

INFLUENZA STAGIONALE E INFLUENZA PANDEMICA: PERCHE' E COME PREVENIRLE

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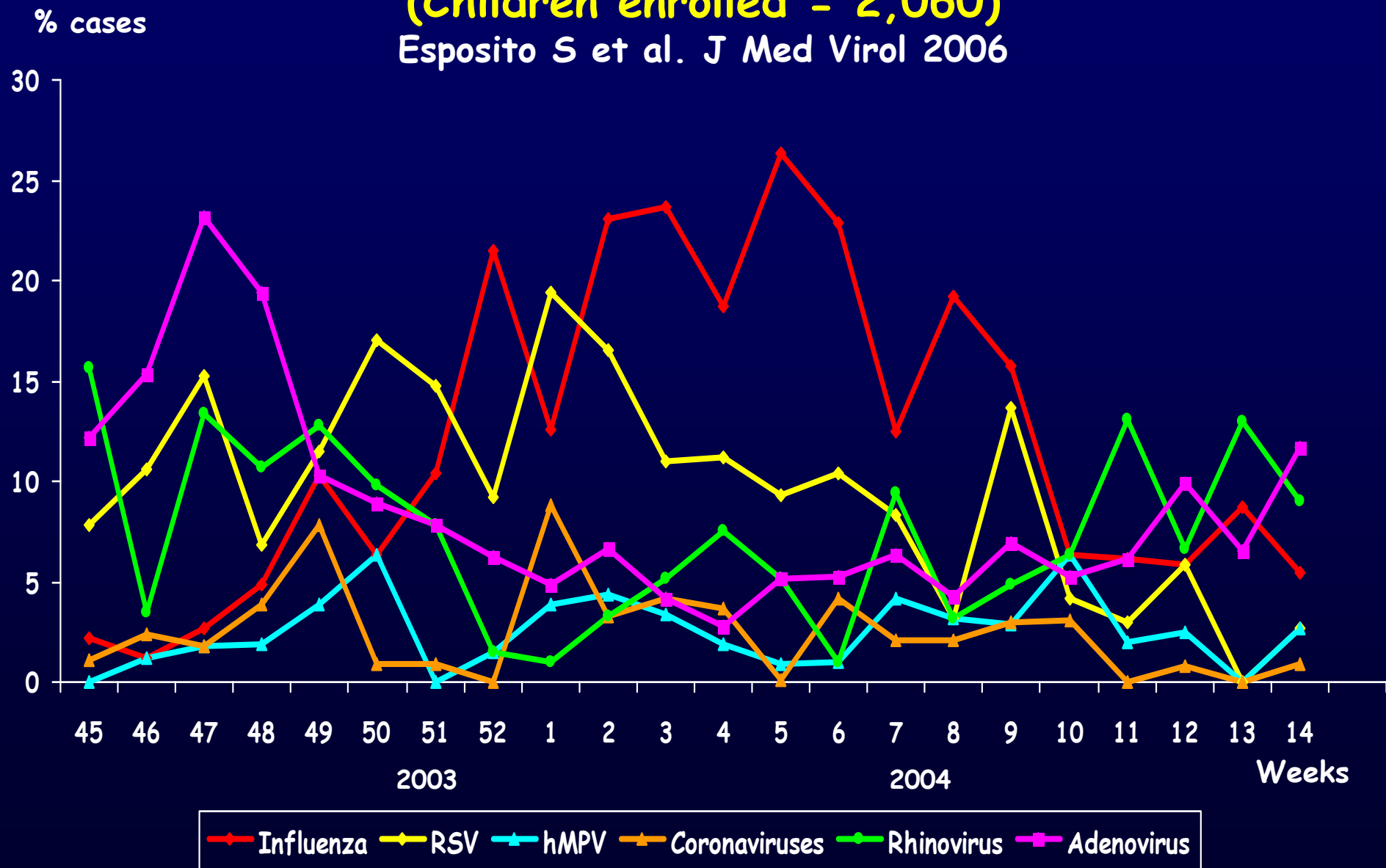
Maggiore Policlinico

Milano

DISTRIBUTION OF RESPIRATORY VIRUSES DURING THE WINTER SEASON 2003-2004

(Children enrolled = 2,060)

Esposito S et al. J Med Virol 2006



HOSPITALIZATION DURING INFLUENZA SEASON ACCORDING TO AGE

(Da Neuzil KM et al. NEJM 2000)

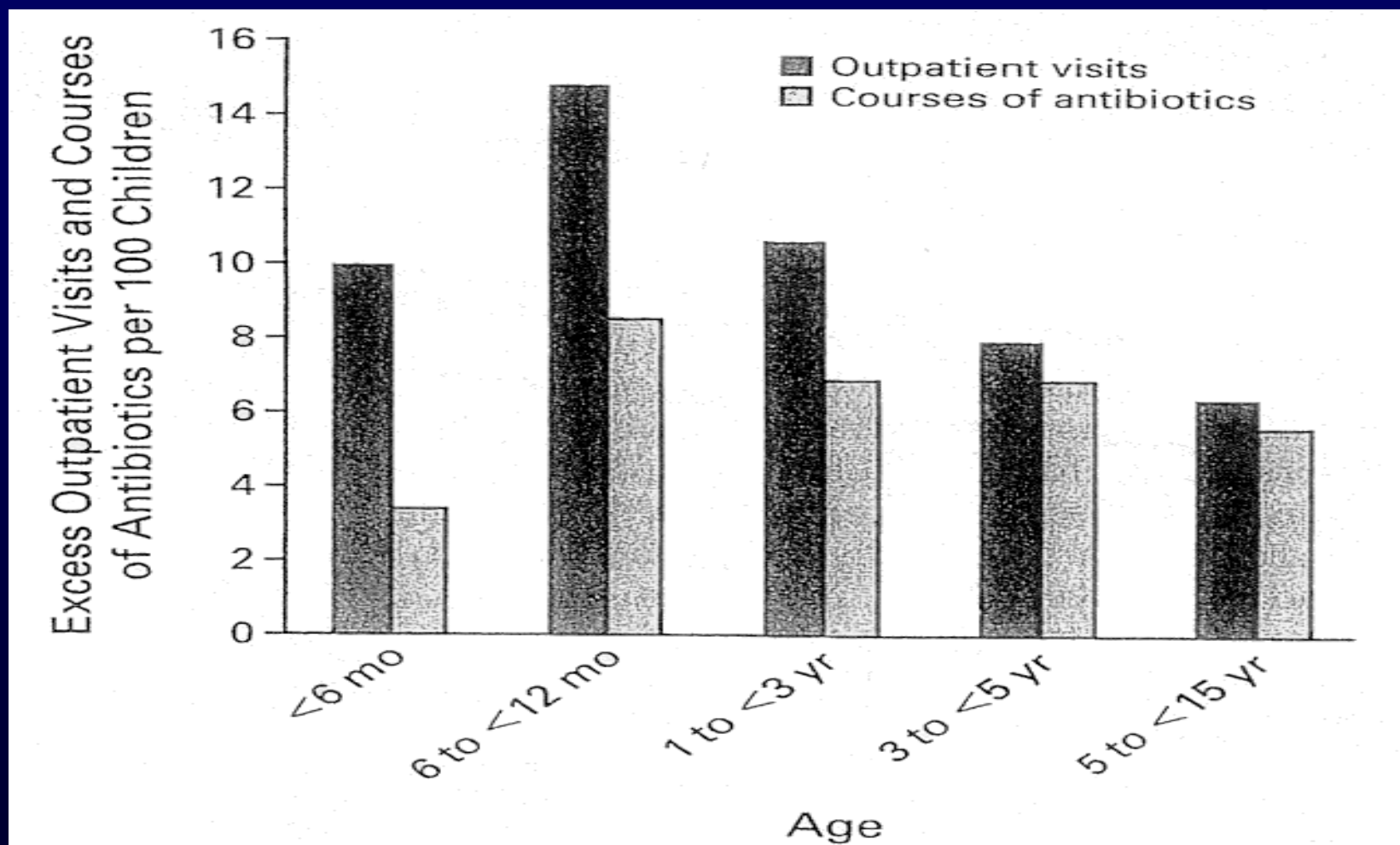
AGE	No. OF PERSON-YEARS	No. OF HOSPITALIZATIONS FOR ACUTE CARDIOPULMONARY CONDITIONS PER 10,000 PERSON-YEARS				No. OF INFLUENZA-ATTRIBUTABLE HOSPITALIZATIONS PER 10,000 PERSON-YEARS*		AVERAGE EXCESS No. OF HOSPITALIZATIONS PER 10,000 CHILDREN PER YEAR (95% CI)†
		INFLUENZA SEASON	PERI-INFLUENZA SEASON	SUMMER	TOTAL	CRUDE	STANDARDIZED‡	
<6 mo	117,205	1964	1497	608	1146	467	449	103.8 (89.0–118.6)
6 to <12 mo	82,997	1117	854	403	675	263	233	49.6 (35.3–63.8)
1 to <3 yr	324,900	464	387	233	325	77	79	18.6 (14.2–23.0)
3 to <5 yr	302,344	232	193	138	173	39	43	8.6 (4.9–12.3)
5 to <15 yr	1,207,697	120	105	86	98	15	22	4.1 (2.8–5.5)

*Values are differences in rates between the influenza season and the peri-influenza season (the base-line values).

†Values are weighted averages of annual excess hospitalizations for a population of 10,000 persons within the specified age group. The excess hospitalizations were calculated for each stratum by multiplying the stratum-specific difference in hospitalization rate by the proportion of the study year covered by the influenza season. CI denotes confidence interval.

‡The weighted average differences in rate between the influenza season and the peri-influenza season were calculated with stratum-specific person-years in all seasons as weights; strata were defined by age group, study year, race, and residence.

INCREASE IN OUTPATIENT VISITS AND ANTIBIOTIC COURSES DURING INFLUENZA SEASON



Neuzil KM et al., N Engl J Med 2000

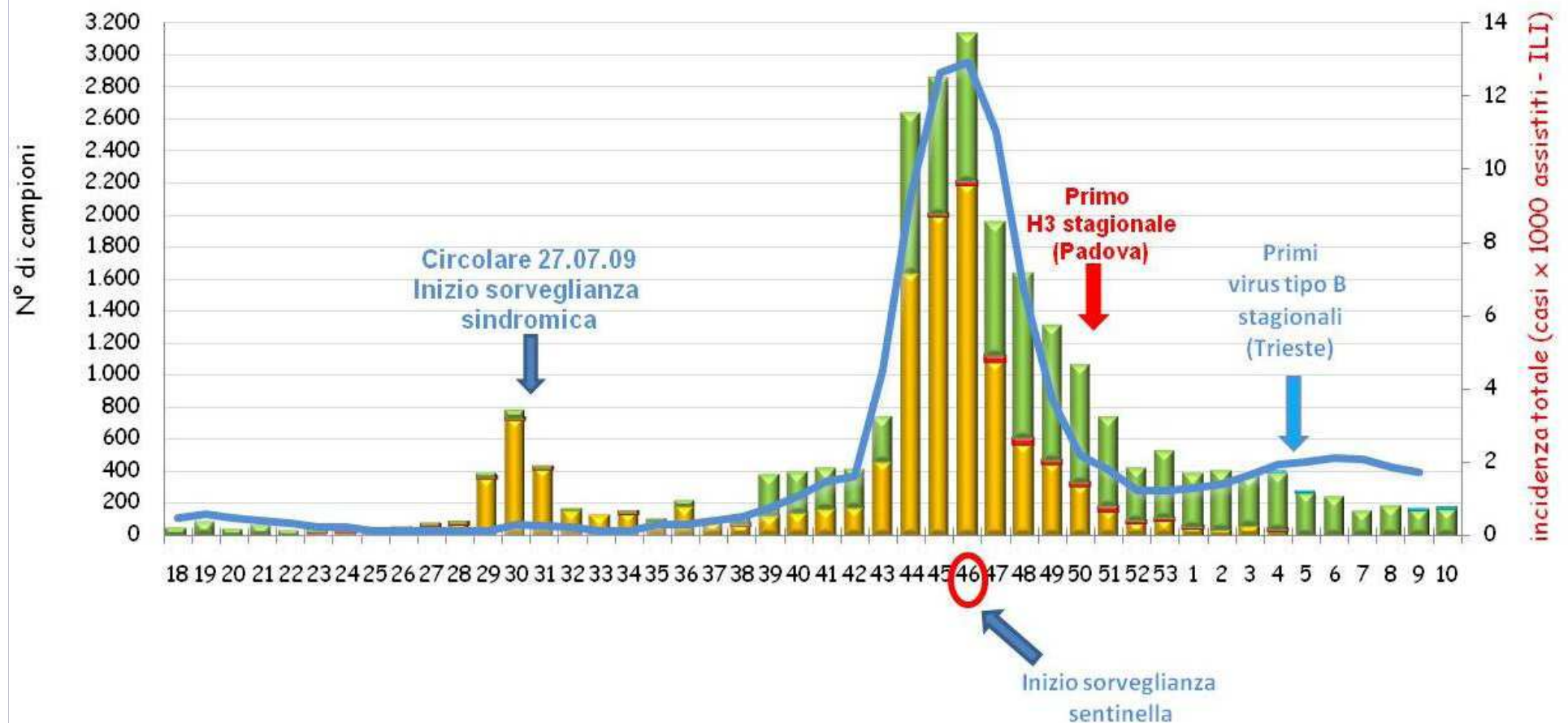
INFLUENZA ASSOCIATED DEATHS AMONG CHILDREN IN THE UNITED STATES

- 153 influenza-related deaths
- Median age of died children was 3 years (63% aged <5 yrs)
- 31% died outside hospital setting
- 29% died within three days after the onset of the illness
- 47% had previously been healthy

