

Efficacité de la vaccination
antigrippale dans la population adulte
et pédiatrique

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Objectifs cliniques de la vaccination et populations cibles

- Objectifs de la vaccination
 - Mortalité, complications (pneumonie)
 - Morbidité simple
 - En fonction de l'âge
 - Populations particulières (asthmatiques, immunodéprimés)
 - Vaccination « altruiste »
- Epidémiologie variable de la grippe saisonnière
 - Variabilité antigénique et adéquation vaccin/virus sauvage
 - Expression clinique infection

Expression clinique de l'infection chez des sujets adultes immunocompétents susceptibles et infectés expérimentalement - revue

- Proportion d'infections symptomatiques **65% (95% CI 56%-73%)**

Influenza virus types and subtypes	Subgroups/participants/events	Pooled estimates (%)	95%CI
A/H1N1	11/228/158	70.8	50.4-85.2
A/H3N2	13/180/107	60.5	50.4-69.8
A/H2N2	2/44/31	72.4	54.8-83.2
B	6/40/25	57.4	35.2-76.9
All	32/492/321	64.8	55.5-73.1

- Proportion of fièvre ($\geq 100^{\circ}\text{F}$ or 37.8°C) **31% (95%CI 24%-40%)**
 - **37% (H1N1), 35% (H3N2), 7.5% (B)*** ($p < 0.001$)

Critères de jugements

- Cliniques
 - Syndrome grippal
 - Toux ou mal de gorge + fièvre ($>37.8^{\circ}\text{C}$)
 - Infection respiratoire aiguë
 - Définition très variable
 - La fièvre n'est pas un critère nécessaire
- Cliniques avec confirmation virologique
- Infection grippale
 - Séroconversion (multiplication x4 du titre HAI post/pre épidémique)

Quelques essais importants : efficacité sur la morbidité non compliquée – adultes

- Syndrome grippal: EV=25% (425 sujets par groupe, double aveugle)

Table 3. Health-Related Benefits Associated with Vaccination.*

STUDY OUTCOME	RATE PER 100 SUBJECTS		DIFFERENCE (95% CI)	VACCINE EFFECTIVENESS %	P VALUE
	PLACEBO GROUP	VACCINE GROUP			
Primary					
Episodes of upper respiratory illness	140	105	35 (17–53)	25	<0.001
Days of sick leave due to upper respiratory illness	122	70	52 (21–84)	43	0.001
Visits to physicians' offices for upper respiratory illness	55	31	24 (8–40)	44	0.004

Nichol KL et al. N Engl J Med 1995;333:889

Quelques essais importants : efficacité sur la morbidité non compliquée – adultes

