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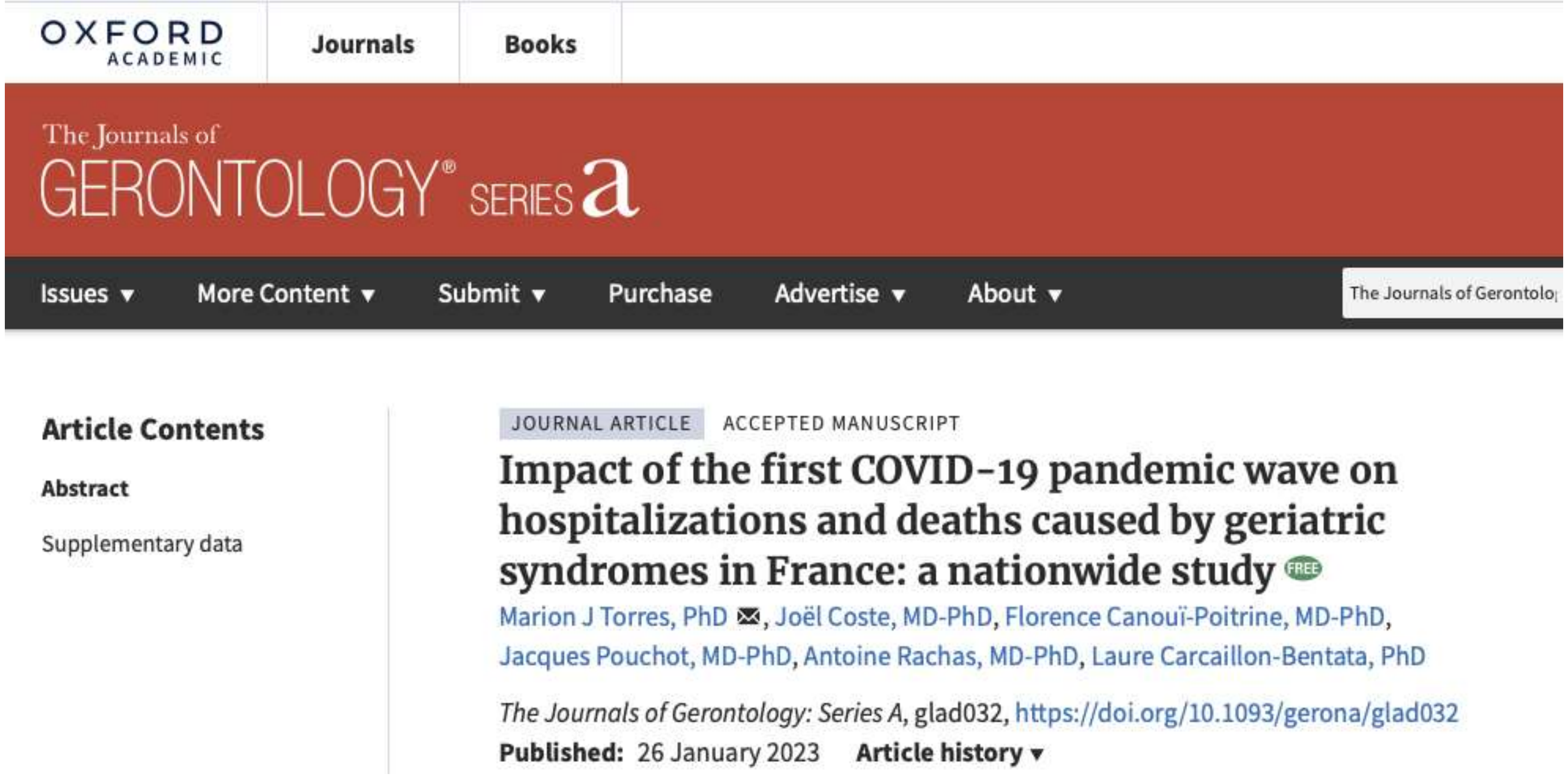
Université Montpellier I
FACULTÉ de MÉDECINE
Montpellier - Nîmes

Quoi de neuf en infectiologie en 2023 ?

Professeur Benoit de Wazieres

Nimes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Impact of the first COVID-19 pandemic wave on hospitalizations and deaths caused by geriatric syndromes in France: a nationwide study FREE

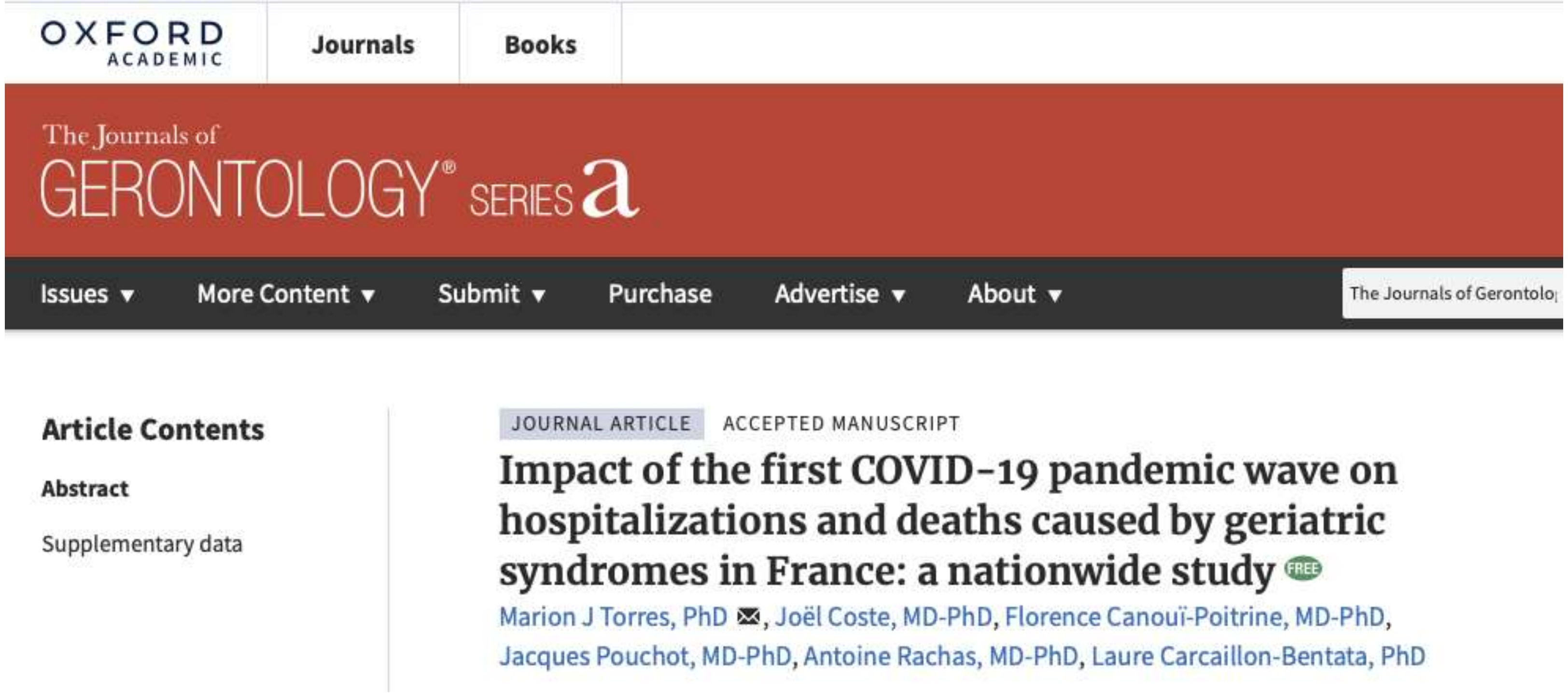
Marion J Torres, PhD ✉, Joël Coste, MD-PhD, Florence Canouï-Poitrine, MD-PhD, Jacques Pouchot, MD-PhD, Antoine Rachas, MD-PhD, Laure Carcaillon-Bentata, PhD

The Journals of Gerontology: Series A, glad032, https://doi.org/10.1093/gerona/glad032

Published: 26 January 2023 **Article history** ▾

- bases du PMSI
- période de confinement du printemps 2020 (17 mars - 12 mai).

https://doi.org/10.1093/gerona/glad032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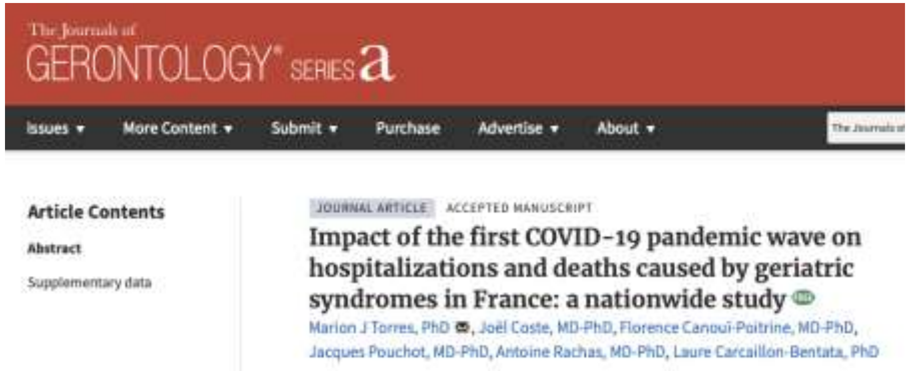
- 314 421 personnes âgées de 65 ans et plus ont été hospitalisées pour une cause autre que la COVID-19, ce qui est inférieur au nombre moyen d’hospitalisations des trois années précédentes qui était de 557 033 (-56 %)

Les 10 syndromes Geriatriques étudiés sont ceux les plus fréquemment cités dans la littérature,

- la démence,
- le déclin cognitif,
- la confusion/désorientation,
- la dépression,
- la dénutrition,
- la déshydratation,
- l’escarre,
- l’incontinence,
- la chute et lésion, avec un focus particulier sur la fracture du col du fémur.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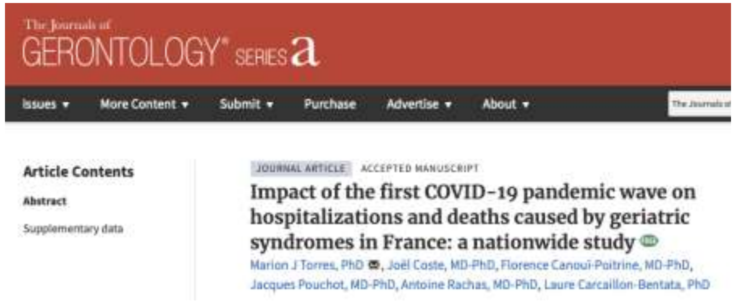
The Journals of Gerontology: Series A, glad032, https://doi.org/10.1093/gerona/glad032

- Diminution très importante des hospitalisations pour syndromes Geriatriques, et de façon concomitante une surmortalité en miroir pour la plupart de ces motifs, notamment à domicile et en institution, durant la période de confinement du printemps 2020 (17 mars - 12 mai).

Diminution des hospitalisations pour SG !

- -59 % pour l’incontinence,
- -51 % pour la dépression,
- -49 % pour le déclin cognitif,
- -43 % pour la démence,
- -37 % pour la dénutrition,
- -37 % pour la déshydratation,
- -36 % pour une escarre, -30 % pour les chutes/lésions,
- - 18% pour la confusion/désorientation et
- -13 % pour les fractures du col du fémur.
- la diminution des hospitalisations pour démence lors du premier confinement était de -61 % dans les territoires les plus touchés (Ile-de-France et Grand Est),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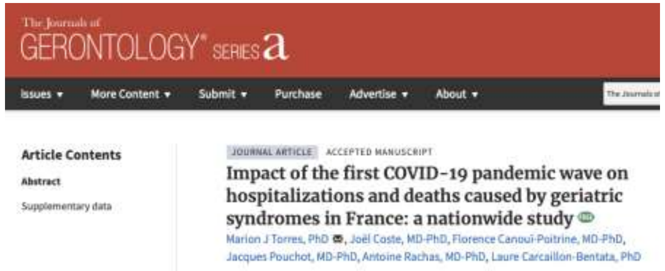
Surmortalité en miroir hors-COVID-19

- +74 % de décès hors-COVID-19 pour confusion/désorientation,
- +44 % pour fracture du col du fémur,
- +32 % pour dépression,
- +20 % pour déshydratation,
- +9 % pour dénutrition,
- +8 % pour chutes/lésions.
- Cette surmortalité était particulièrement observée à domicile et en maisons de retraite.
- Par exemple, la surmortalité lors du premier confinement pour dénutrition était de 39 % à domicile et 40 % en institution (Ehpad, USLD) alors qu’à l’hôpital il y avait une sous-mortalité de -12 %.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DE L'AUTONOMIE
ET DES PERSONNES
HANDICAPÉES
Liberté
Égalité
Fraternité

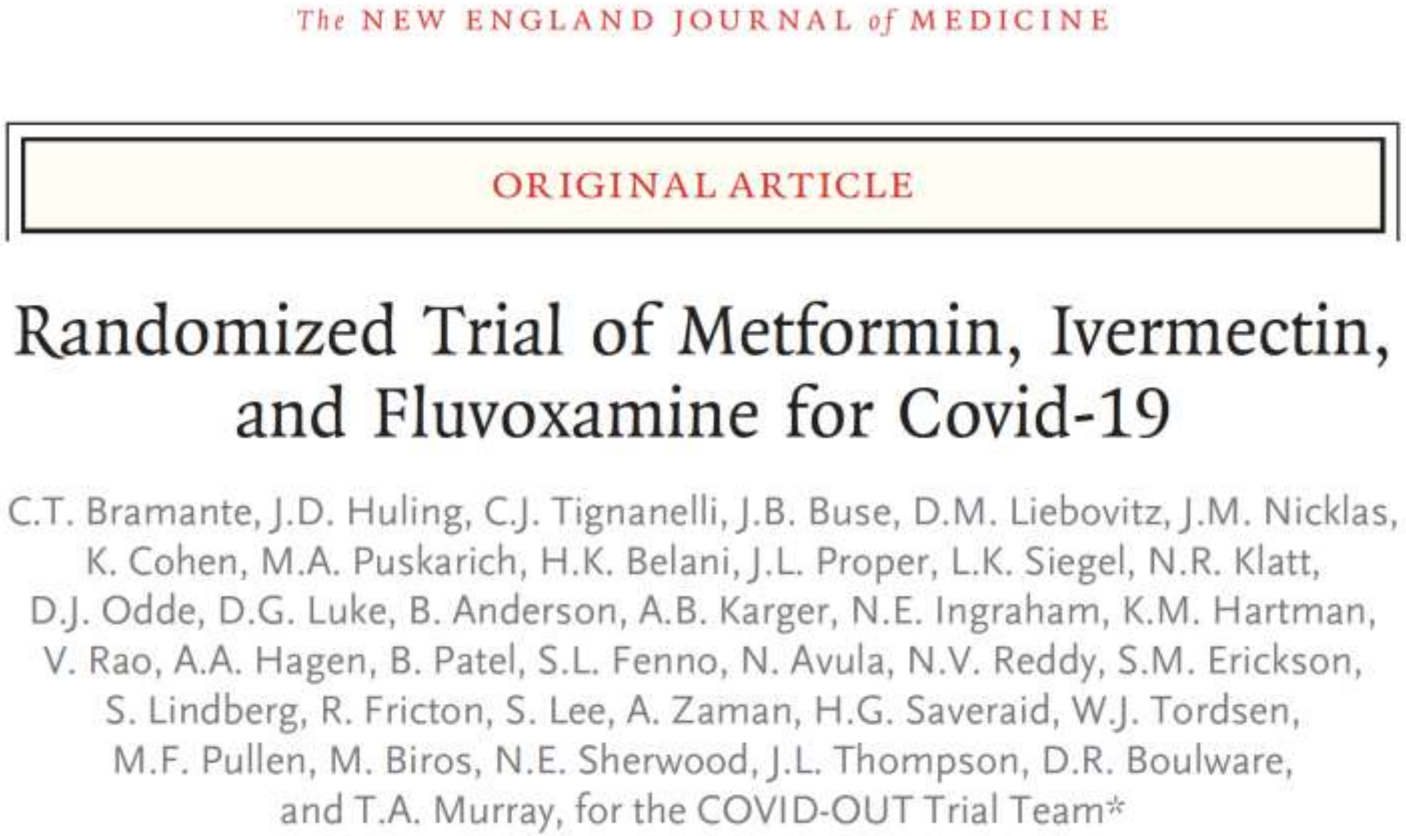
17/03/2023

ACTUALISATION DES CONSIGNES D'ISOLEMENT ET DE DEPISTAGE DANS LES ETABLISSEMENTS ET SERVICES ACCOMPAGNANT DES PERSONNES AGEES ET DES PERSONNES EN SITUATION DE HANDICAP

CONDUITE A TENIR AUTOUR D’UNE SITUATION DE CAS GROUPE D’IRA

La détection d’un cas groupé de grippe (5 cas en 4 jours) ou de Covid (3 cas en 7 jours) parmi les résidents ou les professionnels des établissements peut conduire la direction à mettre en place des mesures de protection complémentaires sur tout l’établissement ou par secteur jusqu’à ce que le cluster soit considéré comme maîtrisé. . Les mesures doivent être adéquates, proportionnées à la situation de l’établissement et limitées dans le temps. Ces mesures doivent être prises en lien avec le dispositif d’appui à la gestion des infections mis en place dans la région (ARS, CPIAS et/ou équipe mobile d’hygiène).