Circolazione virus influenzali epidemici e pandemici in Italia (rete Influnet)

campioni positivi B campioni raccolti campioni positivi A campioni positivi A/H1N1v Incidenza

aggiornamento al 17/03/2010

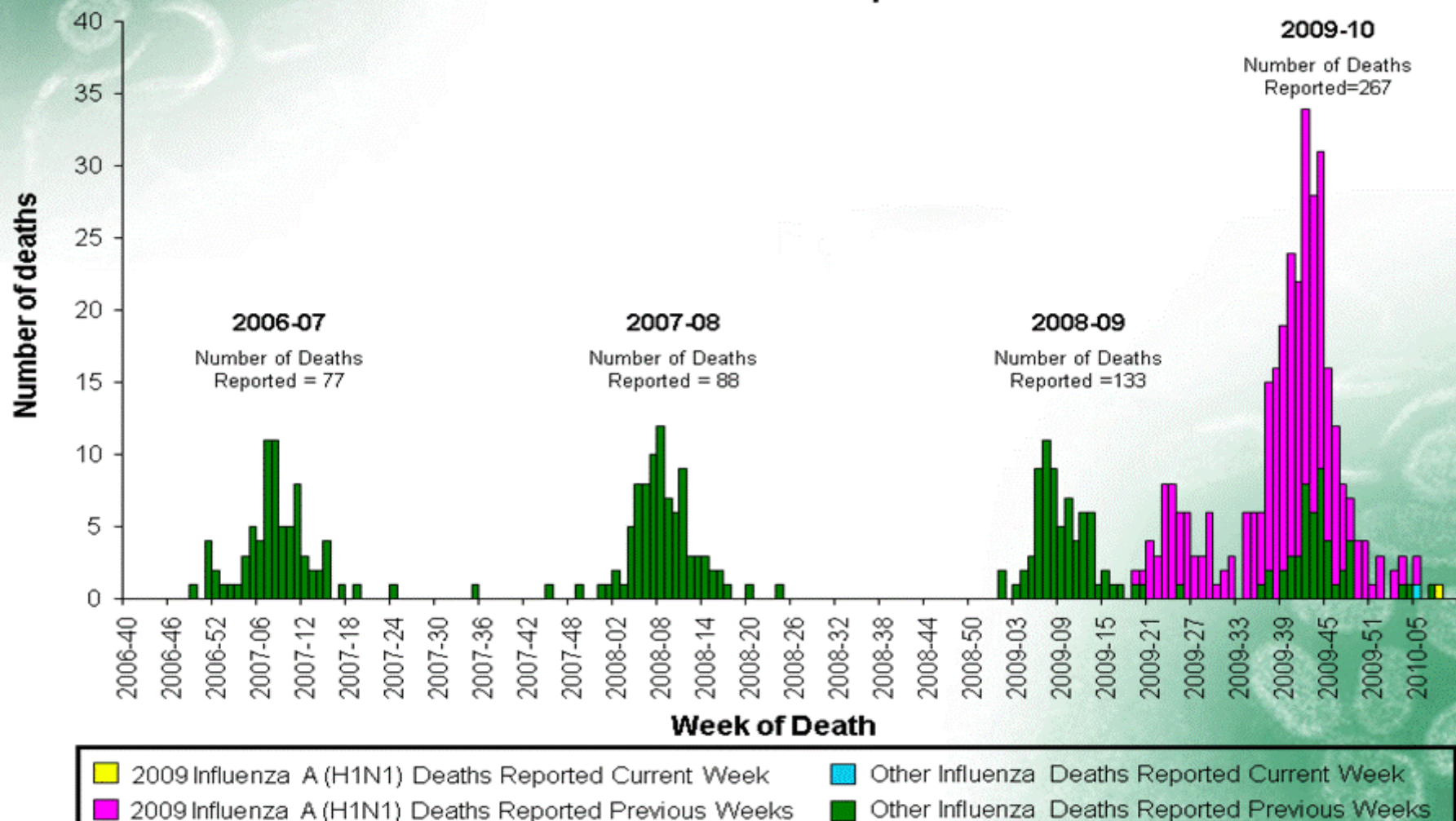


FLUVIEW



A Weekly Influenza Surveillance Report Prepared by the Influenza Division

Number of Influenza-Associated Pediatric Deaths by Week of Death: 2006-07 season to present



Characteristic/Status	No. of patients (N = 36)	(%)
Age group		
0–6 mos	2	(6)
6–23 mos	3	(8)
24–59 mos	2	(6)
5–8 yrs	5	(14)
9–12 yrs	13	(36)
13–17 yrs	11	(30)
Sex		
Male	18	(50)
Female	18	(50)
Race/Ethnicity		
White, non-Hispanic	15	(42)
Black, non-Hispanic	6	(17)
Hispanic	12	(33)
Asian	3	(8)
High-risk medical conditions[†]		
Neurodevelopmental condition [§]	22	(61)
Chronic pulmonary condition	10	(28)
Congenital heart disease	3	(8)
Metabolic or endocrine condition	2	(6)
Immuno suppression	2	(6)
Any high-risk condition	24	(67)
Multiple neurodevelopmental conditions	13	(36)
Neurodevelopmental condition with chronic pulmonary condition	9	(25)
Antiviral treatment		
None	12	(39)
≤2 days after illness onset	4	(13)
>2 days after illness onset	12	(39)
Timing of treatment initiation unknown	3	(10)
Unknown	5	(14)
Invasive bacterial coinfection		
Yes	10	(28)
No	13	(36)
No specimens collected	8	(22)
Unknown	5	(14)

* As of August 8, 2009.

TABLE 2. Selected demographic characteristics and high-risk medical condition, antiviral treatment, and invasive bacterial coinfection status of children whose deaths were associated with 2009 pandemic influenza (H1N1) virus infection — influenza-associated pediatric mortality case reporting, United States, April–August 2009*

MMWR September 4th, 2009

Fattori di rischio per influenza stagionale o pandemica grave in bambini ricoverati in Canada

(Da O'Riordan S et al. CMAJ 2009)

Risk factor	All children admitted to hospital			Children admitted to intensive care unit		
	Pandemic H1N1 influenza <i>n</i> = 58	Seasonal influenza A <i>n</i> = 200	<i>p</i> value*	Pandemic H1N1 influenza <i>n</i> = 12	Seasonal influenza A <i>n</i> = 28	<i>p</i> value*
Asthma†	13 (22)	11 (6)	< 0.001	5 (42)	2 (7)	0.017
Chronic lung disease‡	2 (3)	13 (6)	0.53	0	5 (18)	0.30
Cardiac disease	4 (7)	20 (10)	0.61	1 (8)	3 (11)	1.0
Hemoglobinopathy	9 (16)	22 (11)	0.36	1 (8)	0	0.30
Immunodeficiency	7 (12)	42 (21)	0.13	0	2 (7)	0.30
Neurologic impairment	10 (17)	26 (13)	0.54	2 (17)	6 (21)	1.0
Age < 2 yr and no underlying medical condition	5 (9)	35 (18)	0.15	1 (8)	3 (11)	1.0
Other	1 (2)	12 (6)	0.31	1 (8)	3 (11)	1.0
None	7 (12)	19 (10)	0.74	1 (8)	4 (14)	1.0

All children aged 6 months–18 years should be vaccinated annually.

Children and adolescents at higher risk for influenza complications should continue to be a focus of vaccination efforts as providers and programs transition to routinely vaccinating all children and adolescents, including those who:

- are aged 6 months–4 years (59 months);
- have chronic pulmonary (including asthma), cardiovascular (except hypertension), renal, hepatic, cognitive, neurologic/neuromuscular, hematological or metabolic disorders (including diabetes mellitus);
- are immunosuppressed (including immunosuppression caused by medications or by human immunodeficiency virus);
- are receiving long-term aspirin therapy and therefore might be at risk for experiencing Reye syndrome after influenza virus infection;
- are residents of long-term care facilities; and
- will be pregnant during the influenza season.

Note: Children aged <6 months cannot receive influenza vaccination. Household and other close contacts (e.g., daycare providers) of children aged <6 months, including older children and adolescents, should be vaccinated.



MMWRTM

Morbidity and Mortality Weekly Report

www.cdc.gov/mmwr

July 31, 2009 / Vol. 58 / No. RR-8

Initial target groups for novel influenza A (H1N1) vaccination programs and a subset of these target groups to receive vaccine if initial vaccine availability is not sufficient to meet demand*

Initial target groups

ACIP recommends that programs and providers provide vaccine to all persons in the following five initial target groups as soon as vaccine is available (order of target groups does not indicate priority):

- pregnant women,
- persons who live with or provide care for infants aged <6 months (e.g., parents, siblings, and daycare providers),
- health-care and emergency medical services personnel,[†]
- children and young adults aged 6 months–24 years, and
- persons aged 25–64 years who have medical conditions that put them at higher risk for influenza-related complications.[§]

Subset of initial target groups

ACIP recommends that all persons in the following subset of the five initial target groups receive priority for vaccination if vaccine availability is not sufficient to meet demand (order of target groups does not indicate priority):

- pregnant women,
- persons who live with or provide care for infants aged <6 months (e.g., parents, siblings, and daycare providers),
- health-care and emergency medical services personnel who have direct contact with patients or infectious material,
- children aged 6 months–4 years, and
- children and adolescents aged 5–18 years who have medical conditions that put them at higher risk for influenza-related complications.[§]

From MMWR, August 28, 2009

October 6, 2009 — On the second day of nationwide vaccination for the influenza A (H1N1) virus, the director of the US Centers for Disease Control and Prevention (CDC) reiterated that the vaccine is safe in an effort to assuage public misgivings.

Ministero del Lavoro, della Salute e delle Politiche Sociali

Ordinanza: Misure urgenti in materia di protezione AH1N1v

Ordinanza
30 sett 2009

1. L'articolo 1, comma 1, dell'Ordinanza 11 settembre 2009 è sostituito dal seguente:

"1. La vaccinazione antinfluenzale con vaccino pandemico A(H1N1) è offerta, a partire dal momento della effettiva disponibilità del vaccino, alle seguenti categorie di persone elencate in ordine di priorità:

- a) personale sanitario e socio-sanitario: personale delle forze di pubblica sicurezza e della protezione civile; personale del corpo nazionale dei vigili del fuoco del Ministero dell'interno; personale delle forze armate; personale che assicura i servizi pubblici essenziali di cui alla legge 12 giugno 1990, n. 146, e successive modificazioni secondo piani di continuità predisposti dai datori di lavoro o per i soggetti autonomi dalle Amministrazioni competenti; donatori di sangue periodici;
- b) donne al secondo o al terzo trimestre di gravidanza; donne che hanno partorito da meno di 6 mesi o, in loro assenza, la persona che assiste il bambino in maniera continuativa;
- c) portatori di almeno una delle condizioni di rischio, di cui al comma 2 dell'art. 1 della Ordinanza 11 settembre 2009, nonché i soggetti fino a 24 mesi nati gravemente pretermine;
- d) bambini di età superiore a 6 mesi che frequentano l'asilo nido; minori che vivono in comunità o istituzionalizzati;
- e) persone di età compresa tra più di 6 mesi e 17 anni, non incluse nei precedenti punti, sulla base degli aggiornamenti della scheda tecnica autorizzativa dell'EMEA;
- f) persone tra i 18 e 27 anni, non incluse nei precedenti punti."

*Ministero del Lavoro, della Salute
e delle Politiche Sociali*

Ordinanza: Misure urgenti in materia di protezione AH1N1v

**Ordinanza
30 sett 2009**

Art. 1

1. Ad integrazione dell'art. 6 dell'Ordinanza dell'11 settembre 2009, la co-somministrazione del vaccino contro l'influenza da virus AH1N1v con il vaccino dell'influenza stagionale può essere praticata ma deve essere eseguita con l'inoculazione dei due vaccini in arti differenti. Per ovviare al possibile effetto sommatorio delle reazioni avverse, in risposta alla co-somministrazione dei due vaccini, si deve ricorrere alla somministrazione di vaccino contro l'influenza stagionale non adiuvato.

Requirements for a pediatric influenza vaccine

- Children have immature immune systems that can limit their responses to vaccination
- The efficacy (prevention of confirmed influenza) of inactivated influenza vaccines in children (1–18 years of age) is approximately 60%¹
- For children <24 months of age, some studies have reported that the efficacy of inactivated vaccines is similar to placebo (37%)^{1,2}
- To overcome these limitations, pediatric influenza vaccines should offer the following:
 - Robust immune responses
 - A favorable tolerability profile
- Adjuvants may be able to overcome these limitations and offer effective and safe pediatric vaccines

1. ECDC. Technical Report of the Scientific Panel on Vaccines and Immunisation. 2007;

2. Jefferson T, *et al.*, *Cochrane Database Syst Rev* 2008; 2:CD004879.

Adjuvants: What role do they play in vaccination?

