VECCHIE E NUOVE VACCINAZIONI

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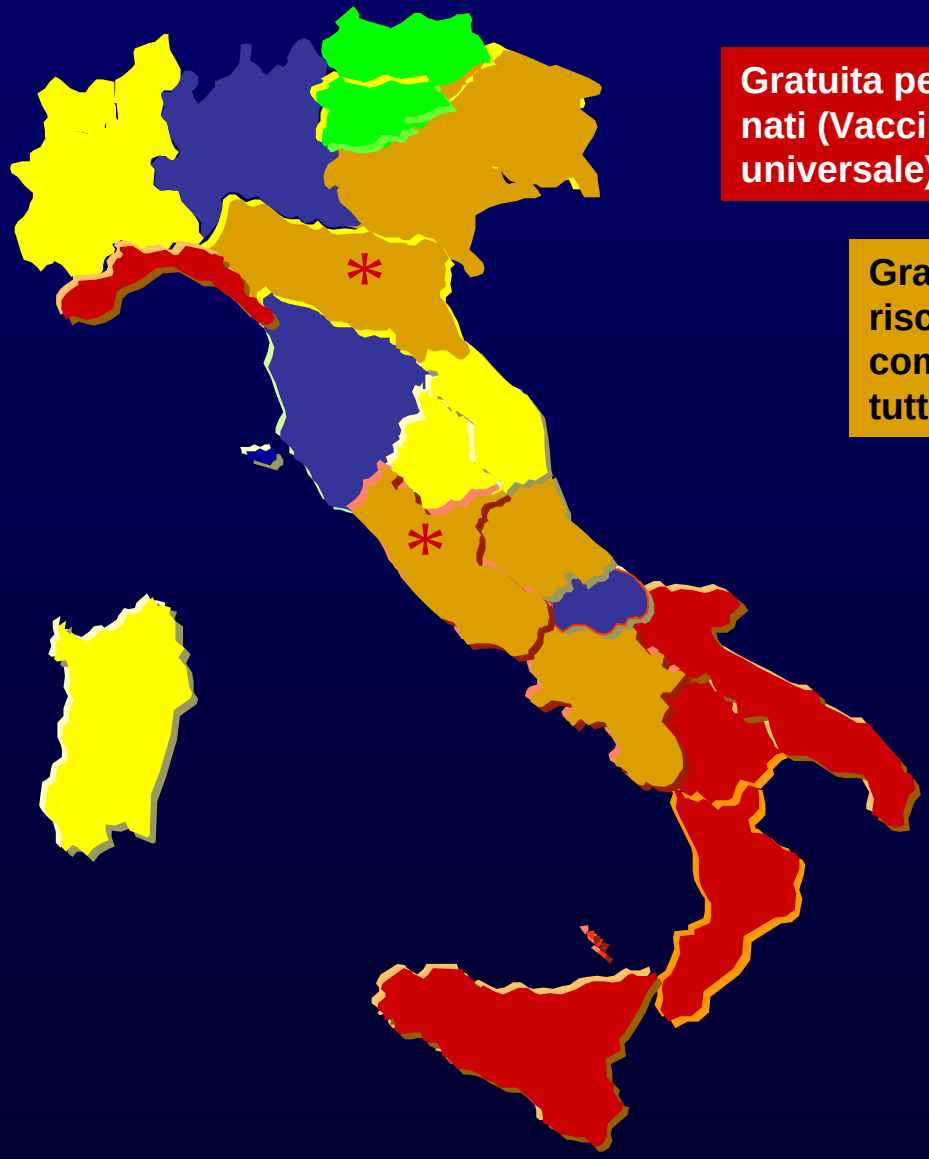
Scelte regionali per la vaccinazione con PCV-7



Gratuita per tutti i nuovi nati (Vaccinazione universale)

Gratuita per bambini a rischio e per frequentanti comunità. Copayment per tutti gli altri

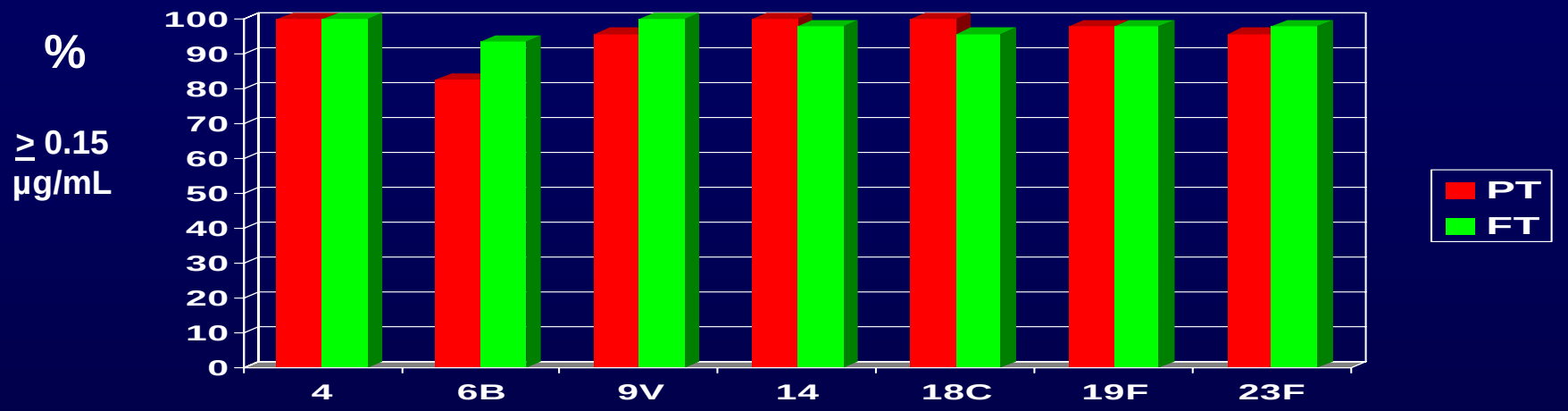
Gratuita per i bambini a rischio e copayment per frequentanti comunità e bambini sani

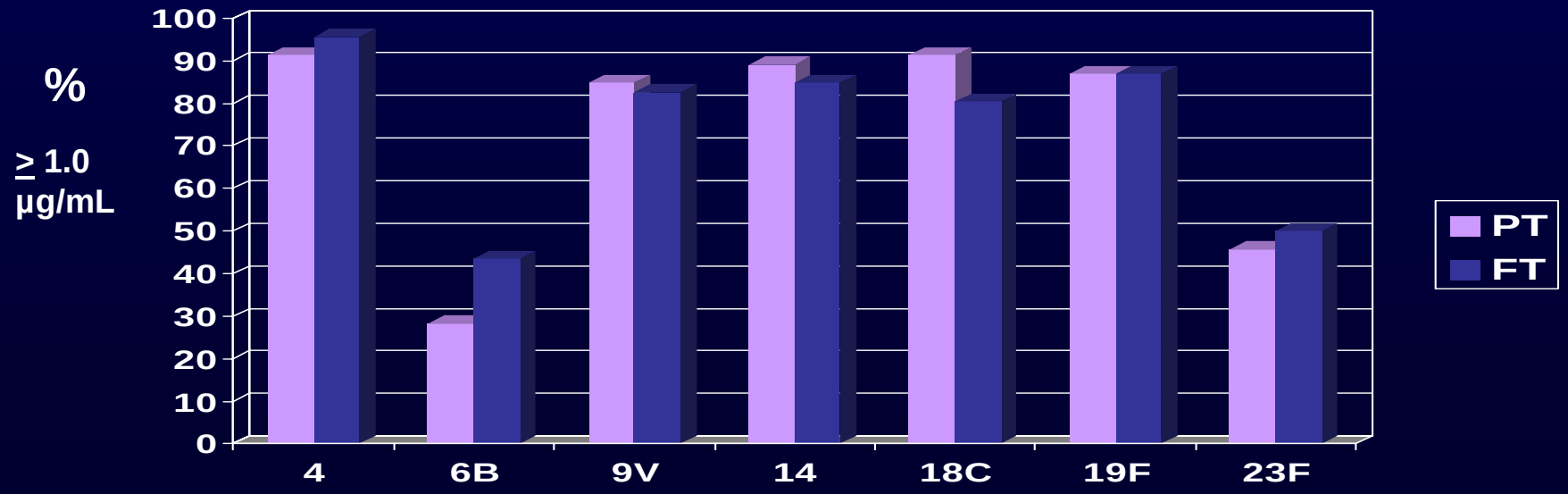
Gratuita per bambini a rischio e copayment per frequentanti comunità

Solo per bambini a rischio

Pre-term (PT) and full-term (FT) infants that reach theoretic protective levels of type-specific IgG antibodies against pneumococcal disease one month after the 2nd dose of PCV

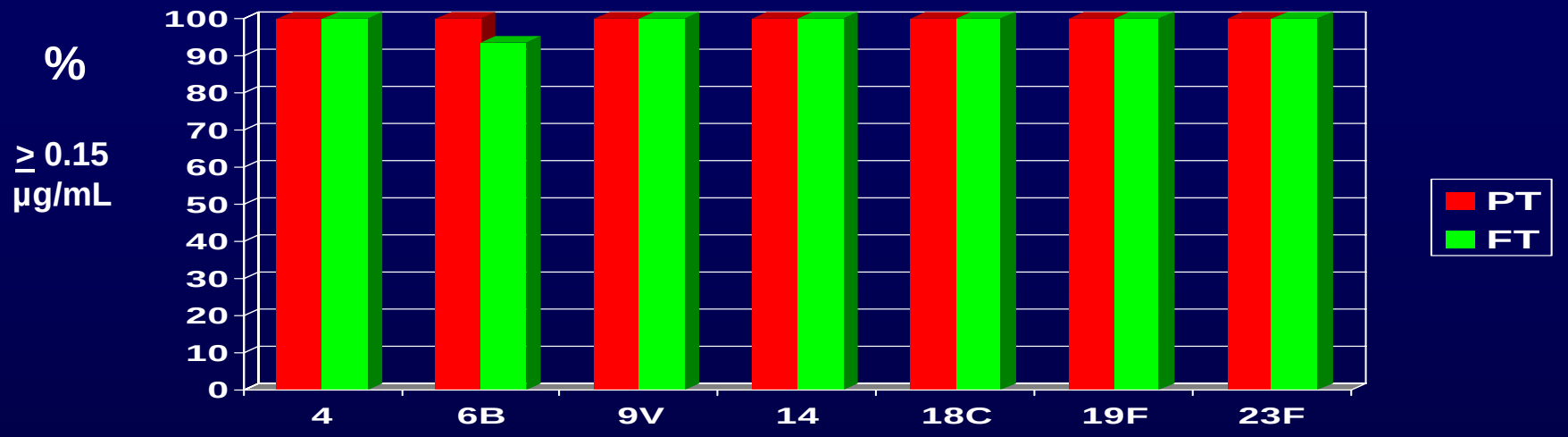
(Esposito S et al. Vaccine 2005)

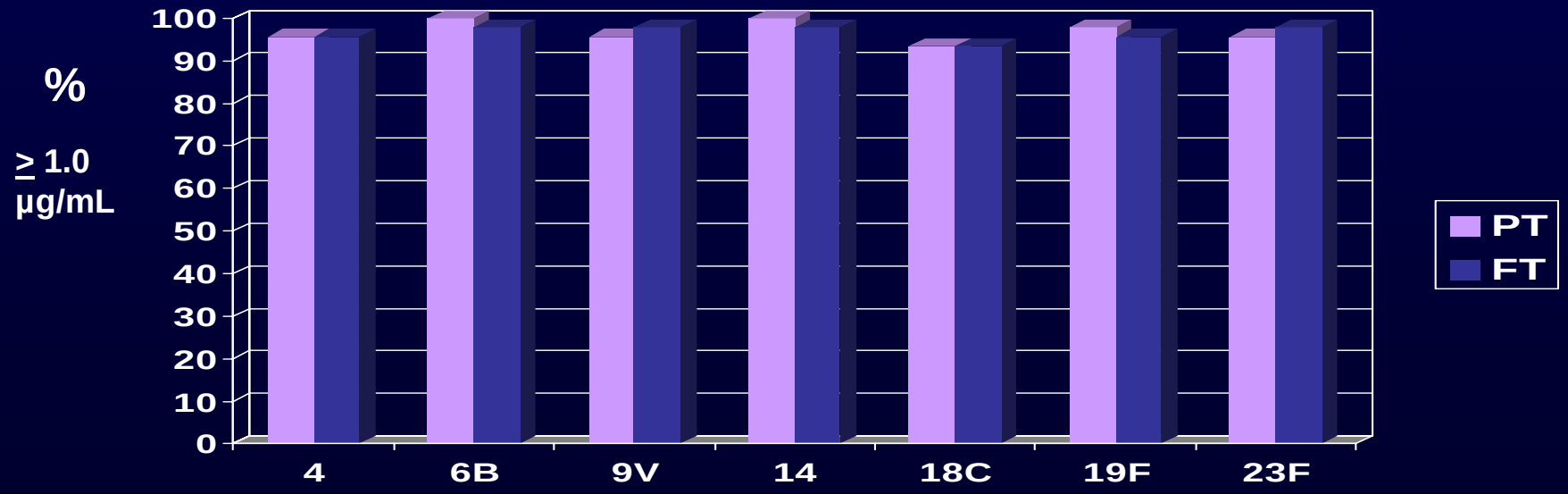




Pre-term (PT) and full-term (FT) infants that reach theoretic protective levels of type-specific IgG antibodies against pneumococcal disease one month after the 3rd dose of PCV