Pour rappel, s'agissant de la Covid, il convient de réaliser un signalement dès le premier cas au lien suivant : https://voozanoo.santepubliquefrance.fr//1828535468/scripts/aindex.php
S'agissant de la grippe (et de la gastroentérite), seuls les cas groupés doivent être signalés en utilisant le formulaire disponible au lien suivant : https://signalement.social-sante.gouv.fr/psig_ihm_utilisateurs/index.html#/choixSignalementPS



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

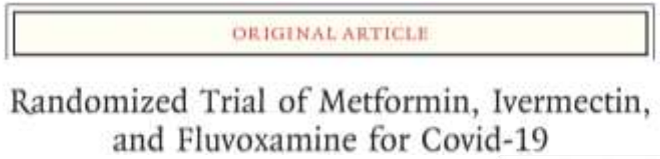
Randomized Trial of Metformin, Ivermectin, and Fluvoxamine for Covid-19

C.T. Bramante, J.D. Huling, C.J. Tignanelli, J.B. Buse, D.M. Liebovitz, J.M. Nicklas, K. Cohen, M.A. Puskarich, H.K. Belani, J.L. Proper, L.K. Siegel, N.R. Klatt, D.J. Odde, D.G. Luke, B. Anderson, A.B. Karger, N.E. Ingraham, K.M. Hartman, V. Rao, A.A. Hagen, B. Patel, S.L. Fenno, N. Avula, N.V. Reddy, S.M. Erickson, S. Lindberg, R. Fricton, S. Lee, A. Zaman, H.G. Saveraid, W.J. Tordsen, M.F. Pullen, M. Biros, N.E. Sherwood, J.L. Thompson, D.R. Boulware, and T.A. Murray, for the COVID-OUT Trial Team*

N Engl J Med 2022;387:599-610.
DOI: 10.1056/NEJMoa2201662
Copyright © 2022 Massachusetts Medical Society.

- *RESULTS*
- *Un total de 1431 patients ont été randomisés ; parmi ces patients, 1323 ont été inclus dans l'analyse primaire.*

- *CONCLUSIONS*
- ***Aucun** des trois médicaments évalués n'a empêché la survenue d'une hypoxémie, d'une visite aux urgences, d'une hospitalisation ou d'un décès associé au Covid-19.*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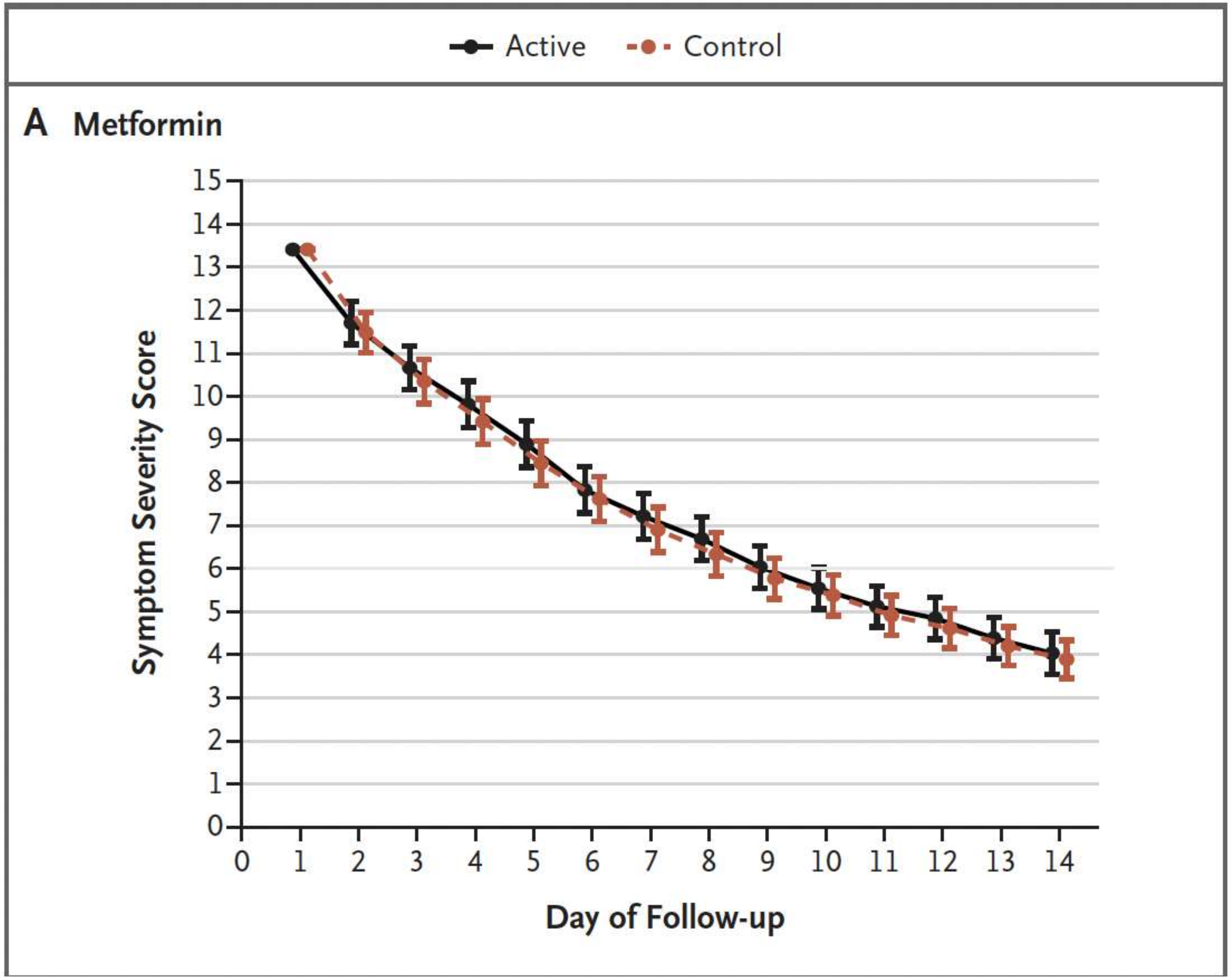
Randomized Trial of Metformin, Ivermectin, and Fluvoxamine for Covid-19



Received: 22 October 2021 | Revised: 29 March 2022 | Accepted: 9 April 2022

DOI: 10.1111/jgs.17828

Journal of the
American Geriatrics Society

30-day mortality following COVID-19 and influenza hospitalization among US veterans aged 65 and older

Benjamin Seligman MD, PhD[1,2,3,4] | **Brian Charest MS, MPH**[5] |
Yuk-Lam Ho MPH[5] | **Hanna Gerlovin PhD**[5] | **Rachel E. Ward PhD**[1,5,6] |
Kelly Cho PhD[5,7] | **Jane A. Driver MD, MPH**[1,7] | **J. Michael Gaziano MD, MPH**[5,7] |
David R. Gagnon MD, MPH, PhD[5,8] | **Ariela R. Orkaby MD, MPH**[1,7]

Journal of the
American Geriatrics Society

30-day mortality following COVID-19 and influenza hospitalization among US veterans aged 65 and older

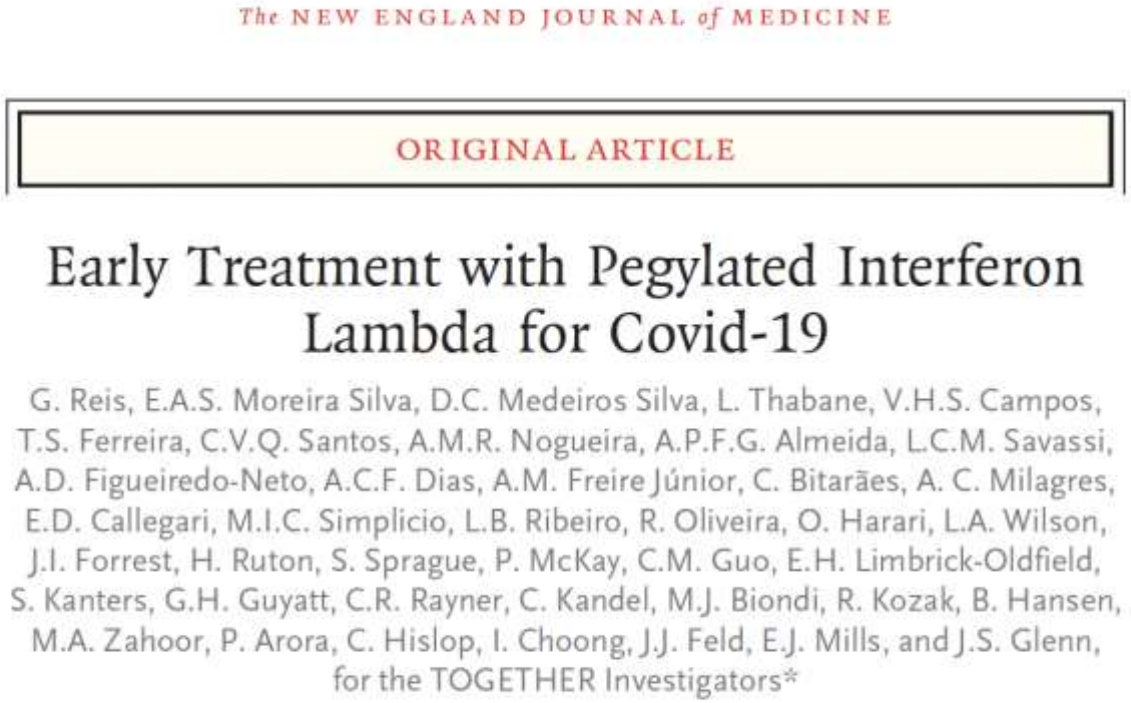
- Etude rétrospective de la mortalité à 30 jours chez les vétérans âgés de 65 ans et plus hospitalisés avec
- le COVID-19 du 1er mars 2020 au 31 décembre 2020 ou avec
- la grippe A/B du 1er septembre 2017 au 31 août 2019
- L'infection au COVID-19 a été déterminée par un test PCR positif et la grippe par des tests PCR

- Veterans Affairs Health Système de soins (VAHCS).

30-day mortality following COVID-19 and influenza hospitalization among US veterans aged 65 and older

- Résultats :
- 15 474 anciens combattants ont été admis avec la COVID-19 et
- 7 867 avec la grippe.
- Les âges moyens (ET) étaient de 76,1 (7,8) et 75,8 (8,3) ans, 97,7 % et 97,4 % étaient des hommes et 66,9 % et 76,4 % étaient de race blanche dans les cohortes COVID-19 et grippe respectivement.
- La mortalité brute à 30 jours (IC à 95 %) était de
    - 18,9 % (18,3 % à 19,5 %) pour la COVID-19 et de
    - 4,3 % (3,8 % à 4,7 %) pour la grippe.

Pour traiter la Covid-19, une seule dose d'interféron pégylé lambda pourrait suffire…



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Early Treatment with Pegylated Interferon Lambda for Covid-19

G. Reis, E.A.S. Moreira Silva, D.C. Medeiros Silva, L. Thabane, V.H.S. Campos, T.S. Ferreira, C.V.Q. Santos, A.M.R. Nogueira, A.P.F.G. Almeida, L.C.M. Savassi, A.D. Figueiredo-Neto, A.C.F. Dias, A.M. Freire Júnior, C. Bitarães, A. C. Milagres, E.D. Callegari, M.I.C. Simplicio, L.B. Ribeiro, R. Oliveira, O. Harari, L.A. Wilson, J.I. Forrest, H. Ruton, S. Sprague, P. McKay, C.M. Guo, E.H. Limbrick-Oldfield, S. Kanters, G.H. Guyatt, C.R. Rayner, C. Kandel, M.J. Biondi, R. Kozak, B. Hansen, M.A. Zahoor, P. Arora, C. Hislop, I. Choong, J.J. Feld, E.J. Mills, and J.S. Glenn, for the TOGETHER Investigators*

Reis G et coll. : Early Treatment with Pegylated Interferon Lambda for Covid-19
N Engl J Med 2023;388:518-28. DOI: 10.1056/NEJMoa2209760