Overcome the limited immune response in populations such as young children

Extend the duration of the immune response by increasing antibody persistence and enhancing the cellular response

Increase the breadth of the immune response, providing heterologous activity

Reduce the antigen dose required in the vaccine to induce an immune response

IMMUNOGENICITY OF TWO DIFFERENT INFLUENZA VACCINES IN CHILDREN AGED 6 MONTHS - 5 YEARS

(Kanra, Marchisio et al., Pediatr Infect Dis J 2004)

Immune Status	Treatment	ITT Population	Seroconversion (% of Subjects)			Seroprotection (% of Subjects)			GMT (Fold Increase)		
			H1N1	H3N2	B	H1N1	H3N2	B	H1N1	H3N2	B
Total	Virusome- adjuvanted split	156	80.1	66.0	90.4	87.8	80.1	90.4	18.08	6.89	37.72
		170	75.9	62.9	89.4	82.9	78.2	89.4	15.77	6.74	35.80
<i>P</i>			0.3559	0.5612	0.7711	0.2142	0.6743	0.7711			
Unprimed	Virusome- adjuvanted split	116	88.8	69.8	94.8	88.8	77.6	94.8	26.99	7.95	49.94
		120	77.5	68.3	93.3	78.3	75.8	93.3	18.01	8.07	43.34
<i>P</i>			0.0208	0.8039	0.6271	0.0306	0.7502	0.6271			
Primed	Virusome- adjuvanted split	40	55.0	55.0	77.5	85.0	87.5	77.5	5.66	4.56	16.71
		50	72.0	50.0	80.0	94.0	84.0	80.0	11.47	4.38	22.63
<i>P</i>			0.0941	0.6370	0.7727	0.1573	0.6388	0.7727			

EFFICACY OF VIROSOMAL-ADJUVANTED INFLUENZA VACCINE IN OTHERWISE HEALTHY CHILDREN AGED 2-5 YEARS

(Esposito et al., Vaccine 2006)

Event	Vaccinated children (<i>n</i> = 202)	Unvaccinated children (<i>n</i> = 101)	Vaccine effectiveness (%) [*]	<i>p</i> -value
Number of upper respiratory tract infections	1.66 ± 0.62	2.47 ± 0.43	33	<0.0001
Number of lower respiratory tract infections	0.32 ± 0.88	0.41 ± 1.32	22	0.004
Number of febrile respiratory illnesses	2.47 ± 1.49	3.32 ± 2.74	26	<0.0001
Number of hospitalisations	0.01 ± 0.23	0.02 ± 0.25	50	0.417
Number of antibiotic prescriptions	1.36 ± 1.28	1.98 ± 1.59	32	<0.0001
Number of antipyretic prescriptions	4.70 ± 2.03	6.59 ± 2.37	29	<0.0001
Missed school days	4.61 ± 6.23	8.84 ± 12.50	48	<0.0001

Mean values ± S.D.

IMPACT OF VIROSOMAL-ADJUVANTED INFLUENZA VACCINE IN CHILDREN AGED 2-5 YEARS ON HOUSEHOLDS (Esposito et al. Vaccine 2006)

Event	Household contacts of vaccinated children (<i>n</i> = 548)	Household contacts of unvaccinated controls (<i>n</i> = 256)	Vaccine effectiveness (%) [*]	<i>p</i> -value
Number of influenza-like illness	3.03 ± 1.68	4.27 ± 1.68	30	0.0005
Number of medical visits for influenza-like illness	2.18 ± 1.37	3.16 ± 1.77	31	0.002
Number of hospitalisations	0	0	0	1.00
Number of antibiotic prescriptions	0.76 ± 0.99	1.40 ± 1.33	46	<0.0001
Number of antipyretic prescriptions	1.01 ± 0.76	1.99 ± 1.46	49	<0.0001
Loss of parental work (days)	1.91 ± 1.43	2.93 ± 2.31	35	0.001
Mothers	3.22 ± 1.86	4.78 ± 2.34	33	0.001
Fathers	0.56 ± 0.46	0.98 ± 1.22	43	<0.0001
Missed school days of siblings	1.43 ± 2.61	2.93 ± 4.10	51	<0.0001
Mean values ± S.D.				

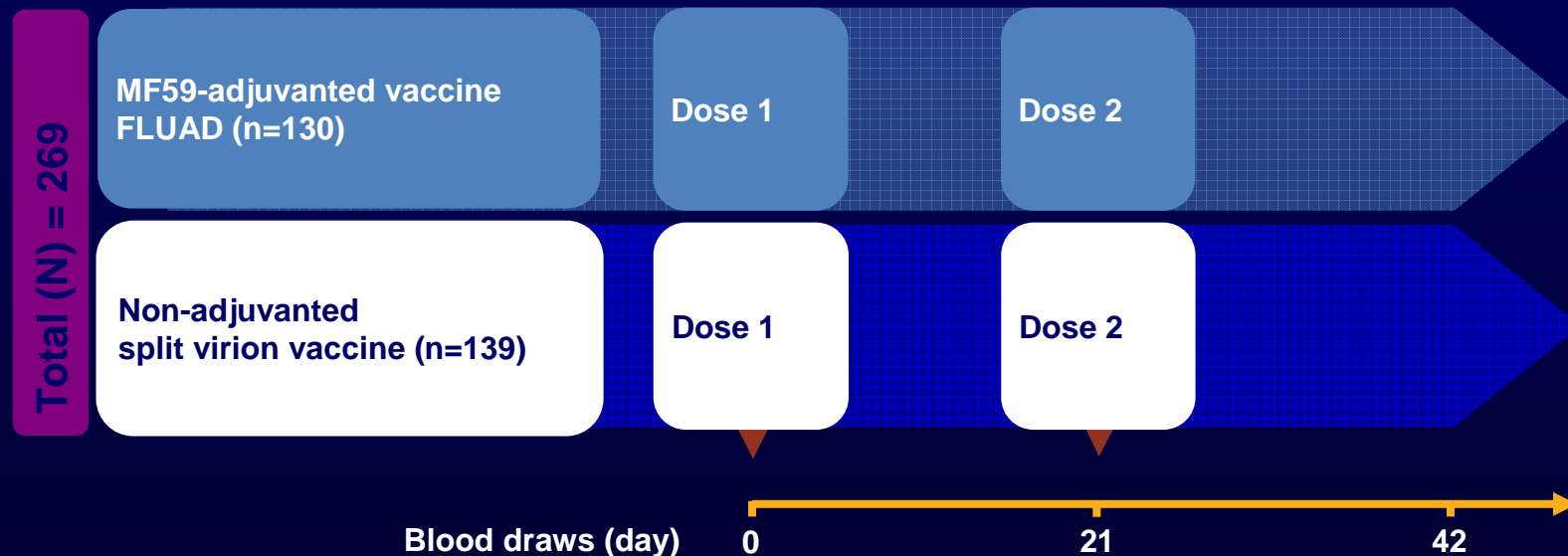
COST-EFFECTIVENESS OF ADJUVANTED INFLUENZA VACCINATION

	No Vaccination of 6-60-Month- Old-Children	Vaccination of 6-24-Month- Old-Children	Vaccination of 6-60-Month- Old-Children
ILI events in Children 6-60 months	4,080,000	3,930,000	3,600,000
ILI events saved in Children 6-60 months	-	150,000	480,000
ILI events in Households	5,670,000	5,520,000	5,130,000
ILI events saved in Households	-	150,000	540,000
ILI events saved in Children and Households	-	300,000	1,020,000
Incremental QALYs	-	900	3000
Incremental costs	-	+ €12,000,000	+ € 30,000,000
incremental cost-effectiveness	-	€13,333/QALY	€10,000/QALY
Incremental costs	-	- €21,000,000	- €63,000,000
Incremental costeffectiveness	-	dominant	dominant

Marchetti et al., Hum Vaccine 2007

FLUAD: Study to evaluate the immunogenicity, safety, and tolerability in healthy children 6–35 months of age*

- Objective: Immunogenicity and tolerability of FLUAD in comparison with non-adjuvanted split-virion vaccine
- Immune responses measured against the vaccine strains: 2006/07 influenza season

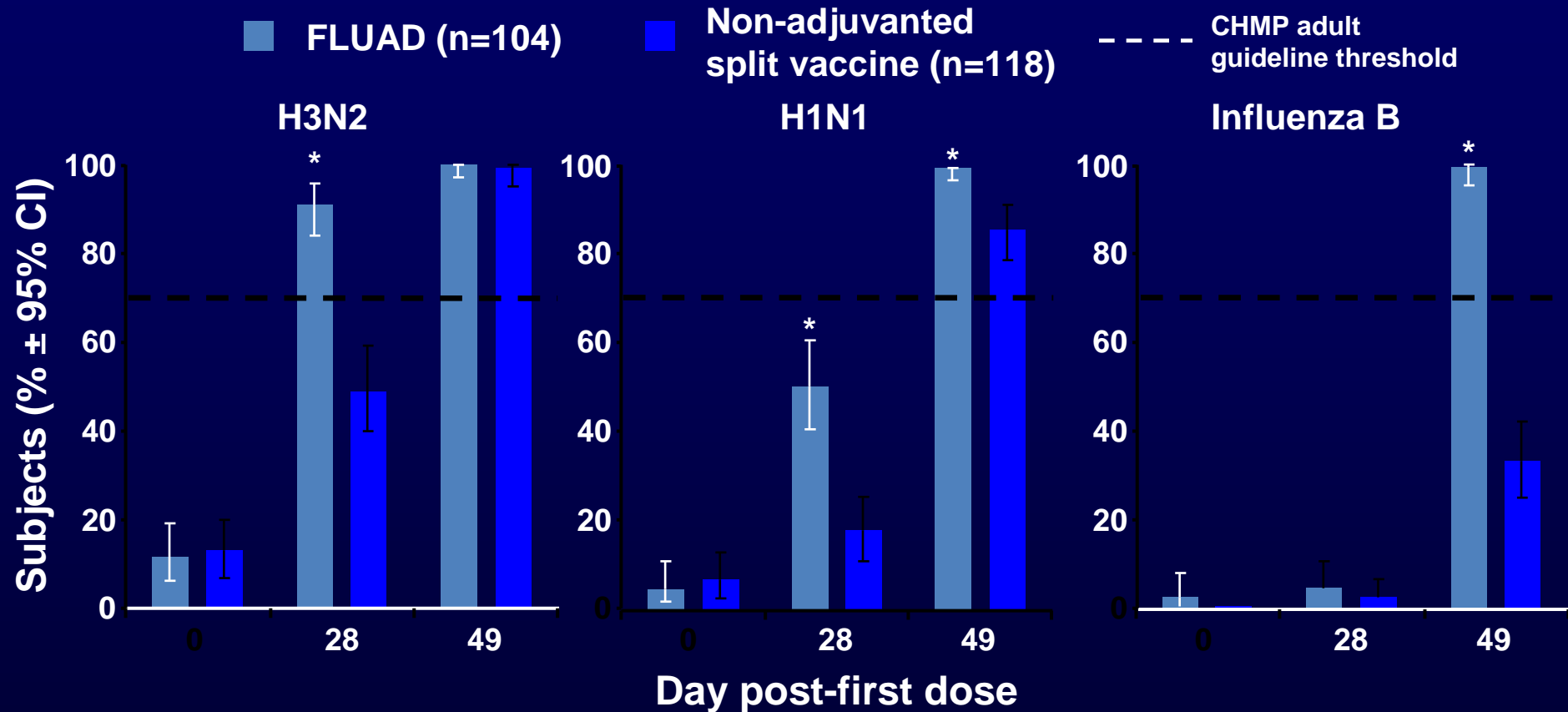


* Not previously vaccinated against influenza

Vesikari T, et al. *Ped Infect Dis J* 2009; 28:563–571.

FLUAD is not licensed in US. FLUAD is recommended for active prophylaxis of influenza in the elderly.