(Esposito S et al., Vaccine 2005)





PCV7: REGIONE LOMBARDIA
AIM

To evaluate the impact of PCV-7 administered at 3, 5 and 11 months of age on respiratory tract infections in very young children

Esposito S et al. 42sd ICAAC 2005

PNEUMO GROUP REGIONE LOMBARDIA - STUDY CHILDREN

	PCV-7	CONTROLS
No. of children initially enrolled	845	779
No. of children who completed the protocol	811 (95.9%)	744 (95.5%)

Esposito S et al. 42sd ICAAC 2005

FREQUENCY OF COMMUNITY ACQUIRED PNEUMONIA (CAP) DURING FOLLOW-UP

	PCV-7 (N.811)	Controls (N.744)	RR	95% CI	*P*
Total CAPs	27	72			
Episodes/ 100 child years	1.7	4.8	0.35	0.22-0.53	<0.001

Esposito S et al. 42sd ICAAC 2005

FREQUENCY OF COMMUNITY ACQUIRED PNEUMONIA (CAP) DURING EACH HALF YEAR OF FOLLOW-UP

	PCV-7 (N.811)	Control (N.744)	RR	95% CI	*P*
CAPs in the I half year of follow-up	9	7			
Episodes/100 child years	2.2	1.9	1.17	0.44-3.16	0.74
CAPs in the II half year of follow-up	3	9			
Episodes/100 child years	0.7	2.4	0.29	0.08-1.11	0.07
CAP in the III half year of follow-up	7	16			
Episodes/100 child years	1.72	4.30	0.40	0.16-0.97	0.04
CAPs in the IV half year of follow-up	8	40			
Episodes/100 child years	1.97	10.7	0.18	0.09-0.39	<0.001

Esposito S et al. 42sd ICAAC 2005

FREQUENCY OF ACUTE OTITIS MEDIA (AOM) DURING FOLLOW-UP

	PCV-7 (N.811)	Controls (N.744)	RR	95% CI	*P*
Total AOMs	637	698			
Episodes/ 100 child years	39.2	46.9	0.83	0.61-1.02	0.02

Esposito S et al. 42sd ICAAC 2005

FREQUENCY OF ACUTE OTITIS MEDIA (AOM) DURING EACH HALF YEAR OF FOLLOW-UP

	PCV-7 (N.811)	Control (N.744)	RR	95% CI	*P*
AOMs in the I half year of follow-up	156	156			
Episodes/100 child years	38.4	41.9	0.91	0.75-1.20	0.06
AOMs in the II half year of follow-up	195	220			
Episodes/100 child years	48.0	59.1	0.81	0.76-1.02	0.04
AOM in the III half year of follow-up	144	162			
Episodes/100 child years	35.5	43.5	0.82	0.62-1.24	0.04
AOMs in the IV half year of follow-up	142	160			
Episodes/100 child years	35.0	43.0	0.81	0.61-1.20	0.04

Esposito S et al. 42sd ICAAC 2005

ANTIBIOTIC COURSES PRESCRIBED DURING FOLLOW-UP

	PCV-7 (N.811)	Controls (N.744)	RR	95% CI	*P*
Total number of antibiotic courses during follow-up	2020	2076			
Courses/100 child years	124	139	0.89	0.83-0.94	0.0001

Esposito S et al. 42sd ICAAC 2005

ANTIBIOTIC COURSES DURING EACH HALF YEAR OF FOLLOW-UP

	PCV-7 (N.811)	Control (N.744)	RR	95% CI	*P*
Total number of antibiotic courses prescribed in the I half year of follow-up	504	454			
Courses/100 child years	122	120	1.01	0.89-1.14	0.87
Total number of antibiotic courses prescribed in the II half year of follow-up	620	658			
Courses/100 child years	153	177	0.86	0.76-0.95	0.004
Total number of antibiotic courses prescribed in the III half year of follow-up	549	562			
Courses/100 child years	135	151	0.89	0.79-1.01	0.06
Total number of antibiotic courses prescribed in the IV half year of follow-up	347	402			
Courses/100 child years	85	108	0.78	0.67-0.90	0.0008

COSTI PER LA GESTIONE DELLE MALATTIE RESPIRATORIE CON O SENZA VACCINO ANTIPNEUMOCOCCO (24 mesi di controllo)

costi diretti SSN (a 30 mesi di età)

DIRETTI SSN	Eur	PCV-7	per paz	Ctrl	per paz
Vaccinazione	€ 132,91	107.789	133	-	-
Otiti	€ 30,59	19.486	24	21.352	29
Polmoniti	€ 2.258,54	60.981	75	162.615	219
TOTALE		**188.256**	**232**	**183.967**	**247**

costi totali (a 30 mesi di età)

DIR+IND	Eur	PCV-7	per paz	Ctrl	per paz
Vaccinazione	€ 150,93	122.405	151	-	-
Otiti	€ 30,59	19.486	24	21.352	26
Polmoniti	€ 2.546,90	68.766	85	183.377	226
TOTALE		**210.658**	**260**	**204.729**	**275**

Esposito S et al. ESPID 2006

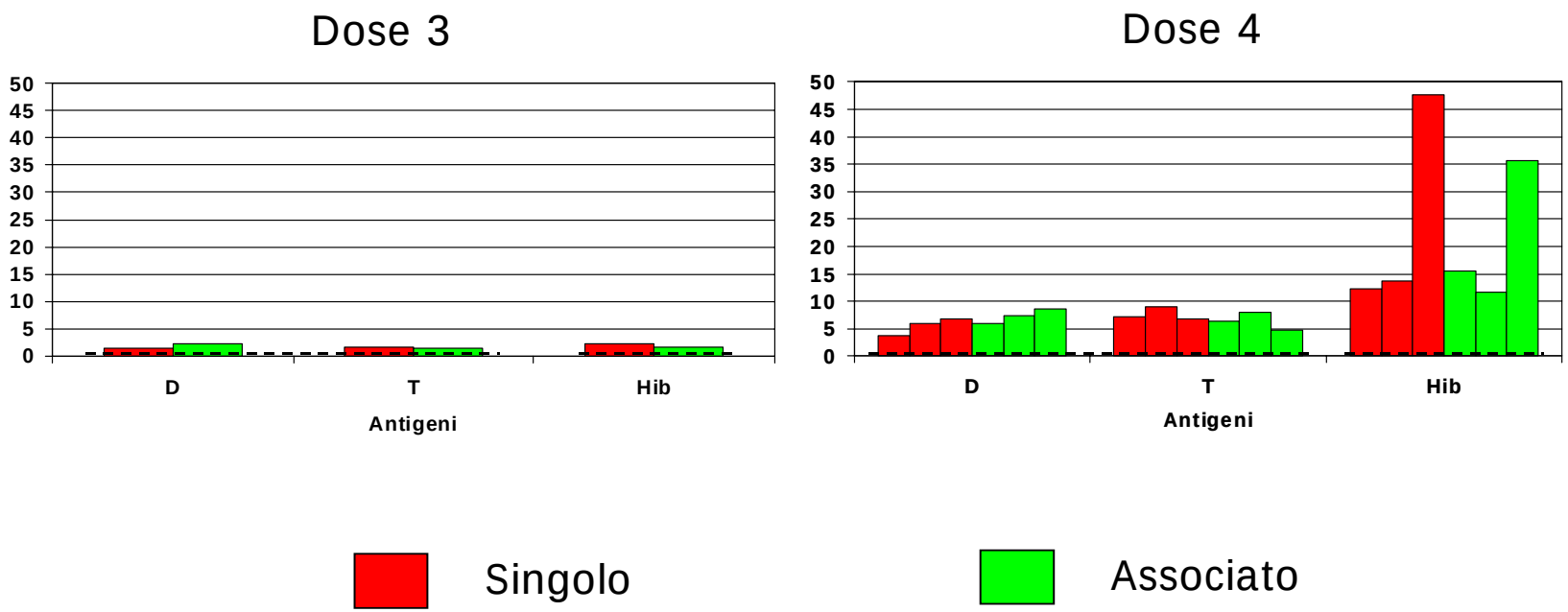
IMPLICAZIONI A LIVELLO LOMBARDIA

(sulla popolazione di nuovi nati 2004 - al variare della copertura vaccinale)

	costi diretti SSN (a 30 mesi di età)		
LOMBARDIA	% copertura	N° soggetti	**Risparmio in €**
	70%	61.116	**916.734**
	80%	69.846	**1.047.696**
	90%	78.577	**1.178.658**

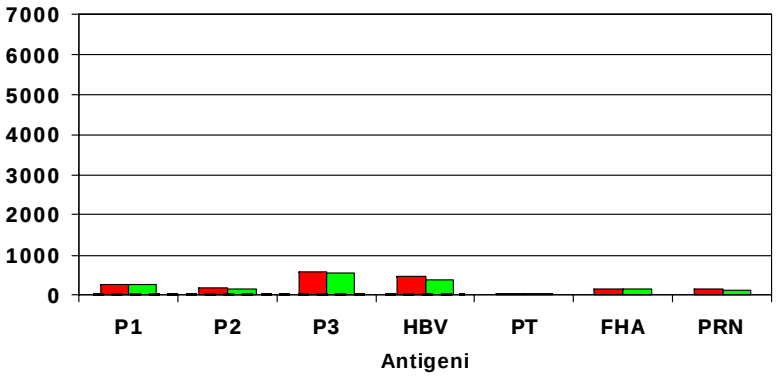
Esposito S et al. ESPID 2006

Esavalente + pneumococco coniugato
Titoli anticorpali (GMT)

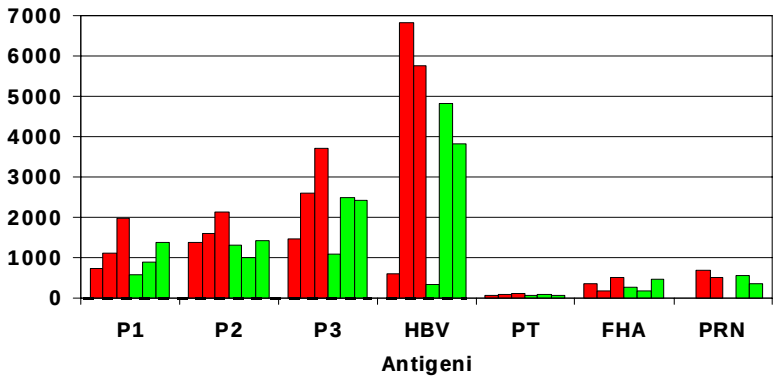


Esavalente + pneumococco coniugato
Titoli anticorpali (GMT)

Dose 3



Dose 4

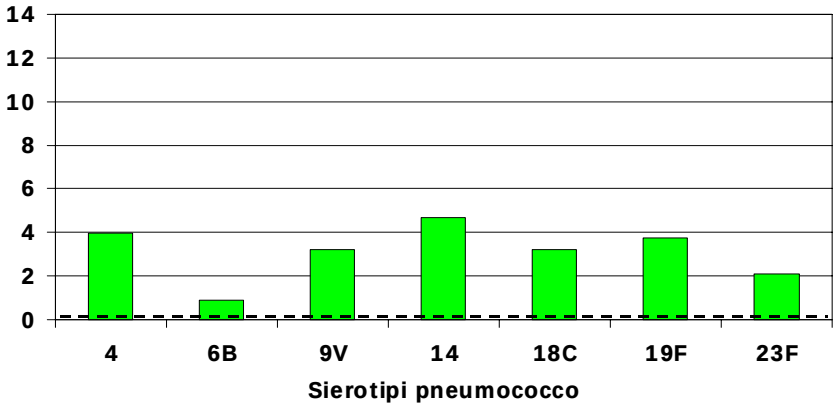


Singolo

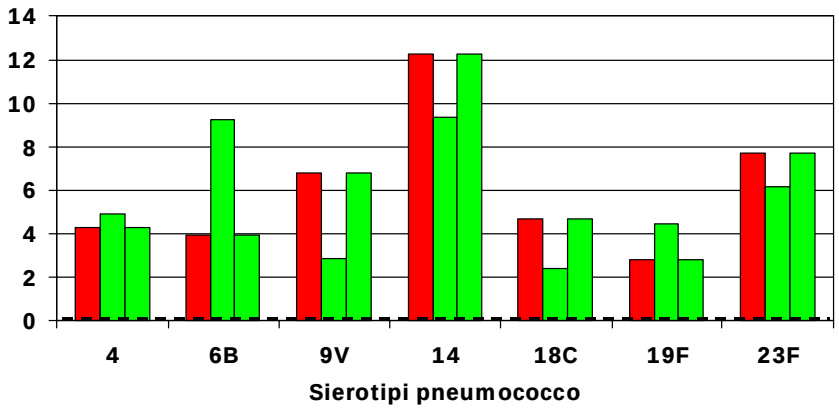
Associato

Esavalente + pneumococco coniugato
Titoli anticorpali (GMT)