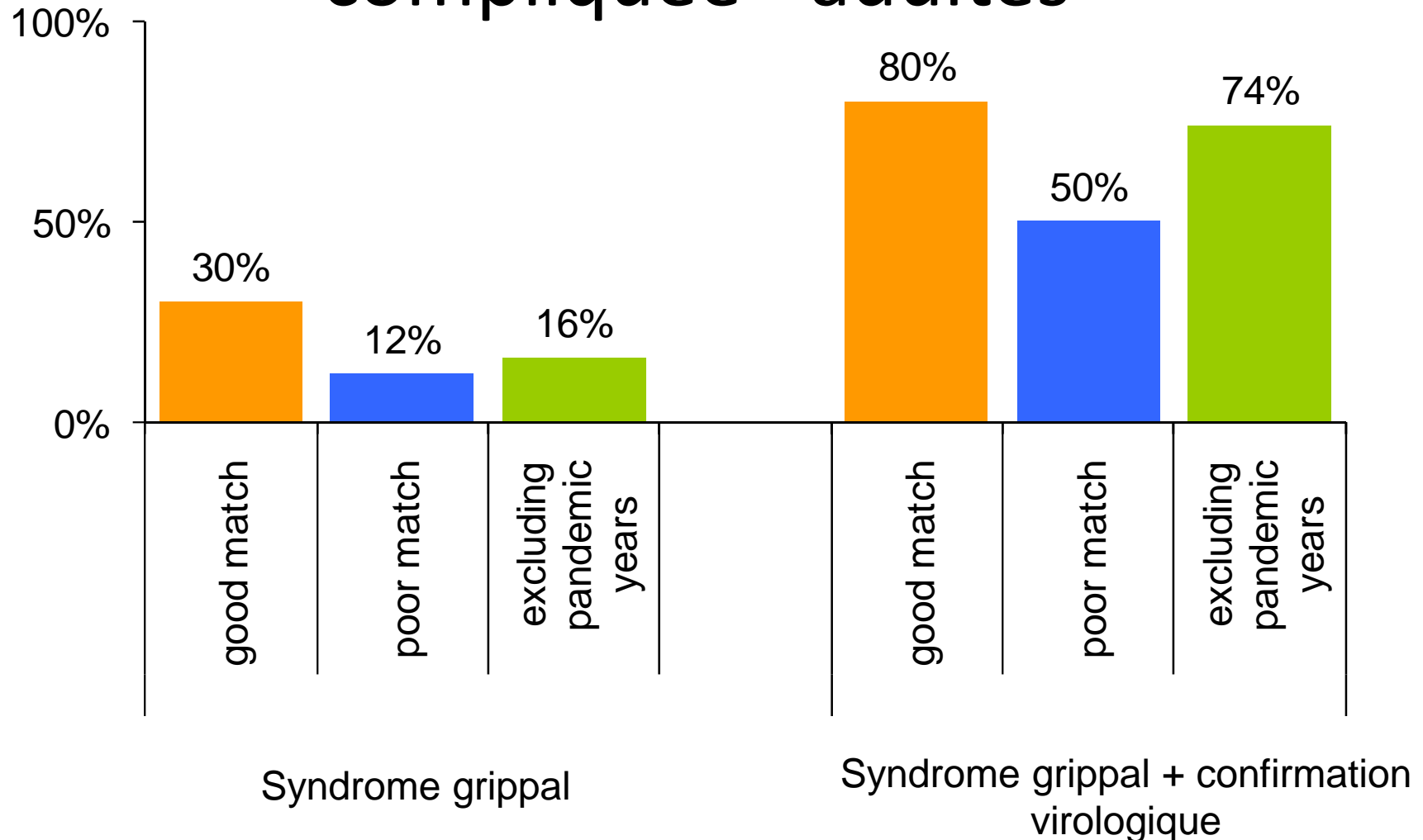
	1997-98			1998-99		
	Vaccinés N=576	Placebo N=554	P	Vaccinés N=582	Placebo N=596	
Syndrome grippal – n (%)	161 (28)	132 (24)	0.25	82 (14)	128 (22)	EV=34% NNV=14
Infection respiratoire aiguë – n (%)	259 (45)	232 (42)	0.57	137 (24)	156 (26)	0.32
Patients prélevés	138	137		141	137	EV=86% NNV=11
Syndrome grippal confirmé	3 (2)	6 (4)	0.33	2 (1)	14 (10)	0.001

↓
Mismatch antigénique: Variant épidémique « éloigné » de la souche vaccinale

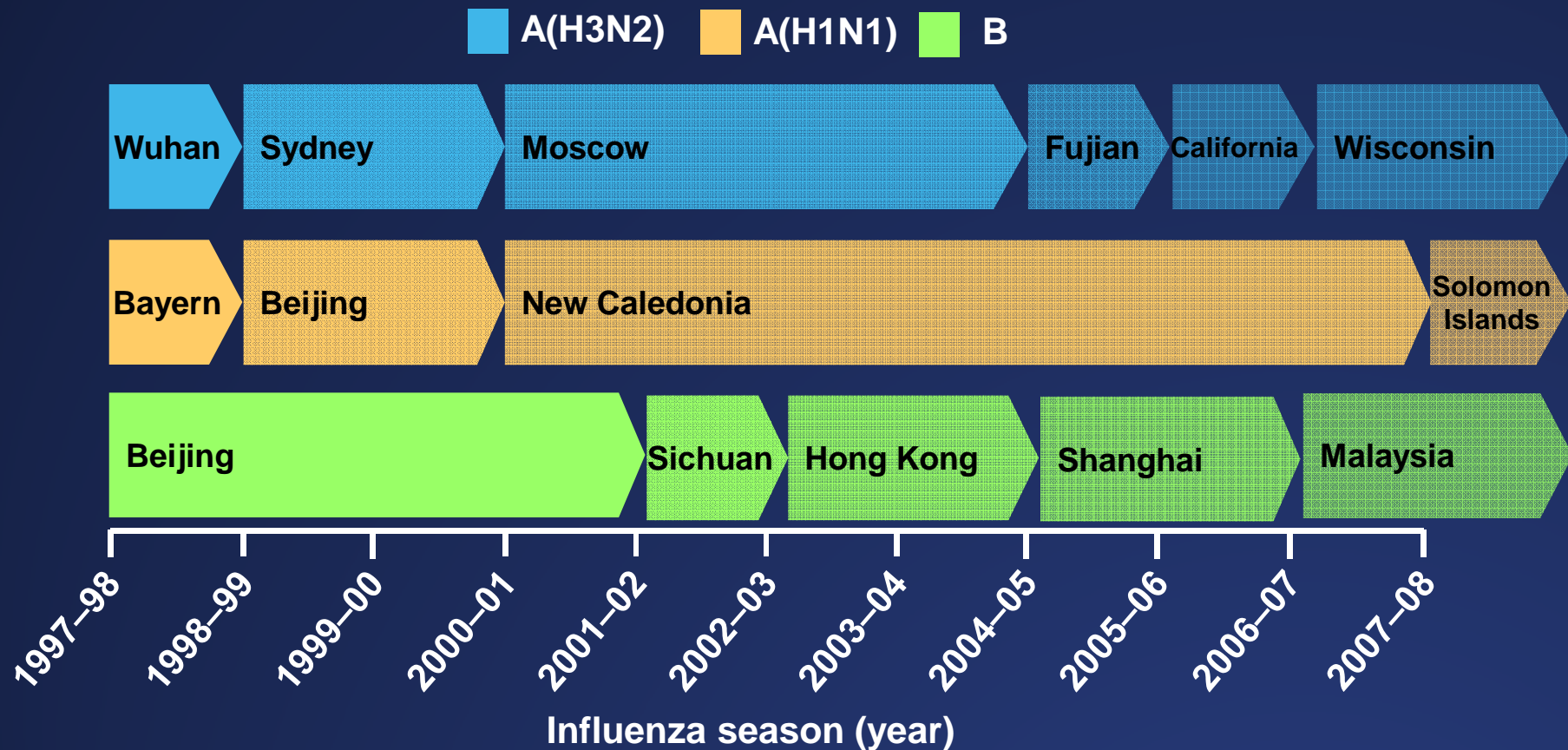
↓
Variant épidémique proche de la souche vaccinale

