manuscript; Ms Mustin and Ms Sisson helped design the study, coordinated CAUTI engagement efforts, maintained the database, performed statistical analyses, and contributed to and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2019-2057

Accepted for publication Apr 27, 2020

Address correspondence to Charles B. Foster, MD, Center for Pediatric Infectious Diseases, Cleveland Clinic Children's, 9500 Euclid Ave, R3, Cleveland, OH 44195. E-mail: fosterc3@ccf.org

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

To cite: Foster CB, Ackerman K, Hupertz V, et al. Catheter-Associated Urinary Tract Infection Reduction in a Pediatric Safety Engagement Network. *Pediatrics*. 2020;146(4):e20192057

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2019-2057

Orchestrated Testing of Formula Type to Reduce Length of Stay in Neonatal Abstinence Syndrome

Heather C. Kaplan, MD, MSCE,[a,b,c] Pierce Kuhnell, MS,[d] Michele C. Walsh, MD, MSEpi,[e,f] Moira Crowley, MD,[e,f] Richard McClead, MD,[g] Scott Wexelblatt, MD,[a,b] Susan Ford, RN, MSN,[e] Lloyd P. Provost, MS,[h] Carole Lannon, MD, MPH,[a,c] Maurizio Macaluso, MD, DrPH,[a,d] OHIO PERINATAL QUALITY COLLABORATIVE

BACKGROUND: Despite the standardization of care, formula feeding varied across sites of the Ohio Perinatal Quality Collaborative (OPQC). We used orchestrated testing (OT) to learn from this variation and improve nonpharmacologic care of infants with neonatal abstinence syndrome (NAS) requiring pharmacologic treatment in Ohio.

METHODS: To test the impact of formula on length of stay (LOS), treatment failure, and weight loss among infants hospitalized with NAS, we compared caloric content (high versus standard) and lactose content (low versus standard) using a 2^2 factorial design. During October 2015 to June 2016, OPQC sites joined 1 of 4 OT groups. We used response plots to examine the effect of each factor and control charts to track formula use and LOS. We used the OT results to revise the nonpharmacologic bundle and implemented it during 2017.

RESULTS: Forty-seven sites caring for 546 NAS infants self-selected into the 4 OT groups. Response plots revealed the benefit of high-calorie formula (HCF) on weight loss, treatment failure, and LOS. The nonpharmacologic treatment bundle was updated to recommend HCF when breastfeeding was not possible. During implementation, HCF use increased, and LOS decreased from 17.1 to 16.4 days across the OPQC.

CONCLUSIONS: OT revealed that HCF was associated with shorter LOS in OPQC sites. Implementation of a revised nonpharmacologic care bundle was followed by additional LOS improvement in Ohio. Despite some challenges in the implementation of OT, our findings support its usefulness for learning in improvement networks.

Full article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2019-0914

abstract

[a]Department of Pediatrics, College of Medicine, University of Cincinnati, Cincinnati, Ohio; [b]Perinatal Institute, [c]James M. Anderson Center for Health Systems Excellence, and [d]Division of Epidemiology and Biostatistics, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio; [e]Division of Neonatology, Department of Pediatrics, Rainbow Babies and Children's Hospital, Cleveland, Ohio; [f]Department of Pediatrics, Case Western Reserve University, Cleveland, Ohio; [g]Department of Pediatrics, Nationwide Children's Hospital, Columbus, Ohio; and [h]Associates in Process Improvement, Austin, Texas

Dr Kaplan led the conceptualization of this work, was the project lead for implementation, was the primary writer of the manuscript, and critically revised the manuscript; Mr Kuhnell conducted the original analyses and contributed to the writing and critical revisions of the manuscript; Ms Ford helped conceptualize this work, was a leader in the implementation of the project as described, and contributed to critical revisions of the manuscript; Drs Crowley, Lannon, McClead, Wexelblatt, and Walsh helped conceptualize this work, served as core faculty in the project implementation as described, and critically revised the manuscript; Mr Provost helped conceptualize the work, assisted in interpretation of the analyses, and critically revised the manuscript; Dr Macaluso helped conceptualized this work (particularly the analytic plan), supervised the original analyses, and contributed to the writing and critical revisions of the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: https://doi.org/10.1542/peds.2019-0914

Accepted for publication Apr 15, 2020

Address correspondence to Heather C. Kaplan, MD, MSCE, Cincinnati Children's Hospital and Medical Center, 3333 Burnet Ave, MLC 7009, Cincinnati, OH 45229. E-mail: heather.kaplan@cchmc.org

To cite: Kaplan HC, Kuhnell P, Walsh MC, et al. Orchestrated Testing of Formula Type to Reduce Length of Stay in Neonatal Abstinence Syndrome. *Pediatrics.* 2020;146(4):e20190914

POLICY STATEMENT Organizational Principles to Guide and Define the Child Health Care System and/or Improve the Health of all Children

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN®

Recommendations for Prevention and Control of Influenza in Children, 2020–2021

Committee on Infectious Diseases

abstract

This statement updates the recommendations of the American Academy of Pediatrics for the routine use of influenza vaccine and antiviral medications in the prevention and treatment of influenza in children during the 2020–2021 season.

The American Academy of Pediatrics (AAP) recommends routine influenza immunization of all children without medical contraindications, starting at 6 months of age. Influenza vaccination is an important intervention to protect vulnerable populations and reduce the burden of respiratory illnesses during the severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) pandemic. Any licensed, recommended, age-appropriate vaccine available can be administered, without preference for one product or formulation over another. Antiviral treatment of influenza with any licensed, recommended, age-appropriate influenza antiviral medication is recommended for children with suspected or confirmed influenza who are hospitalized, have severe or progressive disease, or have underlying conditions that increase their risk of complications of influenza. Antiviral treatment may be considered for any previously healthy, symptomatic outpatient not at high risk for influenza complications in whom an influenza diagnosis is confirmed or suspected, if treatment can be initiated within 48 hours of illness onset, and for children whose siblings or household contacts either are younger than 6 months or have a high-risk condition that predisposes them to complications of influenza.

DOI: https://doi.org/10.1542/peds.2020-024588

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: Dr Munoz has a royalties relationship with Up to Date and is a member of the data safety monitoring boards of Pfizer and Moderna.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: Dr Munoz had a previous research relationship with BioCryst and research relationships with the European Society of Pediatric Infectious Diseases (ESPID) and International Neonatal and Maternal Immunization Symposium (INMIS).

To cite: Infectious Diseases Con. Recommendations for Prevention and Control of Influenza in Children, 2020–2021. *Pediatrics.* 2020;146(4):e2020024588

UPDATES FOR THE 2020–2021 INFLUENZA SEASON

1. The composition of the influenza vaccines for 2020–2021 has been updated. The recommended influenza A(H1N1)pdm09 and A(H3N2) components and the influenza B/Victoria component of the vaccine are new for this season. The B/Yamagata component is unchanged from the previous season. All quadrivalent influenza vaccines include these 4 components. The trivalent vaccines do not include influenza B/Yamagata.

2. All pediatric vaccines are quadrivalent. There are no trivalent vaccines available for children.
3. The vaccine formulations available for children 6 through 35 months of age have been updated. Afluria Quadrivalent will be the only vaccine for children 6 through 35 months of age with a dosing volume of 0.25 mL. Fluzone Quadrivalent, which is licensed in a 0.25-mL and a 0.5-mL dosing volume, will likely be available only in a 0.5-mL dosing volume for this age group this season. The dosing volume for the 2 other vaccines available for this age group, Fluarix and FluLaval, is 0.5 mL. The AAP has no preference for one product over another.
4. Children 6 months through 8 years of age who are receiving influenza vaccine for the first time, who have received only 1 dose ever before July 1, 2020, or whose vaccination status is unknown should be offered vaccination as soon as influenza vaccines become available and should receive 2 doses of vaccine, ideally by the end of October. Children needing only 1 dose of influenza vaccine, regardless of age, should also receive vaccination ideally by the end of October.
5. The contraindications for live attenuated influenza vaccine (LAIV) have been updated to harmonize with recommendations of the Advisory Committee on Immunization Practices (ACIP). Although there are no reports of additional safety risks for LAIV in children with immunodeficiencies, anatomic or functional asplenia, cochlear implants, or active cerebrospinal fluid leaks, because the vaccine is a live attenuated product, it is not recommended in these populations.
6. The importance of influenza vaccination during the SARS-CoV-2 pandemic is discussed.

INTRODUCTION

Children consistently have the highest attack rates of influenza in the community during seasonal influenza epidemics. They play a pivotal role in the transmission of influenza virus infection to household and other close contacts and can experience substantial morbidity, including severe or fatal complications from influenza infection.[1] Children younger than 5 years, especially those younger than 2 years, and children with certain underlying medical conditions are at increased risk of hospitalization and complications attributable to influenza.[1] School-aged children bear a large influenza disease burden and are more likely to seek influenza-related medical care compared with healthy adults.[1,2] Reducing influenza virus transmission among children decreases the burden of childhood influenza and transmission of influenza virus to household contacts and community members of all ages.[1,2] Influenza vaccination is particularly important during the severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) pandemic to reduce the burden of respiratory illnesses and hospitalizations and preserve the capacity of the health care infrastructure. The American Academy of Pediatrics (AAP) recommends routine influenza vaccination and antiviral agents for the prevention and treatment of influenza in children, respectively.

SUMMARY OF RECENT INFLUENZA SEASONS IN THE UNITED STATES

2017–2018 and 2018–2019 Influenza Seasons

The 2017–2018 influenza season had an important impact in pediatric patients. It was the first classified as a high-severity season for all age groups, with high levels of outpatient clinic and emergency department visits for influenza-like illness, high rates of influenza-related hospitalization, and high mortality.[3–5] Influenza A (H3N2) predominated early, followed by a second wave of influenza B/Yamagata from March 2018 onward. Although hospitalization rates for children that season did not exceed those reported during the 2009 pandemic, they did surpass rates reported in previous high-severity A(H3N2)-predominant seasons. Excluding the 2009 pandemic, the 188 pediatric deaths reported during the 2017–2018 season (approximately half of which occurred in otherwise healthy children) were the highest reported since influenza-associated pediatric mortality became a nationally notifiable condition in 2004.[3–5] Among pediatric deaths of children 6 months and older who were eligible for vaccination and for whom vaccination status was known, approximately 80% had not received influenza vaccine during the 2017–2018 season.[3] Influenza vaccine effectiveness (VE) for the 2017–2018 season in children is shown in Table 1.[4]

The 2018–2019 season was of moderate severity, with similar hospitalization rates in children as during the 2017–2018 season (71/100 000 among children 0 through 4 years old and 20.4/100 000 among children 5 through 17 years old), which were higher than those observed in previous seasons from 2013–2014 to 2016–2017.[7] Among 1132 children hospitalized with influenza and for whom data were available, 55% had at least 1 underlying medical condition; the most commonly reported underlying conditions were asthma or reactive airway disease (26%), neurologic disorders (15.6%), and obesity (11.6%).[8] A total of 144 influenza-associated pediatric deaths were reported. The 2017–2018 influenza season was the longest-lasting season reported in the United States in the past decade, with elevated levels of

TABLE 1 Adjusted Vaccine Effectiveness (VE) in Children in the United States, by Season, as Reported by the Centers for Disease Control and Prevention (CDC), US Influenza Vaccine Effectiveness Network

Influenza Type/Age Group	2017–2018	2018–2019	2019–2020[a]
	H3N2 and B/Yamagata VE% (95% CI)	H1N1 and H3N2 VE% (95% CI)	B/Victoria and H1N1 VE% (95% CI)
Influenza A and B			
Overall all ages	38 (31 to 43)	29 (21 to 35)	45 (36 to 53)
6 mo–17 y	Not reported	Not reported	55 (42 to 65)
6 mo–8 y	68 (55 to 77)	48 (37 to 58)	NA
9–17 y	32 (16 to 44)	7 (–20 to 28)	NA
Influenza A(H1N1)pdm09			
Overall all ages	62 (50 to 71)	44 (37 to 51)	37 (19 to 52)
6 mo–17 y	Not reported	Not reported	51 (22 to 69)
6 mo–8 y	87 (71 to 95)	59 (47 to 69)	Not reported
9–17 y	70 (46 to 67)	24 (–18 to 51)	Not reported
Influenza A(H3N2)			
Overall all ages	22 (12 to 31)	9 (–4 to 20)	NA
6 mo–17 y	Not reported	Not reported	NA
6 mo–8 y	54 (33 to 69)	24 (1 to 42)	NA
9–17 y	18 (-6 to 36)	3 (–30 to 28)	NA
Influenza B Victoria			
Overall all ages	76 (45 to 89)	Not reported	50 (39 to 50)
6 mo–17 y	Not reported	Not reported	56 (42 to 67)
6 mo–8 y	Not reported	Not reported	Not reported
9–17 y	Note reported	Not reported	Not reported
Influenza B yamagata			
Overall all ages	48 (39 to 55)	Not reported	NA
6 mo–17 y	Not reported	Not reported	NA
6 mo–8 y	77 (49 to 90)	Not reported	NA
9–17 y	28 (1 to 48)	Not reported	NA

Vaccine effectiveness is estimated as 100% × (1 − odds ratio [ratio of odds of being vaccinated among outpatients with CDC's real-time RT-PCR influenza-positive test results to the odds of being vaccinated among outpatients with influenza-negative test results]); odds ratios were estimated using logistic regression. Adjusted for study site, age group, sex, race/ethnicity, self-rated general health, number of days from illness onset to enrollment, and month of illness using logistic regression.

[a] Interim results as of February 21, 2020.[6]

influenza-like illness activity for a total duration of 21 consecutive weeks (compared with an average duration of 16 weeks).[7] Variations in circulating strains affected vaccine efficacy. Influenza A(H1N1)pdm09 viruses predominated from October to mid-February, and influenza A(H3N2) viruses were identified more frequently from February to May. Influenza B (B/Victoria lineage predominant) represented approximately 5% of circulating strains. Most characterized influenza A(H3N2) viruses were antigenically distinct from the A(H3N2) component of the 2018–2019 vaccine. The vaccine's A(H3N2) virus belonged to subclade 3C.2a1. Cocirculation of multiple genetically diverse subclades of A(H3N2) was documented. Circulating viruses identified belonged to subclade 3C.2a1 or clade 3C.3a, with 3C.3a viruses accounting for >70% of the A(H3N2) in the United States. This likely contributed to an overall lower vaccine effectiveness (VE) against influenza A(H3N2) this season, despite achieving the highest vaccination coverage reported in the last decade in children (62.6% overall) (Table 1 and Fig 1).[7,9]

2019–2020 Influenza Season

The 2019–2020 influenza season was unusual and complicated by the emergence of the SARS-CoV-2 pandemic in early 2020. Influenza activity began early in October 2019, continuing through mid-March 2020, with an abrupt decline after the implementation of social distancing measures for mitigation of the pandemic. Although influenza B/Victoria viruses predominated early in the season, influenza A(H1N1)pdm09 viruses were the most predominant circulating strain this season. Influenza A(H3N2) and B/Yamagata lineage represented approximately 4.1% and 0.8% of circulating strains, respectively. The majority of characterized influenza A(H1N1)pdm09 (82.5%) and influenza B/Victoria (59.7%) viruses were antigenically similar to the viruses included in the 2019–2020 influenza vaccine. Less than half (46.5%) of influenza A(H3N2) viruses were antigenically similar to the A(H3N2) component of the 2019–2020 vaccine. During this season, the predominant A(H3N2) circulating clade was 3C.2a, subclade 3C.2a1, with cocirculation of a small proportion of 3C.3a, in contrast to the 2018–2019 season, when 3C.3a strains predominated. Preliminary estimates of the effectiveness of the 2019–2020 seasonal influenza vaccines against medically attended influenza illness from the US Flu VE Network are shown in Table 1.[6] These are preliminary data and are not vaccine specific. Susceptibility to available antiviral agents remains greater than 99% for all circulating strains, but 0.5% of A(H1N1)pdm09 isolates tested by the Centers for Disease Control and Prevention (CDC) exhibited highly reduced inhibition to oseltamivir and peramivir. Reduced susceptibility to baloxavir has not been reported in the United States to date.

The 2019–2020 season was of moderate severity, although 3 peaks of influenza-like illness activity and the highest hospitalization rates in children, 68.2 per 100 000 population overall, were reported this season. The first peak of activity occurred in early January, likely associated with influenza B circulation; the second peak occurred in February, when

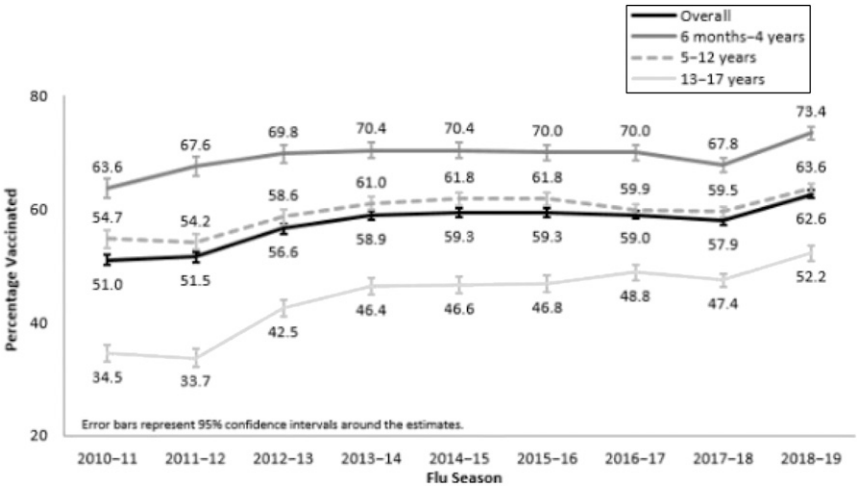


FIGURE 1

Influenza vaccination coverage in children 6 months to 17 years of age in the United States, 2010 to 2019. Source: Centers for Disease Control and Prevention (https://www.cdc.gov/flu/fluvaxview/coverage-1819estimates.htm).

influenza A(H1N1)pdm09 became predominant; and the third peak in March is thought to be associated with cocirculation of influenza and SARS-CoV-2. The CDC has now established a separate surveillance report for novel coronavirus disease 2019 (COVID-19)-like illness.[10] The cumulative influenza hospitalization rates per 100 000 population were 95.1 among children 0 through 4 years old, and 24.8 among children 5 through 17 years old. Hospitalization rates in children 0 to 4 years old were higher than those seen for this age group during the 2009 influenza pandemic, higher than the rate in adults 50 to 64 years old this season (91.8/100 000), and the highest on record for this age group. Among 168 children hospitalized with influenza and for whom data were available, 57.1% had no recorded underlying condition, and 42.9% had at least 1 underlying medical condition; the most commonly reported underlying conditions were asthma or reactive airway disease (19.7%), neurologic disorders (17.0%), and obesity (11.9%).

As of June 6, 2020, the following data were reported by the CDC:

- There were 182 laboratory-confirmed influenza-associated pediatric deaths. Most (63.0%) of those children died after being admitted to the hospital. The median age of the pediatric deaths was 6.1 years (range, 2 months to 17 years).
  - Seventy of the pediatric deaths were associated with influenza A viruses, and 112 were associated with influenza B viruses.
- Among the 168 children with known medical history, 42.9% of deaths occurred in children who had at least 1 underlying medical condition recognized by the Advisory Committee on Immunization Practices (ACIP) to increase the risk of influenza-attributable disease severity. Therefore, most (57.1%) had no known underlying medical conditions.
- The majority of the deaths occurred in children between 2 through 12 years of age: 37.4% were 5- through 11-year-olds, 20.9% were 2- through 4-year-olds, 20.3% were 12- through 17-year-olds, 15.9% were 6- through 23-month-olds, and 5.5% were younger than 6 months.
- Among 63 children who died and were tested, 46.0% had a bacterial coinfection.
- Among 141 children who were 6 months or older at the time of illness onset, and therefore, would have been eligible for influenza vaccination and for whom vaccination status was known, most (74%) were unvaccinated. Only 37 (26%) had received at least 1 dose of influenza vaccine (30 had complete vaccination, and 7 had received 1 of 2 ACIP-recommended doses).

INFLUENZA MORBIDITY AND MORTALITY IN CHILDREN

Influenza viruses are a common cause of acute lower respiratory tract infection (ALRTI) in children. Pediatric hospitalizations and deaths caused by influenza can be substantial. A recent study estimated that globally, influenza virus accounts for 7% of all ALRTIs, 5% of ALRTI hospitalizations, and 4% of ALRTI deaths in children younger than 5 years.[11] In the United States, the rates of influenza-associated hospitalization for children younger than 5 years consistently exceed the rates for children 5 through 17 years of age, and during the 2019–2020 season, they exceeded the hospitalization rates of adults 50 to 64 years of age.[8] Children 5 through 17 years of age also experienced higher than usual hospitalization rates during the 2019–2020 season. The impact of the anticipated SARS-CoV-2 cocirculation with influenza in the 2020–2021 season is unknown at this time. Elevated rates of influenza-like illness hospitalization and mortality were observed toward the end of the 2019–2020 season, suggesting the possibility of comorbidity. It is, therefore, particularly important that children are protected against influenza

through timely vaccination in the 2020–2021 influenza season.

