

# BEST OF INFECTIO- GÉRIATRIE 2025

DR  
THIBAUT  
FRAISSE



GINGER

 Centre  
**HOSPITALIER**  
Alès • Cévennes

**GInGer**  
Groupe Infectio-Gériatrie



# Les Publications du GInGér

## GInGér 2025

- Recommandations Pneumonies d'inhalation et prévention des récurrences
- Recommandations Antibiothérapie sous cutanée (en cours)
- Recommandations IU masculines (en cours)
- Livre blanc sur les infections respiratoires à prévention vaccinale (SFGG, MCOOR)
- Étude Vaxisenior accepté JAMDA 11/12/2025 à 9h (N Weil et al.)

Veille bibliographique sur les études GInGer

~ 2025 (9)

[Characteristics of tuberculosis in elderly adults: A multicenter French study.](#) Trichet, M.; Lanoix, J.; Diamantis, S.; Forestier, E.; Fraisse, T.; Brochard-Libois, J.; et al. *Infectious Diseases Now*, 105226. December 2025.

[Evaluation of subcutaneous amoxicillin/clavulanic acid pharmacokinetics as an alternative to the intravenous route in older patients—the PhASAge Study.](#) Grégoire, N.; Mbarga, D.; Mirfendereski, H.; Stanke-Labesque, F.; Breilh, D.; Forestier, E.; et al. *Journal of Antimicrobial Chemotherapy*, dkaf381. November 2025.

[Pneumocystis pneumonia in older non-HIV-infected patients: a French, multicentre, retrospective, cohort study.](#) Barraud, A.; Larcher, R.; Gavazzi, G.; Fourmy, A.; Verdon, R.; Ancellin, S.; et al. on behalf GInGer (Groupe Infectio-Gériatrie) *Pneumonia*, 17(1): 34. December 2025.

[Antibiotics at life's end: key role in treating end-of-life pneumonia?](#) Fraisse, T.; Putot, A.; Forestier, E.; Gavazzi, G.; Vayne-Bossert, P.; Roubaud-Baudron, C.; and Prendki, V. *Expert Review of Respiratory Medicine*, 19(4): 279–286. April 2025.

[Aspiration pneumonia guidelines – Société de Pathologie Infectieuse de Langue Française 2025.](#) Diamantis, S.; Fraisse, T.; Bonnet, E.; Prendki, V.; Andréjak, C.; Auquier, M.; et al. *Infectious Diseases Now*, 55(5): 105081. August 2025.

[Prevention of aspiration pneumonia recurrences.](#) Fraisse, T.; Prendki, V.; Putot, A.; Garcia-Carmona, C.; Perrin, M.; Chebib, N et al. *Infectious Diseases Now*, 55(6): 105102. September 2025.

[Antibiotic susceptibility according to age of clinical strains from hospital respiratory samples: A nationwide study.](#) Putot, A.; Couve-Deacon, E.; Ploy, M.; Fraisse, T.; Lanoix, J.; Prendki, V.; and Diamantis, S. *Infectious Diseases Now*, 55(7): 105133. November 2025.

[National survey on aspiration pneumonia in elderly hospitalized or institutionalized patients in France in 2023.](#) Vieilledent, L.; Fraisse, T.; Gavazzi, G.; Baudron, C.; Diamantis, S.; Gallien, S.; et al. *Infectious Diseases Now*, 55(7): 105113. November 2025.

[Pharmacokinetics of Subcutaneous and Intravenous Ceftriaxone in an Older Population: The PhASAge Study.](#) Roubaud-Baudron, C.; Fauchon, H.; Stanke-Labesque, F.; Paccalin, M.; Breilh, D.; Grégoire, et al. *Open Forum Infectious Diseases*, 12(6): ofaf313. May 2025



# Résistances bactériennes



# Résistances bactériennes

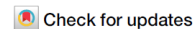
npj | antimicrobials & resistance

Article



<https://doi.org/10.1038/s44259-025-00144-w>

## **The effect of commonly used non-antibiotic medications on antimicrobial resistance development in *Escherichia coli***



Hanbiao Chen<sup>1</sup>, Sylvia A. Sapula<sup>1</sup>, John Turnidge<sup>2</sup> & Henrietta Venter<sup>1</sup> ✉

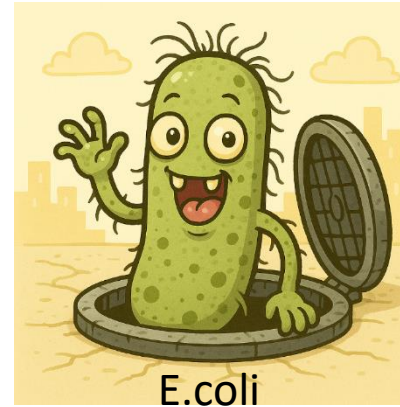
- Dans la lutte contre l'antibio-résistance le bon usage des antibiotiques est un élément clé
- Un certain nombre de médicaments non antibiotiques contribuent à l'augmentation des résistances bactériennes
  - Modification du microbiote (IPP ...)
  - Effet direct antibactérien des statines
  - Effet favorisant la transformation bactérienne et les échanges génétiques plasmidiques (AINS)
  - Effet sur mutations (ISRS)
  - Sélection de pompes à efflux multi-drogues
- Ces traitements représentent 95 % des molécules vs AB

# Résistances bactériennes

9 Molécules à usage « fréquent » chez le patient âgé

Diclofenac\*  
Ibuprofène\*  
Pseudoéphédrine\*  
Tramadol\*

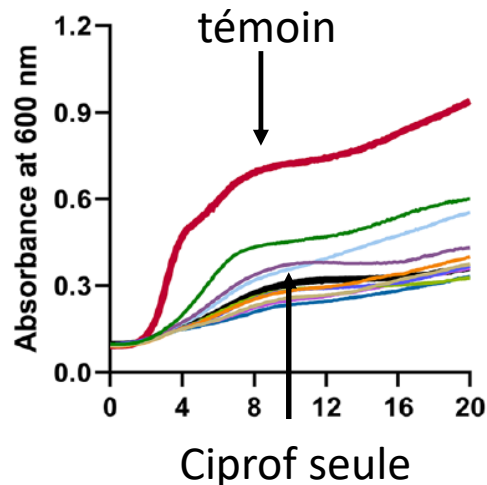
Atorvastatine  
Acétaminophène  
Furosémide  
Metformine  
Témozépam



CIPROFLOXACINE

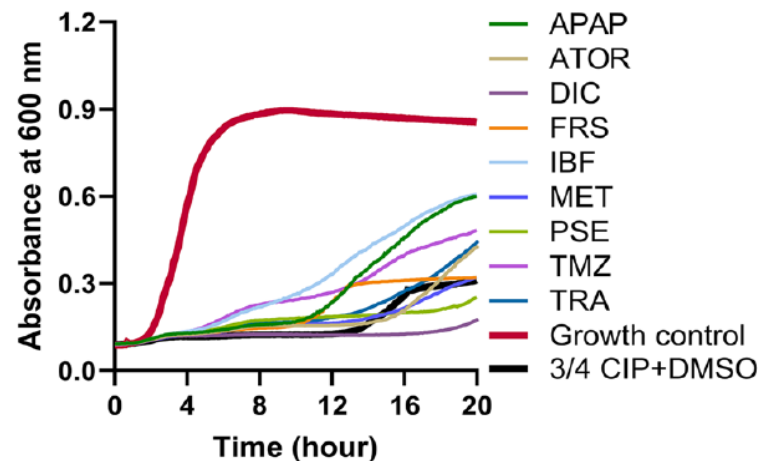
(C)

E coli BW25113



(D)

E coli 6146 (résident EHPAD)

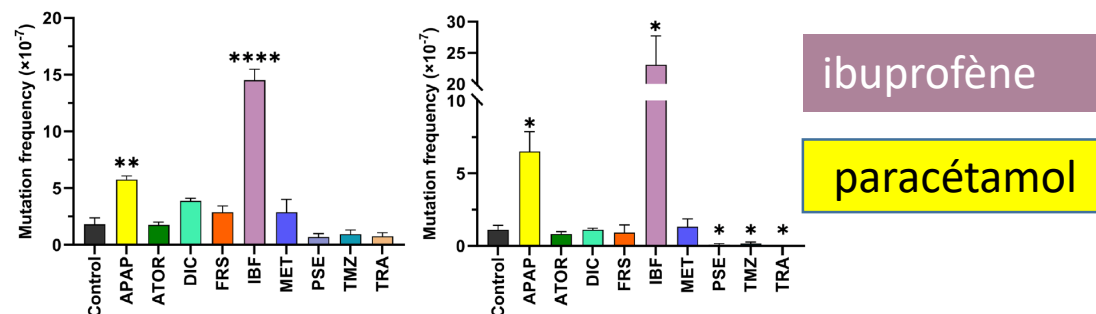


En présence d'ibuprofène, diclofenac ou  
acétaminophène  
La croissance est + rapide et +  
importante

