Comunicare ed affrontare la complessità (=credibilità)

Rotavirus

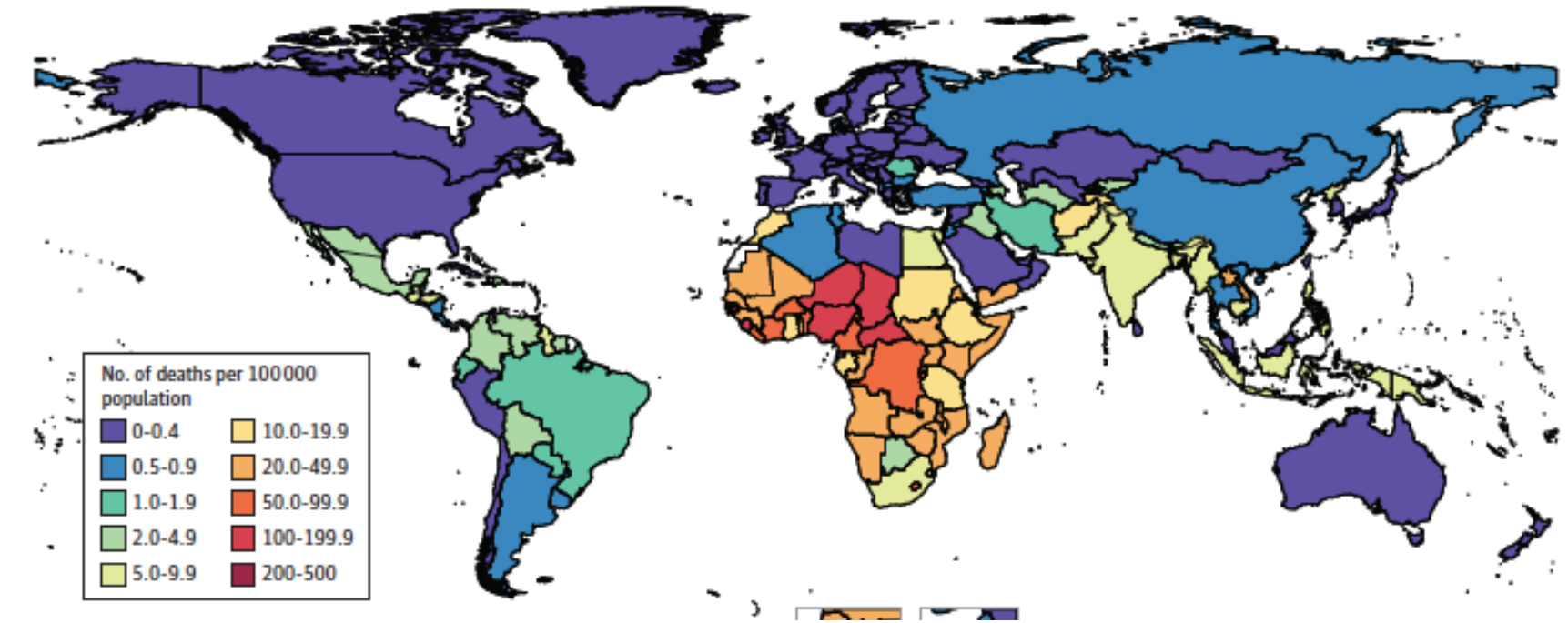
JAMA Pediatrics | Original Investigation

Rotavirus Vaccination and the Global Burden of Rotavirus Diarrhea Among Children Younger Than 5 Years

Christopher Troeger, MPH; Ibrahim A. Khalil, MD; Puja C. Rao, MPH; Shujin Cao, MS; Brigette F. Blacker, MPH; Tahmeed Ahmed, MD; George Armah, PhD; Julie E. Bines, MD; Thomas G. Brewer, MD; Danny V. Colombara, PhD; Gagandeep Kang, MD; Beth D. Kirkpatrick, MD; Carl D. Kirkwood, PhD; Jason M. Mwenda, PhD; Umesh D. Parashar, MD; William A. Petri Jr, MD; Mark S. Riddle, MD; A. Duncan Steele, PhD; Robert L. Thompson, PhD; Judd L. Walson, MD; John W. Sanders, MD; Ali H. Mokdad, PhD; Christopher J. L. Murray, DPhil; Simon I. Hay, FMedSci; Robert C. Reiner Jr, PhD

JAMA Pediatr. doi:10.1001/jamapediatrics.2018.1960
Published online August 13, 2018.