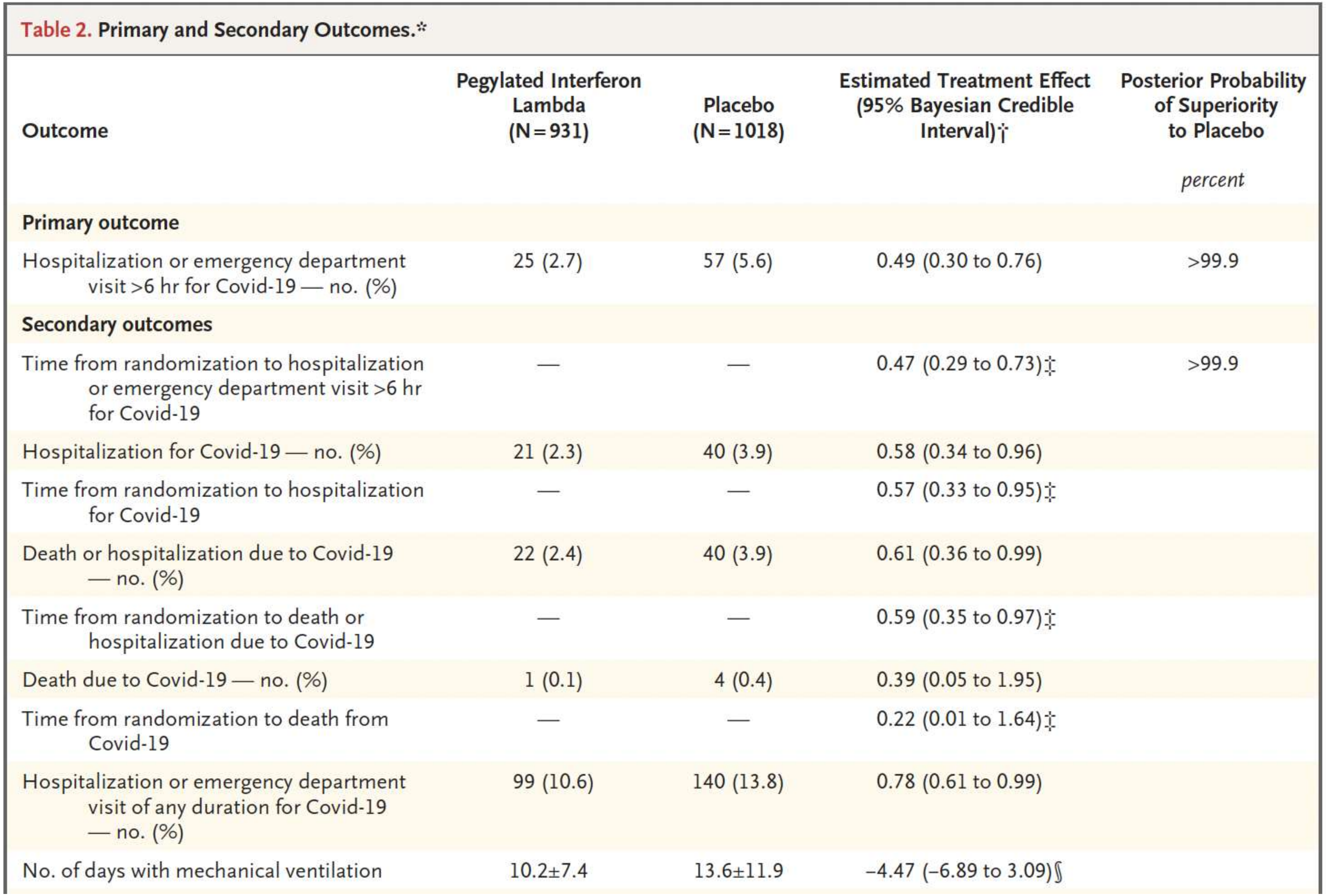
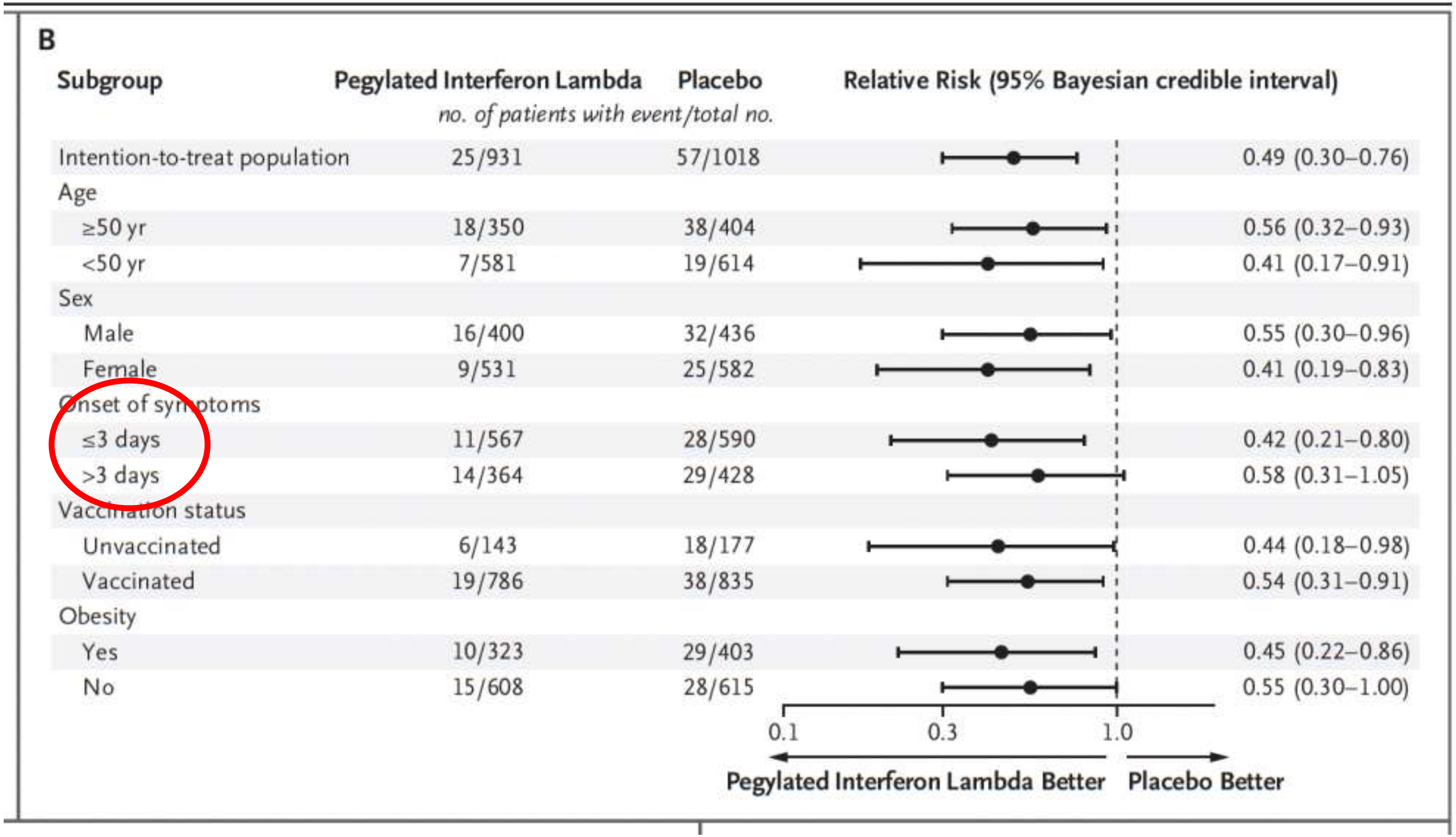
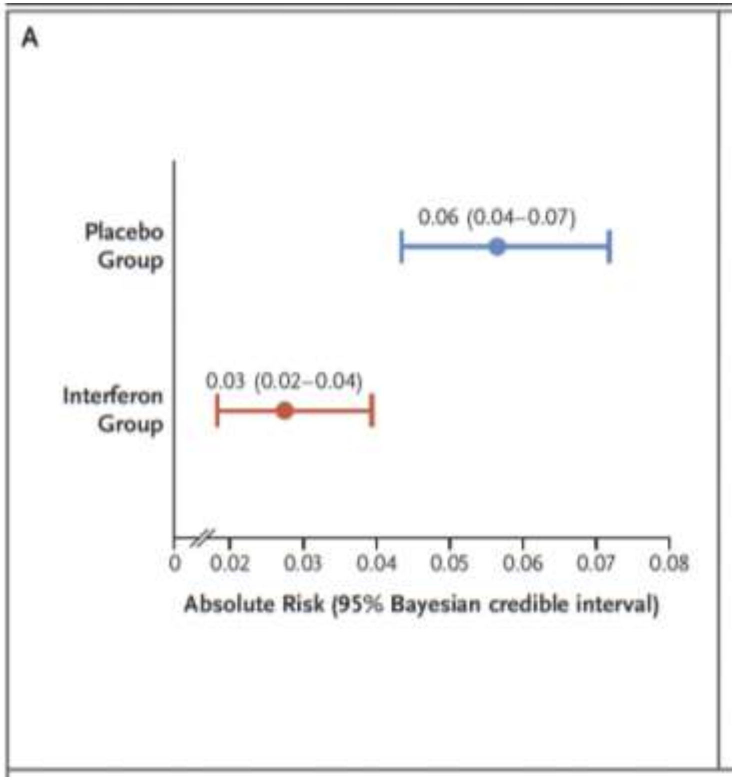


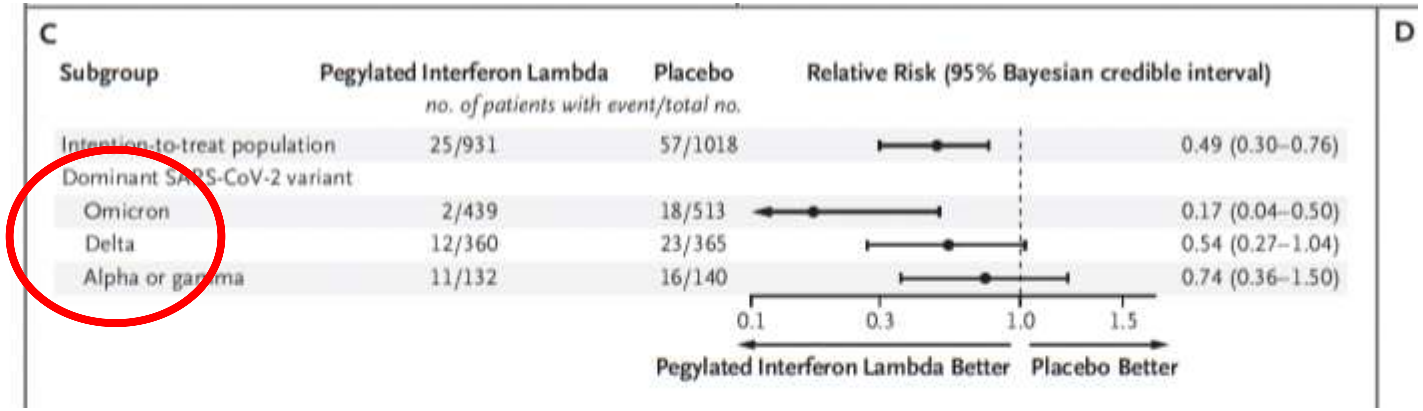
Table 2. Primary and Secondary Outcomes.*

Outcome	Pegylated Interferon Lambda (N=931)	Placebo (N=1018)	Estimated Treatment Effect (95% Bayesian Credible Interval)†	Posterior Probability of Superiority to Placebo
				percent
Primary outcome				
Hospitalization or emergency department visit >6 hr for Covid-19 — no. (%)	25 (2.7)	57 (5.6)	0.49 (0.30 to 0.76)	>99.9
Secondary outcomes				
Time from randomization to hospitalization or emergency department visit >6 hr for Covid-19	—	—	0.47 (0.29 to 0.73)‡	>99.9
Hospitalization for Covid-19 — no. (%)	21 (2.3)	40 (3.9)	0.58 (0.34 to 0.96)	
Time from randomization to hospitalization for Covid-19	—	—	0.57 (0.33 to 0.95)‡	
Death or hospitalization due to Covid-19 — no. (%)	22 (2.4)	40 (3.9)	0.61 (0.36 to 0.99)	
Time from randomization to death or hospitalization due to Covid-19	—	—	0.59 (0.35 to 0.97)‡	
Death due to Covid-19 — no. (%)	1 (0.1)	4 (0.4)	0.39 (0.05 to 1.95)	
Time from randomization to death from Covid-19	—	—	0.22 (0.01 to 1.64)‡	
Hospitalization or emergency department visit of any duration for Covid-19 — no. (%)	99 (10.6)	140 (13.8)	0.78 (0.61 to 0.99)	
No. of days with mechanical ventilation	10.2±7.4	13.6±11.9	−4.47 (−6.89 to 3.09)§	

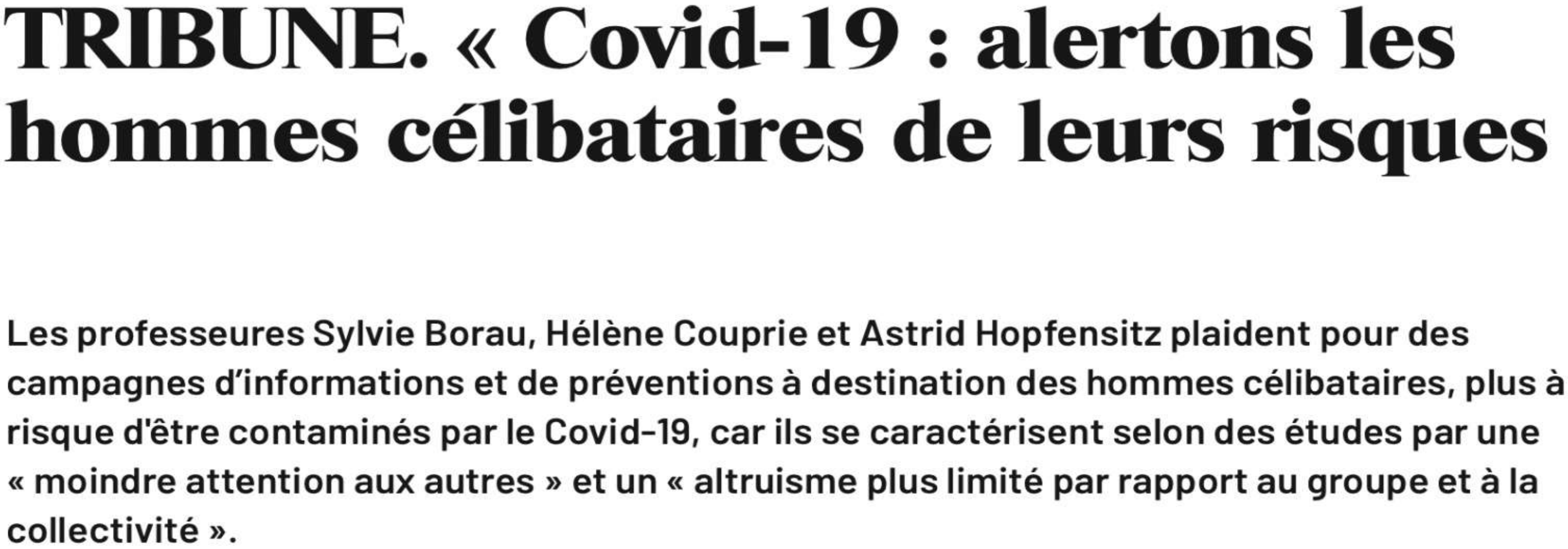


Subgroup	Pegylated Interferon Lambda	Placebo	Relative Risk (95% Bayesian credible interval)
	no. of patients with event/total no.		
Intention-to-treat population	25/931	57/1018	0.49 (0.30–0.76)
Age			
≥50 yr	18/350	38/404	0.56 (0.32–0.93)
<50 yr	7/581	19/614	0.41 (0.17–0.91)
Sex			
Male	16/400	32/436	0.55 (0.30–0.96)
Female	9/531	25/582	0.41 (0.19–0.83)
Onset of symptoms			
≤3 days	11/567	28/590	0.42 (0.21–0.80)
>3 days	14/364	29/428	0.58 (0.31–1.05)
Vaccination status			
Unvaccinated	6/143	18/177	0.44 (0.18–0.98)
Vaccinated	19/786	38/835	0.54 (0.31–0.91)
Obesity			
Yes	10/323	29/403	0.45 (0.22–0.86)
No	15/608	28/615	0.55 (0.30–1.00)





Subgroup	Pegylated Interferon Lambda	Placebo	Relative Risk (95% Bayesian credible interval)
	no. of patients with event/total no.		
Intention-to-treat population	25/931	57/1018	0.49 (0.30–0.76)
Dominant SARS-CoV-2 variant			
Omicron	2/439	18/513	0.17 (0.04–0.50)
Delta	12/360	23/365	0.54 (0.27–1.04)
Alpha or gamma	11/132	16/140	0.74 (0.36–1.50)

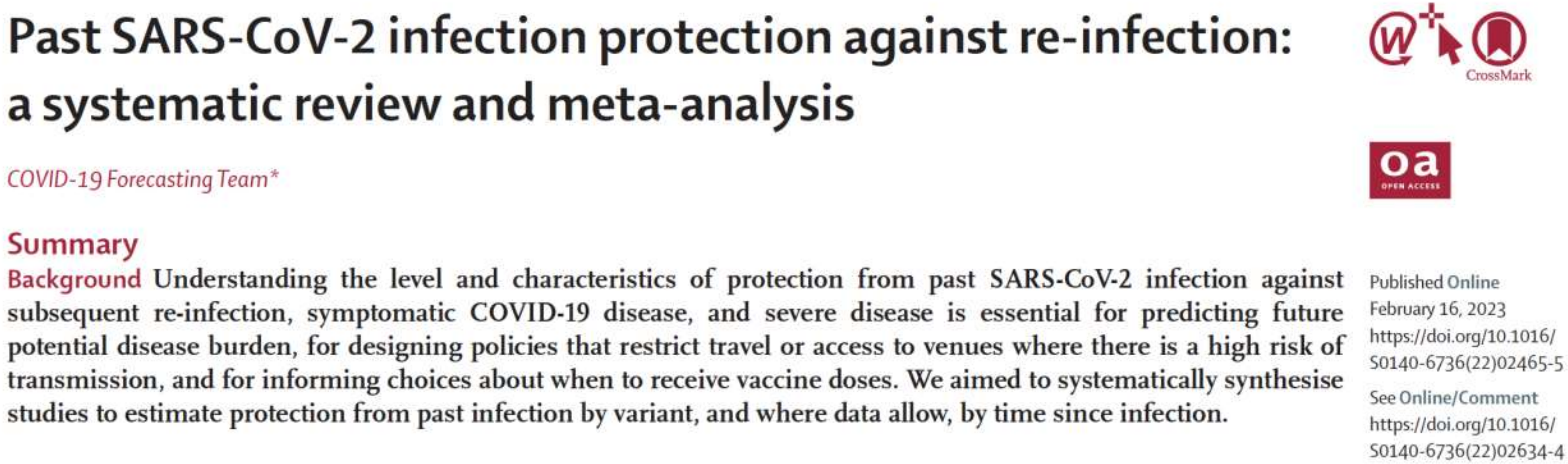


TRIBUNE. « Covid-19 : alertons les hommes célibataires de leurs risques

Les professeures Sylvie Borau, Hélène Couprie et Astrid Hopfensitz plaident pour des campagnes d'informations et de préventions à destination des hommes célibataires, plus à risque d'être contaminés par le Covid-19, car ils se caractérisent selon des études par une « moindre attention aux autres » et un « altruisme plus limité par rapport au groupe et à la collectivité ».

les hommes sont, depuis le début de la pandémie, *deux fois* plus nombreux à décéder du Covid que les femmes.
Leur immunité est probablement plus faible face à ce virus.
Mais on sait également que les célibataires sont *1.5 à 2 fois plus nombreux* que les personnes mariées à décéder de la maladie.

l'élément qui distingue surtout le célibataire de l'homme marié est sa *moindre attention aux autres, son altruisme plus limité par rapport au groupe et à la collectivité*. Il a, moins que l'homme marié, des scrupules moraux et surtout un moindre sentiment d'appartenance à un collectif.



