Impacts direct et indirects de la vaccination anti-grippale

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Liens d’intérêt

Consultants, Groupes de travail, and advisory boards :
Pfizer/ BioMérieux/ Sanofi-Pasteur MSD/Astellas/AstraZeneca/
Sanofi / MSD/Novovax/Moderna / Seqirus / Viatris/ Thermofisher

Institut de Santé Publique : Haute Autorité Santé/DGS/ANSM/OMS

Syndicat : Aucun
Invitation pour congrès : Eisai, Pfizer, Sanofi Pasteur, Novartis, Pfizer, MSD,
URPS Pharmacie (France),

Sociétés Savantes : ESCMID, EUGMS , SFGG, SPILF, EICA, CMI

Yuichiro Miura

Preambule 1

Hank Jones

If Ageing is Universal, Intrinseque, Progressive and somehow Deleterious

Ageing is

Environment (comorbidites) → **HETEROGENEOUS** ← Genetic Epigenetic

80% OF >80 Y POP. AT HOME WITHOUT ADL DISABILITY

The older persons
One trigger = several complications

Numerous unexpected complications

Iatrogenic events,
Health care Associated Infection
Falls
Malnutrition
Immobilisation / pressure sores
Delirium /behavioural disorders
Complications of Chronic Diseases

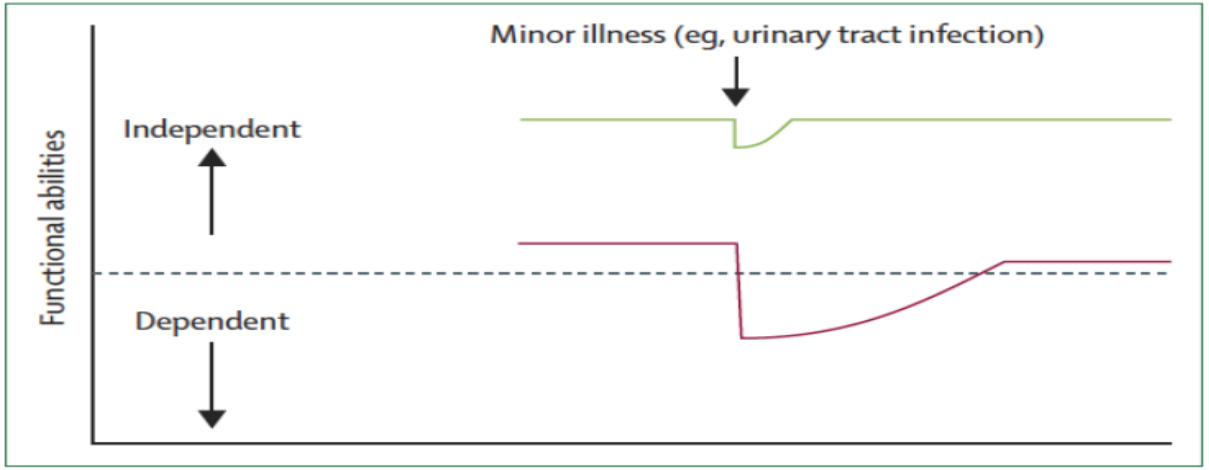


Figure 1: **Vulnerability of frail elderly people to a sudden change in health status after a minor illness**

Disability

↗↗ in hospital length of stay and ↗↗↗ cost

Vaccination as Individual / Collective issues

- Diseases and complications of the Diseases
- Vaccine : Efficacy- effectiveness / Adverse drug reaction ratio
- Cost /Effectivness ratio

Incidence and prevalence of the disease

Cost (dis+complications) versus cost (Vacinne /ADR)

Individual perception of

Efficacy- effectiveness / Adverse drug reaction ratio

Collective Vaccine policies (Public Health policies)

Individual interest / Collective interest

Cost /Effectiveness ratio

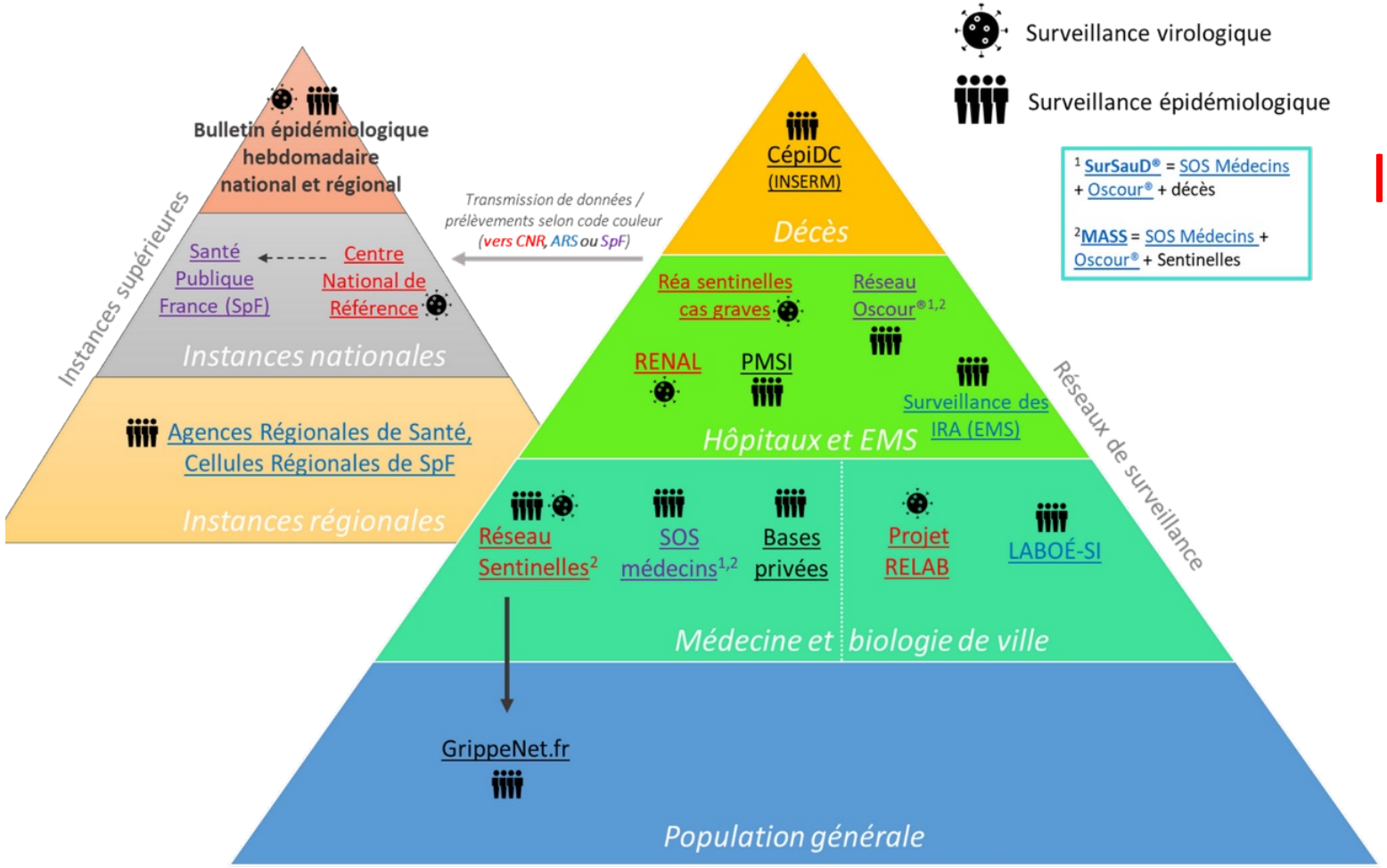
Balinska MA 2004, **Salgado CD** 2004

Preambule 3

How Surveillance system is organized an exemple

various virological and epidemiological surveillance networks with sentinel networks.

SPF coordination



Incidence of flu

=

estimation

from virological culture to Flu PCR

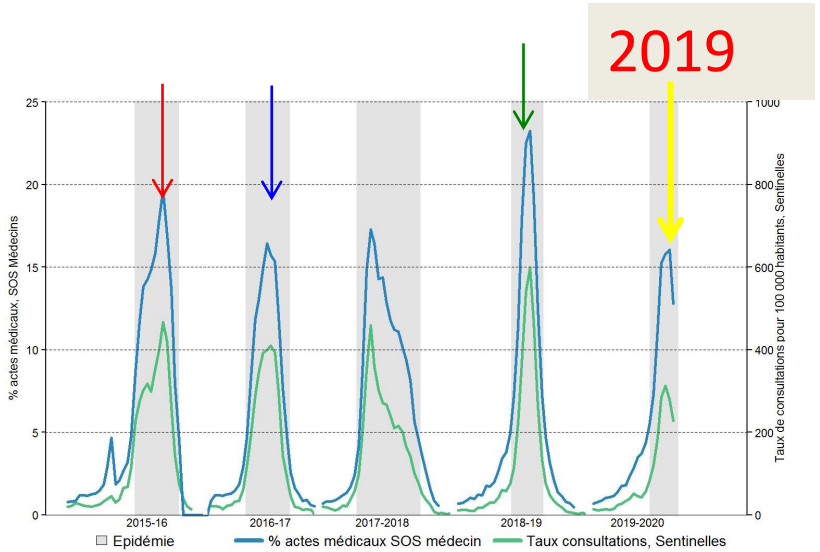
to PCR in hospital
to PCR in community

Despite large, NO interconnections, …. High risk of UNder-estimation

Le fardeau direct et indirects de la grippe chez le sujet âgé

Les vaccins protègent ils ?

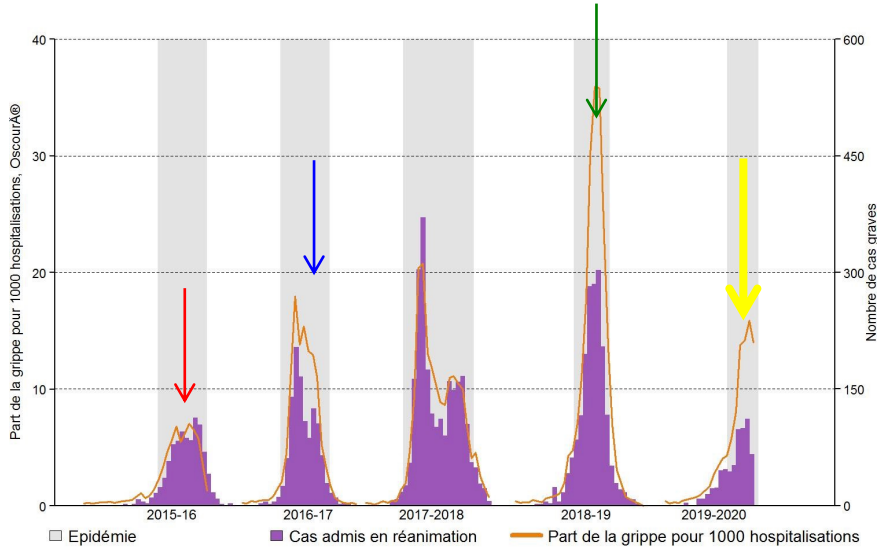
Grippe est variable : region localisation,saisons