Dose 3



Dose 4



Singolo

Associato

LOCAL REACTIONS WITHIN 7 DAYS OF THE THIRD VACCINATION, ACCORDING TO THE VACCINE USED

LOCAL REACTION	HEXAVAC (N=503)	HEXAVAC + PREVENAR (N=558)	INFANRIX-HEXA (N=273)	INFANRIX-HEXA + PREVENAR (N=283)
All local reactions	110 (21.9%)°	129 (23.1%)	41 (15.0%)°	69 (24.4%)
Erythema	71 (14.1%)°	84 (15.1%)*	14 (5.1%)°	25 (8.8%)*
Swelling/ tenderness	85 (16.9%)	86 (15.4%)	37 (13.6%)	46 (16.3%)
Use of drugs for local reactions	52 (10.3%)°	57 (10.2%)	15 (5.5%)°	31 (11.0%)

°= $p < 0.05$

Esposito S et al. ESPID 2005

SYSTEMIC REACTIONS AND USE OF ANTIPYRETIC WITHIN 7 DAYS OF THIRD VACCINATION, ACCORDING TO THE VACCINES USED

SYSTEMIC REACTION	HEXAVAC (N=503)	HEXAVAC + PREVENAR (N=558)	INFANRIX-HEXA (N=273)	INFANRIX-HEXA + PREVENAR (N=283)
All systemic reactions	172 (34.2%)*	272 (48.7%)*	103 (37.7%)°	133 (47.0%)°
Fever > 39°C Duration (days)	124 (24.7%)* 19 (3.8%) 1 (1h-4d)	204 (36.6%)* 34 (6.1%) 1 (2h-4d)	74 (27.1%)° 12 (4.4%) 1 (6h-2d)	101 (35.7%)° 18 (6.4%) 1 (6h-2d)
Irritability	70 (13.9%)	87 (15.6%)	34 (12.5%)	46 (16.3%)
Decreased appetite	10 (2.0%)	15 (2.7%)	12 (4.4%)	9 (3.2%)
Excessive crying	6 (1.2%)**	7 (1.3%)	3 (1.1%)**	0
Drowsiness	5 (1.0%)	7 (1.3%)	5 (1.8%)	9 (3.2%)
Restless sleep	0**	2 (0.4%)°°	5 (1.8)**	6 (2.1)°°

*,**,°,°° = $p < 0.05$

Esposito S et al. ESPID 2005

OSPEDALIZZAZIONE (CASI/ANNO) PER VARICELLA NEGLI U.S.A. IN ERA PREVACCINALE (1988-1995)

(da Galil et al. Pediatr Infect Dis J 2002)

Age (yr)	Male	Female	Total	Rate/10 000 Varicella Cases	Rate/10 000 Population
< 1	756 (60.6)	491 (39.4)*	1247 (11.7)	64.8	3.1
1–4	2119 (60.9)	1358 (39.1)	3477 (32.7)	23.0	2.3
5–9	853 (49.3)	879 (50.7)	1732 (16.3)	11.3	1.0
10–19	386 (49.3)	396 (50.7)	782 (7.4)	21.6	0.4
20–49	1810 (63.1)	1058 (36.9)	2868 (27.0)	210.7	0.2
20+	1998 (58.9)	1396 (41.1)	3394 (31.9)	143.9	0.2
Total	6112 (57.5)	4520 (42.5)	10632 (100)	26.8	0.4

* Number in parentheses, percent.

CAUSE DI OSPEDALIZZAZIONE PER VARICELLA NEGLI U.S.A. IN ERA PREVACCINALE

(da Galil et al. Pediatr Infect Dis J 2002)

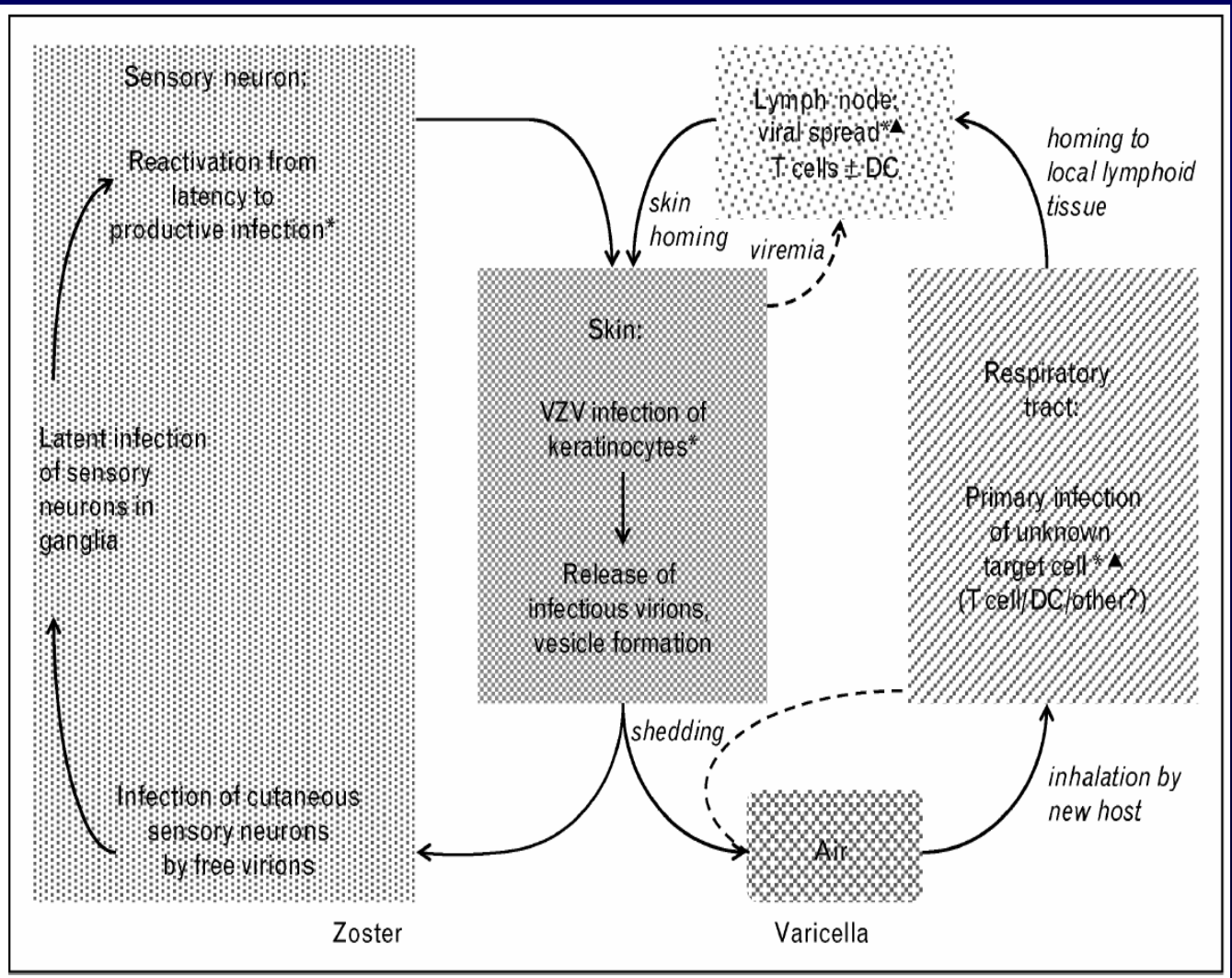
Complication	Annual No. of Persons Hospitalized with Specified Varicella Complication	Rate of Complications/10 000 Varicella Cases	Rate of Complications/10 000 Population
Lower respiratory infection	3154 (2132–4174)*	7.93 (7.02–8.85)	0.12 (0.08–0.16)
Viral (including varicella) pneumonitis	2222 (1429–3015)	5.59 (4.94–6.24)	0.09 (0.06–0.12)
Bacterial pneumonia	1022 (506–1538)	2.57 (2.26–2.89)	0.04 (0.02–0.06)
Fluid/electrolyte disturbance	2049 (1367–2730)	5.16 (4.56–5.75)	0.08 (0.05–0.11)
Skin/soft tissue infection	1895 (1163–2625)	4.77 (4.21–5.32)	0.07 (0.05–0.10)
Encephalitis	999 (579–1419)	2.51 (2.21–2.82)	0.04 (0.02–0.06)
≥ 1 complication	6952 (4957–8946)	17.49 (15.50–19.49)	0.27 (0.20–0.35)

* Number in parentheses, 95% CI.

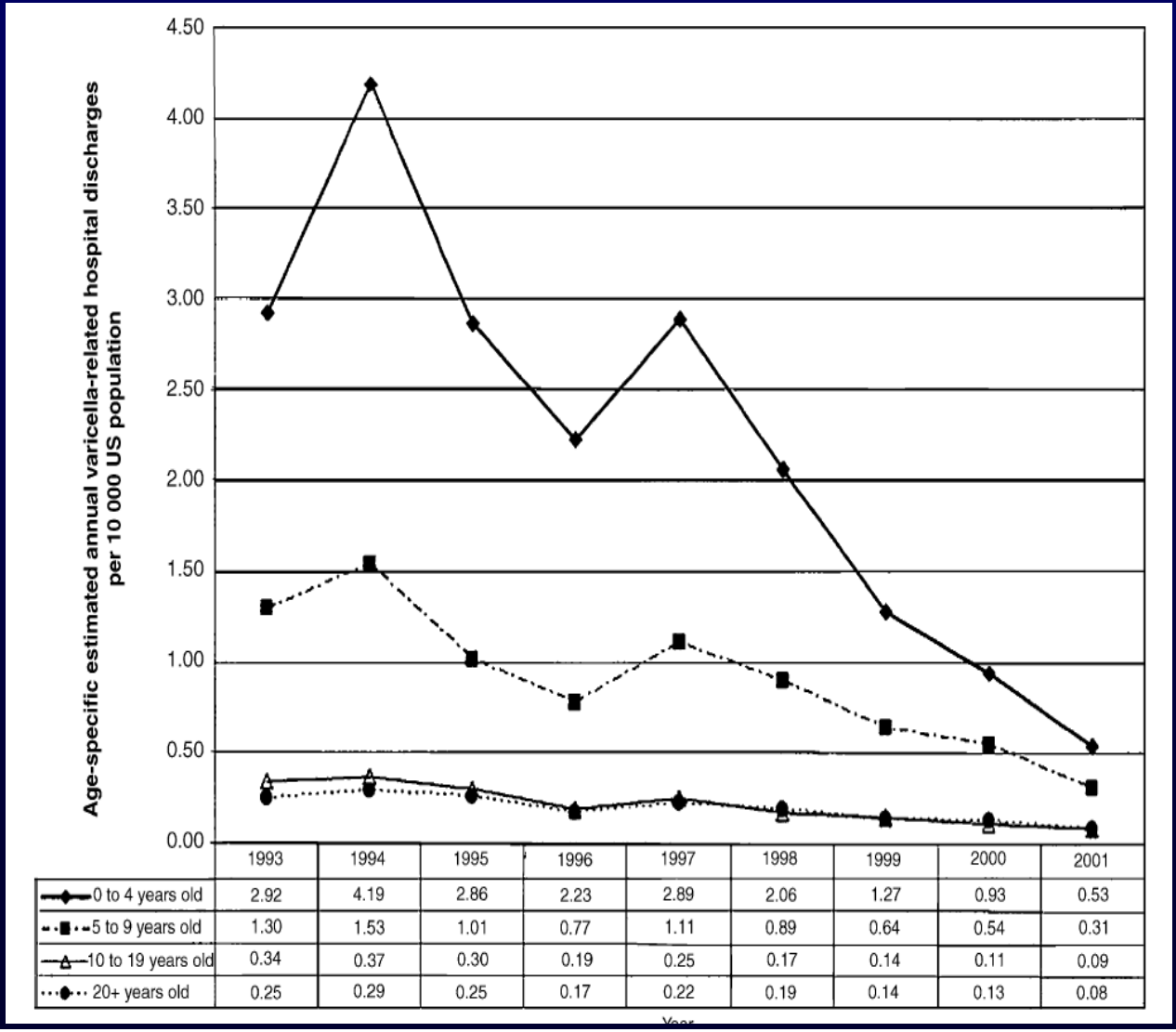
PATOGENESI DELL'HERPES ZOSTER

(da Hambleton Curr Opinion Infect Dis 2005)

Triangle indicates possible sites of action of humoral activity, and asterisk indicates potential targets for cell-mediated immune regulation. DC, dendritic cell.