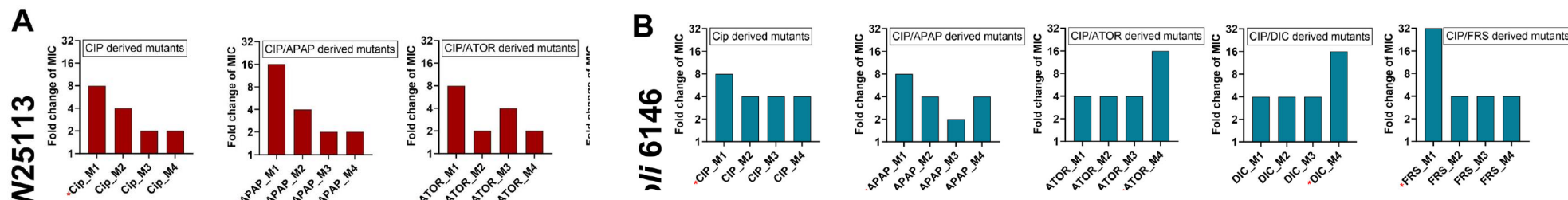
# Résistances bactériennes

## 1- L'exposition aux MNAB induit des mutations chez E coli

Fréquence de mutation



## 2- L'exposition aux MNAB induit des mutations de R à ciprofloxacine

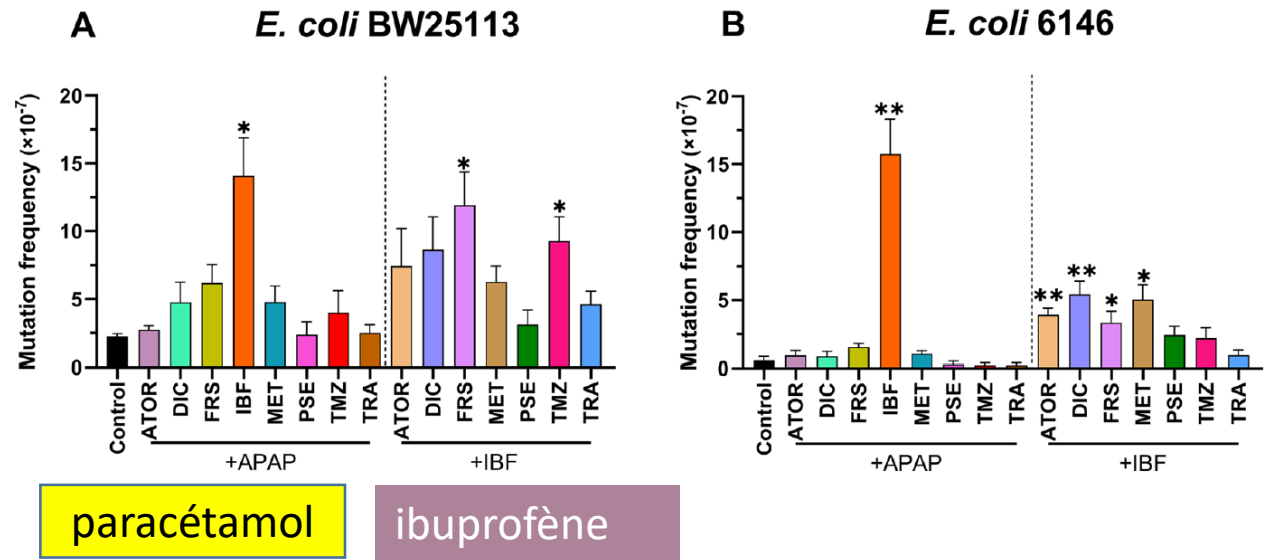
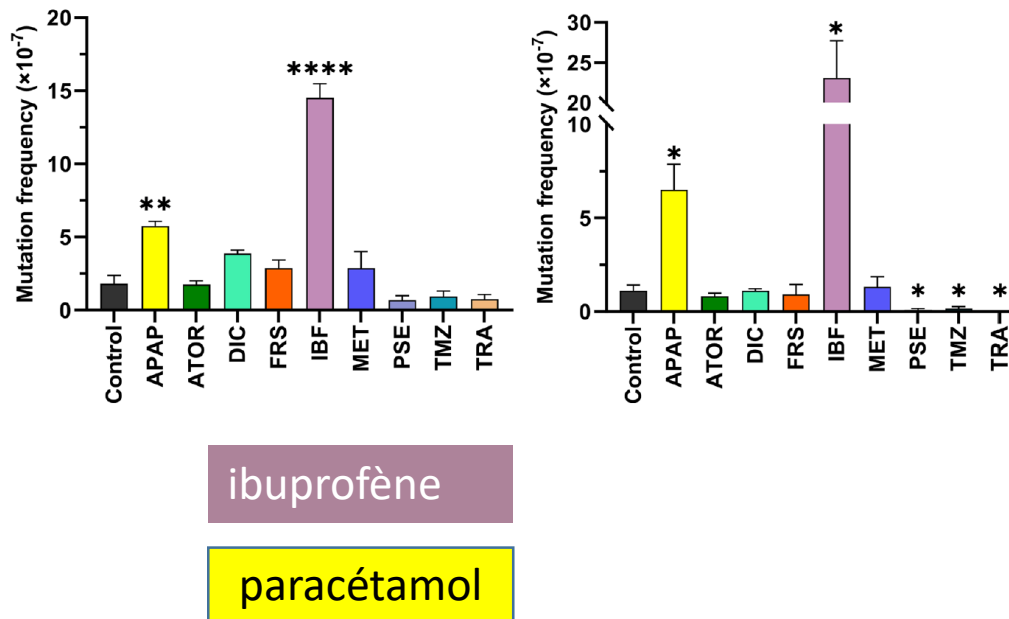


## 3- L'exposition aux MNAB induit des résistances multiples

Parmi les mutants sélectionnés, certains avaient R ceftazidime, cefepime, minocycline

# Résistances bactériennes

## 4- L' association de 2 MNAB se potentialise



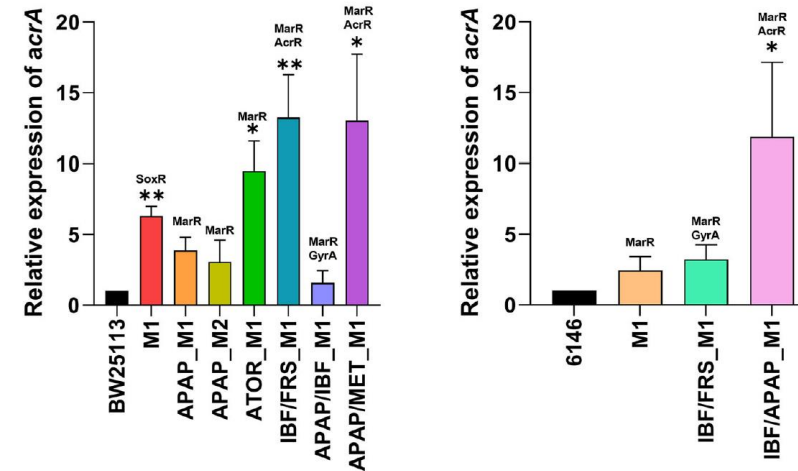
Si on met acetaminophene ou ibuprofene+ 1 autre MNAB on potentialise les mutations

# Résistances bactériennes

## Séquencage des mutants

Mutation  
de la cible  
(GyrA)

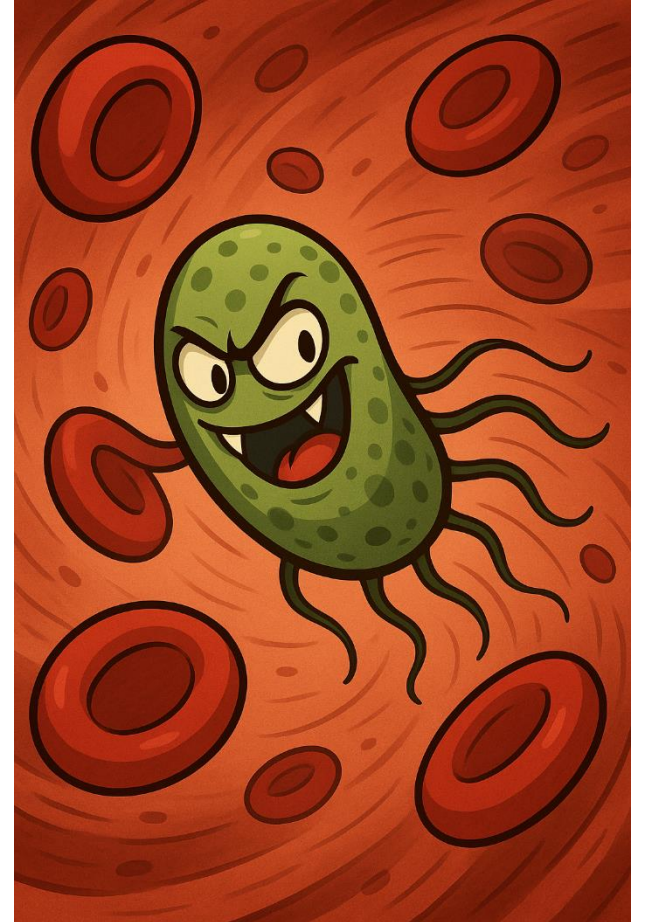
Mutation gène  
régulateur pompe  
d'efflux (acr A..;)



- Les médicaments non antibiotiques (en particulier acétaminophène, les AINS, et le furosémide) ont un impact sur la résistance aux FQ en particulier par les pompes d'efflux
- Les pompes d'efflux sont un mécanisme de résistance non spécifique de la bactérie (stress) et leur hyperexpression est associée à une moins bonne réparation de l'ADN (favorise les résistances)



# Sepsis et bactériémies



# Sepsis

Un programme transversal = Parcours de soins

- Facteurs de risque de sepsis (âge, défaillances d'organe, fragilité, cancers et ttt immunosuppresseurs, diabète, dénutrition, maladie de système...)
- Dépister le sepsis face à une infection

Rechercher chez un adulte, la présence de 3 ou plus des 6 variables cliniques

- a. Age >65 ans
- b. Température >38°C
- c. Pression artérielle systolique  $\leq 110$  mmHg
- d. Fréquence cardiaque >110/min
- e. Saturation périphérique en O<sub>2</sub>  $\leq 95\%$
- f. Troubles des fonctions supérieures

- Agir sans délai en ville
- Traiter (surviving sepsis campaign)
  - Accès veineux et Remplissage par cristalloïdes
  - Prélever des hémocultures et débuter antibiothérapie (3h, 1h en cas de choc)
  - Surveillance continue?
  - Mobiliser passif, verticaliser, faire marcher.....
- Après l'épisode: rééduquer, suivi
- Prévention: vaccin et mesures d'hygiène