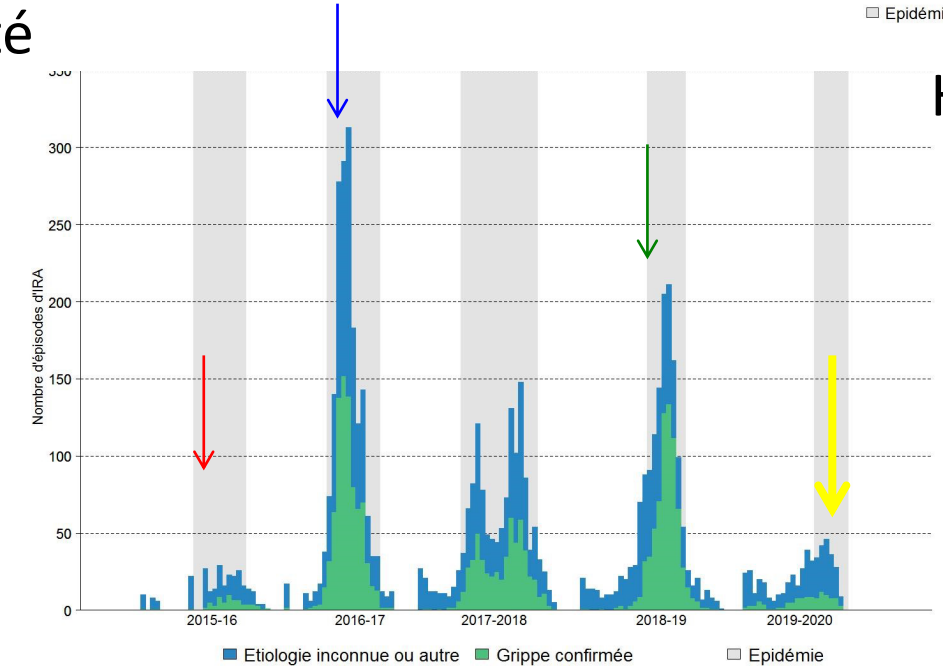
syndrome grippal communauté

2-6 M D'INFECTIONS

> 8 000- 44 000 HOSPIT.



Hospitalisation et réanimation



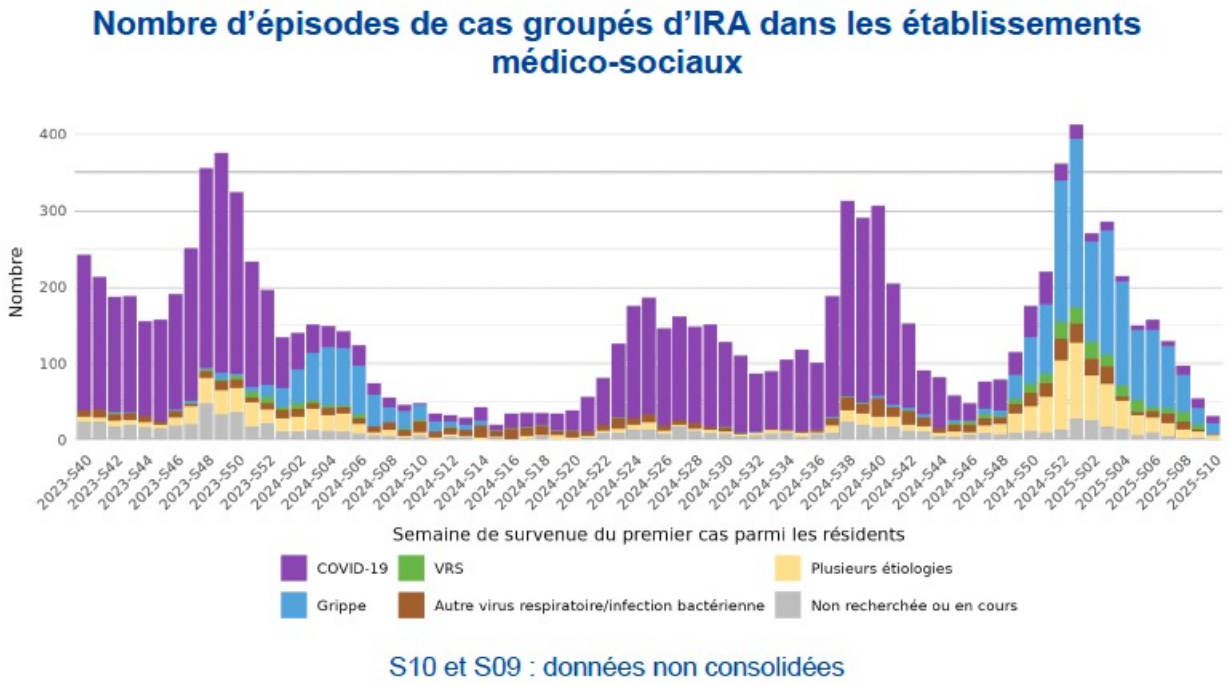
saison 2015-2019

Lemaitre M et al. Influenza Other Respi Viruses. 2022, BEH 2020, Santé publique France, bilan des épidémies de 2011-2012 à 2021-2022 https://www.santepubliquefrance.fr/maladies-et-traumatismes/maladies-et-infections-respiratoires/grippe/documents/rapport-synthese/fardeau-de-la-grippe-en-france-metropolitaine-bilan-des-donnees-de-surveillance-lors-des-epidemies-2011-12-a-2021-22,

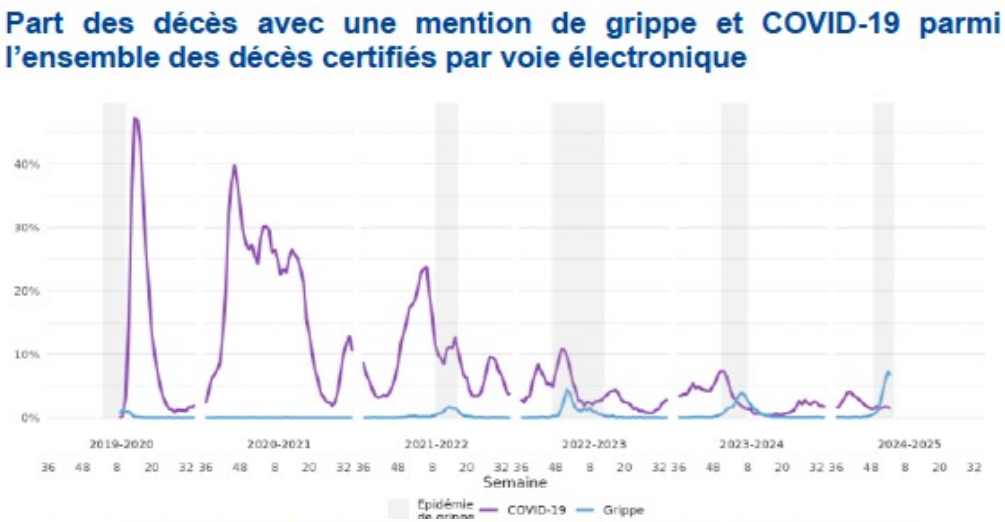
Bulletin
Santé publique France
Infections respiratoires aiguës
Semaine 03 (13 au 19 janvier 2025). Publication : 22 janvier 2025
ÉDITION NATIONALE

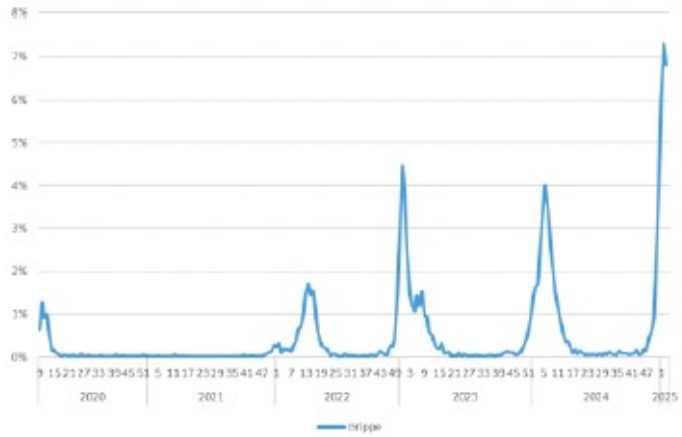
et……aussi?

