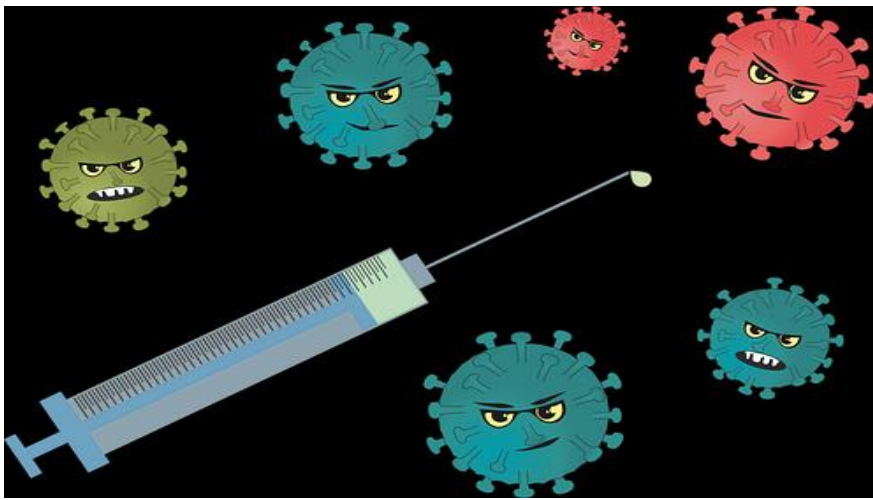




Indications des vaccins chez le patient diabétique

Nathalie Viget
JEDI
14/11/2019



Chez le diabétique

- **2 vaccins spécifiques**
 - Grippe
 - Pneumocoque
- **+ le calendrier vaccinal en vigueur**
- **Aucune contre-indication liée au terrain diabétique**



Modification des réponses vaccinales?

Réponses vaccinales ?

- Enfants : étude 36 enfants, âge moyen 10 ans , appariés DM1 vs contrôles:
 - pas de différence réponse tétanos, diphtérie, *haemophilus influenzae*, pneumocoque conjugué (Ag T-dépendants)
 - Moins bonne réponse après rappel par vaccin pneumocoque non conjugué
- Adultes : étude 20 DM1 vs DM2 vs contrôles
 - DM1: moins bonne réponse vaccin hépatite A, typhoïde (Ag T-dépendants) et réponse identique vaccin pneumocoque non conjugué
 - DM2: pas de différence

Eisenhut, clinical Vaccine Immunology 2016
Eibl, Clinical Immunol 2002

Réponses vaccinales ?

- grippe : étude 105 DM2 vs controles
 - pas de différence immunogénicité
 - Age facteur négatif réponse
 - pas influence durée diabète, insuline, HBA1C
 - Moins effets secondaires

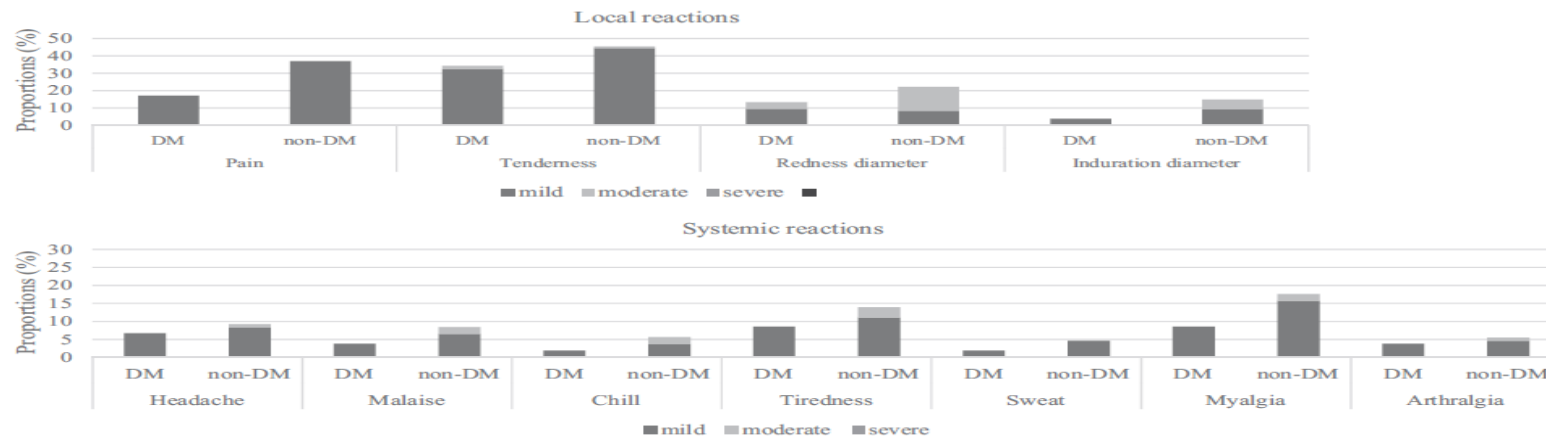


FIG 2 Solicited local and systemic adverse reactions within 7 days after vaccination. All local reactions were statistically different between the diabetes mellitus (DM) group and non-DM group. All systemic reactions were statistically similar between the DM group and non-DM group.



