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Background. A clinical endpoint of moderate-to-severe (M/S) influenza has been proposed in children, defined as fever >39°C, otitis media, lower respiratory tract infection, or serious extrapulmonary manifestations. This definition has not been evaluated against clinically relevant outcomes like hospitalization, emergency room care, antimicrobial use, and child/parental absenteeism.

Methods. We conducted a prospective observational study of children aged 6 months–8 years with influenza at the Children's Hospital Colorado Emergency Department (ED) and its affiliates during two influenza seasons (2016–2017 and 2017–2018). Children with influenza-like-illness (ILI) were enrolled and tested for influenza by polymerase chain reaction (PCR). Parents of influenza cases and matched influenza-negative controls were contacted 2 weeks later for follow-up. The primary outcome was hospitalization for M/S influenza vs. mild influenza. Secondary outcomes included recurrent ED visits, antimicrobial use, child/parental absenteeism. Interim analyses were conducted using SAS v9.4.

Results. Among the 1,480 enrolled children with ILI, 410 (28%) tested positive for influenza by PCR. The median age of influenza cases was 4.0 years (IQR 2.2–6.1), and 20% were considered high-risk for influenza complications. Of influenza cases, 284 (69%) met the definition for M/S influenza. Among M/S influenza subjects, 8.4% were hospitalized, compared with 1.6% with mild influenza (risk difference (RD) 6.9%; 95% CI: 3.0–10.8, $P < 0.01$). Subjects with M/S influenza were more likely to receive antibiotics (RD 12.0%, 95% CI: 3.4–20.6, $P < 0.01$) with a trend to higher antiviral use (RD 6.9%, 95% CI: −0.7–14.5, $P = 0.09$). There was no significant difference for recurrent ED visits nor child/parental absenteeism. After adjusting for comorbidities, age, and influenza strain, the relative risk (RR) of hospitalization or recurrent ED visits was higher among those with M/S influenza vs. mild influenza (RR 2.18, 95% CI: 1.02–4.64, $P = 0.04$).

Conclusion. Children with M/S influenza have a higher risk of hospitalization compared with mild disease. This proposed definition is a useful clinical endpoint to study the public health and clinical impact of influenza interventions in children.

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987. Repeated Exposure to an Adjuvanted Quadrivalent Subunit Influenza Virus Vaccine (aQIV): A Randomized, Observer Blind, Multicenter Study

Wendy Daly, MD[1]; Keith Ramsey, DO[2]; Aino Forsten, MD[3]; Esther Heijnen, MD, PhD[4]; Brett Leav, MD[5]; Janine Oberye, MSc[6]; Bin Zhang, ScD[5]; Filippo Pacciarini, PhD[7] and Timo Vesikari, MD, PhD[8]; [1]Brownsboro Park Pediatrics, Louisville, Kentucky, [2]Jordan Ridge Kids & Teens, West Jordan, Utah, [3]Pori Vaccine Research Clinic, Pori, Finland, [4]Seqirus BV, Amsterdam, Netherlands, [5]Seqirus, Inc., Cambridge, Massachusetts, [6]Seqirus Netherlands BV, Amsterdam, Netherlands, [7]Seqirus S.r.l., Sienna, Italy, [8]Vaccine Research Center, University of Tampere, Tampere, Finland

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Background. The safety, immunogenicity, and efficacy associated with administration of of aQIV in children 6 months through 5 years of age was investigated.[1] Although enhanced immunogenicity in children was demonstrated for MF59-adjuvanted influenza vaccines after first administration, the impact of repeated vaccination on immunogenicity and safety has not been evaluated.

Methods. A total of 607 subjects who participated in parent study, now aged 12 months through 6 years, were enrolled the subsequent year and received a single dose of study vaccine. Enrolled subjects received the same type of influenza vaccine administered in the parent study (aQIV or nonadjuvanted comparator). Blood samples were taken for immunogenicity assessment prior to the second year vaccination, and 21 and 180 days after vaccination.

Results. At baseline, approximately 12 months after vaccination in the parent study, subjects in the aQIV group had significantly greater geometric mean titer (GMT) values against all four homologous strains compared with subjects in the nonadjuvanted vaccine group. After year 2 vaccination, CBER criteria for seroconversion and hemagglutination inhibition (HI) titer ≥1:40 were met for the aQIV group for all four homologous strains tested at Day 22. At both Day 22 and Day 181, subjects who received aQIV had significantly greater GMT values for HI against all four homologous strains compared with those who received nonadjuvanted vaccine. Increased immune response of aQIV vs. nonadjuvanted vaccine was also observed for the selected heterologous strains tested at baseline, Day 22 and Day 181. In terms of safety, transient and generally mild to moderate reactogenicity was more commonly observed in the aQIV group vs. the nonadjuvanted group, but overall safety profiles were similar and comparable to the parent study.

Conclusion. This first-year revaccination study in young children confirms enhanced immunogenicity and similar safety profile after repeat aQIV vaccination compared with repeat nonadjuvanted influenza vaccination.

