



Pediatric outpatient ARI visits and antibiotic use attributable to serotypes in higher valency PCVs

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Disclosures

- Laura King has received consulting fees from Merck for unrelated work.
- Joseph Lewnard has received consulting fees and grants from Pfizer, Merck, and VaxCyte for related and unrelated work.
- All other authors report no conflicts.

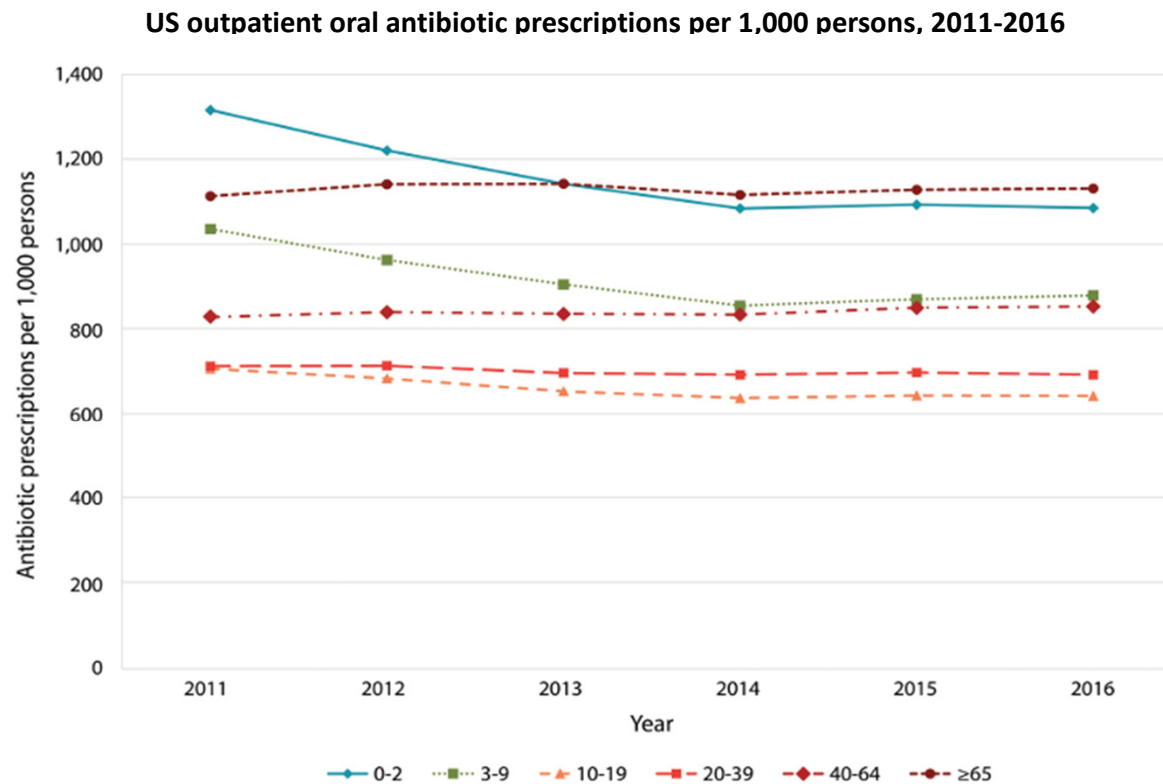
Overview

- Background and study objective
- Pediatric outpatient visit and antibiotic prescription incidence
- Acute otitis media vaccine serotype attributable proportion and incidence
- Sinusitis and pneumonia vaccine serotype attributable proportion and incidence
- Summary and conclusions

Outpatient respiratory infections: a sizeable burden

- ~1,200 acute respiratory infection (ARI) visits per 1,000 children in a commercially-insured population in 2018¹
- ~250 ARI-associated antibiotic prescriptions per 1,000 children issued from doctor's offices and emergency departments in the US annually (2014-15)²
- Limited knowledge of the proportion of ARI visits and antibiotic prescriptions attributable to *Streptococcus pneumoniae*

Reductions in antibiotic use concurrent with PCV uptake



Study objective

Visits and antibiotic prescriptions attributable to additional serotypes in higher-valency PCVs =

Incidence of all cause
pediatric outpatient visits
and antibiotic prescriptions
for AOM, pneumonia, and
sinusitis



Proportion of outpatient
disease caused by *S.*
pneumoniae PCV15 13 and
PCV20 13 serotypes*

*PCV15-13/PCV20-13 serotypes: serotypes in PCV15/PCV20 not in PCV13

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Proportion of outpatient
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All-cause incidence estimation methods