Modification des réponses vaccinales?

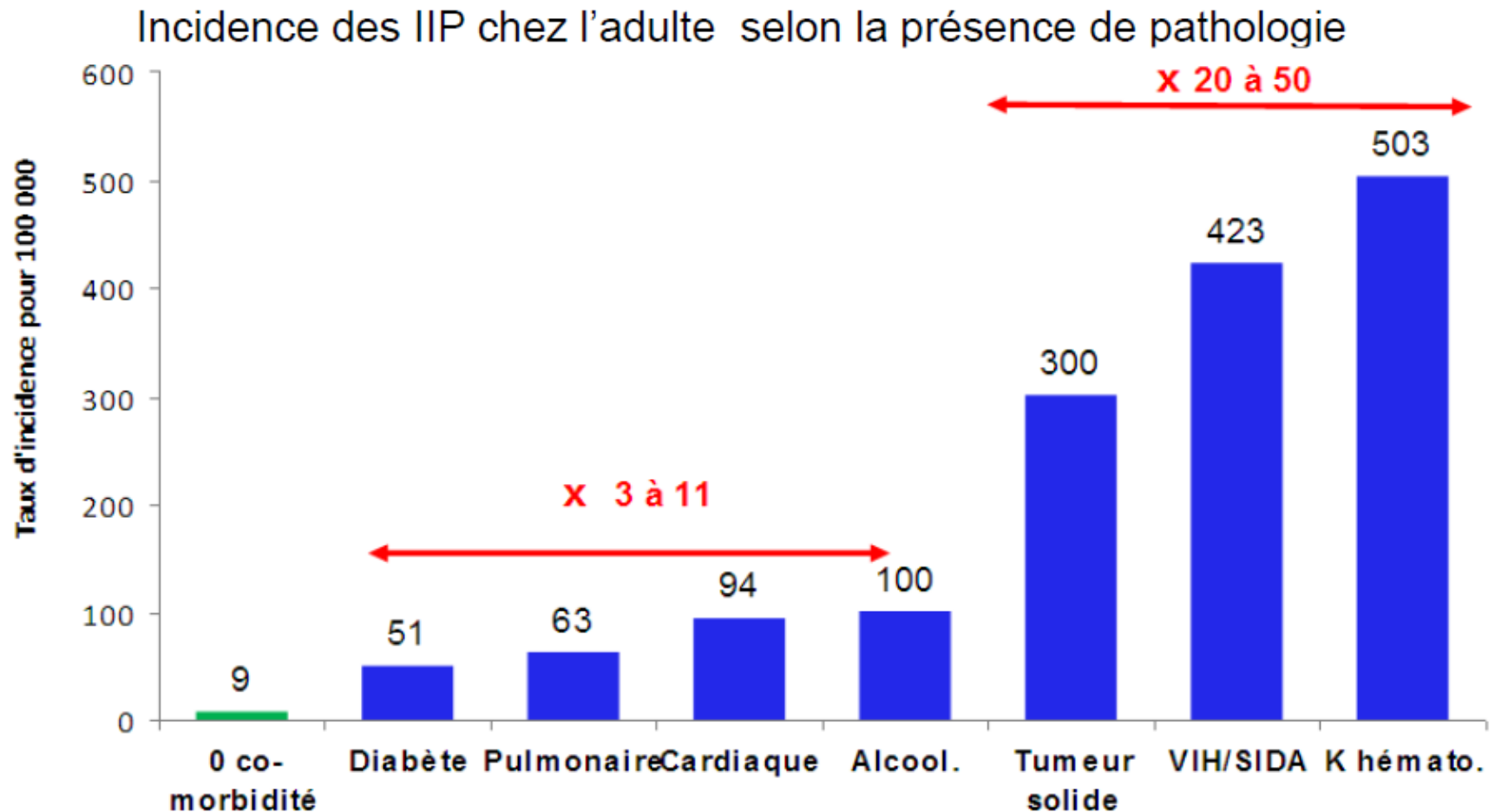
Pas de schéma spécifique
des vaccins pour les diabétiques



Sur-risque grippe et
pneumocoque?

Incidence des IIP et co-morbidités

↑ des IIP en cas de co-morbidités immunodépression (VIH, cancer), pathologies chroniques rénales, cardiaques, pulmonaires, diabète et alcoolisme, tabagisme



Impact of Diabetes Mellitus on Mortality Associated With Pneumonia and Influenza Among Non-Hispanic Black and White US Adults

American Journal of Public Health

November 1999, Vol. 89, No. 11

Valdez et al.