HIGH-RISK GROUPS IN PEDIATRICS

Children and adolescents with certain underlying medical conditions have a high risk of complications from influenza (Table 2). While universal influenza vaccination is recommended for everyone starting at 6 months of age, emphasis should be placed in ensuring that people in high-risk groups and their household contacts and caregivers receive annual influenza vaccine.

EFFECTIVENESS OF INFLUENZA VACCINATION ON HOSPITALIZATION AND MORTALITY

Several studies demonstrate that influenza vaccination can effectively decrease hospitalization in children where universal pediatric immunization has been implemented. In a study during the 2015–2016 season conducted by the United States New Vaccine Surveillance Network (NVSN), among 1653 children enrolled from 7 pediatric hospitals, the adjusted VE in children with complete influenza immunization against any influenza-associated hospitalization was 56% (95% confidence interval [CI], 34% to 71%), against A(H1N1)pdm09 was 68% (95% CI, 36% to 84%), and against B viruses was 44% (95% CI, –1% to 69%).[17] A study in children 6 months to 8 years of age conducted in Israel over 3 influenza seasons from 2015 to 2017 demonstrated that over all seasons, fully vaccinated children had a VE against hospitalization of 53.9% (95% CI, 38.6% to 68.3%), while partial vaccination was not effective (25.6%; 95% CI, –3% to 47%).[18] In this study, a VE against hospitalization as high as 60% to 80% was observed when circulating and vaccine influenza A and B strains matched. After establishing free vaccination for preschool children and children at risk because of comorbid medical conditions in Australia in 2018, VE of influenza vaccine in preventing influenza hospitalization was estimated to be 78.8% (95% CI, 66.9% to 86.4%).[19] In the United Kingdom, during the 2018–2019 season, the overall adjusted VE against influenza-confirmed hospitalization was reported to be 53% (95% CI, 33.3% to 66.8%), with protection varying by strain. Protection was 63.5% (95% CI, 34.4% to 79.7%) against influenza A(H1N1)pdm09, but there was no protection against influenza A(H3N2).[20] Finally, a systematic review and meta-analysis of 28 studies conducted by Kalligeros et al[21] concluded that influenza vaccine offered significant protection against any type of influenza-related hospitalization in children 6 months through 17 years of age, with VE of 57.5% (95% CI, 54.8% to 65.5%). Strain-specific VE was higher for influenza A(H1N1)pdm09 (75.1%; 95% CI, 54.8% to 93.3%) and influenza B (50.9%; 95% CI, 41.7% to 59.9%), compared with influenza A(H3N2) (40.8%; 95% CI, 25.6% to 55.9%). As expected, children who were fully vaccinated were better protected (VE 61.8%; 95% CI, 54.4% to 69.1%) compared with those who were partially vaccinated (VE 33.91%; 95% CI, 21.1% to 46.7%). Notably, VE was higher in children younger than 5 years of age (61.7%; 95% CI, 49.3% to 74.1%) than in children 6 to 17 years old (54.4%; 95% CI, 35.1% to 73.6%). In the United States, the CDC estimates that during the 2018–2019 season, influenza vaccination prevented 20% of projected hospitalizations associated with infection with A(H1N1)pdm09 virus among children 5 through 17 years, and 43% among children 6 months through 4 years.[22]

Historically, up to 80% of influenza-associated pediatric deaths have occurred in unvaccinated children 6 months and older. Influenza vaccination is associated with

TABLE 2 People at High Risk of Influenza Complications

Children <5 y, and especially those <2 y,[a] regardless of the presence of underlying medical conditions
Adults ≥50 y, and especially those ≥65 y
Children and adults with chronic pulmonary (including asthma and cystic fibrosis); hemodynamically significant cardiovascular disease (except hypertension alone); or renal, hepatic, hematologic (including sickle cell disease and other hemoglobinopathies), or metabolic disorders (including diabetes mellitus)
Children and adults with immunosuppression attributable to any cause, including that caused by medications or by HIV infection
Children and adults with neurologic and neurodevelopment conditions (including disorders of the brain, spinal cord, peripheral nerve, and muscle such as cerebral palsy, epilepsy, stroke, intellectual disability, moderate to severe developmental delay, muscular dystrophy, or spinal cord injury)
Children and adults with conditions that compromise respiratory function or handling of secretions (including tracheostomy and mechanical ventilation)[12]
Women who are pregnant or postpartum during the influenza season
Children and adolescents <19 y who are receiving long-term aspirin therapy or salicylate-containing medications (including those with Kawasaki disease and rheumatologic conditions) because of increased risk of Reye syndrome
American Indian/Alaska Native people[b]
Children and adults with extreme obesity (ie, BMI [BMI] ≥40 for adults, and based on age for children)
Residents of chronic care facilities and nursing homes

Source: Adapted from Centers for Disease Control and Prevention. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices—United States, 2020–21 influenza season. *MMWR Recomm Rep.* 2020; in press.

[a] The 2019–2020 CDC recommendations state: Although all children younger than 5 years old are considered at higher risk for complications from influenza, the highest risk is for those younger than 2 years old, with the highest hospitalization and death rates among infants younger than 6 months old.

[b] American Indian/Alaska Native (AI/AN) children have higher rate of influenza complications.[13–16] Most at-risk AI/AN children will also qualify in other high-risk categories to receive appropriate antiviral treatment. In the setting of a shortage, AI/AN children should be prioritized to receive influenza vaccine or anti-viral medications according to local public health guidelines.

reduced risk of laboratory-confirmed influenza-related pediatric death.[23] In one case-cohort analysis comparing vaccination uptake among laboratory-confirmed influenza-associated pediatric deaths with estimated vaccination coverage among pediatric cohorts in the United States from 2010 to 2014, Flannery et al[23] found that only 26% of children had received vaccine before illness onset, compared with an average vaccination coverage of 48%. Overall VE against influenza-associated death in children was 65% (95% CI, 54% to 74%). More than half of children in this study who died of influenza had ≥1 underlying medical condition associated with increased risk of severe influenza-related complications; only 1 in 3 of these at-risk children had been vaccinated; yet, VE against death in children with underlying conditions was 51% (95% CI, 31% to 67%). Similarly, influenza vaccination reduces by three quarters the risk of severe, life-threatening laboratory-confirmed influenza in children requiring admission to the ICU.[24] The influenza virus type might also affect the severity of disease. In a study of hospitalizations for influenza A versus B, the odds of mortality were significantly greater with influenza B than with influenza A and not entirely explained by underlying health conditions.[25]

SEASONAL INFLUENZA VACCINES

The seasonal influenza vaccines licensed for children and adults for the 2020–2021 season are shown in Table 3. More than one product may be appropriate for a given patient, and vaccination should not be delayed to obtain a specific product.

All 2020–2021 seasonal influenza vaccines contain the same influenza strains as recommended by the World Health Organization (WHO) and the US Food and Drug Administration (FDA)'s Vaccines and Related Biological Products Advisory Committee (VRBPAC) for the Northern Hemisphere.[26] Both influenza A(H1N1) and A(H3N2) and the B/Victoria components are different in this season's vaccine. The B/Yamagata component is unchanged. The influenza A strains are different for egg-based versus cell- or recombinant-based vaccines this year on the basis of their optimal characteristics for each platform, but all are matched to the strains expected to circulate in the 2020–2021 season.

1. Quadrivalent vaccines contain:
   a. Influenza A(H1N1) component:
      i. Egg-based vaccines: A/Guangdong-Maonan/SWL1536/2019 (H1N1) pdm09-like virus (new this season)
      ii. Cell- or recombinant-based vaccines: A/Hawaii/70/2019 (H1N1) pdm09-like virus (new this season)
   b. Influenza A(H3N2) component:
      i. Egg-based vaccines: A/Hong Kong/2671/2019 (H3N2)-like virus (new this season)
      ii. Cell- or recombinant-based vaccines: A/Hong Kong/45/2019 (H3N2)-like virus (new this season)
   c. B/Victoria component:
      i. All vaccines: B/Washington/02/2019-like virus (B/Victoria/2/87 lineage) (new this season)
   d. B/Yamagata component:
      i. All vaccines: B/Phuket/3073/2013-like virus (B/Yamagata/16/88 lineage) (unchanged).
2. Trivalent vaccines do not include the B/Yamagata component.

Inactivated Influenza Vaccine

For the 2020–2021 season, all licensed inactivated influenza vaccines (IIVs) for children in the United States are quadrivalent unadjuvanted vaccines, with specific age indications for available formulations (Table 3). Four are egg-based (seed strains grown in eggs), and one is cell culture-based (seed strains grown in Madin-Darby canine kidney cells). All inactivated egg-based vaccines (Afluria Quadrivalent, Fluarix Quadrivalent, Flulaval Quadrivalent, and Fluzone Quadrivalent) are licensed for children 6 months and older and available in single-dose, thimerosal-free, prefilled syringes. The only pediatric cell culture-based vaccine (Flucelvax Quadrivalent) is licensed for children 4 years and older.[1]

A quadrivalent recombinant baculovirus-expressed hemagglutinin influenza vaccine (RIV4, Flublok Quadrivalent) is licensed only for people 18 years and older. A new quadrivalent high-dose inactivated influenza vaccine (HD-IIV4, Fluzone High Dose Quadrivalent) containing 4 times the amount of antigen for each virus strain than the standard dose vaccines, is licensed only for people 65 years and older. A trivalent high-dose formulation is no longer available. Both trivalent and quadrivalent MF-59 adjuvanted inactivated vaccines (aIIV3 Fluad and aIIV4 Fluad Quadrivalent) are now licensed for people 65 years and older. The quadrivalent formulation is new this year (licensed in February 2020).[1] Adjuvants may be included in a vaccine to elicit a more robust immune response, which could lead to a reduction in the number of doses required for children. In one pediatric study, the relative vaccine efficacy of a MF-59 adjuvanted influenza vaccine was significantly greater than nonadjuvanted vaccine in the 6- through 23-month age group.[27] Adjuvanted seasonal influenza vaccines are not licensed for children in the United States.

Children 36 months (3 years) and older can receive any age-appropriate licensed IIV, administered at a 0.5-mL dose containing 15 μg of hemagglutinin (HA) from each strain. Children 6

TABLE 3 Recommended Seasonal Influenza Vaccines for Different Age Groups: United States, 2020–2021 Influenza Season

Vaccine	Trade Name (Manufacturer)	Age Group	Presentation Hemagglutinin Antigen Content (IIVs and RIV4) or Virus Count (LAIV4) per dose for Each Antigen	Thimerosal Mercury Content (μg Hg/0.5-mL dose)	CPT Code
Quadrivalent standard dose – egg-based vaccines					
IIV4	Afluria Quadrivalent (Seqirus)	6–35 mo	0.25-mL prefilled syringe[a] (7.5 μg/0.25 mL)	0	
		≥36 mo	0.5-mL prefilled syringe (15 μg/0.5 mL)	0	90686
		≥6 mo	5.0-mL multidose vial[b] (15 μg/0.5 mL)	24.5	90688
IIV4	Fluarix Quadrivalent (GlaxoSmithKline)	≥6 mo	0.5-mL prefilled syringe (15 μg/0.5 mL)	0	90686
IIV4	FluLaval Quadrivalent (GlaxoSmithKline)	≥6 mo	0.5-mL prefilled syringe (15 μg/0.5 mL)	0	90686 90688
IIV4	Fluzone Quadrivalent (Sanofi Pasteur)	≥6 mo	0.5-mL prefilled syringe (15 μg/0.5 mL)[c]	0	90686
		≥6 mo	0.5-mL single-dose vial (15 μg/0.5 mL)	0	90687
		≥6 mo	5.0-mL multidose vial[b] (15 μg/0.5 mL)	25	90688
Quadrivalent standard dose – cell-based vaccines					
ccIIV4	Flucelvax Quadrivalent (Seqirus)	≥4 y	0.5-mL prefilled syringe (15 μg/0.5 mL)	0	90674
		≥4 y	5.0 mL multidose vial (15 μg/0.5 mL)	25	90756
Standard dose – egg-based with adjuvant vaccines					
aIIV3 MF-59 adjuvanted	Fluad Trivalent Seqirus	≥65 y	0.5-mL prefilled syringe (15 μg/0.5 mL)	0	90653
aIIV4 MF-59 adjuvanted	Fluad Quadrivalent Seqirus	≥65 y	0.5-mL prefilled syringe (15 μg/0.5 mL)	0	90653
Quadrivalent high dose – egg-based vaccine					
IIV4	Fluzone High-dose (Sanofi Pasteur)	≥65 y	0.7-mL prefilled syringe (60 μg/0.7 mL)	0	90662
Recombinant vaccine					
RIV4	Flublok Quadrivalent (Sanofi Pasteur)	≥18 y	0.5-mL prefilled syringe (45 μg/0.5 mL)	0	90682
Live attenuated vaccine					
LAIV4	FluMist Quadrivalent (MedImmune)	2–49 y	0.2-mL prefilled intranasal sprayer (Virus dose: 10 6.5–7.5 FFU/0.2 mL)	0	90672

Data sources: Centers for Disease Control and Prevention. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP)—United States, 2020–2021 influenza season. *MMWR Recomm Rep.* 2020; in press. Implementation guidance on supply, pricing, payment, CPT coding, and liability issues can be found at www.aapredbook.org/implementation. (Table has been reformatted and updated).

[a] For Afluria Quadrivalent, children 6 through 35 months of age should receive 0.25 mL per dose; people ≥36 months (≥3 years) of age should receive 0.5 mL per dose.

[b] For vaccines that include a multidose vial presentation a maximum of 10 doses can be drawn from a multidose vial.

[c] The 7.5-μg/0.25-mL dosing volume is no longer available this season.

through 35 months of age may receive any age-appropriate licensed IIV without preference for one over another. Several vaccines have been licensed for children 6 through 35 months of age since 2017 (Table 3). All are quadrivalent, but the dose volume and, therefore, the antigen content vary among different IIV products. In addition to a 0.25-mL (7.5 μg of HA per vaccine virus) Fluzone Quadrivalent vaccine, a 0.5-mL formulation of Fluzone Quadrivalent containing 15 μg of HA per vaccine virus per dose was licensed in January 2019 after these 2 formulations were shown to have comparable safety and immunogenicity in a single randomized, multicenter study.[28–30] Only the 0.5-mL Fluzone product is expected to be available this season. In addition, 2 other vaccines, Fluarix Quadrivalent[31] and FluLaval Quadrivalent,[32] are licensed for a 0.5-mL dose in children 6 through 35 months of age. These 2 vaccines do not have a 0.25-mL dose formulation. Afluria Quadrivalent is the only pediatric vaccine that has a 0.25-mL (7.5 μg of HA per vaccine virus) presentation for children 6 through 35 months of age. Afluria Quadrivalent 0.5 mL (15 μg of HA per vaccine virus) is licensed for children 3 years and older only.[33]

Given that different formulations of IIV for children 6 through 35 months of age are available, care should be taken to administer the appropriate volume and dose for each product. In each instance, the recommended volume may be administered from an appropriate prefilled syringe, a single-dose vial, or multidose vial, as supplied by the manufacturer. For vaccines that include a multidose vial presentation, a maximum of 10 doses can be drawn from a multidose vial. Importantly, dose volume is different from the number of doses needed to complete vaccination. Children 6 months through 8 years of age who require 2 doses of vaccine for the

2020–2021 season should receive 2 separate doses at the recommended dose volume specified for each product.

Inactivated influenza vaccines are well tolerated in children and can be used in healthy children as well as those with underlying chronic medical conditions. The most common injection site adverse reactions following administration of IIV in children are injection site pain, redness, and swelling. The most common systemic adverse events are drowsiness, irritability, loss of appetite, fatigue, muscle aches, headache, arthralgia, and gastrointestinal tract symptoms.

IIV can be administered concomitantly with other inactivated or live vaccines. During the 2 influenza seasons spanning 2010–2012, there were increased reports of febrile seizures in the United States in young children who received trivalent IIV (IIV3) and the 13-valent pneumococcal conjugate vaccine (PCV13) concomitantly. Subsequent retrospective analyses of past seasons demonstrated a slight increase in the risk of febrile seizures in children 6 through 23 months of age when PCV13 vaccines were administered concomitantly with IIV.[34] The concomitant administration of IIV3, PCV13, and diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP) was associated with the greatest relative risk estimate, corresponding to a maximum additional 30 febrile seizure cases per 100 000 children vaccinated, compared with the administration of the vaccines on separate days. In contrast, data from the Post-Licensure Rapid Immunization Safety Monitoring (PRISM) program of the FDA, revealed that there was no significant increase in febrile seizures associated with concomitant administration of these 3 vaccines in children 6 through 59 months of age during the 2010–2011 influenza season.[35]

Similarly, in a subsequent sentinel CBER/PRISM surveillance report evaluating influenza vaccines and febrile seizures, there was no evidence of an elevated risk of febrile seizures in children 6 through 23 months of age following IIV administration during the 2013–2014 and 2014–2015 seasons, noting that the risk of seizures after PCV13 or concomitant PCV13 and IIV was low compared with a child's lifetime risk of febrile seizures from other causes.[36] Using a self-controlled interval study design, Baker et al[37] further evaluated the relative risk of febrile seizures following IIV or PCV13 in children 6 through 23 months, using the PRISM health care claims during those same 2 influenza seasons. When the febrile seizure rate was compared in a risk interval (0–1 days post vaccination) versus a control interval (14–20 days after vaccination), adjusting by age, calendar time, and concomitant administration of the other vaccine, an elevated risk of febrile seizures was identified after vaccination with PCV13 (incidence rate ratio [IRR], 1.80; 95% CI, 1.29 to 2.52), but not after IIV (IRR, 1.12; 95% CI, 0.80 to 1.56). Furthermore, in a study of children 12 to 16 months of age vaccinated during the 2017–2018 season, no difference was observed in the occurrence of fever when IIV administration was delayed for 2 weeks after PCV13 and DTaP vaccination (9.3%) compared with PCV13, DTaP and IIV given on the same day (8.1%) (adjusted risk ratio [aRR], 0.87; 95% CI, 0.36 to 2.19).[38] On the basis of these findings, simultaneous administration of IIV with PCV13 and/or other vaccines continues to be recommended for the 2020–2021 influenza season when these vaccines are indicated. Overall, the benefits of timely vaccination with same-day administration of IIV and PCV13 or DTaP outweigh the risk of febrile seizures. Vaccine-proximate febrile seizures rarely have any long-term sequelae, similar to nonvaccine–proximate febrile seizures.

Thimerosal-containing vaccines are not associated with an increased risk of autism spectrum disorder in children. Thimerosal from vaccines has not been linked to any neurologic condition. The American Academy of Pediatrics (AAP) supports the current WHO recommendations for use of thimerosal as a preservative in multiuse vials in the global vaccine supply.[39] Despite the lack of evidence of harm, some states have legislation restricting the use of vaccines that contain even trace amounts of thimerosal. The benefits of protecting children against the known risks of influenza are clear. Therefore, to the extent permitted by state law, children should receive any available formulation of IIV rather than delaying vaccination while waiting for reduced thimerosal-content or thimerosal-free vaccines. IIV formulations that are free of even trace amounts of thimerosal are widely available (Table 3).

Live Attenuated (Intranasal) Influenza Vaccine

The intranasal live attenuated influenza vaccine (LAIV) was initially licensed in the United States in 2003 for people 5 through 49 years of age as a trivalent formulation (LAIV3), and the approved age group was extended to 2 years of age in 2007. The quadrivalent formulation (LAIV4) licensed in 2012 was first available during the 2013–2014 influenza season, replacing LAIV3. The most commonly reported reactions of LAIV in children are runny nose or nasal congestion, headache, decreased activity or lethargy, and sore throat.

The CDC conducted a systematic review of published studies evaluating the effectiveness of LAIV3 and LAIV4 in children from the 2010–2011 to the 2016–2017 influenza seasons, including data from United States and European studies.[40] The data suggested that the

effectiveness of LAIV3 or LAIV4 for influenza A(H1N1)pdm09 strain was lower than that of IIV in children 2 through 17 years of age. LAIV was similarly effective against influenza B and A/H3N2 strains in some age groups compared with IIV. LAIV was not recommended by the CDC or AAP for use in children during the 2016–2017 and 2017–2018 seasons, given concerns about its effectiveness against A(H1N1)pdm09. For the 2017–2018 season, a new A(H1N1) pdm09-like virus strain (A/Slovenia/2903/2015) was included in LAIV4, replacing the prior A/Bolivia/559/2013 strain. A study conducted by the LAIV4 manufacturer evaluated viral shedding and immunogenicity associated with the LAIV4 formulation containing the new A(H1N1) pdm09-like virus among US children 24 to 48 months of age.[41] Shedding and immunogenicity data suggested that the new influenza A(H1N1)pdm09-like virus included in its latest formulation had improved replicative fitness over previous LAIV4 influenza A(H1N1)pdm09-like vaccine strains, resulting in an improved immune response, comparable with that of the LAIV3 available prior to the 2009 pandemic. Shedding and replicative fitness are not known to correlate with efficacy, and no published effectiveness estimates for this revised formulation of the vaccine against influenza A(/H1N1)pdm09 viruses were available prior to the start of the 2018–2019 influenza season, because influenza A(/H3N2) and influenza B viruses predominated during the 2017–2018 Northern Hemisphere season. Therefore, for the 2018–2019 influenza season, the AAP recommended IIV4 or IIV3 as the primary choice for influenza vaccination in children, with LAIV4 use reserved for children who would not otherwise receive an influenza vaccine and for whom LAIV utilization was appropriate for age (2 years and older) and health status (ie, healthy, without any underlying chronic medical condition).