Proportion of subjects with an HI titer $\geq 1:40$ following two doses of vaccine



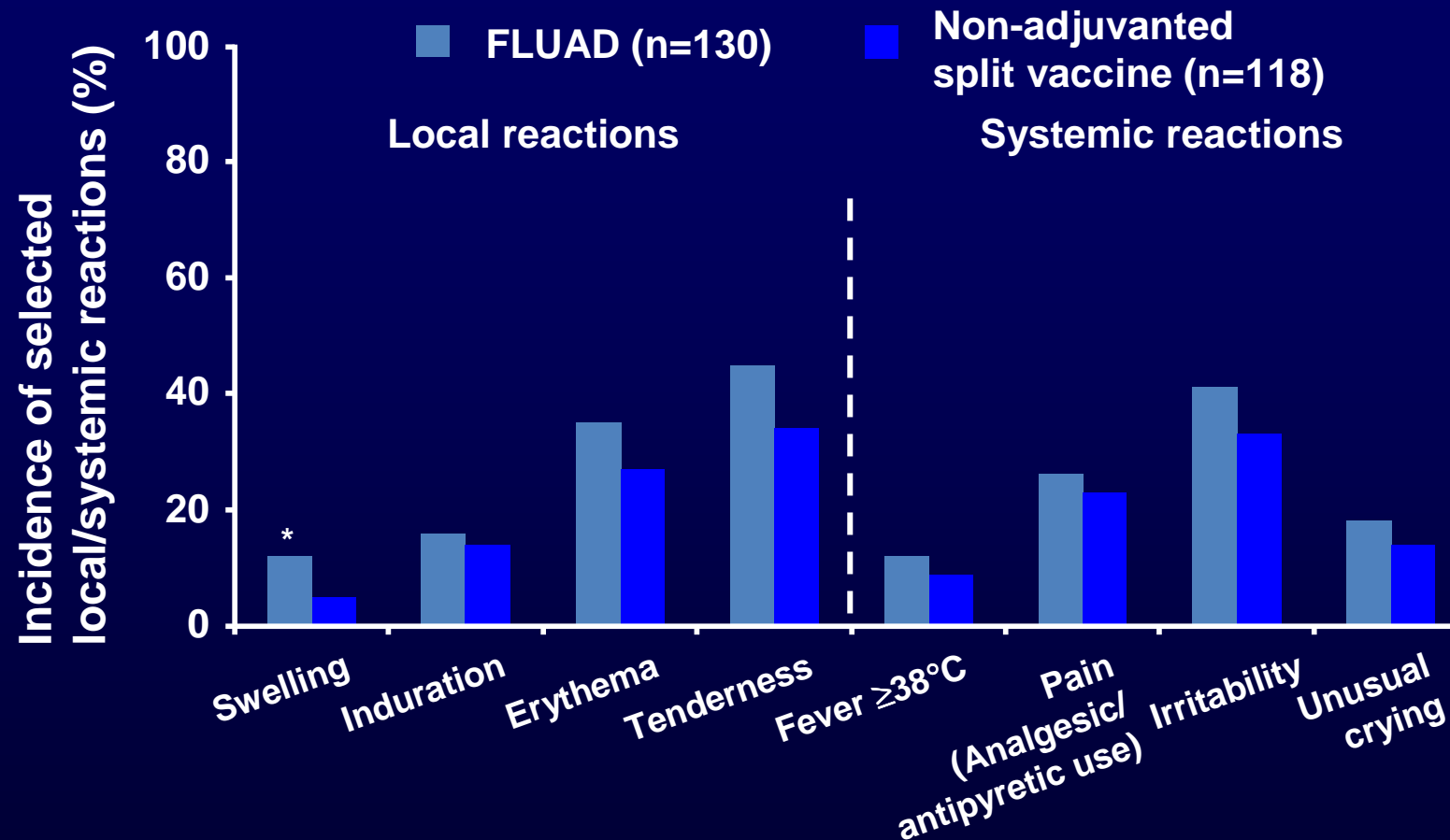
FLUAD induced higher rates of seroprotection against all tested strains, including influenza B, than the non-adjuvanted vaccine

* $P=0.001$ FLUAD vs. split

Vesikari T, et al. *Ped Infect Dis J* 2009; 28:563–571.

FLUAD is not licensed in US. FLUAD is recommended for active prophylaxis of influenza in the elderly.

Overall rates of local and systemic reactions following vaccination



Rates of reactions were comparable between FLUAD and the non-adjuvanted split vaccine

* $P=0.033$ FLUAD vs. split

Vesikari T, et al. *Ped Infect Dis J* 2009; 28:563–571.

FLUAD is not licensed in US. FLUAD is recommended for active prophylaxis of influenza in the elderly.

Summary of clinical trial data for FLUAD

- FLUAD was immunogenic in children 6–35 months of age
 - Higher seroprotection rates than non-adjuvanted vaccine ($P=0.001$)
 - Day 49 seroprotection rate against influenza B was 99% compared with 33% for non-adjuvanted vaccine
- FLUAD demonstrated a favorable tolerability profile
 - Rates of local and systemic reactions were similar to non-adjuvanted vaccine
 - Injection site swelling was more common with FLUAD
 - Most reactions were mild and of short duration

FLUAD was well tolerated in children and induced greater and broader immune responses than non-adjuvanted split vaccine

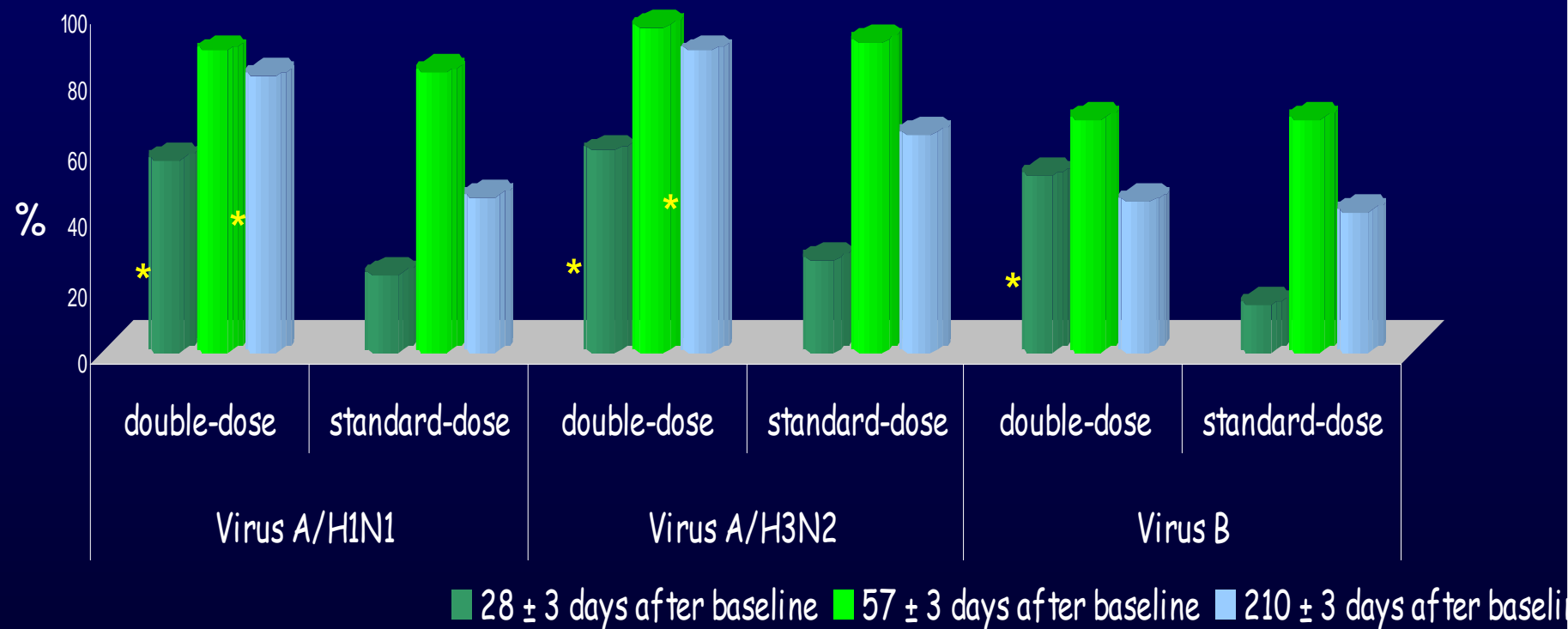
DOUBLE DOSE VS STANDARD DOSE OF VIROSOMAL ADJUVANTED VACCINE

(Esposito S et al., ESPID 2010)

- Healthy children aged 6-35 months who had not been previously vaccinated against influenza
- Children were randomly assigned 1:2 to receive 2 doses 4-week apart of 0.25 mL (standard dose, SD) or 0.50 mL (double dose, DD) of seasonal virosomal-adjuvanted influenza vaccine (Inflexal V, Crucell), separated by an interval of four weeks
- Blood samples were collected pre-vaccination, 4 weeks after each dose and 6 months after the second dose
- Local and systemic reactions were recorded for the 14 days after vaccine administration

SEROCONVERSION RATES (%)

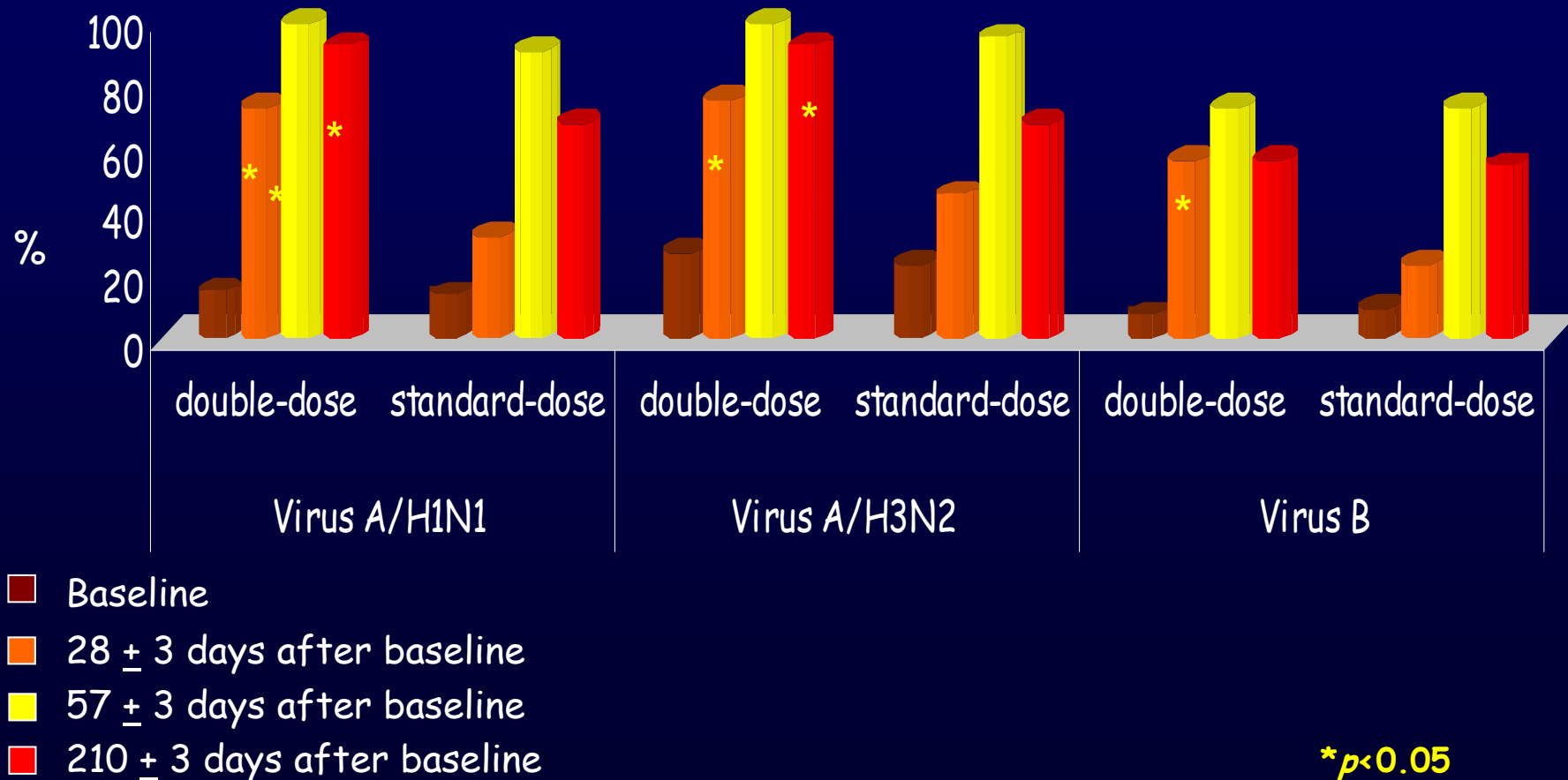
(Esposito S et al., ESPID 2010)