D'après Bridges CB et al. JAMA 2000;284:1655-63

Effacité sur la morbidité non compliquée - adultes



Antigenic drift



▶ Recommended strains have changed 12 times since 1997–1998 due to antigenic drift

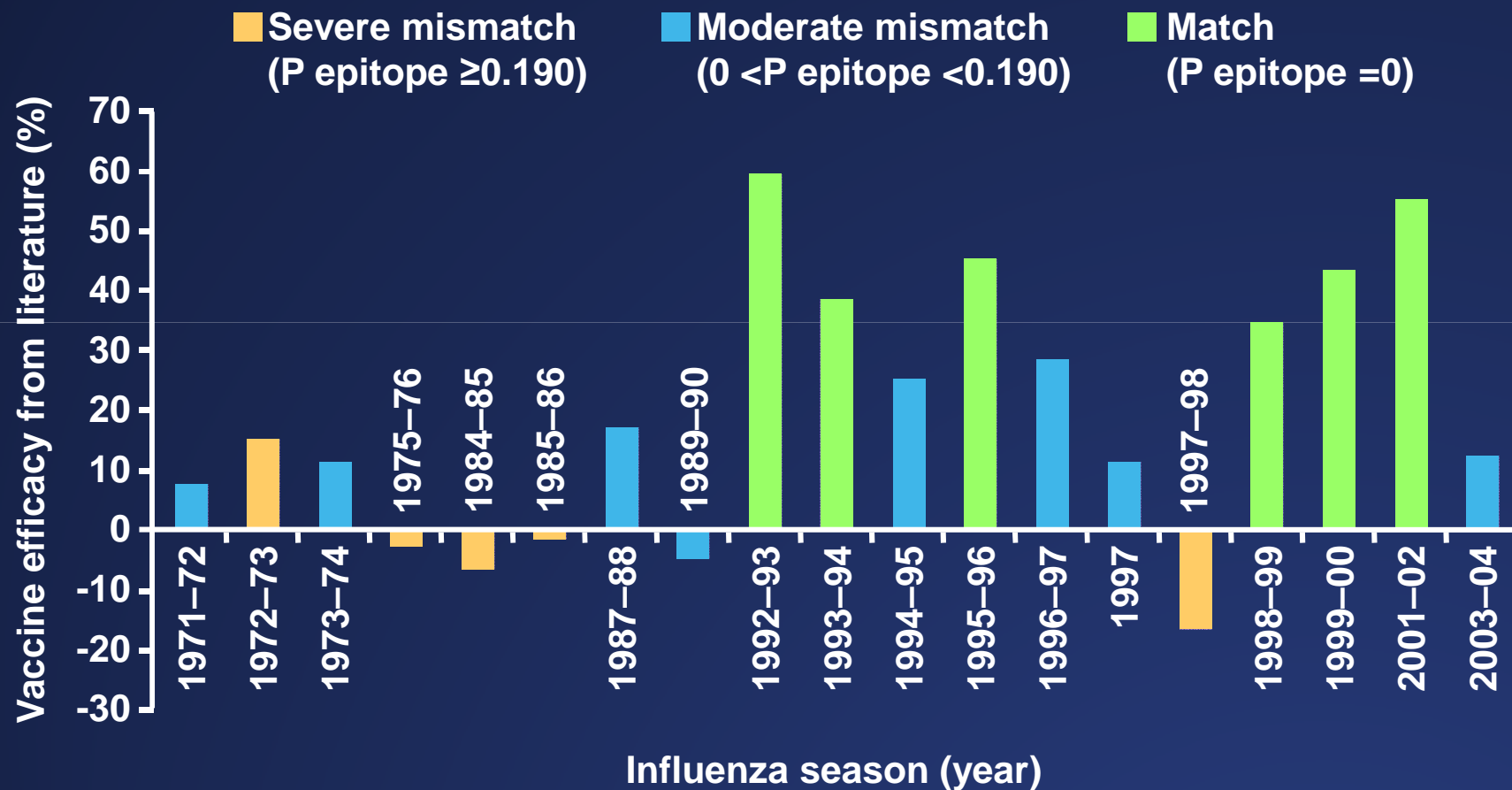
Antigenic distance and vaccine efficacy

- ▶ Antigenic/sequence distance between the vaccine strain and the circulating strain = the proportion of amino acid differences in the dominant epitope