Past SARS-CoV-2 infection protection against re-infection: a systematic review and meta-analysis

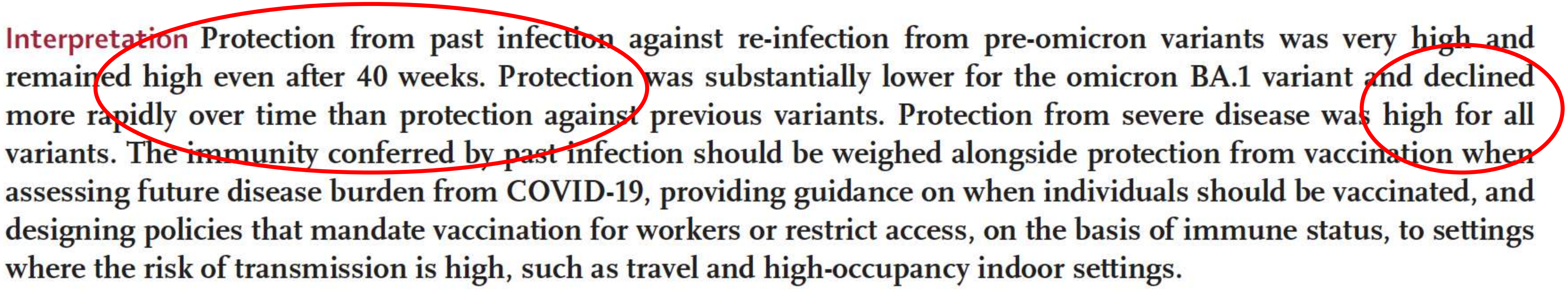
*COVID-19 Forecasting Team**

Published Online
February 16, 2023
https://doi.org/10.1016/
S0140-6736(22)02465-5

See Online/Comment
https://doi.org/10.1016/
S0140-6736(22)02634-4

Summary

Background Understanding the level and characteristics of protection from past SARS-CoV-2 infection against subsequent re-infection, symptomatic COVID-19 disease, and severe disease is essential for predicting future potential disease burden, for designing policies that restrict travel or access to venues where there is a high risk of transmission, and for informing choices about when to receive vaccine doses. We aimed to systematically synthesise studies to estimate protection from past infection by variant, and where data allow, by time since infection.



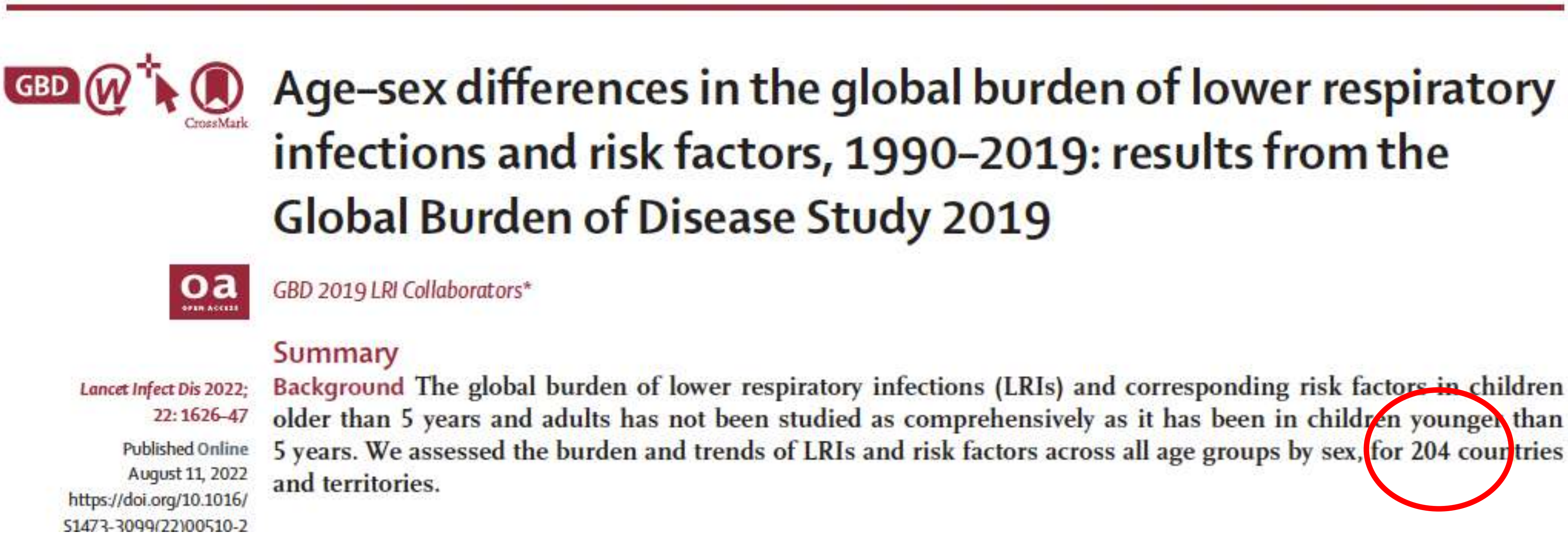
Interpretation Protection from past infection against re-infection from pre-omicron variants was very high and remained high even after 40 weeks. Protection was substantially lower for the omicron BA.1 variant and declined more rapidly over time than protection against previous variants. Protection from severe disease was high for all variants. The immunity conferred by past infection should be weighed alongside protection from vaccination when assessing future disease burden from COVID-19, providing guidance on when individuals should be vaccinated, and designing policies that mandate vaccination for workers or restrict access, on the basis of immune status, to settings where the risk of transmission is high, such as travel and high-occupancy indoor settings.

Diphtérie

Du 1er janvier au 30 novembre 2022, 55 cas de diphtérie ont été rapportés en France, dans 9 régions de métropole, ainsi qu'à la Réunion et à Mayotte.
nombre de cas
C. ulcerans est resté stable, "en comparaison aux autres années, le nombre de cas de
C. diphtheriae est nettement plus élevé que la moyenne",

> 47 cas depuis le début de l'année, contre une moyenne de 6,6 cas par an ces cinq dernières années.

chez des personnes migrantes (n=24) mais également chez des voyageurs (n=5).
Vingt-cinq cas étaient des formes cutanées,



Age–sex differences in the global burden of lower respiratory infections and risk factors, 1990–2019: results from the Global Burden of Disease Study 2019

*GBD 2019 LRI Collaborators**

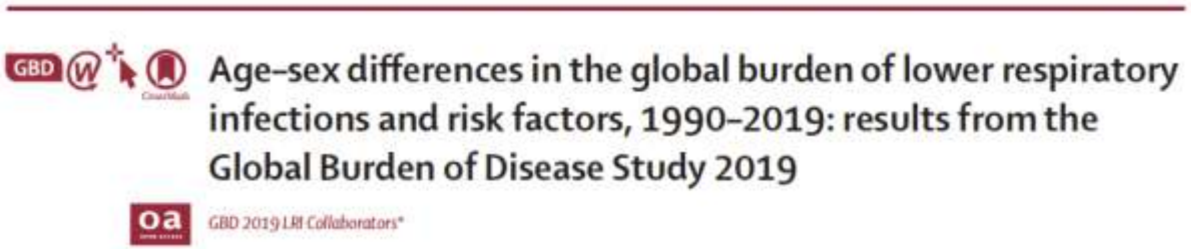
Lancet Infect Dis 2022; 22: 1626–47

Published Online
August 11, 2022

https://doi.org/10.1016/S1473-3099(22)00510-2

Summary

Background The global burden of lower respiratory infections (LRIs) and corresponding risk factors in children older than 5 years and adults has not been studied as comprehensively as it has been in children younger than 5 years. We assessed the burden and trends of LRIs and risk factors across all age groups by sex, for 204 countries and territories.



Age–sex differences in the global burden of lower respiratory infections and risk factors, 1990–2019: results from the Global Burden of Disease Study 2019

GBD 2019 LRI Collaborators*

The global pneumococcal conjugate vaccine coverage (third dose) among young children was estimated to be 47·9%

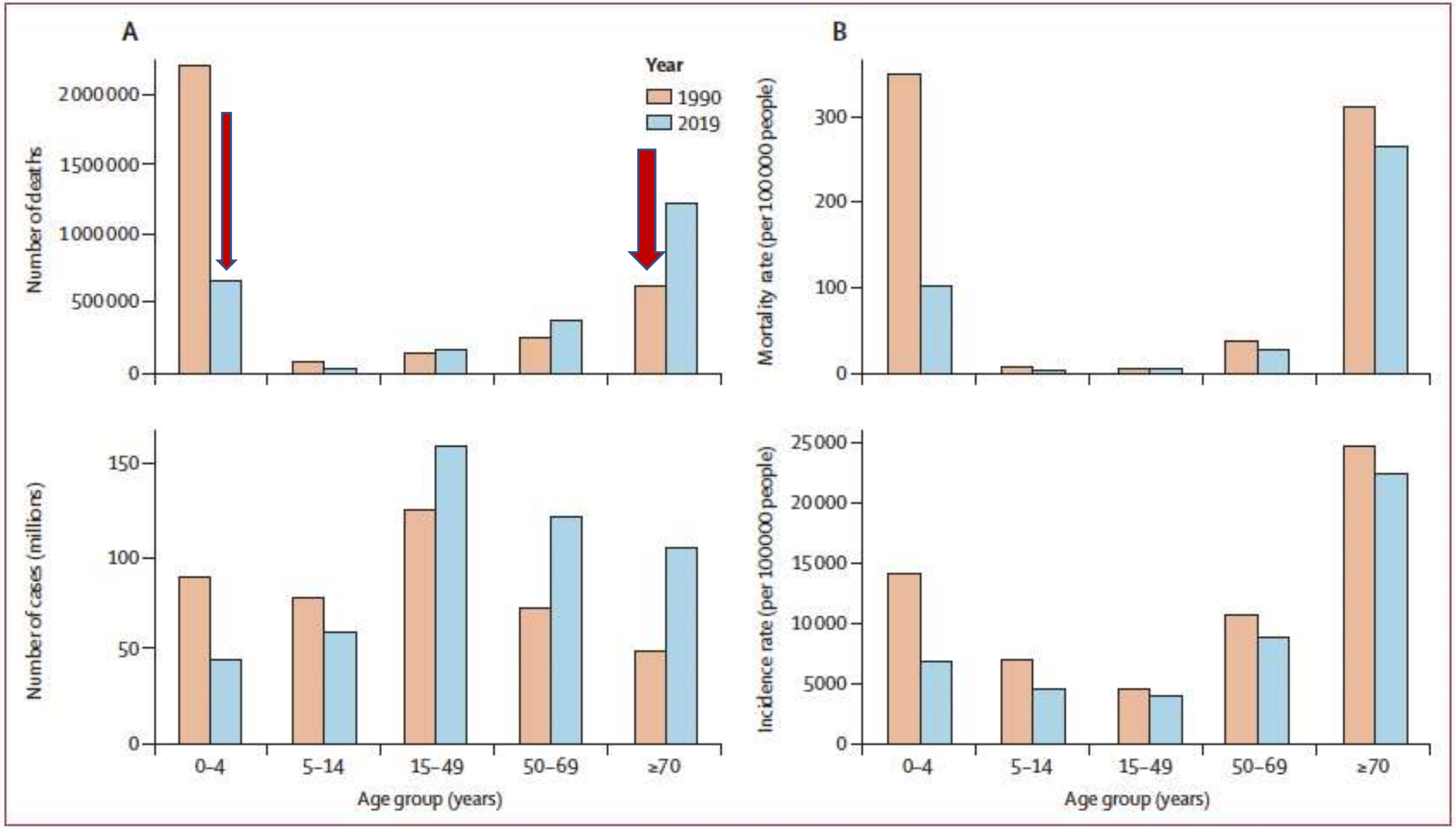
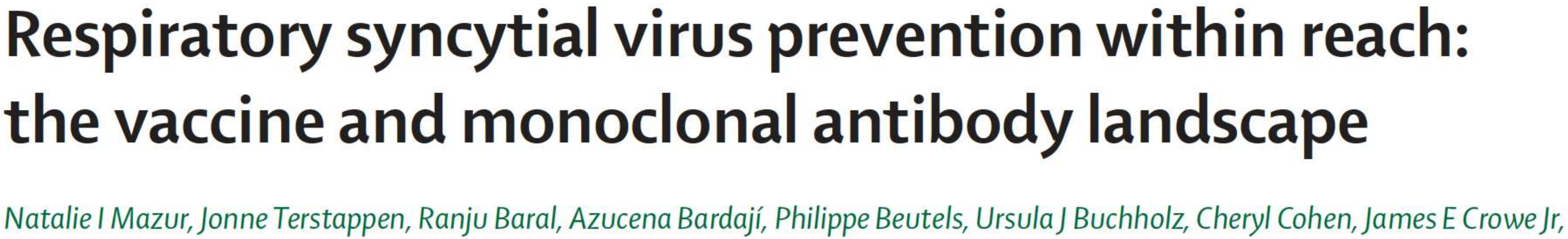


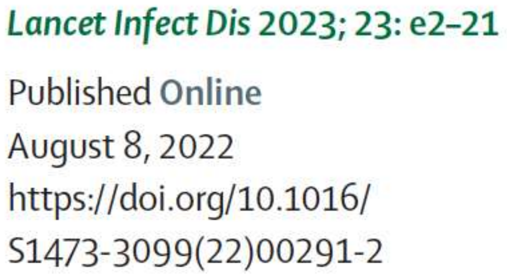
Figure 1: Incidence and mortality counts (A) and rates (B) due to lower respiratory infections for both sexes combined in 1990 and 2019, by age group



Respiratory syncytial virus prevention within reach: the vaccine and monoclonal antibody landscape

Natalie I Mazur, Jonne Terstappen, Ranju Baral, Azucena Bardají, Philippe Beutels, Ursula J Buchholz, Cheryl Cohen, James E Crowe Jr,

La prévention du virus respiratoire syncytial à portée de main :
des vaccins et des anticorps monoclonaux



Lancet Infect Dis 2023; 23: e2–21

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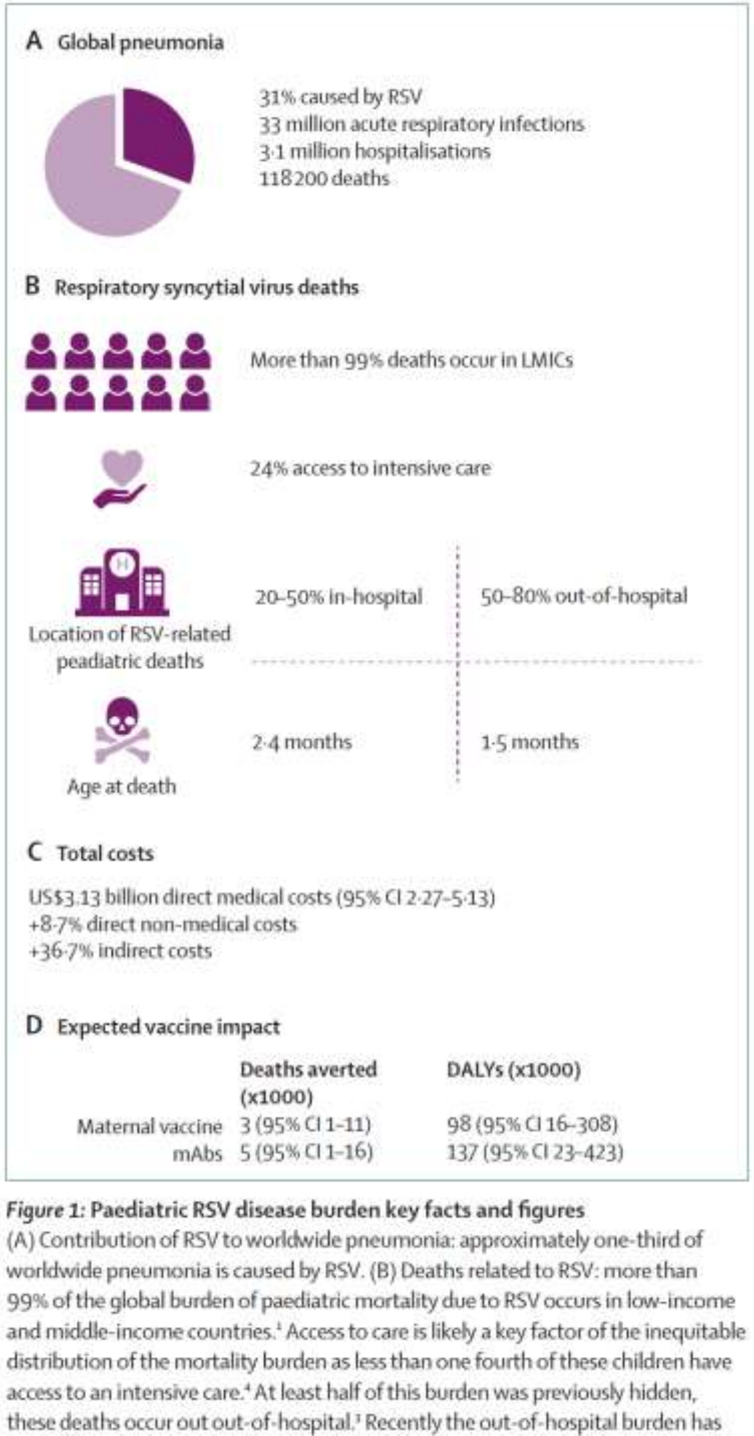
S1473-3099(22)00291-2