**RECOMMANDER**  
LES BONNES PRATIQUES

**RECOMMANDATION**

Prise en charge du sepsis du nouveau-né, de l'enfant et de l'adulte :  
recommandations pour un parcours de soins intégré

# Sepsis présentation et mortalité

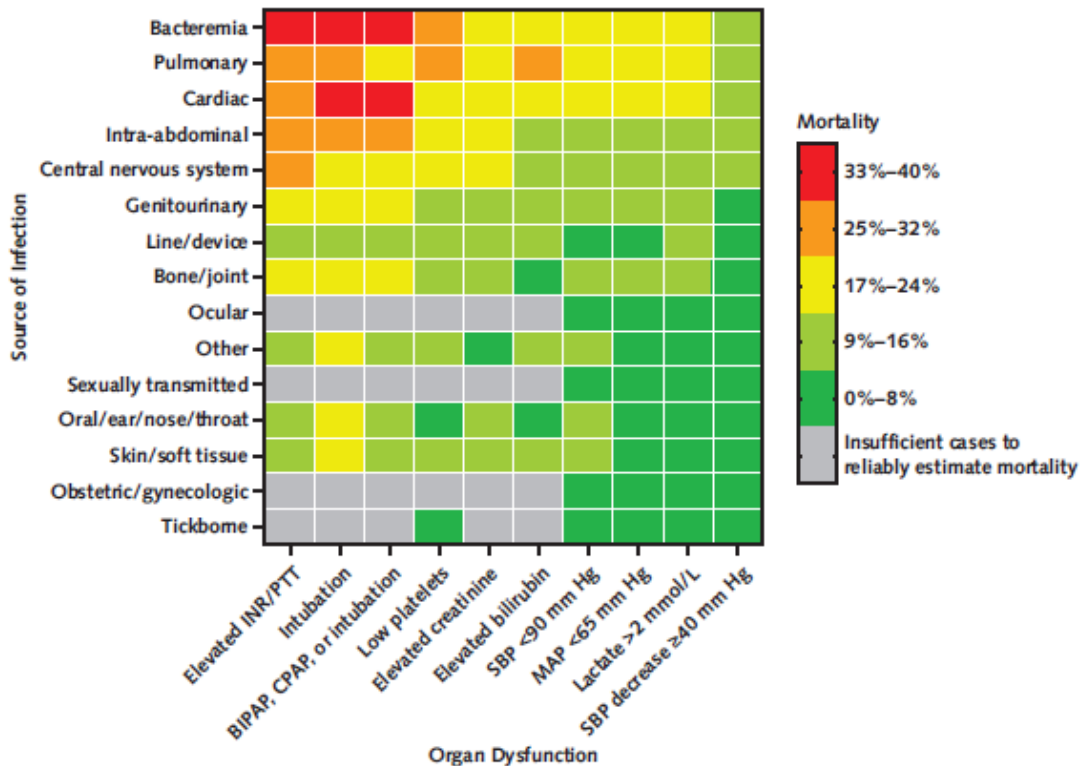
Annals of Internal Medicine

OBSERVATIONS: BRIEF RESEARCH REPORTS

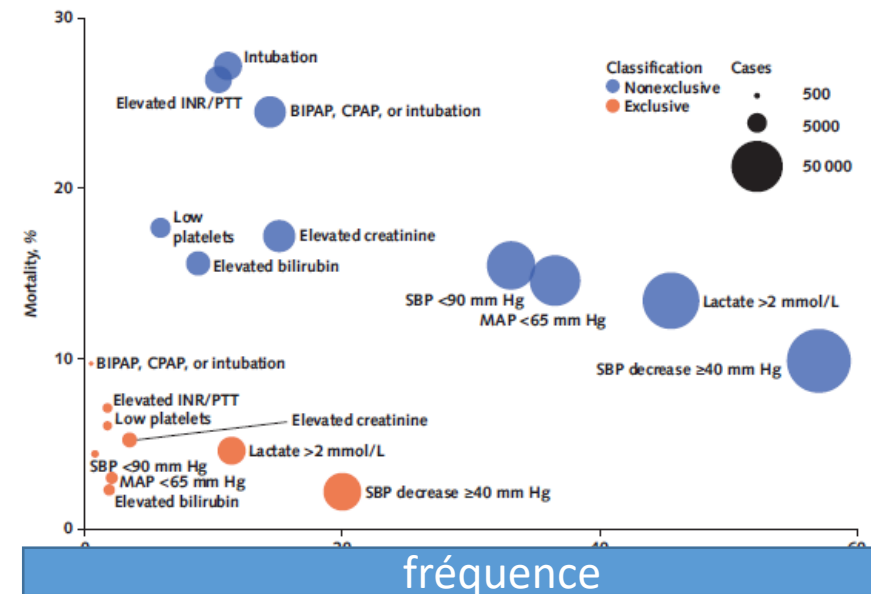
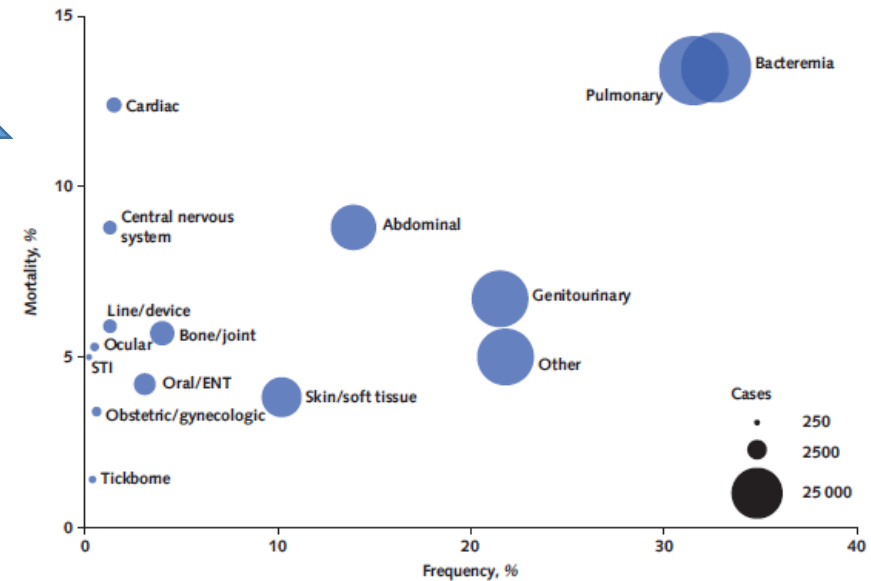
Heterogeneity of Sepsis Presentations and Mortality Rates

Bielberg et al, 2024

75 000 sepsis  
Age moyen 67 ans



m o r t a l i t é



# Atypie sémiologique



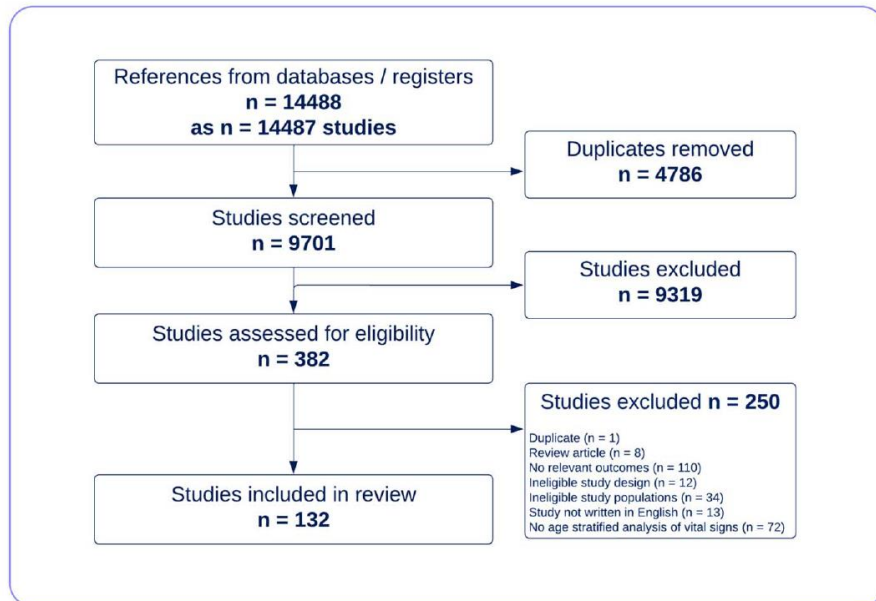
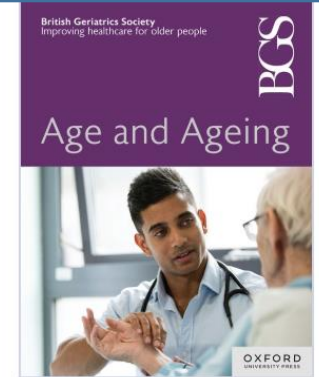


# clinique Infections bactériennes fn âge

## SYSTEMATIC REVIEW

### Is age associated with different vital signs in adults presenting to hospital with bacterial infection? A systematic review and meta-analysis

PHOEBE TUPPER<sup>1</sup>, OLIVER REDFERN<sup>1</sup> , CHARLOTTE H. HARRISON<sup>1</sup>, STEPHEN GERRY<sup>2</sup> ,  
CHRISTOPHER BIGGS<sup>1</sup>, BETHANY WALKER<sup>1</sup>, PETER WATKINSON<sup>1,3,4</sup>



### Patients Hospitalisés pour infection bactérienne suspectée ou prouvée

(Poumon, urine, bactériémie, peau et T mou, endocardite, intra abdominal, méningite)



- 132 études
- 110.475 patients
  - ✓ Données T° (114), FC (64), FR (43)
  - ✓ Inf clinique (67), bact (41)

