

▶ Evaluation of the use of
the 10-valent
pneumococcal conjugate
vaccine in Brazil

9th International Global Health Conference

May 2019

Pneumococcal vaccine

- ▶ Country Characteristics and National Immunization Program
- ▶ Vaccine type and schedule
- ▶ Vaccination Coverage
- ▶ Effectiveness
 - ▶ Control case
 - ▶ Cases only
- ▶ Surveillance data
 - ▶ Meningitis
 - ▶ Pneumonia
 - ▶ Serotypes



Largest country in South America

27 states and 5 regions

5565 municipalities

Population in 2010: 192 million

Birth cohort: 2700000

75% Lives in urban areas

Features National Immunization Program

- ▶ Completely free program
Participation of the three levels of government: federal, state and municipal
Vaccination rooms: 37731
Municipal units: 32183
Private Units: 1420
State Units: 582
Federal Units: 449
Special Immunobiology Center: 23

Vaccines of the National Immunization Program

▶ Children

- ▶ BCG
- Hepatitis B
- Pentavalent/DTP
- VIP / VOP
- Rotavirus
- Meningococcus C
- Pneumococcal 10-valent
- Yellow fever
- Hepatitis A
- MMR
- Varicella
- Influenza

▶ Adolescents

- HPV
- Meningococcus C
- dT (adult)

▶ Elderly

- Influenza
- DT (adult)

▶ Pregnant women

- Influenza
- dTP acellular
- dT (adult)

10-valent pneumococcal conjugate vaccine (Synflorix -GSK)

- ▶ Introduced in the national calendar in 2010

Recommended Calendar

2 doses in children under one year (2 and 4 months)

1 booster dose at 12 months of age

1 dose for children 2 to 4 years of age for children who have not received any dose previously

Vaccination coverage

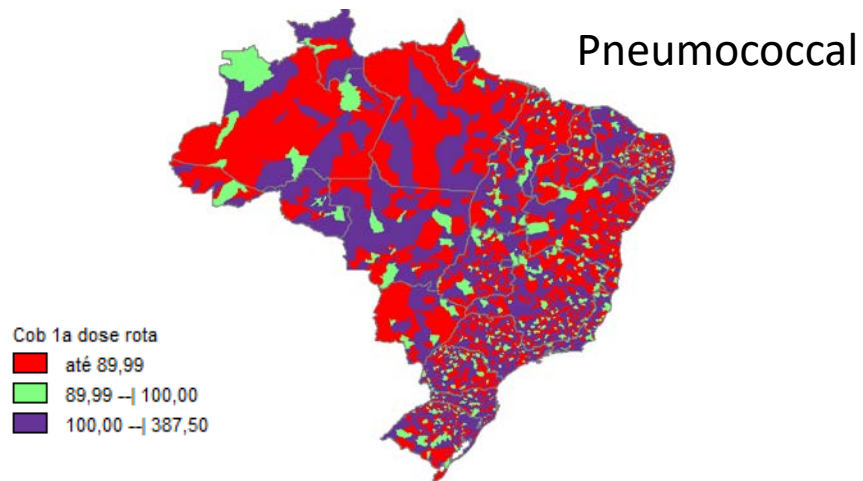
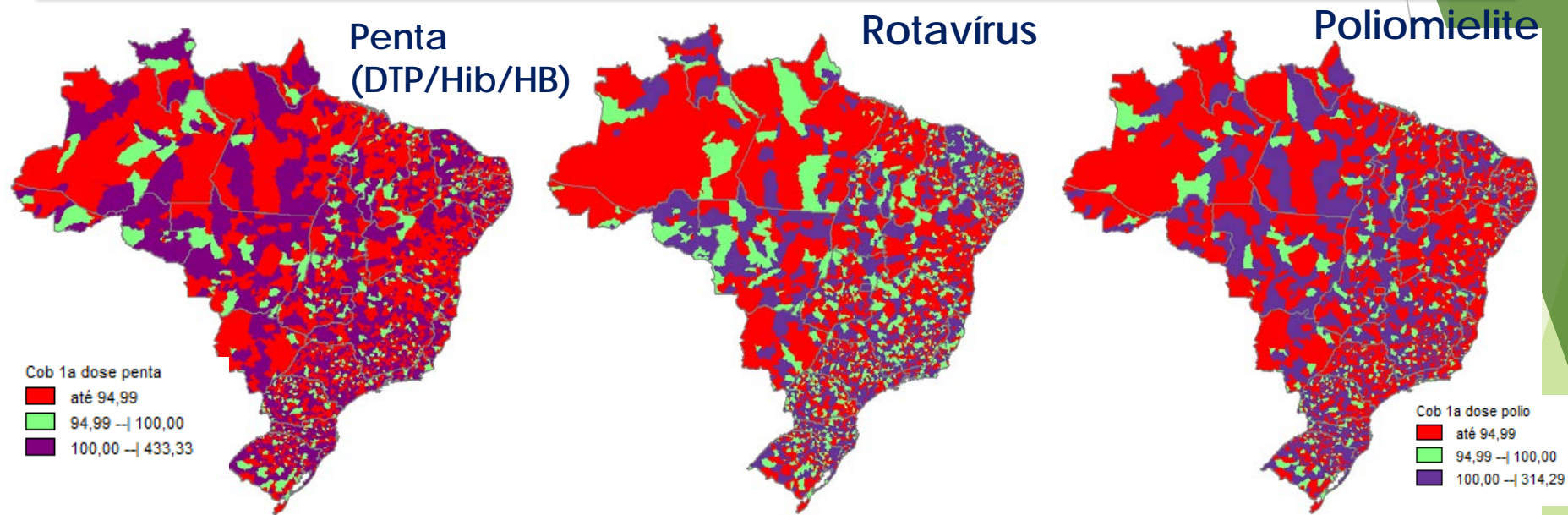
Vaccination coverage - 10-valent pneumococcal conjugate vaccine according to age and year. Brazil, 2011-2018

Year	< 1 year	Booster dose
2011	81.7	
2012	88.4	
2013	93.6	93.1
2014	93.5	88.0
2015	94.2	88.4
2016	95.0	84.1
2017	91.1	74.8
2018	87.2	61.2

Homogeneity of 10-valent pneumococcal conjugate vaccine second year. Brazil, 2011-2017

Year	Homogeneity
2011	47.0
2012	49.3
2013	56.8
2014	48.8
2015	60.7
2016	59.5
2017	54.5