A Global pneumonia

31% caused by RSV
33 million acute respiratory infections
3·1 million hospitalisations
118 200 deaths

B Respiratory syncytial virus deaths

More than 99% deaths occur in LMICs

24% access to intensive care

Location of RSV-related peadiatric deaths	20–50% in-hospital	50–80% out-of-hospital
Age at death	2·4 months	1·5 months

C Total costs

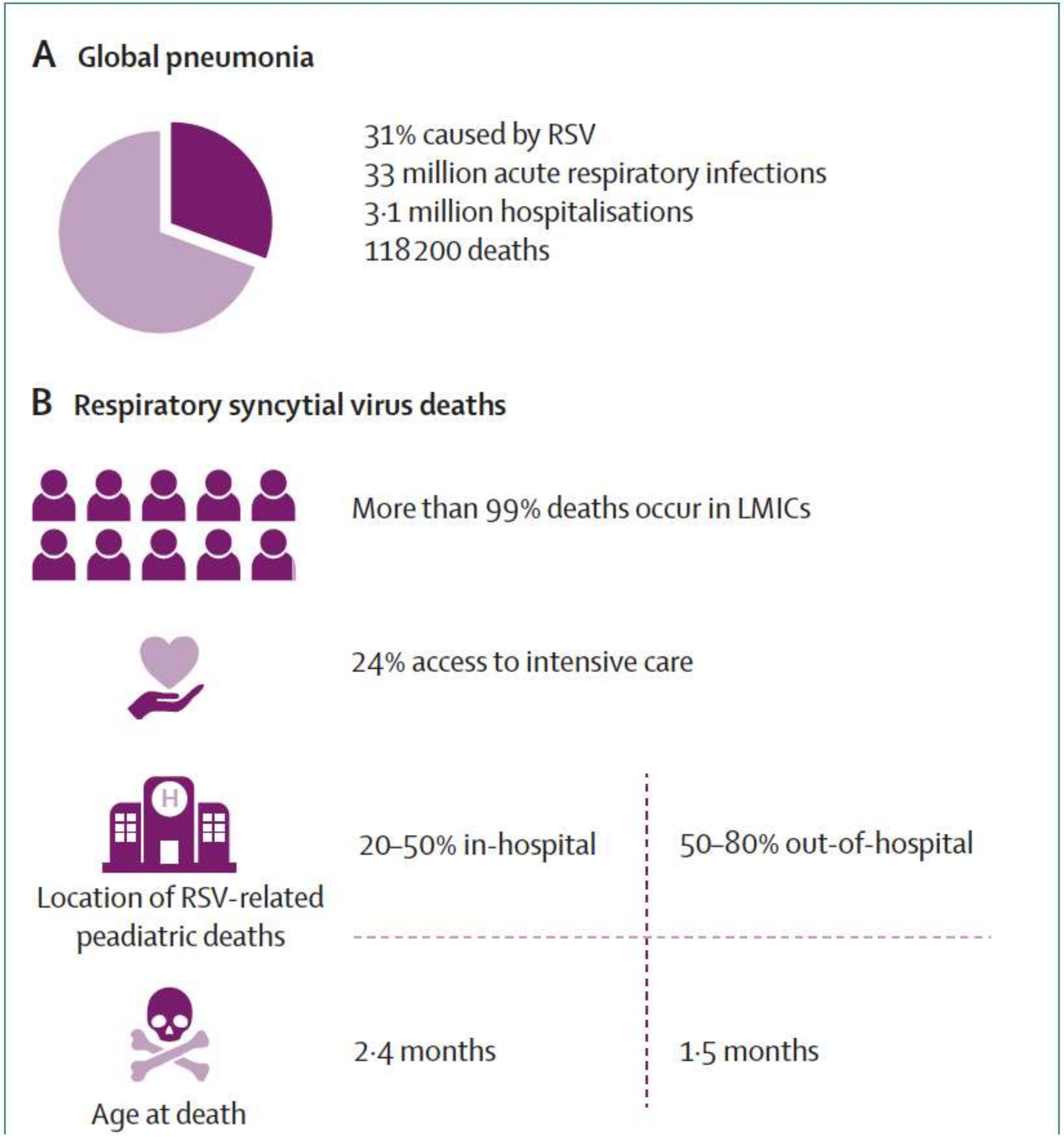
US$3.13 billion direct medical costs (95% CI 2·27–5·13)
+8·7% direct non-medical costs
+36·7% indirect costs

D Expected vaccine impact

	Deaths averted (x1000)	DALYs (x1000)
Maternal vaccine	3 (95% CI 1–11)	98 (95% CI 16–308)
mAbs	5 (95% CI 1–16)	137 (95% CI 23–423)

***Figure 1:* Paediatric RSV disease burden key facts and figures**
(A) Contribution of RSV to worldwide pneumonia: approximately one-third of worldwide pneumonia is caused by RSV. (B) Deaths related to RSV: more than 99% of the global burden of paediatric mortality due to RSV occurs in low-income and middle-income countries.[1] Access to care is likely a key factor of the inequitable distribution of the mortality burden as less than one fourth of these children have access to an intensive care.[4] At least half of this burden was previously hidden, these deaths occur out out-of-hospital.[3] Recently the out-of-hospital burden has

le fardeau mondial de la mortalité pédiatrique due au VRS se produit dans les pays à revenu faible et intermédiaire



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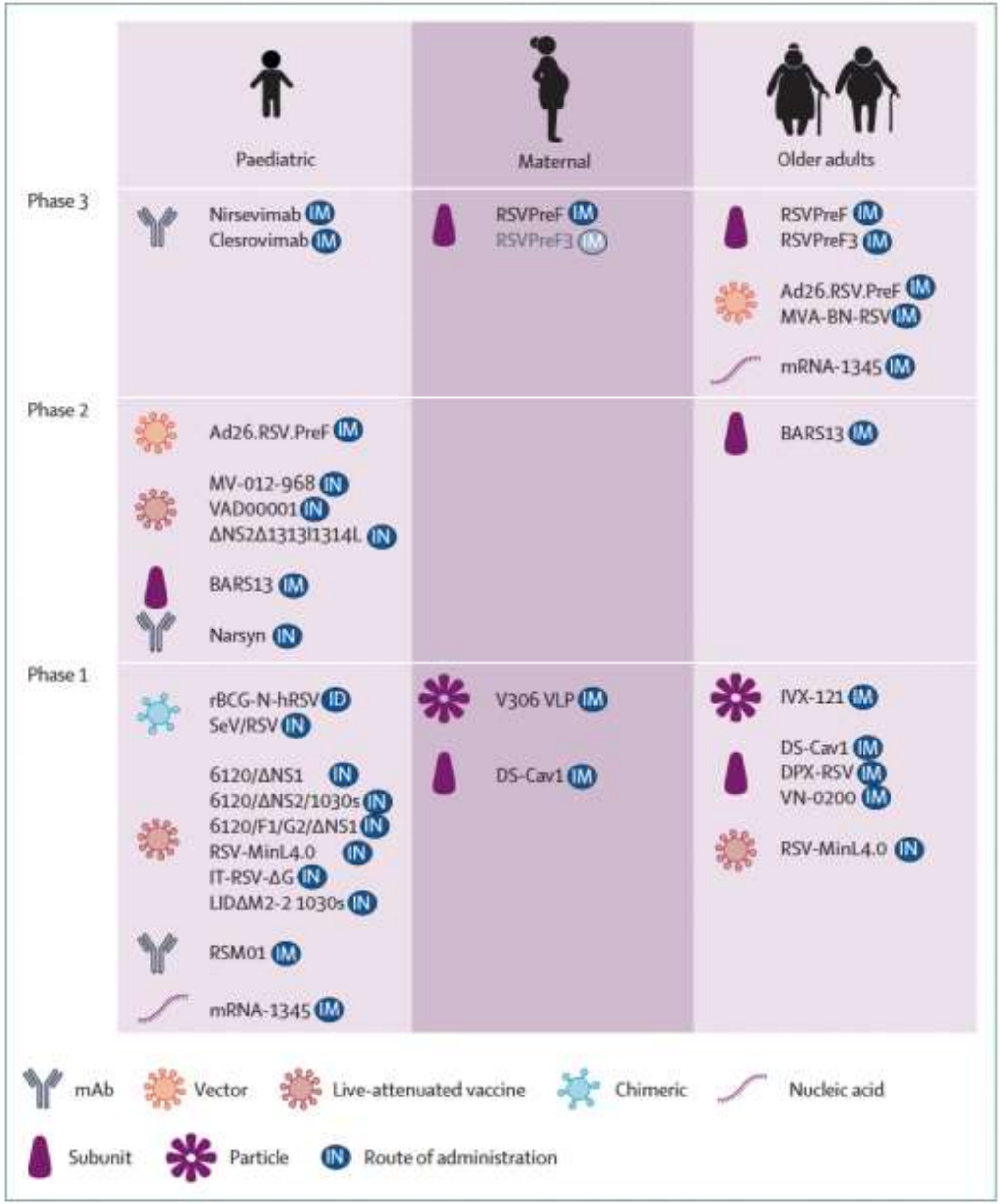
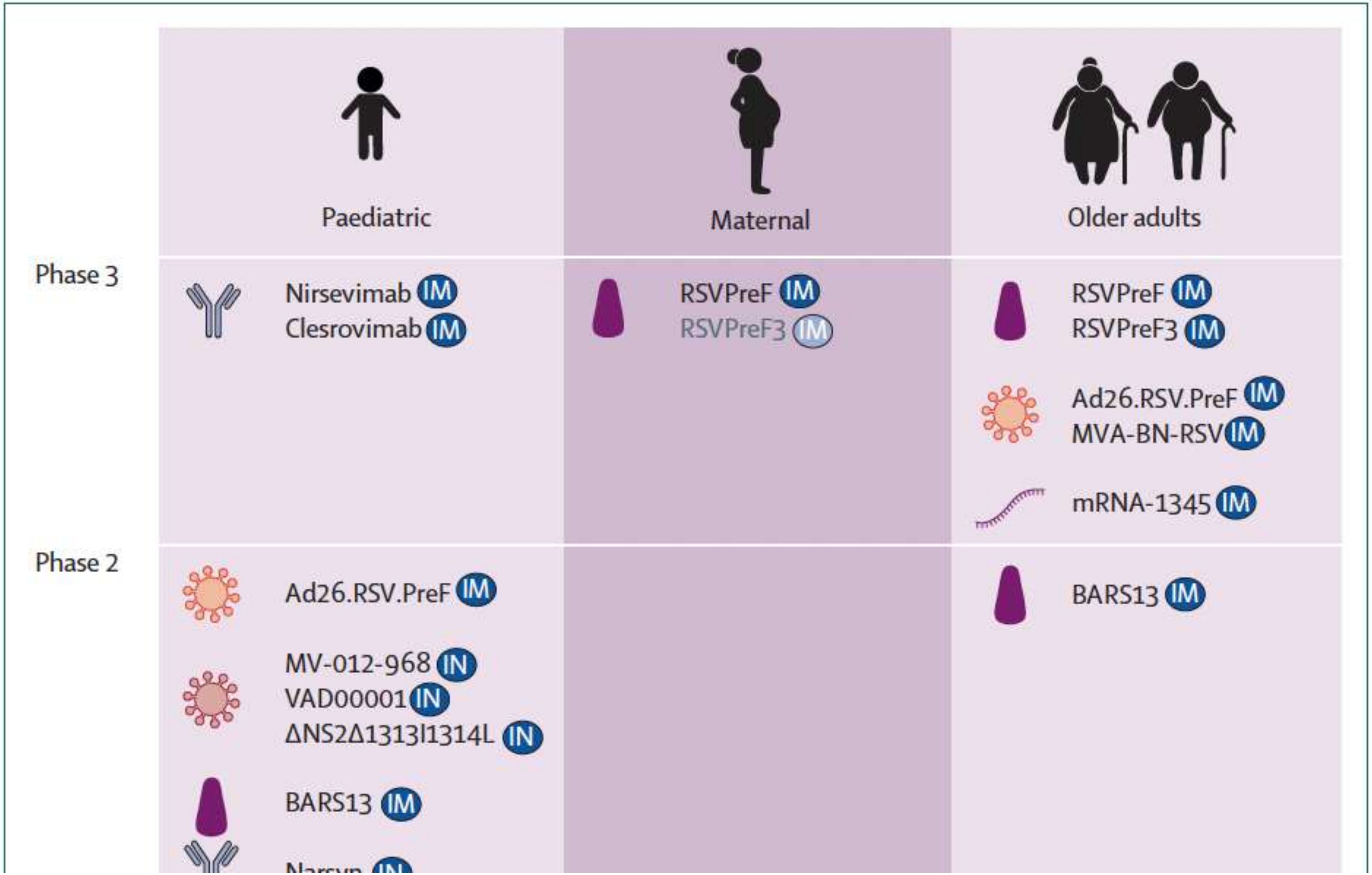

Paediatric
Maternal
Older adults
Phase 3
Nirsevimab IM
Clesrovimab IM
RSVPreF IM
RSVPreF3 IM
RSVPreF IM
RSVPreF3 IM
Ad26.RSV.PreF IM
MVA-BN-RSV IM
mRNA-1345 IM
Phase 2
Ad26.RSV.PreF IM
MV-012-968 IN
VAD00001 IN
ΔNS2Δ1313I1314L IN
BARS13 IM
Narsyn IN
BARS13 IM
Phase 1
rBCG-N-hRSV ID
SeV/RSV IN
6120/ΔNS1 IN
6120/ΔNS2/1030s IN
6120/F1/G2/ΔNS1 IN
RSV-MinL4.0 IN
IT-RSV-ΔG IN
LIDΔM2-2 1030s IN
RSM01 IM
mRNA-1345 IM
V306 VLP IM
DS-Cav1 IM
IVX-121 IM
DS-Cav1 IM
DPX-RSV IM
VN-0200 IM
RSV-MinL4.0 IN
mAb
Vector
Live-attenuated vaccine
Chimeric
Nucleic acid
Subunit
Particle
IN Route of administration

Figure 3: **RSV vaccine and monoclonal antibody agents by target population**

Vaccine candidates and monoclonal antibidies are categorised into three different target populations: paediatric, maternal, and older adults (aged >60 years) and clinical phase of development (ie, phase 1, 2, or 3). Different immunisation approaches are indicated by the key. Light grey text indicates development halted. IM=intramuscular. IN=intranasal. ID=intradermal. RSV=respiratory syncytial virus. PreF=prefusion protein. PostF=postfusion protein.