* $p < 0.05$

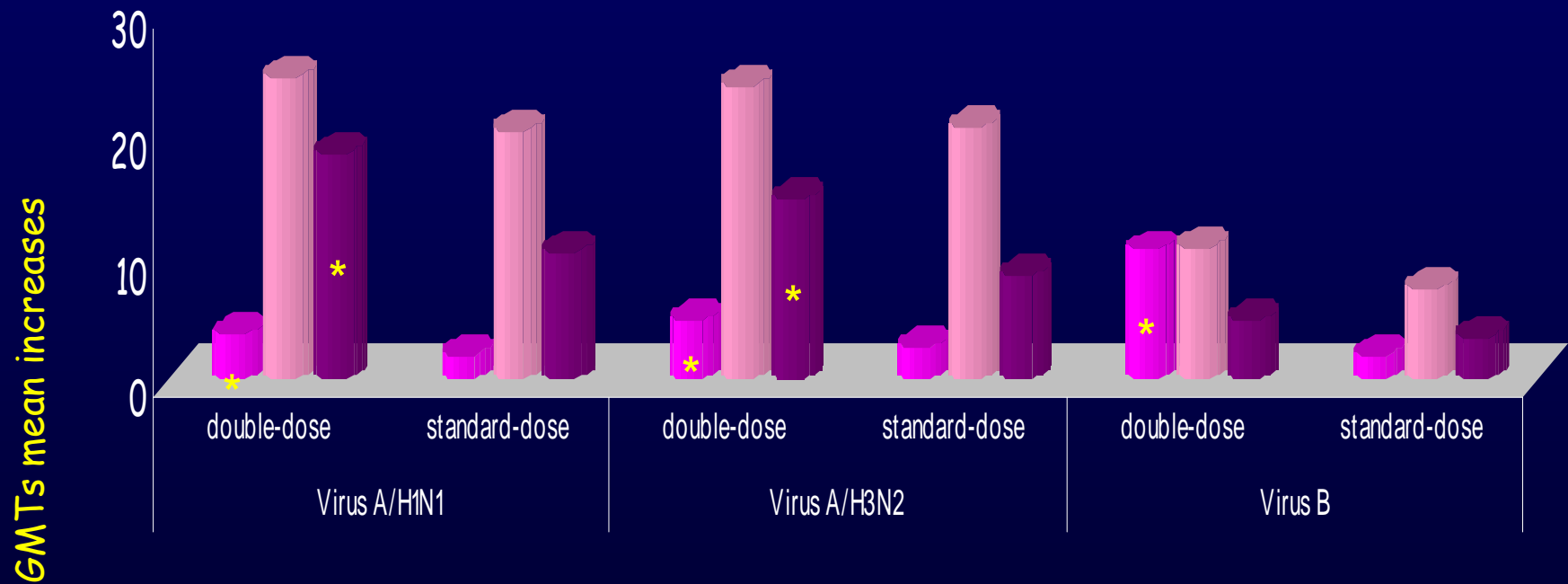
SEROPROTECTION RATES (%)

(Esposito S et al., ESPID 2010)



GEOMETRIC MEAN TITRES

(Esposito S et al., ESPID 2010)

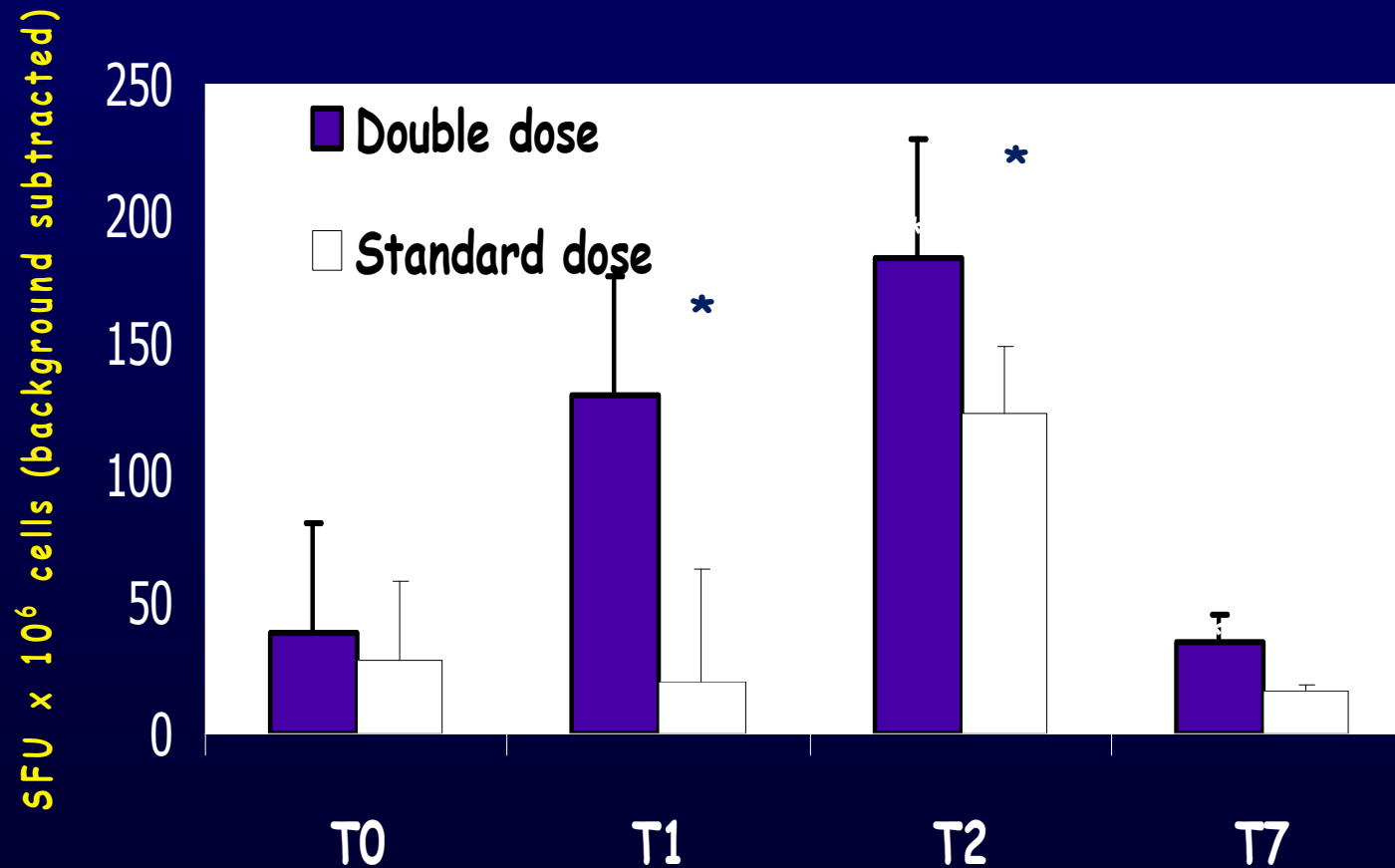


■ 28 ± 3 days after baseline ■ 57 ± 3 days after baseline ■ 210 ± 3 days after baseline

* $p < 0.05$

FLU-SPECIFIC IFN- γ -SECRETING CD8+ T CELLS

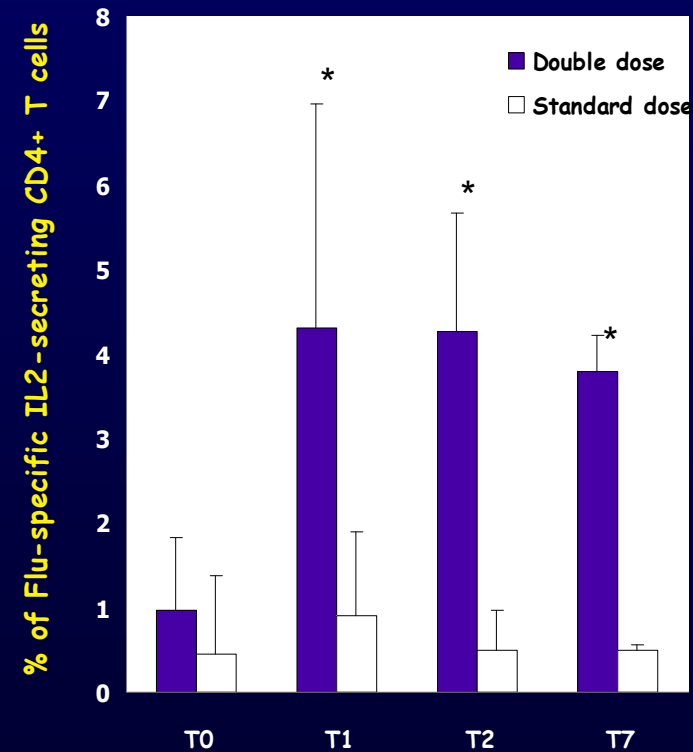
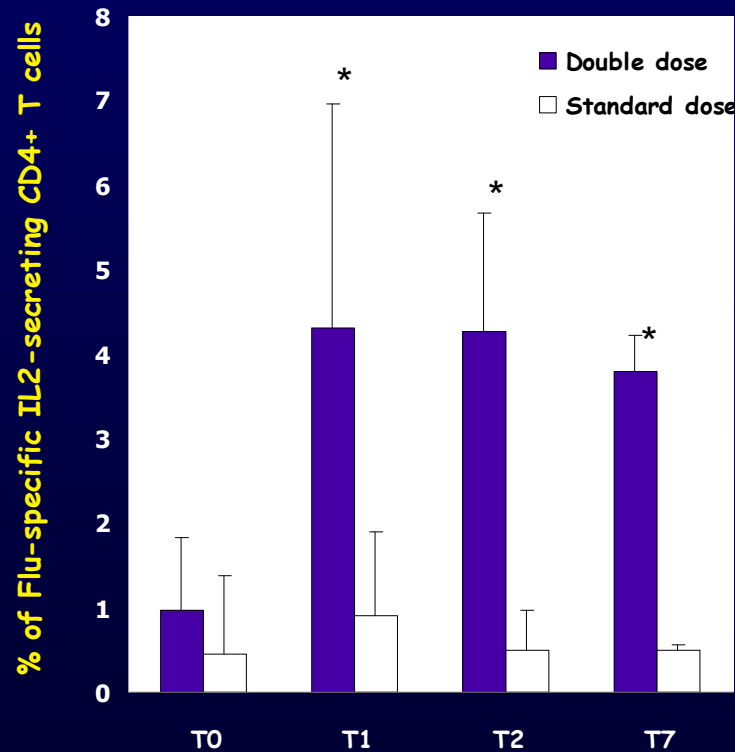
(Esposito S et al., ESPID 2010)



* $p < 0,05$

PERCENTAGES OF IL-2- AND IFN- γ -PRODUCING CD4+ T CELLS

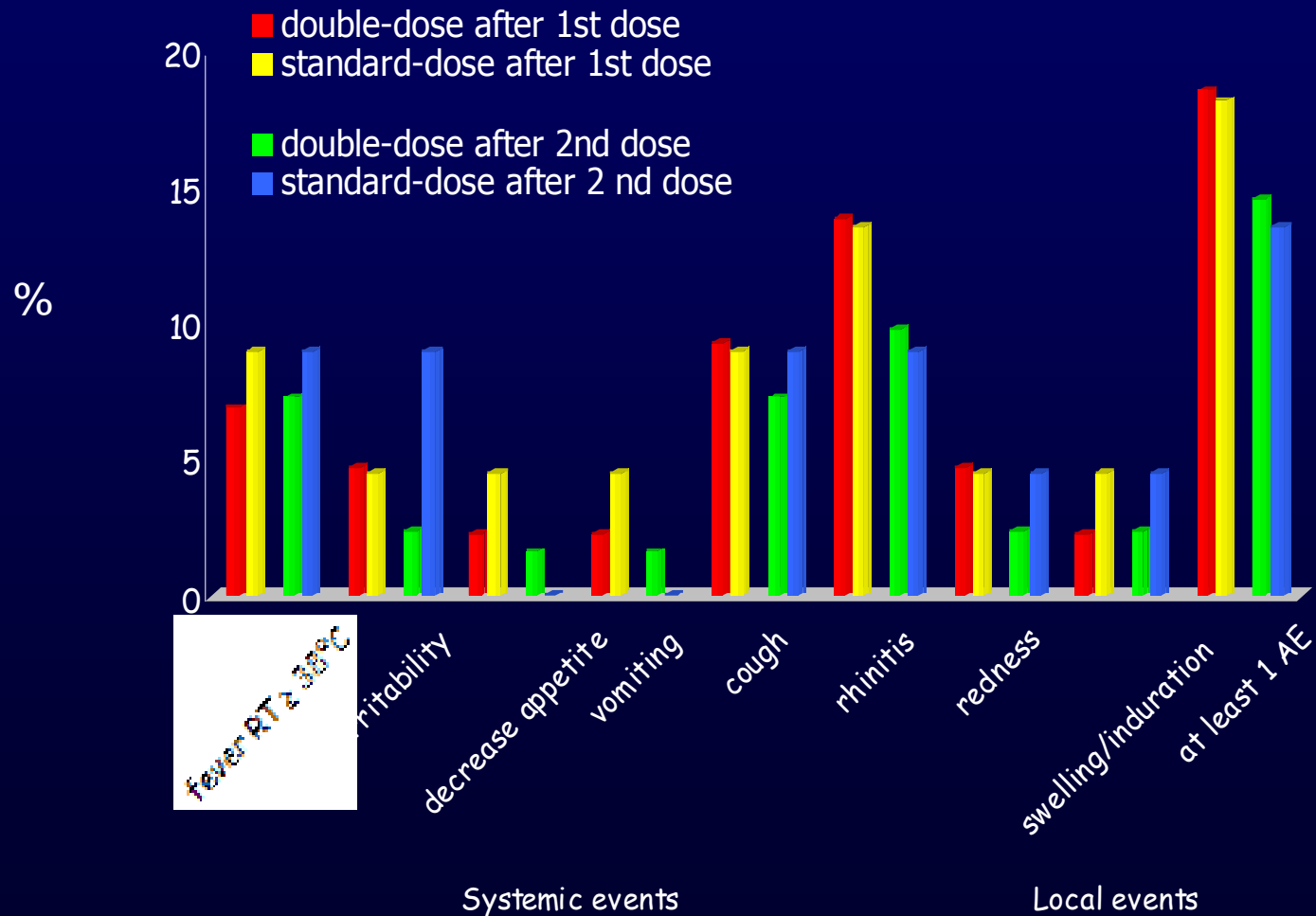
(Esposito S et al., ESPID 2010)