Setting	Data source for number of visits and antibiotics	Data source for person years at risk
Physician offices	NAMCS 2016, 2018	US Census 2016, 2018
Emergency departments	NHAMCS 2016, 2018	US Census 2016, 2018
Alternative outpatient settings	MarketScan Commercial and Medicaid Databases 2016-2018	MarketScan Commercial and Medicaid Databases 2016-2018

Total incidence = incidence in physician offices and emergency departments + incidence in all other outpatient settings

All-cause visit and antibiotic prescription incidence in children by condition

Condition	Outpatient visits per 1000 person-years (95% CI)	Antibiotic prescriptions per 1000 person-years (95% CI)
AOM	146 (116, 180)	124 (103, 149)
Sinusitis	40 (27, 58)	39 (24, 60)
Pneumonia	21 (14, 30)	17 (13, 21)
Total	208 (168, 254)	181 (148, 218)

Visits and antibiotic prescriptions attributable to additional serotypes in higher-valency PCVs =

Incidence of pediatric outpatient visits and antibiotic prescriptions for AOM, pneumonia, and sinusitis



Proportion of outpatient disease caused by *S. pneumoniae* PCV15 13 and PCV20 13 serotypes

Challenges in estimating the proportion of outpatient disease caused by *S. pneumoniae*

- Children frequently colonized with pneumococcus
- Samples not regularly obtained from infection site in outpatient disease
- Few studies conducted for non-AOM ARIs in pediatric outpatients

Proportion and incidence of outpatient AOM caused by PCV15-13 and PCV20-13 serotypes

Three approaches to estimating PCV15-13 and PCV20-13 attributable proportions in [AOM](#)

1. Vaccine probe: use vaccine effectiveness against disease associated with all etiologies to estimate attributable proportion
2. Pneumococcal prevalence and serotype distribution from middle ear fluid in children with AOM
3. Differential nasopharyngeal (NP) carriage between sick and healthy children and NP carriage serotype distribution in children with AOM

AOM pneumococcal and vaccine serotype attributable percents

Method	AOM attributable percent (95% CI)		
	All pneumococcal serotypes	PCV15-13 serotypes	PCV20-13 serotypes
Vaccine probe	16.7 (4.3, 41.9)	0.9 (0.2, 2.3)	4.5 (1.1, 11.5)
Middle ear fluid	22.3 (17.1, 27.5)	1.0 (0.7, 1.4)	5.1 (3.9, 6.4)
Differential NP carriage	14.0 (2.0, 26.0)	0.7 (0.1, 1.5)	3.7 (0.5, 7.1)

Estimated pediatric outpatient visits for AOM attributable to PCV15-13 and PCV20-13 serotypes

Method	Incidence per 1000 person-years (95% CI)		Annual number in thousands* (95% CI)	
	PCV15-13 serotypes	PCV20-13 serotypes	PCV15-13 serotypes	PCV20-13 serotypes
Vaccine probe	1.3 (0.3, 3.5)	6.5 (1.6, 17.1)	92 (23, 257)	477 (121, 1,251)
Middle ear fluid	1.5 (1.0, 2.2)	7.4 (5.2, 10.2)	109 (72, 161)	543 (381, 747)
Differential NP carriage	1.0 (0.1, 2.2)	5.4 (0.8, 10.7)	76 (11, 165)	397 (56, 787)

**Estimated using 2018 census estimate for children <18 years*

Estimated pediatric outpatient antibiotic prescriptions for AOM attributable to PCV15-13 and PCV20-13 serotypes

Method	Incidence per 1000 person-years (95% CI)		Annual number in thousands* (95% CI)	
	PCV15-13 serotypes	PCV20-13 serotypes	PCV15-13 serotypes	PCV20-13 serotypes
Vaccine probe	1.1 (0.3, 3.0)	5.6 (1.4, 14.5)	79 (19, 217)	408 (104, 1,065)
Middle ear fluid	1.3 (0.9, 1.8)	6.3 (4.5, 8.5)	93 (63, 135)	464 (333, 626)
Differential NP carriage	0.9 (0.1, 1.9)	4.6 (0.7, 9.1)	65 (9, 139)	340 (48, 666)

**Estimated using 2018 census estimate for children <18 years*

Proportion and incidence of outpatient pneumonia and sinusitis caused by PCV15-13 and PCV20-13 serotypes

Two approaches to estimating PCV15-13 and PCV20-13 attributable proportions in pneumonia and sinusitis

1. Vaccine probe: use vaccine effectiveness to estimate attributable proportion
2. Differential NP carriage between sick and healthy children and NP carriage serotype distribution in children with AOM