TABLE 2—Race-, Sex-, and Age-Specific Estimations of Relative Risk (RR) and Attributable Fractions for Deaths Associated With Pneumonia and Influenza Among People With Diabetes vs People Without Diabetes: National Health Interview Survey (NHIS; 1987–1989) and National Mortality Followback Survey (NMFS; 1986)

	Weighted Size of Living Population (NHIS)		Weighted No. of Deaths Associated With Pneumonia and Influenza (NMFS)		RR (People With vs People Without Diabetes) (95% Confidence Interval)	Attributable Fraction in the Exposed, % (95% Confidence Interval) ^a	Attributable Fraction in Population, % (95% Confidence Interval) ^b
	With Diabetes	Without Diabetes	With Diabetes	Without Diabetes			
White men, age, y							
25–64	1 227 512	46 591 715	1 340	10 676	4.8 (2.3, 10.0)	79.0 (56.5, 90.0)	9.0 (3.3, 19.2)
≥65	868 592	9 475 653	9 512	53 654	1.9 (1.4, 2.7)	48.3 (28.6, 63.0)	7.9 (3.6, 13.5)
Black men, age, y							
25–64	308 433	5 669 065	728	3 302	4.0 (2.1, 7.8)	75.3 (52.4, 87.2)	14.3 (5.7, 27.0)
≥65	131 761	834 217	963	5 421	1.1 (0.6, 2.2)	... ^c	... ^c
White women, age, y							
25–64	1 199 699	48 315 946	1 080	4 670	9.3 (3.9, 22.4)	89.3 (74.4, 95.5)	17.1 (6.7, 34.7)
≥65	1 206 988	13 445 800	13 436	55 484	2.7 (2.0, 3.6)	62.9 (50.0, 72.2)	13.3 (8.3, 19.0)
Black women, age, y							
25–64	352 487	6 951 811	567	1 140	9.8 (4.6, 20.7)	89.8 (78.3, 95.2)	30.9 (15.5, 50.0)
≥65	276 490	1 133 478	890	3 872	0.9 (0.5, 2.0)	... ^c	... ^c

^a(RR – 1)/RR.

^bPrevalence of diabetes(RR – 1)/[1 + Prevalence of diabetes(RR – 1)].

^cRR statistically indistinguishable from 1.



Couvertures vaccinales?

Couvertures vaccinales

- Jamais très bonnes!
 - Grippe: entre 26 et 64%
 - Pneumocoque: entre 2,8% et 22% (sauf 52% USA)
 - Hépatite B: 17% (USA et Espagne)
 - Zona: 27% (USA)
- Facteurs influençant la non-vaccination
 - Manque d'information par le médecin!
 - Age, niveau d'éducation, insulinothérapie, peur des effets secondaires...

*Moreno-Fernandez, prim Care diab 2019 (online)
Almusalam, J Fam Med prim Care 2019
Almotairy, J Fam Med prim Care 2019
Gorska-ciebiada, Post High Med Dosw 2015
Satman, Hum Vacc Imm 2013
Villaroel, NCHS data brief 2016*