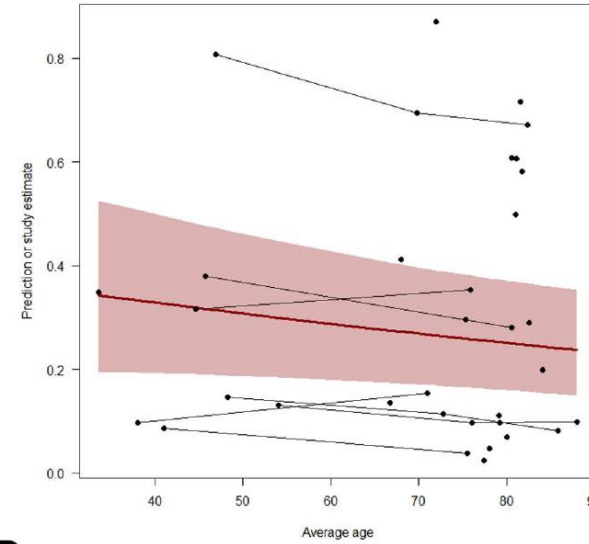
# clinique Infections bactériennes fn âge



**37762 Patients**  
**Moins de tachycardie**  
**FC moins rapide (-5bpm)**

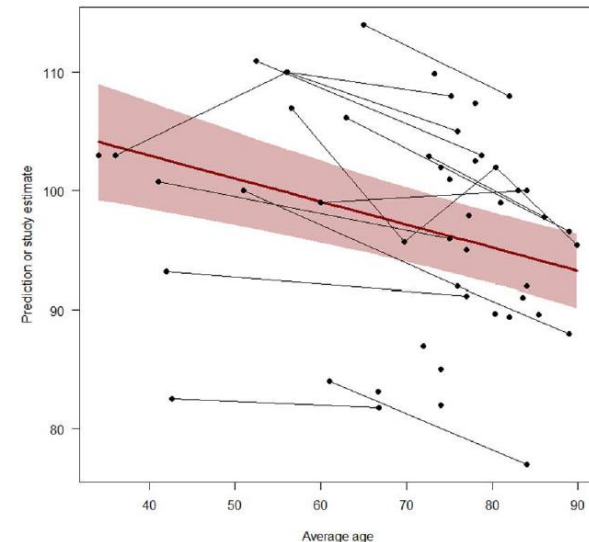


**Pas de différence selon**  
**âge pour survenue**  
**d'hypotension.**  
**TAS plus élevée chez SA**



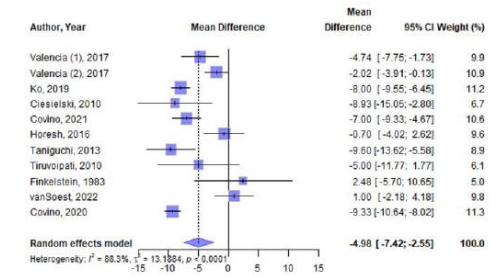
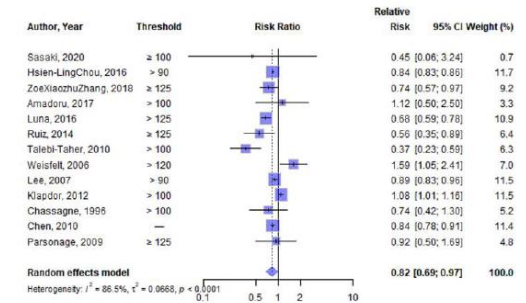
**B**

HR



**D**

**FC >90 à 125**

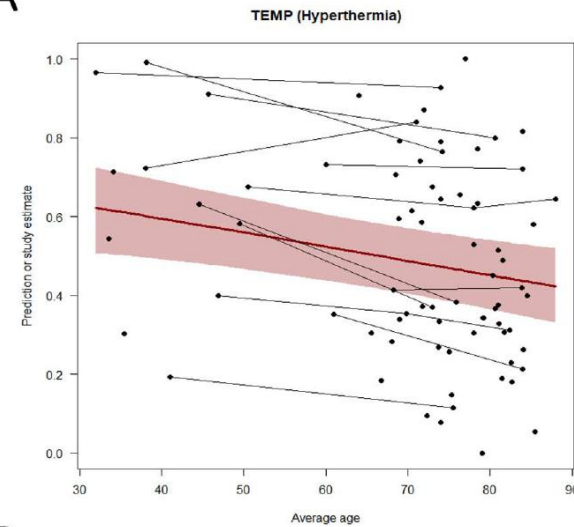


# clinique Infections bactériennes fn âge

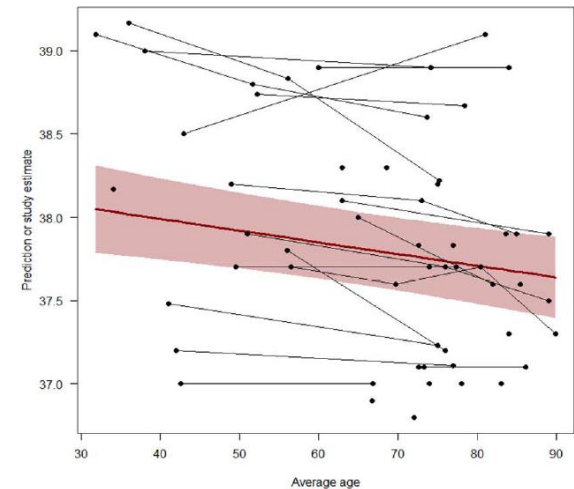


**38696 Patients**  
**Moins de fièvre**  
**T° moins élevée (-0,14°C)**  
**Hypothermie pas plus**  
**fréquente chez S âgé**

**A**

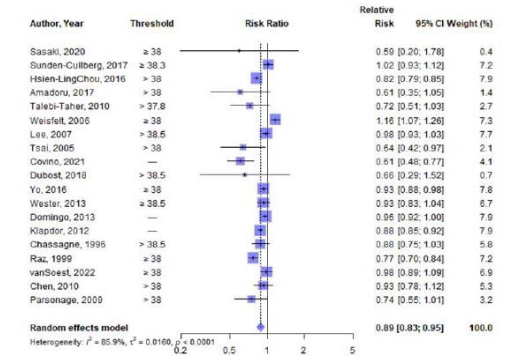


**B**

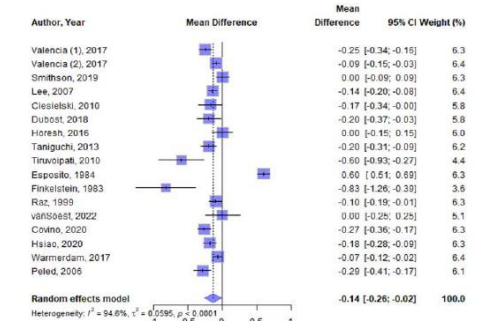


**C**

**Seuil fièvre 37,8 à 38,5°**



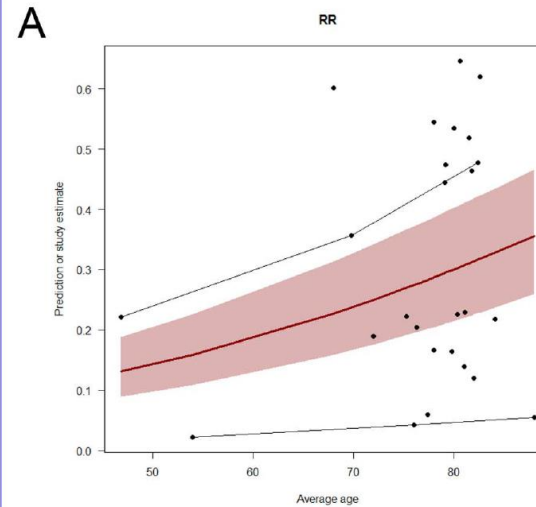
**D**



# clinique Infections bactériennes fn âge

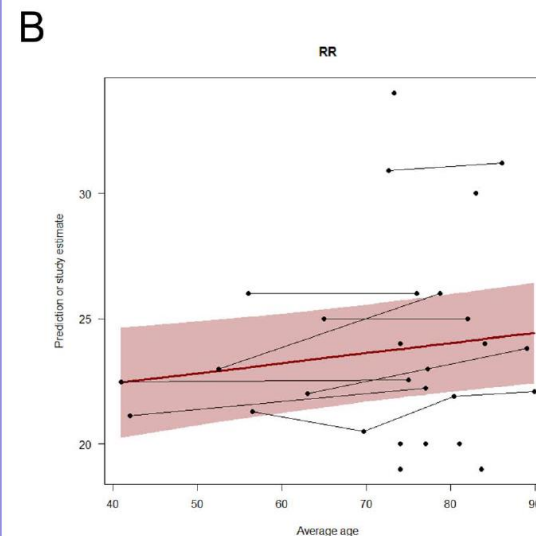
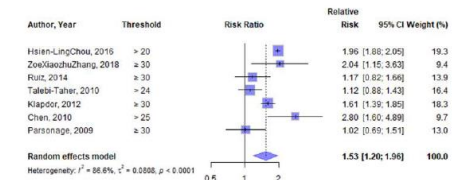


**31748 Patients**  
**Plus de tachypnée**  
**FR plus rapide (+1cpm)**  
**Pas de différence de SaO2**



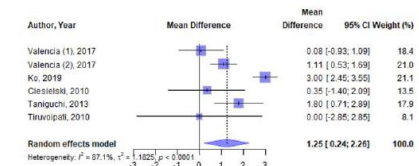
**C**

Fqce tachypnée



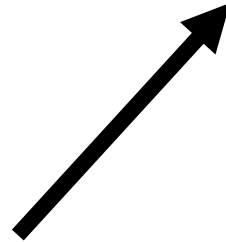
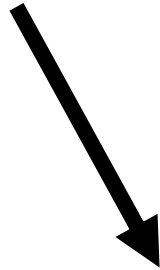
**D**