Simultaneous vaccine versus vaccine coverage (Dose 1) 2016 BRAZIL

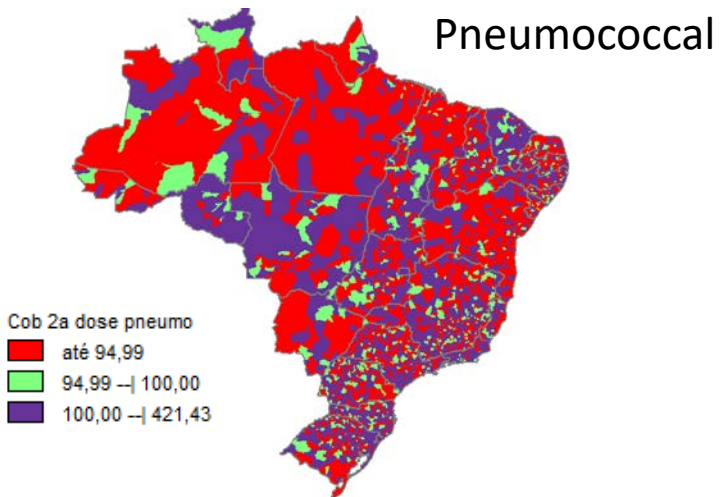
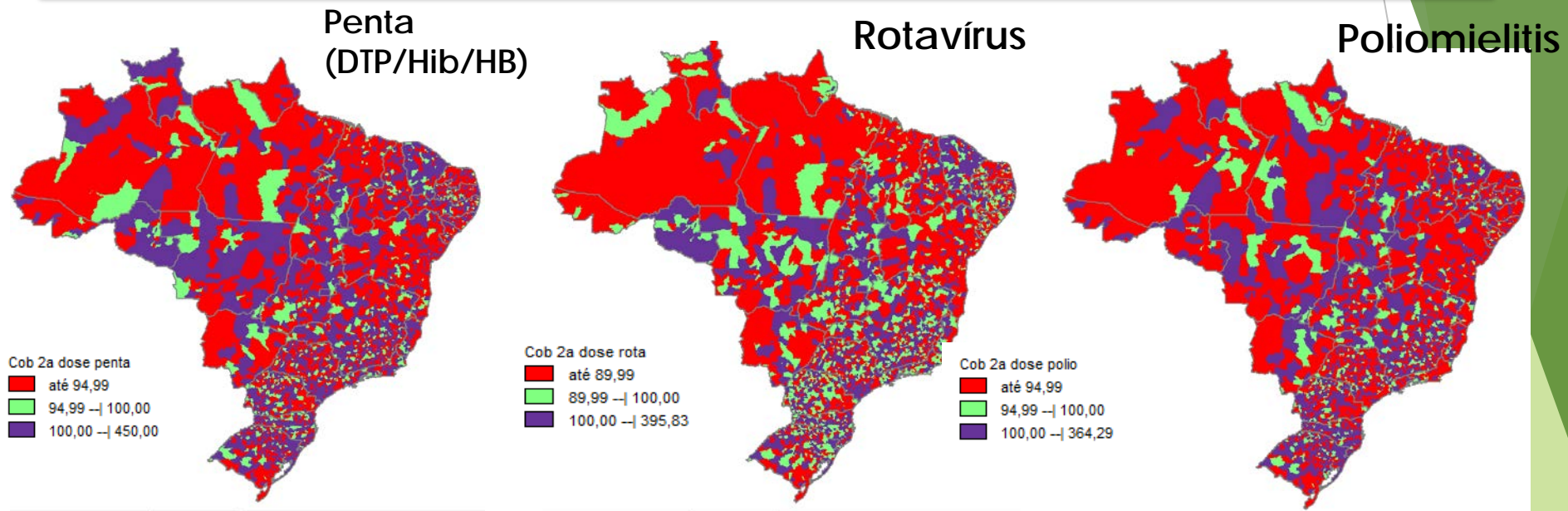


Recommended at 2 months

Vaccine / age (2 months)	Dose No. (Coverage)
Penta (DTP/Hib/HB)	2.858.165 (96,0%)
Poliomielitis	2.515.165 (84,5%)
Pneumococcal	2.875.460 (96,6%)
Rotavírus	2.709.804 (91,0%)

Simultaneous vaccine versus vaccine coverage (Dose 2) 2016

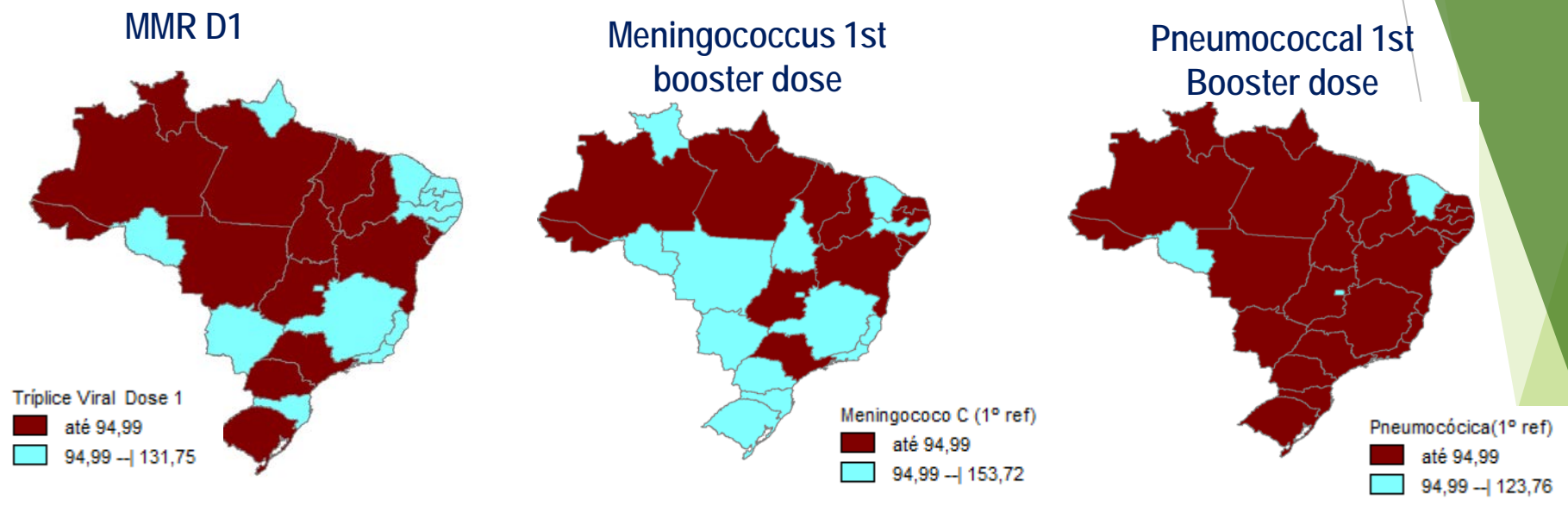
BRAZIL



Recommended at 4 months

Vaccine / age (4 months)	Dose No. (Coverage)
Penta (DTP/Hib/HB)	2.798.015 (94,0%)
Poliomielitis	2.490.621 (83,6%)
Pneumococcal	2.875.460 (95,3%)
Rotavírus	2.709.804 (95,3%)

Simultaneous vaccine versus vaccine coverage (Booster dose) 2016 BRAZIL



Recommended at 12 months

Vaccine / age (12 months)	Doses (Coverage)
<i>Pneumococcal</i>	2.502.837 (84,09%)
<i>Meningococcus C</i>	2.792.904 (93,83%)
<i>MMR</i>	2.839.093 (95,39%)