données françaises: “trajectoire” patients diabétiques/vaccin grippe

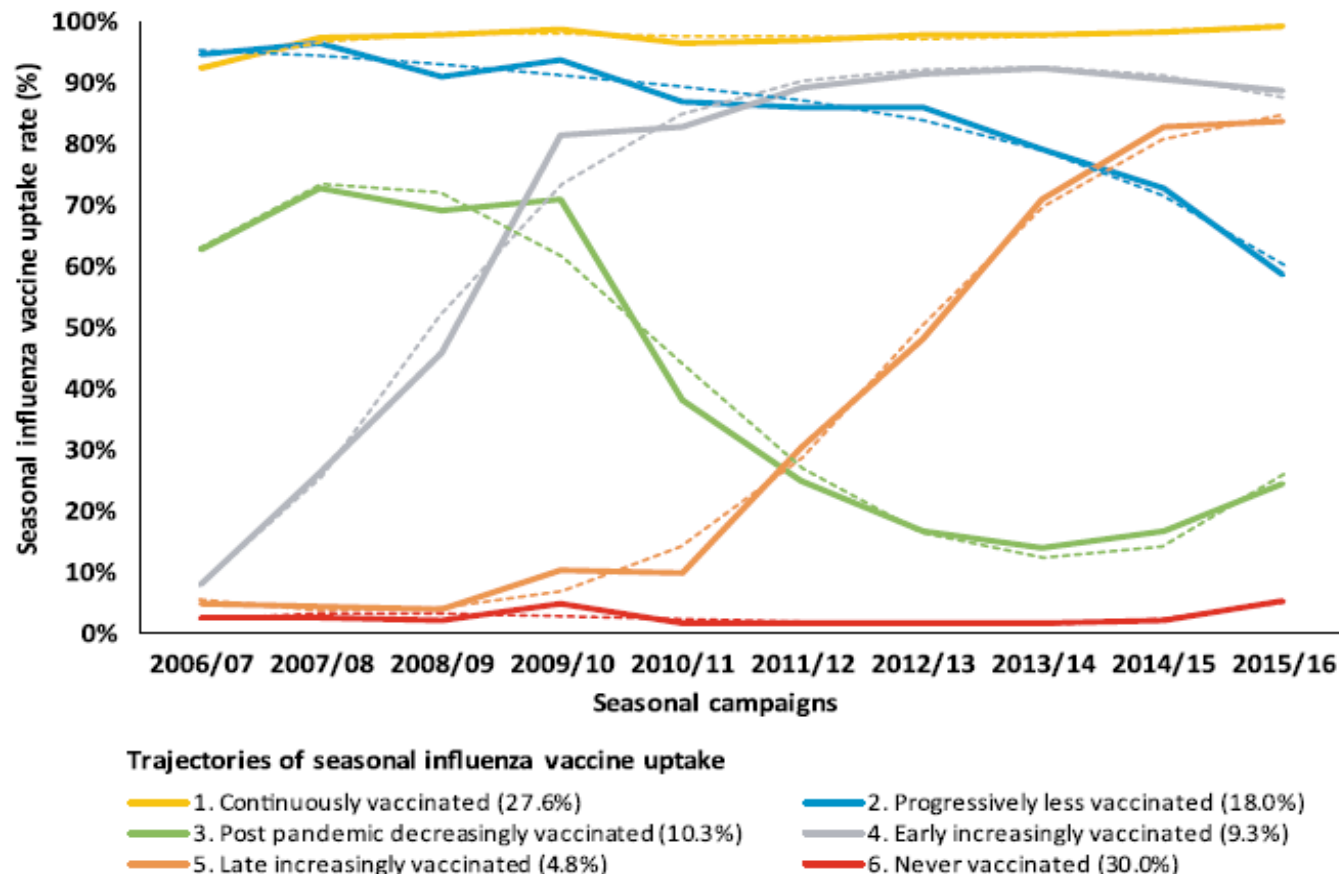


Fig. 1 Observed (solid lines) and predicted (dashed lines) probability of seasonal influenza vaccine uptake among people with diabetes during each season of follow-up for each of six classes identified by the group-based trajectory model^a (EGB, France, 2006/07–2015/16, $n = 15,766^b$).

^a Third-degree polynomials were used for the specifications of all trajectories, except for the “Early increasingly vaccinated” trajectory, for which a second-degree polynomial was used. ^b Among individuals with at least two full years of follow-up ($n = 15,766$, 90.2%), to enable calculation of two variables included in the model (i.e., diabetes treatment intensification and course of weighted individual chronic condition score during follow-up)

“trajectoire” patients diabétiques/vaccin grippe

Table 2 Risk factors for membership in SIV-uptake trajectories – group-based trajectory model, multinomial logistic regression^a (EGB, France, 2006/07–2015/16, *n* = 15,766^b)

	Trajectory (ref. 1. Continuously vaccinated - n = 4344 (27.6%))				
	2. Progressively less vaccinated n = 2832 18.0%	3. Post pandemic decreasingly vaccinated n = 1627 10.3%	4. Early increasingly vaccinated n = 1472 9.3%	5. Late increasingly vaccinated n = 763 4.8%	6. Never vaccinated n = 4728 30.0%
Adjusted risk ratio [95% confidence interval]					
Sociodemographic characteristics					
Age at inclusion > 65	2.89 [2.47;3.33]	0.68 [0.60;0.78]	0.33 [0.28;0.38]	0.14 [0.11;0.18]	0.56 [0.52;0.61]
Women	0.82 [0.75;0.91]	1.38 [1.26;1.51]	0.99 [0.88;1.10]	0.98 [0.83;1.14]	1.09 [1.05;1.14]
Clinical characteristics					
Type and treatment of diabetes at inclusion					
Type 1 ^c	0.99 [0.83;1.16]	1.11 [0.95;1.30]	0.76 [0.59;0.97]	0.53 [0.37;0.76]	0.85 [0.76;0.94]
Other types -- no antidiabetic drug	1.18 [1.01;1.36]	1.61 [1.39;1.85]	3.04 [2.77;3.29]	2.10 [1.69;2.56]	1.62 [1.54;1.68]
Diabetes treatment intensification ^d during follow-up	0.76 [0.68;0.84]	1.04 [0.94;1.15]	1.23 [1.09;1.39]	1.25 [1.06;1.47]	0.96 [0.91;1.01]
Weighted individual chronic condition score ^e at inclusion ≥ median	1.16 [1.04;1.28]	0.87 [0.78;0.97]	0.77 [0.68;0.87]	0.81 [0.68;0.96]	0.75 [0.71;0.80]
Course of weighted individual chronic condition score ^e during follow-up					
Stable	1.33 [1.06;1.60]	0.81 [0.55;1.13]	0.68 [0.40;1.11]	0.83 [0.40;1.62]	1.45 [1.33;1.57]
Increasing	0.99 [0.90;1.08]	0.73 [0.66;0.81]	1.19 [1.05;1.34]	1.21 [1.02;1.43]	0.89 [0.83;0.94]
Hospitalized during follow-up					
For diabetes and its complications	1.05 [0.94;1.16]	1.23 [1.11;1.37]	1.01 [0.88;1.15]	1.02 [0.85;1.22]	1.05 [1.00;1.11]
For influenza and its complications	1.32 [1.16;1.48]	1.44 [1.22;1.67]	1.46 [1.20;1.75]	1.30 [0.91;1.81]	0.98 [0.87;1.09]
Healthcare utilization					
Frequent consultations during follow-up, with:					
General practitioner	1.92 [1.76;2.07]	1.02 [0.91;1.14]	0.95 [0.83;1.07]	0.80 [0.66;0.96]	0.85 [0.80;0.90]
Endocrinologist	0.77 [0.65;0.91]	0.70 [0.59;0.83]	0.82 [0.69;0.97]	0.64 [0.49;0.83]	0.84 [0.78;0.91]
Cardiologist	1.00 [0.90;1.11]	0.79 [0.69;0.92]	0.87 [0.74;1.01]	0.71 [0.55;0.91]	0.79 [0.73;0.86]
Change of general practitioner during follow-up	0.73 [0.66;0.81]	0.98 [0.89;1.08]	0.94 [0.84;1.05]	1.13 [0.97;1.31]	0.93 [0.88;0.97]



vaccination grippe

Vaccin grippe

- Indications calendrier vaccinal: diabètes de type 1 et 2
- 2 vaccins tétravalents: Influvactetra°, Vaxigriptetra°