Figure 1. Geographic Distribution of Rotavirus-Associated Mortality Rates Among Children Younger Than 5 Years in 2016



The New England Journal of Medicine

INTUSSUSCEPTION AMONG INFANTS GIVEN AN ORAL ROTAVIRUS VACCINE

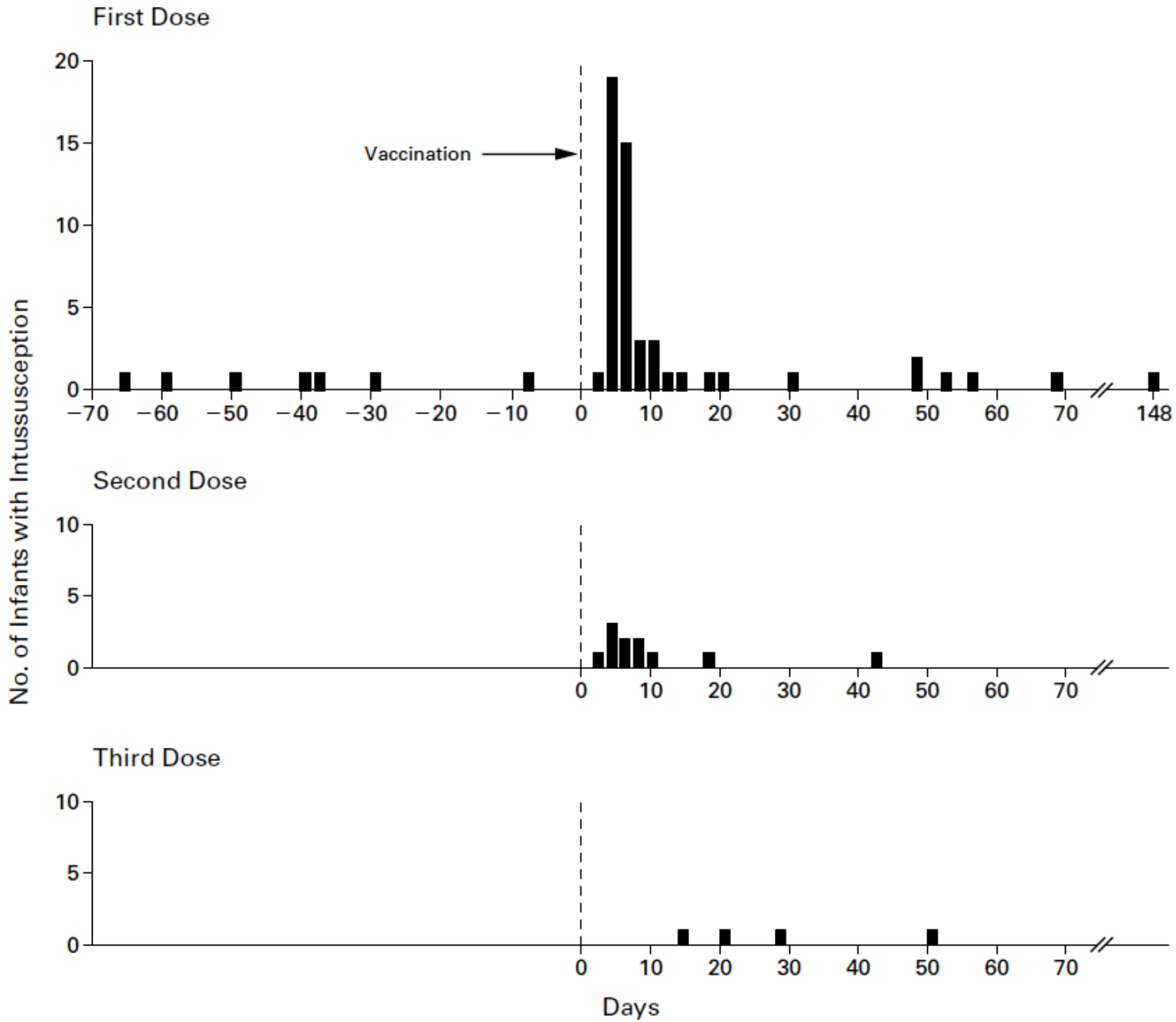
TRUDY V. MURPHY, M.D., PAUL M. GARGIULLO, PH.D., MEHRAN S. MASSOUDI, PH.D., M.P.H., DAVID B. NELSON, B.S., AISHA O. JUMAAN, PH.D., M.P.H., CATHERINE A. OKORO, M.S., LYNN R. ZANARDI, M.D., M.P.H., SABEENA SETIA, M.P.H., ELIZABETH FAIR, M.P.H., CHARLES W. LEBARON, M.D., MELINDA WHARTON, M.D., M.P.H., AND JOHN R. LIVINGOOD, M.D., FOR THE ROTAVIRUS INTUSSUSCEPTION INVESTIGATION TEAM*