IRA en EHPADs

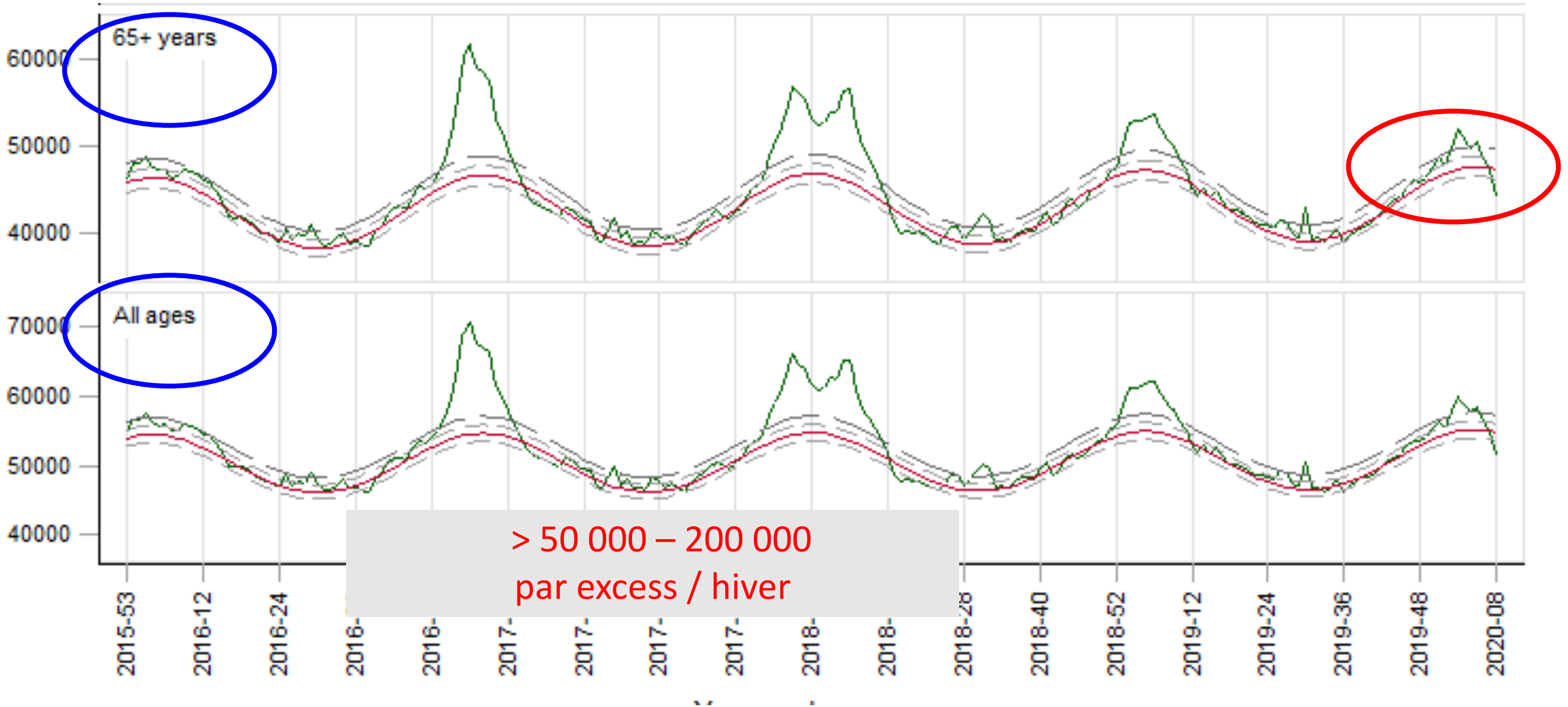


Mortalité





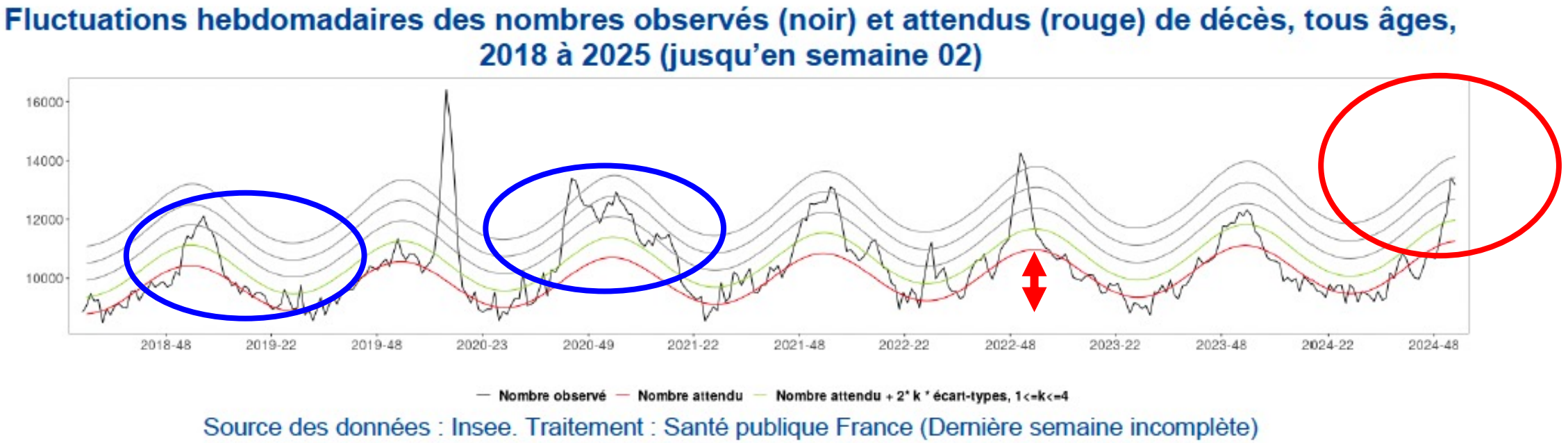
Grippe mortalité- Europe > COVID



> 50 000 – 200 000
par excess / hiver

http://www.euromomo.eu

Grippe mortalité- Europe- variable

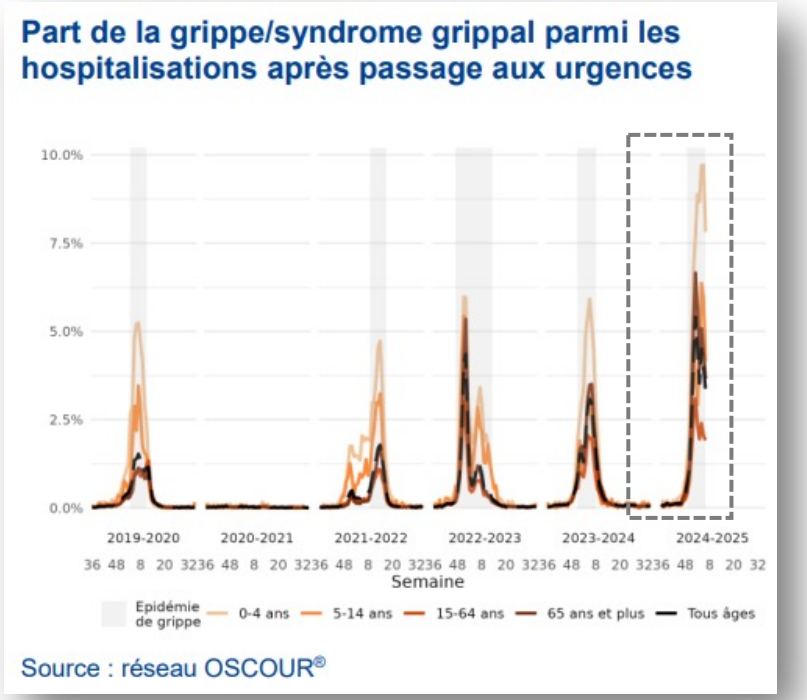


↕ sans compter « l'exces normal »

http://www.euromomo.eu

Une dernière saison grippale intense, et une protection insuffisante des 65 ans et plus par les vaccins standards

Saison grippale 2024/25 intense
Pic d'hospitalisation ~x2 vs saison précédente[1]



Santé publique France

Saison 2024-25[1] : 29 000 hospitalisations après passage aux urgences**, dont ~18 000 hospitalisations de patients 65 ans+**

Efficacité insuffisante des vaccins standards pour les adultes âgés de 65 ans et plus[2]

Eurosurveillance

RAPID COMMUNICATION

Influenza vaccine effectiveness against detected infection in the community, France, October 2024 to February 2025

François Blanquart[1], Vincent Vieillefond[2], Benoit Visseaux[3], Claire Nour Abou Chakra[4], Marta C Nunes[4,5], Alexandra Jacques[6], Stephanie Haim-Boukobza[7], Laurence Josset[8,9], Valentin Wehrle[10], Guillaume Deleglise[11], Thomas Duret[11], Marie Anne Rameix-Welti[12,13], Bruno Lina[8,9], Vincent Enouf[13], on behalf of the RELAB study group[14], Antonin Bal[8,9]

Réseau RELAB en France
(laboratoires de ville)

- Données d'efficacité vaccinale grippe en vie réelle intérimaires pour la saison 2024/25 (données finales à venir)
- **Seuls les vaccins standards étaient disponibles**

Efficacité vaccinale absolue en vie réelle [IC 95%]	
Tous âges	42% [37 ; 46]
65 ans et plus	**22% [13 ; 30]**

1. Bulletins Santé Publique France; 2. Blanquart F, al. *Euro Surveill*. 2025;30(7):2500074. doi:10.2807/1560-7917.ES.2025.30.7.2500074

Grippe hospitalisation France

Paramètre	65-74 ans	75-84 ans	≥85 ans	Ensemble 65+	Source
Durée médiane séjour (jours)	8 [7-8] Durée moyenne de séjour : 9,5	8 [8-9] Durée moyenne de séjour 75+ : 10,5	10 [9-10]	8	Lemaitre *et al.* Nuttens *et al.* Demont *et al.*
Transfert USI (%)	14,9 19,8 26,6	8,3 (75 +) 13,8 13,4 (75+)	6,3	15	Demont *et al.* Lemaitre *et al.* Nuttens *et al.*
Mortalité hospitalière (%)	6,1	6,6	9,3	7,0	Lemaitre *et al.* Nuttens *et al.*
Ventilation mécanique (%)	61,0 (si USI)	61,0 (si USI)	61,0 (si USI)	61,0	Piroth *et al.*

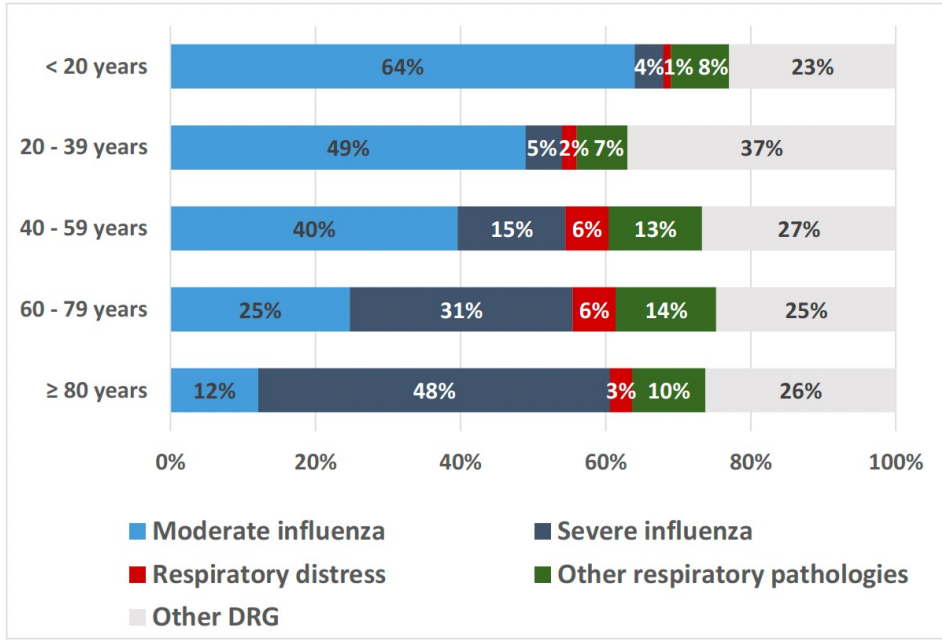


Figure 6. Distribution du type de diagnostic de grippe principal par âge, période 2012-2017 (116).

Type de réhospitalisation	65-74 ans	75-84 ans	≥85 ans	Ensemble	Source
Toutes causes (%)	27,7	26,0	21,9	20,6	Lemaitre *et al.*
Causes respiratoires (%)	6,8	6,0	5,5	4,8	
Causes cardiaques (%)	6,3	6,3	5,8	2,8	

Rapport livre Blanc Infections respiratoires : https://preventionvaccinale-seniors.fr/

PUGG 2016/2017 : les conséquences de la grippe en vie réelle

Hôpital n=515

Décompensation d'organe	57.8%
Réanimation	5.25%
Durée de séjour	16.1 j
ATBthérapie	58.7%
Mortalité	12.2%
Admission EHPAD	14%

EHPADs n=245

Décompensation d'organe	52%
Hospitalisation	17.2%
Durée de séjour	7.4 j
Taux de mortalité	13 %
Taux de mortalité hospitalisés	25%

PUGG : Pratique et Usage en Gériatrie et Gérontologie
n : nombre de cas de grippes confirmées / PCR saison 2016-17

Gavazzi G en preparation 2024

Gavazzi G et al. La grippe dans la population âgée, analyse de 515 cas de grippe virologiquement prouvés durant la saison 2016-2017 en France. Poster présenté au congrès EuGMS 2018. https://sfgg.org/enquetes-pugg/enquete-pugg-2017-la-grippe-chez-le-sujet-age/,

PUGG 2016/2017 : Evolution Intrahospitalière n=515

Décompensation d'organes	57.2%
Décompensation Cardiaque	44.4%
Respiratoire	17.7%
AVC	0.8%
Confusion	22.8%
Insuffisance Rénale	14.2%

PUGG : Pratique et Usage en Gériatrie et Gérontologie
n : nombre de cas de grippes confirmées / PCR saison 2016-17

Gavazzi G en preparation 2022

Gavazzi G et al. La grippe dans la population âgée, analyse de 515 cas de grippe virologiquement prouvés durant la saison 2016-2017 en France. Poster présenté au congrès EuGMS 2018. https://sfgg.org/enquetes-pugg/enquete-pugg-2017-la-grippe-chez-le-sujet-age/,

Impact de la Grippe, l'iceberg, un exemple

8x
increased risk of **stroke**[1]

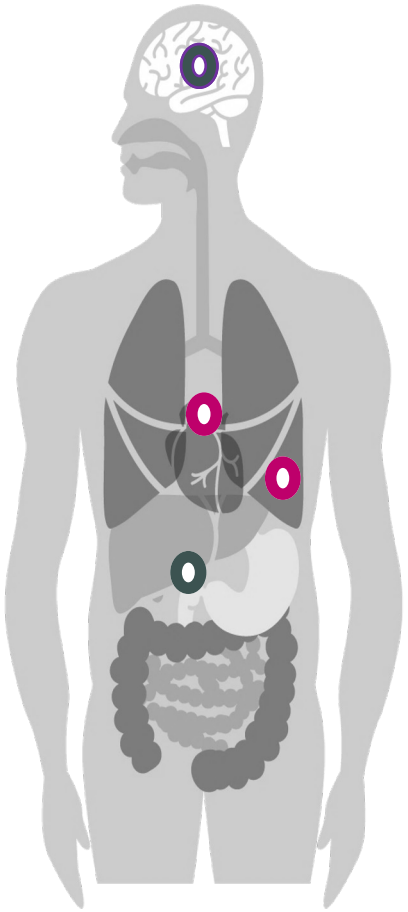
Neurological

23-35%
experience **loss of independence**[2,2bis]

Loss of autonomy

75%
increased abnormal **glycemic events**[3]

Diabetic complications



Cardiovascular

10x
increased risk of **heart attack**[1,bis]

Lower respiratory

8x
increased risk of **pneumonia***[4]

*in children under age 14

1 bis Addario A *Geroscience* 2023 4.