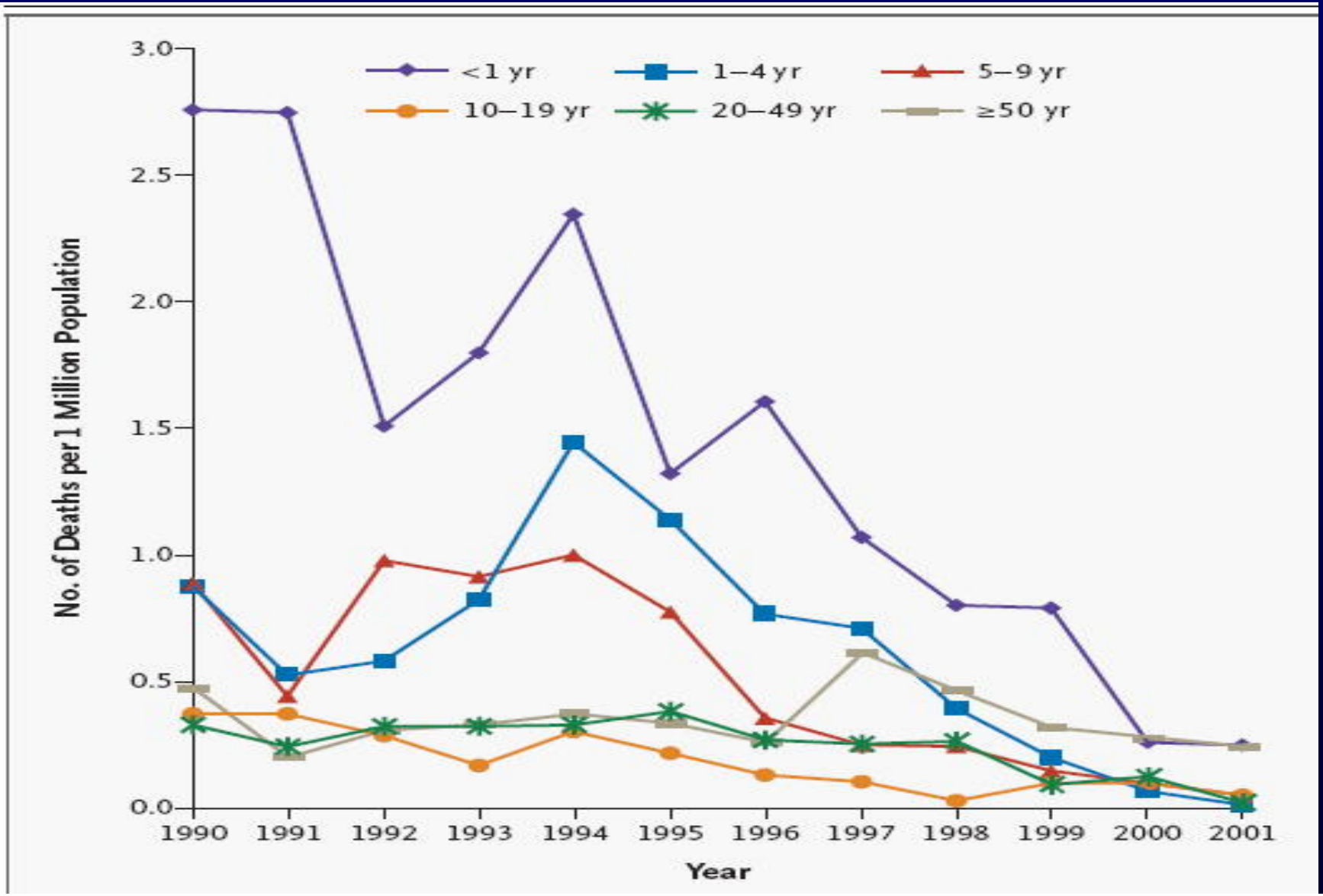
OSPEDALIZZAZIONI PER VARICELLA NEGLI U.S.A. DOPO L'INTRODUZIONE DEL VACCINO (1995)



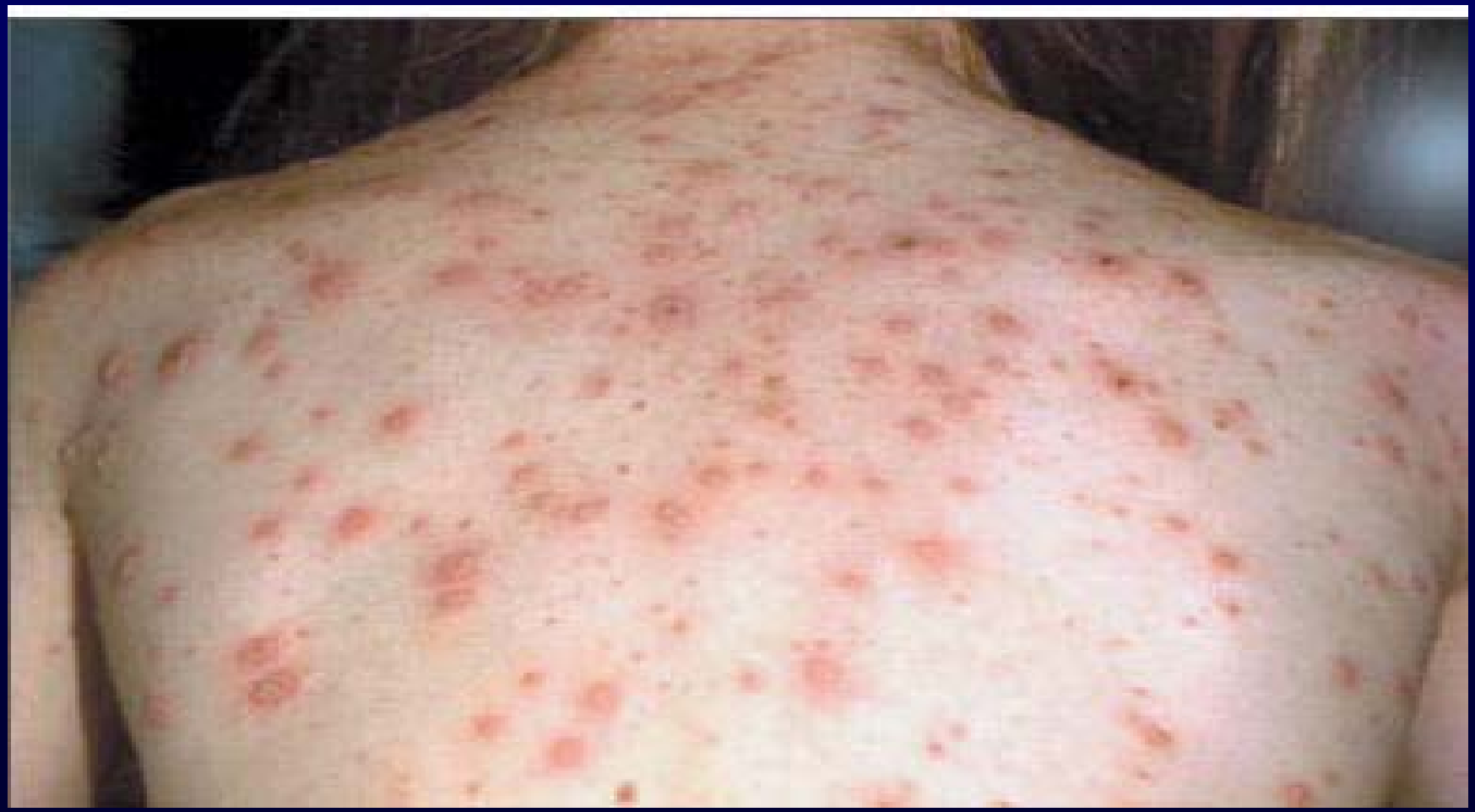
	1993	1994	1995	1996	1997	1998	1999	2000	2001
0 to 4 years old	2.92	4.19	2.86	2.23	2.89	2.06	1.27	0.93	0.53
5 to 9 years old	1.30	1.53	1.01	0.77	1.11	0.89	0.64	0.54	0.31
10 to 19 years old	0.34	0.37	0.30	0.19	0.25	0.17	0.14	0.11	0.09
20+ years old	0.25	0.29	0.25	0.17	0.22	0.19	0.14	0.13	0.08

MORTALITA' DA VARICELLA NEGLI U.S.A

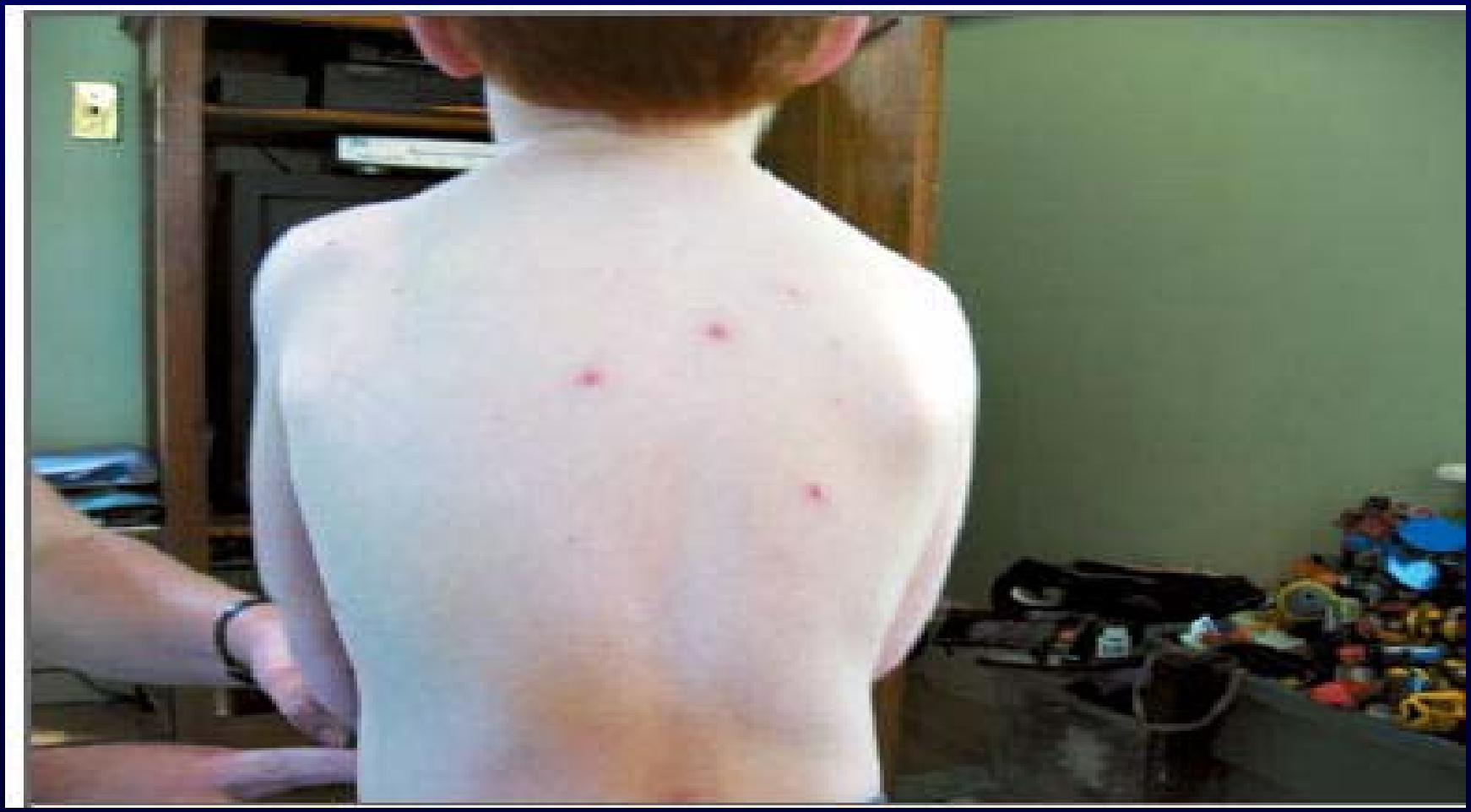
(Da Nguyen et al. NEJM 2005)



VARICELLA NATURALE



VARICELLA IN VACCINATO



MMRV: PERCHÉ, PROBLEMI E SOLUZIONI - I

- La varicella è malattia molto comune, clinicamente più importante di quanto finora creduto, anche nel bambino sano. Deve, se possibile, essere evitata
- Esiste un vaccino a base di virus vivi attenuati che si è dimostrato efficace e sicuro
- Il momento migliore per la vaccinazione è l'inizio del secondo anno di vita, proprio quando si deve somministrare l'MMR
- Per favorirne l'accettazione sembra logico combinare i vaccini, tanto più che per entrambi sembra opportuno eseguire la somministrazione di una seconda dose

MMRV: PERCHÉ, PROBLEMI E SOLUZIONI - II

- Le prime formulazioni (Merck) del vaccino combinato MMRV ottenute inserendo nel classico MMR le stesse quantità di virus VZ utilizzate nel vaccino singolo si sono rivelate poco immunogene (per il VZ) per l'interferenza esercitata dal virus del morbillo nei confronti di quello VZ
- Dopo vari tentativi, il problema è stato risolto aumentando in modo consistente la quantità di virus VZ nel nuovo combinato
- D'altra parte, i primi studi del vaccino MMRV GSK non avevano creato problemi similari
- In ogni caso, si è dovuto verificare, per entrambi i vaccini MMRV, la persistenza dell'immunità, l'efficacia e la effettiva sicurezza sia immediata che a distanza

IMMUNOGENICITÀ A BREVE E LUNGO TERMINE DEL VACCINO MMRV (MERCK)