FRespiratoire





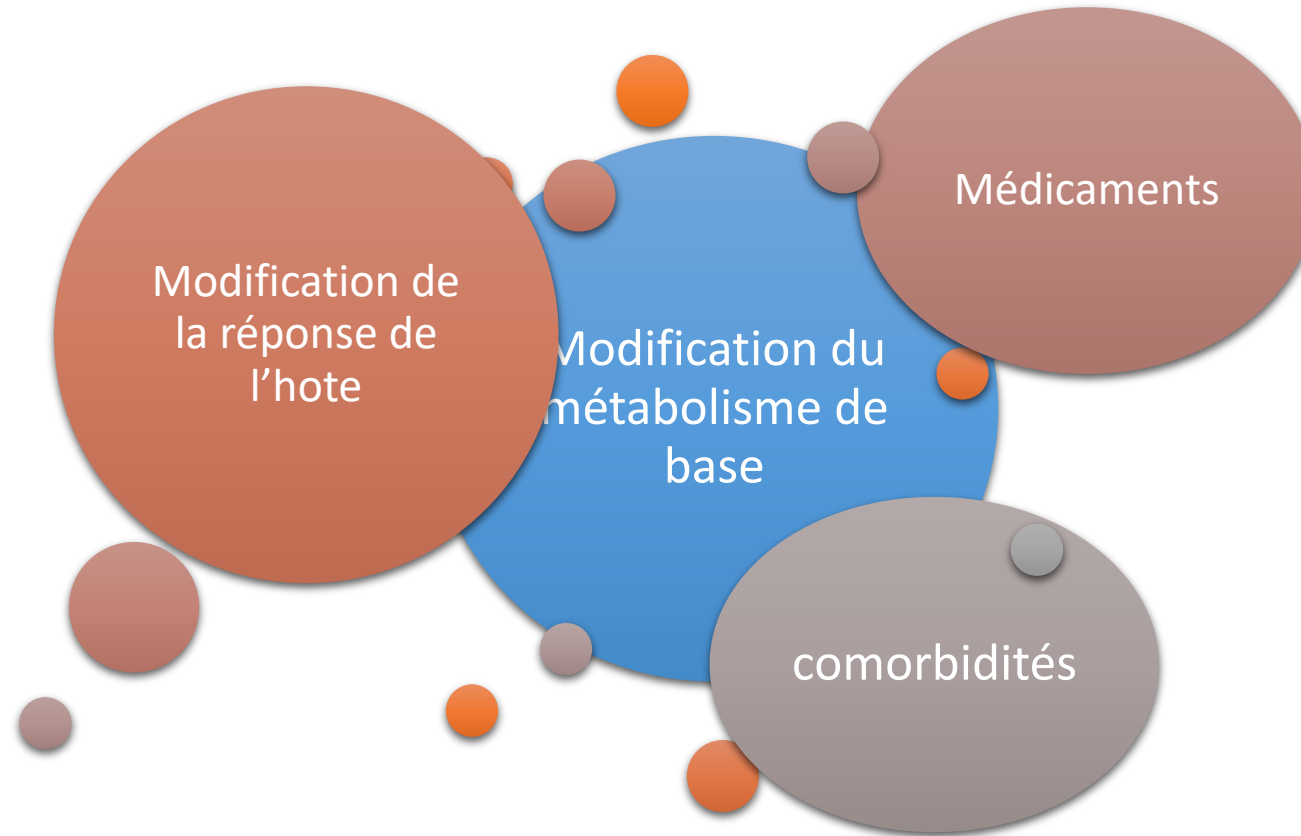
# clinique Infections bactériennes fn âge



Pensez à mesurer la  
Fréquence respiratoire

- **Grande hétérogénéité selon les études (ancienneté, type d'inf, documentation...)**
  - ⇒ analyse de sous groupe par type d'infection, selon documentation microbiologique... tendance retrouvée mais NS
- **De nombreux biais dans les études**  
129/132 à haut risque (sélection des patients, mesure des constantes rétrospective...)
- **Des différences statistiques mais faibles cliniquement (0,14°C, 1cpm)**

# clinique Infections bactériennes fn âge



La fragilité et les comorbidités=> Sd gériatrique  
hospitalisation plus précoce chez lesP âgés

vaccins



# Couverture vaccinale



Date de publication : 18 juillet 2025

ÉDITION NATIONALE

**Couvertures vaccinales contre la grippe  
et la Covid-19 des résidents et des professionnels  
en établissements sociaux et médico-sociaux (ESMS)**

**Résultats clés**

Enquête 2600 EHAD (35%) 2024-2025

	grippe	COVID
Résidents EHPAD	82,7%	63,6%
Personnel	21%	4,3%
AS/pers d service/ASH	17%	3,2%
Médecins/pharmacien	56%	30%

Tableau 6. Raisons pour lesquelles le nombre d'actions mises en place pour promouvoir la vaccination antigrippale a baissé ou que peu d'actions sont mises en place, saison 2024-2025, France (n= 482)

Raisons	Proportions d'Ehpad répondants	
	%	IC95%
Forte réticence à la vaccination au sein de l'équipe	71,4	67,1 - 75,4
Turn over des équipes	26,6	22,7 - 30,7
Impression que les actions ne sont pas efficaces	19,1	15,7 - 22,9
Moins de temps	19,1	15,7 - 22,9
Manque de personnel	17,0	13,8 - 20,7
Manque de motivation	13,3	10,4 - 16,6
Absence de médecin ou d'IDE coordonnateur	2,7	1,4 - 4,6

Des couvertures vaccinales grippe/COVID inférieures aux objectifs  
Tendance à la baisse se confirme surtout COVID  
Chez les soignants (-16% vs 2007)  
Stabilité de la vaccination antigrippale des résidents



# Couverture vaccinale



Accueil > Économie et Société

## Grippe : l'Assemblée adopte la vaccination obligatoire des résidents d'Ehpad et des soignants

Alors que la mesure avait été rejetée en première lecture dans le cadre de l'examen du budget de la Sécurité sociale, les députés ont adopté la vaccination obligatoire des résidents d'Ehpad et des soignants exerçant à titre libéral, ce vendredi 5 décembre.



*DGS-Urgent n°2025-27 : Mise à disposition de doses complémentaires pour la campagne de vaccination contre la grippe saisonnière 2025-2026 et rappel des modalités d'immunisation du nouveau-né contre le VRS*

Mesdames, Messieurs,

Compte tenu de l'évolution de la situation épidémique, deux points sont portés à votre attention :

### 1. Concernant la grippe saisonnière

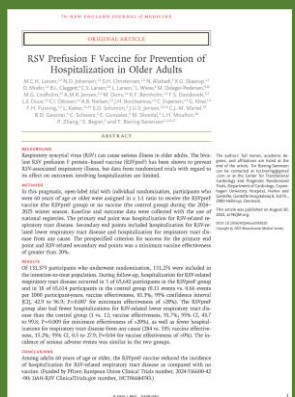
Grâce à votre engagement, **plus de 10,3 millions de patients ont déjà été vaccinés contre le virus de la grippe en ville depuis octobre.** Cette dynamique est essentielle pour atteindre les objectifs de couverture vaccinale et protéger les populations à risque.

Afin de maintenir la tendance, nous invitons les professionnels qui n'auraient plus de stocks suffisants à s'approvisionner sans attendre auprès de leur grossiste-répartiteur ou directement auprès du laboratoire.

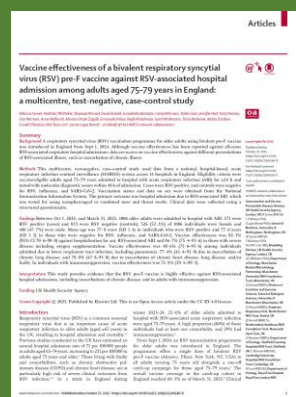
# Efficacité vaccinale VRS



**JAMA 2025**  
**Vaccins VRS**  
**Hospitalisations**  
**D surie et al**



**NEJM 2025**  
**Vaccin VRS (Abrysvo)**  
**Hospitalisations**  
**MCH Lassen et al**



**Lancet Inf dis 25**  
**Vaccin VRS (Abrysvo)**  
**Hospitalisations**  
**R Symes et al**

Étude observationnelle cas  
témoin > 60 ans

N=6951 (821 VRS+ cas)  
Hospitalisations  
15% de vaccinés

EV 2 saisons **58%**  
S1 69%,  
S2 48%

EV plus faible ID et patho CV  
EV idem Arexvy vs Abrysvo

Étude CDC

Essai clinique randomisé  
pragmatique (phase IV)

**131 276 (ITT) (65642vs65634)**  
Hospitalisations liées VRS  
1 saison 2024-2025

**EV 83 %, (1 saison)**  
EV Hospit cardio respi 10% (cf sous  
etude JAMA 2025, Lassen et al)

EIG similaires entre les 2 groupes  
5 attribués au vaccin (PF, malaise...)

consortium danois, **support PFIZER**

Étude observationnelle rétrospective  
cas/témoins 75-79 ans

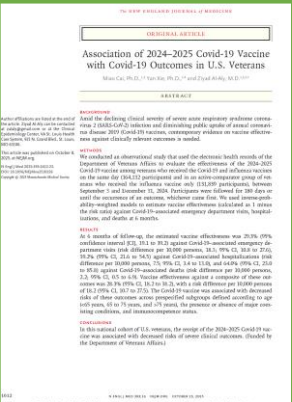
N= 1006 (173 cas H VRS+)  
Hospitalisation  
Taux de vaccination 32%

**EV (1 saison) 82%**  
EV forme sévère (O2) 86,7%  
EV exacerbation comorb; 78%

EV 73% ID ou patho CV 77%

UK Health Security Agency

# Efficacité vaccinale COVID



## NEJM 2025 Vaccin COVID Cs Urgences Hospitalisations M Cai et al

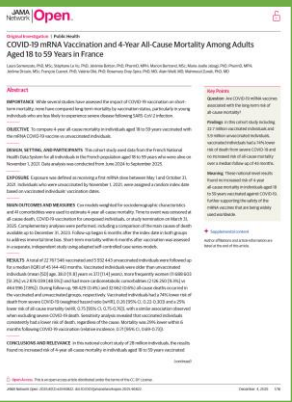
Cohorte observationnelle 2024-25, vétérans US

164.132 vaccin grippe+covid  
131.839 vaccin grippe

EV Passage urgences 29%  
EV hospit 39%  
EV décès 64%  
Confirmé en sous groupe

Biais sélection (vétérans)  
Même Variant moins sévère

Département des vétérans



## JAMA network 2025 Vaccins COVID Mortalité Long terme L Semenzato et al

Cohorte nationale (18-59 ans),  
Existe-t-il surmortalité à long terme lié au vaccin?