1. Warren-Gash C, et al. Eur respir J. 2018
2. Andrew MK, et al. J Am Geriatr Soc. 2021.

2 bis. Gavazzi G SFFG / SPILF PUGG 2017

1. Samson SI, et al. J Diabetes Sci Technol. 2019
2. Kubale J et al., Clin Inf Dis. 2021

Le fardeau direct et indirects de la grippe chez le sujet âgé

Les vaccins protègent ils ?

Influenza and vaccines

Efficacy- Efficiency : incidence (C-NH) / hospitalisation / mortality / autres

Definition of cases : Lab confirmed (PCR) – ILI (grippe presumée) – TROD ?-

Type of vaccines : SD- HD-Adjuvanted, cell based (… coming m RNA)

Type of studies : Real life RCT - RCT-Observational studies (case-control), cohorts,

Today I France : 2 vaccines vailable

Effectiveness of influenza vaccines in preventing severe influenza illness among adults: A systematic review and meta-analysis of test-negative design case-control studies

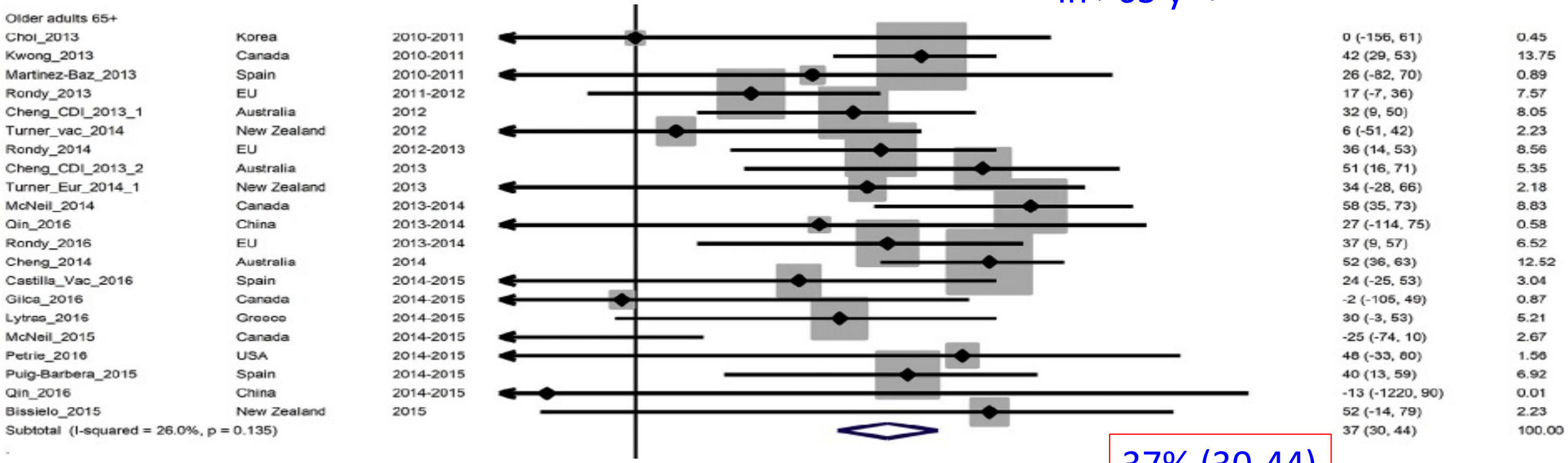
Journal of Infection (2017)

Marc Rondy [a,b,*], Nathalie El Omeiri [c], Mark G. Thompson [d], Alain Levêque [c], Alain Moren [a], Sheena G. Sullivan [e]

Efficacy

SD
Incidence

In >65 y +



37% (30-44)

Very often :Lower efficacy when H3N2 is predominant : 31% (12-51)

MINISTÈRE
DE LA SANTÉ, DES FAMILLES,
DE L'AUTONOMIE
ET DES PERSONNES HANDICAPÉES

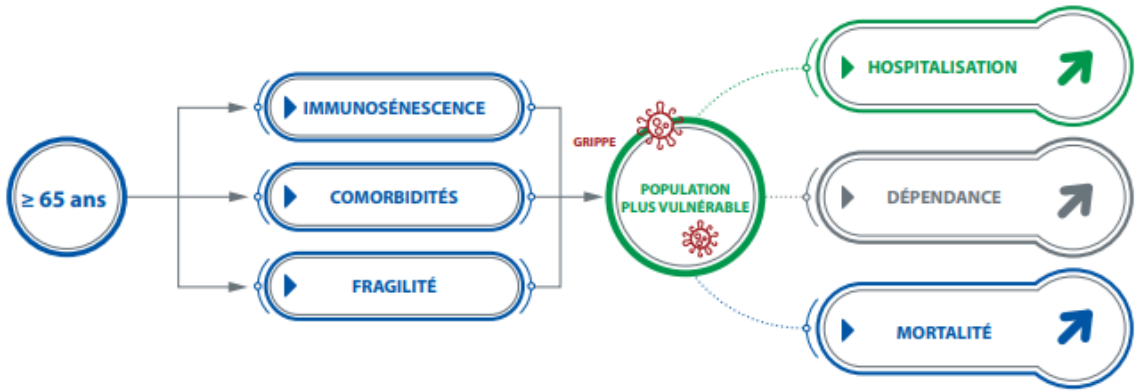
Liberté
Égalité
Fraternité

Calendrier des vaccinations et recommandations vaccinales 2026

Avril 2026

Grippe saisonnière	Une dose de vaccin au cours de la campagne vaccinale annuelle. Il est recommandé de vacciner les personnes âgées de 65 ans et plus, préférentiellement avec les vaccins Efluelda (vaccin hautement dosé) et Fluad (vaccin avec adjuvant). Les vaccins à dose standard peuvent également être utilisés chez cette population.

Améliorer les vaccins antigrippaux [1]



Stratégies :

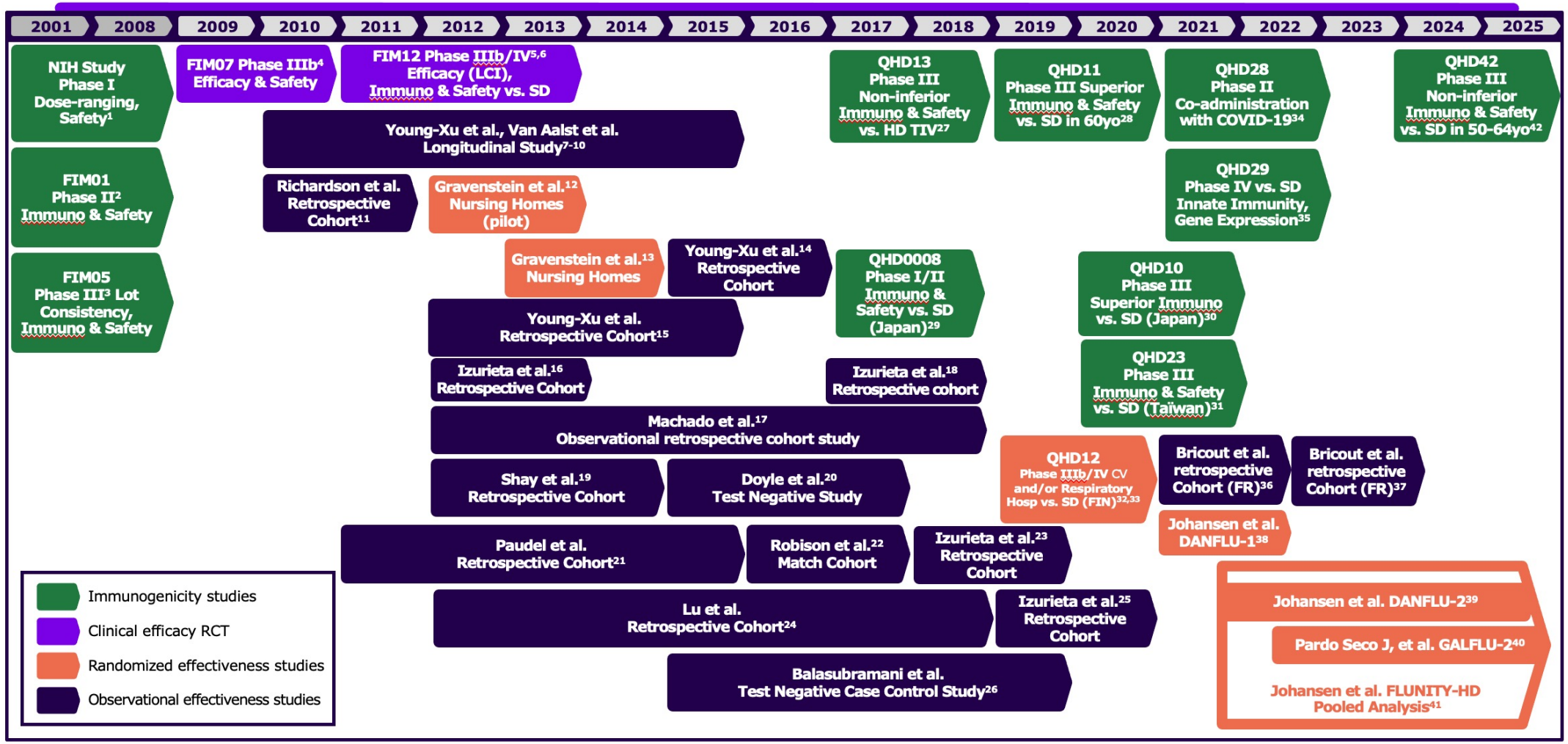
- Autres voies d' administration
- Doses
- Ajout d'adjuvant
- Technologie: mRNA, conjugaison, vecteurs
- Autres voies de stimulation
- Combinaison des stratégies

- résultats : stratégies disponibles en France pour la prévention de la grippe :
  - Augmenter les doses (HD – Haute Dose) : vaccin grippal HD (4 fois plus d'antigène que le vaccin grippe standard) a montré une immunogénicité supérieure
  - Ajouter un adjuvant (MF59) : vaccin grippal à dose standard avec l'ajout d'un adjuvant (MF59) a montré une immunogénicité supérieure

Conrad A, et al. Burden of influenza in the elderly: a narrative review. *Curr Opin Infect Dis*. 2023;36(4):296-302. doi:10.1097/QCO.0000000000000931

High Dose vaccine Efficiency

All kind Studies
RCT: HD/SD



Randomized effectiveness studies = RCT en vie réelle =

Effectiveness of high-dose influenza vaccine against hospitalisations in older adults (FLUNITY-HD): an individual-level pooled analysis