Epidemiological studies

	Exposure*	Contributing strata†	Crude effectiveness (95% CI)	Adjusted effectiveness (95% CI)‡
Overall				
Vaccine-type invasive pneumococcal disease§	Up to date for age for number of PCV10 doses	61/147	86.5% (73.2 to 93.2)	83.8% (65.9 to 92.3)
Vaccine-related invasive pneumococcal disease¶	Up to date for age for number of PCV10 doses	21/75	83.7% (58.7 to 93.6)	77.9% (41.0 to 91.7)
Non-vaccine-type invasive pneumococcal disease	Up to date for age for number of PCV10 doses	18/94	25.4% (-79.2 to 68.9)	37.5% (-65.4 to 76.4)
Children eligible for one catch-up dose at 12-23 months**				
Vaccine-type invasive pneumococcal disease	One dose	29/44	70.3% (24.0 to 88.4)	68.0% (17.6 to 87.6)
Vaccine-related invasive pneumococcal disease	One dose	11/15	51.0% (-103.1 to 88.2)	40.6% (-190.2 to 87.8)
Non-vaccine-type invasive pneumococcal disease	One dose	6/10	-94.9% (-1047.3 to 66.9)	-72.6% (-972.1 to 72.2)
Overall by number of doses††				
Vaccine-type invasive pneumococcal disease	At least one dose	78/147	83.7% (70.1 to 91.2)	81.9% (64.4 to 90.8)
Vaccine-type invasive pneumococcal disease	Two doses	15/124	90.5% (72.4 to 96.7)	89.9% (64.1 to 96.6)
Vaccine-type invasive pneumococcal disease	At least two doses	17/124	96.6% (88.6 to 99.0)	95.9% (84.0 to 98.9)
Vaccine-type invasive pneumococcal disease	Three doses	4/108	97.5% (87.2 to 99.5)	96.4% (80.2 to 99.3)
Vaccine-type invasive pneumococcal disease	At least three doses	5/108	96.7% (86.1 to 99.2)	95.4% (78.1 to 99.0)
Vaccine-type invasive pneumococcal disease	Four doses	1/80	73.5% (-20.4 to 94.2)	67.7% (-58.0 to 93.4)
Overall by clinical syndrome				
Pneumonia or bacteraemia (vaccine-type)	Up to date for age for number of PCV10 doses	26/75	88.2% (67.1 to 95.7)	81.3% (46.9 to 93.4)
Meningitis (vaccine-type)	Up to date for age for number of PCV10 doses	35/72	85.1% (61.6 to 94.2)	87.7% (61.4 to 96.1)
Invasive pneumococcal disease due to individual serotypes				
14	Up to date for age for number of PCV10 doses	29/72	87.2% (61.8 to 95.7)	87.7% (60.8 to 96.1)
6B	Up to date for age for number of PCV10 doses	11/32	87.5% (47.2 to 97.1)	82.8% (23.8 to 96.1)
19A	Up to date for age for number of PCV10 doses	9/26	90.2% (56.5 to 97.8)	82.2% (10.7 to 96.4)
3	Up to date for age for number of PCV10 doses	9/28	5.5% (-278.4 to 76.4)	7.8% (-271.9 to 77.1)
6A	Up to date for age for number of PCV10 doses	6/24	36.3% (-184.4 to 85.7)	14.7% (-311.6 to 82.3)
23F	Up to date for age for number of PCV10 doses	9/18	85.6% (7.7 to 97.7)	57.8% (-336.7 to 95.9)
PCV7 serotypes‡‡	Up to date for age for number of PCV10 doses	61/146	86.5% (73.2 to 93.2)	83.2% (64.7 to 92.1)

Indirect cohort analysis of 10-valent pneumococcal conjugate vaccine effectiveness against vaccine-type and vaccine-related invasive pneumococcal disease

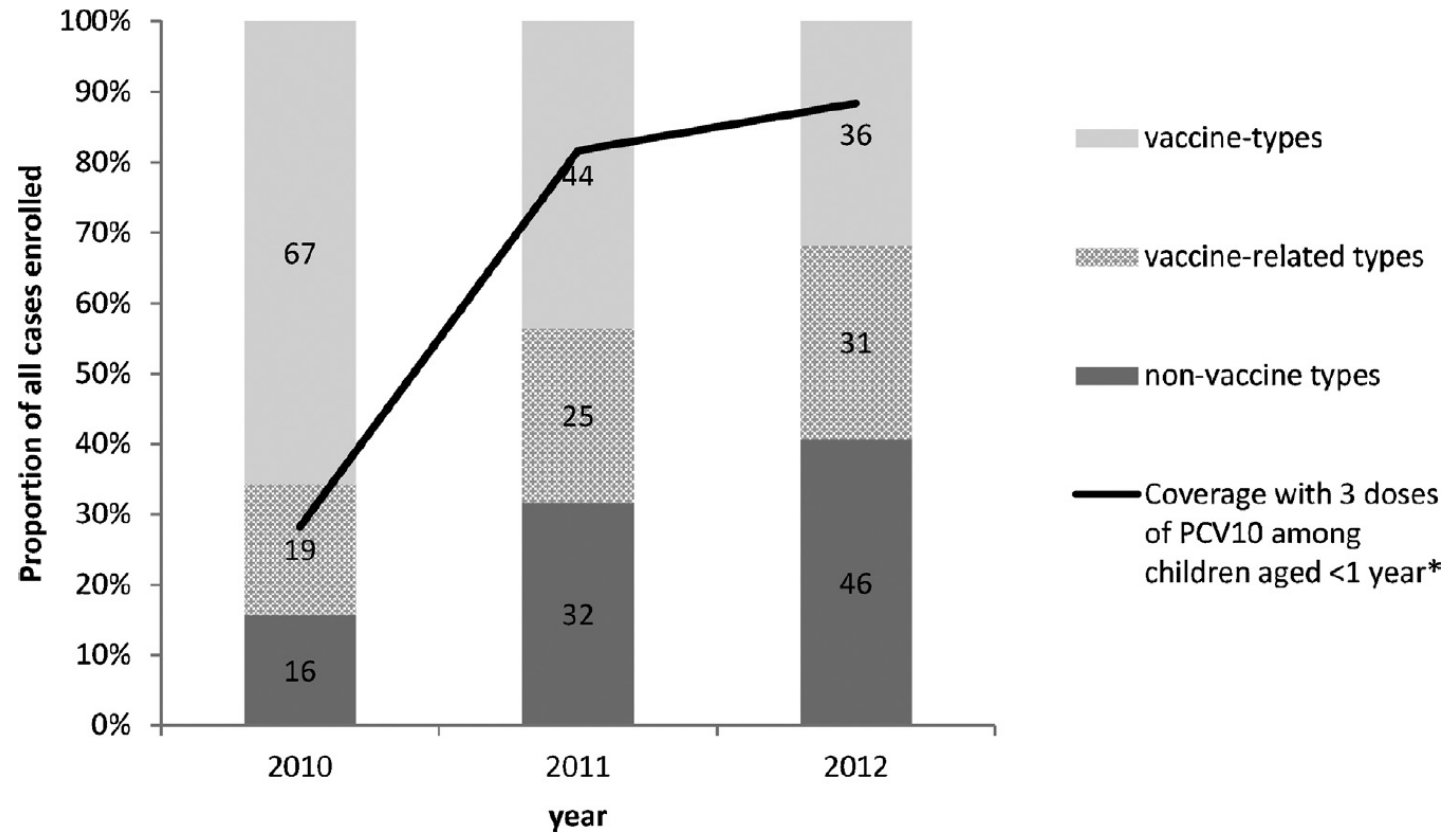


Fig. 1. Proportion of invasive pneumococcal disease cases due to vaccine serotypes, vaccine-related serotypes and non-vaccine serotypes enrolled in study by year and coverage with 3 doses of PCV10 among children aged <1 year. The numbers within each section of the bar represent the number of isolates. *National coverage data for 3 doses of PCV10 among children aged <1 year obtained from <http://pni.datasus.gov.br>.