Vaccine (assay)		Variable	MMRV Combined Lots (N = 2915)	MMR + V (N = 1012)
Measles (ELISA)	6 weeks	Response rate† (95% CI)	97.1% (2437/2509) (96.4%, 97.7%)	97.7% (841/861) (96.4%, 98.6%)
		GMT (95% CI)	2985.0 (2870.9, 3103.7)	2138.3 (2007.2, 2277.9)
	1 yr	Antibody persistence rate‡ (95% CI)	99.0% (1622/1638) (98.4%, 99.4%)	99.1% (576/581) (98.0%, 99.7%)
		GMT (95% CI)	3548.2 (3384.3, 3720.2)	2166.0 (2010.7, 2333.3)
Mumps (ELISA)	6 weeks	Response rate† (95% CI)	96.0% (2409/2509) (95.2%, 96.7%)	97.9% (854/872) (96.8%, 98.8%)
		GMT (95% CI)	95.9 (92.3, 99.6)	89.7 (84.7, 94.9)
	1 yr	Antibody persistence rate‡(95% CI)	96.7% (1676/1733) (95.8%, 97.5%)	96.2% (587/610) (94.4%, 97.6%)
		GMT (95% CI)	105.0 (99.5, 110.8)	84.1 (77.0, 91.9)
Rubella (ELISA)	6 weeks	Response rate† (95% CI)	98.8% (2501/2532) (98.3%, 99.2%)	99.2% (859/866) (98.3%, 99.7%)
		GMT (95% CI)	89.2 (86.4, 92.1)	103.6 (98.2, 109.4)
	1 yr	Antibody persistence rate‡(95% CI)	99.6% (1796/1804) (99.1%, 99.8%)	99.5% (620/623) (98.6%, 99.9%)
		GMT (95% CI)	126.2* (121.2, 131.4)	159.0* (148.5, 170.2)
Varicella (gpELISA)	6 weeks	≥1.25 gpELISA units (seroconversion rate†)	99.5%% (1853/1863) (99.0%, 99.7%)	99.1% (662/668) (98.1%, 99.7%)
		≥5 gpELISA units (95% CI) (response rate†)	93.5% (2180/2331) (92.4%, 94.5%)	95.0% (772/813) (93.2%, 96.4%)
		GMT (95% CI)	17.9 (17.2, 18.7)	17.6 (16.6, 18.7)
	1 yr	Antibody persistence rate‡ (95% CI)	97.5% (1512/1550) (96.7%, 98.3%)	97.5% (537/551) (95.8%, 98.6%)
		GMT (95% CI)	42.7 (40.3, 45.4)	37.6 (34.0, 41.7)

REAZIONI AVVERSE SUCCESSIVE ALL'USO DI MMRV (MERCK)

(da Lieberman Pediatr Infect Dis J 2006)

Variable	MMRV								MMR + V			
	Lot 1 (n = 985)		Lot 2 (n = 968)		Lot 3 (n = 962)		Combined Lots (n = 2915)		V (n = 1012)		MMR (n = 1012)	
	N	Percent	N	Percent	N	Percent	N	Percent	N	Percent	N	Percent
Subjects with follow up	969	(98.4%)	950	(98.1%)	941	(97.8%)	2860	(98.1%)	993	(98.1%)	993	(98.1%)
Subjects with one or more adverse experiences	807	83.3	771	81.2	780	82.9	2358	82.4	779			80.5
Subjects with one or more injection site adverse experiences	318	32.8	330	34.7	329	35.0	997	34.2	397			38.2
Subjects with one or more vaccine-related injection site adverse experiences	317	32.7	328	34.5	326	34.6	971	34.0	375			37.8
Erythema	149	15.4	163	17.2	163	17.3	475	16.6	136	13.7	134	13.5
Pain/tenderness/soreness	221	22.8	246	25.9	230	24.4	697	24.4	262	26.4	266	26.8
Swelling	89	9.2	86	9.1	86	9.1	261	9.1	91	9.2	80	8.1
Subjects with one or more systemic adverse experiences	760	78.4	717	75.5	797	78.3	2214	77.4	728			73.3
Subjects with one or more vaccine-related systemic adverse experiences	312	32.2	306	32.2	313	33.3	931	32.6	227			27.9
Elevated temperature (≥38.9°C or abnormal)	376	39.0	360	38.3	374	40.0	1110	39.1	325			33.1
Diarrhea	80	8.3	80	8.4	77	8.2	237	8.3	82			8.3
Vomiting	59	6.1	49	5.2	60	6.4	168	5.9	61			6.1
Irritability	105	10.8	101	10.6	119	12.6	325	11.4	86			8.7
Cough	57	5.9	56	5.9	61	6.5	174	6.1	61			6.1
Upper respiratory infection	280	28.9	248	26.1	249	26.5	777	27.2	245			24.7
Rhinorrhea	58	6.0	65	6.8	58	6.2	181	6.3	60			6.0
Rash (nonspecific)	59	6.1	51*	5.4	54	5.7	164	5.7	45			4.5
Diaper rash	72	7.4	78	8.2	80	8.5	230	8.0	86			8.7
Viral exanthema	54	5.6	41	4.3	47	5.0	142	5.0	45			4.5
Otitis media	133	13.7	109	11.5	133	14.1	375	13.1	117			11.8

IMMUNOGENICITA' DI MMRV (GSK)

(da Knuf et al. Pediatr Infect Dis J 2006)

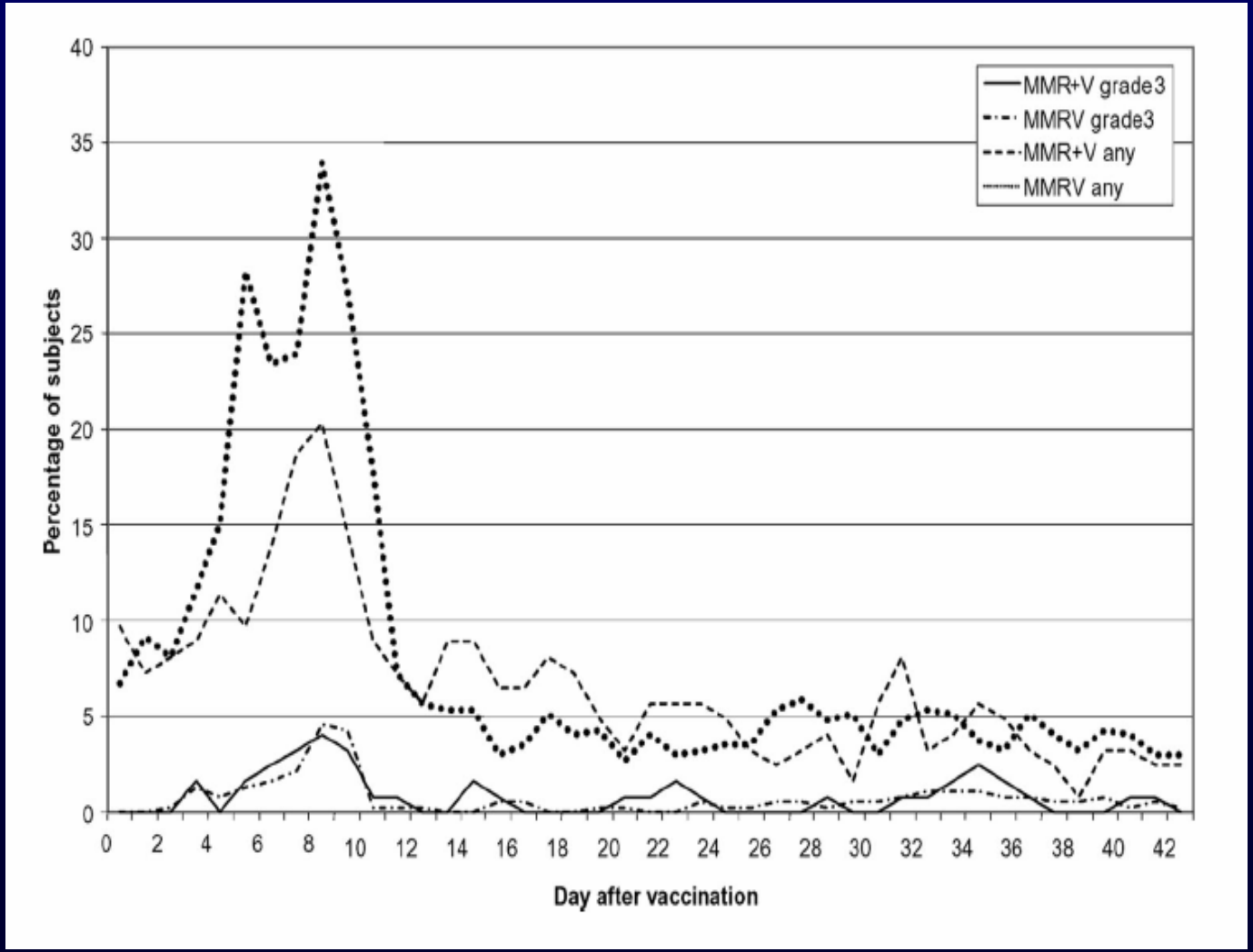
Vaccine	N	Seroconversion*				GMTs		
		n	%	95% CI		Value	95% CI	
				LL	UL		LL	UL
Measles								
MMRV	307	307	100	98.8	100	6103.9	5639.6	6606.4
MMR+V	108	108	100	96.6	100	3719.2	3183.7	4344.7
Mumps								
MMRV	307	301	98.0	95.8	99.3	1465.4	1343.8	1598.0
MMR+V	108	107	99.1	94.9	100	1667.8	1441.7	1929.3
Rubella								
MMRV	307	307	100	98.8	100	101.5	94.6	108.8
MMR+V	108	108	100	96.6	100	107.0	95.3	120.2
Varicella								
MMRV	306	306	100	98.8	100	4932.1	4215.1	5771.0
MMR+V	108	108	100	96.6	100	155.2	126.2	190.5

*Titer ≥ assay cutoff in initially seronegative subjects.

N indicates number of subjects with available results; n, number of seropositive subjects at a given time point; %, percent of subjects with titer for antimeasles ≥150 mIU/mL, antimumps ≥231 units/mL, antirubella ≥4 IU/mL and antivaricella ≥4 dilution^{-1}; u/UL, lower/upper limit of 95% CI.

ANDAMENTO DELLA FEBBRE CON MMRV (GSK)

(da Knuf et al. Pediatr Infect Dis J 2006)

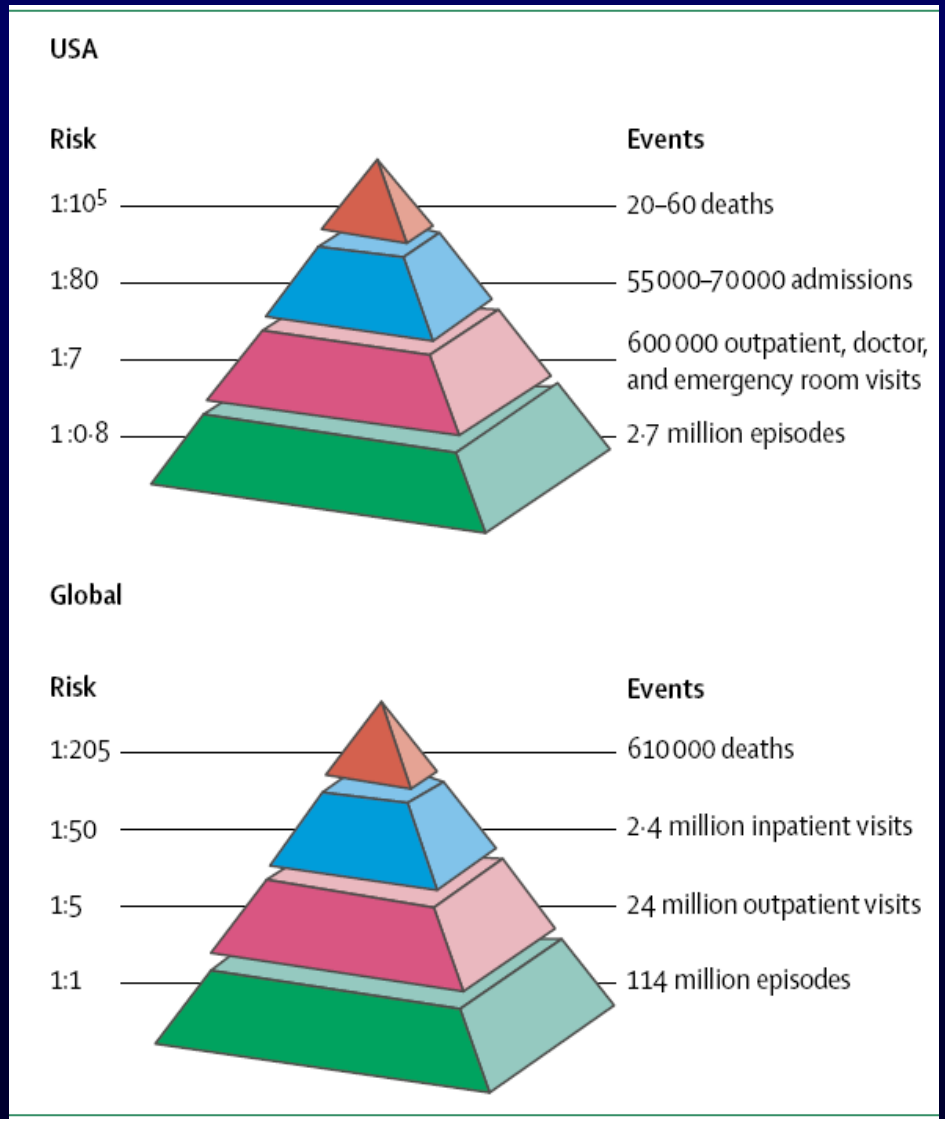


VACCINAZIONE ANTIVARICELLA: CONCLUSIONI

- Sia l'efficacia sia i vantaggi economici sono tanto maggiori quanto più elevata è la copertura vaccinale
- Con coperture vaccinali basse, se pur con vantaggi economici, si ha un aumento dei casi di varicella negli adolescenti e negli adulti
- L'introduzione del vaccino MMRV permette di raggiungere rapidamente elevate coperture vaccinali sfruttando l'effetto di trascinamento del vaccino anti-morbillo
- Con il vaccino MMRV la prospettiva della vaccinazione universale diventa perseguibile

IMPATTO DELLA DIARREA DA ROTAVIRUS

(da Glass et al. Lancet 2006)