Niklas Dyrby Johansen, Daniel Modin, Jacobo Pardo-Seco, Carmen Rodriguez-Tenreiro-Sánchez, Matthew M Loiacono, Rebecca C Harris, Marine Dufournet, Robertus van Aalst, Ayman Chit, Carsten Schade Larsen, Lykke Larsen, Lothar Wiese, Michael Dalager-Pedersen, Brian L Claggett, Kira Hyldekær Janstrup, Carmen Duran-Parrondo, Marta Piñeiro-Sotelo, Martín Cribeiro-González, Mónica Conde-Pájaro, Susana Mirás-Carballal, Juan-Manuel González-Pérez, Scott D Solomon, Pradeesh Sivapalan, Cyril Jean-Marie Martel, Jens Ulrik Stæhr Jensen, Federico Martinón-Torres, Tor Biering-Sørensen, for the DANFLU-2 Study Group and the GALFLU Trial Team**

Lancet 2025; 406: 2425–34

JAMA Network Open

Original Investigation | Infectious Diseases

High-Dose vs Standard-Dose Influenza Vaccines in Older Adults
A Meta-Analysis

Kristoffer Grundtvig Skaarup, MD; Mats C. H. Lassen, MD; Kaveh Hosseini, MD, MPH; Niklas Dyrby Johansen, MD, PhD; Matthew M. Loiacono, PhD; Rebecca C. Harris, PhD; Sandrine I. Samson, PhD; Arto A. Palmu, MD, PhD; Kevin McConeghy, PharmD, MS; Stefan Gravenstein, MD, MPH; Orly Vardeny, PharmD, MS; Brian Claggett, PhD; Scott D. Solomon, MD; Federico Martinón-Torres, MD, PhD; Tor Biering-Sørensen, MD, MPH, MSc, PhD

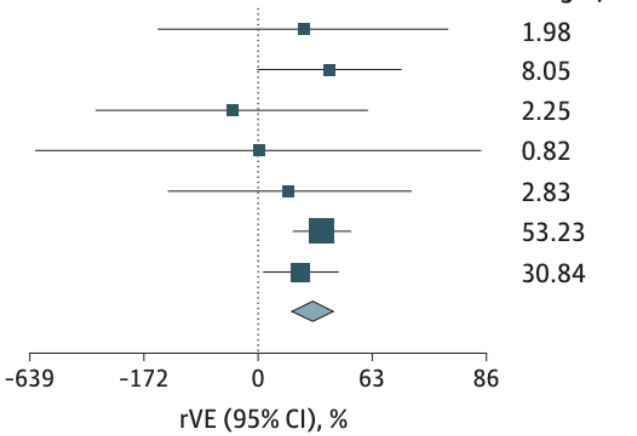
High Dose vaccine Efficiency Vs Standard Dose : HOSPITALISATION

A Hospitalization for influenza

Source	No. with an event/total No. (%) HD-IIV	SD-IIV	rVE (95% CI), %	Weight, %
DiazGranados et al,[5] 2015	4/15 990 (0.03)	6/15 993 (0.04)	33.3 (-136.2 to 81.2)	1.98
Gravenstein et al,[7] 2017	15/26 100 (0.1)	28/25 781 (0.1)	47.1 (1.0 to 71.7)	8.05
Vardeny et al,[6] 2021	6/2010 (0.3)	5/2077 (0.2)	-24.0 (-305.7 to 62.1)	2.25
Johansen et al,[18] 2023	2/6245 (0.03)	2/6232 (0.03)	0.2 (-608.2 to 85.9)	0.82
Palmu et al,[12] 2024	6/16 549 (0.04)	8/16 544 (0.05)	25.0 (-116.0 to 74.0)	2.83
Johansen et al,[9] 2025	101/166 218 (0.1)	179/166 220 (0.1)	43.6 (28.0 to 55.8)	53.23
Pardo-Seco et al,[10] 2025	63/67 093 (0.1)	92/66 789 (0.1)	31.8 (6.1 to 50.5)	30.84
Overall			38.5 (26.5 to 48.5)	

$I^2 = 0.00\%$

Cochran Q statistics = 2.83; $P = .83$



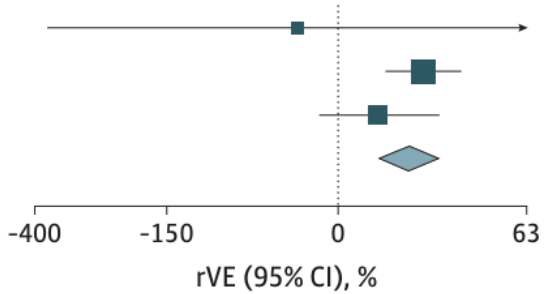
CLINICAL DEFINITION
-38,5%

B Hospitalization for laboratory-confirmed influenza

Source	No. with an event/total No. (%) HD-IIV	SD-IIV	rVE (95% CI), %	Weight, %
Johansen et al,[18] 2023	5/6245 (0.1)	4/6232 (0.1)	-24.7 (-364.3 to 66.5)	1.48
Johansen et al,[9] 2025	177/166 218 (0.1)	276/166 220 (0.2)	35.9 (22.6 to 46.9)	71.96
Pardo-Seco et al,[10] 2025	72/67 093 (0.1)	89/66 789 (0.1)	19.5 (-9.9 to 41.0)	26.56
Overall			31.2 (19.3 to 41.4)	

$I^2 = 13.36\%$

Cochran Q statistics = 2.31; $P = .32$



LAB-CONFIRMED
-31.2%

High Dose vaccine Efficiency Vs Standard Dose : HOSPITALISATION

JAMA Network Open

Original Investigation | Infectious Diseases

High-Dose vs Standard-Dose Influenza Vaccines in Older Adults

A Meta-Analysis

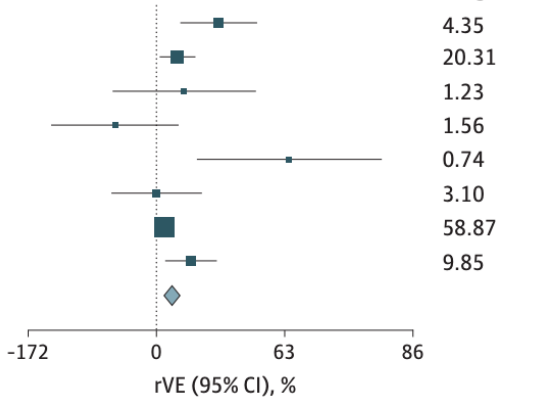
Kristoffer Grundtvig Skaarup, MD; Mats C. H. Lassen, MD; Kaveh Hosseini, MD, MPH; Niklas Dyrby Johansen, MD, PhD; Matthew M. Loiacono, PhD; Rebecca C. Harris, PhD; Sandrine I. Samson, PhD; Arto A. Palmu, MD, PhD; Kevin McConeghy, PharmD, MS; Stefan Gravenstein, MD, MPH; Orly Vardeny, PharmD, MS; Brian Claggett, PhD; Scott D. Solomon, MD; Federico Martinón-Torres, MD, PhD; Tor Biering-Sørensen, MD, MPH, MSc, PhD

C Hospitalization for pneumonia or influenza

Source	No. with an event/total No. (%) HD-IIV	SD-IIV	rVE (95% CI), %	Weight, %
DiazGranados et al,[5] 2015	70/15 990 (0.4)	114/15 993 (0.7)	38.6 (17.4 to 54.4)	4.35
Gravenstein et al,[7] 2017	373/26 100 (1.4)	434/25 781 (1.7)	15.1 (2.6 to 26.0)	20.31
Gravenstein et al,[17] 2018	22/1423 (1.5)	27/1406 (1.9)	19.5 (-40.7 to 53.9)	1.23
Vardeny et al,[6] 2021	36/2010 (1.8)	27/2077 (1.3)	-37.8 (-126.1 to 16.0)	1.56
Johansen et al,[18] 2023	10/6245 (0.2)	28/6232 (0.4)	64.4 (26.7 to 82.7)	0.74
Palmu et al,[12] 2024	62/16 549 (0.4)	62/16 544 (0.4)	0.0 (-42.1 to 29.7)	3.10
Johansen et al,[9] 2025	1138/166 218 (0.7)	1210/166 220 (0.7)	5.9 (-2.0 to 13.2)	58.87
Pardo-Seco et al,[10] 2025	174/67 093 (0.3)	227/66 789 (0.3)	23.7 (7.1 to 37.4)	9.85
Overall			11.5 (5.9 to 16.8)	

$I^2 = 65.49\%$

Cochran Q statistics = 20.28; $P < .01$



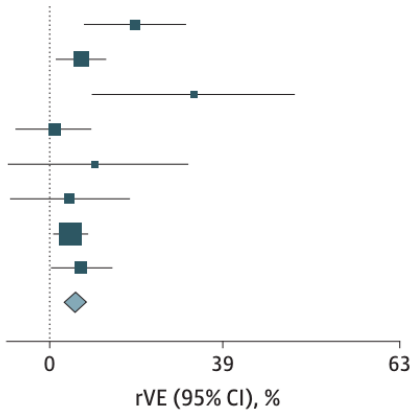
PNEUMONIA/FLU
-11,5%

A Hospitalization for cardiorespiratory disease

Source	No. with an event/total No. (%) HD-IIV	SD-IIV	rVE (95% CI), %	Weight, %
DiazGranados et al,[5] 2015	332/15 990 (2.1)	423/15 993 (2.6)	21.5 (9.5 to 31.9)	4.63
Gravenstein et al,[7] 2017	1512/26 100 (5.8)	1633/25 781 (6.3)	8.5 (2.1 to 14.5)	20.33
Gravenstein et al,[17] 2018	73/1423 (5.1)	109/1406 (7.8)	33.8 (11.8 to 50.3)	1.13
Vardeny et al,[6] 2021	518/2010 (25.8)	542/2077 (26.1)	1.2 (-9.5 to 11.0)	8.70
Johansen et al,[18] 2023	103/6245 (1.6)	117 /6232 (1.9)	12.2 (-14.2 to 32.4)	1.36
Palmu et al,[12] 2024	257 /16 549 (1.6)	272/16 544 (1.6)	5.5 (-11.9 to 20.2)	3.27
Johansen et al,[9] 2025	3735/166 218 (2.2)	962/166 220 (2.4)	5.7 (1.5 to 9.8)	47.89
Pardo-Seco et al,[10] 2025	985/67 093 (1.5)	1071/66 789 (1.6)	8.5 (0.2 to 16.0)	12.68
Overall			7.5 (4.7 to 10.3)	

$I^2 = 46.0\%$

Cochran Q statistics = 13.0; $P = .07$



FOR CARDIO REPSIRATORY
- 7,5 %

NO IMPACT ON ALL cause of death

High Dose vaccine Efficiency Vs Standard Dose : HOSPITALISATION

DRIVEN

- **National retrospective cohort study**, National Assurance system database seasons 2021-22 et 2022-23,
  - **21/22 : 2 millions** 65 +, ~400 000 with HD
  - **22/23 : 3,4 millions** 65+ ~ 670 000 with HD
- **Objective: Measuring** relative efficacy HD Vs SD
- jugement : **hospitalisations with a « influenza » code**

	Incidence hospitalisation grippe vaccinés HD	Incidence hospitalisation grippe vaccinés SD	EVr
Hospitalisations pour grippe - saison 2021/22	70/100 000	90/100 000	**23%** (95% IC, 8.4-35.8)
Hospitalisations pour grippe - saison 2022/23	125/100 000	173/100 000	**27%** (95% IC, 19.8-34.3)

