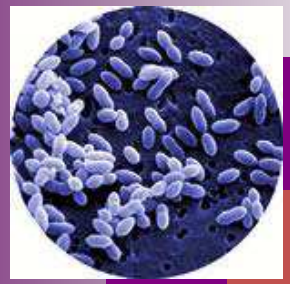


INFECÇÕES PNEUMOCÓCICAS e ROTAVIRUS

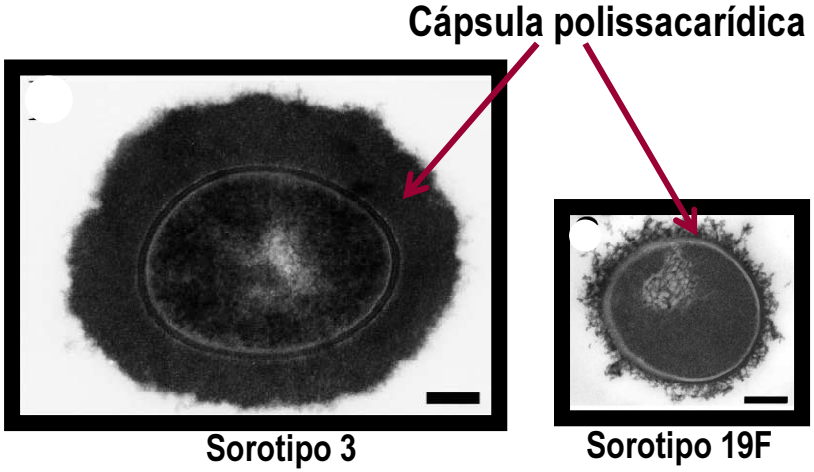
Eitan N Berezin
Professor tTtular Pediatria Fac Ciencias Médicas Santa Casa SP
Comite de Vacinas Ministério da Saude BRASIL
Secretario geral- SLIPE
eberezin2003@yahoo.com

Population of Brazil	190,755,799
Population of capital cities	
Recife	1,537,704
Belo Horizonte	2,375,151
São Paulo	11,253,503
Curitiba	1,751,907
Porto Alegre	1,409,351

Infecções Pneumocócicas (Streptococcus pneumoniae)

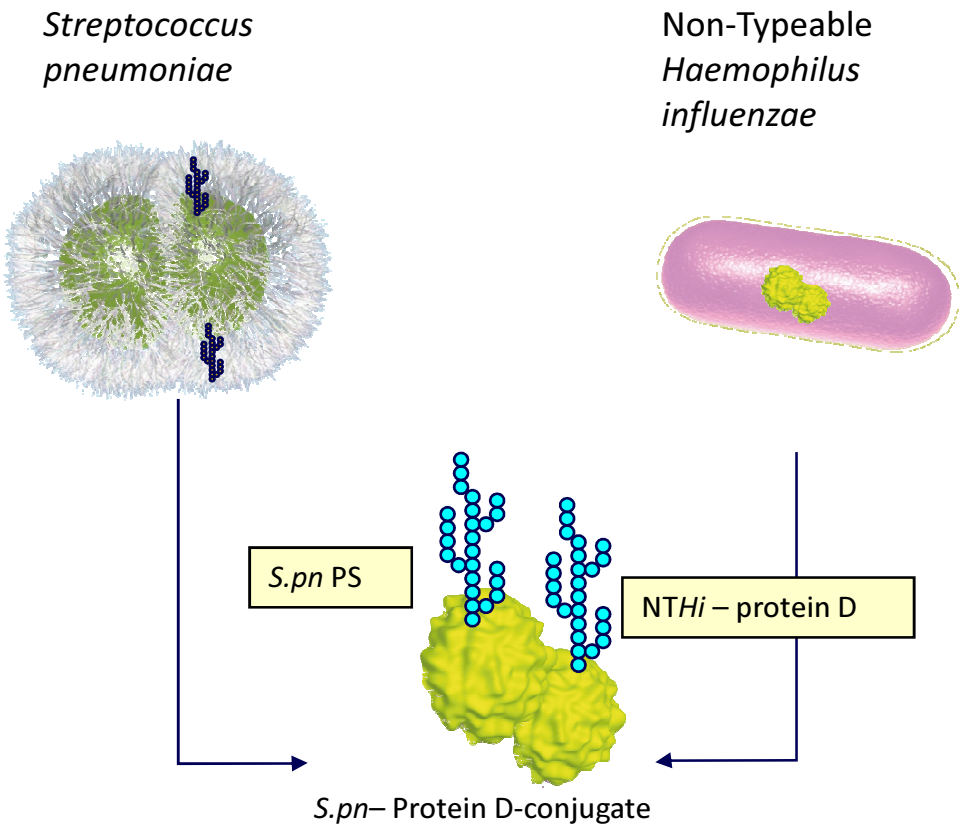
- Bactérias gram positivas dispostas em cachos e encapsuladas

- Existem atualmente descritos 92 sorotipos capsulares, entre os quais o 14, 6B, 1, 19F, 23F, 6A, 18C, 5, 19A, 9V, 4, 7F e 3



Hammerschmidt et al. IAI 2005; 73:4653

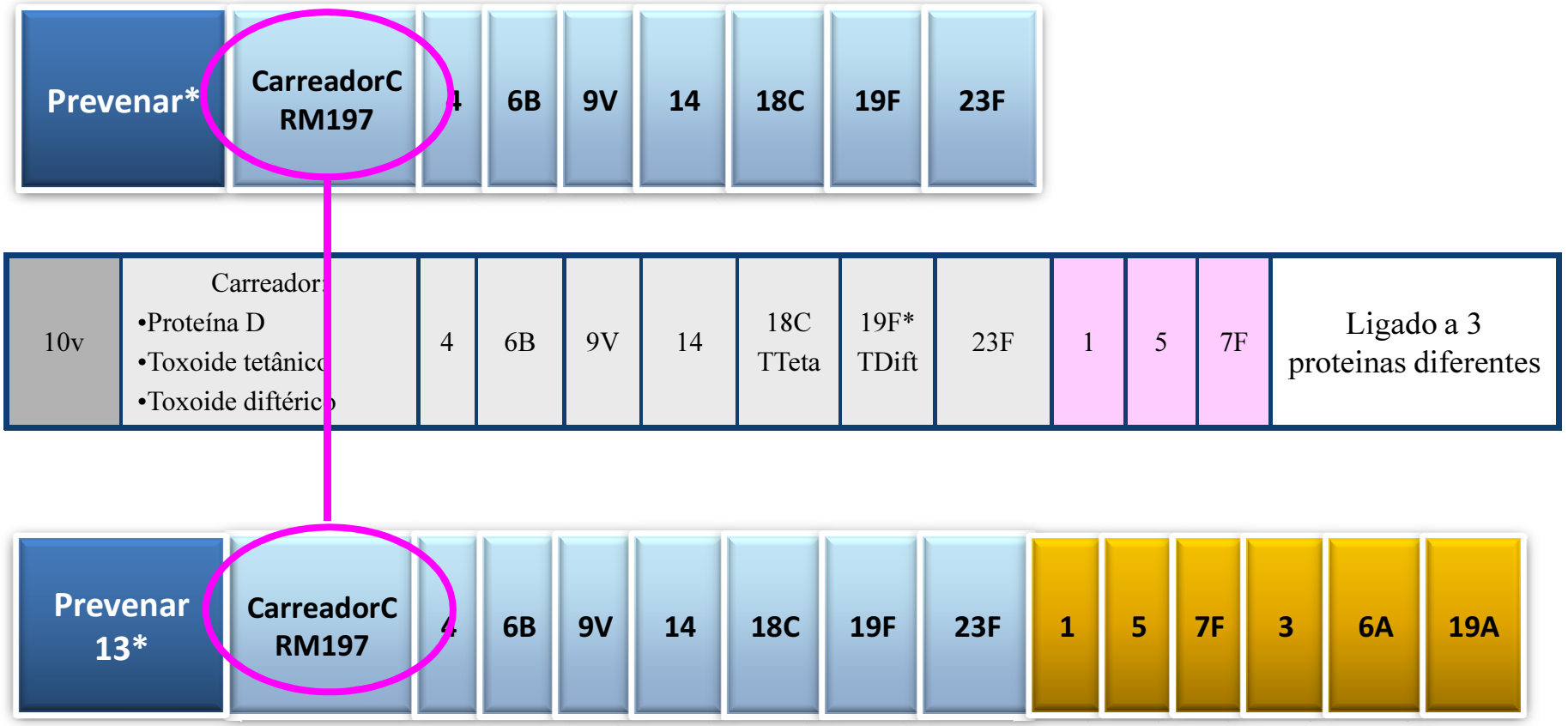
Protein D Carrier para Vacina Pneumocócica



Pneumococcus *Haemophilus influenzae* Protein D Conjugate Vaccine (PHiD-CV)

Esta Vacina além da proteção para Pneumococo pode ter proteção para Hi não Tipavel – apesar de ainda faltar dados para este fato

VACINAS PNEUMOCÓCICAS CONJUGADAS



BR 2010: Implantação da vacina anti-pneumocócica conjugada 10V

Constituída por 10 sorotipos de pneumococo:

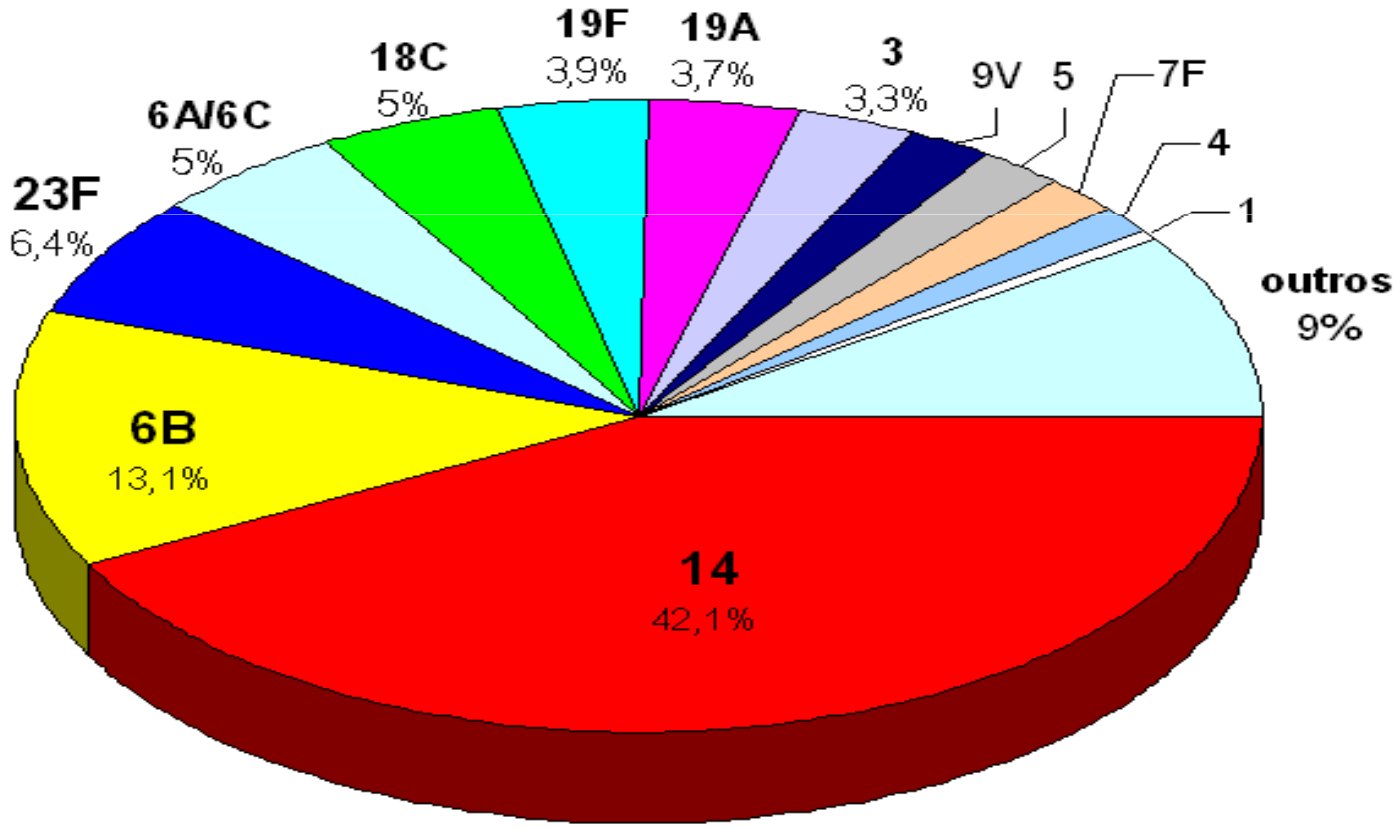
1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F