22,7 Millions Exposé vaccin ARN  
5,7 Millions Non vacciné (1/11/20)

Vaccinés+ âgés, + comorbidés, + femmes, - défavorisés  
  
Mortalité toute cause -25% (vaccin), H COVID -74%  
Effet sur mortalité persiste Covid exclus (K, CV...)  
Possible biais de comportement/social

Mortalité à 6 mois -29% (COVID +++)  
Pas de surmortalité à long terme voir réduction

EPI-PHARE (ANSM-CNAM)



## Lancet Inf dis 2025 Vaccin Covid Hospitalisation CH Hansen et al

Cohorte danoise nationale sur registre  
Tous les danois > 65 ans (1/10/24)

894 560 participants  
Couverture vaccinale 91,7% ( dans les 4 mois)

88,8% BNT162b2.JN.1 et  
11,2% mRNA1273JN.1  
  
Vaccin BNT 70% Hospit, 76% décès  
Vaccin mRNA 84,9% Hospit, 95,8% décès  
Pop non comparable (mRNA + jeune,-com)

EV sur variants KP31, XEC  
Pas de baisse de protection à 4 mois

Registres nationaux danois

[illegible]

Épidémie précoce, longue et intense  
29 000 H, 14000 décès,

**EV 47%[26-63]**  
EV (<65 ans) 59% [28-73]  
EV (>65 ans) 38% [3-60]

Santé publique France

**466 000 patients**  
233000 HD vs 233000 SD  
EIG identique ( $\approx 16000$ )

↓8,8% hospitalisations pour grippe ou  
pneumonie  
-31,9% H pour grippe confirmée  
**Pas de ≠ mortalité** toute cause,

**SANOFI**

Inf ambu 2122 patients  
Inf hosp 42752 patients (61%exclus)  
**Couverture 15-29%**

Circulation AH1N1 pdm09 59%  
A H2N2 27%

EV ambu 50%, **H 49%** (H1>H3)  
EV âgés 38%, comorbides 52%

Réseau surveillance GISAID, OMS, CDC



# Efficacité vaccinale

## SPECIAL ARTICLE

### Updated Evidence for Covid-19, RSV, and Influenza Vaccines for 2025–2026

J. Scott,<sup>1</sup> M.S. Abers,<sup>2</sup> H.K. Marwah,<sup>3</sup> N.C. McCann,<sup>4</sup> E.A. Meyerowitz,<sup>2</sup> A. Richterman,<sup>5</sup> D.F. Fleming,<sup>6</sup> E.J. Holmes,<sup>6</sup> L.E. Moat,<sup>6</sup> S.G. Redepennig,<sup>6</sup> E.A. Smith,<sup>6</sup> C.J. Stoddart,<sup>6</sup> M.E. Sundaram,<sup>7</sup> A.K. Ulrich,<sup>8</sup> C. Alba,<sup>8</sup> C.J. Anderson,<sup>8</sup> M.K. Arpey,<sup>6</sup> E. Borre,<sup>9</sup> J. Ladines-Lim,<sup>5</sup> A.J. Mehr,<sup>6</sup> K. Rich,<sup>9</sup> C. Watts,<sup>5</sup> N.E. Basta,<sup>10</sup> J. Jarolimova,<sup>11</sup> R.P. Walensky,<sup>12</sup> and C.M. Dugdale<sup>13</sup>

## ABSTRACT

### BACKGROUND

Changes in the vaccine advisory process in the United States have disrupted immunization guidance, which reinforces the need for independent evidence review to inform decisions regarding immunization for respiratory viruses during the 2025–2026 season.

### METHODS

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### RESULTS

Of 17,263 identified references, 511 studies met the inclusion criteria. Covid-19 mRNA vaccines against the XBB.1.5 subvariant had pooled vaccine effectiveness against hospitalization of 46% (95% confidence interval [CI], 34 to 55; from cohort studies) and 50% (95% CI, 43 to 57; from case–control studies) among adults and 37% (95% CI, 29 to 44) among immunocompromised adults. In a case–control study, vaccines against the KP.2 subvariant showed an effectiveness of 68% (95% CI, 42 to 82). Maternal RSV vaccination (for infant protection), nirsevimab for infants, and RSV vaccines in adults who were 60 years of age or older showed vaccine effectiveness of 68% or more against hospitalization. Influenza vaccination had a pooled vaccine effectiveness of 48% (95% CI, 39 to 55) in adults between the ages of 18 and 64 years and 67% (95% CI, 58 to 75) in children against hospitalization. Safety profiles were consistent with previous evaluations. The diagnosis of myocarditis associated with Covid-19 vaccines occurred at rates of 1.3 to 3.1 per 100,000 doses in male adolescents, with lower risk associated with longer dosing intervals. The RSVpreF vaccine was associated with 18.2 excess cases of Guillain–Barré syndrome per million doses in older adults; a significant association with preterm birth was not observed when the vaccine was administered at 32 to 36 weeks’ gestation.

### CONCLUSIONS

Ongoing peer-reviewed evidence supports the safety and effectiveness of immunizations against Covid-19, RSV, and influenza during the 2025–2026 season. (Funded by the Center for Infectious Disease Research and Policy and the Alumbra Innovations Foundation.)

The authors’ full names, academic degrees, and affiliations are listed at the end of the article. Jake Scott can be contacted at [scottja@stanford.edu](mailto:scottja@stanford.edu) or at the Division of Infectious Diseases and Geographic Medicine, Stanford University School of Medicine, 300 Pasteur Dr., Stanford, CA 94305.

Jake Scott, Michael S. Abers, Harleen K. Marwah, Nicole C. McCann, Eric A. Meyerowitz, and Aaron Richterman and Nicole E. Basta, Jana Jarolimova, Rochelle P. Walensky, and Caitlin M. Dugdale contributed equally to this article.

This article was published on October 29, 2025, at [NEJM.org](https://www.nejm.org).

DOI: 10.1056/NEJMsa2514268

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# Efficacité vaccinale

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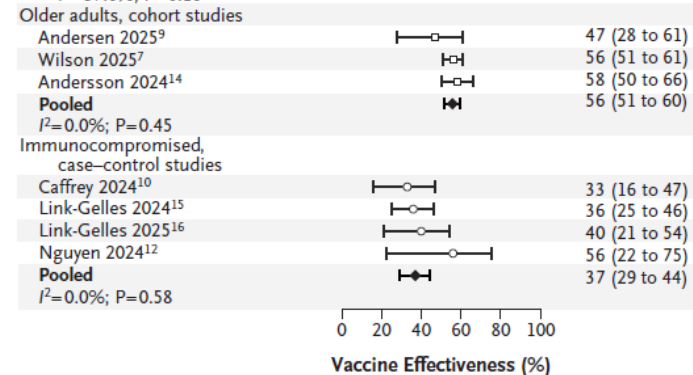
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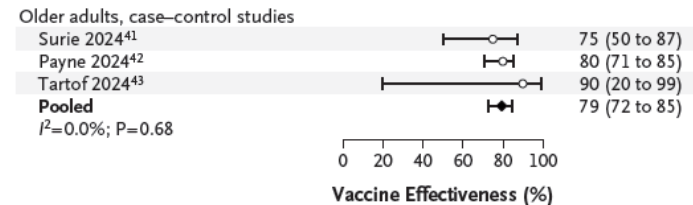
This article was published on October 29, 2025, at [NEJM.org](https://www.nejm.org).

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**Figure 1. Meta-Analysis of Vaccine Effectiveness against Hospitalization for Covid-19.<sup>7-16</sup>**

Forest plots show population-specific vaccine effectiveness against hospitalization for coronavirus disease 2019 (Covid-19) on the basis of case-control and cohort studies. Circles indicate case-control studies, and squares indicate cohort studies; diamonds represent pooled estimates. Heterogeneity ( $I^2$  and  $P$  value) are displayed for pooled data at the bottom of each population analysis. In sensitivity analyses, studies that were deemed to have a moderate or high risk of bias were excluded; findings were similar to the primary results (Fig. S7 in the Supplementary Appendix).



**Figure 2. Meta-Analysis of Vaccine Effectiveness against Hospitalization for RSV.<sup>26-43</sup>**

Forest plots show population-specific vaccine effectiveness against hospitalization for respiratory syncytial virus (RSV) on the basis of case-control and cohort studies.

### Vaccin ARN COVID Sujet âgé

-56% hospitalisations

-58% décès (65-79 ans)

- 48% décès (80 ans)

### Vaccins VRS Sujet âgé

-79% hospitalisation

# Efficacité vaccinale

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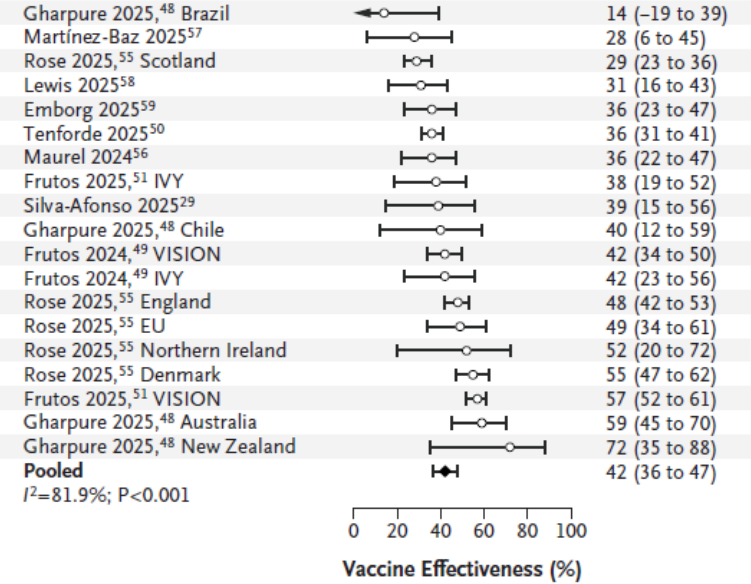
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This article was published on October 29, 2025, at [NEJM.org](https://www.nejm.org).