A/Brisbane/02/2018 (H1N1)pdm09, actuellement prédominante à l'échelle mondiale ;

A/Kansas/14/2017 (H3N2) ;

B/Colorado/06/2017 (lignée Victoria/2/87) ;

B/Phuket/3073/2013 (lignée Yamagata/16/88)..

- Vaccination par le pharmacien, la sage-femme ou l'infirmier possible pour l'adulte dès la première fois.
- Bon ALD vierge téléchargeable ville/hopital



Vaccin grippe

Vaccins tétravalents ~~Fluarix~~ Tetra® et Vaxigrip Tetra®

Âge	Dose	Nombre de doses
De 6 mois à 35 mois	0,5 mL**	1 ou 2*
De 3 ans à 8 ans	0,5 mL	1 ou 2*
À partir de 9 ans	0,5 mL	1

*2 doses à un mois d'intervalle en primovaccination, 1 dose en rappel annuel.

**La vaccination avec les vaccins grippaux tétravalents est effectuée avec une dose entière dès l'âge de 6 mois

Vaccin tétravalent : Influvac Tetra®

Ce vaccin dispose d'une AMM à partir de l'âge de 3 ans

Âge	Dose	Nombre de doses
A partir de 3 ans	0,5 mL**	1 ou 2*
A partir de 9 ans	0,5 mL	1

*2 doses à un mois d'intervalle en primovaccination, 1 dose en rappel annuel.

**La vaccination avec les vaccins grippaux tétravalents est effectuée avec une dose entière dès l'âge de 6 mois

Efficacité ?

Table 2 Pooled crude and adjusted odd ratios of influenza vaccine effectiveness (per outcome) during influenza-season and off-season in vaccinated vs. unvaccinated diabetic patients

Age-group (years)	Outcome/Design	No of studies included	Crude OR (95% CI)	I ²	No of studies included	Adjusted OR (95% CI)	I ²	No of studies included	Off-season adjusted OR (95% CI)	I ²
0–17	No studies	0	–	–	0	–	–	0	–	–
18–64	All-cause mortality									
	Case-control studies	1	0.46 (0.11–1.89)	NA ¹	1	0.76 (0.07–8.06)	NA ¹	0	–	NA ¹
	All-cause hospitalization									
	Case-control studies	2	0.32 (0.19–0.54)	0%	3	0.42 (0.19–0.94)	77%	1	0.73 (0.65–0.83)	NA ¹
	Influenza/pneumonia hospitalization									
	Case-control studies	0	–	–	1	0.57 (0.46–0.72)	NA ¹	1	0.88 (0.68–1.14)	NA ¹
	Influenza-like illness									
	Cohort studies	1	0.76 (0.50–1.15)	NA ¹	0	–	–	0	–	–
	Case-control studies	0	–	–	1	0.99 (0.97–1.01)	NA ¹	1	1.00 (0.90–1.12)	NA ¹
≥65	All-cause mortality									
	Cohort studies	3	0.54 (0.37–0.79)	90%	2	0.62 (0.57–0.68)	0%	1	0.70 (0.37–1.31)	NA ¹
	Case-control studies	2	0.39 (0.35–0.43)	0%	2	0.44 (0.36–0.53)	0%	0	–	–
	All-cause hospitalization									
	Cohort studies	1	0.83 (0.72–0.95)	NA ¹	0	–	–	1	0.91 (0.71–1.17)	NA ¹
	Case-control studies	2	0.89 (0.81–0.98)	0%	3	0.77 (0.60–0.99)	94%	1	0.66 (0.59–0.74)	NA ¹
	Influenza/pneumonia hospitalization									
	Case-control studies	1	0.20 (0.07–0.61)	NA ¹	1	0.55 (0.47–0.66)	NA ¹	1	0.48 (0.32–0.70)	NA ¹
	Influenza-like illness									
	Case-control studies	0	–	–	1	0.87 (0.84–0.90)	NA ¹	1	0.82 (0.70–0.96)	NA ¹
Not reported	Influenza/pneumonia hospitalization									
	Cohort studies	1	1.75 (0.10–32.68)	NA ¹	0	–	–	0	–	–
	Influenza-like illness									
	Cohort studies	1	0.34 (0.02–5.85)	NA ¹	0	–	–	0	–	–

OR, Odds ratio; 95% CI, 95% Confidence interval; ¹Only one study.

Efficacité ?