	Paediatric	Maternal	Older adults
Phase 3	Nirsevimab IM Clesrovimab IM	RSVPreF IM RSVPreF3 IM	RSVPreF IM RSVPreF3 IM Ad26.RSV.PreF IM MVA-BN-RSV IM mRNA-1345 IM
Phase 2	Ad26.RSV.PreF IM MV-012-968 IN VAD00001 IN ΔNS2Δ1313I1314L IN BARS13 IM Narsyn IN		BARS13 IM

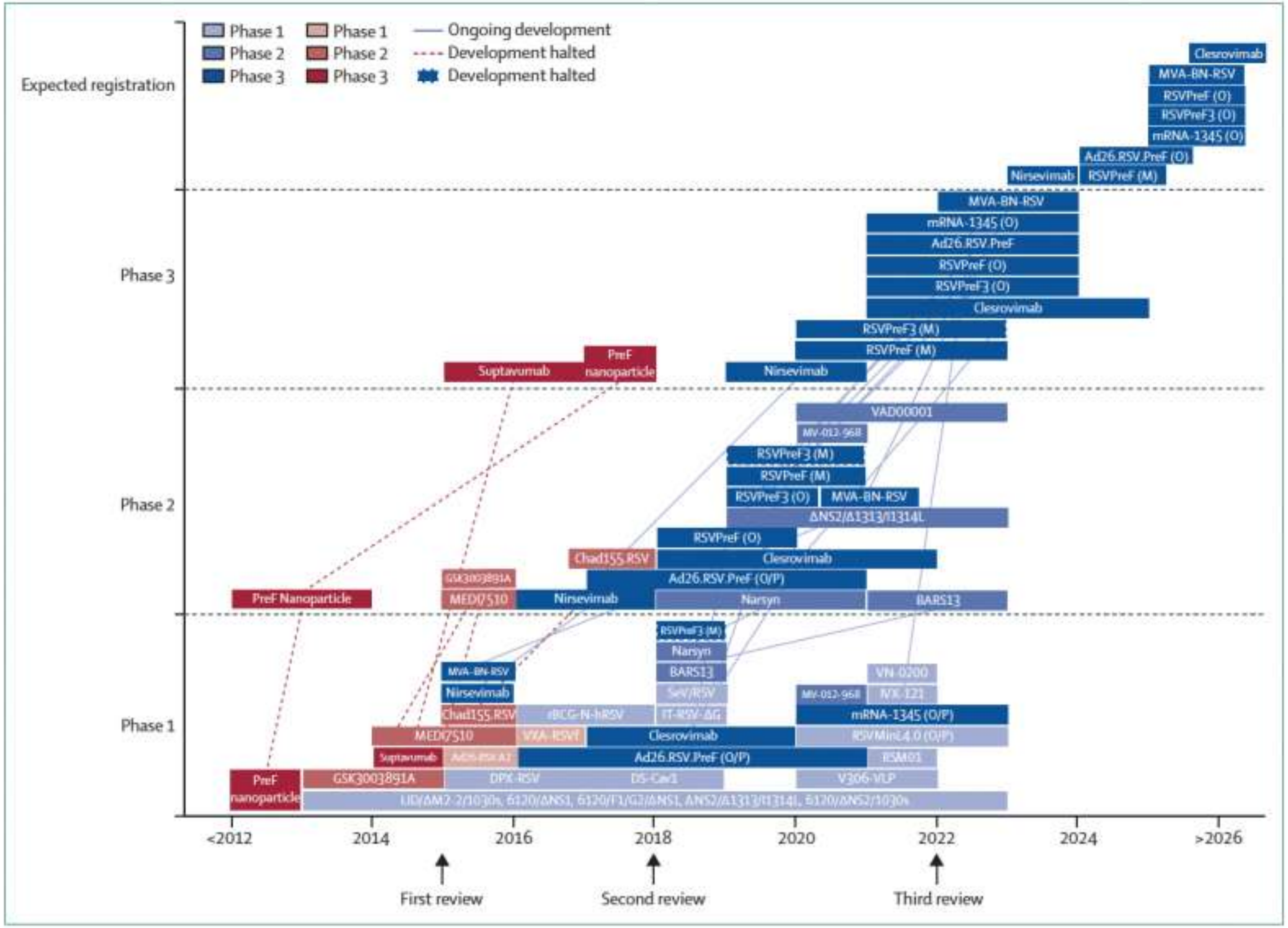


Figure 4: **Historical perspective of RSV vaccine and immunoprophylaxis development over the last 10 years and expected market access**

Candidates that are in ongoing development (blue) or no longer in development (red) are presented at the timing of the clinical trials rounded off to full years. The darkness of the colour represents the furthest development (phase 1, 2, or 3) of the candidate. Candidates with multiple clinical trials are connected with full or dotted lines to show the speed of development. Live attenuated viruses by the same manufacturer are summarised in one box as development of these candidates largely overlaps. The timing of current and previous RSV vaccine landscape reviews is shown at the bottom. RSV=respiratory syncytial virus. PreF=prefusion protein. The development of RSVPreF (M) was not discontinued but instead halted (dotted box). Expected registration was estimated by adding 1 year after published interim results, or if not available by adding 1 year to the estimated completion year published on ClinicalTrials.gov. In case of a phase 1/2 or 2/3 trial, the trial has only been placed in the furthest developed stage.

Correspondence to:
Prof Louis Bont, Department of Pediatric Infectious Disease & Immunology, Wilhelmina Children's Hospital, University Medical Center Utrecht, Lundlaan 6, 3584EA Utrecht, The Netherlands
l.bont@umcutrecht.nl

See Online for appendix

For **Vaccines for the World Conference** see https://www.resvinet.org/rsvvw21.html

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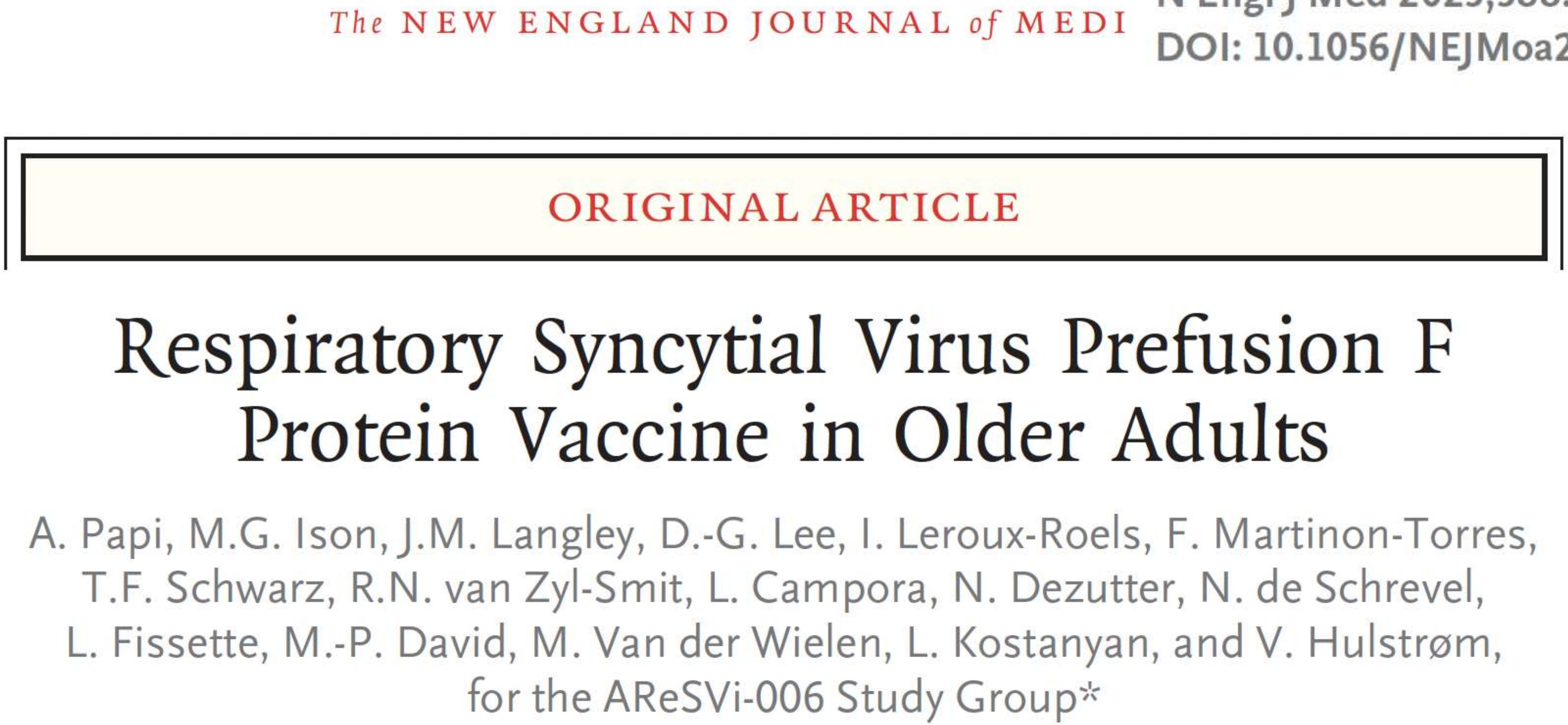


The NEW ENGLAND JOURNAL of MEDI

ORIGINAL ARTICLE

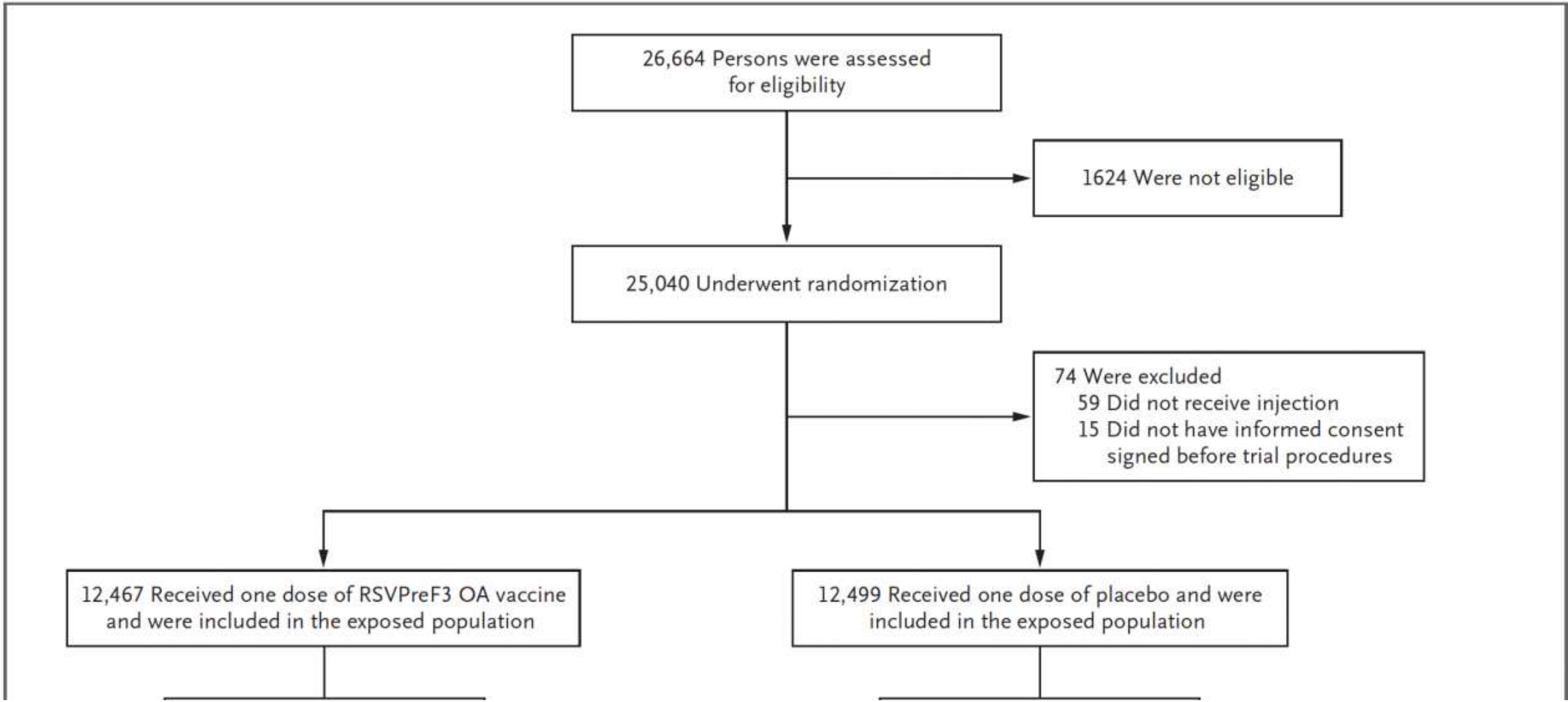
Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults

A. Papi, M.G. Ison, J.M. Langley, D.-G. Lee, I. Leroux-Roels, F. Martinon-Torres,
T.F. Schwarz, R.N. van Zyl-Smit, L. Campora, N. Dezutter, N. de Schrevel,
L. Fissette, M.-P. David, M. Van der Wielen, L. Kostanyan, and V. Hulstrøm,
for the AReSVi-006 Study Group*

Supported by GlaxoSmithKline Biologicals.

AS01E-adjuvanted RSV prefusion F protein–based candidate vaccine (RSVPreF3 OA)

Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults



26,664 Persons were assessed for eligibility

1624 Were not eligible

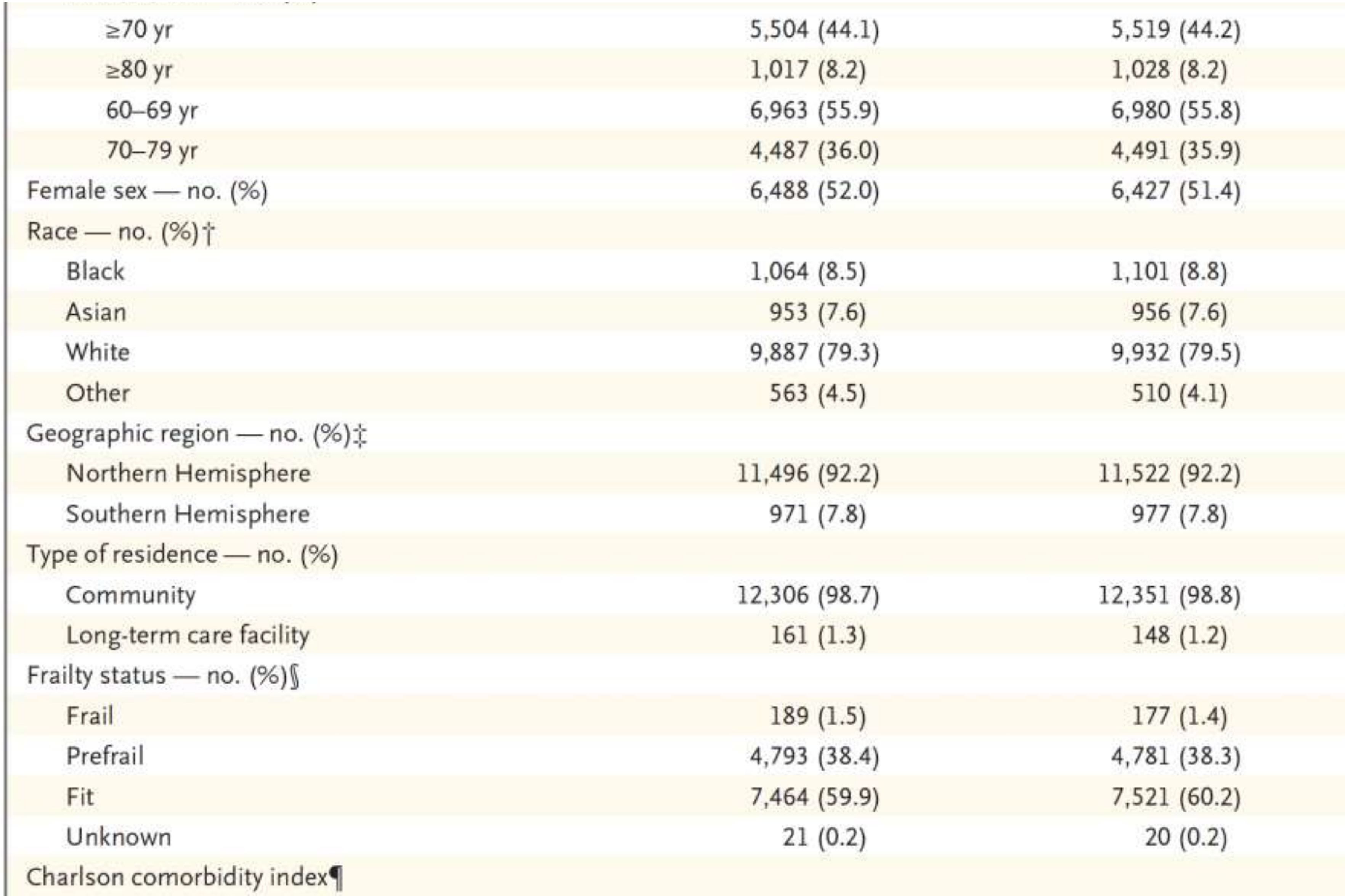
25,040 Underwent randomization

74 Were excluded
- 59 Did not receive injection
- 15 Did not have informed consent signed before trial procedures

12,467 Received one dose of RSVPreF3 OA vaccine and were included in the exposed population