In February 2019, the AAP Committee of Infectious Diseases (COID) reviewed available data on influenza epidemiology and vaccine effectiveness for the 2018–2019 season and agreed that harmonizing recommendations between the AAP and CDC for the use of LAIV in the 2019–2020 season was appropriate. After the February 2020 ACIP meeting, the AAP COID reviewed available epidemiologic and effectiveness data for the previous and current seasons to inform recommendations for the 2020–2021 season. Despite the early circulation of A(H1N1)pdm09 during the 2018–2019 season and its predominance during the 2019–2020 season, low utilization of LAIV4 in the United States population has limited the evaluation of product-specific vaccine effectiveness, and no additional US data on LAIV4 VE are available. Although the proportion of LAIV used for vaccination is unknown, interim overall VE (not specific to a type of vaccine) for the 2019–2020 influenza season shows reassuring protection in children against circulating influenza A and B strains (Table 1).[6] Furthermore, influenza vaccine coverage rates in children are stable.[9] In European surveillance networks where uninterrupted utilization of LAIV has continued from the 2016–2017 through the 2019–2020 seasons, the only country with LAIV VE estimates, the United Kingdom, reported final VE against medically attended influenza for the 2018–2019 season in children 2 through 17 years of age of 49.9% (95% CI, –14.3% to 78.0%) for A(H1N1)pdm09 and of 27.1% (95% CI, –130.5% to 77%) for A(H3N2).[42] The final adjusted VE in the United States (where mostly IIV was used) for 2018–2019 against A(H1N1)pdm09 was 59% (95% CI, 47% to 69%) for children 6 months through 8 years of age but only 24% (95% CI, –18% to 51%) for children 9 through 17 years and for A(H3N2) 24% (95% CI, 1% to 42%) in children 6 months through 8 years of age, and 3% (95% CI, –30% to 28%) in children 9 through 17 years of age.[43] Direct comparisons cannot be made given differences in reporting of VE for various age groups. Other countries that use LAIV (Canada, Finland) have not reported LAIV4-specific VE in past several seasons. Small case numbers and low LAIV use may also limit accurate VE calculations in these countries. In general, as long as use of LAIV is low relative to IIV, it will be difficult to estimate LAIV VE accurately. Furthermore, important variability in VE against all strains is reported for both IIV and LAIV.

Influenza VE varies from season to season and is affected by many factors, including age and health status of the recipient, influenza type and subtype, existing immunity from previous infection or vaccination, and degree of antigenic match between vaccine and circulating virus strains. It is possible that VE also differs among individual vaccine products; however, product-specific comparative effectiveness data are lacking for most vaccines. Additional experience over multiple influenza seasons will help to determine optimal utilization of the available vaccine formulations in children. The AAP will continue to monitor annual influenza surveillance and VE reports to update influenza vaccine recommendations if necessary.

CONTRAINDICATIONS AND PRECAUTIONS

Anaphylactic reactions to any vaccine are considered a contraindication to vaccination. The AAP recommends that children who have had an allergic reaction after a previous dose of any influenza vaccine should be evaluated by an allergist to determine whether future receipt of the vaccine is appropriate. Similarly, consultation

with an infectious disease specialist may be sought to assess potential contraindications and precautions and to determine which influenza vaccine is most appropriate to ensure immunization in special circumstances.

Minor illnesses, with or without fever, are not contraindications to the use of influenza vaccines, including among children with mild upper respiratory infection symptoms or allergic rhinitis. In children with a moderate to severe febrile illness (eg, high fever, active infection, requiring hospitalization, etc), on the basis of the judgment of the clinician, vaccination should be deferred until resolution of the illness. Children with confirmed COVID-19 can receive influenza vaccine when the acute illness has resolved. Children with an amount of nasal congestion that would notably impede vaccine delivery into the nasopharyngeal mucosa should have LAIV vaccination deferred until resolution.

A precaution for vaccination is a condition in a recipient that might increase the risk or seriousness of a possible vaccine-related adverse reaction. A precaution also may exist for conditions that might compromise the ability of the host to develop immunity after vaccination. Vaccination may be recommended in the presence of a precaution if the benefit of protection from the vaccine outweighs the potential risks.

History of Guillain-Barré syndrome (GBS) following influenza vaccine is considered a precaution for the administration of influenza vaccines. GBS is rare, especially in children, and there is a lack of evidence on risk of GBS following influenza vaccine in children. Nonetheless, regardless of age, a history of GBS less than 6 weeks after a previous dose of influenza vaccine is a precaution for administration of influenza vaccine. GBS may occur after influenza infection. The benefits of influenza vaccination might outweigh the risks for certain people who have a history of GBS (particularly if not associated with prior influenza vaccination) and who also are at high risk for severe complications from influenza.

Specific precautions for LAIV include a diagnosis of asthma in children 5 years and older and the presence of certain chronic underlying medical conditions, including metabolic disease, diabetes mellitus, other chronic disorders of the pulmonary or cardiovascular systems, renal dysfunction, or hemoglobinopathies. Although the safety of LAIV has not been definitely established in these situations, IIV can be considered. In a study comparing a large cohort of children 2 through 17 years old with asthma who received LAIV instead of IIV under established practice guidelines from 2007 to 2016, the occurrence of asthma exacerbation within 21 to 42 days of vaccination was not higher compared with children who received IIV.[44] In a prospective open-label phase IV study conducted in the United Kingdom, 478 children aged 2 to 18 years with physician-diagnosed asthma or recurrent wheezing received LAIV, with no significant change in asthma symptoms or exacerbation in the 4 weeks after vaccination.[45] However, 14.7% of patients eventually reported a severe asthma exacerbation after vaccination, requiring treatment. In post-licensure surveillance of LAIV (including LAIV3 and LAIV4), the Vaccine Adverse Event Reporting System (VAERS), jointly sponsored by the FDA and CDC, has not identified any new or unexpected safety concerns, including in people with a contraindication or precaution (https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/vaers/).

People who should not receive LAIV are listed below.

People in Whom LAIV is Contraindicated

- Children younger than 2 years.
- Children 2 through 4 years of age with a diagnosis of asthma or history of recurrent wheezing or a medically attended wheezing episode in the previous 12 months because of the potential for increased wheezing after immunization. In this age range, many children have a history of wheezing with respiratory tract illnesses and are eventually diagnosed with asthma.
- Children with new cochlear implants or active cerebrospinal fluid leaks.
- Children who have a known or suspected primary or acquired immunodeficiency or who are receiving immunosuppressive or immunomodulatory therapies.
- Children with anatomic or functional asplenia, including from sickle cell disease.
- Close contacts and caregivers of those who are severely immunocompromised and require a protected environment.
- Children and adolescents receiving aspirin or salicylate-containing medications.
- Children who have received other live-virus vaccines within the previous 4 weeks (except for rotavirus vaccine); however, LAIV can be administered on the same day with other live-virus vaccines if necessary.
- Children taking an influenza antiviral medication and until 48 hours (oseltamivir, zanamivir) and up to 2 weeks (peramivir and baloxavir) after stopping the influenza antiviral therapy. If a child recently received LAIV but has an influenza illness for which antiviral agents are appropriate, the antiviral agents should be given. If antiviral agents are necessary for treatment within 5

to 7 days of LAIV immunization, reimmunization is indicated because of the potential effects of antiviral medications on LAIV replication and immunogenicity.

- Pregnant women.

LAIV and Immunocompromised Hosts

The inactivated influenza vaccine is the vaccine of choice for anyone in close contact with a subset of severely immunocompromised people (ie, those in a protected environment). IIV is preferred over LAIV for contacts of severely immunocompromised people because of a theoretical risk of infection attributable to LAIV strain in an immunocompromised contact of an LAIV-immunized person. Available data indicate a very low risk of transmission of the virus from both children and adults vaccinated with LAIV. Health care personnel (HCP) immunized with LAIV may continue to work in most units of a hospital, including the NICU and general oncology ward, using standard infection control techniques. As a precautionary measure, people recently vaccinated with LAIV should restrict contact with severely immunocompromised patients for 7 days after immunization, although there have been no reports of LAIV transmission from a vaccinated person to an immunocompromised person. In the theoretical scenario in which symptomatic LAIV infection develops in an immunocompromised host, LAIV strains are susceptible to antiviral medications.

INFLUENZA VACCINES AND EGG ALLERGY

There is strong evidence that egg-allergic individuals can safely receive influenza vaccine without any additional precautions beyond those recommended for any vaccine.[46,47] The presence of egg allergy in an individual is not a contraindication to receive IIV or LAIV. Vaccine recipients with egg allergy are at no greater risk for a systemic allergic reaction than those without egg allergy. Therefore, precautions such as choice of a particular vaccine, special observation periods, or restriction of administration to particular medical settings are not warranted and constitute an unnecessary barrier to immunization. It is not necessary to inquire about egg allergy before the administration of any influenza vaccine, including on screening forms. Routine prevaccination questions regarding anaphylaxis after receipt of any vaccine are appropriate. Standard vaccination practice for all vaccines in children should include the ability to respond to rare acute hypersensitivity reactions. Children who have had a previous allergic reaction to the influenza vaccine should be evaluated by an allergist to determine whether future receipt of the vaccine is appropriate.

INFLUENZA VACCINES DURING PREGNANCY AND BREASTFEEDING

Influenza vaccine is recommended by the ACIP, the American College of Obstetrics and Gynecology (ACOG), and the American Academy of Family Physicians (AAFP) for all women, during any trimester of gestation, for the protection of mothers against influenza and its complications.[1,48] Substantial evidence has accumulated regarding the efficacy of maternal influenza immunization in preventing laboratory-confirmed influenza disease and its complications in both mothers and their infants in the first 2 to 6 months of life.[48–53] Pregnant women who are immunized against influenza at any time during their pregnancy provide protection to their infants during their first 6 months of life, when they are too young to receive influenza vaccine themselves, through transplacental passage of antibodies.[50–58] Infants born to women who receive influenza vaccination during pregnancy can have a risk reduction of up to 72% (95% CI, 39% to 87%) for laboratory-confirmed influenza hospitalization in the first few months of life.[56]

It is safe to administer inactivated influenza vaccine to pregnant women during any trimester of gestation and postpartum. Any licensed, recommended, and age-appropriate influenza vaccine may be used, although experience with the use of RIV4 in pregnant women is limited. LAIV is contraindicated during pregnancy. Data on the safety of influenza vaccination at any time during pregnancy continues to support the safety of influenza immunization during pregnancy.[48,50–55,59] In a 5-year retrospective cohort study from 2003 to 2008 with more than 10 000 women, influenza vaccination in the first trimester was not associated with an increase in the rates of major congenital malformations.[60] Similarly, a systematic review and meta-analysis of studies of congenital anomalies after vaccination during pregnancy, including data from 15 studies (14 cohort studies and 1 case-control study) did not show any association between congenital defects and influenza vaccination in any trimester, including the first trimester of gestation.[61] Assessments of any association with influenza vaccination and preterm birth and small-for-gestational-age infants have yielded inconsistent results, with most studies reporting a protective effect or no association against these outcomes.[62,63] A cohort study from the Vaccines and Medications in Pregnancy Surveillance System (VAMPSS) of vaccine exposure during the 2010–2011 through 2013–2014 influenza seasons found no significant association of spontaneous abortion with influenza vaccine exposure in the first trimester or within the first 20 weeks of gestation.[64] One observational Vaccine Safety Datalink (VSD) study conducted during the 2010–2011 and 2011–2012 influenza seasons indicated an association between receipt of IIV containing

H1N1pdm09 and risk of spontaneous abortion, when an H1N1pdm-09-containing vaccine had also been received the previous season.[65] A follow-up study conducted by the same investigators with a larger population and stricter outcome measures did not show this association and further supported the safety of influenza vaccine during pregnancy.[66]

Women in the postpartum period who did not receive influenza vaccination during pregnancy should be encouraged to discuss with their obstetrician, family physician, nurse midwife, or other trusted provider receiving influenza vaccine before discharge from the hospital. Vaccination during breastfeeding is safe for mothers and their infants.

Breastfeeding is strongly recommended to protect infants against influenza viruses by activating innate antiviral mechanisms, specifically type 1 interferons. Human milk from mothers vaccinated during the third trimester also contains higher levels of influenza-specific immunoglobulin A (IgA).[67] Greater exclusivity of breastfeeding in the first 6 months of life decreases the episodes of respiratory illness with fever in infants of vaccinated mothers. For infants born to mothers with confirmed influenza illness at delivery, breastfeeding is encouraged, and guidance on breastfeeding practices can be found at https://www.cdc.gov/breastfeeding/breastfeeding-special-circumstances/maternal-or-infant-illnesses/influenza.html and https://www.cdc.gov/flu/professionals/infectioncontrol/peri-post-settings.htm. Breastfeeding should be encouraged even if the mother or infant has influenza illness. The mother should pump and feed expressed milk if she or her infant are too sick to breastfeed. If the breastfeeding mother requires antiviral agents, treatment with oral oseltamivir is preferred. The CDC does not recommend use of baloxavir for treatment of pregnant women or breastfeeding mothers. There are no available efficacy or safety data in pregnant women, and there are no available data on the presence of baloxavir in human milk, the effects on the breastfed infant, or the effects on milk production.

VACCINE STORAGE AND ADMINISTRATION

The AAP Storage and Handling Tip Sheet provides resources for practices to develop comprehensive vaccine management protocols to keep the temperature for vaccine storage constant during a power failure or other disaster (https://www.aap.org/en-us/Documents/immunization_disasterplanning.pdf). The AAP recommends the development of a written disaster plan for all practice settings. Additional information is available (www.aap.org/disasters). During the COVID-19 pandemic, the AAP recommends that influenza vaccine administration follow CDC guidance for administration of immunizations (https://www.cdc.gov/vaccines/pandemic-guidance/index.html). Vaccination in the medical home is ideal to ensure that pediatric patients receive other vaccinations and routine care in a timely manner and receive catch-up immunizations if delays have occurred because of the pandemic. In general, infection-prevention measures should be in place for all patient encounters, including screening for symptoms, physical distancing, respiratory and hand hygiene, and surface decontamination. In addition to standard precautions and hand hygiene, during the COVID-19 pandemic, it is recommended that vaccine administrators wear a surgical face mask (not N95 or respiratory) at all times and eye protection if the level of community spread is moderate or elevated. Administration of LAIV intranasally is not an aerosol-generating procedure; however, vaccine administrators are advised to wear gloves when injecting LAIV given the potential to coming in contact with respiratory secretions. Gloves used for intranasal or intramuscular vaccine administration should be changed with every patient. Gowns are not required.

Inactivated Influenza Vaccines

IIVs for intramuscular (IM) injection are shipped and stored at 2°C to 8°C (36°F–46°F); vaccines that are inadvertently frozen should not be used. These vaccines are administered intramuscularly into the anterolateral thigh of infants and young children and into the deltoid muscle of older children and adults. Given that various IIVs are available, careful attention should be used to ensure that each product is used according its approved age indication, dosing, and volume of administration (Table 3). A 0.5-mL unit dose of any IIV should not be split into 2 separate 0.25-mL doses. If a lower dose than recommended is inadvertently administered to a child 36 months or older (eg, 0.25 mL), an additional 0.25-mL dose should be administered to provide a full dose of 0.5 mL as soon as possible. The total number of full doses appropriate for age should be administered. If a child is inadvertently vaccinated with a formulation only approved for adults, the dose should be counted as valid.

Live Attenuated Influenza Vaccine

The cold-adapted, temperature-sensitive LAIV4 formulation is shipped and stored at 2°C to 8°C (35°F–46°F) and administered intranasally in a prefilled, single-use sprayer containing 0.2 mL of vaccine. A removable dose-divider clip is attached to the sprayer to facilitate administration of 0.1 mL separately into each nostril. If the child sneezes immediately after administration, the dose should not be repeated.

VACCINE DOSING RECOMMENDATIONS

The number of seasonal influenza vaccine doses recommended for children during the 2020–2021 influenza season depends on the child's age at the time of the first administered dose and vaccine history. The recommendations are unchanged from previous years, as shown in Fig 2.

- Influenza vaccines are not licensed for administration to infants younger than 6 months and should not be used in this age group.
- Children 9 years and older need only 1 dose, regardless of previous vaccination history.
- Children 6 months through 8 years of age:
  - Need 2 doses if they have received fewer than 2 doses of any trivalent or quadrivalent influenza vaccine (IIV or LAIV) before July 1, 2020, or if their vaccination status is unknown. The interval between the 2 doses should be at least 4 weeks. Two doses should be administered to children who receive their first dose before their ninth birthday, even if their ninth birthday occurs during the same season.
  - Require only 1 dose if they have previously received 2 or more total doses of any trivalent or quadrivalent influenza vaccine (IIV or LAIV) before July 1, 2020. The 2 previous doses do not need to have been received during the same influenza season or consecutive influenza seasons.

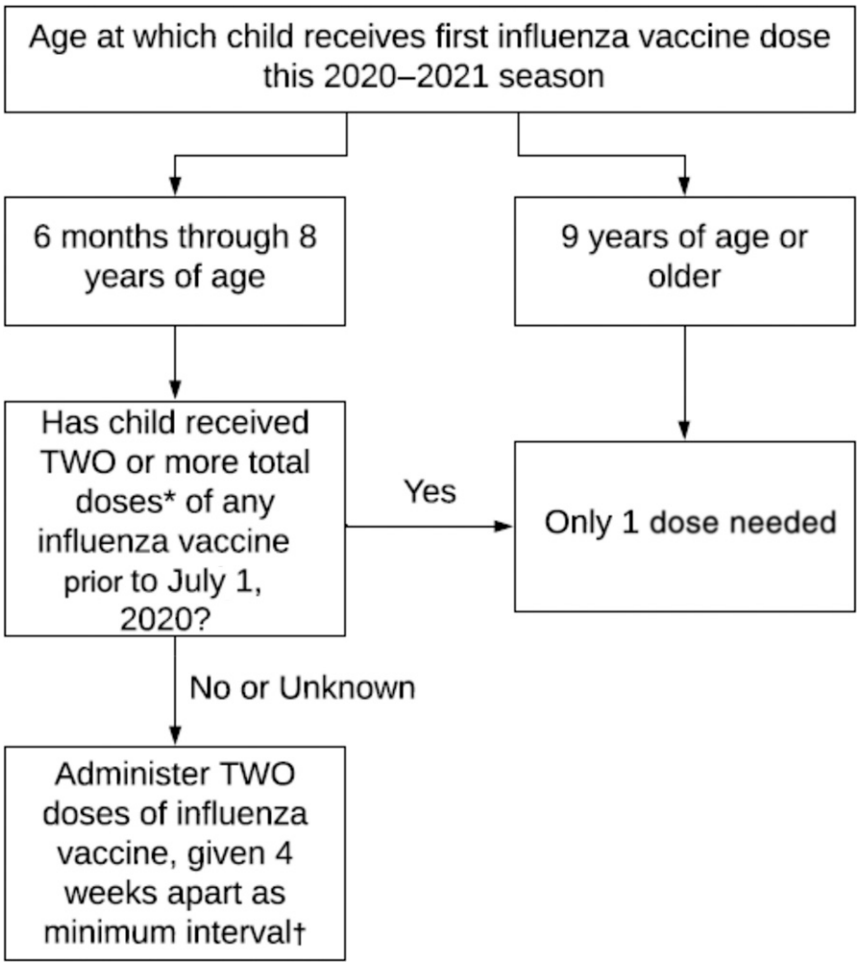


FIGURE 2
Number of 2020–2021 seasonal influenza vaccine doses for children based on age and prior vaccination history. * The 2 doses need not have been received during the same season or consecutive seasons. † Administer 2 doses based on age at receipt of the first dose of influenza vaccine during the season. Children who receive the first dose before their ninth birthday should receive 2 doses, even if they turn 9 years old during the same season.

TIMING OF VACCINATION AND DURATION OF PROTECTION

Although peak influenza activity in the United States tends to occur from January through March, influenza can circulate from early fall (October) to late spring (May), with one or more disease peaks. Predicting the onset and duration or the severity of the influenza season with accuracy is impossible. It is also challenging to balance public health strategies needed to achieve high vaccination coverage with achieving optimal individual immunity for protection against influenza at the peak of seasonal activity, knowing that the duration of immunity after vaccination can wane over time. Initiation of influenza vaccination before influenza is circulating in the community and continuing to vaccinate throughout the influenza season are important components of an effective influenza vaccination strategy, particularly this season, when circulation of SARS-CoV-2 is expected to continue.