Conjugada :

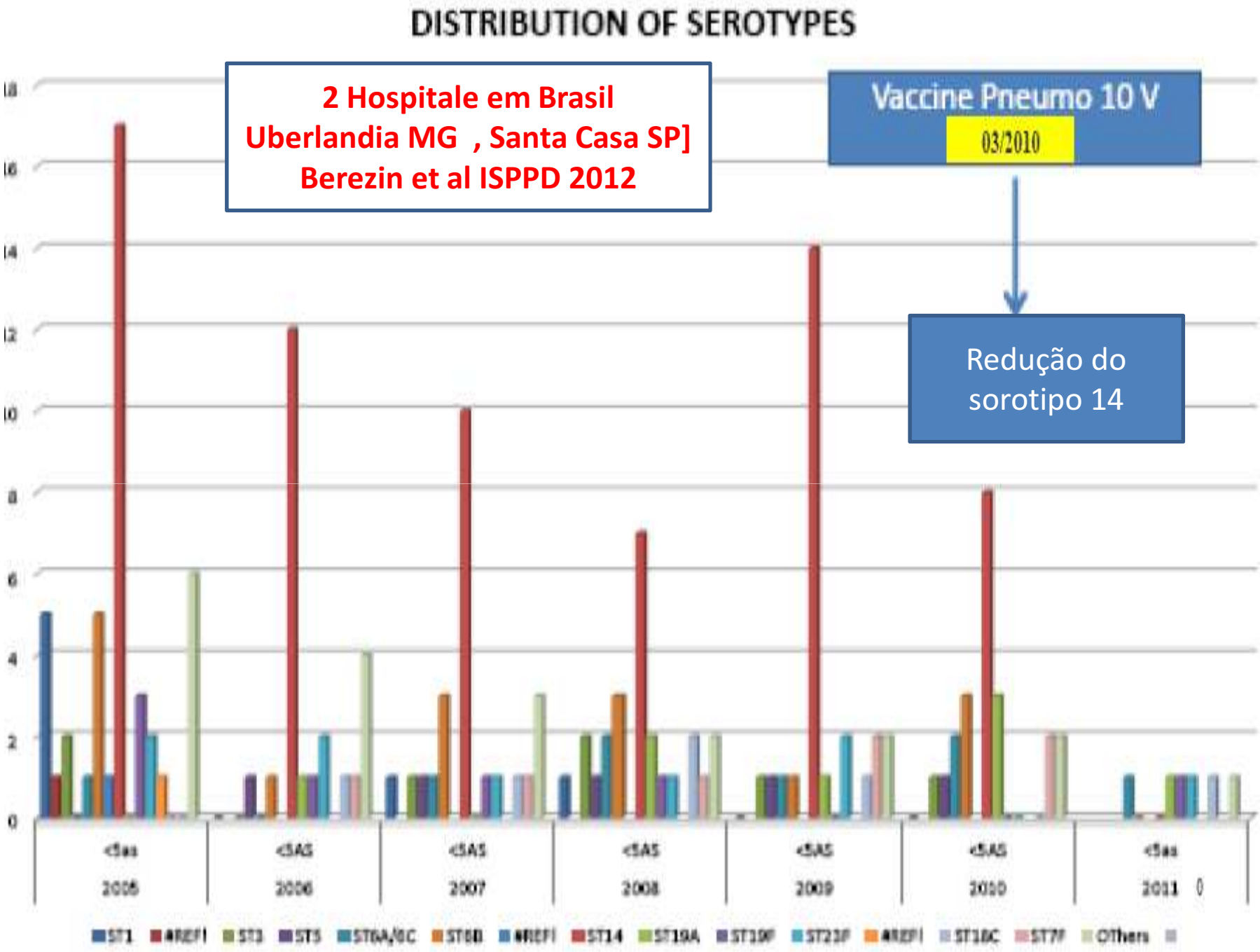
- **8 ST: proteína D de *Haemophilus influenzae***
- **2 ST: carreadores de toxóide diftérico (DT) e de toxóide tetânico (TT ou T)**

Sorotipos em crianças < 2 anos – Brasil

Sireva 2007 e 2008: sorotipos de 544 pneumococos isolados de amostras de sítios estéreis de crianças <2anos



Sireva 2007 e 2008 (*vigilância hospitalar)


DISTRIBUTION OF SEROTYPES
2 Hospitale em Brasil
Uberlandia MG , Santa Casa SP]
Berezin et al ISPPD 2012
Vaccine Pneumo 10 V
03/2010
Redução do sorotipo 14
<5as 2005
<5AS 2006
<5AS 2007
<5AS 2008
<5AS 2009
<5AS 2010
<5as 2011
ST1
ST3
ST5
ST6A/6C
ST6B
ST14
ST19A
ST19F
ST23F
ST18C
ST7F
Others

Serotype distribution of *Streptococcus pneumoniae* isolated from patients with invasive pneumococcal disease in Brazil before and after ten-pneumococcal conjugate vaccine implementation

Base Hospitalar

Silvia R. dos Santos[a,b], Lilian F. Passadore[a], Elizabeth H. Takagi[b], Cristiane M. Fujii[a], Cristina R.M. Yoshioka[a], Alfredo E. Gilio[a], Marina B. Martinez[a,b,*]

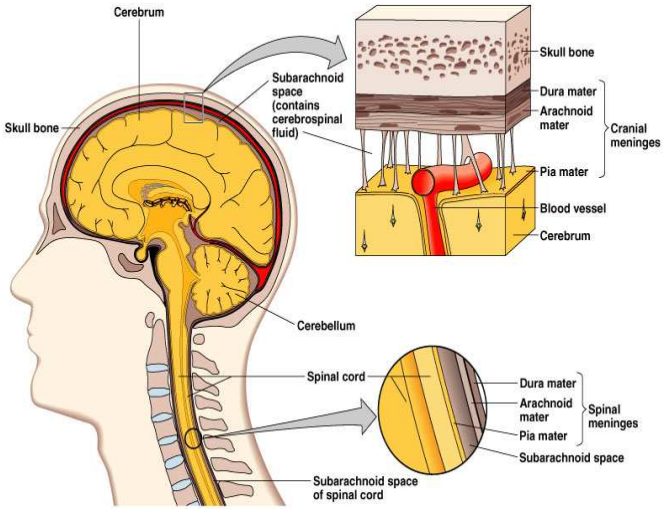
Vaccination periods[b]					
Age group (year)	Pre-implementation		Post-implementation		
	No. of cases	Incidence[a]	No. of cases	Incidence[a]	*p*
All serotypes					
All ages	178	3.49	81	2.99	NS
<2	80	20.30	9	3.97	<0.0012
=2<15	31	3.35	13	2.52	NS
>15	67	1.72	59	3.16	NS
PCV10 serotypes					
All ages	124	2.38	27	1.03	NS
<2	65	16.47	1	0.44	0.0002
=2<15	26	2.81	5	0.97	NS
>15	33	0.85	21	1.13	NS
Non-PCV 10 serotypes					
All ages	54	1.04	51	1.95	NS
<2	15	3.80	7	3.11	NS
=2<15	5	5.41	7	1.35	NS
>15	34	0.88	37	1.98	NS

[a] Incidence is number of cases/1000 people; NS: not significant.

[b] Vaccination periods: pre-implementation period, January 2006–June 2010; post-implementation period, July 2010–September 2012. Statistical analyses were performed using Fisher's exact test as appropriate. We considered $p < 0.05$ to be significant. All *p* values are two sided. Statistical analyses were performed with Statistica (version 6.1

Impacto em Meningite

Meningites por pneumococo no Brasil

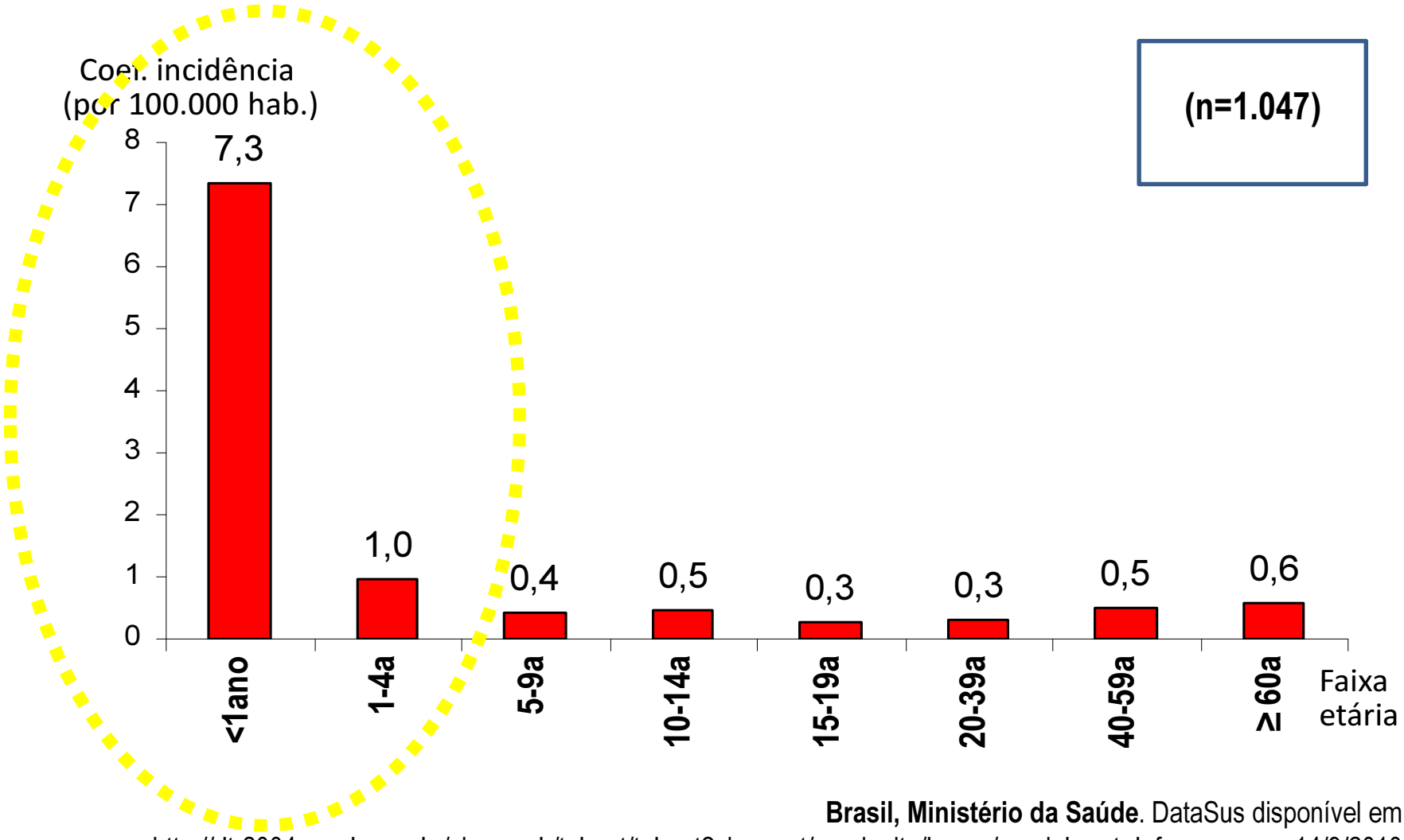


- Segunda bactéria mais comum (~1.000 casos / ano)
- Taxa de letalidade ~ 27,5%
- Coef. incidência anual de
  ~ 7 casos/100.000
  crianças <1ano de idade