Table 2Crude and adjusted estimates of PCV10 effectiveness against invasive pneumococcal disease for ≥ 1 doses and for up-to-date schedule for age^a

Serotype	Cases with ≥ 1 dose PCV10/total (%)	Effectiveness ≥ 1 doses		Cases UTD for PCV10/total (%)	Effectiveness up-to-date schedule ^b	
		Crude	Adjusted ^c		Crude	Adjusted ^c
Vaccine-types	61/147 (41.5)	85.4 (72.7, 92.3)	72.8 (44.1, 86.7)	32/147 (21.8)	85.1 (69.8, 92.7)	73.9 (41.9, 88.3)
Vaccine-related types	48/75 (64.0)	63.5 (25.4, 82.2)	61.3 (14.5, 82.5)	22/75 (29.3)	67.4 (26.9, 85.5)	64.8 (15.3, 85.4)
<i>Individual vaccine serotypes</i>						
14	28/72 (38.9)	86.9 (73.3, 93.6)	75.4 (43.2, 89.4)	16/72 (22.2)	85.5 (67.2, 93.6)	75.8 (37.4, 90.7)
6B	16/32 (50.0)	79.5 (50.7, 91.5)	69.7 (16.5, 89.0)	9/32 (28.1)	77.5 (38.7, 91.7)	65.0 (-8.5, 88.7)
23F	7/18 (38.9)	86.9 (61.2, 95.6)	76.6 (14.6, 93.6)	2/18 (11.1)	92.7 (63.5, 98.6)	86.6 (22.9, 97.7)
18C	6/9 (33.3)	89.7 (54.6, 97.7)	86.6 (30.6, 97.4)	3/9 (33.3)	80.0 (10.2, 95.5)	76.4 (-26.3, 95.6)
19F	4/8 (50.0)	79.5 (9.3, 95.4)	46.3 (-253.1, 91.8)	1/8 (12.5)	90.0 (3.5, 99.0)	77.6 (-188.9, 98.3)
<i>Individual vaccine-related serotypes</i>						
19A	15/26 (57.7)	72.0 (28.0, 89.1)	71.3 (16.6, 90.1)	12/26 (38.5)	63.6 (-2.3, 87.1)	63.4 (-16.8, 88.6)
6A	16/24 (66.7)	59.0 (-12.1, 85.0)	51.0 (-52.2, 84.2)	6/24 (25.0)	70.0 (-0.3, 91.0)	62.2 (-42.2, 89.9)

^a 0 doses used as reference group for all analyses.^b Partially vaccinated were excluded from the analysis of the effectiveness of an up-to-date schedule.^c Adjusted for date of admission/medical attention, age at illness, day care attendance and receipt of at least one diphtheria–tetanus–pertussis vaccine dose.

Impact assessment

- ▶ Early efficacy for community-based pneumonia Goiânia, Brazil
Cross-sectional study comparing vaccinated and non-vaccinated children 6 to 9 months post-introduction
Community-acquired pneumonia
Effectiveness of vaccination 40%, 95% CI 1.4 - 63.2

Hospitalization due to pneumonia from 0 to 2 years old, 2005 -2011
- ▶ High vaccination coverage
Belo Horizonte -40.3 95% CI -50.9 to -27.4
Curitiba -37.6 95% CI - 49.6 to -22.7
Recife - 49.3 95% CI -61.6 a - 33.1
- ▶ Low vaccination coverage
São Paulo -13.4 95% CI 26.0 to 1.4
Porto Alegre -23.5 95% CI -41.6 a 0.2

Table 1. Distribution of invasive *Streptococcus pneumoniae* serotype 19A (n = 673) by age group (<5 years, 5–49 years and ≥50 years) in the pre-PCV10 period (2005–2009) and in the post-PCV10 periods (2011–2015 and 2016–2017).

Age group	Spn	2005–2009†	2011–2015†		2016–2017		χ^2 for trend	<i>p</i> -value
		no. (%)	no. (%)	% change*	no. (%)	% change*		
<5 years	19A	44 (3.2)	126 (15.5)	384.7	92 (31.2)	875.3	230.0	<0.001
	total	1,376	813		295			
5–49 years	19A	43 (2.5)	104 (5.2)	106.6	87 (14.7)	484.1	105.1	<0.001
	total	1,712	2,004		593			
≥50 years	19A	17 (2.5)	87 (5.1)	106.3	73 (11.3)	359.9	54.8	<0.001
	total	693	1,719		647			
All ages	19A	104 (2.8)	317 (7.0)	154.1	252 (16.4)	496.9	296.2	<0.001
	total	3,781	4,536		1,535			

19A: total number of invasive *Streptococcus pneumoniae* serotype 19A in the period; total: total number of invasive *Streptococcus pneumoniae* strains in the period; bold: *p*-value <0.05 was considered statistically significant;

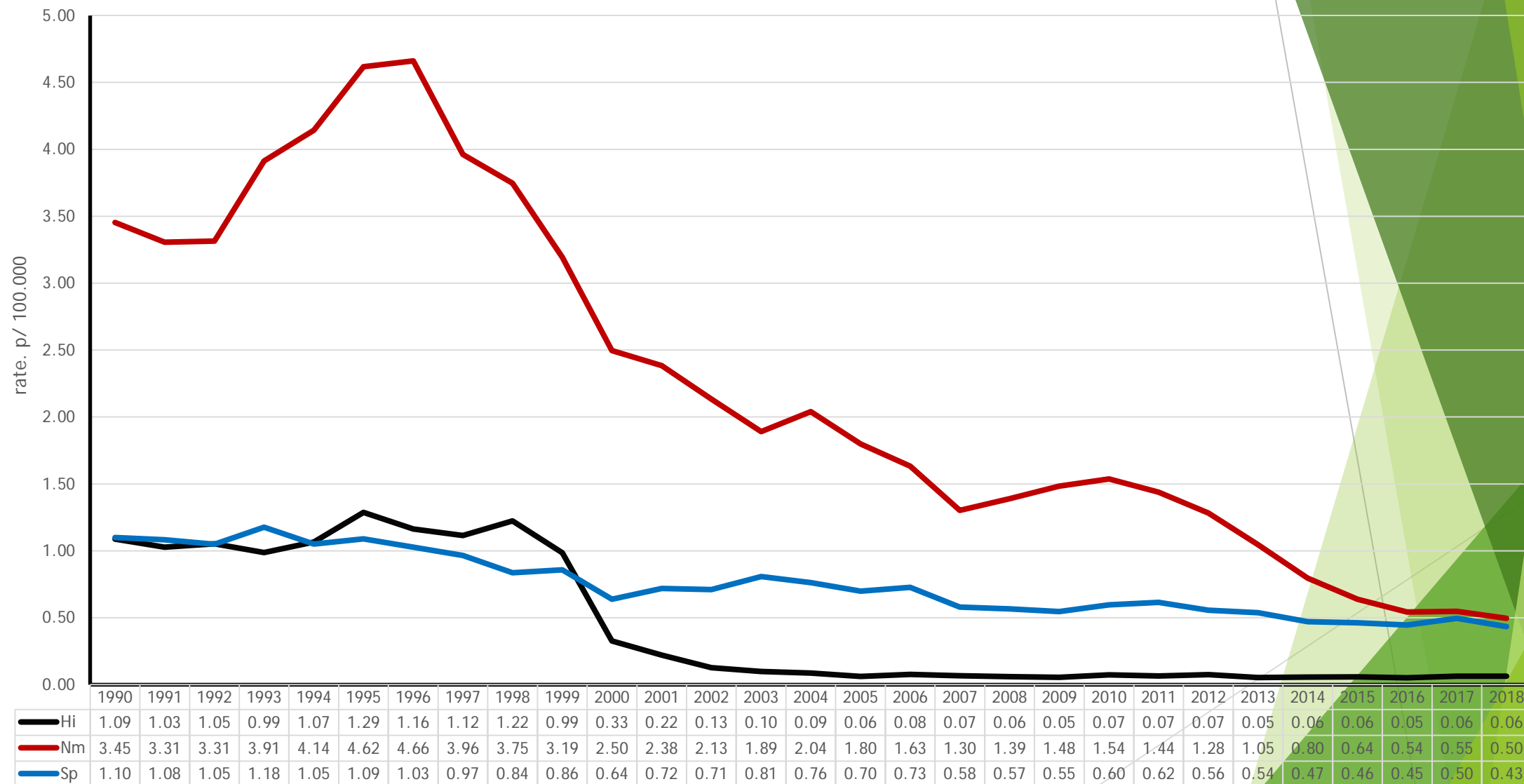
* Pre-PCV10 period used as reference;

† Inclusion of frequency of Spn19A previously reported [31].