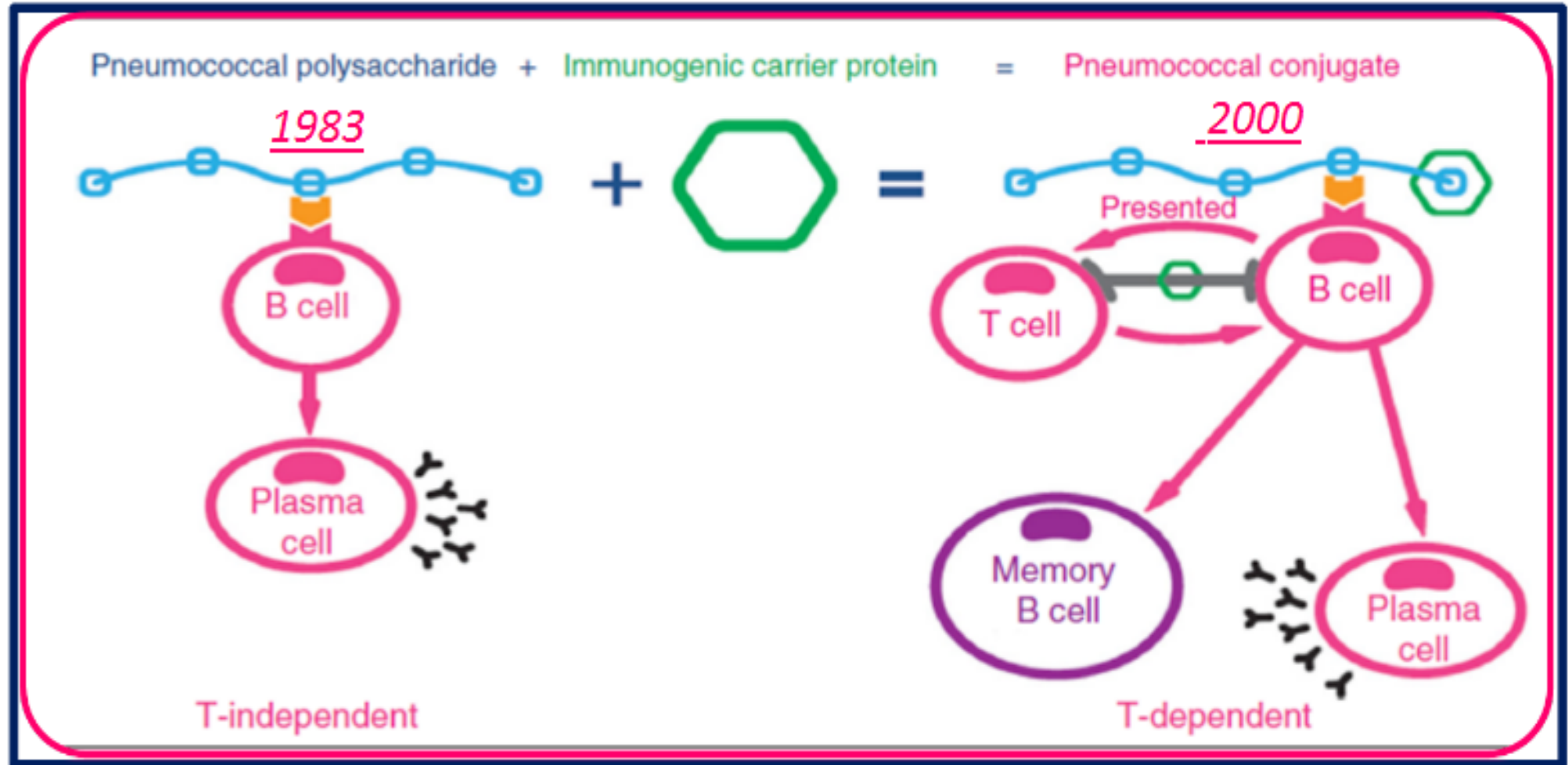
Table 4 – Influenza vaccine's effectiveness measured in terms of risk reduction (%) for each studied outcome.

Outcomes	Authors	18–65 years		>65 years	
		Adjusted risk reduction [IC95%]	p	Adjusted risk reduction [IC95%]	p
All-cause mortality	Heymann			67.9% [58.3–75.3]	Missing
	Looijmans	26% [(–760)–93]	0.819	44% [20–96]	0.039
	Rodriguez			33% [4–53]	0.031
	Wang			56% [46–64]	<0.01
Total hospitalizations	Lau	28% [24–32]	<0.001	33% [30–36]	<0.001
	Wang			12% [4–19]	<0.01
	Heymann			13% [3–23]	Missing
Hospitalization for pneumonia/influenza	Wang			14% [3–23]	<0.05
	Lau	43% [28–54]	<0.001	45% [34–53]	<0.001
Hospitalization for pneumonia, acute respiratory disease, prednisolone-treated chronic bronchitis, emphysema, asthma, myocardial infarction, congestive heart failure, stroke or diabetes dysregulation or death	Looijmans	72% [46–85]	<0.001	39% [(–5)–65]	0.076
Hospitalization for pneumonia/influenza or all-cause death in 96–97	Hak			50% [37–60]	<0.001
Hospitalization for pneumonia/influenza or all-cause death in 97–98	Hak			21% [6–34]	0.009
Hospitalization for pneumonia, acute respiratory disease, prednisolone-treated chronic bronchitis, emphysema, asthma, myocardial infarction, congestive heart failure, stroke or diabetes dysregulation	Looijmans	70% [39–85]	0.001	14% [(–88)–60]	0.706
Hospitalization for primary viral and bacterial and acute and chronic bronchitis, ketocidosis or diabetic coma	Colquhoun			79% [19–95]	Missing
Hospitalization for respiratory failure	Wang			33% [14–48]	<0.01
Hospitalization in an intensive care unit	Wang			70% [53–81]	<0.01
Hospitalization for influenza-like illnesses	Lau	1% [(–1)–3]	0.402	13% [10–6]	<0.001