Complete influenza vaccination by the end of October is recommended by the CDC and AAP. Children who need 2 doses of vaccine should receive their first dose as soon as possible when vaccine becomes available, to allow sufficient time for receipt of the second dose ≥4 weeks after the first, before the onset of the influenza season. Children who require only 1 dose of influenza vaccine should also ideally be vaccinated by end of October; however, recent data (mostly in adults) suggests that very early vaccination (July or August) might be associated with suboptimal immunity

before the end of the influenza season.

Although the evidence is limited in children, recent reports raise the possibility that early vaccination might contribute to reduced protection later in the influenza season.[68–79] In these studies, vaccine effectiveness decreased within a single influenza season, and this decrease was correlated with increasing time after vaccination. However, this decay in VE was not consistent across different age groups and varied by season and virus subtypes. In some studies, waning VE was more evident among older adults and younger children[71,73] and with influenza A(H3N2) viruses more than influenza A(H1N1) or B viruses.[72,75,77] A multiseason analysis from the US Influenza Vaccine Effectiveness Network found that VE declined by approximately 7% per month for influenza A (H3N2) and influenza B and by 6% to 11% per month for influenza A (H1N1)pdm09 in individuals 9 years and older.[70] VE remained greater than 0 for at least 5 to 6 months after vaccination. A more recent study including children older than 2 years also found evidence of declining vaccine effectiveness with an odds ratio increasing approximately 16% with each additional 28 days from vaccine administration.[80] In another study evaluating VE from the 2011–2012 through the 2013–2014 influenza seasons demonstrated 54% to 67% protection from 0 to 180 days after vaccination.[74] Finally, a multiseason study in Europe from 2011–2012 through 2014–2015 showed a steady decline in VE down to 0% protection by 111 days after vaccination.[75]

Further evaluation is needed before any policy change in timing of influenza administration is made. An early onset of the influenza season is a concern when considering delaying vaccination. Until there are definitive data that determine whether waning immunity influences VE in children, administration of influenza vaccine should not be delayed to a later date, because this increases the likelihood of missing influenza vaccination altogether.[81] Providers may continue to offer vaccine until June 30th of each year when the seasonal influenza vaccine expires, because the duration of influenza circulation is unpredictable. Furthermore, a person may experience more than one influenza infection during a given season because of the various cocirculating strains. Although influenza activity in the United States is typically low during the summer, influenza cases and outbreaks can occur, particularly among international travelers, who may be exposed to influenza year-round, depending on destination.

VACCINE IMPLEMENTATION

The AAP Partnership for Policy Implementation has developed a series of definitions using accepted health information technology standards to assist in the implementation of vaccine recommendations in computer systems and quality measurement efforts. This document is available at www2.aap.org/informatics/PPI.html. In addition, the AAP has developed implementation guidance on supply, payment, coding, and liability issues; these documents can be found at www.aapredbook.org/implementation.

HCP, influenza campaign organizers, and public health agencies are encouraged to collaborate to develop improved strategies for planning, distribution, communication, and administration of vaccines. For example, pediatricians can play a key role in educating and assisting early childhood education centers and schools in educating parents on the importance of influenza immunization. Resources for effective communication and messaging strategies are available on the AAP Web site – promoting vaccinations and providing resources for pediatricians to communicate with patients, families, and the communities they serve (https://www.aap.org/en-us/about-the-aap/aap-press-room/campaigns/immunizations/Pages/default.aspx and https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/immunizations/Influenza-Implementation-Guidance/Pages/Patient-Family-and-Community.aspx).

Pediatricians and other pediatric health care providers should plan to make influenza vaccine easily accessible for all children. Examples include sending alerts to families that vaccine is available (eg, e-mails, texts, letters, patient portals, practice-specific websites, or social media platforms); creating walk-in influenza vaccination clinics; extending hours beyond routine times during peak vaccination periods; administering influenza vaccine during both well child examinations and sick visits as well as in hospitalized patients, especially those at high risk of influenza complications, before hospital discharge (unless medically contraindicated); implementing standing orders for influenza vaccination; considering how to immunize parents, adult caregivers, and siblings (see risk management guidance associated with adult immunizations at http://pediatrics.aappublications.org/content/129/1/e247) at the same time as children; and working with other institutions (eg, schools, child care programs, local public health departments, and religious organizations) or alternative care sites, such as pharmacies and hospital emergency departments, to expand venues for administering vaccine. If a child receives influenza vaccine outside of his or her medical home, such as at a pharmacy, retail-based clinic, or another practice setting, appropriate documentation of vaccination should be provided to the patient to be shared with his or her

medical home and entered into the state or regional immunization information system (ie, registry).

Concerted efforts among the aforementioned groups, plus vaccine manufacturers, distributors, and payers, are necessary to prioritize distribution appropriately to the primary care office setting and patient-centered medical home before other venues, especially when vaccine supplies are delayed or limited. Payers should eliminate remaining "patient responsibility" cost barriers to influenza vaccine where they still exist. Similar efforts should be made to eliminate the vaccine supply discrepancy between privately insured patients and those eligible for vaccination through the Vaccines for Children (VFC) program. American Indian/Alaska Native children, who are eligible for vaccines through the VFC program, are at higher risk for influenza complications and should be prioritized in a vaccine shortage (Table 2).

Population health can benefit from pediatricians' discussions about vaccine safety and effectiveness. Pediatricians and their office staff can influence vaccine acceptance by explaining the importance of annual influenza vaccination for children and emphasizing when a second dose of vaccine is indicated. The AAP and CDC have created communication resources to convey these important messages and to help the public understand influenza recommendations. Resources will be available on *Red Book Online* (https://redbook.solutions.aap.org/selfserve/ssPage.aspx?SelfServeContentId=influenza-resources).

The AAP supports mandatory influenza vaccination programs for all HCP in all settings, including outpatient settings. Optimal prevention of influenza in the health care setting depends on the vaccination of at least 90% of HCP, which is consistent with the national *Healthy People 2020* target for annual influenza vaccination among HCP. Vaccine coverage among HCP was 81.1% during the 2018–2019 season, up from 78.4% the previous year.[82] Influenza vaccination programs for HCP benefit the health of employees, their patients, and members of the community, especially because HCP frequently come into contact with patients at high risk of influenza illness in their clinical settings. Mandatory influenza immunization for all HCP is considered to be ethical, just, and necessary to improve patient safety. For the prevention and control of influenza, HCP must prioritize the health and safety of their patients, honor the requirement of causing no harm, and act as role models for both their patients and colleagues by receiving influenza vaccination annually.

INFLUENZA VACCINE COVERAGE

Although national influenza vaccination coverage among children has not declined in the past several seasons, overall vaccination coverage remains suboptimal (Fig 1). Achieving high coverage rates of influenza vaccine in infants and children is a priority to protect them against influenza disease and its complications. Timely influenza vaccination is particularly important during the 2020–2021 influenza season, given the concurrent SARS-CoV-2 pandemic.

The AAP and CDC recommend vaccine administration at any visit to the medical home before and during influenza season when it is not contraindicated, at specially arranged vaccine-only sessions, and through cooperation with community sites, schools, and Head Start and child care facilities to provide influenza vaccine. The CDC has developed guidance for the planning of vaccination clinics during the COVID-19 pandemic (https://www.cdc.gov/vaccines/hcp/admin/mass-clinic-activities/index.html?deliveryName=USCDC_7_3-DM33813). It is important that annual delivery of influenza vaccine to primary care medical homes should be timely to avoid missed opportunities. If alternate venues, including pharmacies and other retail-based clinics, are used for vaccination, a system of patient record transfer is crucial to maintain the accuracy of immunization records. Immunization information systems should be used whenever available and prioritized to document influenza vaccination. Two-dimensional barcodes have been used to facilitate more efficient and accurate documentation of vaccine administration with limited experience to date. Additional information concerning current vaccines shipped with 2-dimensional barcodes can be found at www.cdc.gov/vaccines/programs/iis/2d-vaccine-barcodes/.

Children's likelihood of being immunized according to recommendations appears to be associated with the immunization practices of their parents. One study found that children were 2.77 times (95% CI, 2.74 to 2.79) more likely to be immunized against seasonal influenza if their parents were immunized.[49] When parents who were previously not immunized had received immunization for seasonal influenza, their children were 5.44 times (95% CI, 5.35 to 5.53) more likely to receive influenza vaccine.

Pediatric offices may choose to serve as a venue for providing influenza vaccination for parents and other care providers of children, if the practice is acceptable to both pediatricians and the adults who are to be vaccinated. Medical liability and payment issues along with medical record documentation requirements need to be considered before a pediatrician begins immunizing adults (see risk management guidance associated

with adult immunizations at http://pediatrics.aappublications.org/content/129/1/e247). Pediatric practices should be aware of payment implications including nonpayment or having the parent inappropriately attributed by a payer as a patient of the pediatrician's office. The AAP supports efforts to overcome these payment barriers with insurance payers to maximize influenza immunization rates. To avoid errors in claims processing and payment and in the exchange of immunization data, pediatricians are reminded that parents should have their own basic medical record, where their influenza vaccination should be documented. Adults should be encouraged to have a medical home and communicate their vaccination status to their primary care provider. Offering adult vaccinations in the pediatric practice setting should not undermine the adult medical home model. Vaccination of close contacts of children at high risk of influenza-related complications (Table 2) is intended to reduce children's risk of exposure to influenza (ie, "cocooning"). The practice of cocooning also may help protect infants younger than 6 months who are too young to be immunized with influenza vaccine.

SURVEILLANCE

Information about influenza surveillance is available through the CDC Voice Information System (influenza update at 1-800-232-4636) or at www.cdc.gov/flu/index.htm. Although current influenza season data on circulating strains do not necessarily predict which and in what proportion strains will circulate in the subsequent season, it is instructive to be aware of 2019–2020 influenza surveillance data and use them as a guide to empirical therapy until current seasonal data are available from the CDC. Information is posted weekly on the CDC Web site (www.cdc.gov/flu/weekly/fluactivitysurv.htm). The AAP offers "What's the Latest with the Flu" messages to highlight those details most relevant for AAP members and child care providers on a monthly basis during influenza season (https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/Pages/What's-the-Latest-with-the-Flu.aspx).

INFLUENZA VACCINATION RECOMMENDATIONS

1. The AAP recommends annual influenza vaccination for *everyone* 6 months and older, including children and adolescents, during the 2020–2021 influenza season.
2. For the 2020–2021 influenza season, the AAP recommends that any licensed influenza vaccine appropriate for age and health status can be used for influenza vaccination in children. Inactivated influenza vaccine (IIV) and live attenuated vaccine (LAIV) are options for children for whom these vaccines are appropriate. This recommendation is based on review of current available data on LAIV and IIV vaccine efficacy (VE). The AAP will continue to review VE data as they become available and update these recommendations if necessary.
3. The AAP does not have a preference for any influenza vaccine product over another for children who have no contraindication to influenza vaccination and for whom more than one licensed product appropriate for age and health status is available. Pediatricians should administer whichever formulation is available in their communities to achieve the highest possible coverage this influenza season.
4. Children 6 through 35 months of age may receive any licensed, age-appropriate IIV available this season, at the dose indicated for the vaccine. No product is preferred over another for this age group. Children 36 months (3 years) and older should receive a 0.5-mL dose of any available, licensed, age-appropriate inactivated vaccine.
5. The number of seasonal influenza vaccine doses recommended to be administered to children in the 2020–2021 influenza season remains unchanged and depends on the child's age at the time of the first administered dose and vaccine history (Fig 2).
6. Children 6 months through 8 years of age who are receiving influenza vaccine for the first time or who have received only 1 dose, before July 1, 2020, or whose vaccination status is unknown should receive 2 doses of influenza vaccine, ideally by the end of October, and vaccines should be offered as soon as they become available. Children needing only 1 dose of influenza vaccine, regardless of age, should also receive vaccination, ideally by the end of October.
7. Efforts should be made to ensure vaccination for children in high-risk groups (Table 2) and their contacts, unless contraindicated.
8. Product-specific contraindications must be considered when selecting the type of vaccine to administer. Children who have had an allergic reaction after a previous dose of any influenza vaccine should be evaluated by an allergist to determine whether future receipt of the vaccine is appropriate.
9. Children with egg allergy can receive influenza vaccine without any additional precautions beyond those recommended for all vaccines.
10. Pregnant women may receive inactivated influenza vaccine at

any time during pregnancy, to protect themselves and their infants, who benefit from the transplacental transfer of antibodies. Women in the postpartum period who did not receive vaccination during pregnancy should be encouraged to receive influenza vaccine before discharge from the hospital. Influenza vaccination during breastfeeding is safe for mothers and their infants.

11. The AAP supports mandatory vaccination of health care personnel as a crucial element in preventing influenza and reducing health care-associated influenza infections, because health care personnel often care for individuals at high risk for influenza-related complications.

INFLUENZA ANTIVIRALS

Antiviral agents available for both influenza treatment and chemoprophylaxis in children of all ages can be found in Table 4 (including doses for preterm infants that have not been evaluated by the FDA) and on the CDC Web site (www.cdc.gov/flu/professionals/antivirals/index.htm). These include the neuraminidase inhibitors (NAIs) (oseltamivir, zanamivir, peramivir) and a selective inhibitor of influenza cap-dependent endonuclease (baloxavir), all of which have activity against influenza A and B viruses.[83]

Oral oseltamivir remains the antiviral drug of choice for the management of illness caused by influenza virus infections. Although more difficult to administer, inhaled zanamivir (Relenza) is an equally acceptable alternative for patients who do not have chronic respiratory disease. Options are limited for children who cannot absorb orally or enterally administered oseltamivir or tolerate inhaled zanamivir. Intravenous (IV) peramivir (Rapivab), a third NAI, was approved in September 2017 as treatment of acute uncomplicated influenza in nonhospitalized children 2 years and older who have been symptomatic for no more than 2 days. The efficacy of peramivir in patients with serious influenza requiring hospitalization has not been established.[83] IV zanamivir is not approved in the United States and has not been available for compassionate use since the 2017–2018 season.[68,69] The FDA-licensed baloxavir marboxil in 2018 for the early treatment of uncomplicated influenza in outpatients 12 years and older who have been ill for no more than 2 days.[84] This antiviral agent for influenza has a different mechanism of action (cap-endonuclease inhibitor) than NAIs and requires only a single oral dose for treatment of uncomplicated influenza. A clinical trial of baloxavir treatment of influenza in hospitalized patients 12 years and older is ongoing (https://clinicaltrials.gov/ct2/show/NCT03684044?cond=baloxavir&rank=6).

INFLUENZA TREATMENT

Randomized controlled trials (RCTs) conducted to date to evaluate the efficacy of influenza antiviral medications among outpatients with uncomplicated influenza have found that timely treatment can reduce the duration of influenza symptoms and fever in pediatric populations.[85–89] Observational studies in pediatric and adult populations suggest that antiviral agents could reduce the risk of certain influenza complications, including hospitalization and death.[90–93] The number of published RCTs in children is limited, and interpretation of the results of these studies needs to take into consideration the size of the study (the number of events might not be sufficient to assess specific outcomes in small studies), the variations in the case definition of influenza illness (clinically diagnosed versus laboratory confirmed), the time of treatment administration in relation to the onset of illness, and the child's age and health status as important variables. A Cochrane review of 6 RCTs involving treatment of 2356 children with clinically diagnosed influenza, of whom 1255 had laboratory-confirmed influenza, showed that in children with laboratory-confirmed influenza, oral oseltamivir and inhaled zanamivir reduced median duration of illness by 36 hours (26%; $P < .001$) and 1.3 days (24%, $P < .001$), respectively.[89] Among the studies reviewed, 1 trial of oseltamivir in children with asthma who had laboratory-confirmed influenza showed only a nonsignificant reduction in illness duration (10.4 hours; 8%; $P = .542$). Oseltamivir significantly reduced acute otitis media in children 1 through 5 years of age with laboratory-confirmed influenza (risk difference [RD], −0.14; 95% CI, −0.24 to −0.04).[89] Another Cochrane review of RCTs in adults and children, which included 20 oseltamivir (9623 participants) and 26 zanamivir trials (14 628 participants),[86] found no effect of oseltamivir in reducing the duration of illness in asthmatic children, but in otherwise healthy children, there was a reduction by a mean difference of 29 hours (95% CI, 12 to 47 hours; $P = .001$). No significant effect was observed with zanamivir. Regarding complications, this review did not find a significant effect of NAIs on reducing hospitalizations, pneumonia, bronchitis, otitis media, or sinusitis in children.[86] More recently, a meta-analysis of 5 new RCTs that included 1598 children with laboratory-confirmed influenza showed that treatment with oseltamivir significantly reduced the duration of illness in this population by 17.6 hours (95% CI, −34.7 to −0.62 hours).[87] When children with asthma were excluded, this difference was larger (−29.9 hours; 95% CI, −53.9 to −5.8 hours). The risk of otitis media was 34% lower in this group as well.

TABLE 4 Recommended Dosage and Schedule of Influenza Antiviral Medications for Treatment and Chemoprophylaxis in Children for the 2020–2021 Influenza Season: United States

Medication	Treatment (5 Days)	Chemoprophylaxis (10 Days)[a]
Oseltamivir[b]		
Adults	75 mg, twice daily	75 mg, once daily
Children ≥12 mo (based on body wt)		
≤15 kg (≤33 lb)	30 mg, twice daily	30 mg, once daily
>15 kg–23 kg (33 lb–51 lb)	45 mg, twice daily	45 mg, once daily
>23 kg–40 kg (>51 lb–88 lb)	60 mg, twice daily	60 mg, once daily
>40 kg (>88 lb)	75 mg, twice daily	75 mg, once daily
Infants 9–11 mo[c]	3.5 mg/kg per dose, twice daily	3.5 mg/kg per dose, once daily
Term infants 0–8 mo[c]	3 mg/kg per dose, twice daily	3 mg/kg per dose, once daily for infants 3–8 mo Not recommended for infants <3 mo old because of limited safety and efficacy data in this age group
Preterm infants[d]		
<38 wks' postmenstrual age	1.0 mg/kg per dose, twice daily	
38 through 40 wks' postmenstrual age	1.5 mg/kg per dose, twice daily	
>40 wks' postmenstrual age	3.0 mg/kg per dose, twice daily	
Zanamivir[e]		
Adults	10 mg (two 5-mg inhalations), twice daily	10 mg (two 5-mg inhalations), once daily
Children ≥7 y for treatment ≥5 y for chemoprophylaxis	10 mg (two 5-mg inhalations), twice daily	10 mg (two 5-mg inhalations), once daily
Peramivir		
Adults	One 600-mg intravenous infusion, given over 15–30 min	Not recommended
Children (2–12 y)	One 12 mg/kg dose, up to 600 mg maximum, via intravenous infusion for 15–30 min	Not recommended
Children (13–17 y)	One 600 mg dose, via intravenous infusion for 15–30 min	Not recommended
Baloxavir		
People ≥12 y who weigh more than 40 kg	40–80 kg: one 40-mg dose, orally ≥80 kg: one 80-mg dose, orally	Not recommended

Sources: 2018 IDSA Guidelines78 and https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm.

[a] CDC recommends for 7 days, and 10 days only if part of institutional outbreak (https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm).

[b] Oseltamivir is administered orally without regard to meals, although administration with meals may improve gastrointestinal tolerability. Oseltamivir is available as Tamiflu in 30-, 45-, and 75-mg capsules and as a powder for oral suspension that is reconstituted to provide a final concentration of 6 mg/mL. For the 6-mg/mL suspension, a 30-mg dose is given with 5 mL of oral suspension, a 45-mg dose is given with 7.5 mL oral suspension, a 60-mg dose is given with 10 mL oral suspension, and a 75-mg dose is given with 12.5 mL oral suspension. If the commercially manufactured oral suspension is not available, a suspension can be compounded by retail pharmacies (final concentration also 6 mg/mL), based on instructions contained in the package label. In patients with renal insufficiency, the dose should be adjusted on the basis of creatinine clearance. For treatment of patients with creatinine clearance 10–30 mL/min: 75 mg, once daily, for 5 days. For chemoprophylaxis of patients with creatinine clearance 10–30 mL/min: 30 mg, once daily, for 10 days after exposure or 75 mg, once every other day, for 10 days after exposure (5 doses). See https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm and IDSA Guidelines.[83]

[c] Approved by the FDA for children as young as 2 weeks of age. Given preliminary pharmacokinetic data and limited safety data, oseltamivir can be used to treat influenza in both term and preterm infants from birth because benefits of therapy are likely to outweigh possible risks of treatment. Of note, the CDC recommends a 3 mg/kg/dose, twice daily, for all infants <12 months old; the IDSA guidelines[83] include both AAP and CDC recommendations.

[d] Oseltamivir dosing for preterm infants. The weight-based dosing recommendation for preterm infants is lower than for term infants. Preterm infants may have lower clearance of oseltamivir because of immature renal function, and doses recommended for full-term infants may lead to very high drug concentrations in this age group. Limited data from the National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group provides the basis for dosing preterm infants using their postmenstrual age (gestational age + chronologic age). For extremely preterm infants (<28 wk), please consult a pediatric infectious disease physician.

[e] Zanamivir is administered by inhalation using a proprietary "Diskhaler" device distributed together with the medication. Zanamivir is a dry powder, not an aerosol, and should not be administered using nebulizers, ventilators, or other devices typically used for administering medications in aerosolized solutions. Zanamivir is not recommended for people with chronic respiratory diseases, such as asthma or chronic obstructive pulmonary disease, which increase the risk of bronchospasm.