HD > 20% Hospitalisation rate reduction les hospitalisations on 2 flu Seasons

Bricout H, et al. *Clin Microbiol Infect*. 2024;30(12):1592-1598. doi:10.1016/j.cmi.2024.08.012

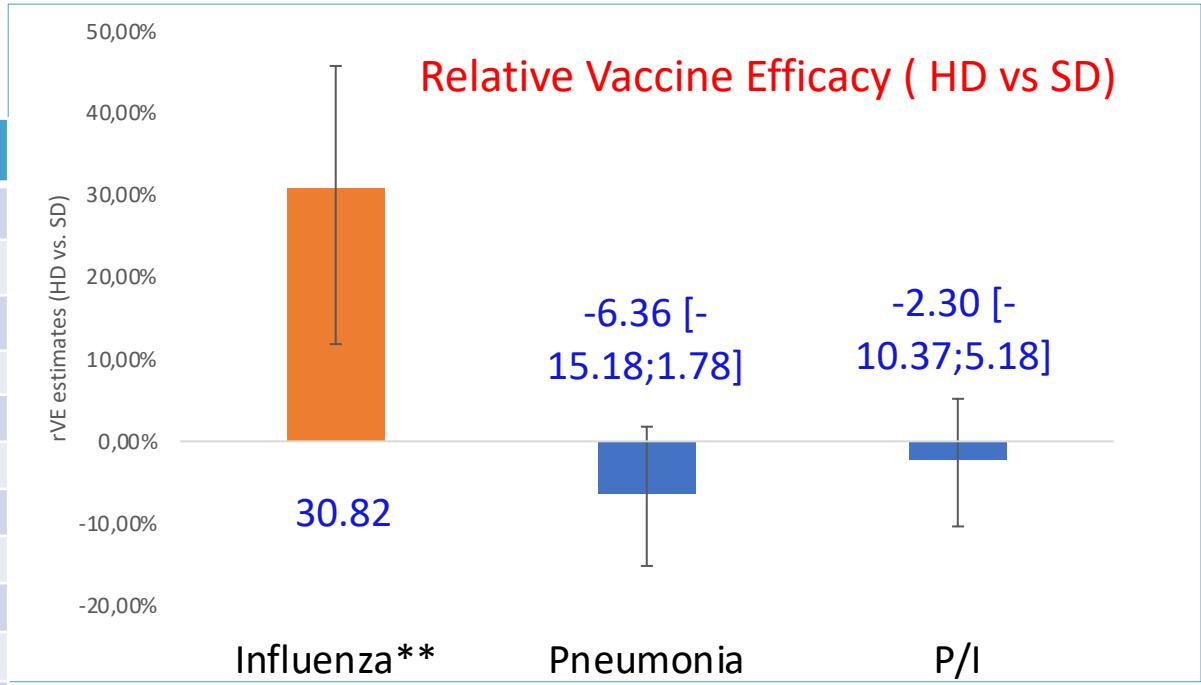
High Dose vaccine Efficiency Vs Standard Dose : Hospitalisation in Nursing Home resident

Administrative database : (SNDS)

n= 123 720 received HD - n= 191 519 received SD

Appariement based on comorbidities age sex etc…

N=	76 858	76 858
Characteristics	**HD**	**SD**
Âge, mean (± STD)	87.76 (7.71)	88.02 (7.78)
Female, n (%)	57.832 (75.25)	57.832 (75.25)
Patients > comorbidities ALD statut, n (%)	59.578 (77.52)	59.405 (77.29)
Death	12.333 (16.05)	12.316 (16.02)
Hospitalisation < 12 months (STD)	0.15 (0.00)	0.13 (0.00)
Flu Vaccination before, n (%)	61.839 (80.46)	66.846 (86.97)
COVID-19 Vaccination, n (%)	73.927 (96.19)	74.091 (96.40)
Pneumococcal vaccination <5 y , n(%)	14.325 (18.64)	13.231 (17.21)
Diabetes	13.139 (17.10)	13.233 (17.22)
COPD	8.168 (10.63)	8.257 (10.74)
cardio-vascular Disease	33.715 (43.87)	33.036 (42.98)
immunodepression	11.964 (15.57)	11.441 (14.89)
> 1 comorbidities	92,61%	92,4%



Gavazzi G Age Ageing submitted

Circulation Jan 2019

ORIGINAL RESEARCH ARTICLE

Influenza Vaccine in Heart Failure

Cumulative Number of Vaccinations, Frequency, Timing, and Survival: A Danish Nationwide Cohort Study

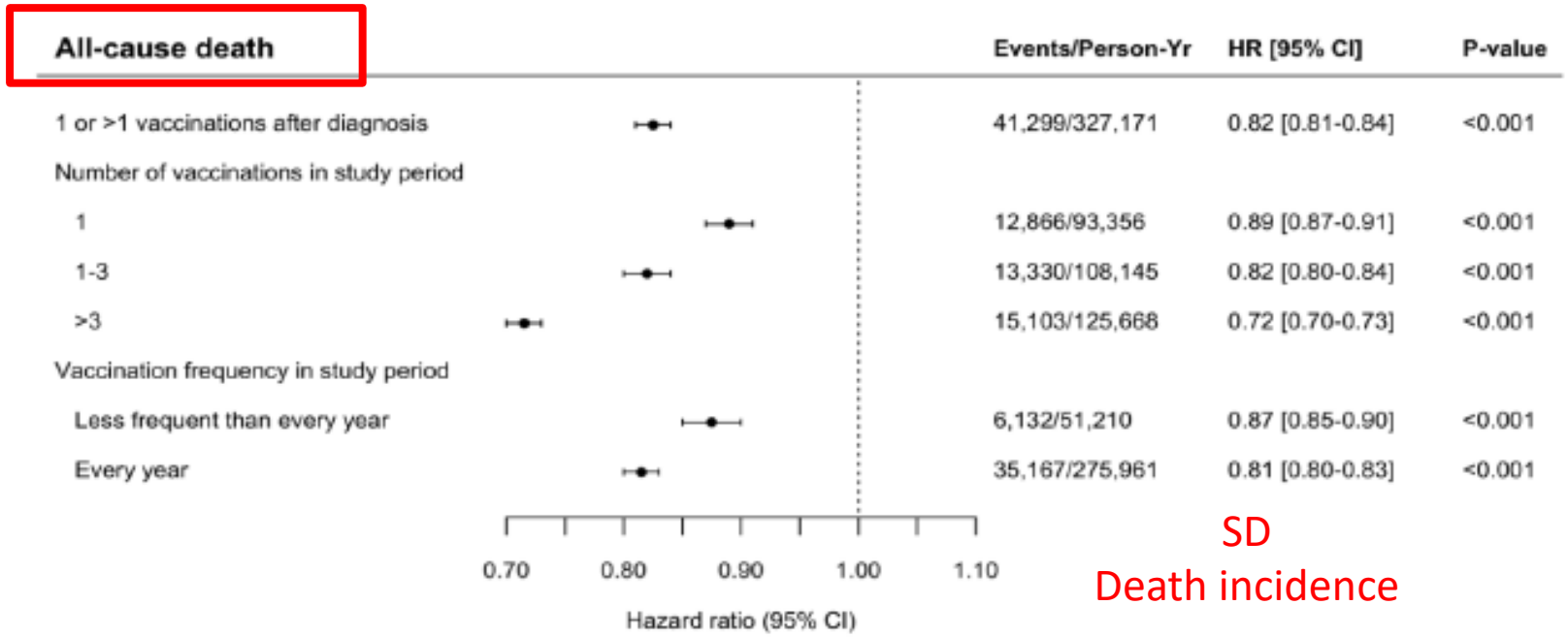
Modin D Circulation 2019

One Flu vaccine shot Protect from cardio-vascular mortality Denmark

Dose effect

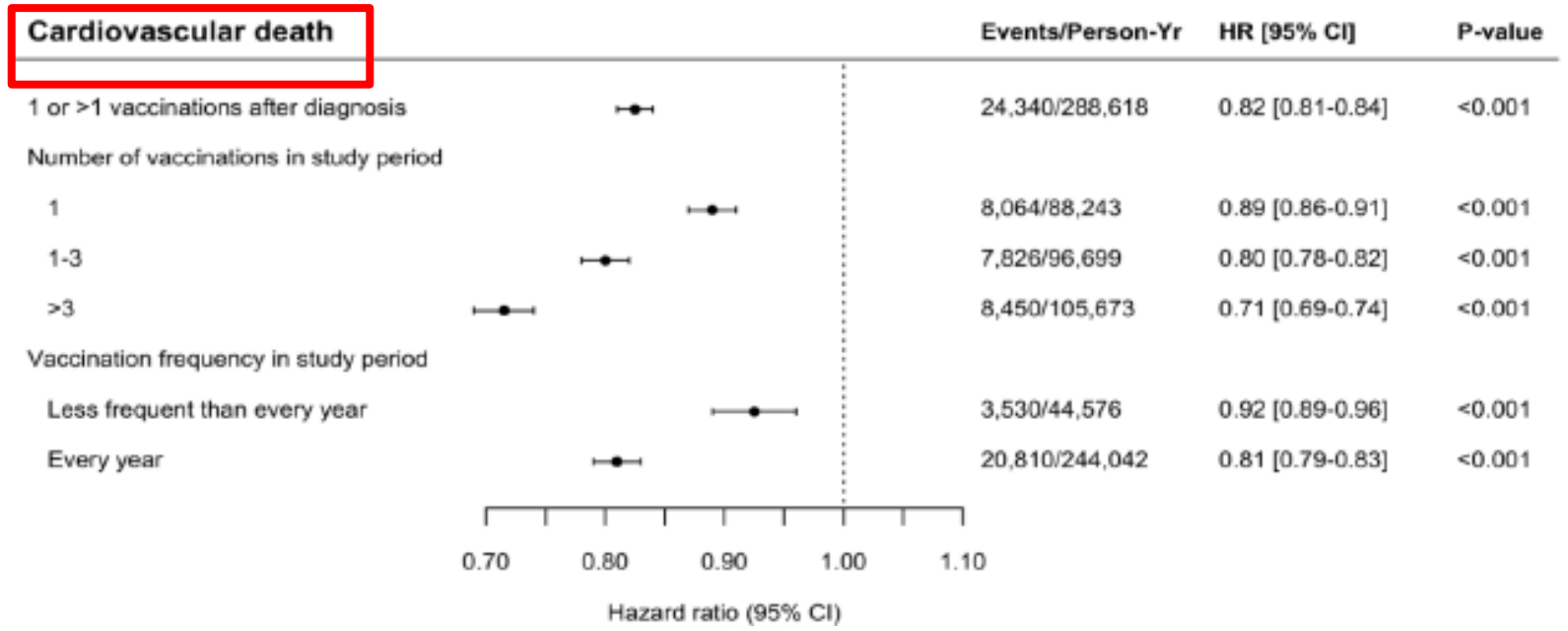
-11% à -28%

As high as statins pills every day



SD

Death incidence



High-Dose vs Standard-Dose Influenza Vaccine in Chronic Kidney Disease

The DANFLU-2 Trial Subgroup Analysis

High-Dose vs Standard-Dose Influenza Vaccine in Chronic Kidney Disease

The DANFLU-2 Trial Subgroup Analysis

Circulation

ORIGINAL RESEARCH ARTICLE

High-Dose Versus Standard-Dose Influenza Vaccine and Cardiovascular Outcomes in Older Adults: The FLUNITY-HD Prespecified Pooled Analysis