Pneumonia pneumococcal and vaccine serotype attributable percents

Method	Pneumonia attributable percent (95% CI)		
	All pneumococcal serotypes	PCV15-13 serotypes	PCV20-13 serotypes
Vaccine probe	18.2 (12.5, 27.3)	0.9 (0.5, 1.5)	4.4 (2.9, 6.7)
Differential NP carriage	11.8 (1.0, 22.7)	0.6 (0.0, 1.2)	2.8 (0.2, 5.5)

Estimated pneumonia pediatric outpatient visits and antibiotic prescriptions attributable to PCV15-13 and PCV20-13 serotypes

Outcome	Method	Incidence per 1000 person-years (95% CI)		Annual number in thousands* (95% CI)	
		PCV15-13 serotypes	PCV20-13 serotypes	PCV15-13 serotypes	PCV20-13 serotypes
Outpatient visits	Vaccine probe	0.2 (0.1, 0.4)	0.9 (0.5, 1.6)	14 (7, 26)	68 (39, 118)
	Differential NP carriage	0.1 (0.0, 0.3)	0.6 (0.1, 1.3)	9 (1, 21)	43 (4, 95)
Antibiotic prescriptions	Vaccine probe	0.1 (0.1, 0.3)	0.7 (0.5, 1.2)	11 (6, 19)	53 (34, 86)
	Differential NP carriage	0.1 (0.0, 0.2)	0.5 (0.0, 1.0)	7 (1, 15)	34 (3, 70)

*Estimated using 2018 census estimate for children <18 years

Sinusitis pneumococcal and vaccine serotype attributable percents

Method	Sinusitis attributable percent (95% CI)		
	All pneumococcal serotypes	PCV15-13 serotypes	PCV20-13 serotypes
Vaccine probe	30.6 (21.0, 45.8)	1.5 (0.9, 2.5)	7.3 (4.9, 11.2)
Differential NP carriage	11.8 (1.0, 22.7)	0.6 (0.0, 1.2)	2.8 (0.2, 5.5)

Estimated [sinusitis](#) pediatric outpatient visits and antibiotic prescriptions attributable to PCV15-13 and PCV20-13 serotypes

Outcome	Method	Incidence per 1000 person-years (95% CI)		Annual number in thousands* (95% CI)	
		PCV15-13 serotypes	PCV20-13 serotypes	PCV15-13 serotypes	PCV20-13 serotypes
Outpatient visits	Vaccine probe	0.6 (0.3, 1.2)	2.9 (1.7, 5.2)	44 (23, 85)	216 (122, 381)
	Differential NP carriage	0.2 (0.0, 0.5)	1.1 (0.1, 2.5)	17 (1, 40)	82 (7, 180)
Antibiotic prescriptions	Vaccine probe	0.6 (0.3, 1.2)	2.9 (1.5, 5.2)	43 (21, 85)	209 (112, 384)
	Differential NP carriage	0.2 (0.0, 0.5)	1.1 (0.1, 2.5)	16 (1, 39)	79 (7, 181)

*Estimated using 2018 census estimate for children <18 years

Summary and conclusions

Point estimate ranges: attributable percent,
number visits, number antibiotic prescriptions

Condition	PCV15-13 serotypes			PCV20-13 serotypes		
	Attributable percent of outpatient disease	Annual no., in thousands		Attributable percent of outpatient disease	Annual no., in thousands	
		Outpatient visits	Antibiotic prescriptions		Outpatient visits	Antibiotic prescriptions
AOM	0.7–1.0	76–109	65–93	3.7–5.1	397–543	340–464
Pneumonia	0.6–0.9	9–14	7–11	2.8–4.4	43–68	34–53
Sinusitis	0.6–1.5	17–44	16–43	2.8–7.3	82–216	79–209
Total*	1.9–3.4	103–168	90–148	9.4–16.8	527–831	458–731

**Individual condition ranges may not sum to total ranges due to simulation methods and rounding*

Study limitations

- Pneumococcal attributable percent, serotype distribution, and vaccine effectiveness estimates based on published data
- Limited data for attributable proportion and serotype distribution in sinusitis and pneumonia
- All-cause incidence data from 2016-2018
- Assumed healthcare utilization constant across serotypes

Conclusions

- Additional serotypes included in higher-valency PCVs account for ~100–830 thousand outpatient visits and ~90–730 thousand antibiotic prescriptions for AOM, pneumonia, and sinusitis among US children annually.
 - PCV15-13 serotypes: 103–168K visits and 90–148K antibiotic prescriptions
 - PCV20-13 serotypes: 527–831K visits and 458–731K antibiotic prescriptions
- The estimated incidence of pediatric outpatient visits and antibiotic prescriptions attributable to PCV20-13 serotypes is **4 – 5 times** the incidence attributable to PCV15-13 serotypes.

Project team

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