N Engl J Med 2001;344:564-72

Bambini < 1 anno di vita
(429 con invaginazione e 1763 controlli sani)

Problema clinico: invaginazione intestinale

Relazione tra invaginazione e vaccinazione per rotavirus?


First Dose
Vaccination
Second Dose
Third Dose
No. of Infants with Intussusception
Days
20
15
10
5
0
−70
−60
−50
−40
−30
−20
−10
0
10
20
30
40
50
60
70
148

The New England Journal of Medicine

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TRUDY V. MURPHY, M.D., PAUL M. GARGIULLO, PH.D., MEHRAN S. MASSOUDI, PH.D., M.P.H., DAVID B. NELSON, B.S., AISHA O. JUMAAN, PH.D., M.P.H., CATHERINE A. OKORO, M.S., LYNN R. ZANARDI, M.D., M.P.H., SABEENA SETIA, M.P.H., ELIZABETH FAIR, M.P.H., CHARLES W. LEBARON, M.D., MELINDA WHARTON, M.D., M.P.H., AND JOHN R. LIVINGOOD, M.D., FOR THE ROTAVIRUS INTUSSUSCEPTION INVESTIGATION TEAM*

Risultato:

Nel gruppo invaginati: 17,2% dei bambini erano vaccinati vs 12% nel gruppo controllo.

P = 0,2

Conclusioni

1. Rapido ritiro dal mercato del vaccino

2. Non riproposto, per ovvi motivi di immagine, neanche nei Paesi in cui il rischio di morte per diarrea è ancora molto alto
(circa 500.000 morti all'anno, nel mondo), da oscurare il rischio potenziale comunque molto basso, e alla fine anche dubbio, dell'invaginazione

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 5, 2006 VOL. 354 NO. 1

Safety and Efficacy of an Attenuated Vaccine against Severe Rotavirus Gastroenteritis

Guillermo M. Ruiz-Palacios, M.D., Irene Pérez-Schael, M.Sc., F. Raúl Velázquez, M.D., Hector Abate, M.D., Thomas Breuer, M.D., SueAnn Costa Clemens, M.D., Brigitte Cheuvart, Ph.D., Felix Espinoza, M.D., Paul Gillard, M.D., Bruce L. Innis, M.D., Yolanda Cervantes, M.D., Alexandre C. Linhares, M.D., Pío López, M.D., Mercedes Macías-Parra, M.D., Eduardo Ortega-Barría, M.D., Vesta Richardson, M.D., Doris Maribel Rivera-Medina, M.D., Luis Rivera, M.D., Belén Salinas, M.D., Noris Pavía-Ruz, M.D., Jorge Salmerón, M.D., Ricardo Rüttimann, M.D., Juan Carlos Tinoco, M.D., Pilar Rubio, M.D., Ernesto Nuñez, M.D., M. Lourdes Guerrero, M.D., Juan Pablo Yarzábal, M.D., Silvia Damaso, M.Sc., Nadia Tornieporth, M.D., Xavier Sáez-Llorens, M.D., Rodrigo F. Vergara, M.D., Timo Vesikari, M.D., Alain Bouckenooghe, M.D., Ralf Clemens, M.D., Ph.D., Béatrice De Vos, M.D., and Miguel O'Ryan, M.D., for the Human Rotavirus Vaccine Study Group*

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 5, 2006 VOL. 354 NO. 1

Safety and Efficacy of an Attenuated Vaccine against Severe Rotavirus Gastroenteritis