vaccination pneumocoque

Vaccins contre les pneumocoques



Faible réponse . Activation des cellules B

Réponse robuste . Immunité mémoire

Hypo- réponse à la revaccination

Réponse persistante et relancée

Sans impact sur le portage pharyngé

Baisse du portage pharyngé

Vaccin pneumocoque

- Indication du calendrier vaccinal: diabète non équilibré par le régime seul

Vaccination contre les infections à pneumocoque (IP)

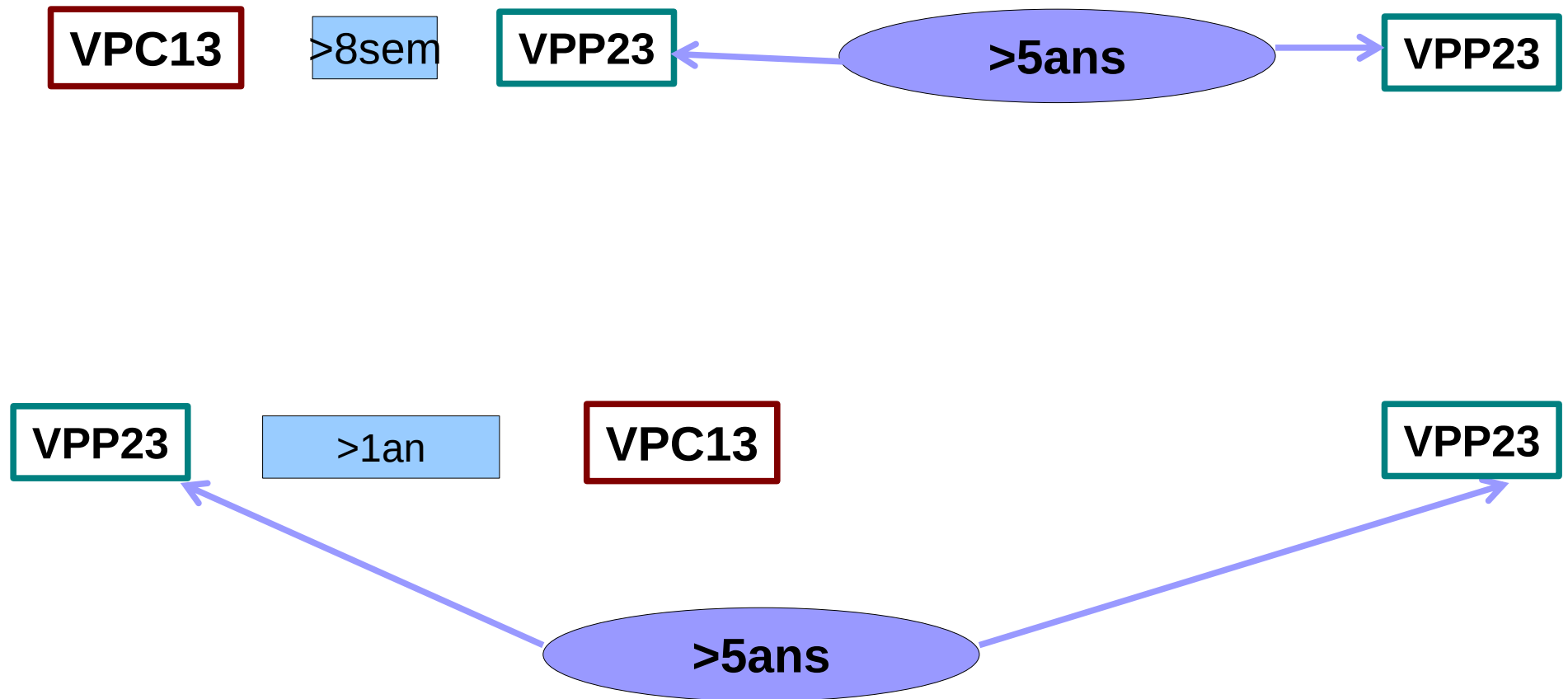
Enfants de moins de 2 ans	Enfants de 2 à 5 ans à risque d'IP	Enfants de plus de 5 ans et adultes à risque d'IP
VPC 13 à l'âge de 2 mois (8 semaines), 4 et 11 mois	Si antérieurement vacciné par VPC 13 VPP23 à l'âge de 24 mois	• Non vaccinés antérieurement : VPC13 puis VPP23 (>S8) • Vaccinés antérieurement : - Avec la séquence VPC13-VPP23 : VPP23 avec un délai d'au moins 5 ans après le dernier VPP23 - Vaccinés depuis plus de 1 an avec le VPP23 : VPC13. Revaccination par VPP 23 avec un délai d'au moins 5 ans après le dernier VPP23
Prématurés et nourrissons à risque d'IP : une dose de vaccin conjugué 13-valent à l'âge de 2 mois (8 semaines), 3 et 4 mois avec un rappel à l'âge de 11 mois	Si non antérieurement vaccinés : deux doses de VPC13 (S0, S8) puis VPP23 (S16)	