Uma carga substancial & uma prioridade de saúde pública no Brasil

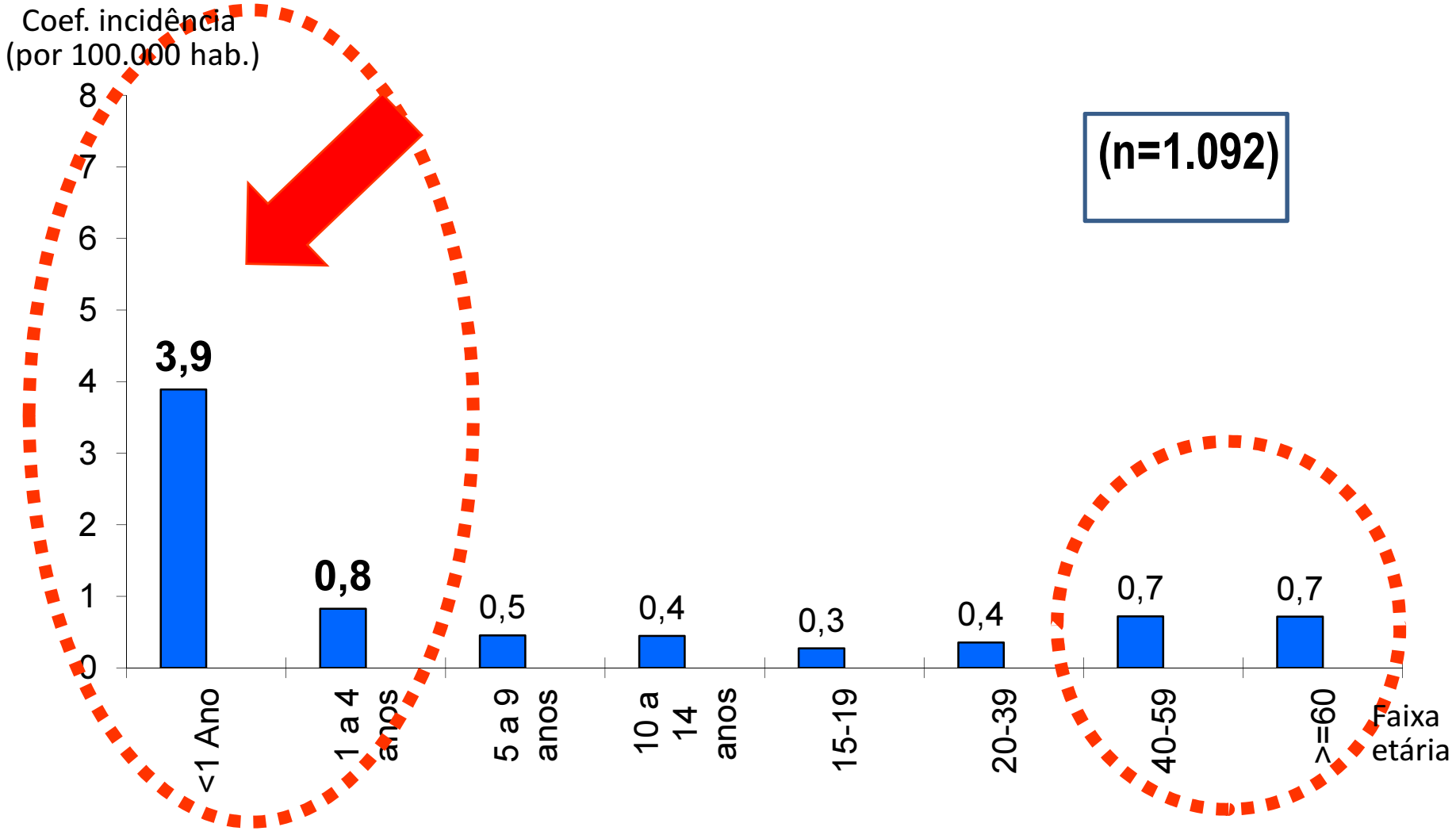
Brandileone M-CC et al. J Infect Dis 2003; 187:1206–12
Brasil, Ministério da Saúde. DataSus (http://www.saude.gov.br) acesso em 14/09/2010

Coef. incidência de meningite pneumocócica por faixa etária – Brasil, 2009



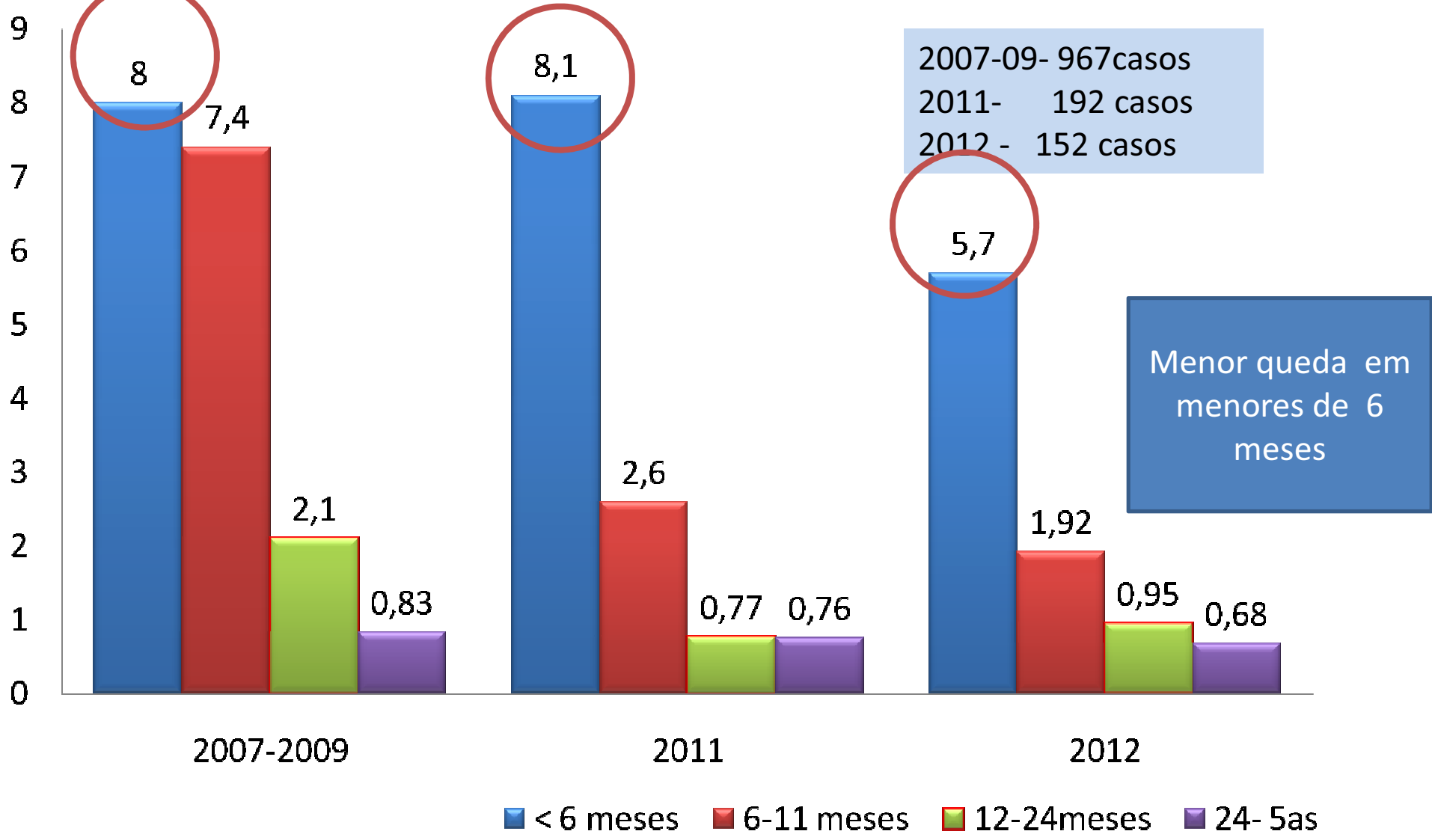
Brasil, Ministério da Saúde. DataSus disponível em http://dtr2004.saude.gov.br/sinanweb/tabnet/tabnet?sinannet/meningite/bases/meninbrnet.def acesso em 14/9/2010

Coef. incidência de meningite pneumocócica por faixa etária – Brasil, 2012



Brasil. Ministério da Saúde do Brasil – DataSus 2012. Disponível em: http://dtr2004.saude.gov.br/sinanweb/tabnet/dh?sinannet/meningite/bases/meninbrnet.def acessado em 08/10/2013.