63225 bambini arruolati in 11 paesi dell'America Latina ed in Finlandia

31673 bambini sono stati vaccinati ed a 31552 viene somministrato un placebo

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 5, 2006 VOL. 354 NO. 1

Safety and Efficacy of an Attenuated Vaccine against Severe Rotavirus Gastroenteritis

Table 2. Risk of Definite Intussusception and Other Serious Adverse Events among Infants Receiving Vaccine or Placebo.*

Adverse Event	HRV Vaccine (N=31,673)		Placebo (N=31,552)		Difference in Risk per 10,000 Infants (95% CI)†	Relative Risk (95% CI)‡	P Value§
	No. of Events	Incidence Rate¶	No. of Events	Incidence Rate¶			
Definite intussusception							
≤31 Days after either dose‖	6	1.89	7	2.21	−0.32 (−2.91 to 2.18)	0.85 (0.30 to 2.42)	0.78
≤31 Days after dose 1‖	1	0.31	2	0.63	−0.32 (−2.03 to 1.20)	0.50 (0.07 to 3.80)	0.56
≤31 Days after dose 2‖	5**	1.57	5††	1.58	−0.01 (−2.48 to 2.45)	0.99 (0.31 to 3.21)	0.99
Between dose 1 and visit 3‡‡	9	2.84	16	5.07	−2.23 (−5.70 to 0.94)	0.56 (0.25 to 1.24)	0.16
Serious adverse event between dose 1 and visit 3							
Overall§§	928	290.99	1047	331.83	−38.84 (−66.02 to −11.73)	0.88 (0.81 to 0.96)	0.005
Hospitalization	886	279.73	1003	317.89	−38.15 (−64.76 to −11.62)	0.88 (0.81 to 0.96)	0.005
Death	56	17.68	43	13.63	4.05 (−2.15 to 10.40)	1.30 (0.87 to 1.93)	0.20

The NEW ENGLAND JOURNAL of MEDICINE

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Safety and Efficacy of an Attenuated Vaccine against Severe Rotavirus Gastroenteritis

Conclusions: Two oral doses of the live attenuated G1P[8] HRV vaccine were highly efficacious in protecting infants against severe rotavirus gastroenteritis, significantly reduced the rate of severe gastroenteritis from any cause, and were not associated with an increased risk of intussusception.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Safety and Efficacy of a Pentavalent Human–Bovine (WC3) Reassortant Rotavirus Vaccine

Timo Vesikari, M.D., David O. Matson, M.D., Ph.D., Penelope Dennehy, M.D., Pierre Van Damme, M.D., Ph.D., Mathuram Santosham, M.D., M.P.H., Zoe Rodriguez, M.D., Michael J. Dallas, Ph.D., Joseph F. Heyse, Ph.D., Michelle G. Goveia, M.D., M.P.H., Steven B. Black, M.D., Henry R. Shinefield, M.D., Celia D.C. Christie, M.D., M.P.H., Samuli Ylitalo, M.D., Robbin F. Itzler, Ph.D., Michele L. Coia, B.A., Matthew T. Onorato, B.S., Ben A. Adeyi, M.P.H., Gary S. Marshall, M.D., Leif Gothefors, M.D., Dirk Campens, M.D., Aino Karvonen, M.D., James P. Watt, M.D., M.P.H., Katherine L. O'Brien, M.D., M.P.H., Mark J. DiNubile, M.D., H Fred Clark, D.V.M., Ph.D., John W. Boslego, M.D., Paul A. Offit, M.D., and Penny M. Heaton, M.D., for the Rotavirus Efficacy and Safety Trial (REST) Study Team

68038 bambini arruolati in USA e Finlandia

34035 bambini nel gruppo "vaccino" e
34003 nel gruppo placebo

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Safety and Efficacy of a Pentavalent Human–Bovine (WC3) Reassortant Rotavirus Vaccine

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Non rischio aumentato di invaginazione

Table 2. Reduction in the Numbers of Hospitalizations and Emergency Department Visits in the Per-Protocol Population of the Large-Scale Study, According to G Serotype Identified in the Subject's Stool.*

Serotype	No. of Cases of Rotavirus Gastroenteritis		Percent Rate Reduction (95% CI)
	Vaccine Group (N=34,035)	Placebo Group (N=34,003)	
G1	16	328	95.1 (91.6–97.1)
G2	1	8	87.6 (<0–98.5)
G3	1	15	93.4 (49.4–99.1)
G4	2	18	89.1 (52.0–97.5)
G9	0	13	100.0 (67.4–100.0)
G12	0	1	100.0 (<0–100.0)