<https://doi.org/10.1371/journal.pone.0208211.t001>

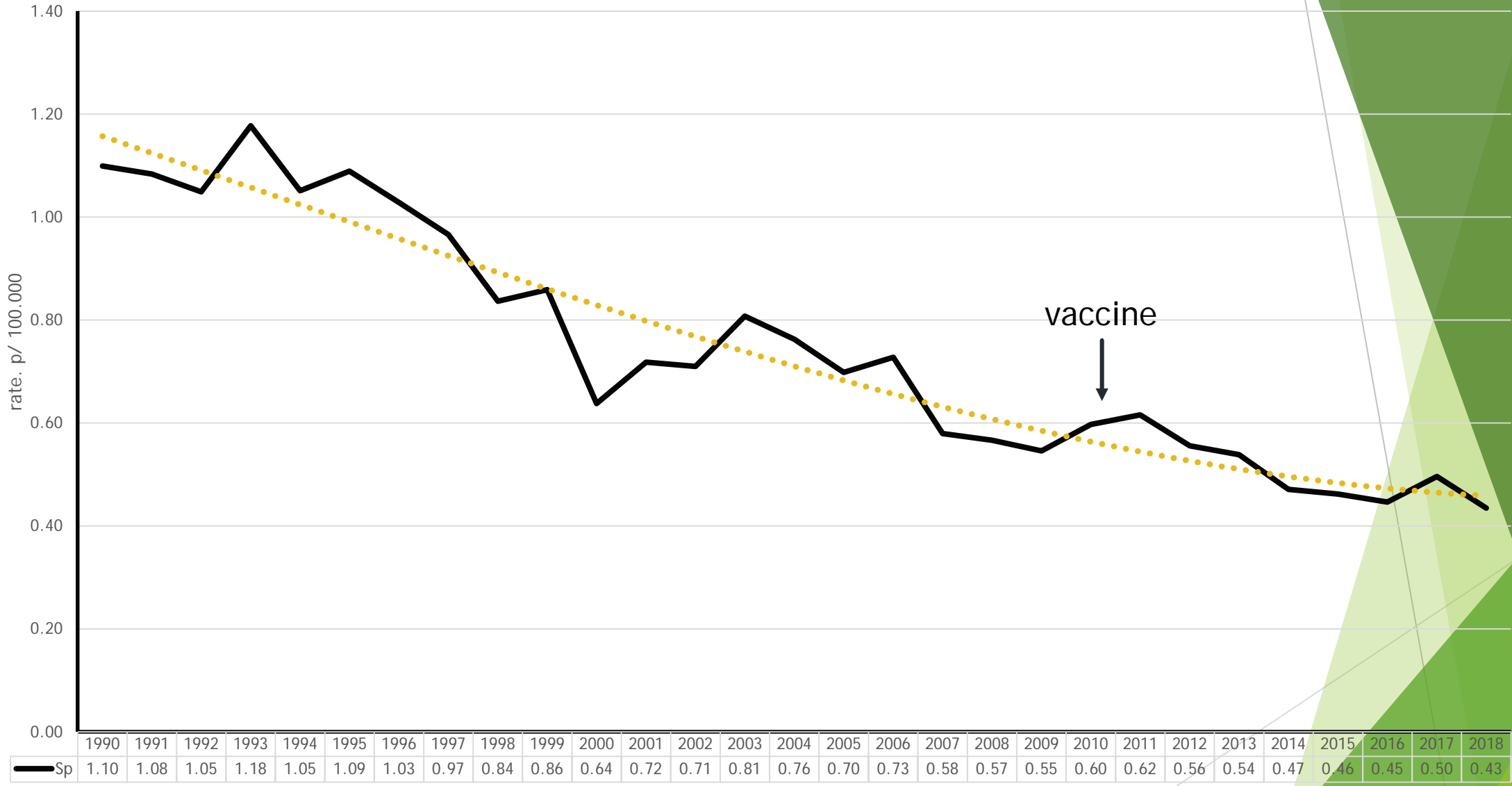
Surveillance data

Bacterial meningitis according to etiology and year. Brazil, 1990-2018



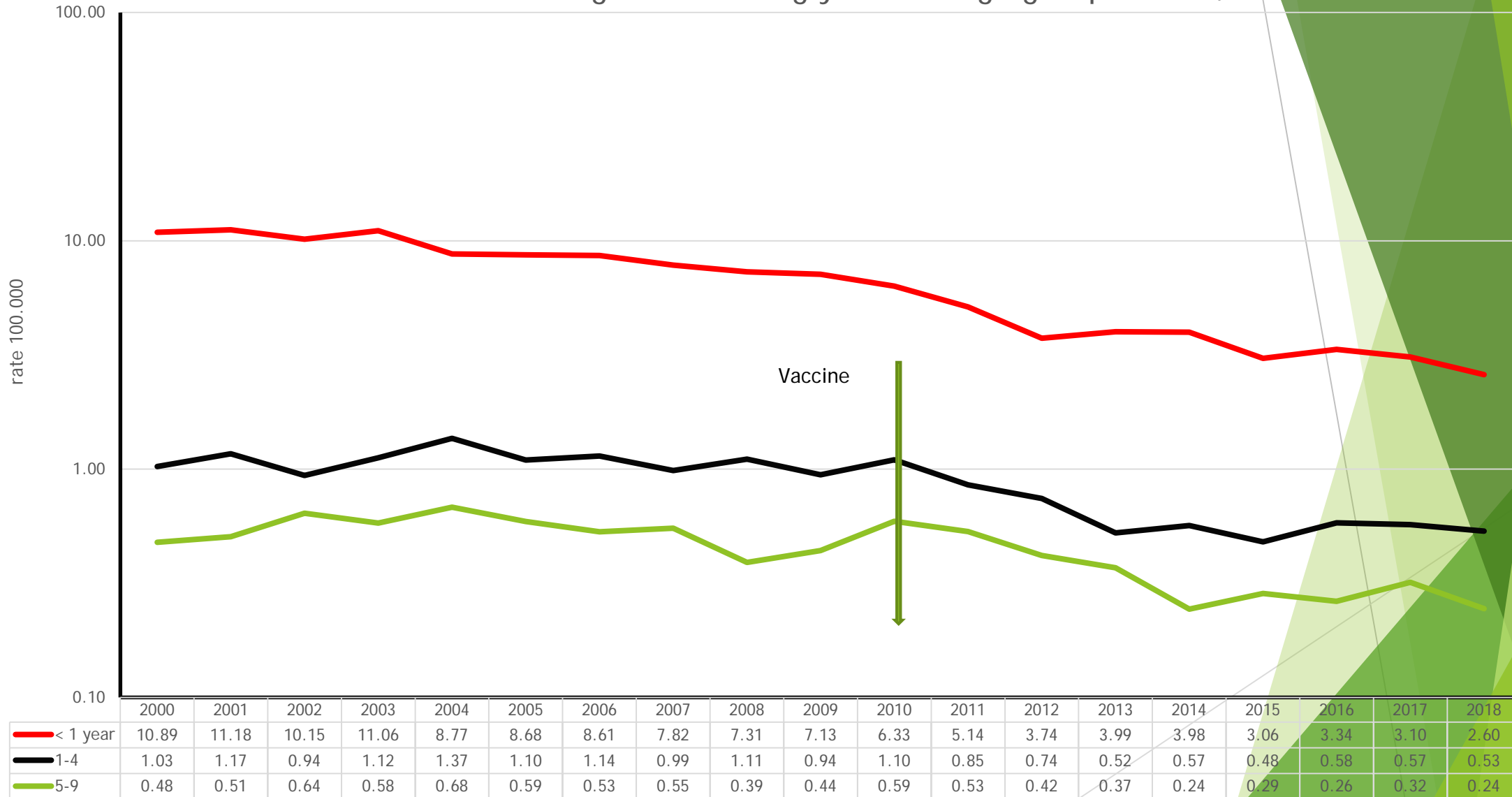
Source : DataSus

Pneumococcal meningitis according to etiology and year. Brazil, 1990-2018