P epitope:
$$\frac{\text{number of amino acid differences in the dominant epitope}}{\text{total number of amino acids in the dominant epitope}}$$

- ▶ Antigenic distance and vaccine efficacy are strongly correlated

Strong correlation between antigenic distance and vaccine efficacy



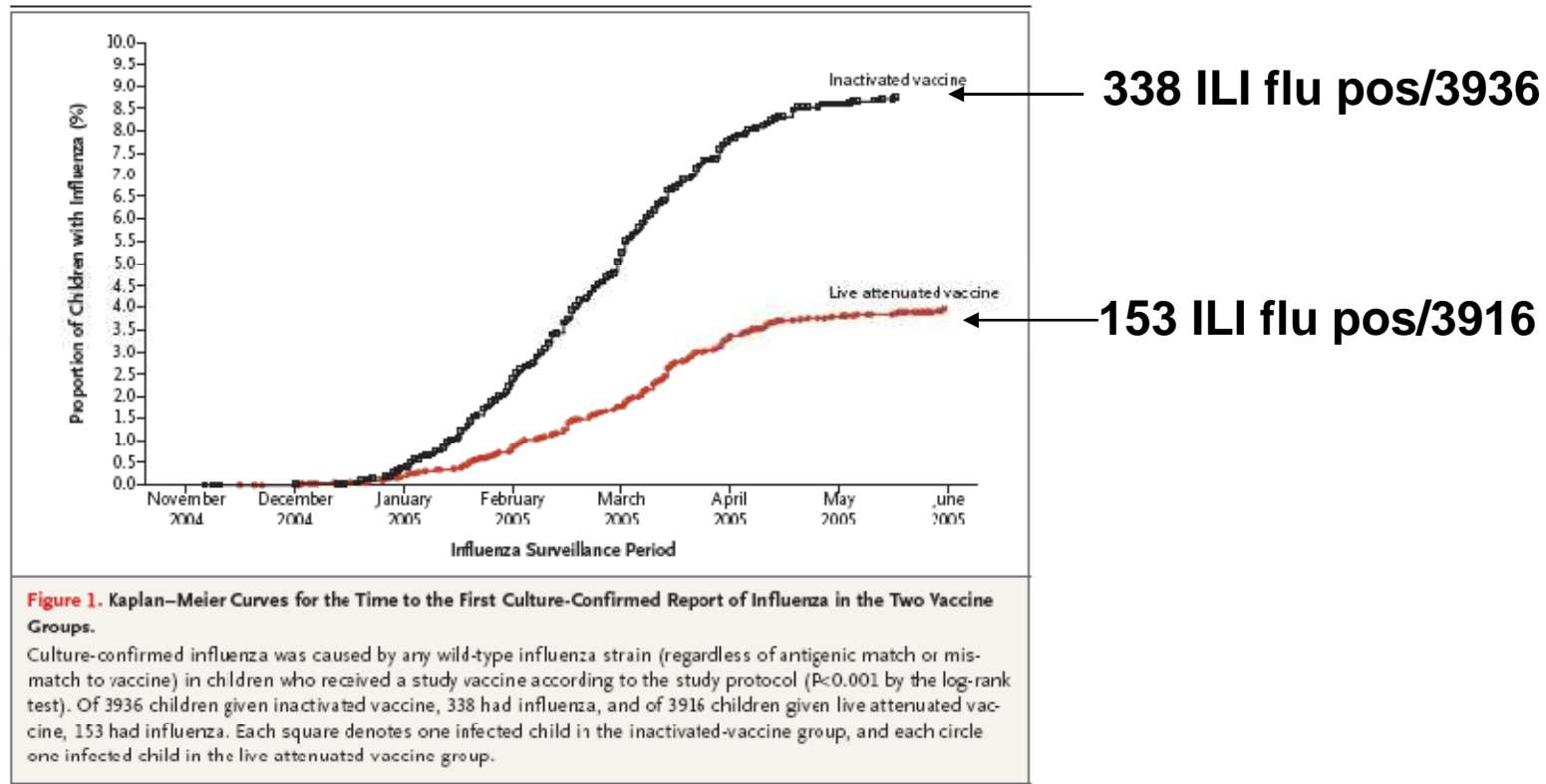
P epitope value defines the degree of antigenic drift