2 vaccins

Non conjugué, 23 valences: PPV23 **Pneumovax°**

Conjugué, 13 valences: VPC13 **Prevenar°**

Vaccin pneumocoque



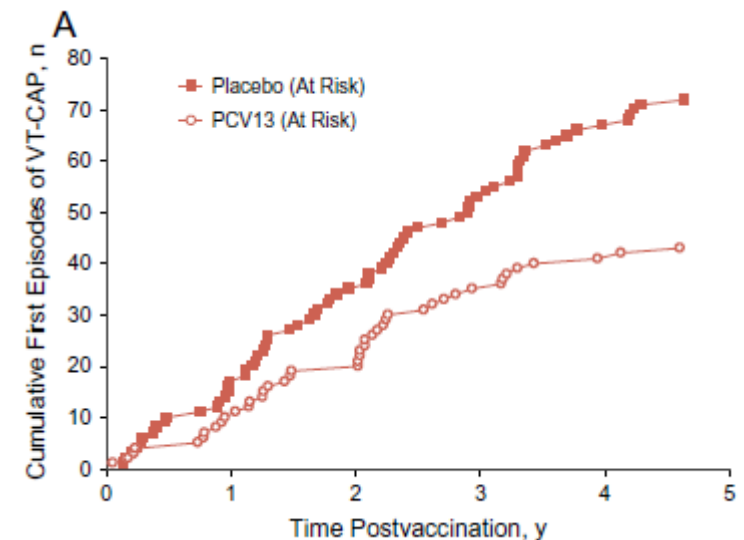
Efficacité?

- PCV13: Analyse données issues étude CAPITA chez les patients à risque (>65 ans)

Table 2
Baseline characteristics of participants stratified by risk classification.

	At risk (n = 41,385)	
	PCV13 (n = 20,680)	Placebo (n = 20,705)
Sex, n (%)		
Female	8313 (40.2)	8095 (39.1)
Male	12,367 (59.8)	12,610 (60.9)
Race, n (%)		
White	20,337 (98.3)	20,369 (98.4)
Nonwhite	339 (1.6)	329 (1.6)
Missing	4 (0.0)	7 (0.0)
Age at enrolment, y		
Mean (SD)	73.1 (5.8)	73.1 (5.8)
Median	72.0	72.0
Min-max	65-101.1	65-99.5
<75, n (%)	13,678 (66.1)	13,654 (65.9)
75-85, n (%)	6200 (30.0)	6275 (30.3)
≥85, n (%)	802 (3.9)	776 (3.7)
Self-reported medical condition, n (%)		
Asthma	2008 (9.7)	2094 (10.1)
Diabetes	5211 (25.2)	5303 (25.6)
Heart disease	10,642 (51.5)	10,657 (51.5)
Liver disease	203 (1.0)	199 (1.0)
Lung disease	4224 (20.4)	4324 (20.9)
Smoking	5175 (25.0)	5147 (24.9)

PCV13 = 13-valent pneumococcal conjugate vaccine.



J.A. Suaya et al./Vaccine 36 (2018) 1477-1483

- PPV23: données rétrospectives patients diab âgés: réduction des infections invasives, des hospitalisations, bénéfice majoré si vaccin grippe

Kuo et al. Medicine (2016) 95:26



Vaccins du calendrier



**Calendrier
des vaccinations
et recommandations
vaccinales 2019**

Mars 2019

Vaccins du calendrier

Vaccination contre la diphtérie, le tétanos, la poliomyélite et la coqueluche

- dTcaP à 25 ans
- Rattrapage coqueluche jusque 39 ans
- Puis coqueluche selon le cocooning
- dTP à 45 ans, 65 ans, puis 75, 85 ans....

dTcaP: boostrix° repevax°

dTP: revaxis°

Vaccins du calendrier

Vaccination contre le zona

- 1 dose à 65 ans, pas de rappel pour l'instant
- Co-administration possible dTP-grippe
- Non avec PPV23

Vaccin Vivant Atténué: zostavax°

Vaccin Inactivé: shingrix° (non disponible France)

- DM2: +de zona, + de complications, + de douleurs post-zostériennes
- vaccin zostavax°: pas de différence efficacité et effets secondaires patient diabétique vs non diabétique

Inoue, Diab Med 2016

Ohfuji, BMC 2019

Papagianni, Diab Ther 2018

Au total

- 2 vaccins spécifiques
 - Grippe
 - Pneumocoque
- Vaccins du calendrier
 - Rappels dTP/dTPcoq
 - zona



Pour en savoir plus..



B. Bauduceau¹, F. Bricaire²,
B. De Wazières³, S. Halimi⁴

Médecine des maladies Métaboliques - Septembre 2018 - Vol. 12 - N°5

Pour la pratique

441



La vaccination, ce n'est pas que
pour les enfants, et c'est indispensable
chez les patients diabétiques !

*Vaccination is not for children only, and is indispensable for patients
with diabetes!*

Merci de votre attention!