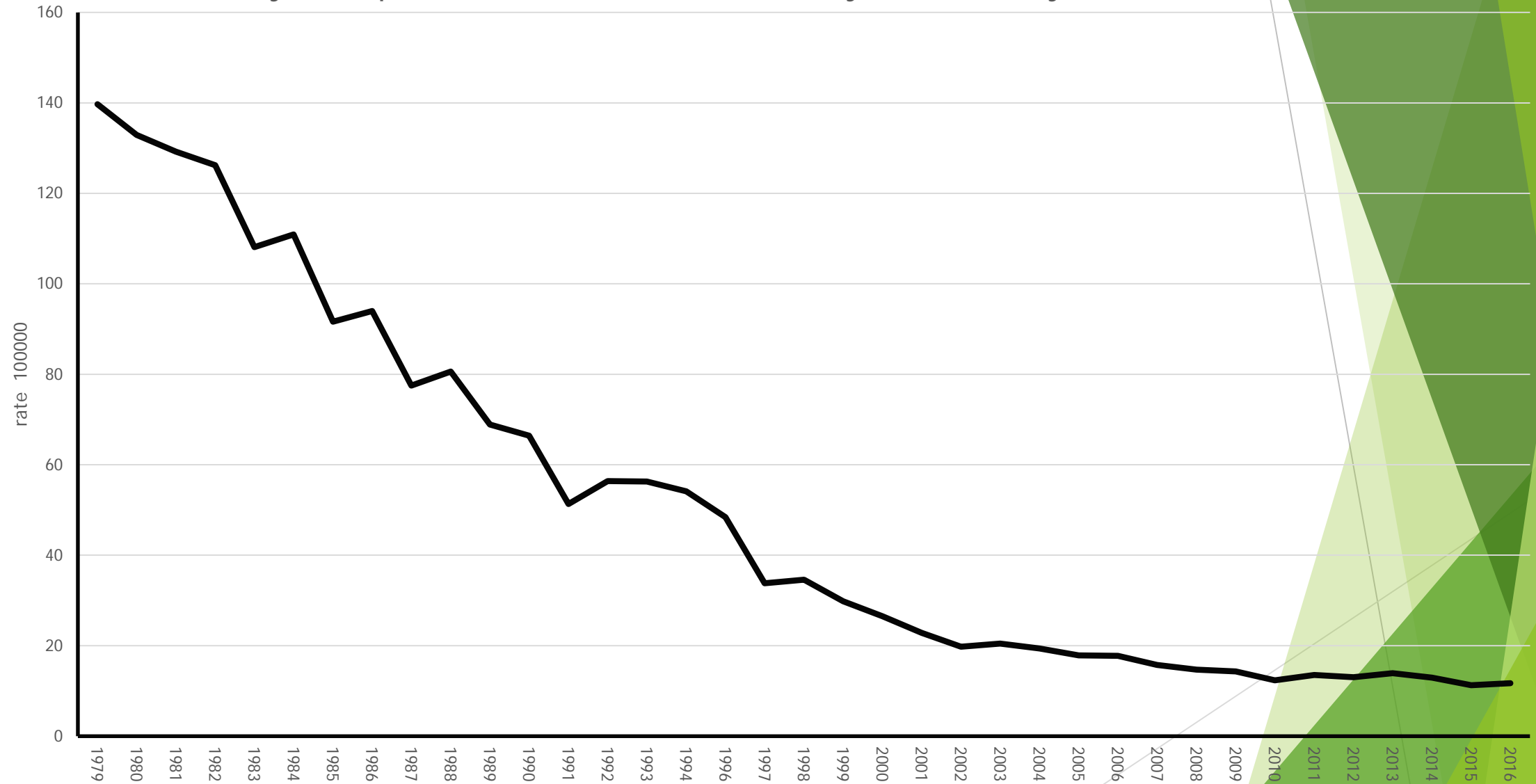
Source : DataSus

Pneumococcal meningitis according year and age group. Brazil, 2000 -2018



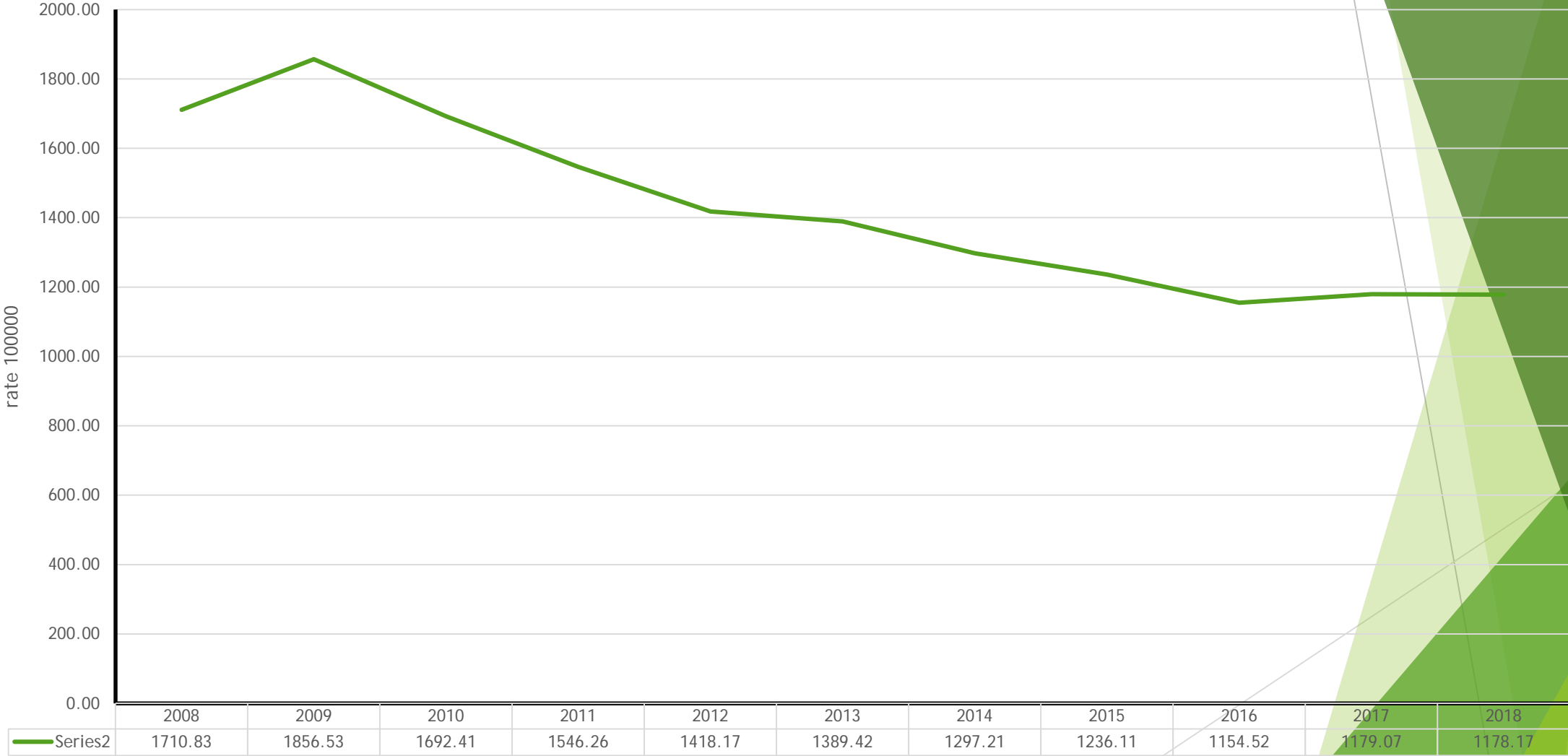
Source : DataSus

Mortality from pneumonia in children under 5 years second year. Brazil, 1979-2016