		HD-IIV	SD-IIV	Crude Relative Vaccine Effectiveness (95% CI)	P Value for Interaction	Number Needed to Vaccinate (95% CI)
		no./total no. (%)				
Hospitalization for influenza or pneumonia						
Overall		1,312/233,311 (0.56)	1,437/233,009 (0.62)	8.8 (1.7 to 15.5)		1,839 (1,049 to 9,756)
By cardiovascular disease at baseline					0.71	
	No	689/179,248 (0.38)	768/179,363 (0.43)	10.2 (0.4 to 19.1)		2,649 (1,511 to 14,051)
	Yes	623/54,061 (1.15)	669/53,639 (1.25)	7.6 (-3.2 to 17.3)		909 (519 to 4,824)
Hospitalization for any cardio-respiratory disease						
Overall		4,720/233,311 (2.02)	5,033/233,009 (2.16)	6.3 (2.5 to 10.0)		730 (463 to 1,832)
By cardiovascular disease at baseline					0.75	
	No	2,282/179,248 (1.27)	2,460/179,363 (1.37)	7.2 (1.7 to 12.4)		1,150 (729 to 2,886)
	Yes	2,438/54,061 (4.51)	2,573/53,639 (4.80)	6.0 (0.6 to 11.1)		329 (208 to 825)
Laboratory-confirmed influenza hospitalization						
Overall		249/233,311 (0.11)	365/233,009 (0.16)	31.9 (19.7 to 42.2)		2,003 (1,511 to 3,233)
By cardiovascular disease at baseline					0.66	
	No	139/179,248 (0.08)	198/179,363 (0.11)	29.8 (12.3 to 43.9)		2,842 (2,145 to 4,589)

Adjuvanted vaccine Efficiency Vs Standard Dose : Hospitalisation

Table 4. Relative effectiveness of the adjuvanted vaccine versus the standard influenza vaccine.

Study	Study description	n	Population	Endpoint	rVE, % (95% CI)
Randomized studies					
McConeghy et al. [108]	Pragmatic cluster randomized study in the 2016/17 season	50,012	Adults aged ≥65 years residing in nursing homes	Respiratory- illness-related hospitalizations	7 (–4, 17)
Observational studies					
Van Buynder et al. 2013 [114]	Prospective community-based case-control study in the 2011/12 season	282	Adults aged ≥65 years	Laboratory-confirmed influenza	63 (4, 86)
Pott et al. 2023 [115]	Test-negative design study using pooled data from the 2012 to 2015 seasons	7,101	Adults aged ≥65 years	Laboratory-confirmed influenza-related hospital admissions	25 (8, 39)
Domnich et al. 2022 [82]	Test-negative case-control study during four seasons (2018/19 to 2021/22)	512	Adults aged ≥65 years		59.2 (14.6, 80.5)
Ku et al. 2024 [116]	Retrospective cohort study during the 2022/23 season	495,119	Adults aged ≥65 years		61.6 (18.1, 82.0)
Lapi et al. 2019 [106]	Case-control study across 15 seasons (2002 to 2016)	43,000	Adults aged ≥65 years	Hospitalization for pneumonia or cerebrovascular/cardiovascular events	39 (4, 61)
Imran et al. 2024 [107]	Retrospective cohort study during the 2019/20 season	4,299,594	Adults aged ≥65 years	Cardiorespiratory hospitalizations	9.0 (7.7, 10.4)
Lapi et al. 2022 [109]	Nested case-control study over 18 influenza seasons (2002 to 2019)	58,252	Adults aged ≥65 years	All-cause hospitalizations	12 (2, 20)

EXPERT REVIEW OF VACCINES
2025, VOL. 24, NO. 1, 350–364
https://doi.org/10.1080/14760584.2025.2499728

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REVIEW

OPEN ACCESS Check for updates

Enhanced influenza vaccination for older adults in Europe: a review of the current situation and expert recommendations for the future

Gaëtan Gavazzi[a,b], Bertrand Fougère[c,d], Olivier Hanon[e,f], Isabel Leroux-Roels[g], Etienne Brochot[h,i], Elodie Blanchard[j], Colin A Russell[k], Marc Paccalin[l] and Tino F Schwarz[m]

Variable good and better efficacy but NO RCT

JAMA Network Open

Original Investigation | Infectious Diseases

Adjuvanted vs High-Dose Influenza Vaccines in Older US Adults

A Cluster Randomized Crossover Study

Amber Hsiao, PhD, MPH; Thomas Leong, MPH; Bruce Fireman, MA; John Hansen, MPH; Ousseny Zerbo, PhD; Karen B. Jacobson, MD, MPH; Lauren D. Liao, PhD; Mendel D. M. Haag, PhD, PharmD; Ian McGovern, MPH; Bin Zhang, ScD, MA; Juliet Dang, PhD, MS; Nicola P. Klein, MD, PhD

Population :> 65 y
Design : cluster randomized crossover study
Location : one center Kaiser Permanente Northern California
Outcomes : Lab confirmed Influenza / Hospitalisation
Seasons : 1 (2023-2024)

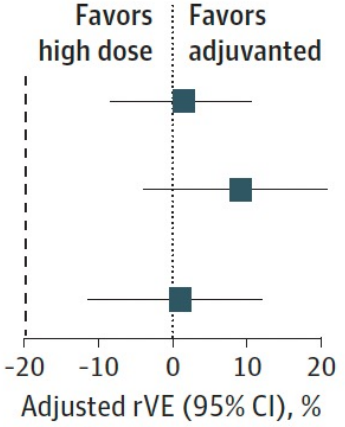
Week	Block A	Block B
1[a] (Aug 7 to Aug 19)	High dose	Adjuvanted
2 (Aug 20 to Aug 26)	Adjuvanted	High dose
3 (Aug 27 to Sep 2)	High dose	Adjuvanted
4 (Sep 3 to Sep 9)	Adjuvanted	High dose
Alternating weekly patterns continue for all 65 facilities to April 16, 2024		
35 (April 7 to April 13)	High dose	Adjuvanted
36[a] (April 14 to April 16)	Adjuvanted	High dose

212 875 Adjuvanted influenza vaccine cohort

216 720 High-dose influenza vaccine cohort

Equivalent pop :all prior Health status in the year ad other RT vaccines

Outcome	Adjuvanted influenza vaccine (n = 212 875)	High-dose influenza vaccine (n = 216 720)	Unadjusted HR (95% CI)	AHR (95% CI)	Adjusted rVE (95% CI), %	AHR *P* value[a]	*P* value for noninferiority test[b]
PCR-confirmed influenza	836 (3.93)	867 (4.00)	0.978 (0.889-1.077)	0.985 (0.895-1.084)	1.5 (-8.4 to 10.5)	.76	<.001
Hospitalized or ED PCR-confirmed influenza	411 (1.93)	466 (2.15)	0.910 (0.796-1.039)	0.909 (0.796-1.039)	9.1 (-3.9 to 20.4)	.16	<.001
Hospitalized all-cause CAP	544 (2.56)	573 (2.64)	0.975 (0.866-1.098)	0.990 (0.880-1.114)	1.0 (-11.4 to 12.0)	.87	<.001



JAMA Network Open. 2026;9(5):e2610120. doi:10.1001/jamanetworkopen.2026.10120

Conclusions : NO DIfference

high-dose (HD) vaccine : safe and well tolerated[1-3]


Clinical Trial > J Infect Dis. 2009 Jul 15;200(2):172-80. doi: 10.1086/599790.

Randomized, double-blind controlled phase 3 trial comparing the immunogenicity of high-dose and standard-dose influenza vaccine in adults 65 years of age and older

Ann R Falsey [1], John J Treanor, Nadia Tornieporth, Jose Capellan, Geoffrey J Gorse

Affiliations + expand

PMID: 19508159 DOI: 10.1086/599790

Both vaccines were *well tolerated* in participants ≥60 years of age, with no safety concerns identified[3]


Human Vaccines & Immunotherapeutics

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/khvi20

Immunogenicity and safety of a quadrivalent high-dose inactivated influenza vaccine compared with a standard-dose quadrivalent influenza vaccine in healthy people aged 60 years or older: a randomized Phase III trial

Stephanie Pepin, Jean-François Nicolas, Henryk Szymanski, Isabel Leroux-Roels, Thomas Schaum, Marc Bonten, Giancarlo Icardi, Anju Shrestha, Cynthia Tabar & The QHD00011 study team

Solicited local reactions[1]	HD (n=2572) n (%)	SD (n=1260) n (%)
Pain	915 (36)	306 (24)
Erythema	384 (15)	136 (11)
Swelling	165 (6)	45 (4)

Reactogenicity of HD* was slightly increased as compared to SD†, but *no major difference* in intensity was observed[1,2]

Solicited local reactions[3]		HD‡ (n=772), %	SD§ (n=761), %
Pain	60-64 y	51.7	23.6
	≥65 y	39.4	18.3
Erythema (Grade 3)	60-64 y	2.1	0.3
	≥65 y	1.3	0.3

- Erythema, induration, swelling, and bruising at the injection site were recorded less frequently
- Most reactions were of Grade 1 or 2 intensity

*high-dose trivalent inactivated influenza vaccine; †Fluzone (Sanofi); ‡high-dose quadrivalent inactivated influenza vaccine (HD-IIV, Fluzone/Efluelda, Sanofi); ; §Influvac Tetra (Mylan)
HD: high-dose; SD: standard-dose.

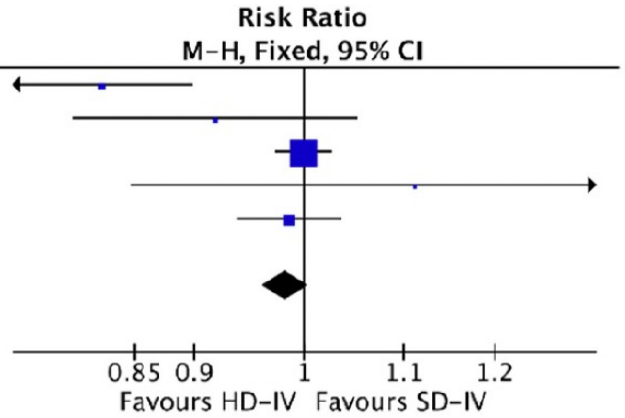
References: 1. Falsey A, et al. *J Infect Dis*. 2009;200:172-80. doi: 10.1086/599790 2. HD SmPC/Label 3. Pepin S, et al. *Hum Vaccin Immunother.* 2021;17(12):5475-5486. doi: 10.1080/21645515.2021.1983387.

Vaccinations – Adverse drug reactions

Study or Subgroup	HD-IV Events	HD-IV Total	SD-IV Events	SD-IV Total	Weight	Risk Ratio M-H, Fixed, 95% CI
DiazGranados 2015	858	15990	1042	15993	7.3%	0.82 [0.75, 0.90]
Johansen 2023	373	6248	405	6229	2.8%	0.92 [0.80, 1.05]
Johansen 2025	9814	166142	9804	165827	68.4%	1.00 [0.97, 1.03]
Palmu 2024	109	16549	98	16544	0.7%	1.11 [0.85, 1.46]
Pardo-Seco 2025	2953	67093	2983	66789	20.8%	0.99 [0.94, 1.04]
Total (95% CI)		**272022**		**271382**	**100.0%**	**0.98 [0.96, 1.00]**
Total events	14107		14332			

Heterogeneity: $Chi^2 = 18.79$, $df = 4$ ($P = 0.0009$); $I^2 = 79\%$

Test for overall effect: $Z = 1.58$ ($P = 0.12$)



Forest plot of any serious adverse event.