Reference

1. Vesikari T et al. Lancet Respir Med 2018;6:345–356.

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988. Effectiveness of Seasonal Influenza Vaccines Against Influenza A(H3N2) Illness Among Children Aged <18 Years, US Flu VE Network, 2010–2018

Brendan L. Flannery, PhD[1]; Jessie Chung, MPH[1]; Michael L. Jackson, PhD, MPH[2]; Lisa A. Jackson, MD, MPH, FIDSA[2]; Arnold S. Monto, MD, FIDSA[3]; Emily T. Martin, MPH, PhD[4]; Edward Belongia, MD[5]; Huong McLean, PhD, MPH[5]; Richard K. Zimmerman, MD MPH, FIDSA[6]; Mary Patricia Nowalk, PhD RD[7]; Manjusha Gaglani, MBBS[8]; Marie R. Griffin, MD, MPH[9]; H. Keipp Talbot, MD, MPH[10]; John J. Treanor, MD[11]; Sarah Spencer, PhD[12] and Alicia M. Fry, MD, MPH[1]; [1]Influenza Division, Centers for Disease Control and Prevention, Atlanta, Georgia, [2]Kaiser Permanente Washington Health Research Institute, Seattle, Washington, [3]Department of Epidemiology, University of Michigan School of Public Health, Ann Arbor, Michigan, [4]Epidemiology, University of Michigan School of Public Health, Ann Arbor, Michigan, [5]Marshfield Clinic Research Institute, Marshfield, Wisconsin, [6]University of Pittsburgh, Pittsburgh, Pennsylvania, [7]Family Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania, [8]Pediatrics, Pediatric Infectious Diseases, Baylor Scott & White Health, Texas A&M University Health Science Center College of Medicine, Temple, Texas, [9]Vanderbilt University Medical Center, Nashville, Tennessee, [10]Infectious Diseases, Vanderbilt University Medical Center, Nashville, Tennessee, [11]Medicine, University of Rochester Medical Center School of Medicine and Dentistry, Rochester, New York, [12]Centers for Disease Control and Prevention, Atlanta, Georgia

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Background. Interim estimates of 2017–2018 influenza vaccine effectiveness (VE) against influenza A(H3N2)-related illness in the United States indicated better protection among young children than among older children and adolescents. We examined VE against influenza A(H3N2) illness during five A(H3N2)-predominant seasons from 2010–2011 through 2016–2017 to investigate differences between VE among younger vs. older children.

Methods. We analyzed data from 11,736 outpatients aged <18 years with medically attended acute respiratory illnesses enrolled at US Flu VE Network study sites during five influenza A(H3N2)-predominant seasons. Respiratory specimens from all enrollees were tested for influenza viruses using reverse transcription PCR. Children with documented receipt of the recommended number of doses of current season inactivated influenza vaccine at least 14 days before illness onset were considered fully vaccinated; partially vaccinated children and those who received live attenuated influenza vaccine were excluded. Vaccine effectiveness was estimated as 100 × (1 – adjusted odds ratio) from multivariable logistic regression adjusting for study site, age, sex, presence of high-risk medical conditions, and days from illness onset to enrollment comparing odds of vaccination among A(H3N2)-positive cases vs. influenza-negative controls.

Results. A total of 1,854 influenza A(H3N2) cases and 9,882 influenza-negative controls were included; 494 (28%) influenza A(H3N2) cases and 3,637 (41%) controls were fully vaccinated before illness onset. VE ranged from 26% (95% confidence interval [CI], −17% to 53%) to 60% (38%–75%) among children aged 6 months–4 years and from 9% (−16% to 29%) to 66% (37%–82%) among 5–17 year olds (figure). During 2012–2013 and 2014–2015, A(H3N2) VE estimates were significantly higher among younger compared with older children ($P < 0.05$); in other seasons before 2017–2018, A(H3N2) VE estimates were similar among younger and older children.

Conclusion. Higher VE against A(H3N2) viruses in younger vs. older children in some seasons suggests immunologic differences in response to vaccine components. Overall, inactivated influenza vaccine provided moderate protection against A(H3N2)-related illness among children.

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989. Clinical Effectiveness of High-Dose Trivalent vs. Quadrivalent Influenza Vaccination Among Veterans Health Administration Patients

Yinong Young-Xu, ScD, MS, MA[1,2]; Ellyn Russo, MS[1]; Nabin Neupane, BS[1]; Melissa Lewis, AD[1] and Yuliya Halchenko, MA[1]; [1]Clinical Epidemiology Program, Veterans Affairs Medical Center, White River Junction, Vermont, [2]Department of Psychiatry, Geisel School of Medicine at Dartmouth, Hanover, New Hampshire

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Background. Despite the widespread availability of several injectable inactivated influenza vaccines (IIV), including the trivalent standard-dose (IIV3-SD) and high-dose (IIV3-HD), and the quadrivalent (IIV4), the US Advisory Committee on Immunization Practices does not currently recommend one over another. The objective of this study was to assess the relative vaccine effectiveness (rVE) of IIV3-HD and IIV4 vs. IIV3-SD.

Methods. rVE was estimated from a retrospective cohort study of Veterans aged 65 years and older who received an IIV during the 2014–2015 influenza season.