Source : DataSus

Hospitalization due to pneumonia in children under 5 years second year. Brazil, 2008 -2018



Source : DataSus

Diseases

Effects

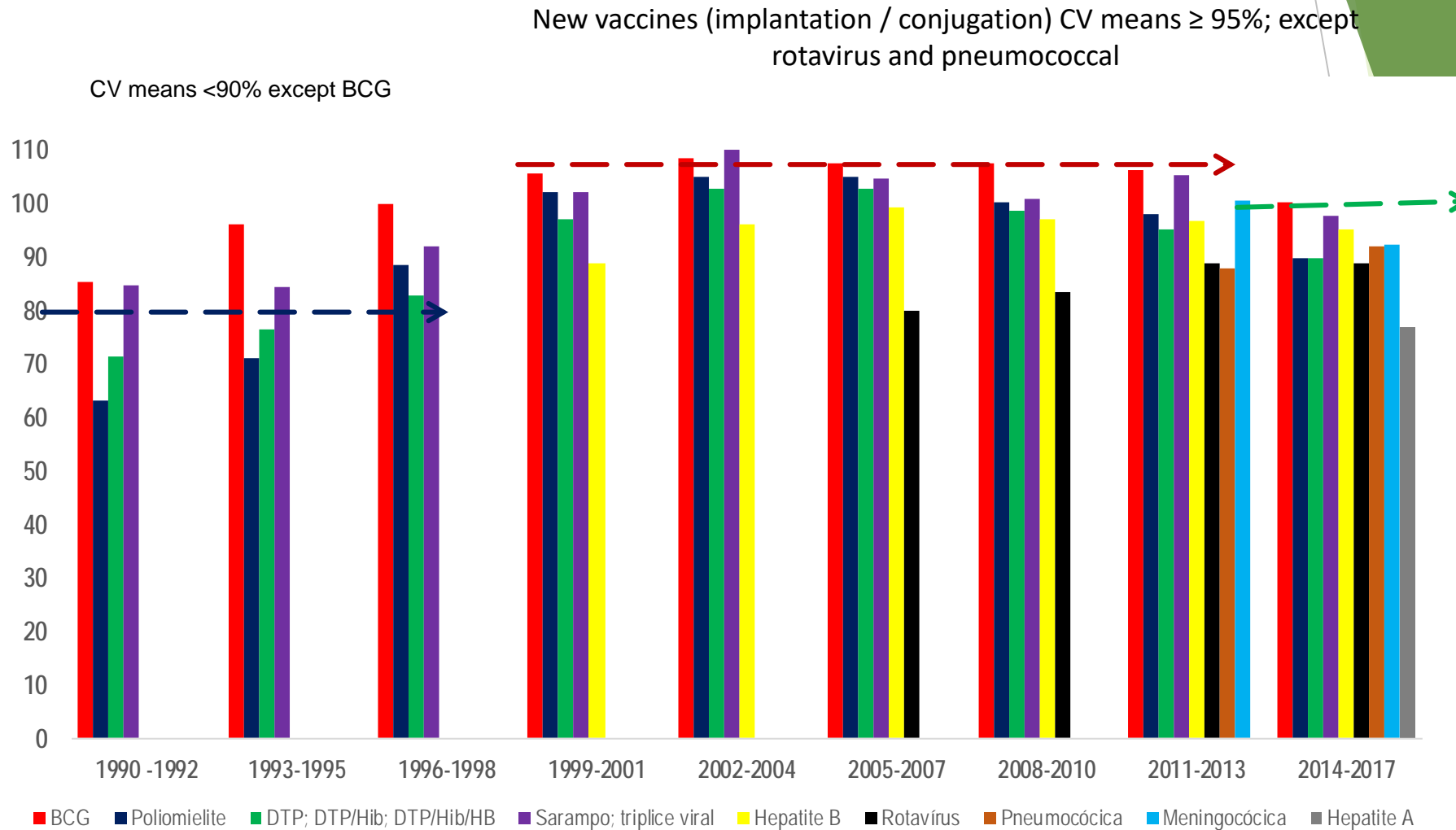
Vaccination

Protection

Infections

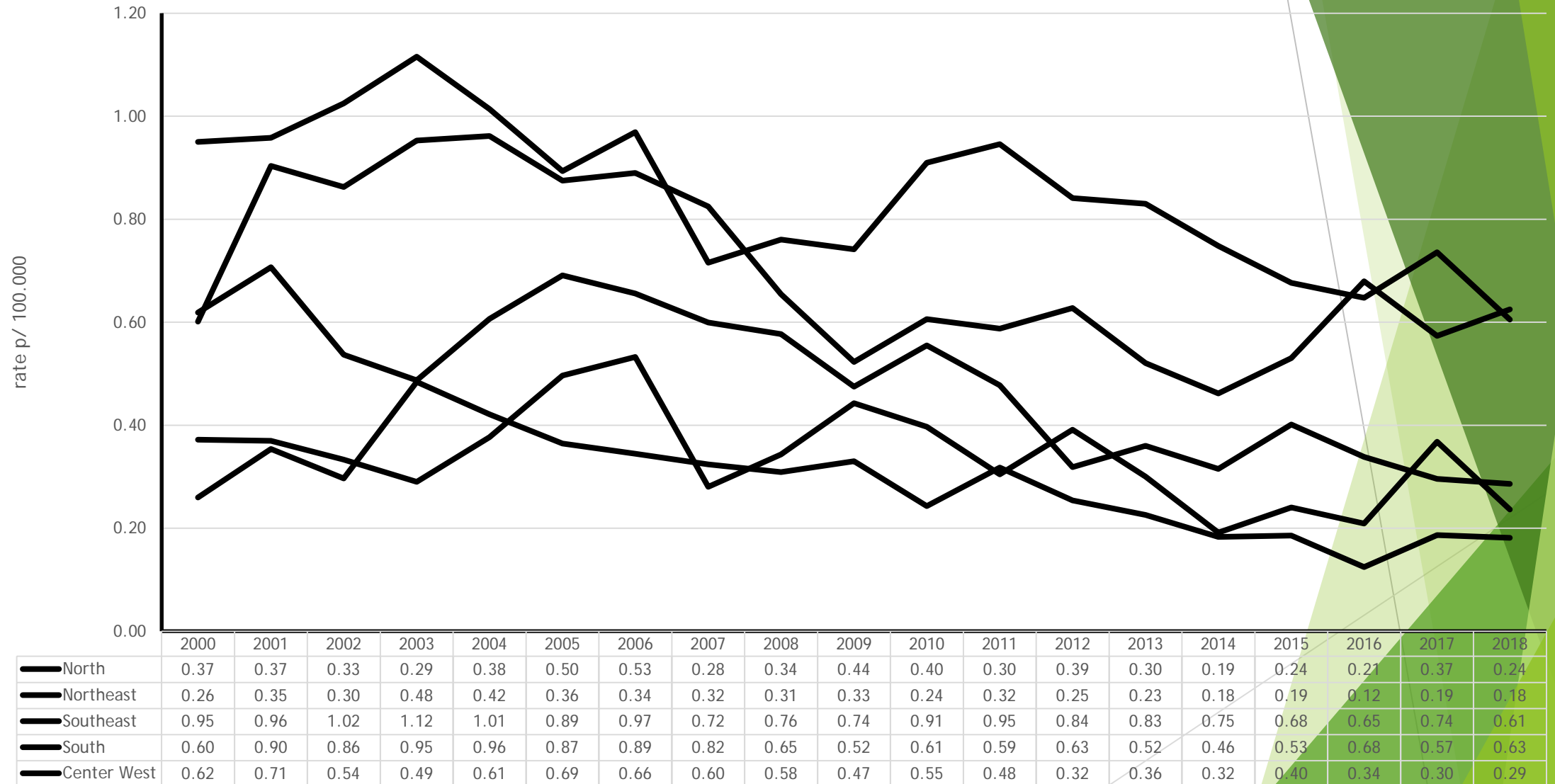
Thank you Gracias Merci Obrigado

Vaccination coverage (CV) averaged over triennia * for children's calendar vaccines: 1990 to 2017