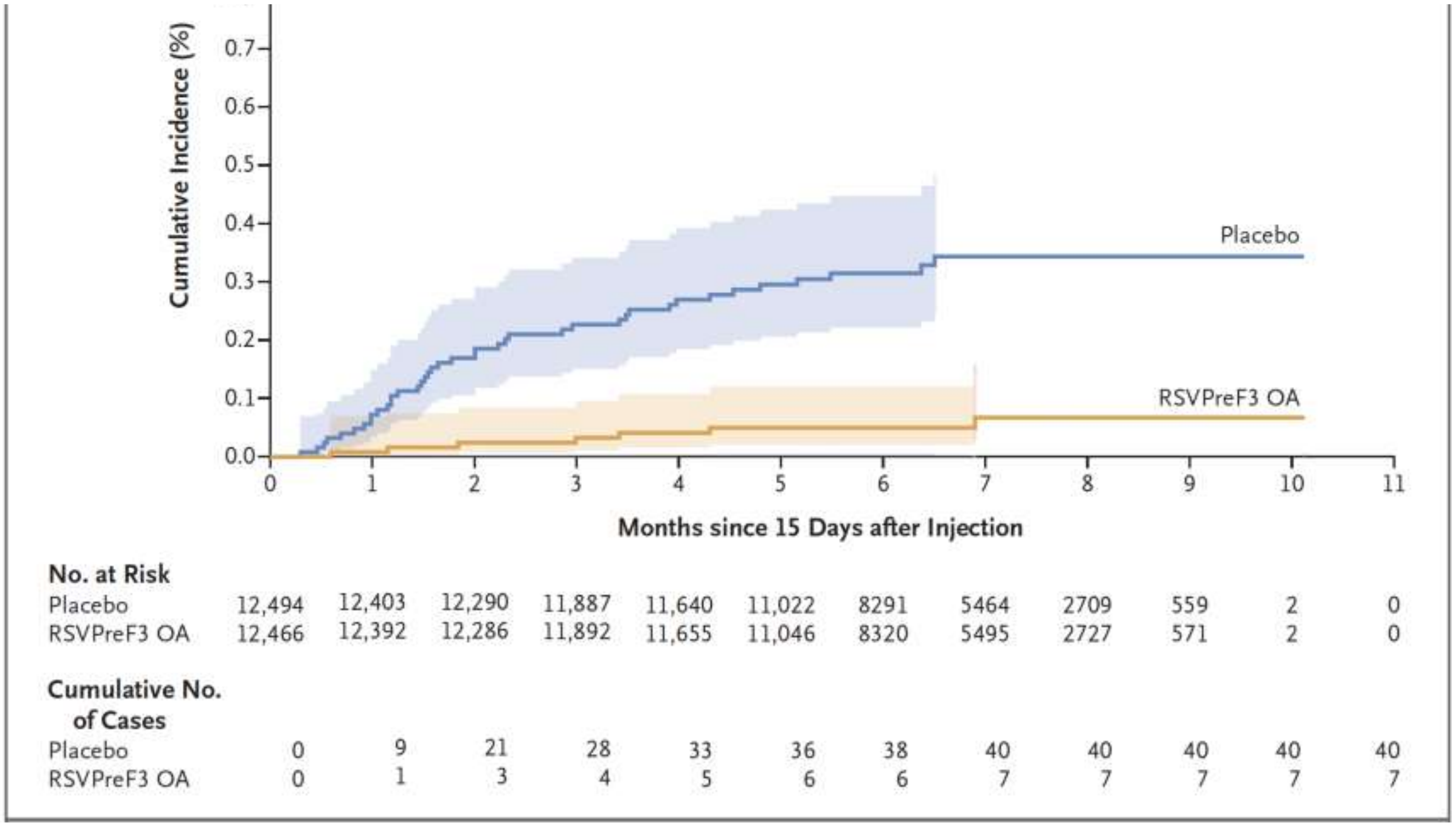
12,499 Received one dose of placebo and were included in the exposed population

Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults



≥70 yr	5,504 (44.1)	5,519 (44.2)
≥80 yr	1,017 (8.2)	1,028 (8.2)
60–69 yr	6,963 (55.9)	6,980 (55.8)
70–79 yr	4,487 (36.0)	4,491 (35.9)
Female sex — no. (%)	6,488 (52.0)	6,427 (51.4)
Race — no. (%)†		
Black	1,064 (8.5)	1,101 (8.8)
Asian	953 (7.6)	956 (7.6)
White	9,887 (79.3)	9,932 (79.5)
Other	563 (4.5)	510 (4.1)
Geographic region — no. (%)‡		
Northern Hemisphere	11,496 (92.2)	11,522 (92.2)
Southern Hemisphere	971 (7.8)	977 (7.8)
Type of residence — no. (%)		
Community	12,306 (98.7)	12,351 (98.8)
Long-term care facility	161 (1.3)	148 (1.2)
Frailty status — no. (%)§		
Frail	189 (1.5)	177 (1.4)
Prefrail	4,793 (38.4)	4,781 (38.3)
Fit	7,464 (59.9)	7,521 (60.2)
Unknown	21 (0.2)	20 (0.2)
Charlson comorbidity index¶		

Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults

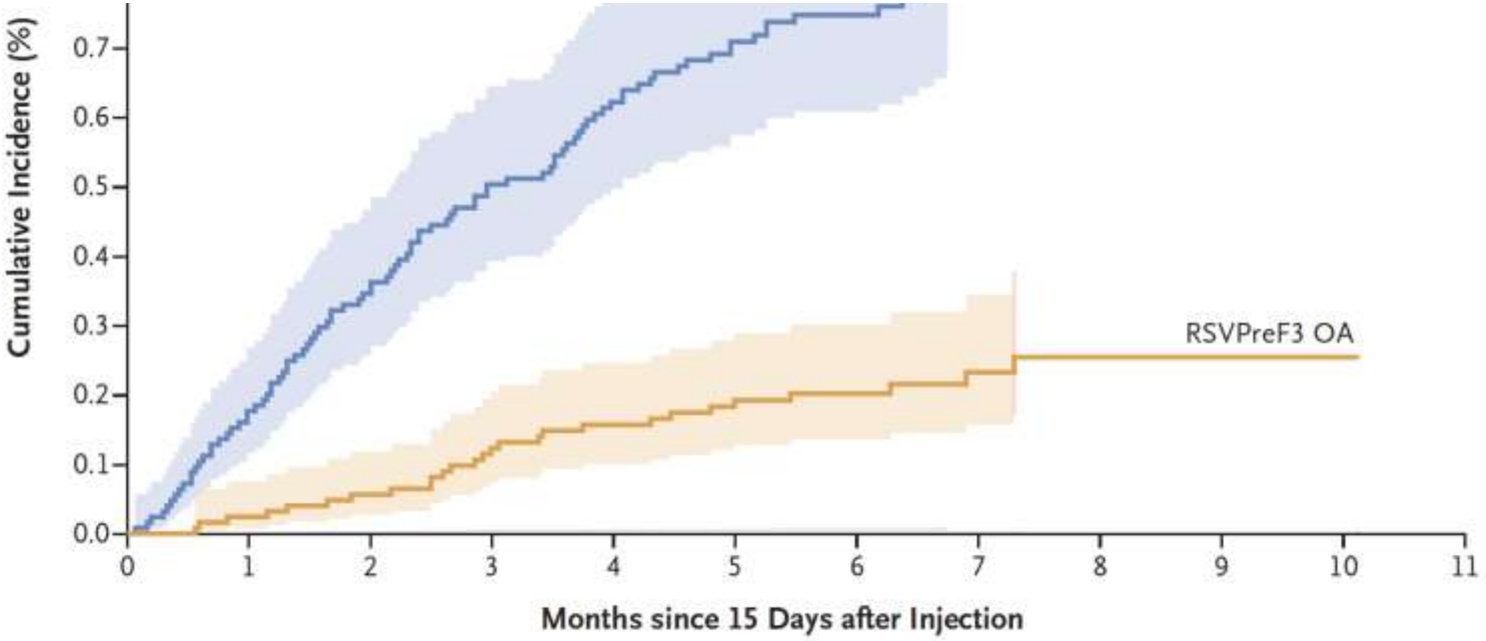


No. at Risk											
Placebo	12,494	12,403	12,290	11,887	11,640	11,022	8291	5464	2709	559	2	0
RSVPreF3 OA	12,466	12,392	12,286	11,892	11,655	11,046	8320	5495	2727	571	2	0

Cumulative No. of Cases												
Placebo	0	9	21	28	33	36	38	40	40	40	40	40
RSVPreF3 OA	0	1	3	4	5	6	6	7	7	7	7	7

incidence of RSV-related lower respiratory tract disease

Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults



No. at Risk

	0	1	2	3	4	5	6	7	8	9	10	11
Placebo	12,494	12,390	12,268	11,853	11,597	10,973	8255	5441	2697	554	2	0
RSVPreF3 OA	12,466	12,390	12,282	11,881	11,641	11,029	8305	5481	2717	570	2	0

Cumulative No. of Cases

	0	1	2	3	4	5	6	7	8	9	10	11
Placebo	0	22	43	62	76	86	90	95	95	95	95	95
RSVPreF3 OA	0	3	7	15	19	23	24	26	27	27	27	27

incidence of RSV-related acute respiratory infection

Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults

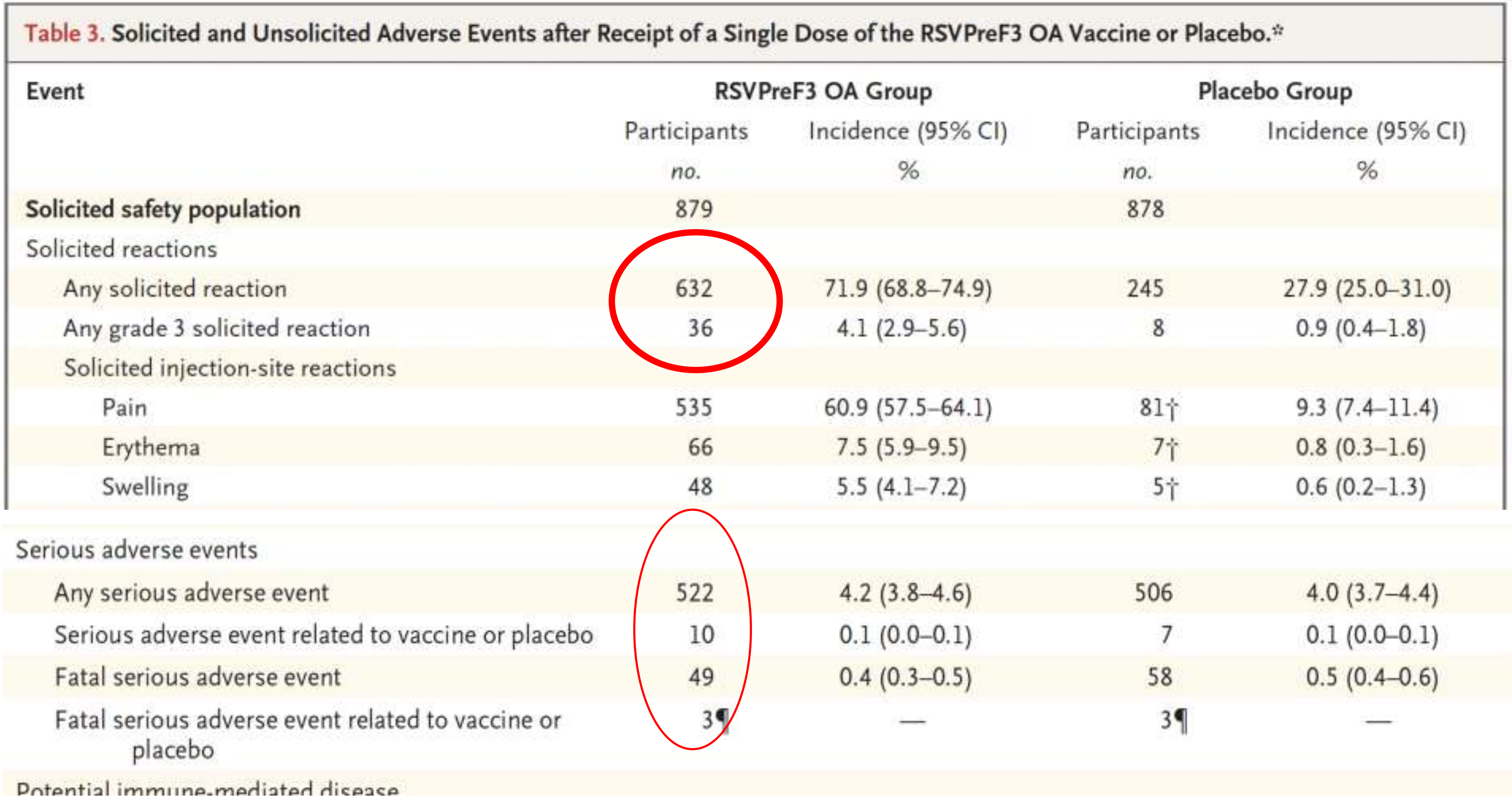


Table 3. Solicited and Unsolicited Adverse Events after Receipt of a Single Dose of the RSVPreF3 OA Vaccine or Placebo.*

Event	RSVPreF3 OA Group		Placebo Group	
	Participants	Incidence (95% CI)	Participants	Incidence (95% CI)
	no.	%	*no.*	%
Solicited safety population	879		878	
Solicited reactions				
Any solicited reaction	632	71.9 (68.8–74.9)	245	27.9 (25.0–31.0)
Any grade 3 solicited reaction	36	4.1 (2.9–5.6)	8	0.9 (0.4–1.8)
Solicited injection-site reactions				
Pain	535	60.9 (57.5–64.1)	81†	9.3 (7.4–11.4)
Erythema	66	7.5 (5.9–9.5)	7†	0.8 (0.3–1.6)
Swelling	48	5.5 (4.1–7.2)	5†	0.6 (0.2–1.3)
Serious adverse events				
Any serious adverse event	522	4.2 (3.8–4.6)	506	4.0 (3.7–4.4)
Serious adverse event related to vaccine or placebo	10	0.1 (0.0–0.1)	7	0.1 (0.0–0.1)
Fatal serious adverse event	49	0.4 (0.3–0.5)	58	0.5 (0.4–0.6)
Fatal serious adverse event related to vaccine or placebo	3¶	—	3¶	—
Potential immune-mediated disease				

Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults

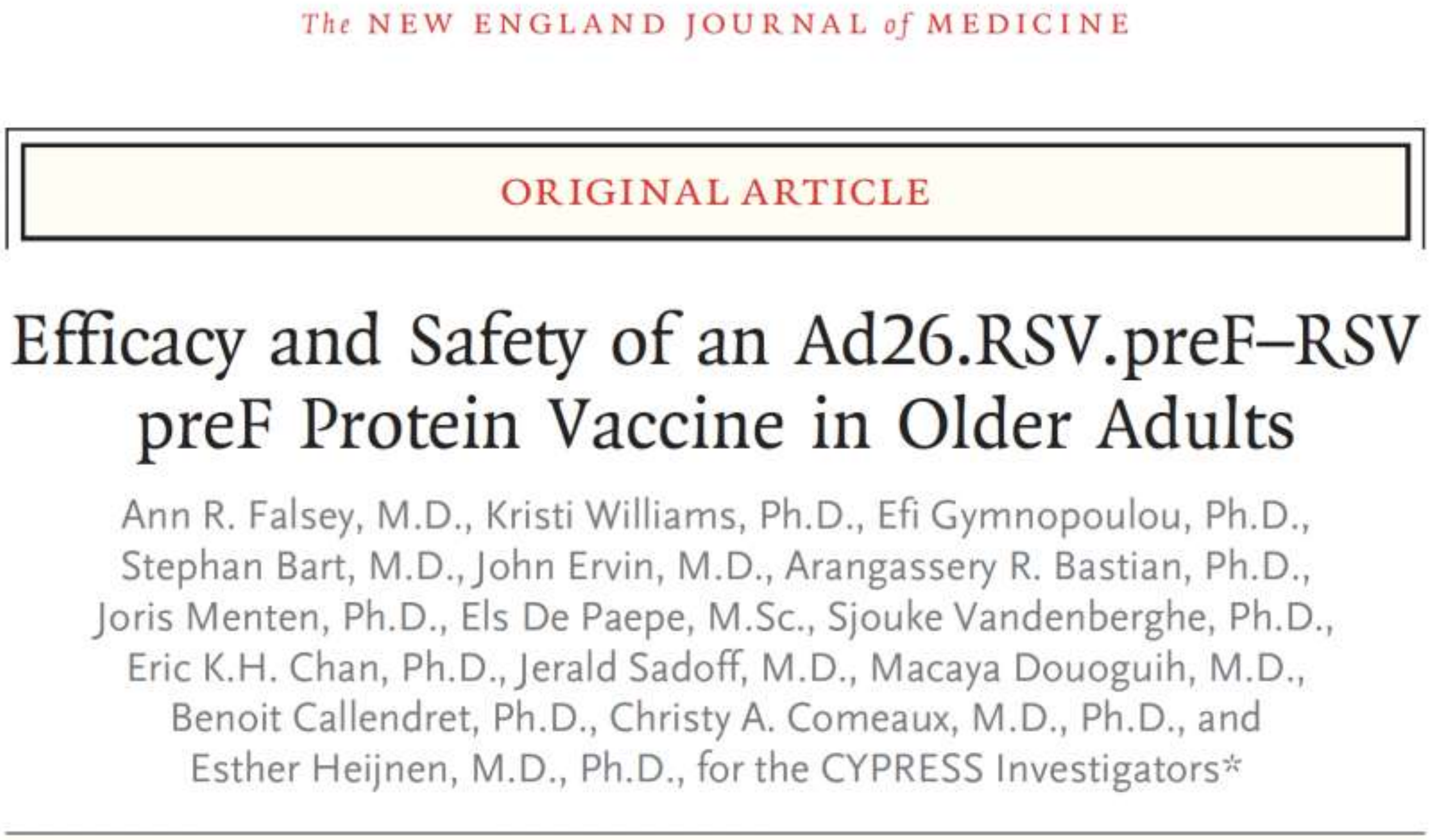
Over a median follow-up of 6.7 months,
vaccine efficacy against RT-PCR–confirmed RSV-related lower
Respiratory tract disease

- 7 cases (1.0 per 1000 participant-years) in the vaccine group and
- 40 cases (5.8 per 1000 participant-years) in the placebo group.

