

Supplemental Digital Content 1: Antibiotic resistance, serotypes and nasopharyngeal carriage of *Streptococcus pneumoniae* (Sp), *Haemophilus influenzae* (Hi) and *Moraxella catarrhalis* (Mc) strains in children with acute otitis media (AOM) in the pre-PCV7, non-generalized PCV7, PCV7, transition and PCV13 periods.

Nasopharyngeal carriage	Pre-PCV7 period 2001-2002 n = 1236 n (%)	Non- generalized PCV7 period 2003-2005 n = 2030 n (%)	PCV7 period 2006-2010 n = 4268 n (%)	Transition PCV7- PCV13 period 2011-2012 n = 1790 n (%)	PCV13 period ≥ 2013 n = 3649 n (%)	P-value
Sp carriage	867 (70.1)^b	1229 (60.5)^b	2488 (58.3)	976 (54.5)	1994 (54.6)	<0.001
Penicillin-susceptible	299 (34.5)	661 (53.8)	1324 (53.2)	608 (62.3)	1274 (63.9)	<0.001
Penicillin–intermediate-resistant	556 (64.1)	560 (45.6)	1155 (46.4)	365 (37.4)	705 (35.4)	<0.001
Penicillin-resistant	12 (1.4)	8 (0.7)	9 (0.4)	3 (0.3)	15 (0.8)	<0.001
Penicillin–non-susceptible	568 (65.5)	568 (46.2)	1164 (46.8)	368 (37.7)	720 (36.1)	<0.001
Erythromycin-susceptible	311 (35.9)	607 (49.4)	1312 (52.8)	659 (67.5)	1505 (75.5)	<0.001

Erythromycin–intermediate-resistant	46 (5.3)	28 (2.3)	32 (1.3)	3 (0.3)	3 (0.1)	< 0.001
Erythromycin -resistant	508 (58.7)	593 (48.3)	1142 (45.9)	314 (32.2)	485 (24.3)	< 0.001
PCV7 vaccine types ^a	535 (61.8)	452 (36.8)	208 (8.4)	31 (3.2)	58 (2.9)	< 0.001
PCV13 vaccine types + 6C ^a	742 (86.7)	831 (67.6)	1089 (43.9)	159 (16.3)	165 (8.3)	< 0.001
Additional serotypes + 6C ^a	207 (23.9)	379 (30.8)	881 (35.5)	128 (13.1)	107 (5.4)	< 0.001
Non-PCV13 and non-6C serotypes ^a	124 (14.3)	398 (32.4)	1389 (56.1)	816 (83.7)	1823 (91.7)	< 0.001
Unknown serotypes	1 (0.1)	0 (0)	10 (0.4)	1 (0.1)	6 (0.3)	0.12
Hi carriage			2115 (49.6)	935 (52.2)	1918 (52.6)	0.02
NT Hi strains ^a			2101 (99.3)	934 (99.9)	1918 (100.0)	< 0.001
β–lactamase-producing			324 (12.5)	116 (12.4)	357 (18.6)	< 0.001
BLNAR +			168 (7.2)	73 (7.9)	115 (6.2)	0.23
β-lactamase + BLNAR -			292 (13.8)	110 (11.8)	326 (17.0)	< 0.001
β-lactamase + BLNAR +			32 (1.5)	6 (0.6)	30 (1.6)	0.11
β-lactamase - BLNAR +			136 (6.4)	67 (7.2)	85 (4.4)	0.004
β-lactamase - BLNAR -			1654 (78.2)	751 (80.4)	1473 (76.9)	0.11
Hi or Sp			3414 (80.0)	1419 (79.3)	2859 (78.3)	0.20

Hi and Sp	1189 (27.8)	492 (27.5)	1053 (28.8)	0.48
Mc carriage	2512 (58.9)	922 (51.5)	2065 (56.6)	<0.001
β-lactamase-producing	2505 (99.7)	911 (98.9)	2033 (98.5)	<0.001

PCV7: 7-valent pneumococcal conjugate vaccine, PCV13: 13-valent pneumococcal conjugate vaccine, NT: non-typable, BLNAR: β-lactamase–negative, ampicillin-resistant

^a on available serotypes; ^b in the pre-PCV7 and non-generalized PCV7 periods, children were enrolled only if they had AOM with fever and/or otalgia