NO Differences

And NO differences regarding :

Cardiovascular SAE
Gastrointestinal SAE
Respiratory SAE
Infection-related SAE

already used in More than 50 millions of individuals
No alert

Khan *BW et al, Reviews in Medical Virology,* 2026

Grippe, Vaccin et trouble neurocognitif ?

Review

Influenza vaccination reduces dementia risk: A systematic review and meta-analysis

Nicola Veronese [a,*], Jacopo Demurtas [b], Lee Smith [c], Jean Pierre Michel [d], Mario Barbagallo [a], Francesco Bolzetta [e], Marianna Noale [f], Stefania Maggi [f]

Descriptive findings of the studies included.

Author, year	Country	Condition	Sample size	Mean age	Percentage of females	Definition of dementia	Follow-up length (years)	Adjustments
Lee et al., 2020	Taiwan	Periodontitis	112,036	> 50 years	51.6	ICD-9	13	Age, sex, medical conditions, medications
Liu et al., 2016	Taiwan	Chronic kidney disease	32,844	> 60 years	43.2	ICD-9	7	Age, sex, diabetes, hypertension, dyslipidemia, cerebrovascular diseases, parkinsonism, epilepsy, substance- and alcohol-use disorders, mood disorder, anxiety disorder, psychotic disorder, sleep disorder, level of urbanization, and monthly income in propensity score
Luo et al., 2020	Taiwan	COPD	19,848	71.9 (7.9)	42.2	ICD-9	11	COPD-related hospitalization, age, sex, diabetes, hypertension, dyslipidemia, cerebrovascular diseases, parkinsonism, epilepsy, substance use and alcohol disorder, mood disorder, anxiety disorder, psychotic disorder, sleep disorder, level of urbanization, monthly income
Verreault et al., 2001	Canada	General population	3682	> 65 years	60.0	DSM-IV	5	Age, sex, education, current smoking, regular alcohol consumption, family history of dementia, activities of daily living and instrumental activities of daily living, antecedents of chronic diseases and perceived health status.
Wiemken et al., 2021	USA	General population	123,747	75.5 (7.3)	38	ICD-9/ICD-10	7.5	None
Summary data			**292,157**	**75.5 (7.4)**	**46.8**	**ICD-9: three studies; ICD-9/ICD-10: one study; DSM-IV: one study**	**9**	

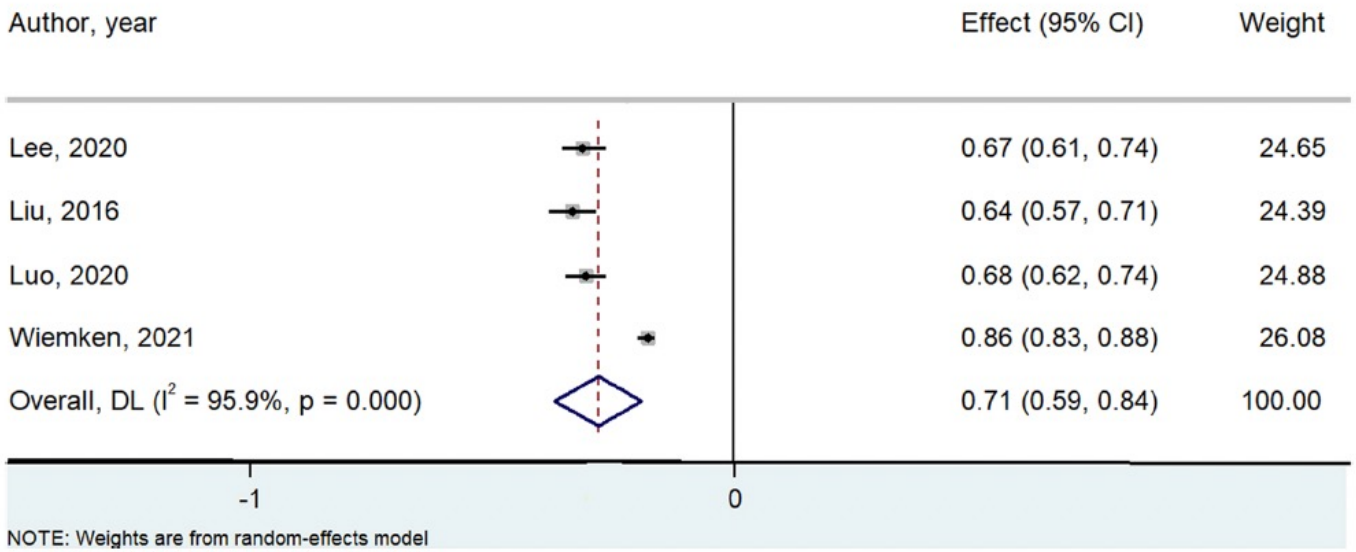


Fig. 2. Association between influenza vaccination and dementia incidence, adjusting for potential confounders.

Flu vaccine prevent flu-associated Disability

SD

PUGG derivated cohort (515 patients in 2017)
Comparison of 243 Influenza hospitalized old patients (> 80y) - vaccinated Versus non vaccinated

	Univariate Analysis				Multivariate analysis**		
	ADL post-hospitalisation		P	n	OR	Intervalle de Confiance à 95%	p
	Médiane	Moyenne					
CARDIAC decomp	3,0	3,3	0,50	12	-1,1	[-2,4 ; 0,2]	0,11
Without cardiac Decomp.	4,5	3,7		38	Réf		
DELIRIUM	2,5	2,8	0,10	11	-0,4	[-1,7 ; 0,8]	0,53
Without Delirium	4,5	3,8		39	Réf		
Charlson Index < 2	3,0	3,4	0,64	17	0,2	[-0,9 ; 1,3]	0,72
CharlsonIndex >=2	4,0	3,7		33	Réf		
Vaccinated	4,5	4,0	<0,01	40	1,8	[0,4 ; 3,2]	0,01
Non vaccinated	2,0	2,3		10	Réf		

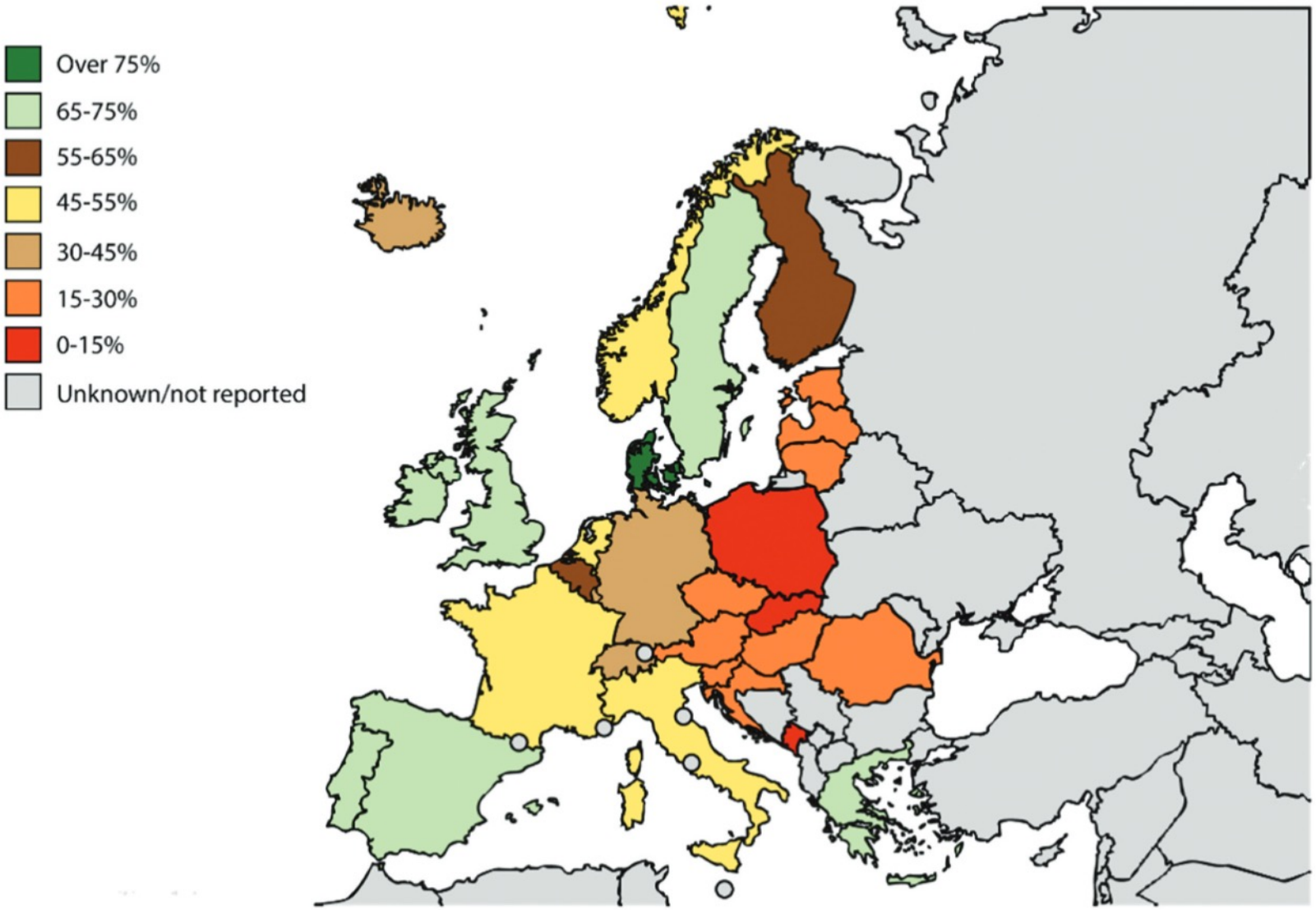
More delirium in the NON vaccinated group

No impact in mortality
No impact in readmission

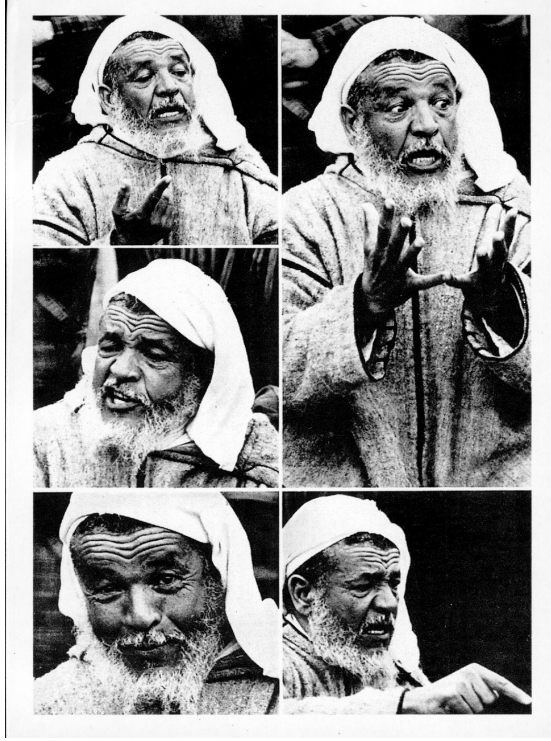
One protecting factor for Disability in influenza assocaited Hospitalisation : Flu vaccination

Bavelele P, Gavazzi G submitted

Vaccine Influenza Uptake



Merci de votre Attention



…raconter….

Save the date
Jeudi
4 décembre,Paris