Gupta *et al.* Vaccine 2006

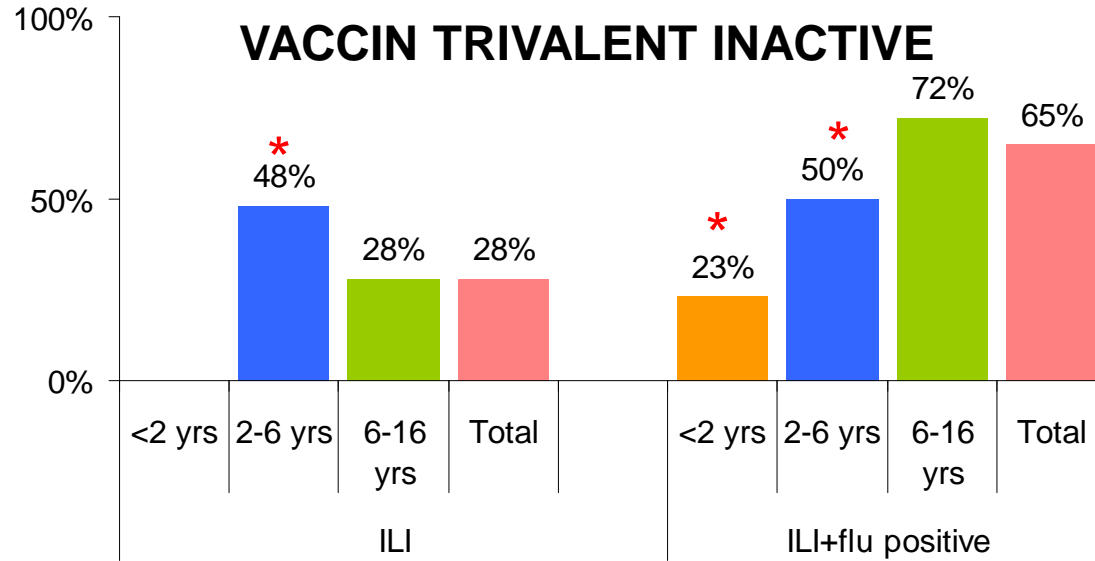
Efficacité sur la morbidité - enfants

- Deux vaccins différents évalués
 - Inactivé
 - Vivant atténué (non commercialisé en Europe)
- 14 essais thérapeutiques contrôlés

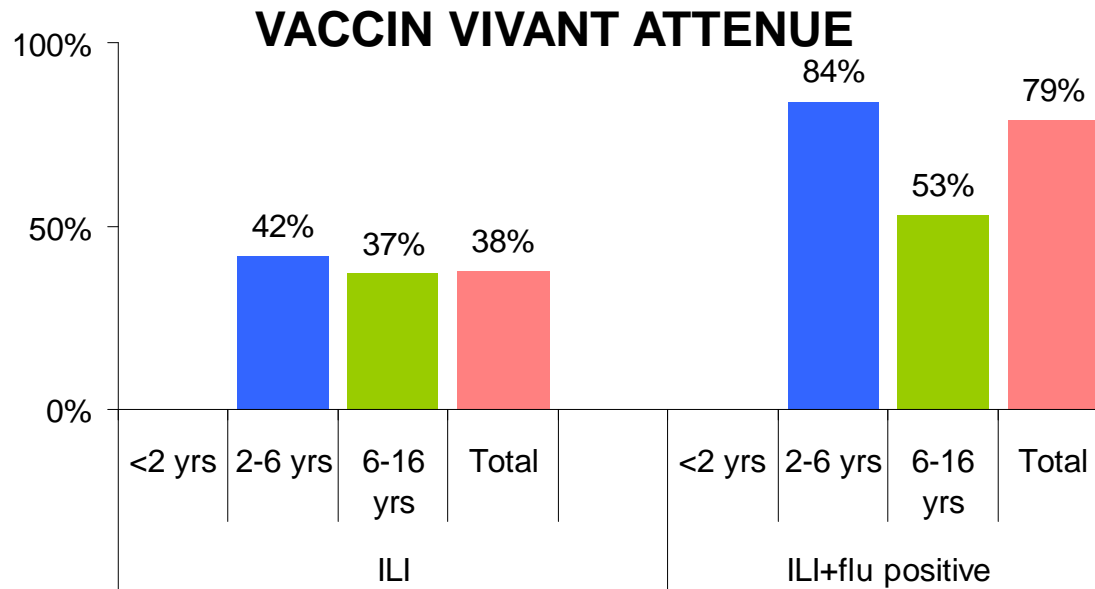
Enfants: efficacité supérieure du vaccin vivant atténuée (< 5 ans)