CARATTERISTICHE DI ROTASHIELD, PRIMO VACCINO ANTIROTAVIRUS

- Vaccino ricombinato tetravalente
- Altamente efficace: riduzione del 90% dei ricoveri per diarrea da Rotavirus negli U.S.A. e del 79% in Venezuela
- Registrato dalla FDA nel 1998
- Somministrato a 600.000 bambini in 9 mesi
- Ritirato dal commercio nel luglio 1999 per la possibile associazione con invaginazione intestinale (1 caso ogni 10.000 nelle prime 2 settimane dopo la I dose)

NUOVI VACCINI ANTIROTAVIRUS - I

(da Glass et al. Lancet 2006)

	Rotarix (GlaxoSmithKline) Monovalent vaccine	RotaTeq (Merck) Pentavalent vaccine
Original strain	Human rotavirus strain 89-12 P1A[8], G1	Bovine rotavirus strain WC3 P7[5], G6
Final vaccine	RIX4414	Five reassortants; G1_WC3 G2_WC3 G3_WC3 GA_WC3 P1A[8]_WC3
Titre	$10^{5\cdot8}$ focus-forming units	$6\cdot7–12\cdot4\times10^{7}$ plaque forming units

NUOVI VACCINI ANTIROTAVIRUS - II

(da Glass et al. Lancet 2006)

	Rotarix (GlaxoSmithKline) Monovalent vaccine	RotaTeq (Merck) Pentavalent vaccine
Dose regimen	Two oral doses Dose 1: 6–14 weeks of age Dose 2: ≥4 weeks later	Three oral doses Dose 1: 6–12 weeks of age Doses 2 and 3: at about 4–10-week intervals
Shelf life at 2–8°C	36 months	24 months
Vaccine interference		
Diphtheria tetanus pertussis, inactivated polio vaccine, *Haemophilus influenzae* type b vaccine, Hepatitis B vaccine	None	None*
Pneumococcal conjugate†	..	..
Oral polio 1 vaccine†	..	..
Post-dose shedding	>50%	~10%

EFFICACIA DEI DUE NUOVI VACCINI ANTIROTAVIRUS

(da Glass et al. Lancet 2006)

	Patients enrolled (n)		Outcomes			Effectiveness (95% CI)
	Vaccine	Placebo	Gastroenteritis outcome	In vaccine group	In placebo group	
Monovalent vaccine (Rotarix, GlaxoSmithKline)						
Finland[74]	245	123	Any	13	23	72 (42–87)
			Severe	3	10	85 (42–97)
Brazil, Mexico, Venezuela*[76]	464	454	Any	15	49	70 (46–84)
			Severe	5	34	86 (63–96)
Latin America†[77]	10 159	10 010	Severe	n/a	n/a	84·7 (71·7–92·4)
			Admission			85·0 (69·6–93·5)
Pentavalent vaccine (RotaTeq, Merck)						
USA, Finland[77]	2834	2839	Any	83	315	74·0 (66·8–79·9)
			Severe	1	51	98·0(88·3–100·0)
USA[84]	650	660	Any	15	54	72·5 (50·6–85·6)
			Moderate/severe	10	42	76·3 (52·0–89·4)
			Severe	0	6	100 (13·0–100·0)

*Subset of infants receiving the final dose of vaccine. †Overall reduction of 41% in admissions due to gastroenteritis of any cause.

RISCHIO DI INVAGINAZIONE CON I DUE NUOVI VACCINI ANTIROTAVIRUS

(da Glass et al. Lancet 2006)

	Site	Follow-up period post-vaccination	Number of participants		Intussusception cases			Relative risk (95% CI)
			Vaccinated	Placebo		Vaccinated	Placebo	
Monovalent (Rotarix, GlaxoSmithKline)	Europe, Asia,	31 days	~31500	~31500	Total	6	7	~0·86 (0·29–2·55)
	Latin America[77]				Dose 1	1	2	~0·50 (0·05–5·51)
					Dose 2	5	5	~1·00 (0·29–3·45)
	Latin America[78]	1 year	10159	10010	Total	4	14	0·28 (0·10–0·81)
Pentavalent (RotaTeq, Merck)	USA, others[84]	42 days	~35150	~35150	Total	6	5	~1·20 (0·37–3·93)
					Dose 1	0	1	~0 (0–17·30)
					Dose 2	4	1	~4·00 (0·45–35·79)
					Dose 3	2	3	~0·67 (0·11–3·99)
		1 year	~35150	~35150	Total	12	15	~0·80 (0·35–1·71)

CARATTERISTICHE DELLE DIARREE VIRALI

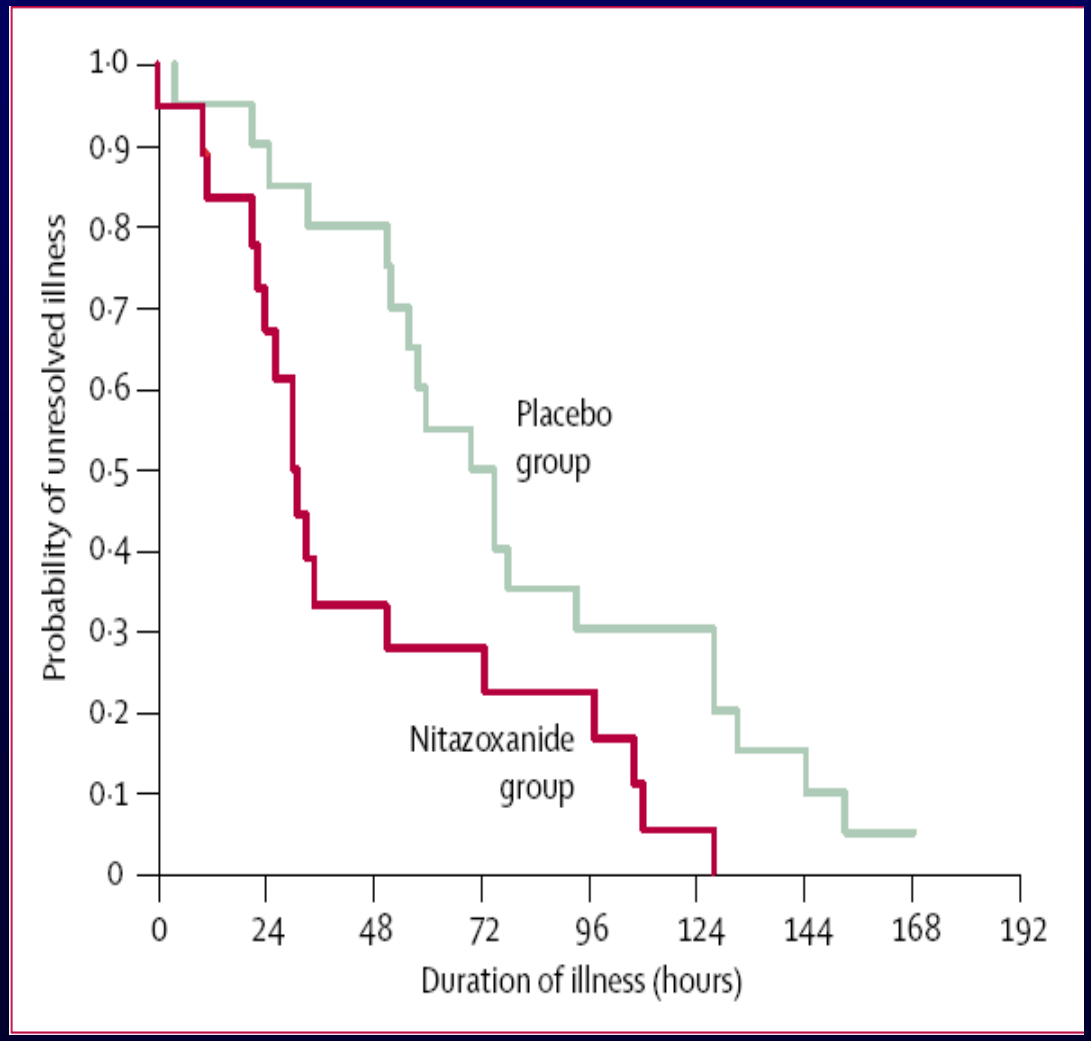
(da Colomba et al. Eur J Clin MIcrobiol Infect Dis 2006)

Characteristic	Rotavirus	Adenovirus	Astrovirus	Norovirus	Dual infection	No viral infection	*p* value
No. (%) of children infected[a]	43 (20)	9 (4.2)	7 (3.2)	21 (9.8)	21 (9.8)	114 (53)	<0.05
No. (%) male[a]	29 (67.4)	8 (88.9)	6 (85.7)	12 (57.1)	10 (47.6)	75 (65.8)	>0.05
Age, months[b, c]	16.4 (6.4–75.2)	78.1 (34.2–151)	115 (66.4–163.6)	25.1 (10.4–152.4)	30,7 (4–161)	35.7 (1.7–165)	<0.05
Days of diarrhoea[b, d]	4 (1–12)	4 (3–8)	4.5 (3–7)	3.5 (1–8)	4 (1–8)	4 (1–14)	>0.05
Maximum number of stools/day[b, d]	7.5 (2–37)	5 (3–8)	13 (3–26)	4.5 (2–20)	5 (2–21)	7 (1–30)	<0.05
Vomiting (%)[a]	33 (76.7)	5 (55.5)	4 (57.1)	12 (57.1)	12 (57.1)	49 (43)	<0.05
Days of vomiting[b, d]	2 (0–5)	1 (0–7)	1.5 (1–5)	1 (0–4)	1 (0–5)	1 (0–9)	<0.05
Fever (%)[a]	28 (65.1)	4 (44.4)	4 (57.1)	11 (52.4)	13 (61.9)	76 (66.7)	>0.05
No. (%) of dehydrated children[a]	23 (53.5)	2 (22.2)	3 (42.8)	9 (42.8)	11 (52.4)	42 (36.8)	>0.05
Days of hospitalisation[b, d]	3 (1–10)	2 (2–2)	2 (2–5)	3 (1–6)	3 (1–5)	2 (1–9)	>0.05
Severity score[b, d]	11 (5–14)	7 (5–10)	11.5 (6–14)	9.5 (5–14)	8 (4–14)	9 (4–14)	<0.05

[a] Chi-square test
[b] Median and (range)
[c] Kruskal-Wallis test
[d] Median test (based on chi-square test)

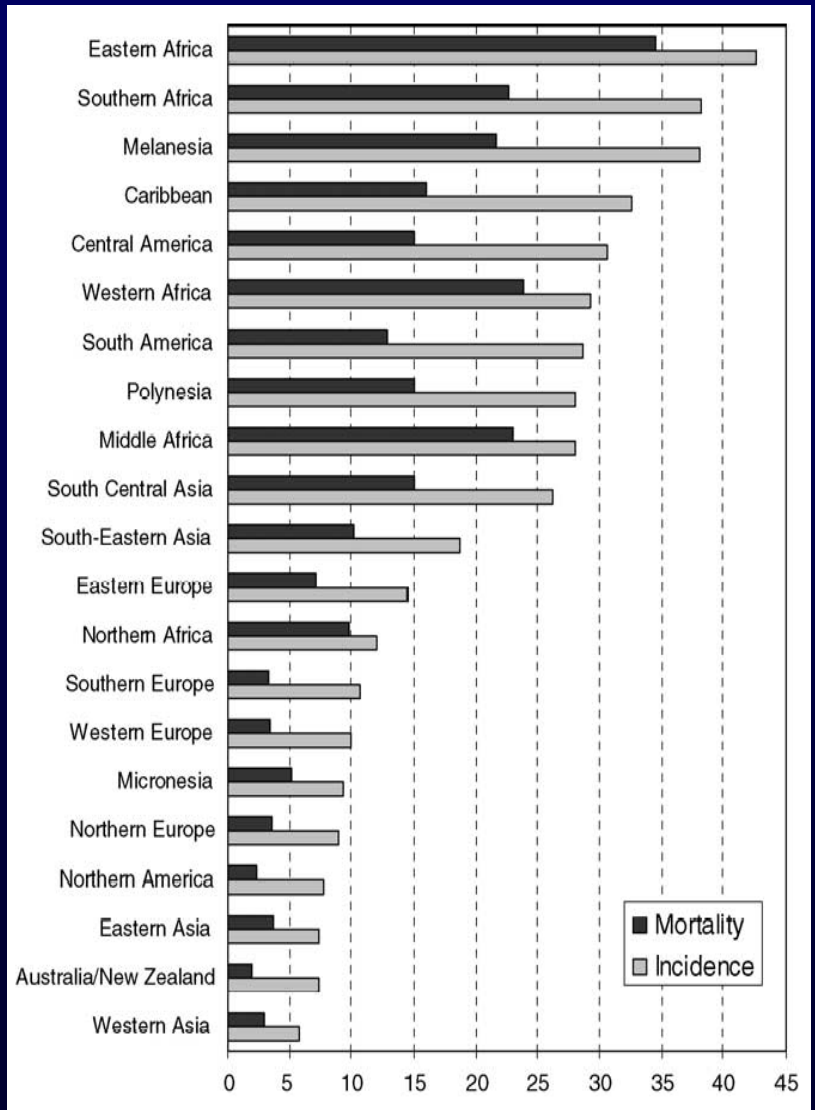
EFFETTO DELLA NITAZOXANIDE SULLA DURATA DELLA DIARREA DA ROTAVIRUS

(da Rossignol et al. Lancet 2006)