Overall, efficacy outcomes are best demonstrated in patients with laboratory confirmed influenza. All these studies confirmed vomiting as an occasional adverse effect of oseltamivir, occurring in approximately 5% of treated patients. The balance between benefits and harms should be considered when making decisions about the use of NAIs for either treatment or chemoprophylaxis of influenza.

Although prospective comparative studies to determine the efficacy of influenza antiviral medications in hospitalized patients or pediatric patients with comorbidities have not been conducted, and prospectively collected data to determine the role of antiviral agents in treating severe influenza are limited, on the basis of information obtained from retrospective observational studies

and meta-analyses conducted to date in both adults and children, most experts support the use of antiviral medications as soon as possible to treat pediatric patients with severe influenza, including hospitalized patients.[88,90–94] An observational epidemiologic study conducted in adult patients hospitalized with severe laboratory-confirmed influenza in Spain over 6 influenza seasons (2010–2016) evaluated the effectiveness of NAIs, concluding that when started early after the onset of symptoms (≤48 hours or ≤5 days), NAI treatment was associated with a reduction in influenza-associated deaths (adjusted odds ratio [aOR], 0.37; 95% CI, 0.22 to 0.63; and aOR, 0.50; 95% CI, 0.32 to 0.79, respectively).[90] However, treatment initiation more than 5 days after the onset of influenza symptoms was not associated with reduction in mortality in hospitalized adults.

Importantly, and despite limited evidence from prospectively conducted trials, treatment with oseltamivir for children with serious, complicated, or progressive disease presumptively or definitively caused by influenza, irrespective of influenza vaccination status (the circulating strains may not be well matched with vaccine strains) or whether illness began greater than 48 hours before admission, is recommended by the AAP, CDC, Infectious Diseases Society of America (IDSA),[83] and Pediatric Infectious Diseases Society (PIDS). Earlier treatment provides better clinical responses. However, treatment after 48 hours of symptoms in adults and children with moderate to severe disease or with progressive disease has been shown to provide some benefit and should be offered.[95–97] In a retrospective study of 653 PICU admissions from 2009 to 2012, the estimated risk of death was reduced in NAI treated cases (OR 0.36, 95% CI: 0.16 to 0.83).[95] No additional benefit exists for double-dose NAI therapy on reduction of mortality or virologic clearance, compared with standard-dose therapy, on the basis of a recent systematic review and meta-analysis of 10 published studies[98] (4 RCT and 6 observational studies) involving 20 947 adult and pediatric patients.

Children younger than 2 years are at an increased risk of hospitalization and complications attributable to influenza. The FDA has approved oseltamivir for treatment of children as young as 2 weeks. Given preliminary pharmacokinetic data and limited safety data, the CDC and AAP support the use of oseltamivir to treat influenza in both term and preterm infants from birth, because benefits of therapy of neonatal influenza are likely to outweigh possible risks of treatment.

Oseltamivir is available in capsule and oral suspension formulations. The available capsule doses are 30, 45, and 75 mg, and the commercially manufactured liquid formulation has a concentration of 6 mg/mL in a 60-mL bottle. If the commercially manufactured oral suspension is not available, the capsule may be opened and the contents mixed with simple syrup or Ora-Sweet SF (sugar free) by retail pharmacies to a final concentration of 6 mg/mL.

In adverse event data collected systematically in prospective trials, vomiting was the only adverse effect reported more often with oseltamivir compared with placebo when studied in children 1 through 12 years of age (ie, 15% of treated children versus 9% receiving placebo). In addition, following reports from Japan of oseltamivir-attributable neuropsychiatric adverse effects, a review of controlled clinical trial data and ongoing surveillance has failed to establish a link between this drug and neurologic or psychiatric events.[99,100]

ANTIVIRAL TREATMENT AND INFLUENZA TESTING CONSIDERATIONS

Clinical judgment (on the basis of underlying conditions, disease severity, time since symptom onset, and local influenza activity) is an important factor in treatment decisions for pediatric patients who present with influenza-like illness. Antiviral treatment should be started as soon as possible after illness onset and should not be delayed while waiting for a definitive influenza test result, because early therapy provides the best outcomes. Influenza diagnostic tests vary by method, availability, processing time, sensitivity, and cost (Table 5), all of which should be considered in making the best clinical decision. Positive and negative predictive values of influenza test results are influenced by the level of influenza activity in the population being tested, the characteristics of a test compared with a gold standard, pretest probability, whether the influenza virus is actively replicating in the person, proper collection and transport of specimens, and proper test procedures. Testing should be performed when timely results will be available to influence clinical management or infection control measures. Given the similarities in clinical presentation, testing for influenza and for SARS-CoV-2 infection should be offered to patients with a febrile respiratory illness or influenza-like illness.

Although decisions on treatment and infection control can be made on the basis of positive rapid influenza diagnostic test (RIDT) results, negative results should not always be used in a similar fashion because of the suboptimal sensitivity and potential for false-negative results. An updated list of RIDTs is available at: https://www.cdc.gov/flu/professionals/diagnosis/table-ridt.html. Positive results of RIDTs are helpful, because they may reduce additional testing to identify

TABLE 5 Comparison of Types of Influenza Diagnostic Tests

Testing Category	Method	Influenza Viruses Detected	Distinguishes Influenza A Virus Subtypes	Time to Results	Performance
Rapid molecular assay	Nucleic acid amplification	Influenza A or B viral RNA	No	15–30 min	High sensitivity; high specificity
Rapid influenza diagnostic test	Antigen detection	Influenza A or B virus antigens	No	10–15 min	Low to moderate sensitivity (higher with analyzer devise); high specificity
Direct and indirect immunofluorescence assays	Antigen detection	Influenza A or B virus antigens	No	1–4 h	Moderate sensitivity; high specificity
Molecular assays (including RT-PCR)	Nucleic acid amplification	Influenza A or B viral RNA	Yes, if subtype primers are used	1–8 h	High sensitivity; high specificity
Multiplex molecular assays	Nucleic acid amplification	Influenza A or B viral RNA, other viral or bacterial targets (RNA or DNA)	Yes, if subtype primers are used	1–2 h	High sensitivity; high specificity
Rapid cell culture (shell vial and cell mixtures)	Virus isolation	Influenza A or B virus	Yes	1–3 d	High sensitivity; high specificity
Viral culture (tissue cell culture)	Virus isolation	Influenza A or B virus	Yes	3–10 d	High sensitivity; high specificity

Negative results may not rule out influenza. Respiratory tract specimens should be collected as close to illness onset as possible for testing. Clinicians should consult the manufacturer's package insert for the specific test for the approved respiratory specimen(s). Specificities are generally high (>95%) for all tests compared with reverse transcriptase-polymerase chain reaction (RT-PCR). FDA-cleared rapid influenza diagnostic tests are CLIA-waived; most FDA-cleared rapid influenza molecular assays are CLIA-waived, depending on the specimen. Source: Uyeki.[83]

alternative causes of the child's influenza-like illness, provide the opportunity for early antiviral treatment, promote appropriate antimicrobial stewardship, and allow the timely implementation of appropriate strategies to prevent transmission. Available FDA-approved rapid molecular assays based on nucleic acid detection are highly sensitive and specific diagnostic tests that can provide rapid results. An updated list of these tests is available here: https://www.cdc.gov/flu/professionals/diagnosis/table-nucleic-acid-detection.html. Molecular assays are preferred in hospitalized patients, because they are more sensitive compared with antigen detection. Early detection, prompt antiviral treatment, and infection control interventions can lead to improved individual patient outcomes and allow for effective cohorting and disease containment. This containment strategy is particularly relevant during the SARS-CoV-2 pandemic.

People with suspected influenza who are at higher risk of influenza complications should be offered treatment with antiviral medications (Table 2). Efforts should be made to minimize treatment of patients who are not infected with influenza. Otherwise healthy children who have suspected influenza with an uncomplicated presentation should be considered for antiviral medication, particularly if they are in contact with other children who either are younger than 6 months (as they are not able to receive influenza vaccine) or have high-risk conditions (including age <5 years) that predispose them to complications of influenza, when influenza viruses are known to be circulating in the community. If there is a local shortage of antiviral medications, local public health authorities should be consulted to provide additional guidance about testing and treatment. In previous years, local shortages of oseltamivir suspension have occurred because of uneven drug distribution, although national shortages have not occurred since 2009, particularly given the availability of the capsule formulation that can be made into a suspension for young children if needed (Table 4).

INFLUENZA CHEMOPROPHYLAXIS

Randomized placebo-controlled studies showed that oral oseltamivir and inhaled zanamivir were efficacious when administered as chemoprophylaxis to household contacts after a family member had laboratory-confirmed influenza.[83] There are no data on IV peramivir or oral baloxavir for chemoprophylaxis. Decisions on whether to administer antiviral chemoprophylaxis should take into account the exposed person's risk of influenza complications, vaccination status, the type and duration of contact, recommendations from local or public health authorities, and clinical judgment. Optimally, postexposure chemoprophylaxis should only be used when antiviral agents can be started within 48 hours of exposure; the lower once-daily dosing for chemoprophylaxis with oral oseltamivir or inhaled zanamivir should not be used for treatment of children symptomatic with influenza. Early, full treatment doses (rather than chemoprophylaxis doses) should be used in high-risk symptomatic patients without waiting for laboratory confirmation.

Chemoprophylaxis should not be considered a substitute for vaccination. Influenza vaccine should always be offered before and throughout the influenza season when not contraindicated. Antiviral medications are important adjuncts to influenza vaccination for control and prevention of influenza disease. Toxicities may be associated with antiviral agents, and indiscriminate use might limit availability. Pediatricians should inform recipients of antiviral chemoprophylaxis that risk of influenza is lowered but still remains while taking the medication, and susceptibility to influenza returns when medication is discontinued. Oseltamivir use is not a contraindication to vaccination with IIV, although LAIV effectiveness will be decreased for the child receiving oseltamivir.[83] No data are available on the impact of inhaled zanamivir, IV peramivir or oral baloxavir on effectiveness of LAIV, but it is likely that all antiviral agents will have some impact on effectiveness of LAIV. Among some high-risk people, both vaccination with IIV and antiviral chemoprophylaxis may be considered. Updates will be available at www.aapredbook.org/flu and www.cdc.gov/flu/professionals/antivirals/index.htm.

ANTIVIRAL RESISTANCE

Antiviral resistance to any drug can emerge, necessitating continuous population-based assessment that is conducted by the CDC. During the 2019–2020 season, >99% of influenza A(/H1N1)pdm09 and B/Victoria viruses tested were susceptible to oseltamivir, peramivir, and zanamivir, and all were susceptible to baloxavir. All tested influenza A(H3N2) and B/Yamagata viruses were susceptible to these antiviral agents. Decreased susceptibility to baloxavir has been reported in Japan, where utilization has been more common,[101–105] and surveillance for resistance among circulating influenza viruses is ongoing in Japan and the United States.[106–108] In contrast, high levels of resistance to amantadine and rimantadine persist among the influenza A viruses currently circulating. Adamantane medications are not recommended for use against influenza unless resistance patterns change.[83]

Viral surveillance and resistance data from the CDC and WHO indicate that the majority of currently circulating influenza viruses likely to cause influenza in North America during the 2020–2021 influenza season continue to be susceptible to oseltamivir, zanamivir, peramivir, and baloxavir (https://www.cdc.gov/flu/weekly/). If a newly emergent oseltamivir- or peramivir-resistant virus is a concern, recommendations for alternative treatment will be available from the CDC and AAP. Resistance characteristics can change for an individual patient over the duration of a treatment course, especially in those who are severely immunocompromised. Up-to-date information on current recommendations and therapeutic options can be found on the AAP Web site (www.aap.org or www.aapredbook.org/flu), through state-specific AAP chapter websites, or on the CDC Web site (www.cdc.gov/flu/).

INFLUENZA ANTIVIRALS RECOMMENDATIONS

Treatment recommendations for antiviral medications for the 2020–2021 influenza season are applicable to infants and children with suspected influenza when influenza viruses are known to be circulating in the community, or when infants or children are tested and confirmed to have influenza. Continuous monitoring of the epidemiology, change in severity, and resistance patterns of influenza virus strains by CDC may lead to new guidance. Oseltamivir (oral), zanamivir (inhaled), peramivir (IV), and baloxavir (oral) are FDA-approved for treatment of uncomplicated influenza virus infection in pediatric outpatients; published data exist to support the use of oseltamivir (oral) for hospitalized and children at high risk. For more serious influenza virus infections, particularly in immune compromised children, seeking the advice of an infectious diseases specialist is suggested.

ANTIVIRAL TREATMENT RECOMMENDATIONS

Regardless of influenza vaccination status, antiviral treatment should be offered as early as possible to:

- Any hospitalized child with suspected or confirmed influenza disease, regardless of duration of symptoms.
- Any child, inpatient or outpatient, with severe, complicated, or progressive illness attributable to influenza, regardless of duration of symptoms.
- Influenza virus infection of any severity in children at high risk of complications of influenza, as listed in Table 2, regardless of duration of symptoms.

Antiviral treatment may be considered for the following individuals:

- Any previously healthy, symptomatic outpatient not at high risk for influenza complications in whom an influenza diagnosis is confirmed or suspected on the basis of clinical judgment, if treatment can be initiated within 48 hours of illness onset.
- Children with suspected or confirmed influenza disease whose siblings or household contacts either are younger than 6 months or have a high-risk condition that predisposes them

to complications of influenza as listed in Table 2.

Shared informed decision making between providers and parents/legally authorized caregivers is encouraged to initiate therapy and monitor children for safety and efficacy while receiving antiviral agents. Efforts should be made to minimize treatment of patients who are not infected with influenza viruses.

ANTIVIRAL CHEMOPROPHYLAXIS RECOMMENDATIONS

Although vaccination is the preferred approach to prevention of infection, chemoprophylaxis during an influenza season is recommended in the following situations:

- For children at high risk of complications from influenza for whom influenza vaccine is contraindicated.
- For children at high risk during the 2 weeks after IIV influenza vaccination, before optimal immunity is achieved. Prophylaxis after LAIV may decrease vaccine efficacy.
- For family members or HCP who are unvaccinated and are likely to have ongoing, close exposure to:
  - unvaccinated children at high risk; or
  - unvaccinated infants and toddlers who are younger than 24 months.
- For control of influenza outbreaks for unvaccinated staff and children in a closed institutional setting with children at high risk (eg, extended-care facilities).
- As a supplement to IIV vaccination among children at high risk, including children who are immunocompromised and may not respond with sufficient protective immune responses following influenza vaccination.
- As postexposure antiviral chemoprophylaxis for family members and close contacts of an infected person if those people are at high risk of complications from influenza.
- For children at high risk of complications and their family members and close contacts, as well as for HCP, when circulating strains of influenza virus in the community are not well matched by seasonal influenza vaccine virus strains, on the basis of current data from the CDC and state or local health departments.

These recommendations apply to routine circumstances, but it should be noted that guidance may change on the basis of updated recommendations from the CDC in concert with antiviral availability, local resources, clinical judgment, recommendations from local or public health authorities, risk of influenza complications, type and duration of exposure contact, and change in epidemiology (resistance, antigenic shift) or severity of influenza. Children who have higher rates of influenza complications, including American Indian/Alaska Native children, should be prioritized to receive influenza antiviral agents in the setting of a shortage according to local public health guidelines (Table 2). Chemoprophylaxis is not routinely recommended for infants younger than 3 months given limited safety and efficacy data in this age group.

FUTURE DIRECTIONS

Safety and effectiveness data for influenza vaccines used during the 2020–2021 influenza season will be analyzed as they become available and reported by CDC as they are each season. Continued evaluation of the safety, immunogenicity, and effectiveness of influenza vaccines, especially for at risk populations, is important. The duration of protection, the potential role of previous influenza vaccination on overall vaccine effectiveness, and vaccine effectiveness by vaccine formulation, virus strain, timing of vaccination, and subject age and health status, in preventing outpatient medical visits, hospitalizations, and deaths continue to be evaluated. For the 2020–2021 influenza season, it will be particularly important to understand the effect of SARS-CoV-2 and influenza virus cocirculation on the epidemiology and morbidity of influenza in the pediatric population. Understanding how to better educate parents about influenza symptoms and how to recognize when to seek medical attention would be informative. Additionally, with limited data on the use of antiviral agents in hospitalized children and in children with underlying medical conditions, prospective clinical trials to inform optimal timing and efficacy of antiviral treatment in these populations are warranted. This is particularly relevant as new antiviral agents or new indications for existing antiviral agents become available. At this time, the FDA has accepted supplemental new drug applications for baloxavir marboxil. One application concerns the treatment of acute, uncomplicated influenza in pediatric patients from 1 year of age through 12 years of age. Another application addresses the use of baloxavir marboxil for postexposure prophylaxis (https://www.biospace.com/article/releases/fda-accepts-genentech-s-new-drug-application-for-xofluza-for-the-treatment-of-influenza-in-children-/).

There is also a need for more systematic health services research on influenza vaccine uptake and refusal as well as identification of methods to enhance uptake. Further investigation is needed about vaccine acceptance and hesitancy and methods to overcome parental concerns and improve coverage. This may include evaluating the strategy of

offering to immunize parents and adult child care providers in the pediatric office setting and understanding the level of family contact satisfaction with this approach; how practices handle the logistic, liability, legal, and financial barriers that limit or complicate this service; and most importantly, how this practice may affect disease rates in children and adults. Furthermore, ongoing efforts should include broader implementation and evaluation of mandatory HCP vaccination programs in both inpatient and outpatient settings.

Efforts should be made to create adequate outreach (eg, mobile integrated health care) and infrastructure to facilitate the optimal distribution of vaccine so that more people are immunized. Given the experience with COVID-19, pediatricians should become more involved in pandemic preparedness and disaster planning efforts. A bidirectional partner dialogue between pediatricians and public health decision makers assists efforts to address children's issues during the initial state, regional, and local plan development stages. Additional information can be found at www.aap.org/disasters/resourcekit and https://pediatrics.aappublications.org/content/pediatrics/early/2017/05/11/peds.2016-3690.full.pdf.

Access to care issues, lack of immunization records, and questions regarding who can provide consent may be addressed by linking children (eg, those in foster care/juvenile justice system or refugee, immigrant, or homeless children) with a medical home, using all health care encounters as vaccination opportunities, and more consistently using immunization registry data.

Development efforts continue for universal influenza vaccines that induce broader protection and eliminate the need for annual vaccination. Understanding the establishment of immunity against influenza in early life and the development of a safe, immunogenic vaccine for infants younger than 6 months are essential. Studies on the effectiveness and safety of influenza vaccines containing adjuvants that enhance immune responses to influenza vaccines or that use novel routes of administration are needed. Efforts to improve the vaccine development process to allow for a shorter interval between identification of vaccine strains and vaccine production continue. New antiviral drugs are in various development phases, given the need to improve options for the treatment and chemoprophylaxis of influenza.

Pediatricians can remain informed of advances and other updates during the influenza season by following the CDC Influenza page (www.cdc/gov/flu) and the AAP *Red Book Online* Influenza Resource Page (www.aapredbook.org/flu).

SUMMARY OF RECOMMENDATIONS

1. The AAP recommends annual influenza vaccination for everyone 6 months and older, including children and adolescents, during the 2020–2021 influenza season.
2. For the 2020–2021 influenza season, the AAP recommends that any licensed influenza vaccine appropriate for age and health status can be used for influenza vaccination in children. Inactivated influenza vaccine (IIV) and live attenuated vaccine (LAIV) are options for children for whom these vaccines are appropriate. This recommendation is based on review of current available data on LAIV and IIV vaccine efficacy (VE). The AAP will continue to review VE data as they become available and update these recommendations if necessary.
3. The AAP does not have a preference for any influenza vaccine product over another for children who have no contraindication to influenza vaccination and for whom more than one licensed product appropriate for age and health status is available. Pediatricians should administer whichever formulation is available in their communities to achieve the highest possible coverage this influenza season.
4. Children 6 through 35 months of age may receive any licensed, age-appropriate IIV available this season, at the dose indicated for the vaccine. No product is preferred over another for this age group. Children 36 months (3 years) and older should receive a 0.5-mL dose of any available, licensed, age-appropriate inactivated vaccine.
5. The number of seasonal influenza vaccine doses recommended to be administered to children in the 2020–2021 influenza season remains unchanged and depends on the child's age at the time of the first administered dose and vaccine history (Fig 2).
6. Children 6 months through 8 years of age who are receiving influenza vaccine for the first time or who have received only 1 dose, before July 1, 2020, or whose vaccination status is unknown, should receive 2 doses of influenza vaccine, ideally by the end of October, and vaccines should be offered as soon as they become available. Children needing only 1 dose of influenza vaccine, regardless of age, should also receive vaccination, ideally by the end of October.
7. Efforts should be made to ensure vaccination for children in high-risk groups (Table 2) and their contacts, unless contraindicated.