Meningite Pneumocócica – Brasil-SINAN - (Taxas:100000) Menores de 2 anos e 0 a 6 meses



Internamentos por Pneumonia em crianças no Brasil

Em 2009: 321.767 internamentos por pneumonia em crianças < 5 anos (Coef.incid.=2.051/100.000)

Em 2012: 242.885 internamentos por pneumonia em crianças < 5 anos (Coef.incid.=1.729/100.000)

Ministério da Saúde/SVS - DataSus Internamentos por Pneumonia 2009 e 2012
http://tabnet.datasus.gov.br/cgi/tabcgi.exe?sih/cnv/niuf.def , Acesso em 21-9-2010 e 08-10-2013
Bricks LF & Berezin E. J Pediatr (Rio J). 2006;82 (3) Supl.:S 67-74

Effect of 10-Valent Pneumococcal Vaccine on Pneumonia among Children, Brazil

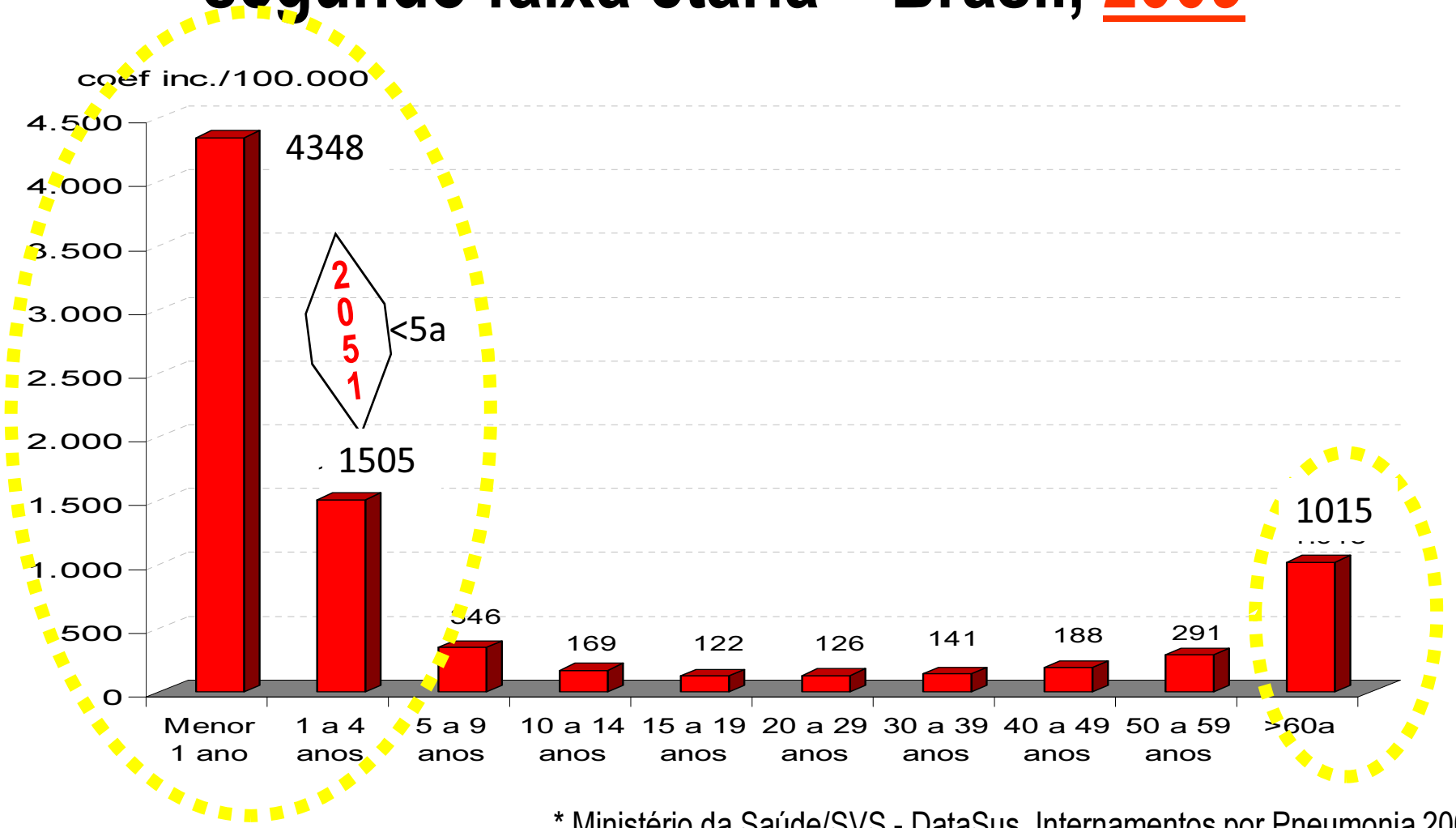
Eliane Terezinha Afonso, Ruth Minamisava, Ana Luiza Bierrenbach, Juan Jose Cortez Escalante, Airlane Pereira Alencar, Carla Magda Domingues, Otaliba Libanio Morais-Neto, Cristiana Maria Toscano, and Ana Lucia Andrade

Pneumonia is most problematic for children in developing countries. In 2010, Brazil introduced a 10-valent pneumococcal conjugate vaccine (PCV10) to its National Immunization Program. To assess the vaccine's effectiveness for preventing pneumonia, we analyzed rates of hospitalization among children 2–24 months of age who had pneumonia from all causes from January 2005 through August 2011. We used data from the National Hospitalization Information System to conduct an interrupted time-series analysis for 5 cities in Brazil that had good data quality and high PCV10 vaccination coverage. Of the 197,975 hospitalizations analyzed, 30% were for pneumonia. Significant declines in hospitalizations for pneumonia were noted in Belo Horizonte (28.7%), Curitiba (23.3%), and Recife (27.4%) but not in São Paulo and Porto Alegre. However, in the latter 2 cities, vaccination coverage was less than that in the former 3. Overall, 1 year after introduction of PCV10, hospitalizations of children for pneumonia were reduced.

Table 2. Annual percent change (trend) and percentage change in rates of hospitalization among children 2 months–2 years of age, Brazil, postvaccination period (January 2005–August 2011)

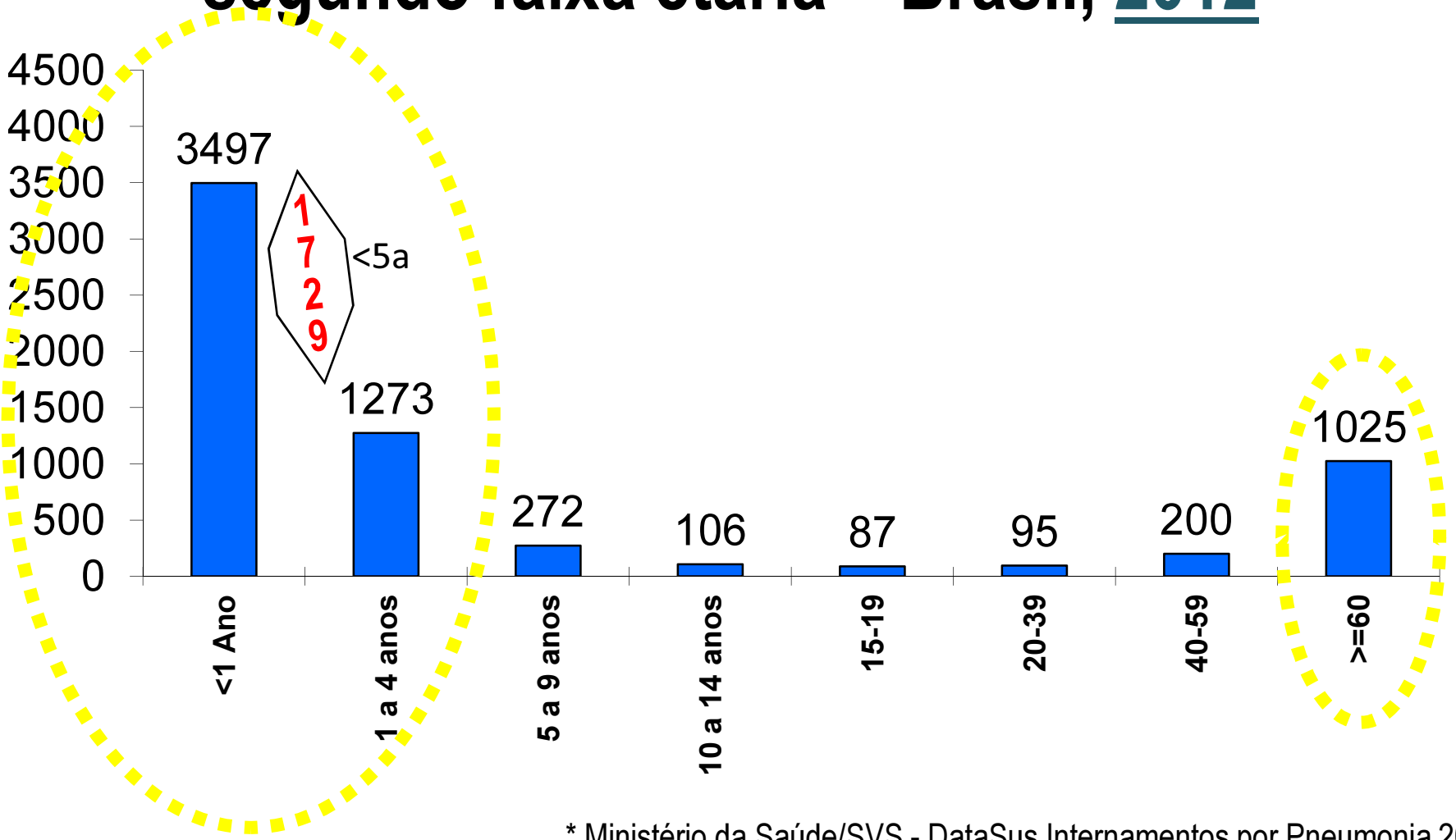
	Hospitalizations for pneumonia		Hospitalizations for nonrespiratory causes		Difference in	
City	% Change (95% CI)	p value	% Change (95% CI)	p value	change	p value
Belo Horizonte	–40.30 (–50.88 to –27.44)	<0.001	–11.61 (–23.48 to 2.10)	0.093	–28.69	0.002
Curitiba	–37.59 (–49.63 to –22.68)	<0.001	–14.27 (–23.94 to –3.38)	0.012	–23.32	0.011
Recife	–49.32 (–61.63 to –33.05)	<0.001	–21.93 (–32.18 to –10.13)	0.001	–27.39	0.007
São Paulo	–13.38 (–26.02 to 1.42)	0.074	–11.60 (–19.31 to –3.15)	0.008	–1.78	0.827
Porto Alegre	–23.51 (–41.60 to 0.18)	0.052	–21.18 (–31.08 to –9.86)	0.001	–2.33	0.845