Effacité vaccinale chez l'enfant.

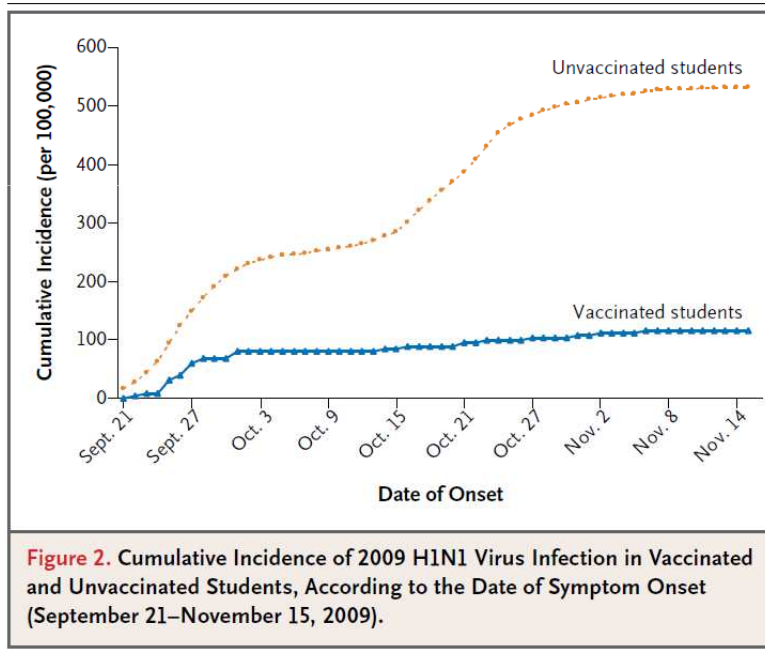


* Non significativement différent de zéro



Et H1N12009 ?

Données observationnelles suggèrent efficacité clinique du vaccin pandémique sur souche 2009



and adjusted PIVE.

Crude and Adjusted PIVE Estimates	Included Population	<i>n</i>	Percent PIVE	95% CI
Crude ^b	All	1,502	79.0	55.8–90.0
	<65 y	1,367	83.3	61.2–92.8
	15–64 y	912	76.6	44.7–90.1
	<15 y	455	100	58.2–100.0 ^c
Adjusted model ^d	No chronic disease	1,190	81.5	53.0–92.7
	All	1502	66.0	23.9–84.8
	<65 y	1,367	71.3	29.1–88.4
	15–64 y	912	65.5	12.3–86.5
	<15 y	455	100	Not calculable ^e
	No chronic disease	1,190	70.2	19.4–89.0