Efficacy and safety of an oral live attenuated human rotavirus vaccine against rotavirus gastroenteritis during the first 2 years of life in Latin American infants: a randomised, double-blind, placebo-controlled phase III study

*Alexandre C Linhares, F Raúl Velázquez, Irene Pérez-Schael, Xavier Sáez-Llorens, Hector Abate, Felix Espinoza, Pío López, Mercedes Macías-Parra, Eduardo Ortega-Barría, Doris Maribel Rivera-Medina, Luis Rivera, Noris Pavía-Ruz, Ernesto Nuñez, Silvia Damaso, Guillermo M Ruiz-Palacios, Béatrice De Vos, Miguel O'Ryan, Paul Gillard, Alain Bouckenooghe, and the Human Rotavirus Vaccine Study Group**

www.thelancet.com Vol 371 April 5, 2008

15000 bambini randomizzati (1:1) in 10 paesi dell'america latina ad assumere una dose di vaccino o placebo

	RIX4414 (N=7205)		Placebo (N=7081)		Relative risk† (95% CI)	Absolute risk	Vaccine efficacy (95% CI)
	Infants with ≥1 episode*	1000 infants-year ratio	Infants with ≥1 episode*	1000 infants-year ratio			
Severe gastroenteritis according to the clinical case definition‡							
All-cause gastroenteritis							
Severe	342	28·5	551	46·7	0·610 (0·531-0·699)	0·078	39·0 (30·1–46·9)
Admission	265	22·1	429	36·4	0·607 (0·519-0·709)	0·061	39·3 (29·1–48·1)
Rotavirus gastroenteritis§							
Severe	32	2·7	161¶	13·6	0·195 (0·129-0·287)	0·023	80·5 (71·3–87·1)
Admission	22	1·8	127	10·8	0·170 (0·103-0·269)	0·018	83·0 (73·1–89·7)
Serotype specific rotavirus gastroenteritis‖							
G1P[8]**	10††	0·8	55‡‡	4·7	0·179 (0·081-0·354)	0·008	82·1 (64·6–91·9)
Pooled P[8], non-G1 (G3, G4, G9)	19§§	1·6	96¶¶	8·1	0·195 (0·112-0·321)	0·014	80·5 (67·9–88·8)
Pooled non-G1 (G2, G3, G4, G9)	24	2·0	105‖‖	8·9	0·225 (0·138-0·353)	0·015	77·5 (64·7-86·2)
Non-G1, non-P[8] (G2P[4])	5	0·4	8	0·7	0·614 (0·158-2·129)	0·001	38·6 (<0–84·2)
Severe rotavirus gastroenteritis with a score of ≥11 on the Vesikari scale***							
Serotype specific gastroenteritis							
G1P[8]**	9†††	0·7	51†††	4·3	0·173 (0·075-0·356)	0·007	82·7 (64·4–92·5)
Pooled P[8], non-G1 (G3, G4, G9)	17†††	1·4	94†††	8·0	0·178 (0·099-0·300)	0·013	82·2 (70·0–90·1)
Pooled non-G1 (G2, G3, G4, G9)	21	1·7	101	8·6	0·204 (0·121-0·329)	0·014	79·6 (67·1-87·9)
Non-G1, non-P[8] (G2P[4])	4	0·3	7	0·6	0·562 (0·121-2·209)	0·001	43·8 (<0–87·9)

Vaccine 28 (2010) 345–351

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

RotaTeq®, a pentavalent rotavirus vaccine: Efficacy and safety among infants in Europe

Timo Vesikari[a,*], Robbin Itzler[b], Aino Karvonen[a], Tiina Korhonen[a], Pierre Van Damme[c], Ulrich Behre[d], Gianni Bona[e], Leif Gothefors[f], Penny M. Heaton[b], Michael Dallas[b], Michelle G. Goveia[b]

Table 5
Hospitalizations and ED visits in Europe for RVGE regardless of serotype in infants followed for up to 2 years.