* $p < 0,05$

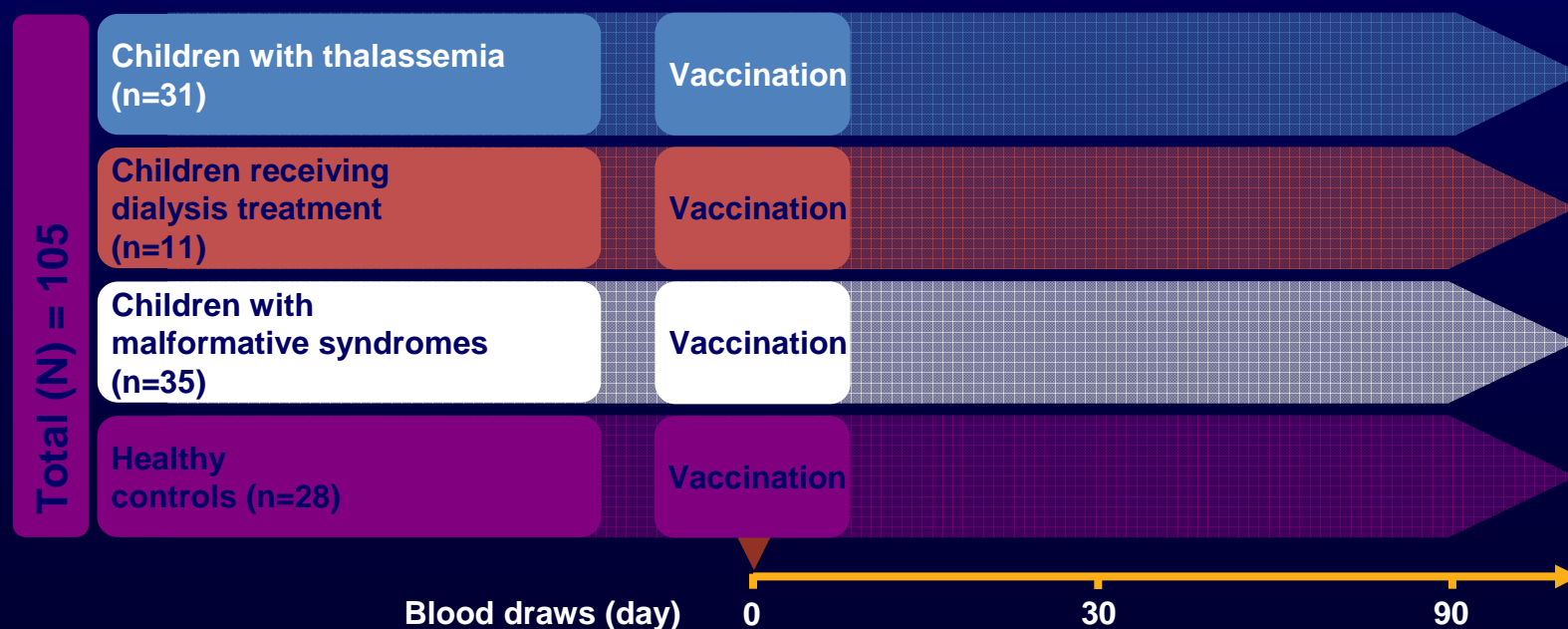
ADVERSE EVENTS

(Esposito S et al., ESPID 2010)



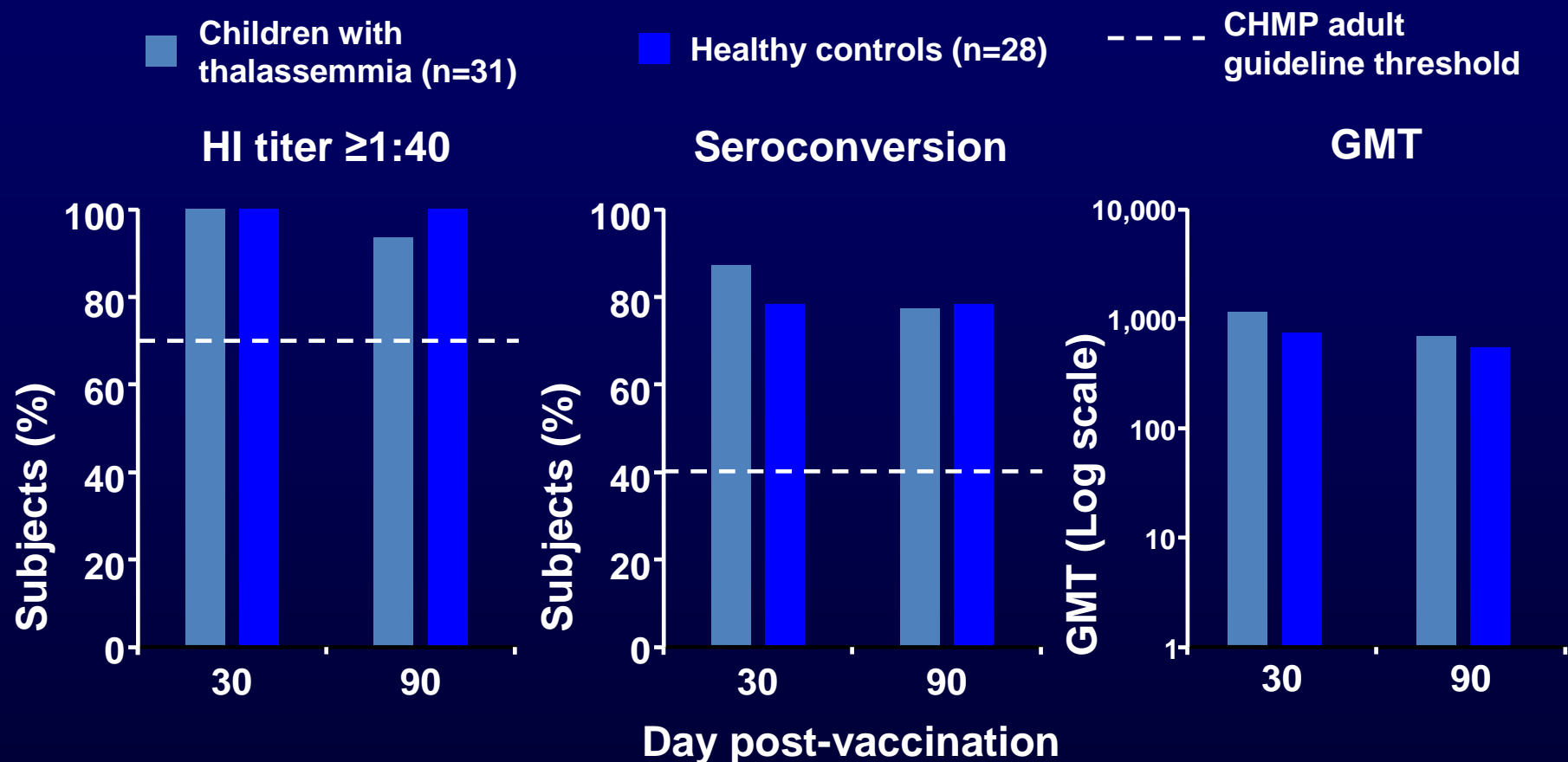
FOCETRIA: Phase IV trial to evaluate immunogenicity and safety in children with chronic disease

- Objective: Immunogenicity and safety of one dose of FOCETRIA in children (3–18 years of age) with chronic disease and healthy controls
- Immune responses* measured against the vaccine strain: Pandemic H1N1 virus A/California/7/2009



* Assays ongoing. Immunogenicity data shown for children with thalassemia and healthy controls
Esposito S. *et al.* Unpublished data.

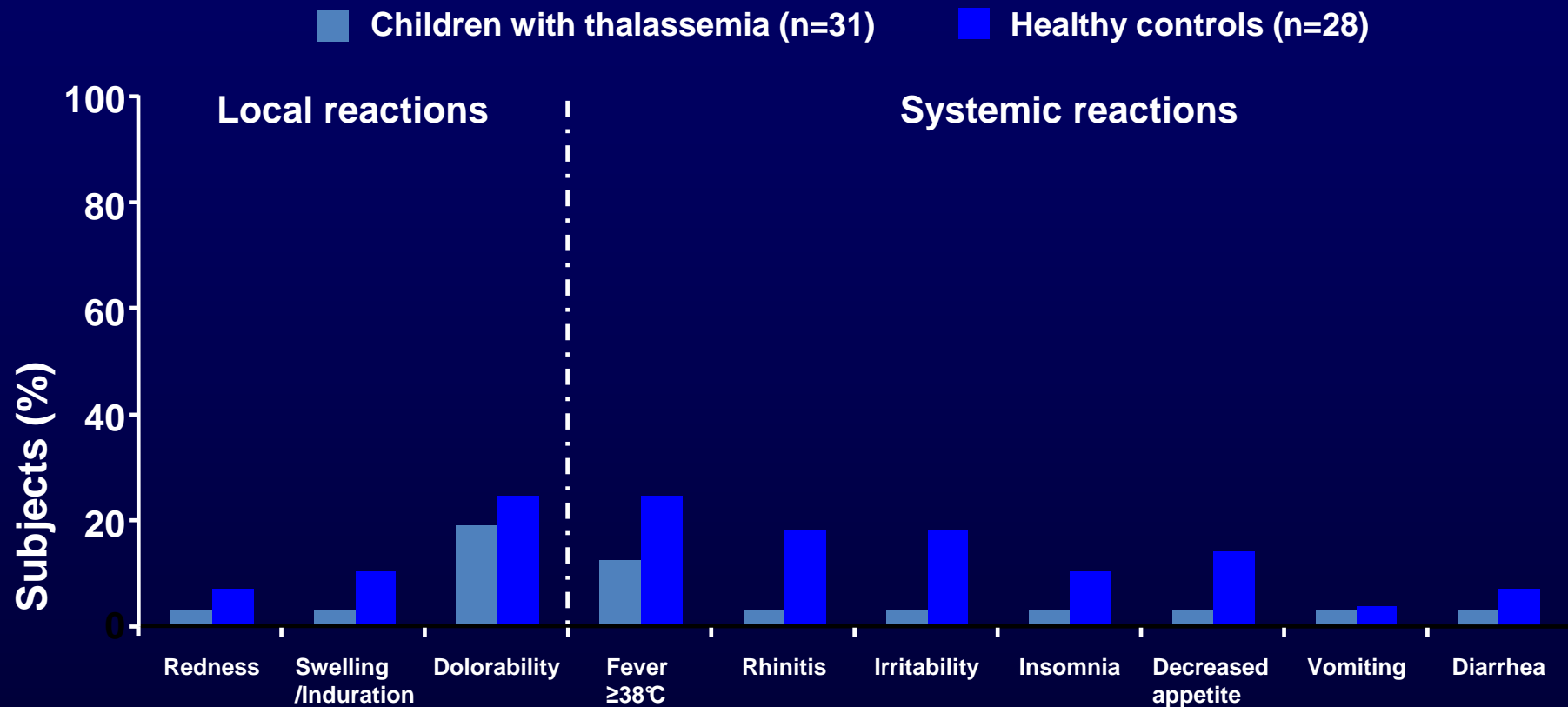
Immune responses following a single dose of FOCETRIA in children with thalassemia



A single dose of FOCETRIA induced immune responses in children with thalassemia which met licensure criteria 30 and 90 days post-vaccination

Esposito S. *et al.* Unpublished data.