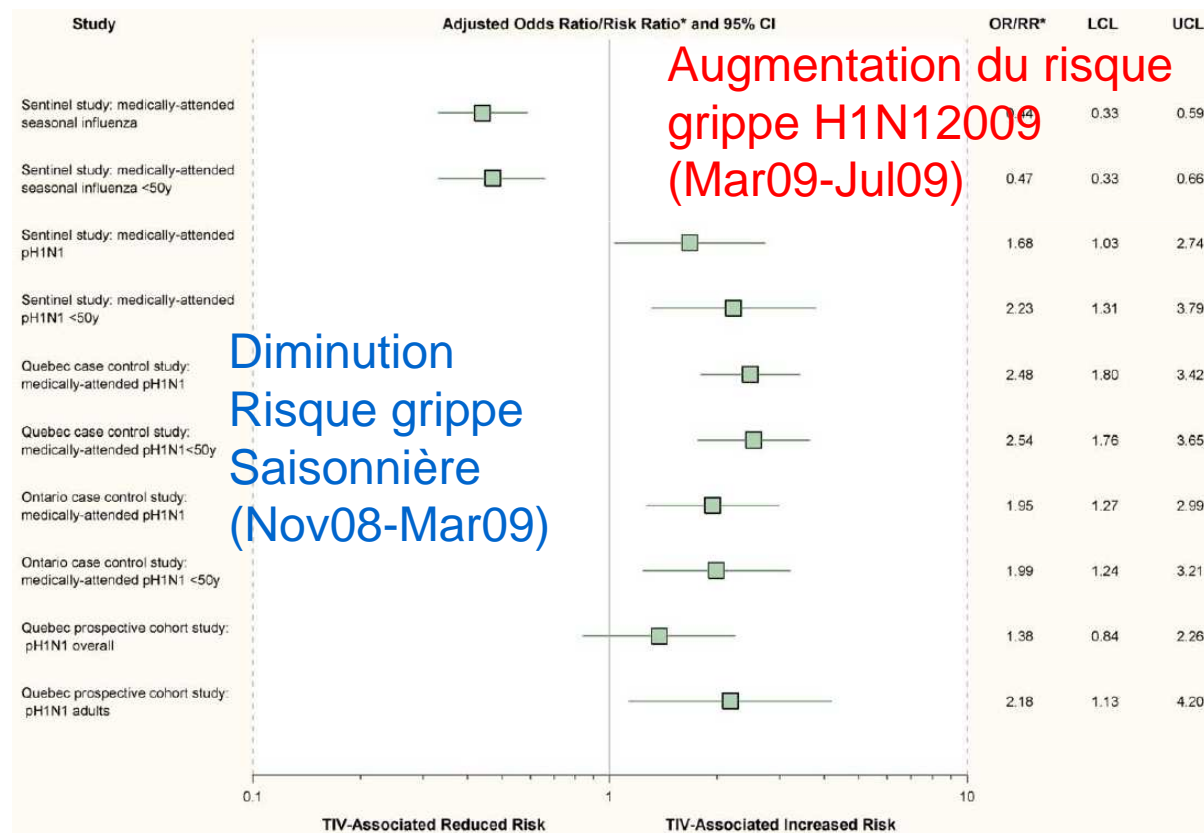
EV: 72% chez les moins de 65ans

Wu J et al. N Engl J Med
2010;363:2416-2423

Valenciano et al. PLoSMed;
8(1): e1000388.

Impact de la vaccination saisonnière sur H1N1 2009

- 4 études observationnelles (3 cas-témoin, 1 étude prospective) au Canada



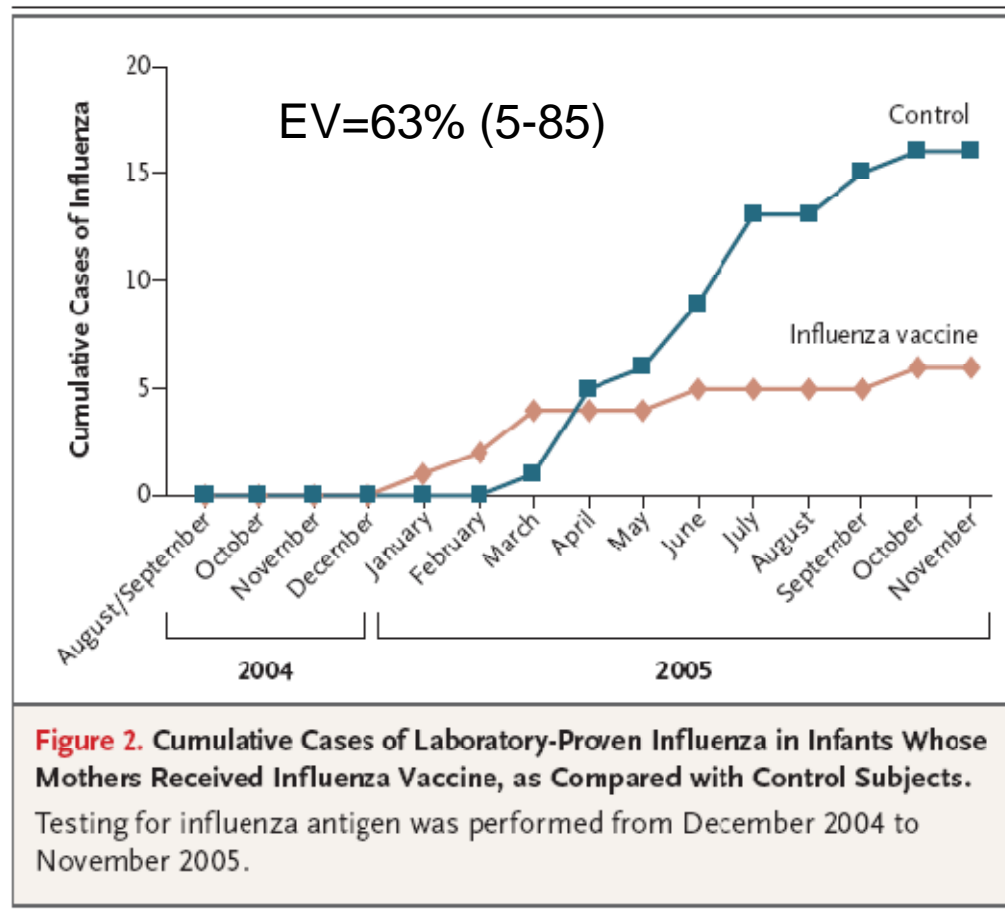
Un essai de vaccination saisonnière vs placebo