DOI: 10.1056/NEJMsa2514268  
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#### Older adults, case–control studies



**Figure 3. Meta-Analysis of Vaccine Effectiveness against Hospitalization for Influenza.<sup>48–59</sup>**

Forest plots show population-specific vaccine effectiveness against hospitalization for influenza on the basis of case–control and cohort studies.

Vaccin grippe Sujet âgé  
-42% hospitalisations

# Sécurité vaccinale

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Vaccin COVID pas de signal spécifique en particulier sur les myocardites

Vaccin VRS

RSV			
Myocardial infarction			
Older adults			
RSVpreF	1	Walsh 2025 <sup>116</sup>	OR, 1.11 (0.72–1.71)
Guillain–Barré syndrome			
Older adults			
RSVpreF	1	Fry 2025 <sup>46</sup>	IRR, 2.4 (1.5–4.0)
RSVPreF3	1	Fry 2025 <sup>46</sup>	IRR, 1.5 (0.9–2.2)

Incidence absolue : 18,2 cas / million

Vaccin grippe: pas de signal SGB, AVC, IDM

Pour conclure

across populations. These findings underscore the enduring value of immunization against respiratory viruses as a cornerstone of preventive care and support the feasibility of maintaining rigorous, evidence-based guidance during periods of institutional disruption.



# Vaccins et troubles cognitifs

## Démence et vaccin contre le zona

Vaccin recombinant antizosterien

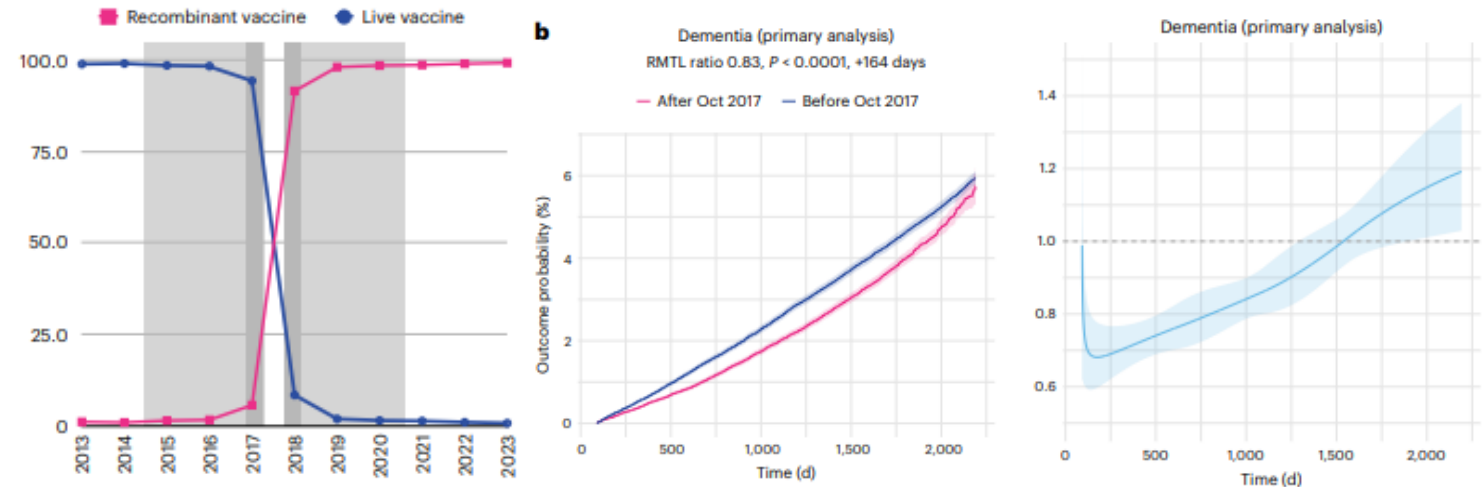
Analyse des dossiers électroniques US

Transition rapide vaccin vivant/recombinant

103000 vaccinés avec vaccin recombinant (95%) et 103000 avec score de propension vacciné avec vaccin vivant (95%)

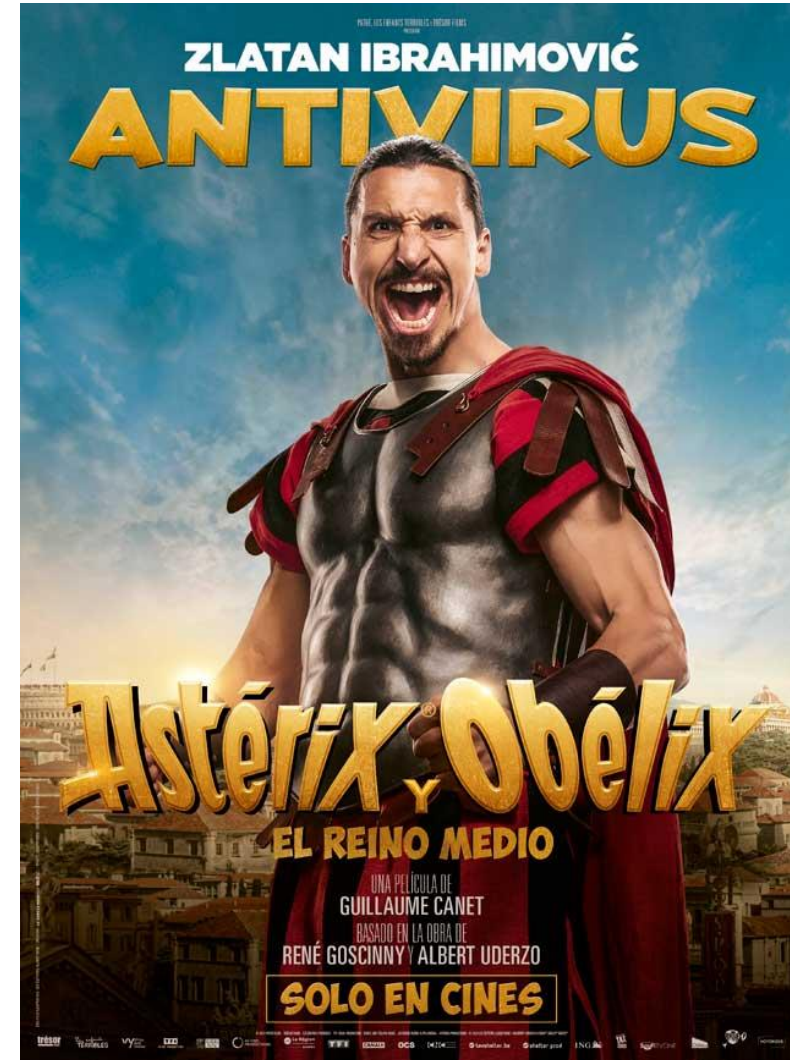
Comparaison incidence de la démence

- Diminution du risque de démence de 17% avec vaccin recombinant à 6 ans IC [0,8-0,87] vs vaccin vivant
- Augmentation du temps de vie sans démence (+164j)
- Effet protecteur pour Homme et femme (> chez femmes)
- Les 2 vaccins contre le zona sont associés à un moindre risque de démence que le vaccin antigrippal et DTP,





antivirus



# Grippe délai de début antiviral

Clinical Infectious Diseases

MAJOR ARTICLE



## Timing of Influenza Antiviral Therapy and Risk of Death in Adults Hospitalized With Influenza-Associated Pneumonia, Influenza Hospitalization Surveillance Network (FluSurv-NET), 2012–2019

Mark W. Tenforde,<sup>1,6</sup> Kameela P. Noah,<sup>1</sup> Alissa C. O'Halloran,<sup>1</sup> Pam Daily Kirley,<sup>2</sup> Cora Hoover,<sup>3</sup> Nisha B. Alden,<sup>4</sup> Isaac Armistead,<sup>4</sup> James Meek,<sup>5</sup> Kimberly Yousey-Hindes,<sup>5</sup> Kyle P. Openo,<sup>6,7,8</sup> Lucy S. Witt,<sup>6,7</sup> Maya L. Monroe,<sup>9</sup> Patricia A. Ryan,<sup>9</sup> Anna Falkowski,<sup>10</sup> Libby Reeg,<sup>10</sup> Ruth Lynfield,<sup>11</sup> Melissa McMahon,<sup>11</sup> Emily B. Hancock,<sup>12</sup> Marisa R. Hoffman,<sup>12</sup> Suzanne McGuire,<sup>13</sup> Nancy L. Spina,<sup>13</sup> Christina B. Folsen,<sup>14</sup> Maria A. Gaitan,<sup>14</sup> Krista Lung,<sup>15</sup> Eli Shultz,<sup>15</sup> Ann Thomas,<sup>16</sup> William Schaffner,<sup>17</sup> H. Keipp Talbot,<sup>17</sup> Melanie T. Crossland,<sup>18</sup> Andrea Price,<sup>18</sup> Svetlana Masalovich,<sup>1</sup> Katherine Adams,<sup>1</sup> Rachel Holstein,<sup>1</sup> Devi Sundaresan,<sup>1</sup> Timothy M. Uyeki,<sup>1</sup> Carrie Reed,<sup>1</sup> Catherine H. Bozio,<sup>1</sup> and Shikha Garg<sup>1</sup>

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**Background.** Pneumonia is common in adults hospitalized with laboratory-confirmed influenza, but the association between timeliness of influenza antiviral treatment and severe clinical outcomes in patients with influenza-associated pneumonia is not well characterized.