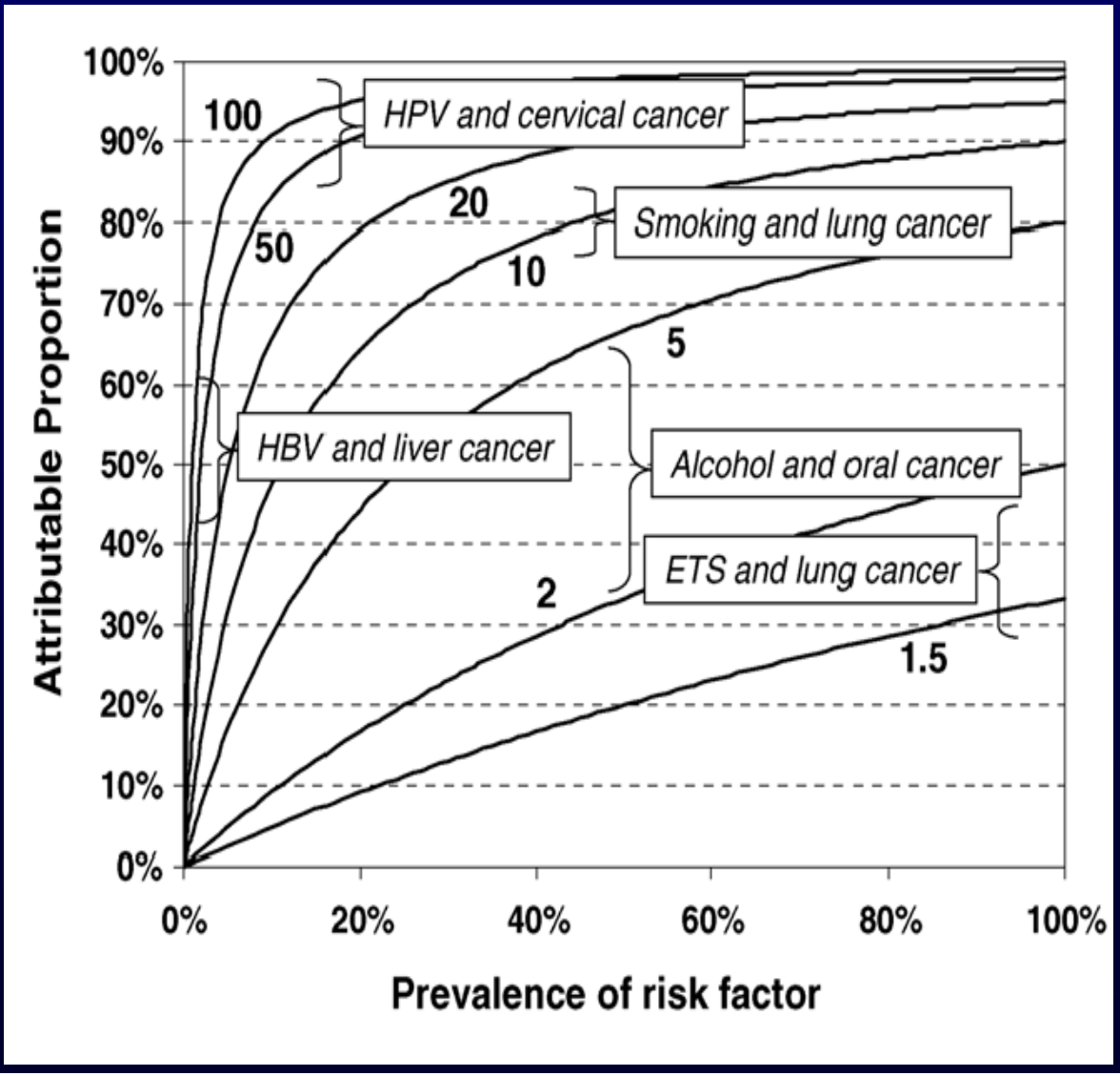
CANCRO CERVICALE: CASI/100.000 DONNE/ANNO

(Globocan 2002)



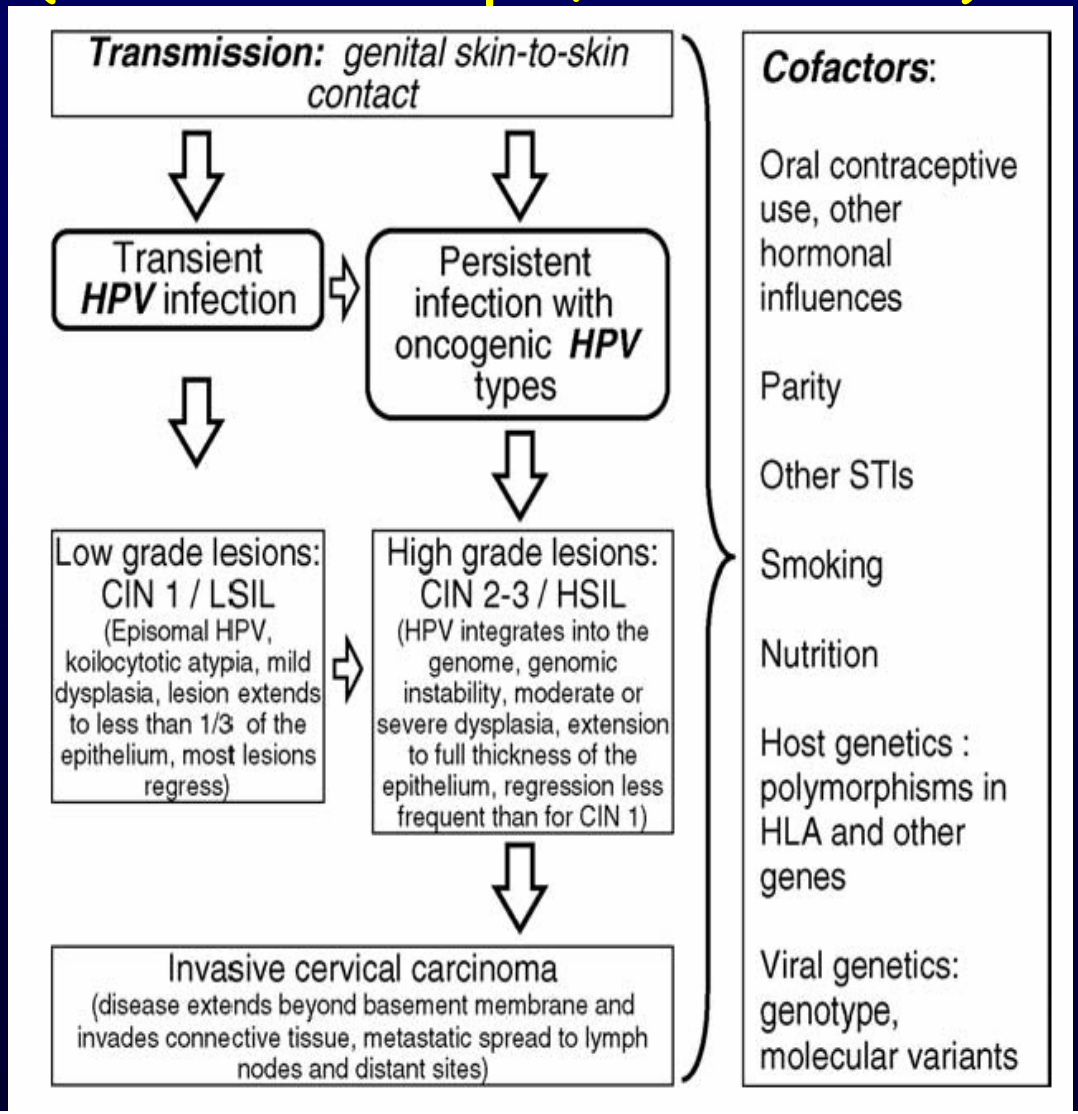
CASI DI MALATTIA IN FUNZIONE DELLA PREVALENZA DI UN FATTORE DI RISCHIO

(da Franco e Harper, Vaccine 2005)



GENESI DEL CANCRO CERVICALE DA HPV

(da Franco e Harper, Vaccine 2005)



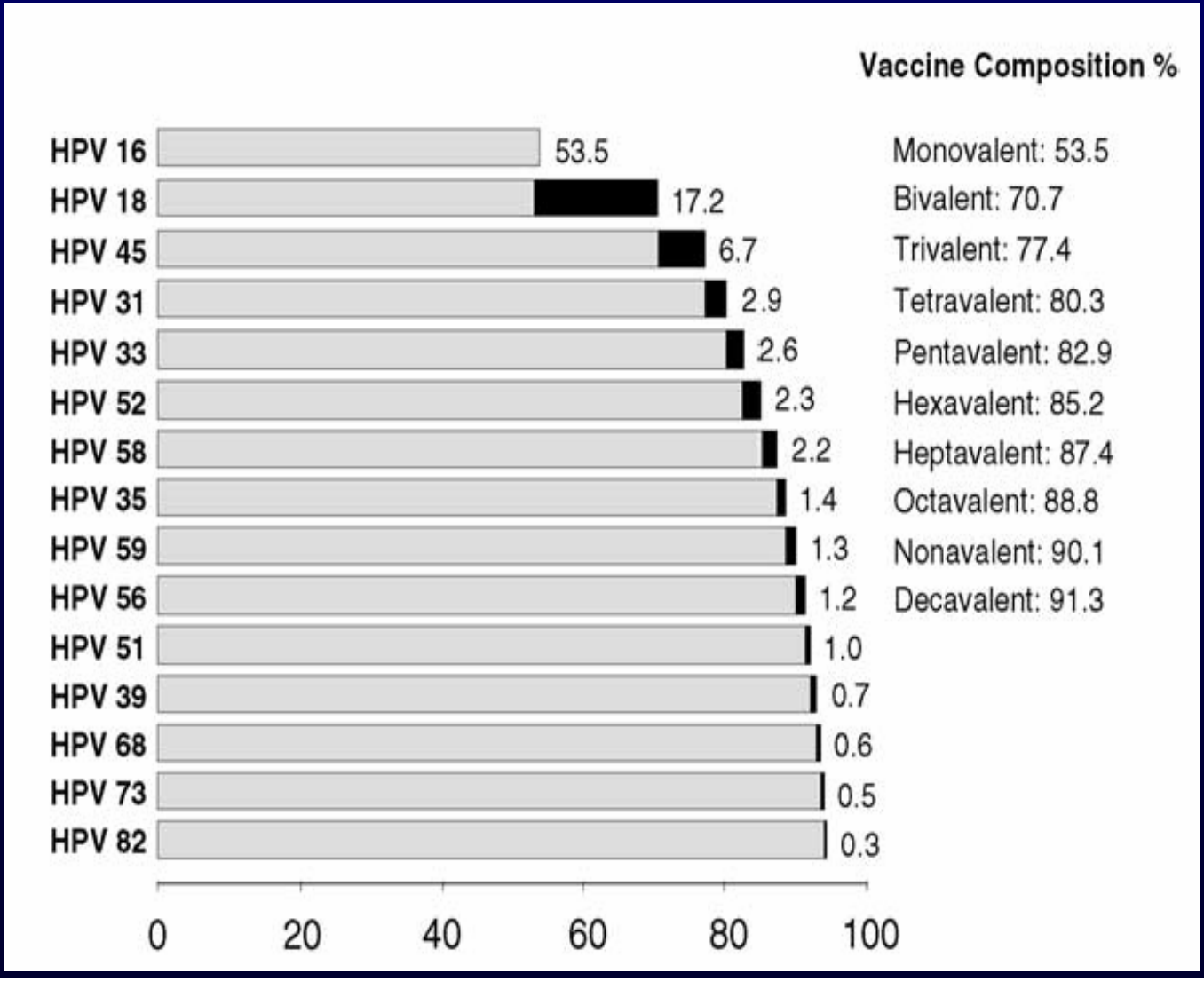
HPV CHE DETERMINANO PATOLOGIA ONCOLOGICA ANO-CERVICALE

(da Stanley. Rev Med Virol 2006)

Lesion	HPV types involved	% cases HPV + ve
Cervical carcinoma	16,18,31,33, 35,39,45,51, 52,66,58,59, 66,(*26,68,73,82**)	> 95
Vulval carcinoma		
Basaloid	16,18	> 50
'warty'	16,18	> 50
keratinising	16	< 10
Penile carcinoma		
Basaloid	16,18	> 50
'warty'	16,18	> 50
keratinising	16	< 10
Vaginal carcinoma	16,18	> 50
Carcinoma Anus	16,18	> 70