Source: CGPNI / SVS / MS * average 4 years in the last period. 1 year old: Viral triple and Hepatitis A; <1 year other vaccines

Pneumococcal meningitis according year and macrorregion. Brazil, 2000-2018



Source : DataSus

Effectiveness of ten-valent pneumococcal conjugate vaccine against invasive pneumococcal disease in Brazil: a matched case-control study

	Cases (n=325)
Age (months)	
Median (range)	13.3 (2.6–53.1)
Clinical syndrome	
Meningitis	158 (49%)
Bacteraemic pneumonia	129* (40%)
Pneumonia with effusion	36 (11%)
Bacteraemia†	2 (<1%)
Method of detection	
Culture of isolate	307 (94%)
PCR of cerebrospinal fluid or pleural fluid	18 (6%)
Serotype	
Vaccine-type‡	151 (46%)
Vaccine-related§	77 (24%)
Non-vaccine¶	97 (30%)
Medical care	
Outpatient	17 (5%)
Admitted to hospitalised without intensive care	187 (58%)
Admitted to hospitalised with intensive care	121 (37%)
Deaths (outcome)	
Overall	77 (24%)
In cases of meningitis	57 (36%)
In cases of pneumonia	19 (12%)
In cases of bacteraemia	1 (50%)

Data are number (%), unless otherwise indicated. PCV10=ten-valent pneumococcal conjugate vaccine. *Includes eight cases with *Streptococcus pneumoniae* detected in both blood and pleural fluid. †Without pneumonia, meningitis, and sepsis. ‡PCV10 serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, and 23F. §Serotypes not included in PCV10, but in the same serogroup as any of the included serotypes. ¶Serotypes not included in PCV10 and not in the same serogroup as any of the included serotypes.

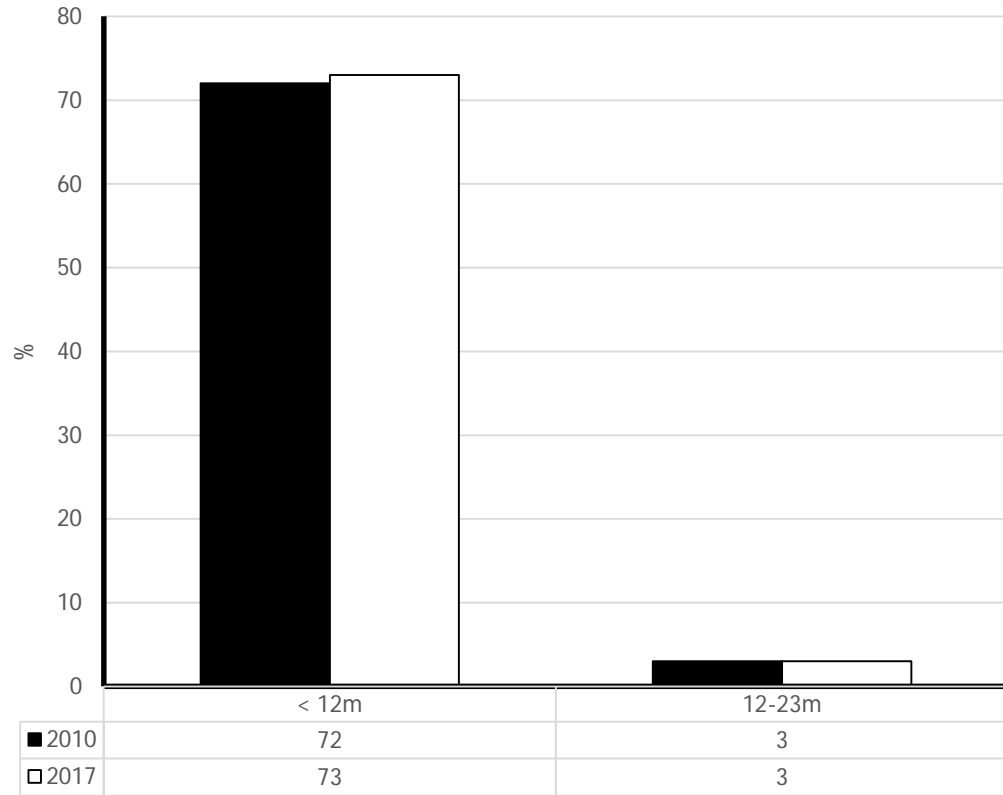
Table 1: Characteristics of eligible cases

	Cases (n=316)	Controls (n=1219)	p value (matched)
Male sex*	173 (55%)	630 (52%)	0.3181
Maternal education less than 12 years*	61 (19%)	255 (21%)	0.2752
Low household income†	147 (47%)	519 (43%)	0.2098
Crowding‡	178 (56%)	664 (54%)	0.5973
Any chronic illness*§	85 (27%)	96 (8%)	<0.0001
Asthma	42 (13%)	71 (6%)	<0.0001
Premature birth (<37 weeks' gestation)*	42 (13%)	82 (7%)	0.0004
Low birthweight (<2500 g)*	39 (12%)	83 (7%)	0.0017
Use of immunosuppressant drugs*	25 (8%)	22 (2%)	<0.0001
Day care (daily attendance)	127 (40%)	357 (29%)	<0.0001
Presence of other children younger than 5 years in the home*	148 (47%)	477 (39%)	0.0110
Exclusive breastfeeding until 3 months of age	177 (56%)	804 (66%)	0.0001
Presence of smoker in the home	113 (36%)	387 (32%)	0.0800
Vaccination history¶			
At least one dose of diphtheria-tetanus-pertussis- <i>Haemophilus influenzae</i> type B	295 (93%)	1196 (98%)	<0.0001
No dose of PCV10	129 (41%)	304 (25%)	Ref
One dose of PCV10	78 (25%)	399 (33%)	<0.0001
Two doses of PCV10	34 (11%)	173 (14%)	<0.0001
Three doses of PCV10	48 (15%)	221 (18%)	<0.0001
Four doses of PCV10	27 (9%)	122 (10%)	<0.0001

Data are number (%), unless otherwise indicated. PCV10=ten-valent pneumococcal conjugate vaccine. Ref=reference. *Missing data were excluded from denominator. †Defined as monthly household income per household member of less than or equal to 50% of the standard monthly minimum wage. ‡Defined as a ratio of the number of household members to number of bedrooms greater than two. §Defined as having one or more of the following: asplenia, sickle cell disease, haemolytic anaemia, HIV/AIDS, cancer, use of immunosuppressant drugs, organ transplant, diabetes, asthma, or chronic pulmonary, cardiovascular, renal, or hepatic disease. ¶Includes only vaccine doses received at least 14 days before reference date, which for cases was the date of hospital admission (or medical attention if not admitted to hospital); for controls, the reference date was that on which their age in days was the same as their corresponding case's age at hospital admission or medical attention.

Table 2: Characteristics of cases and controls in the PCV10 effectiveness analysis*

% Serotype included in pneumococcal 10v vaccine of IPD according year and age. Brazil, 2010 e 2017



Serotype 19A in IPD according year and age. Brazil, 2010 and 2017