**Methods.** We included adults aged ≥18 years hospitalized with laboratory-confirmed influenza and a discharge diagnosis of pneumonia over 7 influenza seasons (2012–2019) sampled from a multistate population-based surveillance network. We evaluated 3 treatment groups based on timing of influenza antiviral initiation relative to admission date (day 0, day 1, days 2–5). Baseline characteristics and clinical outcomes were compared across groups using unweighted counts and weighted percentages accounting for the complex survey design. Logistic regression models were generated to evaluate the association between delayed treatment and 30-day all-cause mortality.

**Results.** A total of 26 233 adults were sampled in the analysis. Median age was 71 years and most (92.2%) had ≥1 non-immunocompromising condition. Overall, 60.9% started antiviral treatment on day 0, 29.5% on day 1, and 9.7% on days 2–5 (median, 2 days). Baseline characteristics were similar across groups. Thirty-day mortality occurred in 7.5%, 8.5%, and 10.2% of patients who started treatment on day 0, day 1, and days 2–5, respectively. Compared to those treated on day 0, adjusted odds ratio for death was 1.14 (95% confidence interval [CI], 1.01–1.27) in those starting treatment on day 1 and 1.40 (95% CI, 1.17–1.66) in those starting on days 2–5.

**Conclusions.** Delayed initiation of antiviral treatment in patients hospitalized with influenza-associated pneumonia was associated with higher risk of death, highlighting the importance of timely initiation of antiviral treatment at admission.

**Keywords.** influenza; hospitalization; antiviral; oseltamivir; mortality.

Influenza is a major cause of morbidity and mortality in the United States (US), leading to hundreds of thousands of hospitalizations and thousands of deaths annually [1]. Globally, an estimated 291 000–645 000 thousand deaths per year occur due to

respiratory complications of influenza [2]. While annual vaccination is the primary intervention to reduce the burden of influenza-related illness and its sequelae, influenza antiviral therapy may also lower the risk of clinical complications after illness onset [3].

Guidelines recommend that adults hospitalized with suspected or confirmed influenza start treatment with influenza antiviral therapy as soon as possible [3]. While most US adults hospitalized with laboratory-confirmed influenza receive antiviral treatment [4, 5], timing of initiation may vary based on when a patient seeks care after illness onset, availability of influenza test results, and clinical suspicion for influenza, among other factors. Pneumonia is the most common acute diagnosis among

Étude observationnelle rétrospective sur 7 saisons grippales  
Population: patients admis pour grippe avec codage de pneumonie  
Exposition: traitement antigrippal J0, J1, J2-J5  
Objectif: mortalité à J30

Received 26 April 2024; editorial decision 18 July 2024; published online 22 August 2024

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Clinical Infectious Diseases® 2025;80(2):461–8

Published by Oxford University Press on behalf of Infectious Diseases Society of America 2024. This work is written by (a) US Government employee(s) and is in the public domain in the US. <https://doi.org/10.1093/cid/ciae427>

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**Results.** A total of 26 233 adults were sampled in the analysis. Median age was 71 years and most (92.2%) had ≥1 non-immunocompromising condition. Overall, 60.9% started antiviral treatment on day 0, 29.5% on day 1, and 9.7% on days 2–5 (median, 2 days). Baseline characteristics were similar across groups. Thirty-day mortality occurred in 7.5%, 8.5%, and 10.2% of patients who started treatment on day 0, day 1, and days 2–5, respectively. Compared to those treated on day 0, adjusted odds ratio for death was 1.14 (95% confidence interval [CI], 1.01–1.27) in those starting treatment on day 1 and 1.40 (95% CI, 1.17–1.66) in those starting on days 2–5.

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## Résultats:

26233 patients, âge médian 71 ans, 92% ont > 1 comorbidité

Oseltamivir 99%, J0 60,9%, J1 29,5%, J2-J5 9,7%

Transfert USI 30%, mortalité 8% (âge médian 79 ans)

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Clinical Infectious Diseases® 2025;80(2):461–8

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OXFORD

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**Results.** A total of 26 233 adults were sampled in the analysis. Median age was 71 years and most (92.2%) had  $\geq 1$  non-immunocompromising condition. Overall, 60.9% started antiviral treatment on day 0, 29.5% on day 1, and 9.7% on days 2–5 (median, 2 days). Baseline characteristics were similar across groups. Thirty-day mortality occurred in 7.5%, 8.5%, and 10.2% of patients who started treatment on day 0, day 1, and days 2–5, respectively. Compared to those treated on day 0, adjusted odds ratio for death was 1.14 (95% confidence interval [CI], 1.01–1.27) in those starting treatment on day 1 and 1.40 (95% CI, 1.17–1.66) in those starting on days 2–5.

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Group	No. / Total (%)	Unadjusted OR	(95% CI)	Adjusted OR	(95% CI)
<b>Overall</b>					
Treatment initiated day 0	15 806/26 233 (60.9)	Ref		Ref	
Treatment initiated day 1	7810/26 233 (29.5)	1.16	(1.03, 1.31)	1.14	(1.01, 1.27)
Treatment initiated days 2–5	2617/26 233 (9.7)	1.41	(1.21, 1.64)	1.40	(1.17, 1.66)
<b>18–64 years</b>					
Treatment initiated day 0	6498/10 812 (60.3)	Ref		Ref	
Treatment initiated day 1	3153/10 812 (29.1)	1.16	(.95, 1.42)	1.16	(.94, 1.43)
Treatment initiated days 2–5	1161/10 812 (10.7)	1.64	(1.25, 2.18)	1.60	(1.20, 2.13)
<b><math>\geq 65</math> years</b>					
Treatment initiated day 0	9308/15 421 (61.2)	Ref		Ref	
Treatment initiated day 1	4657/15 421 (29.7)	1.16	(1.00, 1.34)	1.14	(.99, 1.30)
Treatment initiated days 2–5	1456/15 421 (9.1)	1.40	(1.17, 1.68)	1.33	(1.09, 1.63)

Received 26 April 2024; editorial decision 18 July 2024; published online 22 August 2024  
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### Limites:

- Pas de distinction précise pneumonie virale et bactérienne
- Sous déclaration possible du ttt préhospitalier
- Pas d'horaire d'administration
- Pas d'étude des autres traitements (antibiotiques, corticoïdes)
- Délai par rapport à l'admission mais pas début des symptômes

Si on décide de traiter il faut traiter précocement les pneumonies associées à la grippe

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# Grippe Baloxavir

Efficacité du Baloxavir pour prévenir la transmission de la grippe (CENTERSTONE study)

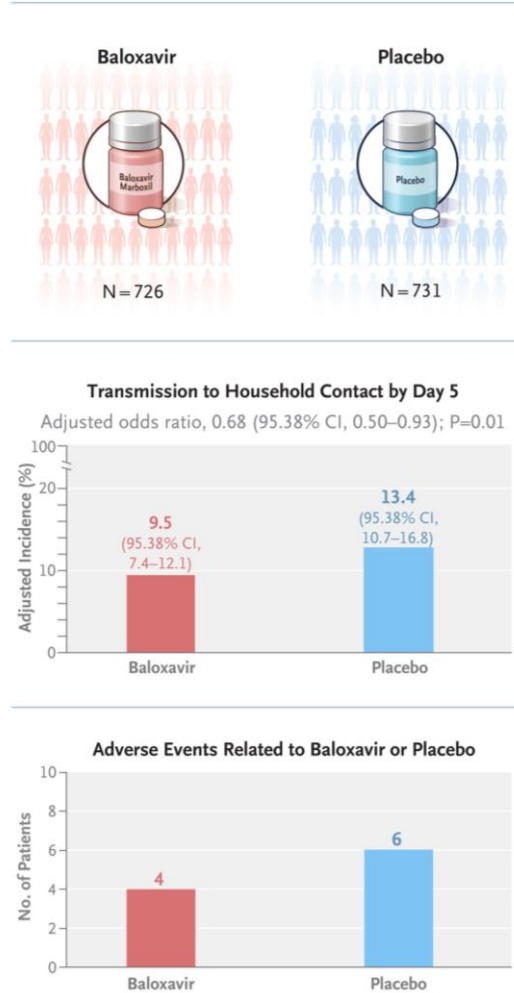
## Rationnel:

Baloxavir = inhibiteur de l'endonucléase cap dépendante du virus de la grippe

« Efficace » pour traiter la grippe et surtout réduction rapide de la charge virale (vs oseltamivir)

## Méthodologie

- Etude de phase IIIb RCT double aveugle
- Multicentrique 15 pays 2019-2024
  - 1457 cas index randomisés
  - suivi de 2681 contacts (famille)
  - Surveillance à J5 (J9)



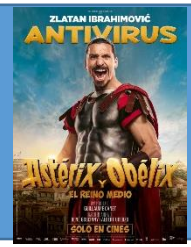
## Résultats

- Réduction 29 % du nombre de cas Ilaires ( $p=0,01$ )
- Réduction des cas symptomatiques 24% ( $p=0,16$ )

Manque de puissance car taux de transmission < celui attendu (effet COVID)

## Intérêts potentiels?

- dans les EHPAD pour arrêter une épidémie?
- en cas de pandémie pour gagner le temps de produire les vaccins?



- Le bon usage concerne tous les médicaments
- Savoir dépister et prendre en charge le sepsis (PNDS) y compris atypique (mesurer la FR)
- Les vaccins pour les virus respiratoires (VRS, COVID, grippe) sont efficaces en vie réelle et bien tolérés
- La couverture vaccinale est faible pour le COVID et la grippe et surtout chez les professionnels
- Les vaccins ont des bénéfices secondaires (troubles cognitifs)
- La recherche sur les antiviraux se poursuit, ils doivent être utilisés le plus tôt possible dans l'infection