PERCENTUALE DI CANCRO CERVICALE ATTRIBUIBILE AI DIVERSI HPV

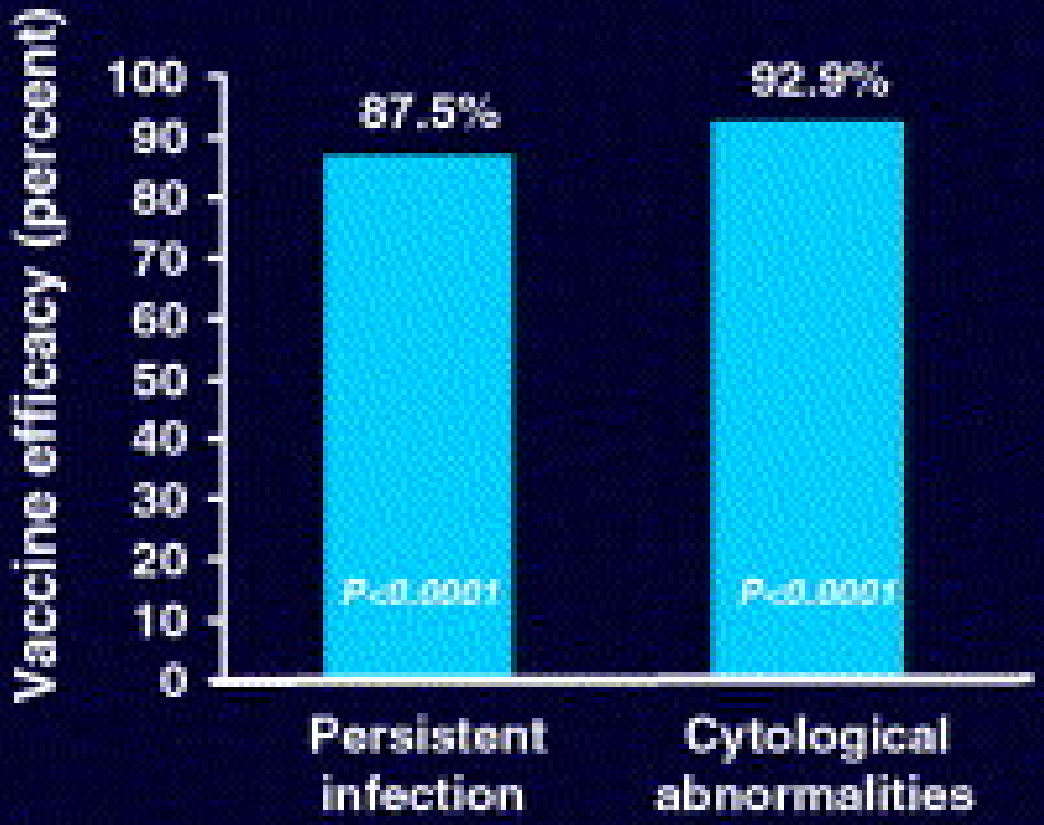
(da Franco e Harper, Vaccine, 2005)



VACCINI ANTI HPV IN STUDIO

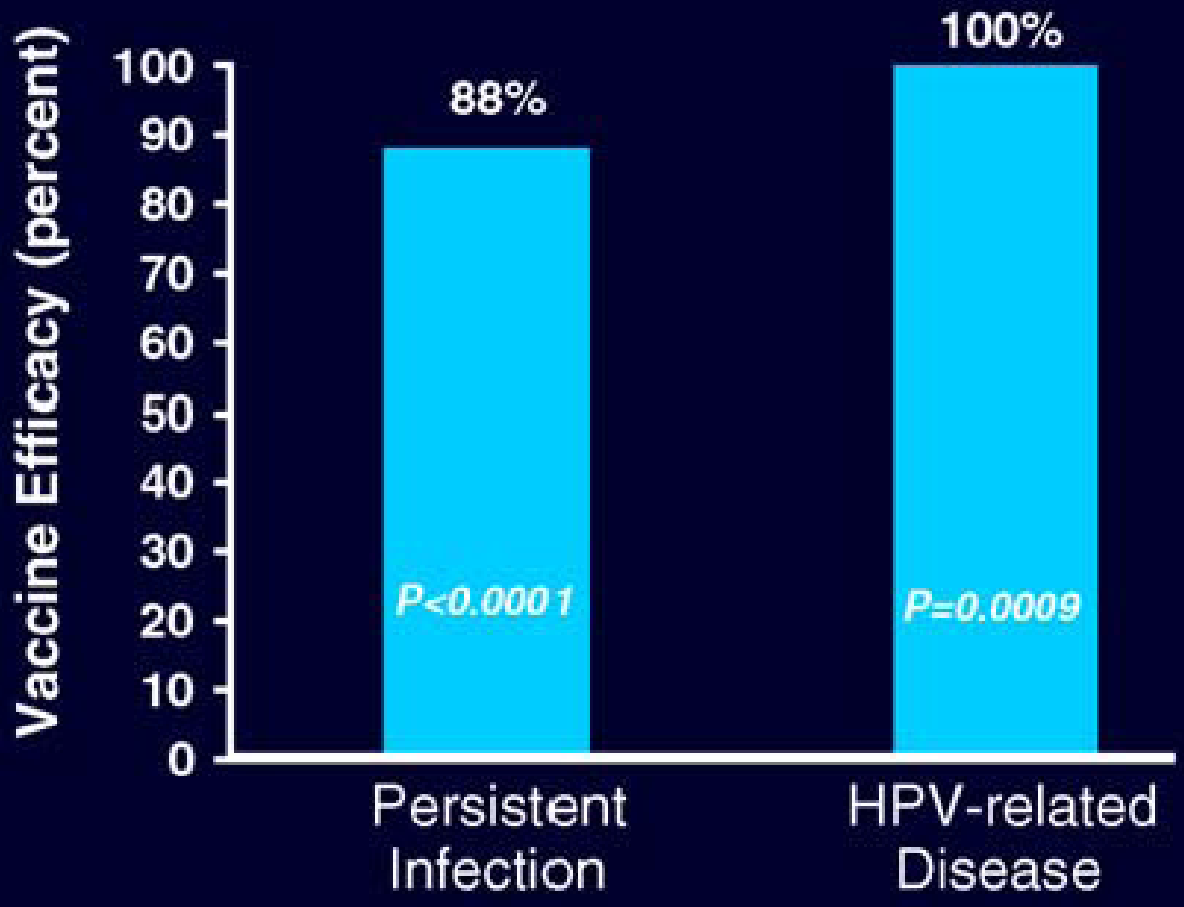
- GSK HPV 16 - 18
- MERCK HPV 6 - 11- 16 -18

Bivalent HPV Vaccine Trial: Intention-to-Treat Efficacy



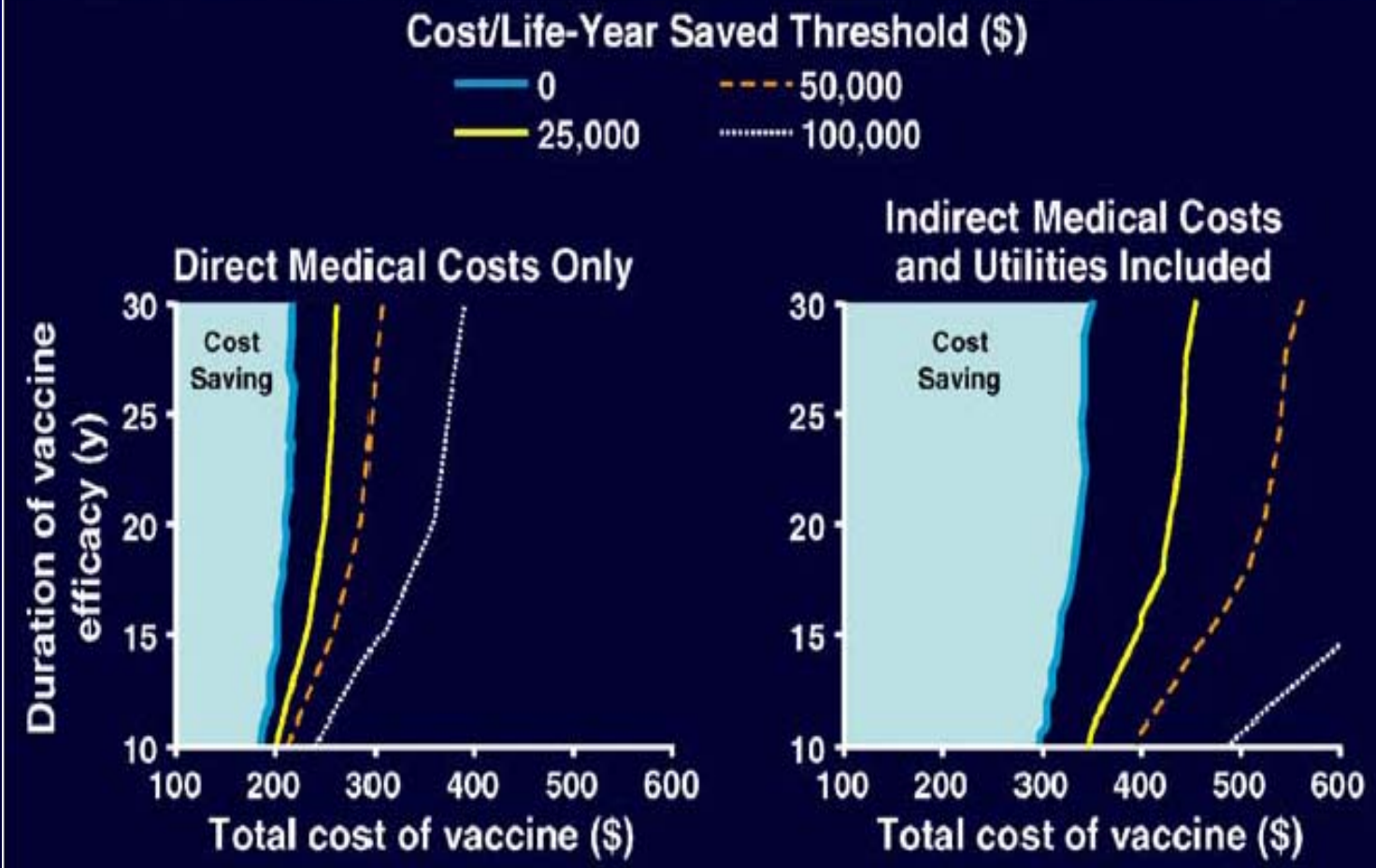
Harper DM et al. *Lancet* 2004;364:1757-65.

Quadrivalent HPV Vaccine Trial: Modified Intention-to-Treat Efficacy



Villa et al. *Lancet* Oncology. 2005;6:271-278.

Two-Way Sensitivity Analysis Varying Duration of HPV-Vaccine Efficacy and Total Cost



da Villa, Vaccine 2006

HPV Vaccine Efficacy Trials

Manufacturer	Vaccine	Location	Participants	Projected End
Merck 	VLPs of L1 protein from HPV 6/11/16/18, made in yeast, aluminum adjuvant	U.S., S. America, Europe	17,800 women, 16 to 26 years old	2007
		U.S., S. America, Europe, Asia	3800 women, 24 to 45 years old	2008
		U.S., S. America, Europe, Asia, Africa	3700 men, 16 to 24 years old	2008
GSK	VLPs of L1 protein from HPV 16/18, made in baculovirus, AS04 adjuvant	U.S., S. America, Europe, Asia Pacific	18,000 women, 15 to 25 years old	2010
		Costa Rica (run by NCI)	12,000 women, 18 to 25 years old	2010

PREVENZIONE DEL CARCINOMA CERVICALE (CC): STRATEGIA ATTUALE

- Finora la prevenzione del CC è stata attuata attraverso il Pap test, esame eseguito dallo specialista ginecologo
- La disponibilità di un vaccino efficace contro l'HPV deve spostare la logica della prevenzione del CC verso la prevenzione delle infezioni che sono la causa della malattia
- Poiché le infezioni da HPV sono sessualmente trasmesse, è ovvio che l'uso del vaccino debba avvenire prima della pubertà e, comunque, prima dell'inizio dell'attività sessuale
- Il pediatra deve sostituire il ginecologo ed assumere il ruolo principale nella gestione del problema

ACIP Provisional Recommendations for the Use of Quadrivalent HPV Vaccine

Date of ACIP vote: June 29, 2006
Date of posting of provisional recommendations: August 14, 2006
Tentative date of publication of recommendations in CDC *Morbidity and Mortality Weekly Report*: November 2006

Provisional recommendations for use of quadrivalent HPV vaccine:

- Routine vaccination with three doses of quadrivalent HPV vaccine is recommended for females 11-12 years of age. The vaccination series can be started in females as young as 9 years of age.

- Catch-up vaccination is recommended for females 13-26 years of age who have not been vaccinated previously or who have not completed the full vaccine series. Ideally, vaccine should be administered before potential exposure to HPV through sexual contact.

- Each dose of quadrivalent HPV vaccine is 0.5 mL, administered intramuscularly.

- Quadrivalent HPV vaccine is administered in a three dose schedule. The second and third doses should be administered 2 and 6 months after the first dose.

- Quadrivalent HPV vaccine can be administered at the same visit when other age appropriate vaccines are provided, such as Tdap, Td and MCV4.

- At present, cervical cancer screening recommendations have not changed for females who receive quadrivalent HPV vaccine.

PROBLEMI DA SUPERARE PER L'INTRODUZIONE DELLA VACCINAZIONE ANTI-HPV IN PEDIATRIA

- Le **adolescenti** possono rifiutare perché:
  1) sono propense a credersi invulnerabili
  2) non avendo confidenza con il pediatra o altri medici si vergognano di parlare di problemi sessuali

- I **genitori** possono essere riluttanti ad accettare la vaccinazione perché:
  1) non vogliono iniziare a discutere di problemi sessuali della figlia per loro molto lontani nel tempo
  2) non credono che la loro figlia possono avere problemi inerenti malattie sessualmente trasmesse
  3) temono che, una volta vaccinata, la loro figlia possa avere più facilmente comportamenti a rischio
  4) non sono certi dell'efficacia del vaccino e temono che non sia sicuro

- Il **pediatra** può avere difficoltà a parlare di problemi sessuali