	Per-protocol analysis[a]			Intention-to-treat analysis[b]		
	RotaTeq® *N* = 14,018	Placebo *N* = 13,988	Rate reduction, % (95% CI)	RotaTeq® *N* = 14,831	Placebo *N* = 14,734	Rate reduction % (95% CI)
Number (rate) of events[c]						
Hospitalizations and ED visits	18 (1.9)	331 (35.2)	94.5 (91.3–96.8)	31 (2.3)	387 (29.4)	92.0 (88.4–94.6)
Hospitalizations	6 (0.6)	138 (14.7)	95.6 (90.3–98.4)	14 (1.1)	172 (13.1)	91.9 (86.0–95.6)
ED visits	12 (1.3)	193 (20.5)	93.8 (88.9–96.9)	17 (1.3)	215 (16.3)	92.1 (87.0–95.4)

Conclusioni

Vaccino sembra non prioritario…**nessuna modifica sulla mortalità**, peraltro già bassa, neanche nei paesi "meno" sviluppati

Da valutare l'effetto, nei paesi industrializzati, sulla diminuzione delle spese sanitarie (aumento della necessità di "sicurezza")

Eur J Health Econ
DOI 10.1007/s10198-014-0624-2

ORIGINAL PAPER

Recommendation of rotavirus vaccination and herd effect: a budget impact analysis based on German health insurance data

Alexander Karmann · Andrea Jurack · Daniel Lukas

Cost-impact study of **rotavirus vaccination** programme in Scotland.
Heggie R, Murdoch H, McIntosh E, Cameron C, Smith-Palmer A, Bouttell J.
Hum Vaccin Immunother. 2018 Nov 5. doi: 10.1080/21645515.2018.1543522.

Vaccinazione di massa risparmio di 500 milioni di sterline

Conclusioni

Forse utile nei paesi in via di sviluppo, ma attualmente costi non permettono il loro utilizzo.

Altre più economiche e facilmente applicabili misure di protezione (zinco, vitamina A) sono risultate molto efficaci sulla mortalità da diarrea.
Sono misure largamente inapplicate.

Inoltre, con un 25 cents al giorno si potrebbe fornire una dieta normocalorica, normoproteica, e arricchita di oligoelementi e vitamine a ogni lattante africano

Direct and possible indirect effects of **vaccination** on **rotavirus** hospitalisations among children in Malawi four years after programmatic introduction.

Bennett A, Pollock L, Jere KC, Pitzer VE, Parashar U, Tate JE, Heyderman RS, Mwansambo C, French N, Nakagomi O, Iturriza-Gomara M, Everett D, Cunliffe NA, Bar-Zeev N; VacSurv Consortium.

Vaccine. 2018 Nov 12;36(47):7142-7148.

Sustained impact of **rotavirus** vaccine introduction on **rotavirus** gastroenteritis hospitalizations in children <5 years of age, Ghana, 2009-2016.

Enweronu-Laryea CC, Armah G, Sagoe KW, Ansong D, Addo-Yobo E, Diamenu SK, Mwenda JM, Parashar UD, Tate JE.

Vaccine. 2018 Nov 12;36(47):7131-7134.

Piano nazionale vaccinale 2017-2019

Il calendario vaccinale del Piano Nazionale di Prevenzione Vaccinale 2017-2019

Vaccino	0gg-30gg	3° mese	4° mese	5° mese	6° mese	7° mese	11° mese	13° mese	15° mese	6° anno	12°-18° anno	19-49 anni	50-64 anni	> 64 anni	Soggetti ad aumentato rischio
DTPa**		DTPa		DTPa			DTPa			DTPa***	dTpaIPV	1 dose dTpa**** ogni 10 anni			(1)
IPV		IPV		IPV			IPV			IPV					
Epatite B	EpB-EpB*	Ep B		Ep B			Ep B								(2)
Hib		Hib		Hib			Hib								(3)
Pneumococco		PCV		PCV			PCV							PCV+PPSV	(4) ^^
MPRV								MPRV		MPRV					(6) ^
MPR								*oppure* MPR + V		*oppure* MPR + V					(5) *****
Varicella															(6)^
Meningococco C								Men C§			Men ACWY coniugato				(7)
Meningococco B*^		Men B	Men B		Men B			Men B							
HPV											HPV°: 2-3 dosi (in funzione di età e vaccino)				(8)
Influenza														1 dose all'anno	(9) °°
Herpes Zoster														1 dose#	(10)
Rotavirus		Rotavirus## (due o tre dosi a seconda del tipo di vaccino)													
Epatite A															(11)