8. Product-specific contraindications must be considered when selecting the type of vaccine to administer. Children who have had an allergic reaction after a previous dose of any influenza vaccine should be evaluated by an allergist to determine whether future receipt of the vaccine is appropriate.
9. Children with egg allergy can receive influenza vaccine without any additional precautions beyond those recommended for all vaccines.
10. Pregnant women may receive inactivated influenza vaccine at any time during pregnancy, to protect themselves and their infants, who benefit from the transplacental transfer of antibodies. Women in the postpartum period who did not receive vaccination during pregnancy should be encouraged to receive influenza vaccine before discharge from the hospital. Influenza vaccination during breastfeeding is safe for mothers and their infants.
11. The AAP supports mandatory vaccination of health care personnel as a crucial element in preventing influenza and reducing health care-associated influenza infections, because health care personnel often care for individuals at high risk for influenza-related complications.
12. Antiviral medications are important in the control of influenza but are not a substitute for influenza vaccination. Pediatricians should promptly identify their patients suspected of having influenza infection for timely initiation of antiviral treatment, when indicated and based on shared decision making between the pediatrician and child's caregiver, to reduce morbidity and mortality. Although best results are observed when the child is treated within 48 hours of symptom onset, antiviral therapy should still be considered beyond 48 hours of symptom onset in children with severe disease or those at high risk of complications.
13. Antiviral treatment should be offered as early as possible to the following individuals, regardless of influenza vaccination status:
    - Any hospitalized child with suspected or confirmed influenza disease, regardless of duration of symptoms.
    - Any child, inpatient or outpatient, with severe, complicated, or progressive illness attributable to influenza, regardless of duration of symptoms.
    - Influenza infection of any severity in children at high risk of complications of influenza infection (Table 2), regardless of duration of symptoms.
14. Treatment may be considered for the following individuals:
    - Any previously healthy, symptomatic outpatient not at high risk for influenza complications in whom influenza is confirmed or suspected on the basis of clinical judgment, if treatment can be initiated within 48 hours of illness onset.
    - Children with suspected or confirmed influenza disease whose siblings or household contacts either are younger than 6 months or have a high-risk condition that predisposes them to complications of influenza (Table 2).
15. Antiviral chemoprophylaxis is recommended after known or suspected exposure influenza in the following situations:
    - For children at high risk of complications from influenza for whom influenza vaccine is contraindicated.
    - For children at high risk during the 2 weeks after influenza vaccination, before optimal immunity is achieved.
    - For family members or HCP who are unvaccinated and are likely to have ongoing, close exposure to:
        - unvaccinated children at high risk; or
        - unvaccinated infants and toddlers who are younger than 24 months.
    - For control of influenza outbreaks for unvaccinated staff and children in a closed institutional setting with children at high risk (eg, extended-care facilities).
    - As a supplement to vaccination among children at high risk, including children who are immunocompromised and may not respond with sufficient protective immune responses following influenza vaccination.
    - As postexposure antiviral chemoprophylaxis for family members and close contacts of an infected person if those people are at high risk of complications from influenza.
    - For children at high risk of complications and their family members and close contacts, as well as HCP, when circulating strains of influenza virus in the community are not well matched by seasonal influenza vaccine virus strains, on the basis of current data from the CDC and state or local health departments.

ADDITIONAL RESOURCES

Lessin HR; Edwards KM; American Academy of Pediatrics, 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(1):e247.

American Academy of Pediatrics, Committee on Infectious Diseases. Policy statement: Influenza immunization for all health care personnel: keep it mandatory. *Pediatrics.* 2015;136(4):809-818.

American Academy of Pediatrics, Committee on Pediatric Emergency Medicine. Preparation for emergencies in the offices of pediatricians and pediatric primary care providers. *Pediatrics.* 2007;120(1):200-212. Reaffirmed June 2011.

American Academy of Pediatrics, Committee on Practice and Ambulatory Medicine, AAP Committee on Infectious Diseases, AAP Committee on State Government Affairs, AAP Council on School Health, AAP Section on Administration and Practice Management. Medical Versus Nonmedical Immunization Exemptions for Child Care and School Attendance. *Pediatrics.* 2016;138(3):e20162145.

Edwards KM, Hackell JM; American Academy of Pediatrics, Committee on Infectious Diseases, Committee on Practice and Ambulatory Medicine. Countering vaccine hesitancy. *Pediatrics.* 2016;138(3):e20162146.

American Academy of Pediatrics, Committee on Pediatric Emergency Medicine; American Academy of Pediatrics Committee on Medical Liability; Task Force on Terrorism. The pediatrician and disaster preparedness. *Pediatrics.* 2006; 117(2):560-565. Reaffirmed September 2013.

American Academy of Pediatrics. Influenza. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2018 Report of the Committee on Infectious Diseases.* 31st ed. Elk Grove Village, IL: American Academy of Pediatrics; 2018: 476–489. Available at: http://aapredbook.aappublications.org/flu.

ABBREVIATIONS

AAP: American Academy of Pediatrics
WHO: World Health Organization
ACIP: Advisory Committee on Immunization Practices
ANE: acute necrotizing encephalopathy
ccIIV4: quadrivalent cell culture-based inactivated influenza vaccine
CDC: Centers for Disease Control and Prevention
FDA: US Food and Drug Administration
GBS: Guillain-Barré syndrome
HA: hemagglutinin
HCP: health care personnel
IAE: influenza-associated encephalopathy
IIV: inactivated influenza vaccine
IIV3: trivalent inactivated influenza vaccine
IIV4: quadrivalent inactivated influenza vaccine
IM: intramuscular
LAIV4: quadrivalent live attenuated influenza vaccine
NAIs: neuraminidase inhibitors
PCR: polymerase chain reaction
PCV13: 13-valent pneumococcal conjugate vaccine
RIV4: quadrivalent recombinant influenza vaccine
SARS-CoV-2: severe acute respiratory syndrome-coronavirus 2
VE: vaccine effectiveness

REFERENCES

1. Grohskopf LA, Alyanak E, Broder KR, et al. Prevention and control of seasonal influenza with vaccines:

recommendations of the Advisory Committee on Immunization Practices, United States, 2020–21 influenza season. *MMWR Recomm Rep*. 2020; 69(RR-8):1–24

2. Shope TR, Walker BH, Aird LD, Southward L, McCown JS, Martin JM. Pandemic influenza preparedness among child care center directors in 2008 and 2016. *Pediatrics*. 2017;139(6):e20163690
3. Garten R, Blanton L, Elal AIA, et al. Update: influenza activity in the United States during the 2017–18 season and composition of the 2018–19 influenza vaccine. *MMWR Morb Mortal Wkly Rep*. 2018;67(22):634–642
4. Centers for Disease Control and Prevention. Vaccine effectiveness tables for 2017-18 season. Available at: https://www.cdc.gov/flu/vaccines-work/2017-2018.html. Accessed May 31, 2019
5. Biggerstaff M, Kniss K, Jernigan DB, et al. Systematic assessment of multiple routine and near real-time indicators to classify the severity of influenza seasons and pandemic in the United States, 2003-2004 through 2015-2016. *Am J Epidemiol*. 2018;187(5):1040–1050
6. Dawood FS, Chung JR, Kim SS, et al. Interim estimates of 2019-20 seasonal influenza vaccine effectiveness–United States, February 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(7):177–182
7. Xu X, Blanton L, Elal AIA, et al. Update: influenza activity in the United States during the 2018-19 season and composition of the 2019-20 influenza vaccine. *MMWR Morb Mortal Wkly Rep*. 2019;68(24):544–551
8. Centers for Disease Control and Prevention. Weekly US influenza surveillance report (FluView). Available at: https://www.cdc.gov/flu/weekly/. Accessed May 31, 2020
9. Centers for Disease Control and Prevention. Flu vaccination coverage, United States, 2018–19 influenza season. Available at: https://www.cdc.gov/flu/fluvaxview/coverage-1819estimates.htm. Accessed May 4, 2020
10. Centers for Disease Control and Prevention. COVIDView: a weekly surveillance study of U.S. COVID-19 activity. Available at: https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview.html. Accessed May 4, 2020
11. Wang X, Li Y, O'Brien KL, et al; Respiratory Virus Global Epidemiology Network. Global burden of respiratory infections associated with seasonal influenza in children under 5 years in 2018: a systematic review and modelling study. *Lancet Glob Health*. 2020;8(4):e497–e510
12. Miyakawa R, Barreto NB, Kato RM, Neely MN, Russell CJ. Early use of anti-influenza medications in hospitalized children with tracheostomy. *Pediatrics*. 2019;143(3):e20182608
13. Centers for Disease Control and Prevention (CDC). Deaths related to 2009 pandemic influenza A (H1N1) among American Indian/Alaska Natives - 12 states, 2009. *MMWR Morb Mortal Wkly Rep*. 2009;58(48):1341–1344
14. Dee DL, Bensyl DM, Gindler J, et al. Racial and ethnic disparities in hospitalizations and deaths associated with 2009 pandemic Influenza A (H1N1) virus infections in the United States. *Ann Epidemiol*. 2011;21(8):623–630
15. Gounder PP, Callinan LS, Holman RC, et al. Influenza hospitalizations among american indian/alaska native people and in the United States general population. *Open Forum Infect Dis*. 2014;1(1):ofu031
16. Hennessy TW, Bruden D, Castrodale L, et al; Investigative Team. A case-control study of risk factors for death from 2009 pandemic influenza A(H1N1): is American Indian racial status an independent risk factor? *Epidemiol Infect*. 2016;144(2):315–324
17. Feldstein LR, Ogokeh C, Rha B, et al. Vaccine effectiveness against influenza hospitalization among children in the United States, 2015-2016 [published online ahead of print February 28, 2020]. *J Pediatr Infect Dis Soc*. doi: 10.1093/jpids/piaa017
18. Segaloff HE, Leventer-Roberts M, Riesel D, et al. Influenza vaccine effectiveness against hospitalization in fully and partially vaccinated children in Israel: 2015-2016, 2016-2017, and 2017-2018. *Clin Infect Dis*. 2019;69(12):2153–2161
19. Blyth CC, Cheng AC, Crawford NW, et al; Paediatric Active Enhanced Disease Surveillance (PAEDS), Influenza Complications Alert Network (FluCAN) Collaboration. The impact of new universal child influenza programs in Australia: vaccine coverage, effectiveness and disease epidemiology in hospitalised children in 2018. *Vaccine*. 2020;38(13):2779–2787
20. Pebody RG, Zhao H, Whitaker HJ, et al. Effectiveness of influenza vaccine in children in preventing influenza associated hospitalisation, 2018/19, England. *Vaccine*. 2020;38(2):158–164
21. Kalligeros M, Shehadeh F, Mylona EK, et al. Influenza vaccine effectiveness against influenza-associated hospitalization in children: a systematic review and meta-analysis. *Vaccine*. 2020;38(14):2893–2903
22. Chung JR, Rolfes MA, Flannery B, et al. Effects of influenza vaccination in the United States during the 2018-2019 influenza season [published online ahead of print January 6, 2020]. *Clin Infect Dis*. doi: 10.1093/cid/ciz1244
23. Flannery B, Reynolds SB, Blanton L, et al. Influenza vaccine effectiveness against pediatric deaths: 2010-2014. *Pediatrics*. 2017;139(5):e20164244
24. Ferdinands JM, Olsho LE, Agan AA, et al; Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network. Effectiveness of influenza vaccine against life-threatening RT-PCR-confirmed influenza illness in US children, 2010-2012. *J Infect Dis*. 2014;210(5):674–683
25. Tran D, Vaudry W, Moore D, et al; members of the Canadian Immunization Monitoring Program Active. Hospitalization for influenza A versus B. *Pediatrics*. 2016;138(3):e20154643
26. World Health Organization. Recommended composition of influenza virus vaccine for use in the 2019-2020 northern hemisphere influenza season. Available at: https://www.who.int/influenza/vaccines/virus/recommendations/2019_20_north/en/. Accessed March 21, 2019
27. Vesikari T, Kirstein J, Devota Go G, et al. Efficacy, immunogenicity, and safety evaluation of an MF59-adjuvanted quadrivalent influenza virus vaccine compared with non-adjuvanted influenza vaccine in children: a multicentre, randomised controlled, observer-blinded, phase 3 trial. *Lancet Respir Med*. 2018;6(5):345–356
28. US Food and Drug Administration. Fluzone quadrivalent. 2018. Available at: https://www.fda.gov/vaccines-blood-

biologics/vaccines/fluzone-quadrivalent. Accessed June 24, 2019

29. Robertson CA, Mercer M, Selmani A, Klein NP, Jeanfreau R, Greenberg DP. Safety and immunogenicity of a full-dose, split-virion, inactivated, quadrivalent influenza vaccine in healthy children 6-35 months of age: a randomized controlled clinical trial. *Pediatr Infect Dis J*. 2019;38(3):323–328
30. Halasa NB, Gerber MA, Berry AA, et al. Safety and immunogenicity of full-dose trivalent inactivated influenza vaccine (TIV) compared with half-dose TIV administered to children 6 through 35 months of age. *J Pediatric Infect Dis Soc*. 2015;4(3):214–224
31. Claeys C, Zaman K, Dbaibo G, et al; Flu4VEC Study Group. Prevention of vaccine-matched and mismatched influenza in children aged 6-35 months: a multinational randomised trial across five influenza seasons. *Lancet Child Adolesc Health*. 2018;2(5):338–349
32. Jain VK, Domachowske JB, Wang L, et al. Time to change dosing of inactivated quadrivalent influenza vaccine in young children: evidence from a phase III, randomized, controlled trial. *J Pediatric Infect Dis Soc*. 2017;6(1):9–19
33. US Food and Drug Administration. Afluria quadrivalent. 2018. Available at: https://www.fda.gov/vaccines-blood-biologics/vaccines/afluria-quadrivalent. Accessed June 24, 2019
34. Duffy J, Weintraub E, Hambidge SJ, et al; Vaccine Safety Datalink. Febrile seizure risk after vaccination in children 6 to 23 months. *Pediatrics*. 2016;138(1): e20160320
35. Thompson CA. Vaccine safety signal from spontaneous system not supported by active surveillance. *Am J Health Syst Pharm*. 2014;71(17): 1432–1433
36. Sentinel. Influenza vaccines and febrile seizures in the 2013-2014 and 2014-2015 influenza seasons. 2017. Available at: https://www.sentinelinitiative.org/sites/default/files/vaccines-blood-biologics/assessments/Influenza-Vaccines-Febrile-Seizures-Final-Report.pdf. Accessed June 24, 2019
37. Baker MA, Jankosky C, Yih WK, et al. The risk of febrile seizures following influenza and 13-valent pneumococcal conjugate vaccines. *Vaccine*. 2020;38(9): 2166–2171
38. Walter EB, Klein NP, Wodi AP, et al. Fever after influenza, diphtheria-tetanus-acellular pertussis, and pneumococcal vaccinations. *Pediatrics*. 2020;145(3): e20191909
39. Global advisory committee on vaccine safety, June 202. *Wkly Epidemiol Rec*. 2012;87(30):277–288
40. Grohskopf LA, Sokolow LZ, Fry AM, Walter EB, Jernigan DB. Update: ACIP recommendations for the use of quadrivalent live attenuated influenza vaccine (LAIV4) - United States, 2018-19 influenza season. *MMWR Morb Mortal Wkly Rep*. 2018;67(22):643–645
41. Mallory RM, Nyborg A, Kalyani RN, Yuan Y, Block SL, Dubovsky F. A study to evaluate the immunogenicity and shedding of live attenuated influenza vaccine strains in children 24-<48 months of age. *Vaccine*. 2020;38(5): 1001–1008
42. Pebody RG, Whitaker H, Ellis J, et al. End of season influenza vaccine effectiveness in primary care in adults and children in the United Kingdom in 2018/19. *Vaccine*. 2020;38(3):489–497
43. Centers for Disease Control and Prevention. US flu VE data for 2018-2019. Available at: https://www.cdc.gov/flu/vaccines-work/2018-2019.html. Accessed May 4, 2020
44. Nordin JD, Vazquez-Benitez G, Olsen A, Kuckler LC, Gao AY, Kharbanda EO. Safety of guidelines recommending live attenuated influenza vaccine for routine use in children and adolescents with asthma. *Vaccine*. 2019;37(30):4055–4060
45. Turner PJ, Fleming L, Saglani S, Southern J, Andrews NJ, Miller E; SNIFFLE-4 Study Investigators. Safety of live attenuated influenza vaccine (LAIV) in children with moderate to severe asthma. *J Allergy Clin Immunol*. 2020; 145(4):1157–1164.e6
46. Kelso JM, Greenhawt MJ, Li JT; Joint Task Force on Practice Parameters (JTFPP). Update on influenza vaccination of egg allergic patients. *Ann Allergy Asthma Immunol*. 2013;111(4): 301–302
47. Greenhawt M, Turner PJ, Kelso JM. Administration of influenza vaccines to egg allergic recipients: a practice parameter update 2017. *Ann Allergy Asthma Immunol*. 2018;120(1):49–52
48. American College of Obstetricians and Gynecologists. ACOG committee opinion No. 732: influenza vaccination during pregnancy. *Obstet Gynecol*. 2018;131(4): e109–e114
49. Robison SG, Osborn AW. The concordance of parent and child immunization. *Pediatrics*. 2017;139(5): e20162883
50. Zaman K, Roy E, Arifeen SE, et al. Effectiveness of maternal influenza immunization in mothers and infants. *N Engl J Med*. 2008;359(15):1555–1564
51. Tapia MD, Sow SO, Tamboura B, et al. Maternal immunisation with trivalent inactivated influenza vaccine for prevention of influenza in infants in Mali: a prospective, active-controlled, observer-blind, randomised phase 4 trial. *Lancet Infect Dis*. 2016;16(9): 1026–1035
52. Madhi SA, Cutland CL, Kuwanda L, et al; Maternal Flu Trial (Matflu) Team. Influenza vaccination of pregnant women and protection of their infants. *N Engl J Med*. 2014;371(10):918–931
53. Steinhoff MC, Katz J, Englund JA, et al. Year-round influenza immunisation during pregnancy in Nepal: a phase 4, randomised, placebo-controlled trial. *Lancet Infect Dis*. 2017;17(9):981–989
54. Shakib JH, Korgenski K, Presson AP, et al. Influenza in infants born to women vaccinated during pregnancy. *Pediatrics*. 2016;137(6):e20152360
55. Nunes MC, Madhi SA. Influenza vaccination during pregnancy for prevention of influenza confirmed illness in the infants: a systematic review and meta-analysis. *Hum Vaccin Immunother*. 2018;14(3):758–766
56. Thompson MG, Kwong JC, Regan AK, et al; PREVENT Workgroup. Influenza vaccine effectiveness in preventing influenza-associated hospitalizations during pregnancy: a multi-country retrospective test negative design study, 2010-2016. *Clin Infect Dis*. 2019; 68(9):1444–1453
57. Nunes MC, Madhi SA. Prevention of influenza-related illness in young infants by maternal vaccination during pregnancy. *F1000 Res*. 2018;7:122

58. Omer SB, Clark DR, Aqil AR, et al; BMGF Supported Maternal Influenza Immunization Trials Investigators Group. Maternal influenza immunization and prevention of severe clinical pneumonia in young infants: analysis of randomized controlled trials conducted in Nepal, Mali and South Africa. *Pediatr Infect Dis J*. 2018;37(5): 436–440

59. Munoz FM, Jackson LA, Swamy GK, et al. Safety and immunogenicity of seasonal trivalent inactivated influenza vaccines in pregnant women. *Vaccine*. 2018; 36(52):8054–8061

60. Sheffield JS, Greer LG, Rogers VL, et al. Effect of influenza vaccination in the first trimester of pregnancy. *Obstet Gynecol*. 2012;120(3):532–537

61. Polyzos KA, Konstantelias AA, Pitsa CE, Falagas ME. Maternal influenza vaccination and risk for congenital malformations: a systematic review and meta-analysis. *Obstet Gynecol*. 2015; 126(5):1075–1084

62. Chambers CD, Johnson D, Xu R, et al; OTIS Collaborative Research Group. Risks and safety of pandemic H1N1 influenza vaccine in pregnancy: birth defects, spontaneous abortion, preterm delivery, and small for gestational age infants. *Vaccine*. 2013;31(44):5026–5032

63. Nordin JD, Kharbanda EO, Vazquez Benitez G, Lipkind H, Vellozzi C, Destefano F; Vaccine Safety Datalink. Maternal influenza vaccine and risks for preterm or small for gestational age birth. *J Pediatr*. 2014;164(5): 1051–1057.e2

64. Chambers CD, Johnson DL, Xu R, et al; OTIS Collaborative Research Group. Safety of the 2010-11, 2011-12, 2012-13, and 2013-14 seasonal influenza vaccines in pregnancy: birth defects, spontaneous abortion, preterm delivery, and small for gestational age infants, a study from the cohort arm of VAMPSS. *Vaccine*. 2016;34(37): 4443–4449

65. Donahue JG, Kieke BA, King JP, et al. Association of spontaneous abortion with receipt of inactivated influenza vaccine containing H1N1pdm09 in 2010-11 and 2011-12. *Vaccine*. 2017;35(40): 5314–5322