Coeficiente de Internações por Pneumonia segundo faixa etária – Brasil, 2009

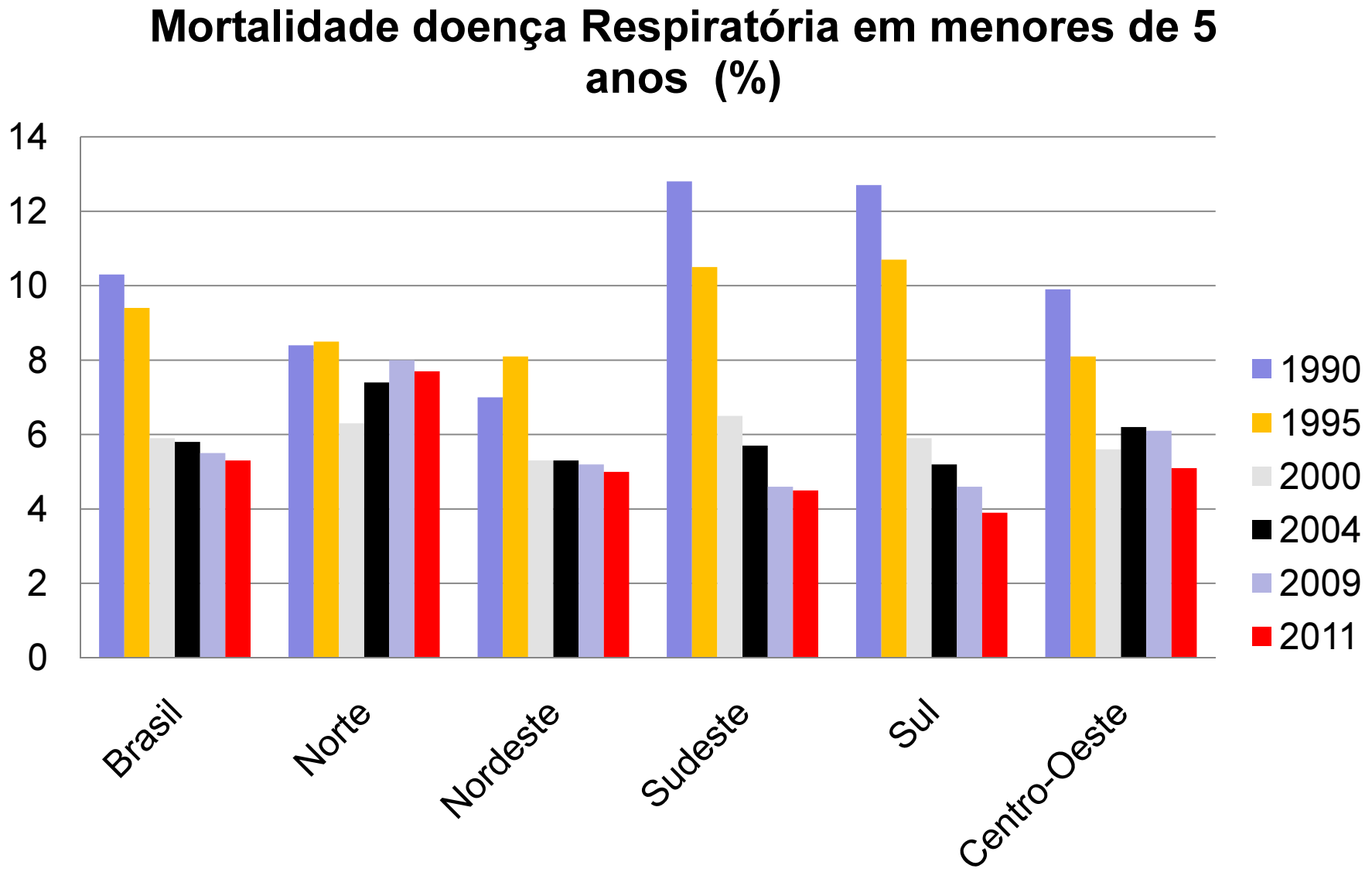


* Ministério da Saúde/SVS - DataSus Internamentos por Pneumonia 2009
Acesso em 21-9-2010 http://tabnet.datasus.gov.br/cgi/tabcgi.exe?sih/cnv/niuf.def

Coeficiente de Internações por Pneumonia segundo faixa etária – Brasil, 2012



* Ministério da Saúde/SVS - DataSus Internamentos por Pneumonia 2012
Acesso em 08-10-2013 http://tabnet.datasus.gov.br/cgi/tabcgi.exe?sih/cnv/niuf.def

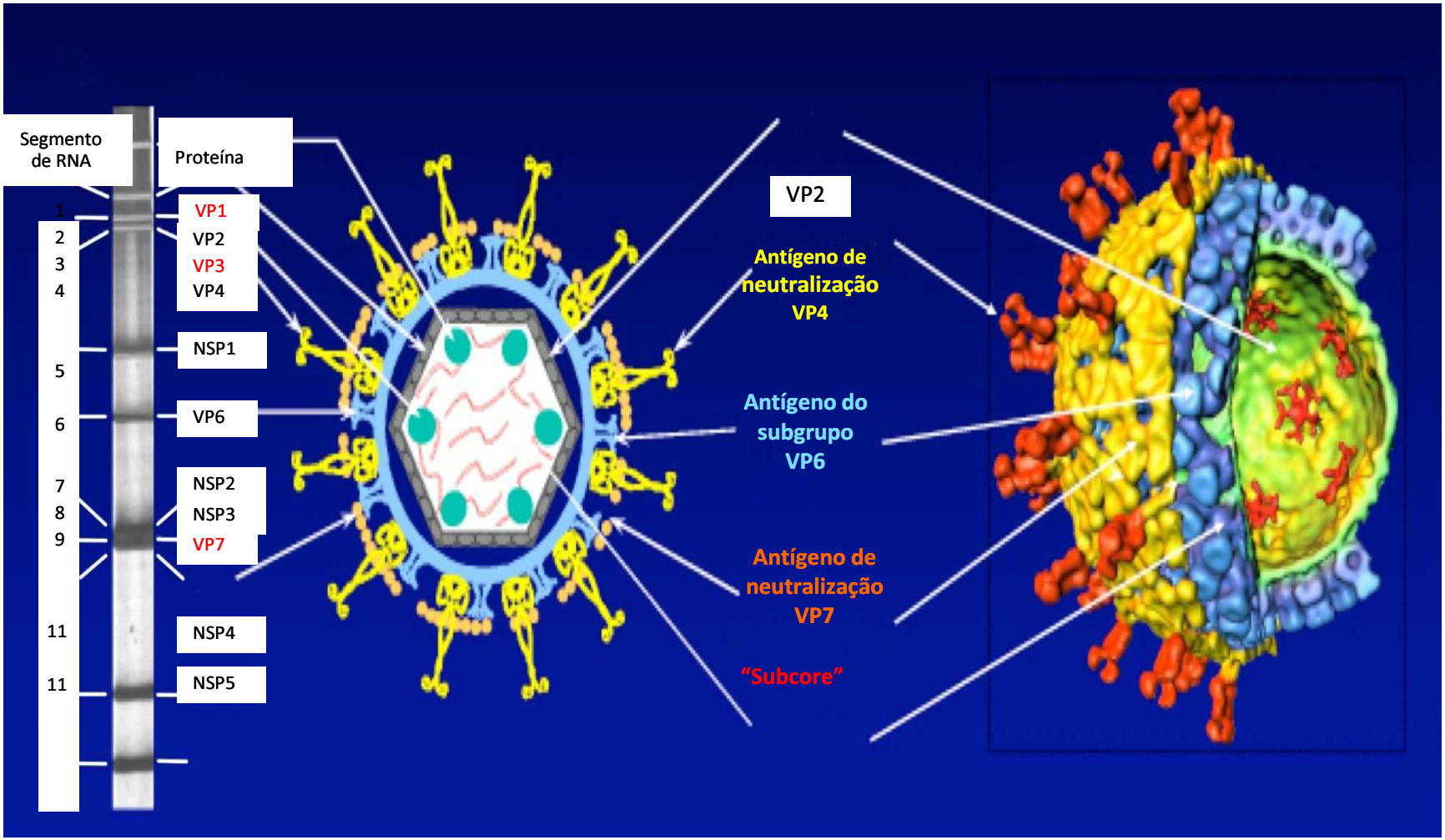

Mortalidade doença Respiratória em menores de 5 anos (%)
14
12
10
8
6
4
2
0
Brasil
Norte
Nordeste
Sudeste
Sul
Centro-Oeste
1990
1995
2000
2004
2009
2011

Conclusoes

- Queda da infeccao invasiva por sorotipos vacinais
- Nao se observou efeito de Rebanho
- Nao se observou substituicao de sorotipos

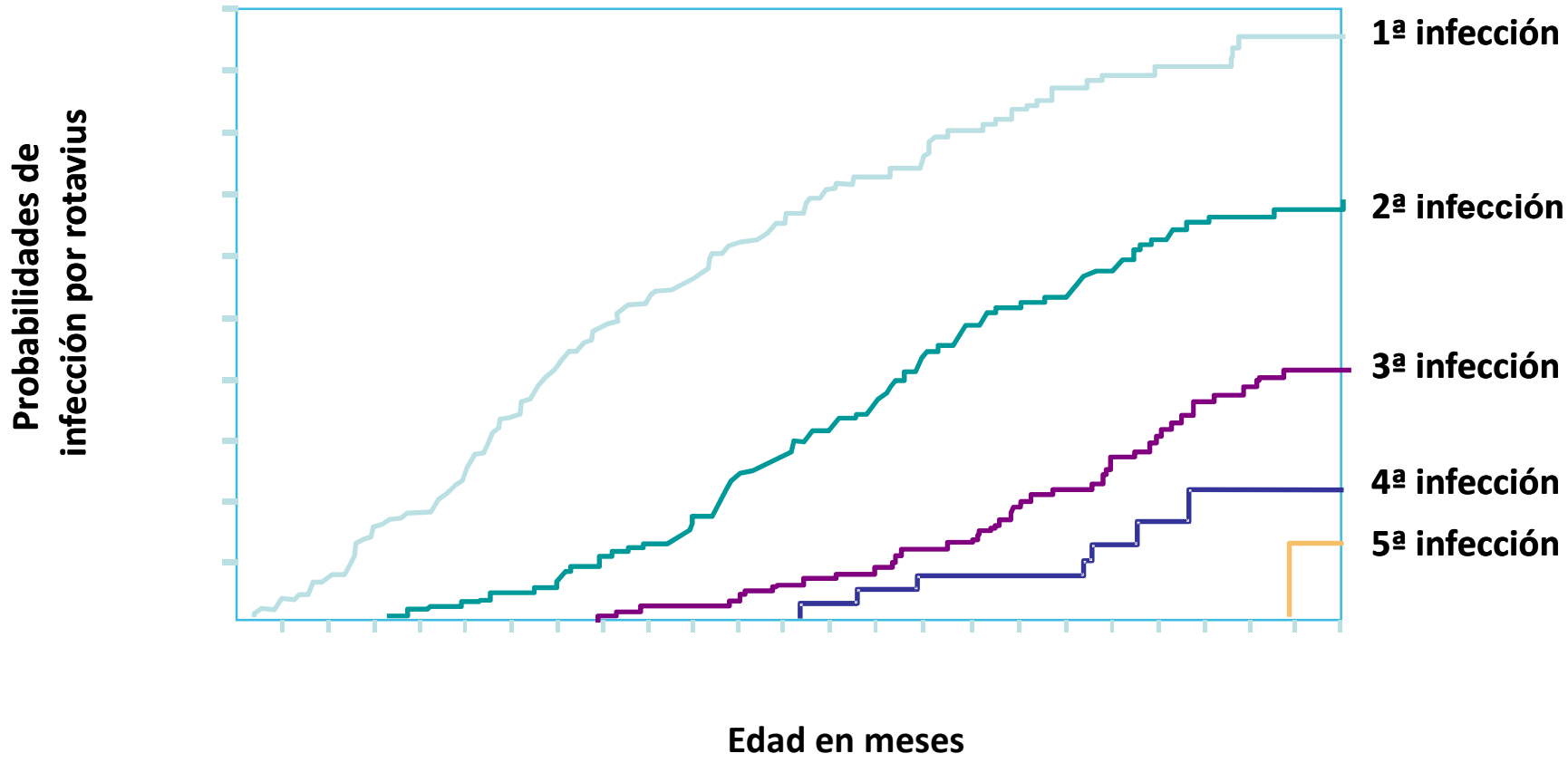
- **Rotavirus**
  Experiencia con la vacuna de Rotavirus en Brasil
- **Dr. Eitan Berezin**
- Profesor Titular de Pediatria Facultad de Ciencias Médicas de Santa Casa de S. Paulo

Estructura del rotavirus



De Kapikian AZ, Hoshino Y, Chanok RM. Rotaviruses. Em: Knipe DM, Howley PM, Griffin DE, et al, eds. Fields Virology. 4ª edição. Philadelphia, PA: Lippincott Williams & Wilkins: 2001:1787-1825. Reimpresso com a permissão. Figura tridimensional à direita: cortesia de B.V.V. Prasad.