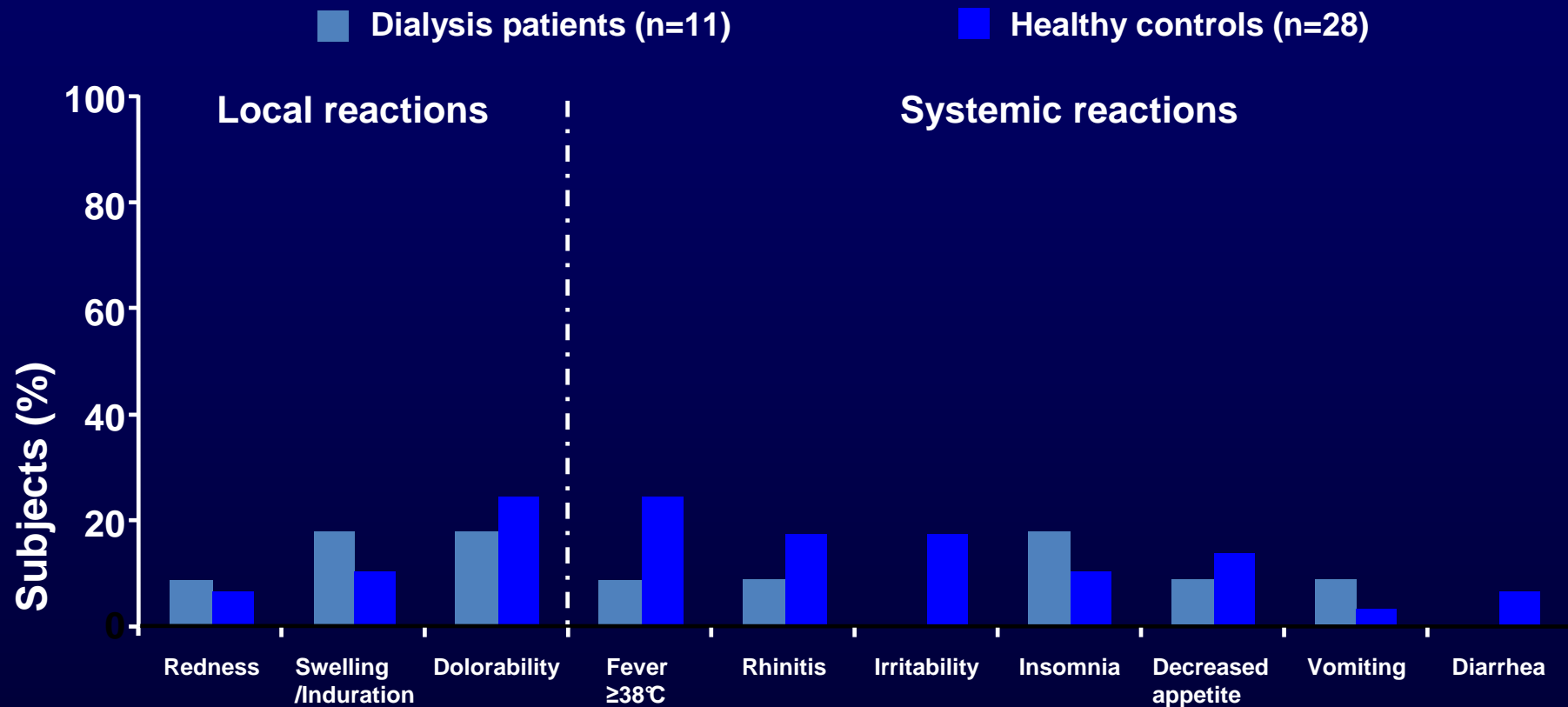
Local and systemic reactions following a single dose of FOCETRIA in children with thalassemia



Rates of local and systemic reactions were comparable between groups
No serious adverse events were observed for either group

Esposito S. *et al.* Unpublished data.

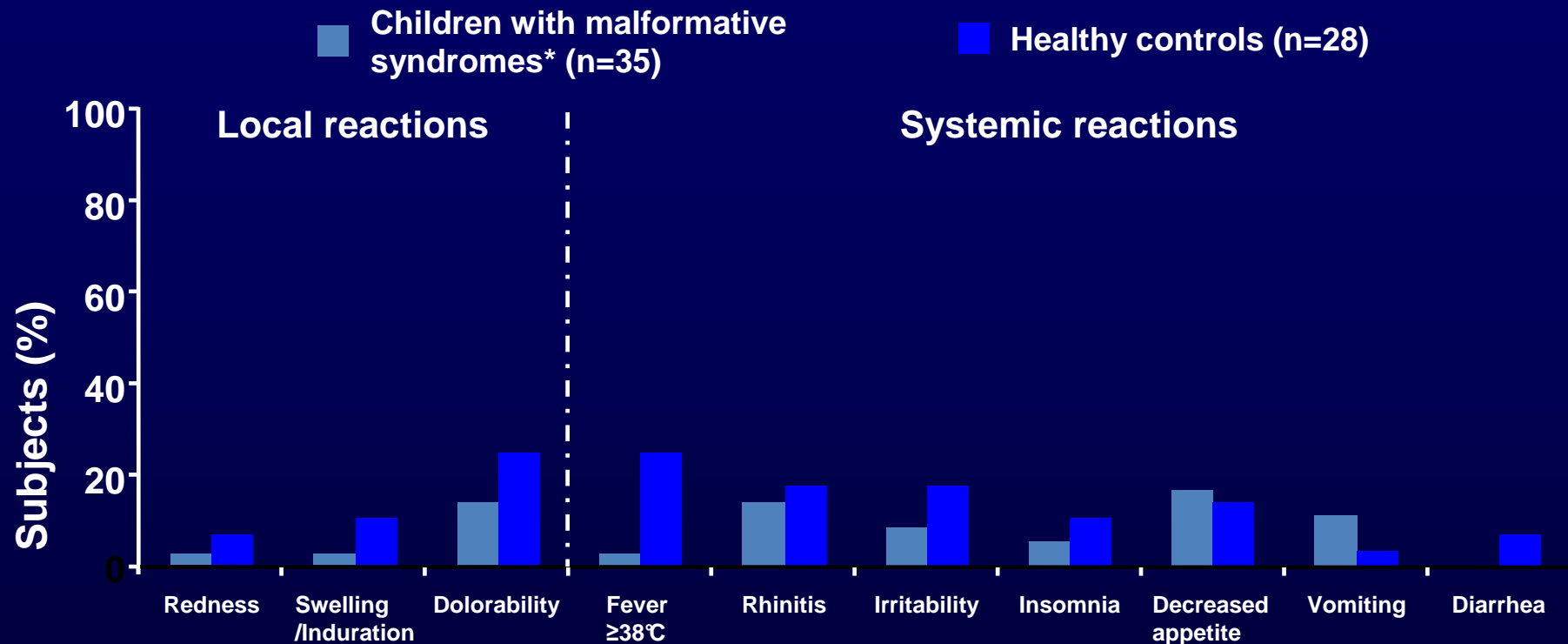
Local and systemic reactions following a single dose of FOCETRIA in children receiving dialysis treatment



Rates of local and systemic reactions were comparable between groups
No serious adverse events were observed for either group

Esposito S. *et al.* Unpublished data.

Local and systemic reactions following a single dose of FOCETRIA in children with malformative syndromes

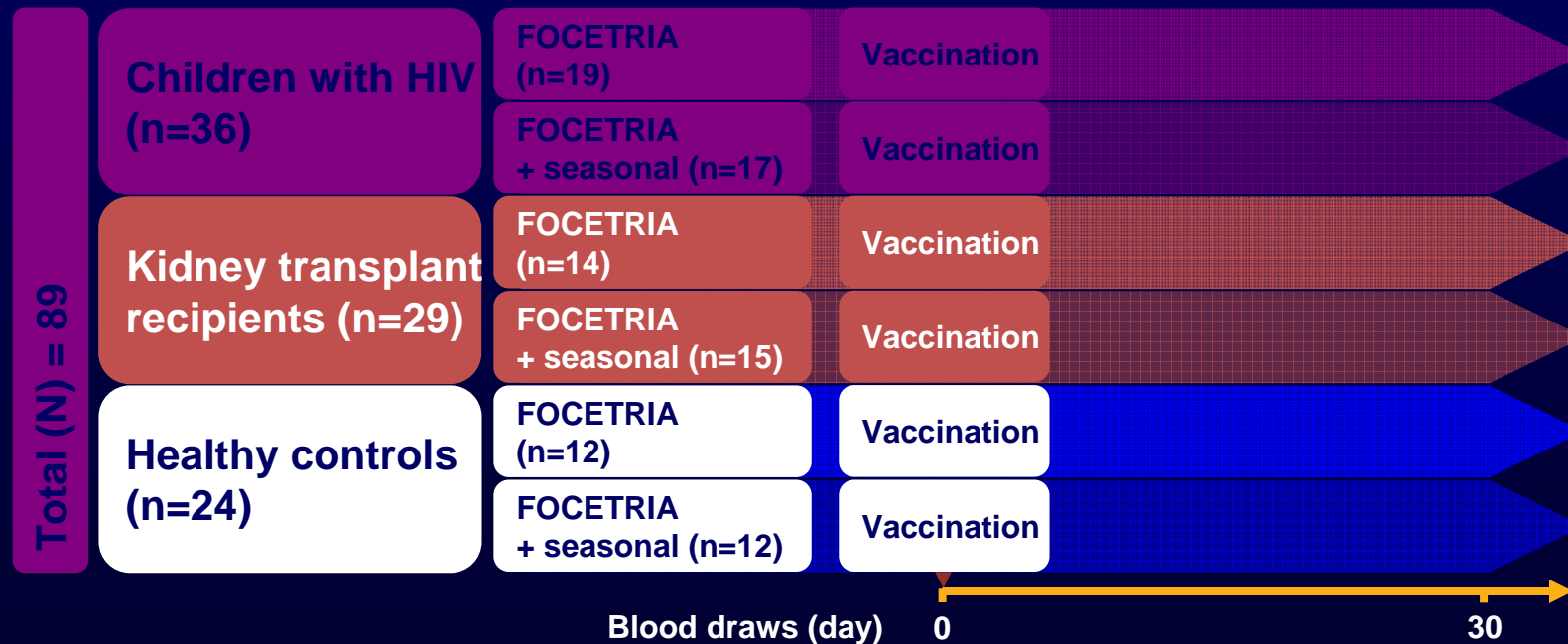


Rates of local and systemic reactions were comparable between groups
No serious adverse events were observed for either group

* Malformations include Angelman syndrome, Ataxia telangiectasia, Cockayne syndrome, Cornelia de Lange syndrome, Deletion of chromosome 22, Down syndrome, Malformative syndrome, Noonan syndrome, Pallister-Killian syndrome, Polimalformative syndrome, Smith Magenis syndrome, Williams syndrome, Wolf Hirschhorn syndrome, suspected NDD syndrome, suspected Noonan syndrome, suspected noonan syndrome with neurofibromatosis. Further details on notes page.
Esposito S. *et al.* Unpublished data.

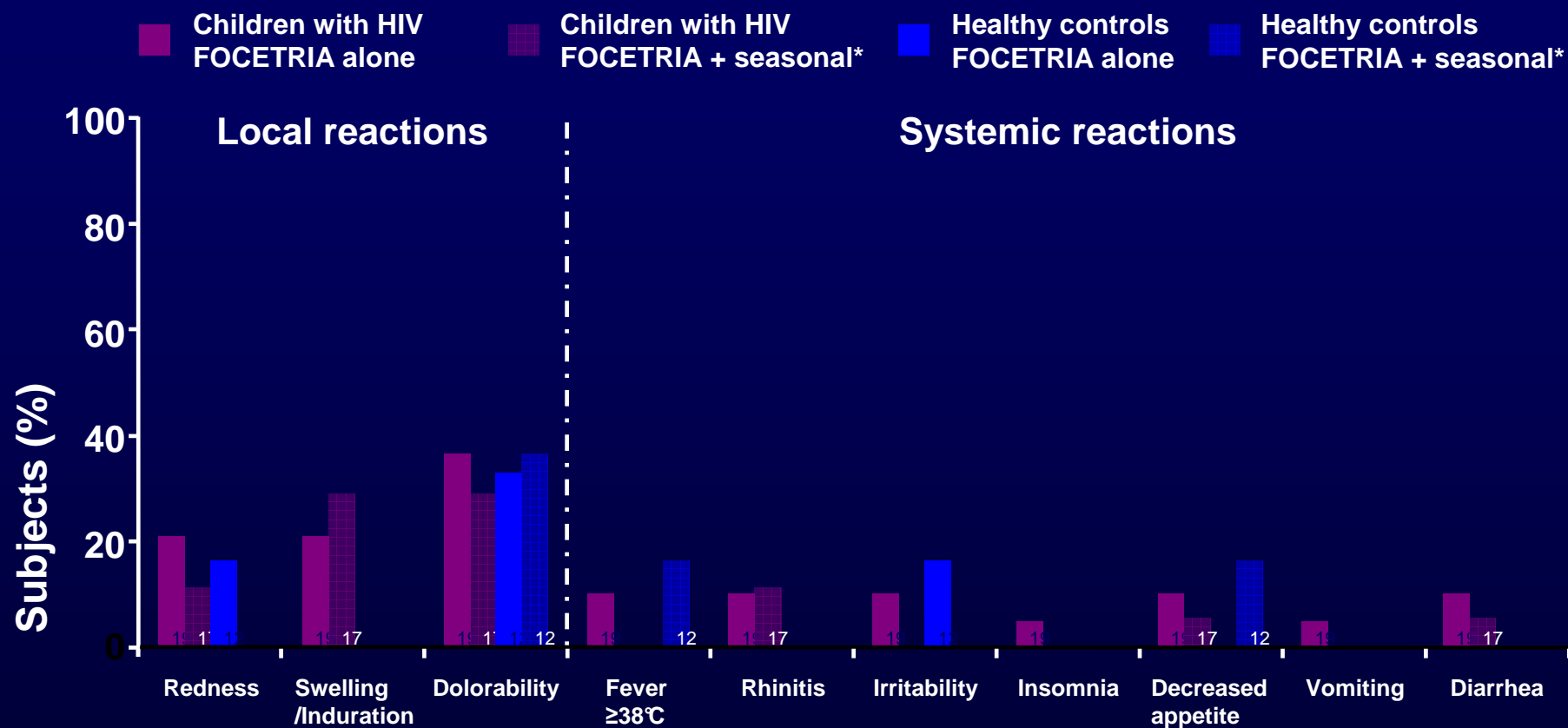
FOCETRIA: Phase III randomized trial, use of FOCETRIA ± seasonal vaccine in immunocompromised children

- Objective: Immunogenicity* and safety of one dose of FOCETRIA ± virosomal-adjuvanted seasonal vaccine† in immunocompromised and healthy children (7–18 years of age)
- Impact of vaccination on HIV RNA and CD4+ cells in children with HIV, or creatinine and urea in kidney transplant recipients, one month post-vaccination



* Assays ongoing, data not shown. † Inflexal V® (Crucell).
Esposito S. *et al.* Unpublished data.