66. Donahue J. Inactivated influenza vaccine and spontaneous abortion in the Vaccine Safety Datalink in 2012-13, 2013-14, and 2014-15. *Vaccine*. 2019; 37(44):6673–6681

67. Schlaudecker EP, Steinhoff MC, Omer SB, et al. IgA and neutralizing antibodies to influenza a virus in human milk: a randomized trial of antenatal influenza immunization. *PLoS One*. 2013;8(8):e70867

68. Bradley JS, Blumer JL, Romero JR, et al. Intravenous zanamivir in hospitalized patients with influenza. *Pediatrics*. 2017;140(5):e20162727

69. Chan-Tack KM, Kim C, Moruf A, Birnkrant DB. Clinical experience with intravenous zanamivir under an Emergency IND program in the United States (2011-2014). *Antivir Ther*. 2015;20(5):561–564

70. Ferdinands JM, Fry AM, Reynolds S, et al. Intraseason waning of influenza vaccine protection: evidence from the US influenza vaccine effectiveness network, 2011-12 through 2014-15. *Clin Infect Dis*. 2017;64(5):544–550

71. Castilla J, Martínez-Baz I, Martínez-Artola V, et al; Primary Health Care Sentinel Network; Network for Influenza Surveillance in Hospitals of Navarre. Decline in influenza vaccine effectiveness with time after vaccination, Navarre, Spain, season 2011/12. *Euro Surveill*. 2013;18(5):20388

72. Kissling E, Valenciano M, Larrauri A, et al. Low and decreasing vaccine effectiveness against influenza A(H3) in 2011/12 among vaccination target groups in Europe: results from the I-MOVE multicentre case-control study. *Euro Surveill*. 2013;18(5):20390

73. Belongia EA, Sundaram ME, McClure DL, Meece JK, Ferdinands J, VanWormer JJ. Waning vaccine protection against influenza A (H3N2) illness in children and older adults during a single season. *Vaccine*. 2015;33(1):246–251

74. Radin JM, Hawksworth AW, Myers CA, Ricketts MN, Hansen EA, Brice GT. Influenza vaccine effectiveness: maintained protection throughout the duration of influenza seasons 2010-2011 through 2013-2014. *Vaccine*. 2016; 34(33):3907–3912

75. Puig-Barberà J, Mira-Iglesias A, Tortajada-Girbés M, et al; Valencia Hospital Network for the Study of Influenza and other Respiratory Viruses (VAHNSI, Spain). Waning protection of influenza vaccination during four influenza seasons, 2011/2012 to 2014/2015. *Vaccine*. 2017;35(43):5799–5807

76. Ray GT, Lewis N, Klein NP, Daley MF, Lipsitch M, Fireman B. Depletion-of-susceptibles Bias in Analyses of Intra-season waning of influenza vaccine effectiveness. *Clin Infect Dis*. 2020;70(7): 1484–1486

77. Kissling E, Nunes B, Robertson C, et al; I-MOVE case–control study team. I-MOVE multicentre case-control study 2010/11 to 2014/15: is there within-season waning of influenza type/subtype vaccine effectiveness with increasing time since vaccination? *Euro Surveill*. 2016;21(16)

78. Pebody R, Andrews N, McMenamin J, et al. Vaccine effectiveness of 2011/12 trivalent seasonal influenza vaccine in preventing laboratory-confirmed influenza in primary care in the United Kingdom: evidence of waning intra-seasonal protection. *Euro Surveill*. 2013; 18(5):20389

79. Petrie JG, Ohmit SE, Truscon R, et al. Modest waning of influenza vaccine efficacy and antibody titers during the 2007-2008 influenza season. *J Infect Dis*. 2016;214(8):1142–1149

80. Ray GT, Lewis N, Klein NP, et al. Intraseason waning of influenza vaccine effectiveness. *Clin Infect Dis*. 2019; 68(10):1623–1630

81. Ferdinands JM, Patel MM, Foppa IM, Fry AM. Influenza vaccine effectiveness. *Clin Infect Dis*. 2019;69(1):190–191

82. Centers for Disease Control and Prevention. Influenza vaccination coverage among health care personnel — United States, 2018–19 influenza season. Available at: https://www.cdc.gov/flu/fluvaxview/hcp-coverage_1819estimates.htm. Accessed May 4, 2020

83. Uyeki TM, Bernstein HH, Bradley JS, et al. Clinical practice guidelines by the Infectious Diseases Society of America: 2018 Update on diagnosis, treatment, chemoprophylaxis, and institutional outbreak management of seasonal influenza. *Clin Infect Dis*. 2019;68(6): e1–e47

84. Heo YA. Baloxavir: first global approval. *Drugs*. 2018;78(6):693–697

85. Dobson J, Whitley RJ, Pocock S, Monto AS. Oseltamivir treatment for influenza in adults: a meta-analysis of randomised controlled trials. *Lancet*. 2015;385(9979):1729–1737

86. Jefferson T, Jones MA, Doshi P, et al. Neuraminidase inhibitors for preventing and treating influenza in healthy adults and children. *Cochrane Database Syst Rev*. 2014;(4):CD008965

87. Malosh RE, Martin ET, Heikkinen T, Brooks WA, Whitley RJ, Monto AS. Efficacy and safety of oseltamivir in children: systematic review and individual patient data meta-analysis of randomized controlled trials. *Clin Infect Dis*. 2018;66(10):1492–1500

88. Uyeki TM. Oseltamivir treatment of influenza in children. *Clin Infect Dis*. 2018;66(10):1501–1503

89. Wang K, Shun-Shin M, Gill P, Perera R, Harnden A. Neuraminidase inhibitors for preventing and treating influenza in children (published trials only). *Cochrane Database Syst Rev*. 2012;(4): CD002744

90. Domínguez A, Romero-Tamarit A, Soldevila N, et al; Surveillance of Hospitalized Cases of Severe Influenza in Catalonia Working Group. Effectiveness of antiviral treatment in preventing death in severe hospitalised influenza cases over six seasons. *Epidemiol Infect*. 2018;146(7):799–808

91. Hsu J, Santesso N, Mustafa R, et al. Antivirals for treatment of influenza: a systematic review and meta-analysis of observational studies. *Ann Intern Med*. 2012;156(7):512–524

92. Muthuri SG, Venkatesan S, Myles PR, et al; PRIDE Consortium Investigators. Effectiveness of neuraminidase inhibitors in reducing mortality in patients admitted to hospital with influenza A H1N1pdm09 virus infection: a meta-analysis of individual participant data. *Lancet Respir Med*. 2014;2(5):395–404

93. Venkatesan S, Myles PR, Leonardi-Bee J, et al. Impact of outpatient neuraminidase inhibitor treatment in patients infected with influenza A(H1N1) pdm09 at high risk of hospitalization: an individual participant data metaanalysis. *Clin Infect Dis*. 2017; 64(10):1328–1334

94. Dawood FS, Jara J, Gonzalez R, et al. A randomized, double-blind, placebo-controlled trial evaluating the safety of early oseltamivir treatment among children 0-9 years of age hospitalized with influenza in El Salvador and Panama. *Antiviral Res*. 2016;133:85–94

95. Louie JK, Yang S, Samuel MC, Uyeki TM, Schechter R. Neuraminidase inhibitors for critically ill children with influenza. *Pediatrics*. 2013;132(6). Available at: www.pediatrics.org/cgi/content/full/132/6/e1539

96. Katzen J, Kohn R, Houk JL, Ison MG. Early oseltamivir after hospital admission is associated with shortened hospitalization: a 5-year analysis of oseltamivir timing and clinical outcomes. *Clin Infect Dis*. 2019;69(1): 52–58

97. Ramirez J, Peyrani P, Wiemken T, Chaves SS, Fry AM. A randomized study evaluating the effectiveness of oseltamivir initiated at the time of hospital admission in adults hospitalized with influenza-associated lower respiratory tract infections. *Clin Infect Dis*. 2018;67(5):736–742

98. Li L, Liu J, Qin K. Comparison of double-dose vs standard-dose oseltamivir in the treatment of influenza: a systematic review and meta-analysis [published online ahead of print June 4, 2020]. *J Clin Pharm Ther*. doi: 10.1111/jcpt.13203

99. Howard A, Uyeki TM, Fergie J. Influenza-associated acute necrotizing encephalopathy in siblings. *J Pediatric Infect Dis Soc*. 2018;7(3):e172–e177

100. Takeuchi S, Tetsuhashi M, Sato D. Oseltamivir phosphate-Lifting the restriction on its use to treat teenagers with influenza in Japan. *Pharmacoepidemiol Drug Saf*. 2019; 28(4):434–436

101. Koszalka P, Tilmanis D, Roe M, Vijaykrishna D, Hurt AC. Baloxavir marboxil susceptibility of influenza viruses from the Asia-Pacific, 2012-2018. *Antiviral Res*. 2019;164:91–96

102. Takashita E, Kawakami C, Morita H, et al; On Behalf Of The Influenza Virus Surveillance Group Of Japan. Detection of influenza A(H3N2) viruses exhibiting reduced susceptibility to the novel cap-dependent endonuclease inhibitor baloxavir in Japan, December 2018. *Euro Surveill*. 2019;24(3):1800698

103. Takashita E, Kawakami C, Ogawa R, et al. Influenza A(H3N2) virus exhibiting reduced susceptibility to baloxavir due to a polymerase acidic subunit I38T substitution detected from a hospitalised child without prior baloxavir treatment, Japan, January 2019. *Euro Surveill*. 2019;24(12):1900170

104. Hayden FG, Sugaya N, Hirotsu N, et al; Baloxavir Marboxil Investigators Group. Baloxavir marboxil for uncomplicated influenza in adults and adolescents. *N Engl J Med*. 2018; 379(10):913–923

105. Omoto S, Speranzini V, Hashimoto T, et al. Characterization of influenza virus variants induced by treatment with the endonuclease inhibitor baloxavir marboxil. *Sci Rep*. 2018;8(1):9633

106. Gubareva LV, Mishin VP, Patel MC, et al. Assessing baloxavir susceptibility of influenza viruses circulating in the United States during the 2016/17 and 2017/18 seasons. *Euro Surveill*. 2019; 24(3):1800666

107. Ince WL, Smith FB, O'Rear JJ, Thomson M. Treatment-emergent influenza virus PA substitutions independent of those at I38 associated with reduced baloxavir susceptibility and virus rebound in trials of baloxavir marboxil [published online ahead of print April 7, 2020]. *J Infect Dis*. doi: 10.1093/infdis/jiaa164

108. Takashita E, Daniels RS, Fujisaki S, et al. Global update on the susceptibilities of human influenza viruses to neuraminidase inhibitors and the cap-dependent endonuclease inhibitor baloxavir, 2017-2018. *Antiviral Res*. 2020; 175:104718

CLASSIFIED ADVERTISEMENTS & ANNOUNCEMENTS

CONTENTS

AAP Career Center
careercenter.aap.org

Classified Advertisements

Advertisements in the Classified Advertising section of PEDIATRICS reach more than 65,000 child health-care professionals and clinicians monthly. PEDIATRICS circulation encompasses 85% of all board certified pediatricians, more than 90% of certified pediatric allergists, cardiologists, and surgeons, and more than 9,000 pediatric residents.

LINE ADS

Line ads: A line ad is a text ad with no logos, and no paragraph formatting. Cost is calculated by word count. To calculate words, either open Microsoft Word and use the word count function, or count each word as one. Web addresses, e-mail addresses, phone numbers, or fax numbers are all calculated as one word. BC/BE is calculated as one word, but Board Certified/Board Eligible is calculated as four. All line ads are packaged with a job posting at www.pedjobs.org. There is no print advertising only. There is online advertising only. When placing your ad, the online compatibility allows you to search the job bank of hundreds of CVs.

If you would like information about placing your ad, please call 443.512.8899 and ask for Pediatrics classifieds.

CLASSIFIED DISPLAY

Classified advertising on a set-size basis (1/2 page, 1/4 page, etc.) also is available in PEDIATRICS. All display ads are packaged with a job posting at www.pedjobs.org. There is no print advertising alone. Rate sheets are furnished upon request. Please call 443.512.8899 and ask for Pediatrics classifieds between the hours of 8:30 am and 5:00 pm Eastern Standard Time for more information.

PLACING AN AD

To confirm an insertion order, send classified ad copy with payment to:

American Academy of Pediatrics
2225 Old Emmorton Road, Suite 201
Bel Air, MD 21015
E-mail ad copy to: rhonda.truitt@wt-group.com

Ad copy may be sent via e-mail in a Word-friendly format or be typewritten. No handwritten or telephone (verbal) orders will be accepted.

DEADLINE

The deadline for placing a classified ad in PEDIATRICS is the 15th of the second month preceding month of issue. Example: January 15th for the March issue.

TERMS

Please note, payment must accompany order. No ads will be placed without prior payment. Make checks payable to: American Academy of Pediatrics. Visa, MasterCard, American Express, and Discover are accepted. Ads will not be placed until payment is collected. An advertiser may cancel an ad without refund.

REPLYING TO A CONFIDENTIAL BOX AD

To reply to an ad with a confidential box number (box #000), please use the following address: Pediatrics Classified Ads, Box _____, 2225 Old Emmorton Road, Suite 201, Bel Air, MD 21015.

CLASSIFIED ADVERTISING POLICY

Although the American Academy of Pediatrics believes classified advertisements published in PEDIATRICS are from reputable sources, the Academy reserves the right to revise or reject advertising copy that is inconsistent with the publication's standards. All advertising is subject to approval.

Ads in PEDIATRICS must be relevant to the practice of medicine. The Academy does not investigate offers made in classified ads and assumes no responsibility concerning them. In consideration for acceptance of an advertisement for publication, the agency and advertiser agree to indemnify and hold the American Academy of Pediatrics harmless against any losses or expenses arising out of publication of such advertisements, including and without limitation, those resulting from claims based on the contents, claims, or subject matter of such advertisements. Every effort is made to avoid mistakes, but the Academy cannot accept responsibility for printing or clerical errors.

Without limiting the American Academy of Pediatrics' terms, conditions, and policies, the American Academy of Pediatrics, in accordance with Department of Justice guidelines:

- Prohibits any job posting that requires U.S. citizenship or lawful permanent residence in the U.S. as a condition of employment, unless otherwise required in order to comply with law, regulation, executive order, or government contract.
- Prohibits any job requirement or criterion in connection with a job posting that discriminates on the basis of citizenship status or national origin.

For complete EEO guidelines please refer to the following resource: http://www.justice.gov/crt/osc/

CONTACT INFORMATION

The Walchli Tauber Group, Inc.
Attn: Rhonda Truitt
2225 Old Emmorton Road, Suite 201
Bel Air, MD 21015
Phone: 443.512.8899 ext. 106
Fax: 443.490.4003
Email: rhonda.truitt@wt-group.com

CONNECTICUT

Largest Concierge Pediatric Practice in the Country

Concierge Care Pediatric Practice is searching for a third General Pediatrician to join our team!! -Usually see only 3 to 10 patients per doctor per day -Hour long Physicals -Home Visits -PCR lab testing in office -Lifestyle of utmost importance -Very happy and supportive team -Partnership track -Competitive salary and benefits. Please email CV to what20happened@gmail.com.

GEORGIA

Integrative Medicine Pediatrician Growing Atlanta Practice

We're currently seeking a Pediatrician with at least three years' conventional medical experience who is also boarded or board eligible in integrative medicine to join the thriving pediatric practice of Dr. Taz Bhatia, a board-certified integrative medicine physician and wellness expert, best-selling author, speaker and guest on programs including The Today Show, Dr. Oz and Live with Kelly & Ryan. Her integration of Eastern medical wisdom with modern science provides a truly distinctive approach to the care of children. The successful candidate will join a team of board-certified, compassionate providers who are conventionally trained, but diagnose and treat their patients by pulling from traditional, integrative, holistic, functional and Chinese medicine to identify underlying health issues and create the best treatment plans possible. This position offers the potential for leadership as growth dictates. Both part-time and full-time candidates are encouraged to apply. Dr. Taz opened her practice, CentreSpringMD, in 2009. She continued to grow adding multiple locations and providers and the launch of CentreSpringMD Spa and CentreSpringMD Pediatrics. For the last 10 years, her practices have served as integrative medical homes for the entire family – pediatric care, adults, prevention and advanced therapy for disease. At CentreSpring Pediatrics, physicians spend more time with their patients, averaging between 30 and 45 minutes per visit. CentreSpring Pediatrics has two locations, both outpatient practices, in the Brookhaven and Johns Creek suburbs of Atlanta, both highly desirable, family-oriented communities with nationally ranked schools, friendly neighborhoods, and an abundance of parkland and recreational opportunities. Here you will have the chance to live in or near Atlanta, ranked by *U.S. News & World Report* in 2020 as one of the Top 100 Best Places to Live in the United States based on affordability, job availability, and quality of life. The state's largest city and capital, Atlanta is home to an abundance of world-class entertainment, recreation, cuisine, shopping, arts and culture. Southern tradition and urban modernism sit side by side. A booming economy and housing market, proximity to an international airport, a diverse population, and mild winters are additional perks associated with living here. Tybee Island, Hilton Head Island, St. Simons Island, and Jekyll Island as well as the white sand beaches of the panhandle of Florida are all within four and half to five and a half hours by car and make great weekend beach options. This is an exceptional opportunity for professional growth in a practice with a decidedly innovative approach to pediatric health care. For more information about this position and for confidential consideration, please contact Glenda Church Smith, Pediatric Search Partners: 877-440-3832; or email glenda@pediatricsearchpartners.com. Pediatric Search Partners is a boutique search consultancy focused solely on pediatric and pediatric subspecialty search and leaders within children's healthcare. To learn more about us, please visit https://www.pediatricsearchpartners.com

LOUISIANA

Chief Quality Officer New Orleans, Louisiana

We're seeking a Chief Quality Officer to join the rapidly growing team at Ochsner Hospital for Children in New Orleans, Louisiana. The ideal candidate will be board certified in general pediatrics as well as the pediatric subspecialty in which they are fellowship-trained, if applicable, and will have administrative experience. MBA, MHA or MMM degree is desirable. Ochsner Hospital for Children offers a level of pediatric care unmatched in Louisiana for everything from well-child check-ups and immunizations to cancer care and heart transplants. Ochsner Hospital for Children provides care to nearly 300 open heart pediatric cases per year, along with liver transplants, BMT, advanced spine surgery, craniofacial and other quaternary services. Located in one of our most vibrant cultural cities, this nonprofit, academic, multi-specialty institution is the recipient of numerous awards, including Healthgrades Distinguished Hospitals for Clinical Excellence, which places Ochsner in the top 5 percent of U.S. hospitals for clinical outcomes. Ochsner Hospital for Children is the only children's hospital in Louisiana or Mississippi ever recognized by *U.S. News & World Report* as a specialty top 50 hospital for pediatric heart care. Ochsner physicians care for over 80,000 children each year at 14 sites across Louisiana including a large, state-of-the-art dedicated pediatric ambulatory campus located at the main hospital campus. The primary care pediatric network throughout the region currently has more than 40 general pediatricians in addition to a large outside referral base and treats more than 55,000 unique pediatric patients annually. Ochsner Hospital for Children includes: •125-bed children's hospital within a hospital •54-bed Level IV Regional NICU, the highest level available in Louisiana •14-bed Level I Pediatric Intensive Care Unit, the highest level available •12-bed state-of-the-art Pediatric CVICU, the only unit of its kind in the Gulf South dedicated to the care of children with cardiovascular and congenital heart defects •46-bed Pediatric Acute Care. This nonprofit, academic, multi-specialty institution also has a combined pediatrics residency program with Tulane University Medical School. Medical students from Tulane and the University of Queensland/Ochsner Clinical School rotate through the division. Academic and research opportunities are available. New Orleans exudes a character all its own and offers a lifestyle that no other U.S. city can match. It's home to an unparalleled blend of cultures. World-class music, dining and shopping are just the beginning. Professional sports, gorgeous city parks, year-round festivals, prestigious academic centers and universities, and Southern hospitality await you. It's easy to understand why residents take great pride in calling New Orleans their home. You'll fall in love the minute you set foot here, both personally and professionally. For complete details and consideration, please forward your CV and cover letter to Glenda Church Smith, Principal, Pediatric Search Partners via email to glenda@pediatricsearchpartners.com. Please contact Glenda by phone at 877-440-3832 or call/text to 214-850-3094.