Probabilidad acumulada de infección por rotavirus en los primeros dos años de vida



Proteción adquirida por infección natural con rotavirus

Resultados seleccionados de infección por rotavirus	Eficacia ajustada despues de cada infección, %*		
	Primera	Segunda	Tercera
Infección asintomática	38	62	74
Diarrea leve	73	75	99
Diarrea moderada a grave	87	100	–

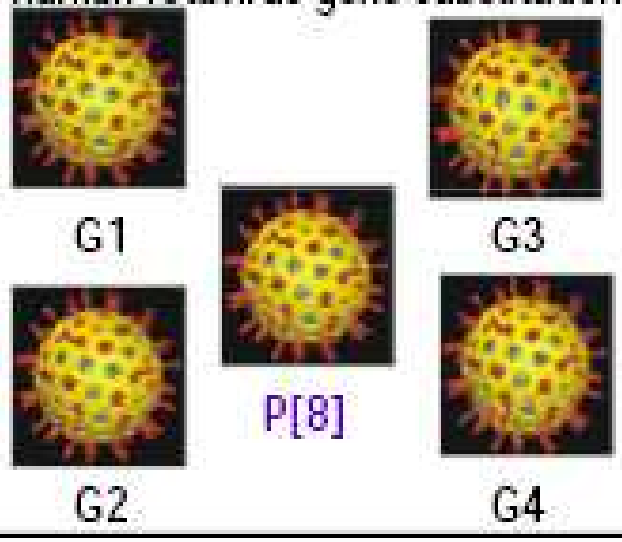
*La eficacia fue calculada como la reducción porcentual del riesgo de un resultado en comparación con el riesgo en los niños que aún no habían sido infectados.

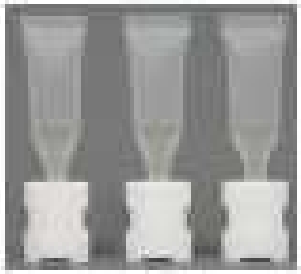
Adaptado de Velazquez FR, Matson DO, Calva JJ, et al. Rotavirus infection in infants as protection against subsequent infections. *N Eng J Med*. 1996;335:1022-1028.

Vaccines Differ in Composition & Schedule

RotaTeq , RV5 (Merck)

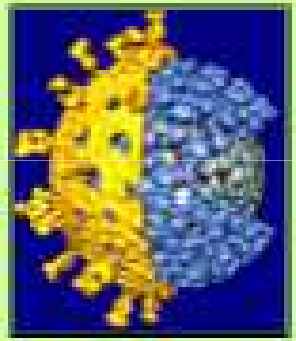
Bovine rotavirus with single human rotavirus gene substitution





Rotarix, RV1 (GSK)

Human rotavirus



G1P[8]

Tabla: Vacuna de Rotavirus, Número de dosis aplicadas y Cobertura vaccinal, Brasil 2006-2008.

Ano	Número de doses aplicadas (n)	Cobertura Vacinal (%)
2006	3.512.890	45,3
2007	5.023.431	79,78
2008	5.144.538	81,33
2009	5.284.604	84,26

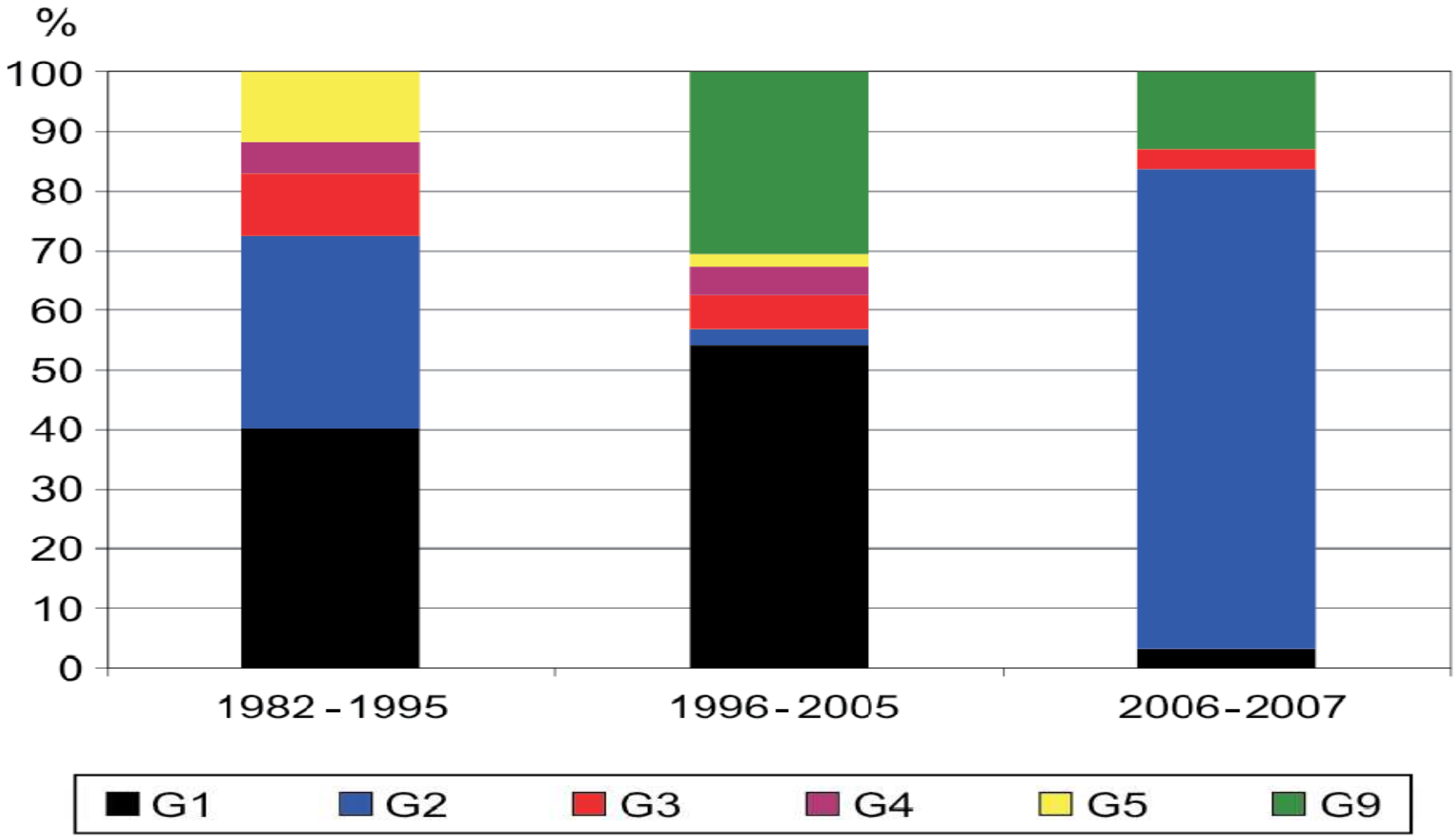
Fonte: (http://pni.datasus.gov.br/inf_estatistica_cobertura.asp)

Predominance of Rotavirus P[4]G2 in a Vaccinated Population, Brazil

Ricardo Q. Gurgel,*† Luis E. Cuevas,†‡
Sarah C.F. Vieira,* Vanessa C.F. Barros,*
Paula B. Fontes,* Eduardo F. Salustino,*
Osamu Nakagomi,§ Toyoko Nakagomi,§
Winifred Dove,† Nigel Cunliffe,†
and Charles A. Hart†

We identified 21 rotaviruses in 129 patients with diarrhea in a Brazilian city with high rotavirus vaccine coverage. All rotaviruses were genotype P[4]G2 with 1 mixed infection with P[NT]G9. Although virus predominance could have occurred randomly, the vaccine may be less protective against P[4]G2. Prospective surveillance is urgently needed.

Serotipos de Rotavirus
Brasil



Decline in Diarrhea Mortality and Admissions after Routine Childhood Rotavirus Immunization in Brazil: A Time-Series Analysis

Greice Madeleine Ikeda do Carmo[1], Catherine Yen[2,3], Jennifer Cortes[2,3], Alessandra Araújo Siqueira[1], Wanderson Kleber de Oliveira[1], Juan José Cortez-Escalante[4], Ben Lopman[2], Brendan Flannery[5], Lucia Helena de Oliveira[6], Eduardo Hage Carmo[1], Manish Patel[2]*

- En Brasil hubo una reducción del 25% en la tasa de hospitalización por gastroenteritis aguda grave en niños menores de 1 año (equivalente a 17.000 hospitalizaciones al año) en el Sistema Único de Salud
- 22% de reducción de muertes por diarrea en el primer año de vida (una reducción de 150 muertes por año).
- Las tasas de hospitalización por gastroenteritis se redujo en todas las regiones de Brasil, no sólo en el Norte y Nordeste, donde los beneficios en términos de reducción de la mortalidad fueron más evidentes .

Decline in Diarrhea Mortality and Admissions after Routine Childhood Rotavirus Immunization in Brazil: A Time-Series Analysis

Greice Madeleine Ikeda do Carmo[1], Catherine Yen[2,3], Jennifer Cortes[2,3], Alessandra Araújo Siqueira[1], Wanderson Kleber de Oliveira[1], Juan José Cortez-Escalante[4], Ben Lopman[2], Brendan Flannery[5], Lucia Helena de Oliveira[6], Eduardo Hage Carmo[1], Manish Patel[2]*

Conclución

Después de tres años de la inclusión de la vacuna contra el rotavirus en el cuidado de la salud ha disminuído la mortalidad y los ingresos por diarrea en Brasil

PLoS Medicine

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 16, 2011 VOL. 364 NO. 24

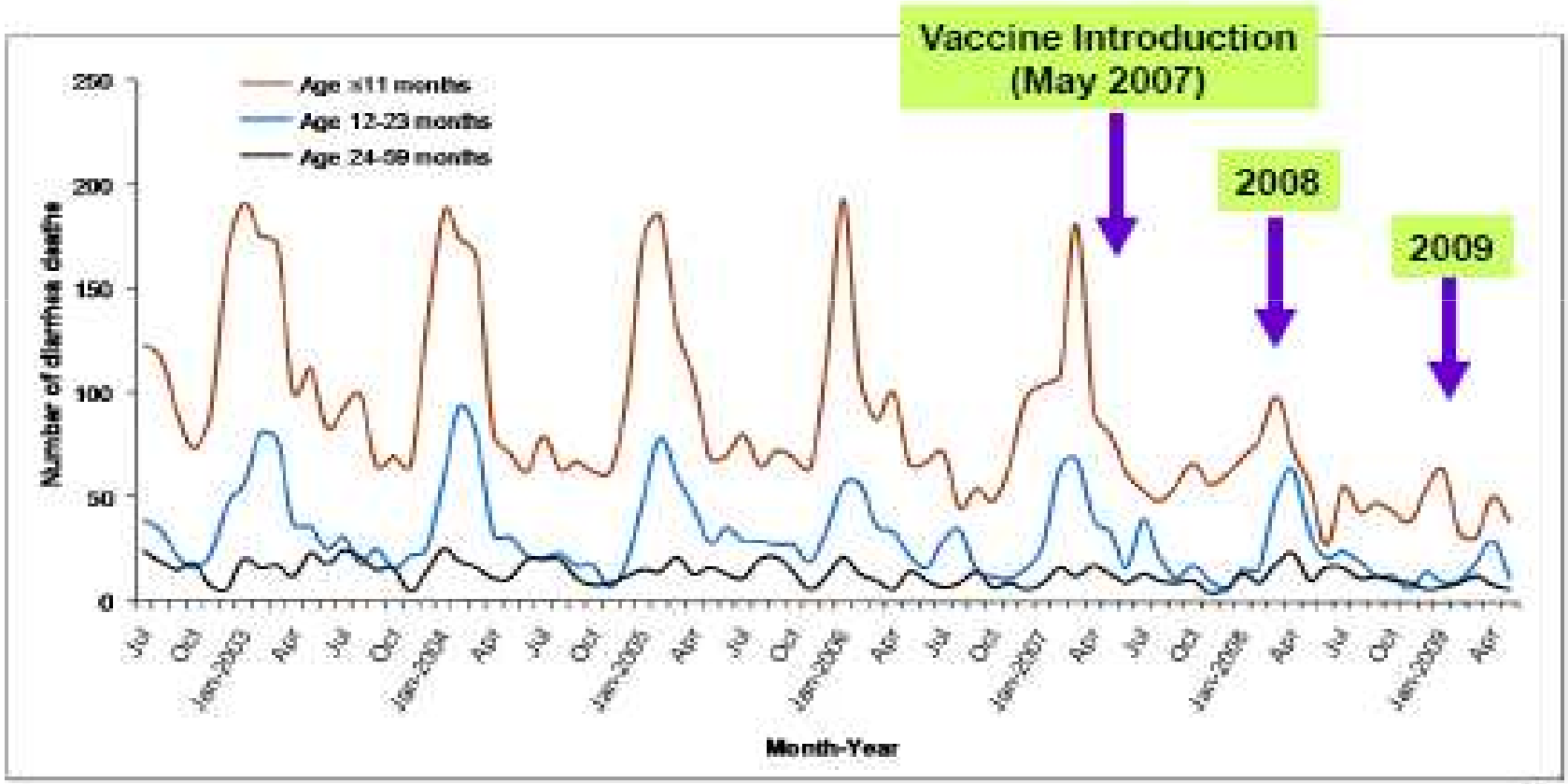
Intussusception Risk and Health Benefits of Rotavirus Vaccination in Mexico and Brazil