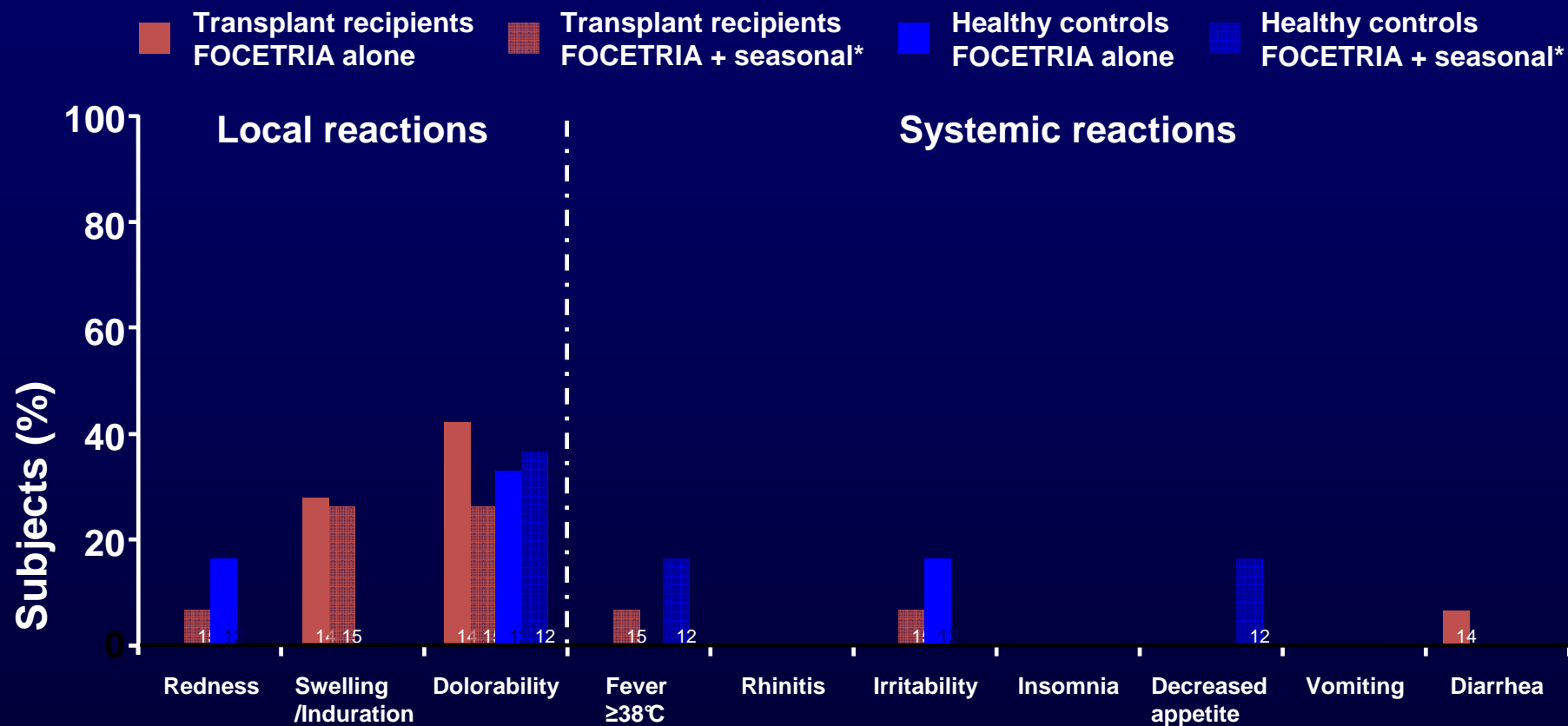
Local and systemic reactions following a single dose of FOCETRIA in children with HIV



FOCETRIA was well tolerated in children with HIV
No serious adverse events were observed for any group

* Inflexal V® (Crucell).
 Esposito S. *et al.* Unpublished data.

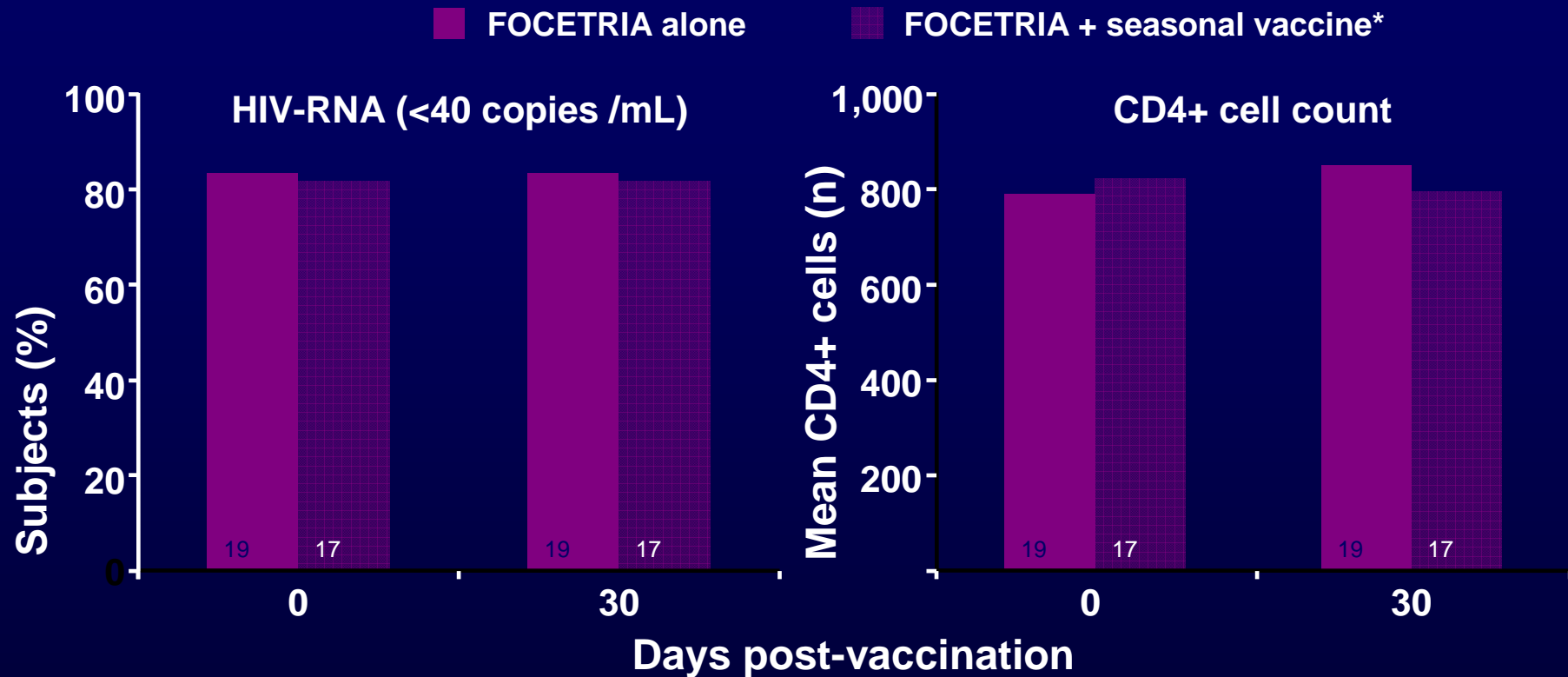
Local and systemic reactions following a single dose of FOCETRIA in children who received a kidney transplant



FOCETRIA was well tolerated in children who received a kidney transplant
No serious adverse events were observed for any group

* Inflexal V® (Crucell).
 Esposito S. *et al.* Unpublished data.

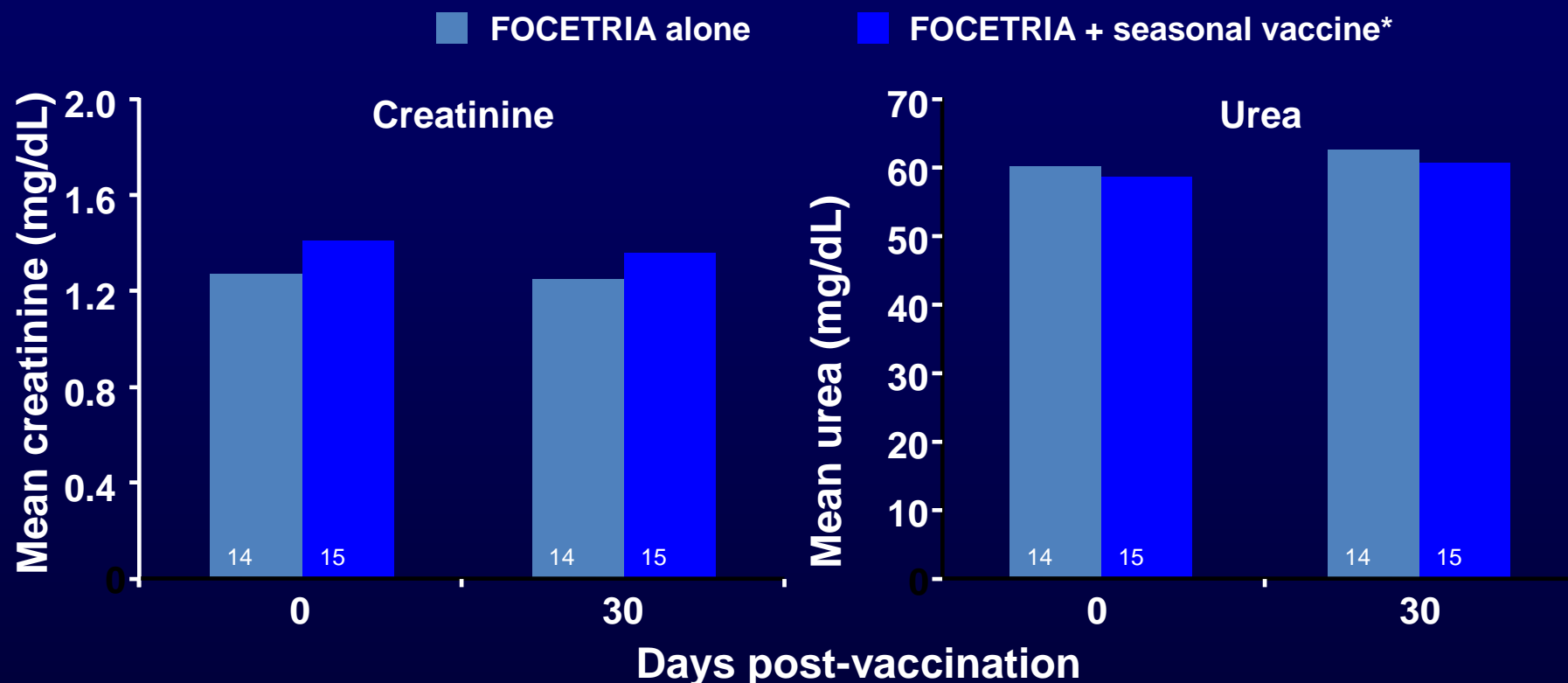
HIV biomarkers following vaccination with FOCETRIA in children with HIV



No significant differences were observed in HIV biomarkers between subjects receiving FOCETRIA and FOCETRIA + a seasonal vaccine

* Inflexal V® (Crucell).
Esposito S. *et al.* Unpublished data.

Kidney function following vaccination with FOCETRIA in children who received a kidney transplant



There were no significant differences in renal function between subjects receiving FOCETRIA and FOCETRIA + a seasonal vaccine

* Inflexal V® (Crucell).
Esposito S. *et al.* Unpublished data.

Summary of clinical trial data for MF59-adjuvanted pandemic vaccines in children

- **MF59-adjuvanted vaccines were immunogenic in children**
 - A single dose of FOCETRIA met all CHMP immunogenicity criteria in children 12–35 months of age irrespective of their baseline serological status
- **MF59-adjuvanted pandemic vaccines demonstrated a favorable tolerability profile**
 - Commonly occurring reactions following vaccination with CELTURA were transient in nature, lasting 1–2 days without treatment
 - FOCETRIA was well tolerated in children 6–35 months of age; most reactions were mild to moderate and transient in nature

MF59-adjuvanted pandemic vaccines met licensure criteria and demonstrated a favorable tolerability profile

Recommended viruses for influenza vaccines for use in the 2010-2011 northern hemisphere influenza season

**It is recommended that the following viruses be
used for influenza vaccines in the 2010-2011
influenza season (northern hemisphere):**

- an an A/California/7/2009 (H1N1)-like virus;**
- an an A/Perth/16/2009 (H3N2)-like virus;**
- a B/Brisbane/60/2008-like virus.**

COSA SUCCEDERA' IL PROSSIMO ANNO?

- Il virus influenzale A/H1N1 andrà incontro a mutazioni?
- Come si porranno le famiglie e gli operatori sanitari nei confronti dell'influenza e della sua prevenzione?
- Come avverrà la comunicazione con le famiglie?
- Come si articolerà la campagna vaccinale?