Associate Chair, Pediatric Primary Care New Orleans Region

Pediatric Search Partners is pleased to partner with Ochsner Hospital for Children, on a newly created leadership opening. We are seeking an **Associate Chair, Pediatric Primary Care for the New Orleans Region** to continue Ochsner's growth and development of primary care pediatrics. **For the fourth year in a row, Ochsner Hospital for Children has been ranked in 2020-21 among the Top 50 Children's Hospitals in the country for pediatric cardiology and heart surgery by *U.S. News and World Report*. Ochsner Hospital for Children is also Louisiana's only ranked children's hospital.** Based on the campus of Ochsner Medical Center in New Orleans, you'll find

an exciting opportunity to join a rapidly growing team of more than 140 pediatric physicians and advanced specialty care in 30 pediatric specialties and subspecialties at 15 locations throughout Louisiana. Responsibilities include continuing the development of a geographically broad network of pediatric primary care providers practicing at the highest possible quality standards on behalf of children throughout the Gulf South Region; and maintenance of solid relationships with the pediatric primary care community outside the Ochsner system, providing the support and communication they need in order for Ochsner Hospital for Children to function as the comprehensive system of care for their patients. The ideal candidate will be a board certified Pediatrician with administrative experience who has successfully developed and/or overseen a multisite pediatric primary care practice. MBA, MHA or MMM degree is desirable. The Associate Chair will report to the System Chair/AMD, Pediatrics and will lead a team of Pediatric Primary Care Site Directors and Physicians. Ochsner Hospital for Children offers a level of pediatric care unmatched in Louisiana for everything from well-child check-ups and immunizations to cancer care and heart transplants. Ochsner Hospital for Children provides care to nearly 300 open heart pediatric cases per year, along with liver transplants, BMT, advanced spine surgery, craniofacial and other quaternary services. Ochsner physicians care for over 80,000 children each year at 15 sites across Louisiana including a large, state-of-the-art dedicated pediatric ambulatory campus located at the main hospital campus. The primary care pediatric network throughout the region currently has more than 40 general pediatricians in addition to a large outside referral base and treats more than 55,000 unique pediatric patients annually. Ochsner Hospital for Children includes: •125-bed children's hospital within a hospital •54-bed Level IV Regional NICU, the highest level available in Louisiana •14-bed Level I Pediatric Intensive Care Unit, the highest level available •12-bed state-of-the-art Pediatric CVICU, the only unit of its kind in the Gulf South dedicated to the care of children with cardiovascular and congenital heart defects •45-bed Pediatric Acute Care •The Michael R. Boh Center for Child Development, dedicated to improving the lives of children and adolescents with developmental disorders •Pediatric Emergency Room. This nonprofit, academic, multi-specialty institution also has a combined pediatrics residency program with Tulane University Medical School. Medical students from Tulane and the University of Queensland/Ochsner Clinical School rotate through the division. Academic and research opportunities are available. New Orleans exudes a character all its own and offers a lifestyle that no other U.S. city can match. It's home to an unparalleled blend of cultures. World-class music, dining and shopping are just the beginning. Professional sports, gorgeous city parks, year-round festivals, prestigious academic centers and universities, and Southern hospitality await you. The north shore of Lake Pontchartrain offers lakefront living with quaint historic town centers and the number-one school district in the state. It's easy to understand why residents take great pride in calling New Orleans their home. You'll fall in love the minute you set foot here, both personally and professionally. For complete details, please forward your CV and cover letter to Glenda Church Smith, Principal, Pediatric Search Partners who is handling the search at glenda@pediatricsearchpartners.com, dial directly at 877-440-3832 or text to 214-850-3094.

Neonatology
New Orleans and Region

Pediatric Search Partners is seeking **Board Eligible/Board Certified Neonatologists** for **Ochsner Hospital for Children** in New Orleans, Louisiana. With the assistance of an experienced group of neonatal nurse practitioners, Ochsner's team of seven board-certified neonatologists directs the Neonatal Intensive Care Unit at Ochsner Baptist Medical Center. Ochsner's NICU was ranked in the top 60 in the United States and features 54 beds, including both private and care by parent rooms. They participate in the Vermont Oxford Network, have received the level IV designation by the State of Louisiana and have long been commended for taking an innovative approach to caring for the sickest newborns in the region. At Ochsner, you will find an incredibly exciting opportunity to join a rapidly growing pediatric team of more than 120 physicians, including subspecialists covering all medical and surgical fields. The group is the region's leading integrated provider of multispecialty care for infants, children, adolescents, and young adults offering a full range of pediatric services, including solid organ transplantation and pediatric cardiovascular surgery. Ochsner Hospital for Children includes: •125-bed children's hospital within a hospital •54-bed Level IV NICU •14-bed Level I Pediatric Intensive Care Unit, the highest level available •12-bed CVICU, the only unit of its kind in the Gulf South dedicated to the care of children with cardiovascular and congenital heart defects •45-bed Pediatric Acute Care •Dedicated state-of-the-art center for child development, the only facility to offer this type of comprehensive care in the region under one roof. Located in one of our most vibrant cultural cities, this nonprofit, academic, multi-specialty institution is the recipient of numerous awards, including Healthgrades' Distinguished Hospitals for Clinical Excellence, which places Ochsner in the top five percent of U.S. hospitals for clinical outcomes. New Orleans exudes a character all its own and offers a lifestyle that no other U.S. city can match. It's home to world-class music, dining and shopping. A city of neighborhoods, New Orleans is best traveled by foot, but you can also hop on one of the city's historic streetcars or join the growing legion of commuters by bicycle. NOLA's neighborhoods each have a distinct architectural flavor and include everything from traditional Antebellum style to historic bungalows and cottages to modern lofts. Professional football and basketball, gorgeous city parks, year-round festivals, prestigious academic centers and universities, and Southern hospitality await you. If you're craving the beach, the Gulf shores of Alabama are about two and a half hours away by car; and the white sands of Pensacola, Florida, are just three hours away. It's easy to understand why residents take great pride in calling New Orleans their home. You'll fall in love the minute you set foot here, both personally and professionally. If you are seeking an exceptional opportunity with a growing organization, please contact Glenda Church Smith, Principal, Pediatric Search Partners for complete details at glenda@pediatricsearchpartners.com, or call directly at 877.440.3832.

System Medical Director, Neonatology
New Orleans

We're seeking a Board Certified Neonatologist for a newly created position as the System Medical Director for Neonatology to join the growing team at Ochsner Hospital for Children in New Orleans, Louisiana. Primary responsibilities: The System Medical Director, Neonatology will serve in a strategic clinical leadership role that will collaborate with senior clinical and administrative leadership across the Women's Services and Pediatrics Centers of Excellence to lead clinical transformation and integration of Ochsner's NICU services (at Baptist, Kenner, West Bank, Slidell and St. Tammany) and staffs into a Ochsner NICU system delivering standardized care of a consistent high quality at the units best matched to the appropriate level of patient care and the family's home location. The focus will be on value creation for care delivery of both high risk and normal newborns utilizing a single team of neonatal providers, current and new digital health technologies, and robust education to support of Ochsner's "birthing platforms" across the New Orleans, North Shore and Bayou regions and resulting in improved care of all babies in the Ochsner system, greater retention of healthy babies at their home hospitals and level-of-care appropriate utilization of higher level nurseries. This includes but is not limited to: Direct oversight of clinical care, including physician and NNP recruiting and retention at the system's Level IV NICU at Ochsner Baptist Hospital as well as recruiting and

retaining top neonatal talent to Ochsner's Level IIII and II NICUs; Creating a NICU network-wide staffing plan; recruiting and retaining to that plan and its growth; and Advancing the group's role in the application of telemedicine to improve the care of babies across the system, both in traditional nurseries and NICUs. Practice Location: The System Neonatology Medical Director will be based at Ochsner Baptist Hospital in Uptown New Orleans with responsibility for 4 lower-level units in the Greater New Orleans area. The position will require local travel. Reports to: System Chair and AMD for Pediatrics with matrixed responsibility to System Chair for Women's Services and Maternal Fetal Medicine **About Ochsner:** Ochsner Health System is Louisiana's largest non-profit, academic, multi-specialty, healthcare delivery system with 30 owned, managed and affiliated hospitals and 60+ health centers. Ochsner employs more than 1,100 physicians in over 90 medical specialties and subspecialties and performs over 600 clinical research studies. Ochsner for Children is a vertically integrated health system, with a pediatric primary care network, a dedicated pediatric emergency department, in-house pediatric intensivists and hospitalists, as well as a dedicated, full-time, pediatric transport team providing ground, rotary and fixed wing transports across the entire Gulf South. Ochsner Hospital for Children has a 33 pediatric bed unit, along with a 14 bed PICU, 12 bed CVICU, and 54 Level IV NICU beds. Ochsner sponsors the combined Tulane-Ochsner pediatric residency program and teaches medical school students from Tulane as well as the University of Queensland. **The Location:** New Orleans exudes a character all its own and offers a lifestyle that no other U.S. city can match. It's home to world-class music, dining and shopping. Professional football and basketball, gorgeous city parks, year-round festivals, prestigious academic centers and universities, and Southern hospitality await you. If you're craving the beach, the Gulf shores of Alabama are about two and a half hours away by car: and the white sands of Pensacola are just three hours away. It's easy to understand why residents take great pride in calling New Orleans their home. You'll fall in love the minute you set foot here, both personally and professionally. For complete details, please forward your curriculum vitae and cover letter to **Glenda Church Smith, Principal, Pediatric Search Partners at glenda@pediatricsearchpartners.com,** or contact by phone at **877-440-3832 or cell/text to 214-850-3094.**

MASSACHUSETTS

Pediatrician

Premier pediatric practice on Boston's North shore is looking for a pediatrician for acute/urgent care full-time or part-time. You will be working alongside a collegial group of three or more additional experienced Pediatricians and Pediatric Nurse Practitioner's with full nursing support, laboratory, and x-ray. Work may include afternoons, evenings, and/or weekends. Visit our website at www.phcapediatrics.com.

TENNESSEE

Medical Director, Neonatology Level II NICU One Hour from Nashville

We're seeking a Medical Director, Neonatology to join Vanderbilt University Medical Center's team overseeing the Level II NICU at Maury Regional Medical Center in Columbia, Tennessee, located just a 50-minute drive from Nashville. The position will also allow the Medical Director to also spend time at the Level IV NICU at Vanderbilt Hospital in Nashville, if desired. Vanderbilt offers a very competitive salary and benefits package. Maury Regional's 255-bed facility is home to more than 200 physicians, has been compared to some of the nation's most prestigious medical centers and has been recognized consistently for performance on publicly reported quality measures. The hospital's NICU team includes Board Certified Neonatologists and Neonatologist Nurse Practitioners provided by Monroe Carell Jr. Children's Hospital at Vanderbilt in Nashville, along with Neonatal Registered Nurses certified by the American Heart Association's Neonatal Resuscitation Program (NRP), respiratory therapists, international board certified lactation consultants, speech/physical/occupational therapists, registered dieticians, and social workers. The Vanderbilt University Medical Center neonatal transport team can provide transfer of babies to the Level IV NICU at Monroe Carell Jr. Children's Hospital. Columbia has been named among *Southern Living* magazine's Best Small Towns of 2019, and after a visit here, you'll quickly understand why. Located just 45 minutes south of Nashville and 75 miles north of Huntsville, Alabama, this charming town includes an historic town square and Main Street with plenty of shops, restaurants and a lively music scene. The new Columbia Arts District, located just blocks from Columbia Town Square, was designed as a haven for artists and includes a variety of eclectic galleries along with additional shops, cafes and other retailers. You'll enjoy the best of small-town life with easy access to Nashville and all of its attractions, from the Grand Ole Opry, Johnny Cash Museum and Country Music Hall of Fame to professional sports, shopping, nightlife, top-notch restaurants and culture. And here's one of the most attractive perks of Columbia life: Tennessee residents pay no state income tax and enjoy a competitive cost of living. For complete details and confidential consideration, please contact Glenda Church Smith, Principal, Pediatric Search Partners: 877.440.3832; 214.850.3094 (cell/text); or email to glenda@pediatricsearchpartners.com.

Developmental-Behavioral Pediatrician Opening in the Only Town Named *Best Town Ever* by *Outside Magazine* More Than Once!

Looking for a great place to live and practice? Your search can end now. We're seeking Developmental-Behavioral Pediatricians who are board certified or board eligible to join Siskin Children's Institute growing team in beautiful Chattanooga, Tennessee. Serving children with special needs and their families since 1950, Siskin Children's Institute achieves its mission through education, pediatric healthcare services, home and community-based programs and outreach services in the field of developmental disabilities. Siskin Children's Institute is affiliated with the Children's Hospital at Erlanger. Founded in 1889, Erlanger is the seventh largest public healthcare system in the United States with more than half a million patients per year. The Children's Hospital at Erlanger is a Comprehensive Regional Pediatric Center, the highest state designation for pediatrics and offers a full complement of pediatric subspecialists. ***Outside* magazine searches the country annually to rank cities with great access to trails and public lands as well as great restaurants and wonderful neighborhoods. Chattanooga is the only city to be recognized as *Best Town Ever* more than once!** Surrounded by mountains with a river running through the heart of its downtown, Chattanooga is a nationally renowned destination in the Southeastern United States with recreation for people of all skill levels and hundreds of miles of trails, world-class events, thousands of acres of conservation and national recognition. The city is also noted for the renaissance of its beautiful downtown and redevelopment of its riverfront. With its scenic beauty, stable population, growing economy, and cooperative, friendly people, it is truly one of the most progressive mid-size cities in the United States. **Within a two-hour drive of Atlanta, Nashville, Birmingham and Knoxville, Chattanooga uniquely offers a quality of life that is hard to duplicate anywhere in the country. And it provides an opportunity to join an established program committed to serving the needs of children in cooperation with a growing, world-class children's hospital.** The Siskin Children's Institute includes the

following: The **Siskin Early Learning Center** provides a high-quality preschool education to young children with and without disabilities, including children with developmental delays, autism spectrum disorder, chromosomal abnormality and brain injury. All children learn and play side by side in an environment that celebrates the accomplishments of every child. The **Siskin Center for Developmental Pediatrics** is a regional developmental pediatric center led by a board-certified developmental-behavioral pediatrician. Children are referred to the center for medical, psychological and cognitive assessment, diagnosis and treatment, including physical, occupational, speech and language, and other therapies as well as counseling and social skills groups. The **Siskin Home & Community-Based Early Intervention** program is designed to help parents, other caregivers and children with special needs gain the knowledge and confidence they need to be successful in life. Through visits with a developmental therapist, families receive information, support, guidance and consultation about improving quality of life both for children and their families. The program can be provided in the home, child care center, the park or other natural settings in the community. **Siskin Outreach Services** provide disability information to families, college students and professional through a dynamic array of programs that weave through the Institute's other areas of focus. Outreach Services offer a lending library, family support and training, consultation services, and professional training in fields related to special needs and early development. In addition to the four-season climate and affordable housing, there is **no state income tax on salaries, wages, bonuses or any other type of income for work.** Chattanooga is also home to several well-known private and parochial schools, including Baylor School, McCallie School and Girls Preparatory School. With a world-class aquarium ranked No. 4 in the country and No. 8 in the world, a variety of urban and outdoor activities, and 57 trail heads within a half-hour drive, you'll be pleasantly surprised by this gem of a town, if you aren't already a fan. For complete details and confidential consideration for this exceptional opportunity, please contact Glenda Smith, Principal, Pediatric Search Partners at **glenda@pediatricsearchpartners.com**, or by phone at **877.440.3832.**

Developmental and Behavioral Pediatrics/Neurodevelopmental Pediatrics

We're seeking a **Board Certified or Board Eligible Developmental and Behavioral Pediatrician** and/or a **Neurodevelopmental Pediatrician** to join the expanding team at **Siskin Children's Institute's brand new office in Nashville, Tennessee,** opening in January 2020. This new facility will offer medical services including developmental assessments and treatment as well as applied behavior analysis therapy for children with special needs. Based in Chattanooga, Siskin Children's Institute is a nonprofit organization with a mission to increase access to assessment, diagnosis, and early intervention for children with developmental disorders including autism spectrum disorder, ADHD, Down syndrome, cerebral palsy and genetic disorders. The organization's expansion into the Nashville area will help shorten wait times and reduce the distance families of special needs children have to travel to see developmental pediatricians who can provide the care their children deserve. You'll join a group of specialists and experts in the areas of developmental pediatrics, behavior psychology, and applied behavior analysis, all of whom work collaboratively with families and take an interdisciplinary approach to identification and intervention for neurodevelopmental concerns. Leading the Nashville practice is Dr. James Van Decar, a neurodevelopmental pediatrician with more than 30 years of experience helping children with special needs and an expert in the evaluation, diagnosis, and management of developmental disabilities in children. You'll love living in Nashville, one of the country's hottest cities and ranked No. 15 on *U.S. News & World Report's* Best Places to Live based on quality of life, job market, value and desirability of the area. Dubbed "Music City, U.S.A.," Nashville enjoys a booming and diverse economy, lower cost of living than other major U.S. cities, great neighborhoods and an entertainment scene that's second to none, from the Grand Old Opry, Country Music Hall of Fame and a slew of live music venues to professional sports, world-class museums, even a thriving craft beer industry. Nashville's central location puts you within two to four hours driving distance of Atlanta, Chattanooga, Knoxville, the Great Smoky Mountains and the Kentucky Bourbon Trail. **Plus, as a resident of Tennessee, you'll pay no state income tax.** For complete details and confidential consideration, please contact Glenda Church Smith, Principal, Pediatric Search Partners, at 877.440.3832 (office), 214.850.3094 (cell/text), or via email at **glenda@pediatricsearchpartners.com**.

NATIONWIDE

Your dream job awaits. Let us help you find it.

Thinking of making a change? Or just starting your search for a new practice setting? Pediatric Search Partners is a specialized boutique search firm with over 30 years of experience. Our sole focus is serving the pediatricians, pediatric subspecialists, healthcare executives and physician leaders dedicated to providing children's healthcare. Since 2009, we've successfully filled more than 500 searches within leading children's hospitals and healthcare organizations across the nation, each of them with a highly personalized approach. Our passion is matching the physicians and executives who care for children with opportunities they truly care about. For complete details and consideration, please contact: Glenda Smith, Principal, Pediatric Search Partners, Phone 877.440.3832, Cell 214.850.3094 or email glenda@pediatricsearchpartners.com.

AAP experience VIRTUAL 2020
National Conference & Exhibition

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

90 Years of Caring for Children—1930–2020

THERE'S STILL TIME TO REGISTER!

Register for the 2020 AAP Virtual National Conference & Exhibition through October 30 and gain access to all of the educational content the conference has to offer!

FLEXIBLE

Watch and learn on your own schedule.

CONVENIENT

Participate wherever you are. No lines. No crowded rooms.

AFFORDABLE

Pay one low price for all the National Conference has to offer. No tickets or sold-out sessions. No travel costs.

VERSATILE

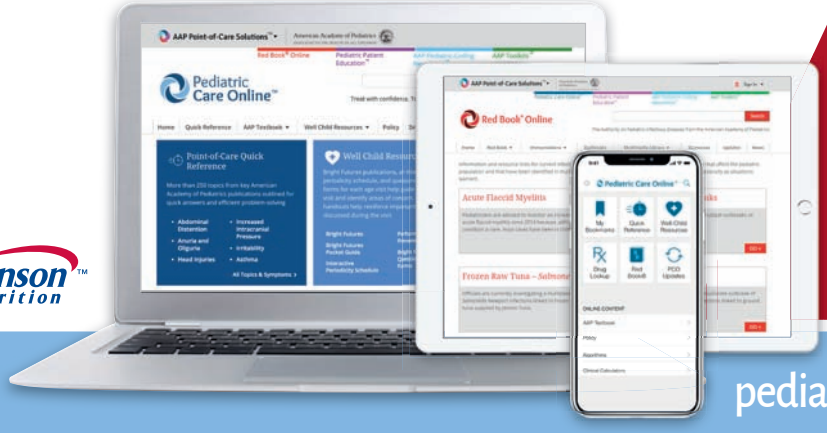
Can't join us October 2-5? Recordings of live sessions and all on-demand content will be available until January 31!

#AAP2020

For more information about the Virtual National Conference, visit AAPexperience.org or email nce@aap.org.

Pediatric Care Online
provides instant access
to the most essential AAP resources in pediatrics today.

Pediatric Care Online™



Founding Sponsor
Mead Johnson Nutrition™

Free trial available!

Pediatricians can request a free 1-month trial. Visit **aap.org/pcotrial** today.

pediatriccare.solutions.aap.org

Exclusive AAP practice resources included in your PCO subscription

- ***Bright Futures Tool and Resource Kit*, 2nd Edition**
- ***Caring for Children With ADHD: A Practical Resource Toolkit for Clinicians*, 3rd Edition**
- ***Caring for Children With Autism Spectrum Disorder: A Practical Resource Toolkit for Clinicians*, 3rd Edition**
- **New! COVID-19–RELATED PATIENT HANDOUTS** including 2019 Novel Coronavirus; Social Distancing; Teens & COVID-19; Tips for Coping with a New Baby.
- **New! Ten key handouts translated into 12 languages** including Chinese (Mandarin), Arabic, and Vietnamese.

shopAAP
shop.aap.org

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

90 Years of Caring for Children—1930–2020

Let's work together to give your pediatric heart patients **high quality cardiac care.**

BEST CHILDREN'S HOSPITALS
U.S.News & World Report
CARDIOLOGY & HEART SURGERY
2020–21

As one of the higher-volume heart programs in the nation, Riley Children's Health provides the most comprehensive approach to pediatric cardiovascular care with expertise and options not available everywhere. With a pediatric cardiovascular program ranked 5th nationally by *U.S. News & World Report*, you can trust your patients will be seen by the most highly skilled congenital heart team, providing care that changes everything.

Let's make referral simple. Learn more about our comprehensive pediatric cardiovascular program by calling 317.94.HEART or visiting rileychildrens.org/heart.

Riley Children's Health
Indiana University Health