Manish M. Patel, Vesta Richardson López-Collada, Marília Mattos Bulhões, Lucia Helena De Oliveira,

CONCLUSIONS

RV1 was associated with a short-term risk of intussusception in approximately 1 of every 51,000 to 68,000 vaccinated infants. The absolute number of deaths and hospitalizations averted because of vaccination far exceeded the number of intussusception cases that may have been associated with vaccination. (Funded in part by the GAVI Alliance and the U.S. Department of Health and Human Services.)

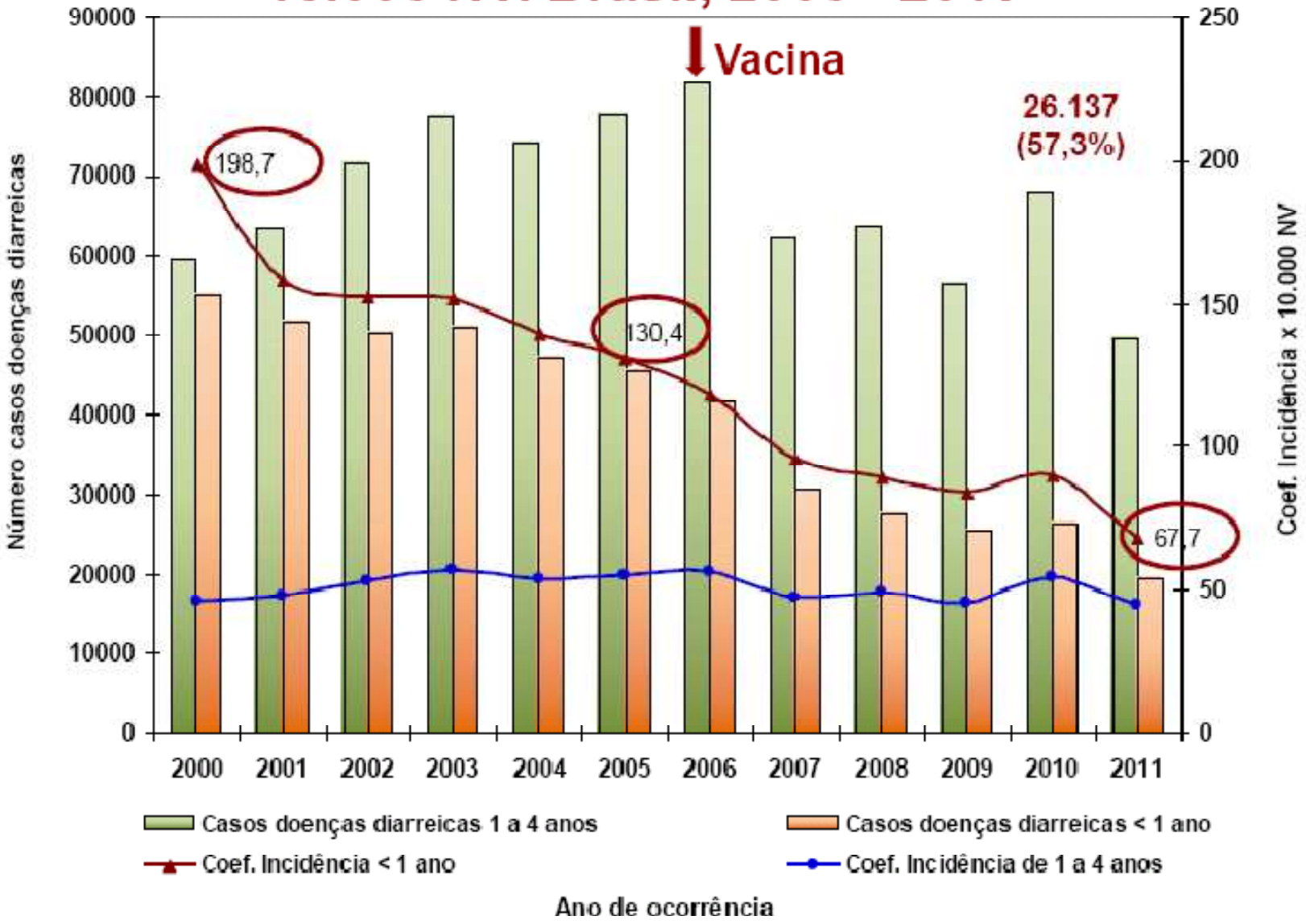
Decline in Winter Childhood Diarrhea Deaths After Vaccine Introduction, Mexico, 2003-09



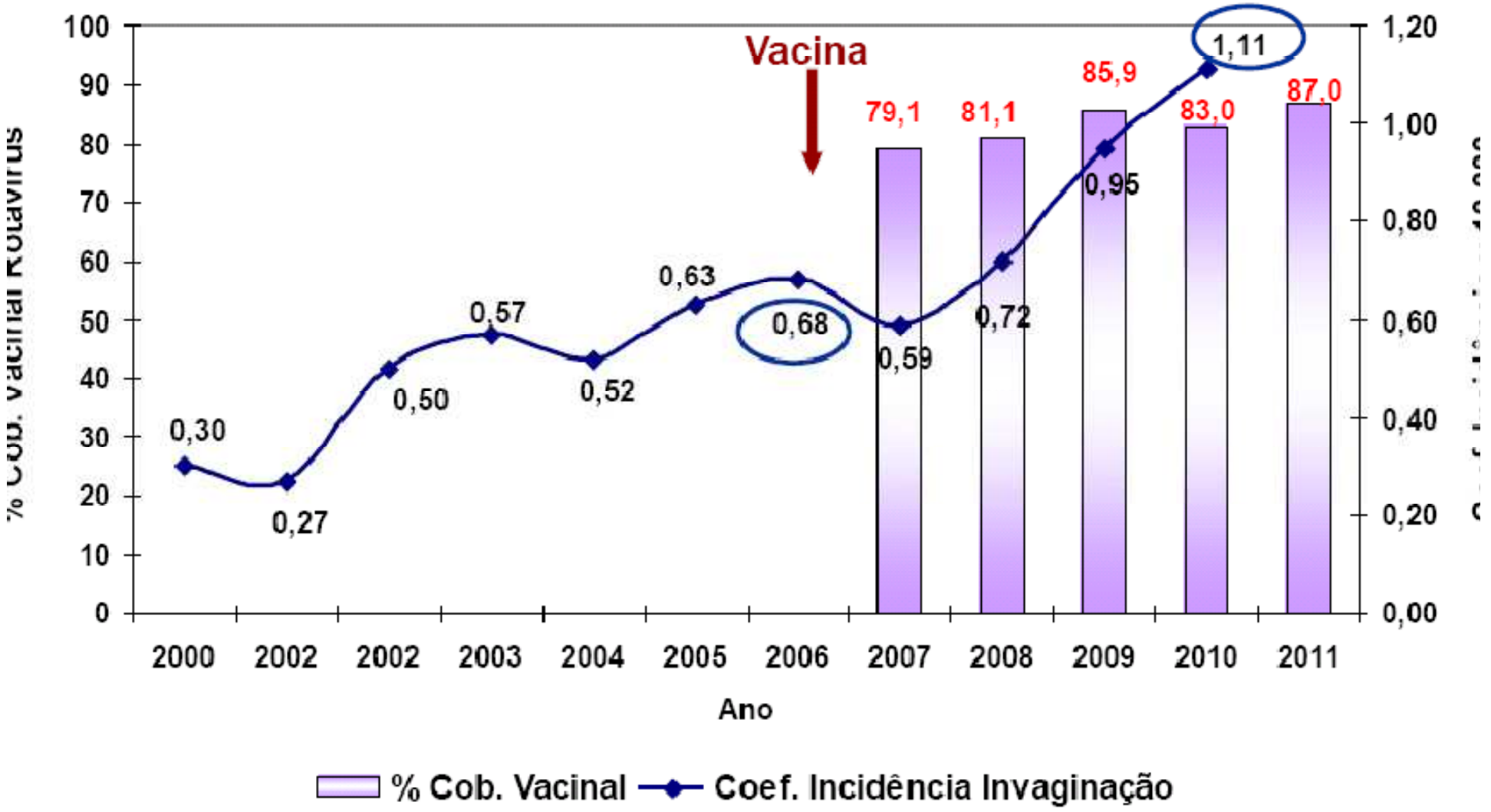
Vacuna contra el rotavirus e invaginación intestinal NEJM 20111

- En México, el riesgo de invaginación intestinal fue de 5,3 veces mayor en los siete días después de la primera dosis de la vacuna y los tiempos de 2,0 a 2,3 de ocho a 21 días después de la dosis 2.
- En Brasil, no fue observado aumento del riesgo después de la primera dosis, pero el riesgo fue de 1,9 a 2,6 veces mayor en los siete días después de la segunda dosis de la vacuna
- Teniendo en cuenta la incidencia natural de la invaginación intestinal en esta época, la asociación observada representa un "exceso" de un caso de invaginación intestinal por 51.000 niños vacunados en México y 1 de cada 68.000 niños vacunados en Brasil.

