

Safety of Guidelines Recommending LAIV for Routine Use in Children and Adolescents with Asthma

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Background

- Children and adolescents with asthma are at increased risk for influenza-related morbidity
- Although the prevalence of pediatric asthma is 9%, asthmatics account for at least one-third of pediatric influenza hospitalizations
- In early years of use LAIV was more effective than IIV in preventing influenza in children
- Pre-licensure clinical trials of LAIV found increased risks for wheezing following vaccination
- Risks highest in children under 2 years
- Resulted in asthma or recurrent wheezing listed as a precaution for LAIV
- Starting in 2018-19 influenza season, LAIV is again recommended by ACIP for use in children in adolescents

Natural Experiment in asthmatic children 2-18 years of age

- Two medical groups within HealthPartners with different immunization guidelines starting in 2010
 - PNMS followed ACIP guidelines and gave IIV to asthmatics from 2007 to 2015
 - HPMG in 2011 implemented care guideline recommending LAIV as vaccine of choice for asthmatics
- Instrumental variable
 - Vaccination guideline followed based on medical group
 - Analyzed guideline impact as ratio of ratios (ROR)

Study population

- Age 2- 18 years
- Multiple influenza season per subject
- Continuous enrollment
 - 1 year before immunization (index date)
 - 42 days after immunization
- Diagnosis of asthma based on previous year
 - For age 2-5 years
 - 2 diagnoses of wheezing, 786.07, respiratory distress, 786.09, bronchiolitis or asthma, 486.xx
 - For age 5-18
 - 2 diagnoses of asthma , 486.xx
- Exclusions
 - Pregnancy or any immune suppression
 - Hospital or ED encounter for a lower respiratory event in 42 days prior to immunization

Study Design

- Pre and Post guideline implementation
 - Pre-implementation: 2007-08 to 2009-10 influenza seasons
 - Both groups used IIV preferentially
 - Post-implementation: 2010-11 to 2014-15 influenza seasons
 - PNMS IIV preferentially
 - HPMG LAIV preferentially
- Intention to treat analysis (by medical group)
 - Pre and post guideline implementation for asthmatic children and adolescents in both medical groups
 - Ratio of ratios analytic approach

Data

Data Source

- Medical records and administrative data

Outcomes

All LREs (ICD-9 codes 466.x, 490, 493.x, 518.81, 518.82, 518.84, 519.11, 786.00, .05-.07, .09 (asthma, wheezing, bronchiolitis)

- Observation periods
 - Day 1-42 outpatient
 - Day 0-42 urgent care, ED and inpatient
 - Day 1-21 outpatient
 - Day 0-21 urgent care, ED, and inpatient
- Algorithm developed to determine asthma exacerbation versus asthma management visits for ambulatory visits

Covariates

- Sociodemographics (sex, age, race, government payer, neighborhood income, neighborhood asthma rate, use of interpreter)
- Asthma classification
 - Intermittent or persistent (algorithm developed)
 - Controlled or not controlled (algorithm developed)

Analytic approach

- Ratio of ratio (ROR) approach was used to estimate the LAIV guideline impact
- A generalized linear model with a Poisson distribution and accounting for multiple seasons per subject was used.
- Models included age and asthma classification variables
- Analysis was performed for the overall population and for children age 2 through 4 years and 5 through 18.

Characteristics of asthmatic children, Pre- and Post-Guideline by medical group, n= 4824 unique children

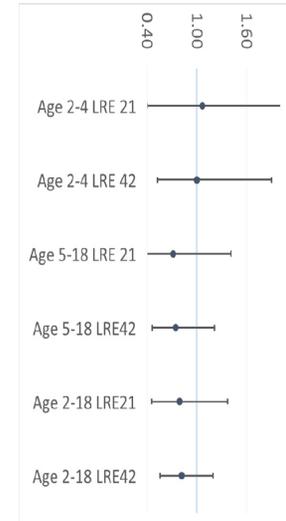
	HPMG		PNMS	
	Pre-Guideline	Post-Guideline	Pre-Guideline	Post-Guideline
Influenza seasons	2007-08 2008-09 2009-10	2010-11 2011-12 2012-13 2013-14 2014-15	2007-08 2008-09 2009-10	2010-11 2011-12 2012-13 2013-14 2014-15
Unique patients	1,755	2,825	587	854
Female	715(41)	1172(42)	715(41)	341(40)
Asian	140(8.0)	264(9.3)	48(8.2)	65(7.6)
Black/African American	379(22)	663(24.0)	90(15)	122(14)
Hispanic	106(6.0)	172(6.1)	27(4.6)	34(4.0)
Other	76(4.3)	119(4.2)	31(5.3)	35(4.1)
White	1054(60)	1607(57)	391(67)	598(70)
Use of Interpreter	24(1.4)	61(2.2)	13(2.2)	11(1.3)
Medicaid	340(19)	809(29)	109(19)	150(18)

Characteristics of asthmatic children seasons, Pre- and Post-Guideline by medical group, n= 7957 child-seasons

	HPMG		PNMS	
	Pre-Guideline	Post-Guideline	Pre-Guideline	Post-Guideline
Child-seasons	2239	3822	748	1148
Age groups				
2-4	640(29)	1083(28)	271(36)	290(25)
5-11	876(39)	1554(41)	269(36)	500(44)
12-18	723(32)	1185(31)	208(28)	358(31)
Received LAIV	522(24)	2576(67)	50(6.7)	128(11)
Mean asthma rate in neighborhood +SD	32.8+20.2	34.2+21.1	29.5+22.0	30.0+19.9
Mean Median Family income in neighborhood (1000) +SD	83.1+30.0	79.1+29.9	97.0+35.4	98.7+35.7
Preventive Care	1370(61)	2338(61)	440(59)	635(55)
Intermittent Asthma	1147(51)	2270(59)	358(48)	566(49)
Controlled Asthma	1796(80)	3091(81)	553(74)	894(78)

* Children counted once per period and medical group; Children may be included in both medical groups or across periods

Adjusted ROR (95%CI)



ROR adjusted for age and intermittent and controlled asthma

Discussion

- We did not observe increased visits for wheezing or LREs with a guideline recommending LAIV for use in all asthmatic children and adolescents
- Limitations
 - Only one geographic area
 - Electronic algorithms can be prone to misclassification of asthma control and severity
 - Retrospective study, may have missed asthma or wheezing events if no insurance claim, outside of our health system, or managed at home
 - Underpowered to conduct sub-group analyses
- Strengths
 - Pre/post ratio of ratios design minimizes bias due to confounding or secular trends
- Policy Implications
 - Guidelines for influenza vaccination in asthmatic children should be based on effectiveness studies



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