Variable	TIV group	Placebo group	P
Study subjects			
No. of study subjects	71	48	
Serologically confirmed infection ^a			
Seasonal A/H1N1	0.08 (0.02–0.15)	0.21 (0.09–0.32)	.10
Seasonal A/H3N2	0.07 (0.01–0.13)	0.12 (0.03–0.22)	.49
Pandemic A/H1N1	0.32 (0.22–0.43)	0.17 (0.06–0.27)	.09
Seasonal B	0.03 (0.00–0.07)	0.08 (0.01–0.16)	.36

Risk factor	Factors Associated with the Risk of Laboratory-Confirmed Pandemic Influenza in household members	No. of study subjects	Adjusted odds ratio ^a (95% confidence interval)
Age <16 years		192	6.60 (2.17–20.13)
Age 16–45 years		163	2.53 (0.80–7.99)
Age >45 years		76	1.00
Female sex		229	1.00
Male sex		202	0.97 (0.55–1.70)
No laboratory-confirmed seasonal influenza A infection		277	1.00
Laboratory-confirmed seasonal influenza A infection		93	0.35 (0.14–0.87)
Did not receive seasonal influenza vaccine		271	1.00
Received seasonal influenza vaccine prior to 2008–2009 season		106	1.11 (0.54–2.26)
Completed study before 1 October 2009		221	1.00
Completed study between 1 October and 20 October 2009		156	2.77 (1.53–4.99)

^a Adjusted for age, sex, laboratory-confirmed seasonal influenza A infection, receipt of TIV, and date of study completion.

Femmes enceintes et ... enfants



- 340 femmes randomisées vaccin inactivé vs vaccin pneumocoque (3^{ème} Trimestre)
- 316 enfants suivis 1,5 ans
- EV sur Infections respiratoires aiguës fébriles enfants : 29%(7-46)
- EV sur Infections respiratoires fébriles chez mère : 36% (4-57)

Femmes enceintes et ... enfants

- Enquête cas témoin : les cas sont des enfants hospitalisés et confirmés virologiquement; les témoins sont des enfants hospitalisés mais négatifs

Table 4. Effectiveness of Influenza Vaccine Given to Mothers During Pregnancy in Preventing Hospitalization for Influenza among Their Infants

Measure	Subjects aged <6 months	Subjects aged ≥6 months
No. (%) of case infants; no. (%) of control infants		
Mother was vaccinated	2 (2.2); 31 (19.9)	1 (4.6); 2 (5.6)
Mother was not vaccinated	89 (97.8); 125 (80.1)	21 (95.5); 34 (94.4)
Vaccine effectiveness (95% CI), %		
Unadjusted	90.7 (59.9–97.8) ^a	–41.4 (–2257.3 to 91.5) ^b
Adjusted ^c	91.5 (61.7–98.1) ^a	...

NOTE. CI, confidence interval.

^a $P = .001$.

^b $P = .809$.

^c The adjusted model for subjects aged <6 months retained vaccination of household contacts and prematurity.

Conclusion: questions en suspens

- Questions cliniques sans réponse
 - Interactions virales/vaccins et efficacité clinique à long terme d'une vaccination répétée
 - Efficacité clinique des vaccins adjuvantés vs non adjuvantés ? Protection croisée ?
- Vers la recherche d'un vaccin « universel » ?

Vaccination with a synthetic peptide from the influenza virus hemagglutinin provides protection against distinct viral subtypes

EDITORIAL COMMENTARY

Taia T. Wang^{a,1}, Gene S. Tan^{a,1}, Rong Hai^a, Natalie Pica^a, Lily Ngai^a, Damian C. Adolfo García-Sastre^{a,d,e}, Thomas M. Moran^{a,f}, and Peter Palese^{a,d,2}

[PNAS 2010;107:18979](#)

Prospecting the Influenza Hemagglutinin to Develop Universal Vaccines

[CID 2011; 52:1010](#)

Ruben O. Donis and Nancy J. Cox

Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia

Induction of unnatural immunity: prospects for a broadly protective universal influenza vaccine

Gary J Nabel & Anthony S Fauci

[Nature Med 2010; 16:1389](#)