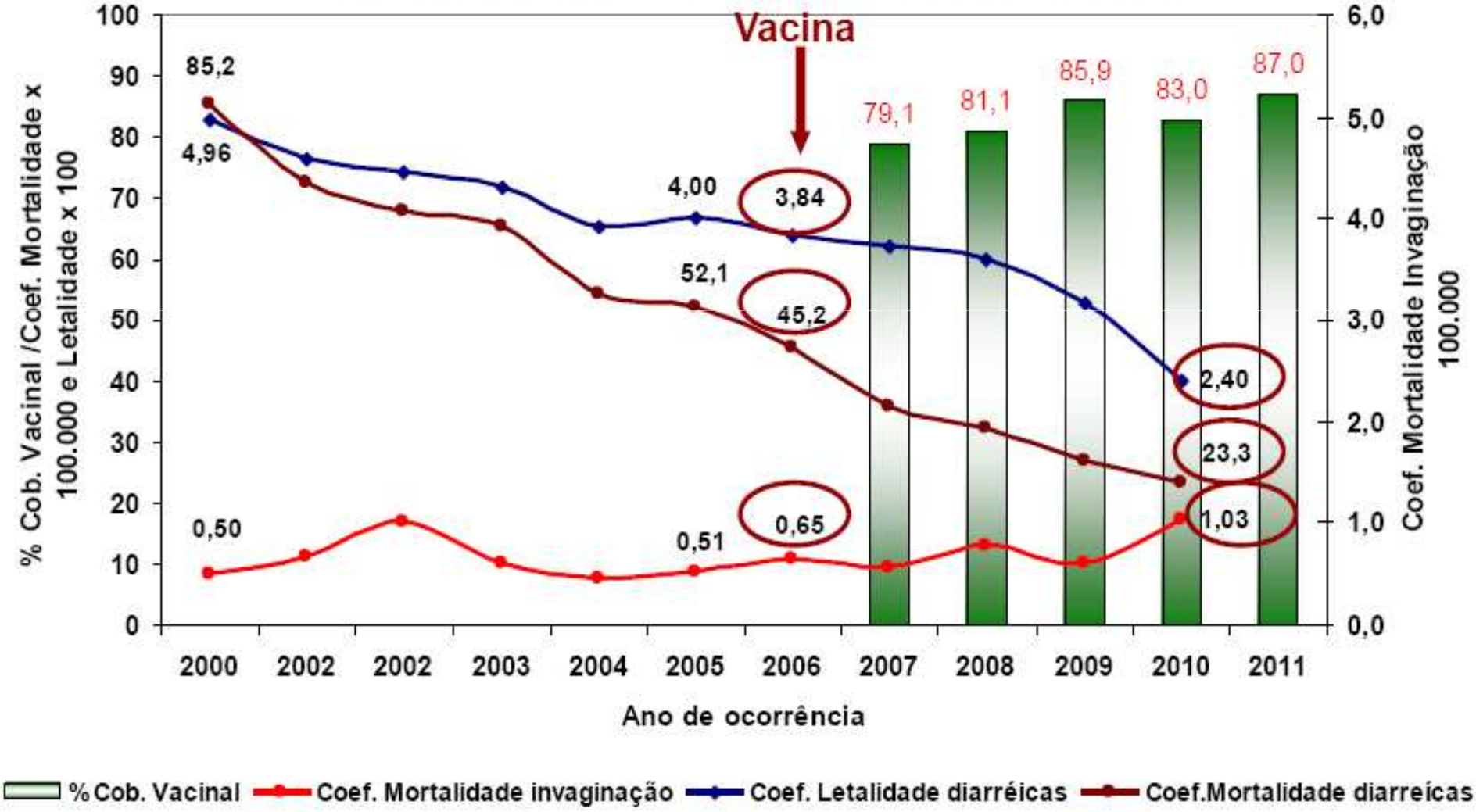
Número de casos de doenças diarreicas em menores de um ano e de 1 a 4 anos com seus coeficientes de incidência x 10.000 NV. Brasil, 2000 - 2011



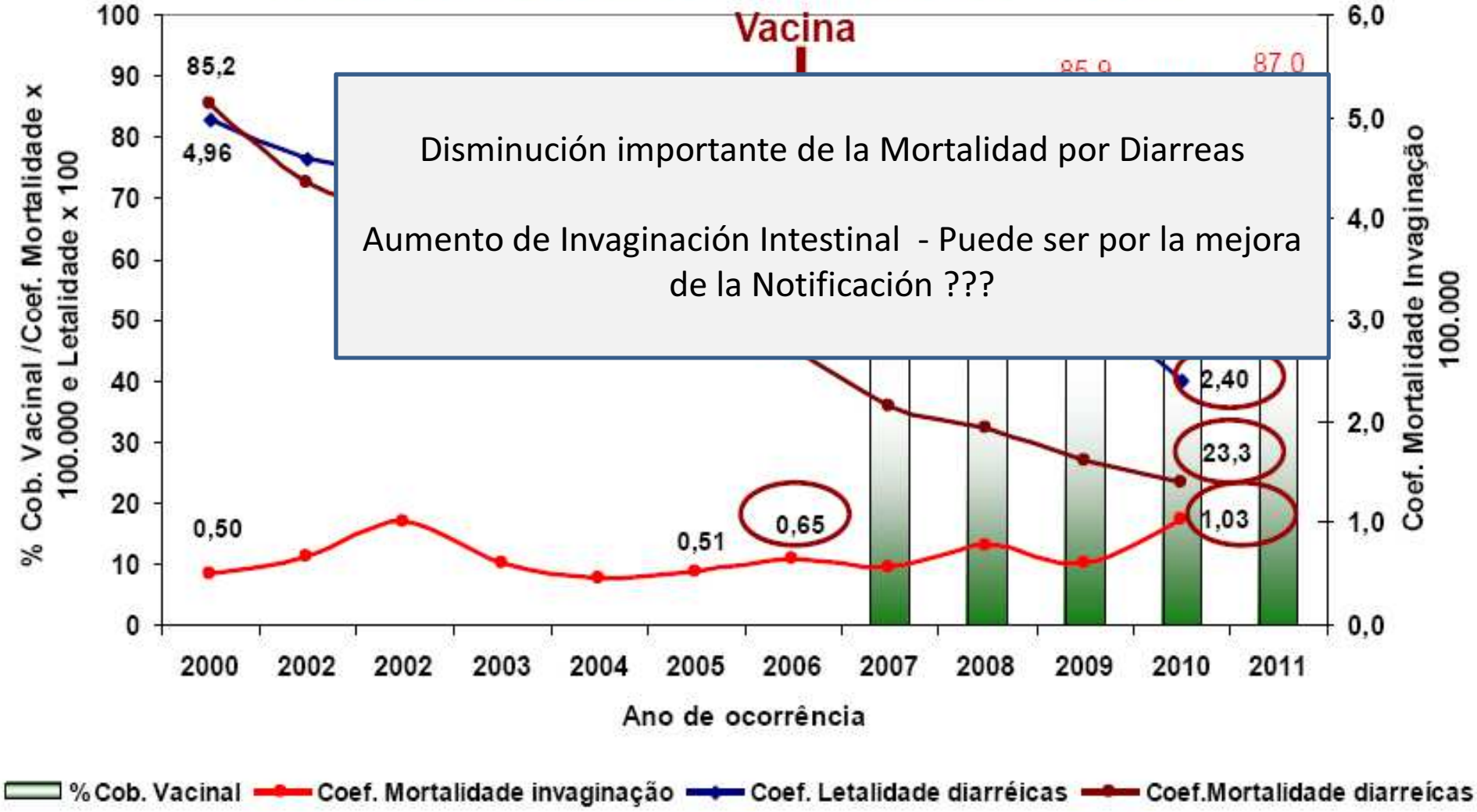
Coeficiente de incidência de invaginação intestinal e cobertura vacinal contra o rotavírus. Brasil, 2000 - 2011



Coeficiente de mortalidade e de letalidade por doenças diarreicas e por invaginação em relação à cobertura vacinal contra o rotavírus, Brasil, 2000 - 2010



Coeficiente de mortalidade e de letalidade por doenças diarreicas e por invaginação em relação à cobertura vacinal contra o rotavírus, Brasil, 2000 - 2010

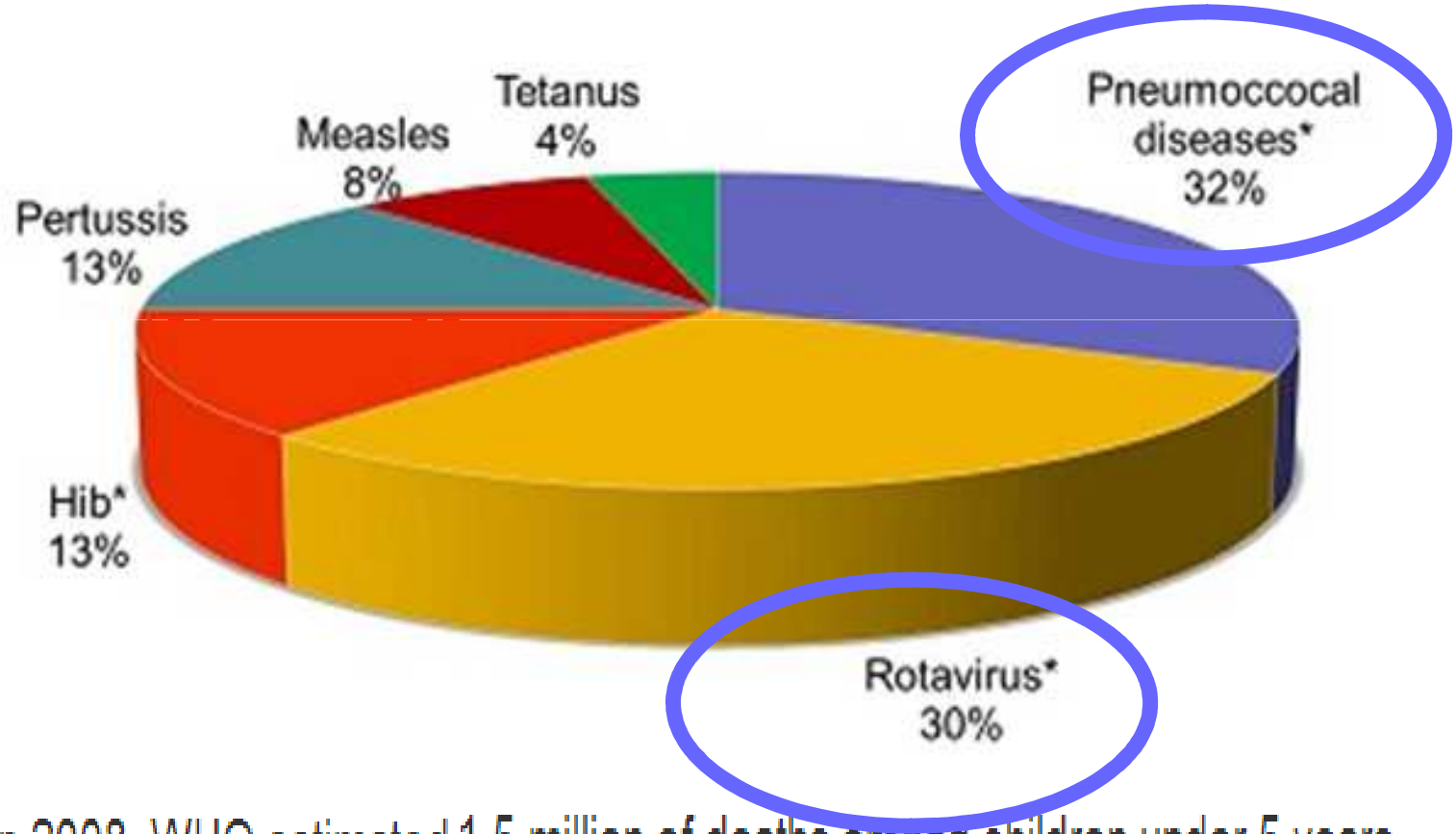


Conclusiones

- La vacuna monovalente esta relacionada a menor número de consultas, internaciones y muertes por diarrea en Brasil
- Aumento de la Notificación de Invaginación Intestinal
- Se observa una cambio en el perfil de genotipos de Rotavirus en todo el país después de la introducción de la vacuna con predominio absoluto del genotipo P[4]G2

Impacto da Doença Pneumocócica e Rotavirus

Causas de morte no mundo por doenças imunopreveníveis



In 2008, WHO estimated 1.5 million of deaths among children under 5 years

Source: Black RE at all. Global, regional, and national causes of child mortality in 2008: a systematic analysis. Lancet. 2010 Jun 5;375(9730):1969-87. Epub 2010 May 11.
* WHO/IVB estimates

http://www.who.int/immunization_monitoring/diseases/en/