L'efficacité du vaccin était de

- 94,1 % contre les maladies graves des voies respiratoires inférieures liées au VRS et de
- 71,7 % contre les infections respiratoires aiguës liées au VRS

N Engl J Med 2023;388:609-20.
DOI: 10.1056/NEJMoa2207566

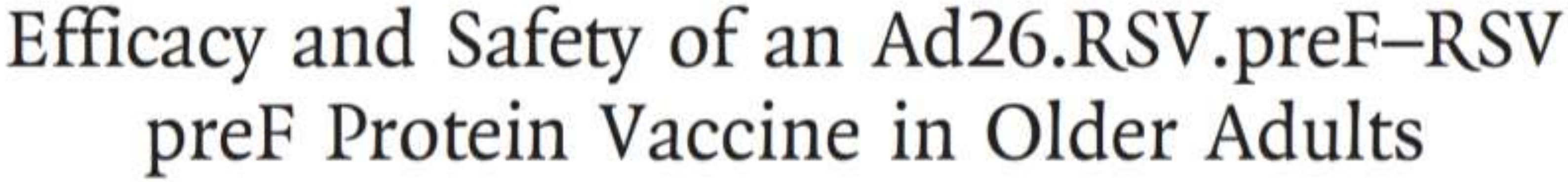


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Efficacy and Safety of an Ad26.RSV.preF–RSV preF Protein Vaccine in Older Adults

Ann R. Falsey, M.D., Kristi Williams, Ph.D., Efi Gymnopoulou, Ph.D., Stephan Bart, M.D., John Ervin, M.D., Arangassery R. Bastian, Ph.D., Joris Menten, Ph.D., Els De Paepe, M.Sc., Sjouke Vandenberghe, Ph.D., Eric K.H. Chan, Ph.D., Jerald Sadoff, M.D., Macaya Douoguih, M.D., Benoit Callendret, Ph.D., Christy A. Comeaux, M.D., Ph.D., and Esther Heijnen, M.D., Ph.D., for the CYPRESS Investigators*



Efficacy and Safety of an Ad26.RSV.preF–RSV preF Protein Vaccine in Older Adults

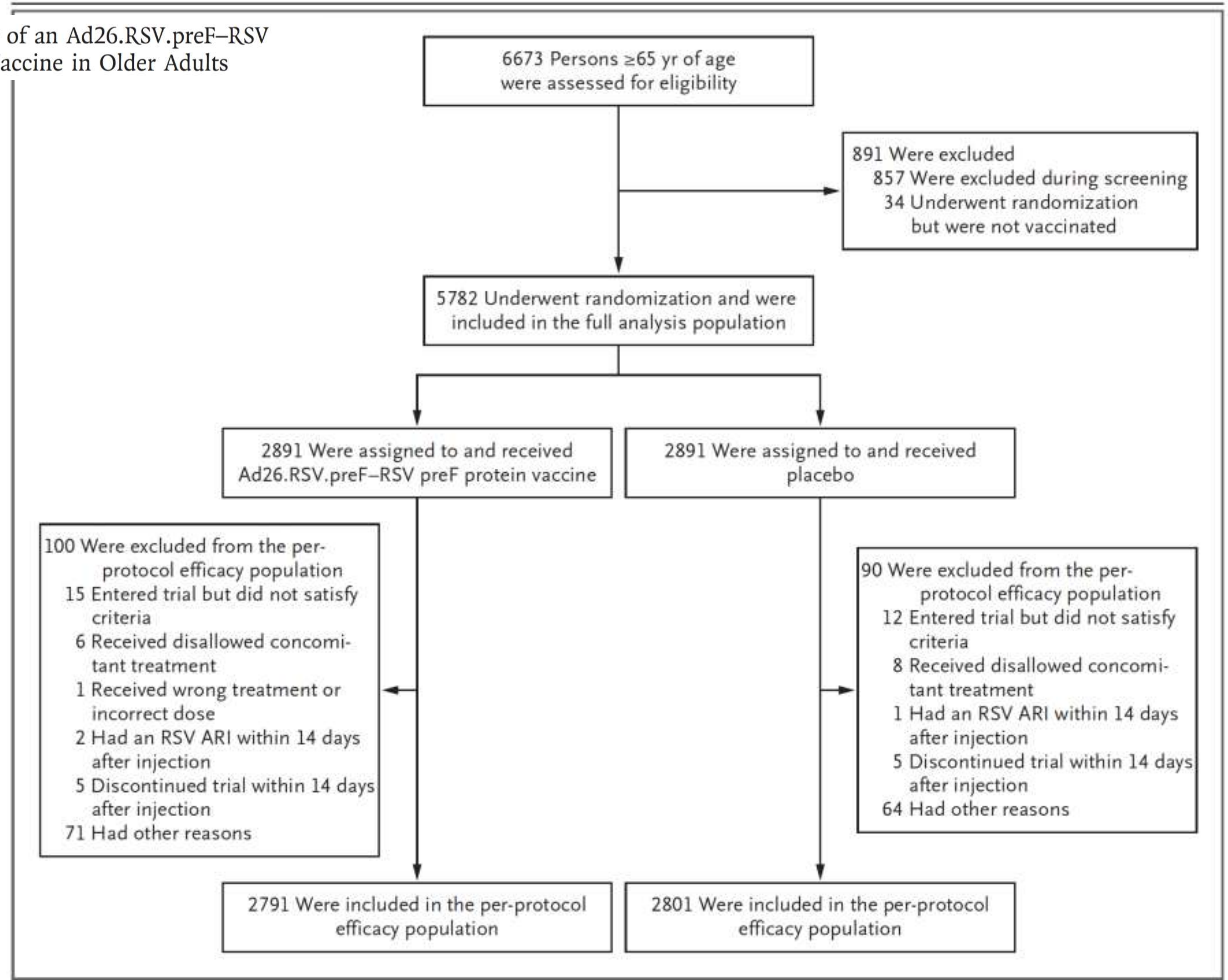
A recombinant, replication-incompetent, adenovirus serotype 26 vector encoding a conformation-stabilized RSV preF protein (Ad26.RSV.preF) and recombinant RSV preF protein, with no adjuvant.

Efficacy and Safety of an Ad26.RSV.preF–RSV preF Protein Vaccine in Older Adults

Trois définitions de cas :

- 3 symptômes ou plus d'infection des voies respiratoires inférieures (définition de cas 1, la maladie la plus grave),
- 2 ou plusieurs symptômes d'infection des voies respiratoires inférieures (définition de cas 2), et soit
- 2 ou plusieurs symptômes d'infection des voies respiratoires inférieures ou un ou plusieurs symptômes d'infection des voies respiratoires inférieures plus au moins un symptôme systémique (définition de cas 3)

Efficacy and Safety of an Ad26.RSV.preF–RSV preF Protein Vaccine in Older Adults



6673 Persons ≥65 yr of age were assessed for eligibility

891 Were excluded
- 857 Were excluded during screening
- 34 Underwent randomization but were not vaccinated

5782 Underwent randomization and were included in the full analysis population

2891 Were assigned to and received Ad26.RSV.preF–RSV preF protein vaccine

2891 Were assigned to and received placebo

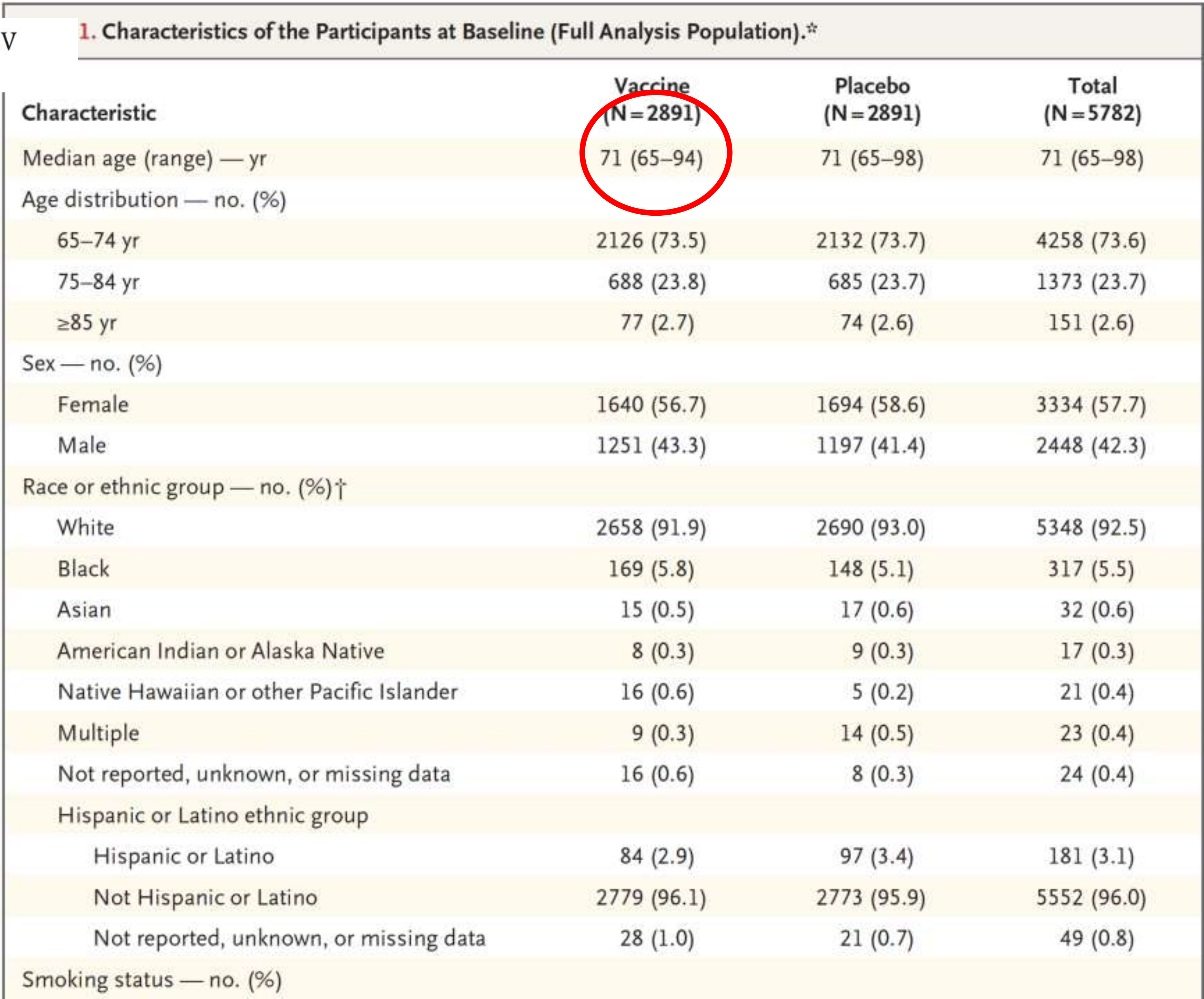
100 Were excluded from the per-protocol efficacy population
- 15 Entered trial but did not satisfy criteria
- 6 Received disallowed concomitant treatment
- 1 Received wrong treatment or incorrect dose
- 2 Had an RSV ARI within 14 days after injection
- 5 Discontinued trial within 14 days after injection
- 71 Had other reasons

90 Were excluded from the per-protocol efficacy population
- 12 Entered trial but did not satisfy criteria
- 8 Received disallowed concomitant treatment
- 1 Had an RSV ARI within 14 days after injection
- 5 Discontinued trial within 14 days after injection
- 64 Had other reasons

2791 Were included in the per-protocol efficacy population

2801 Were included in the per-protocol efficacy population

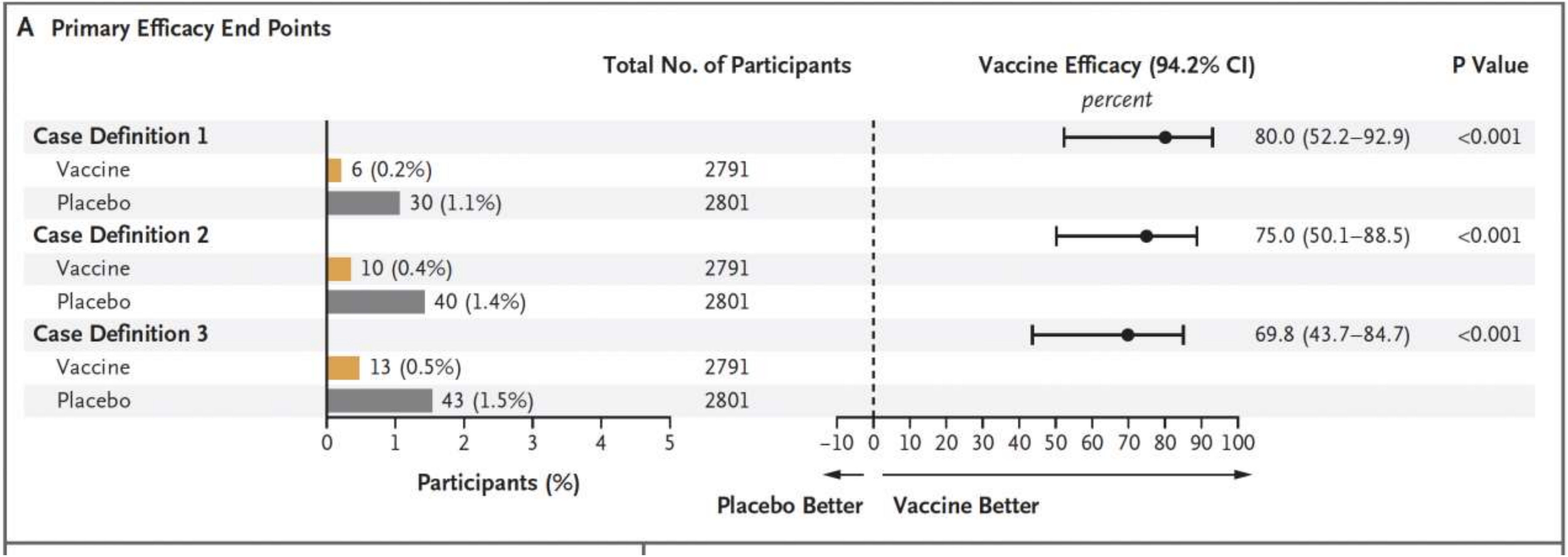
Efficacy and Safety of an Ad26.RSV.preF–RSV preF Protein Vaccine in Older Adults



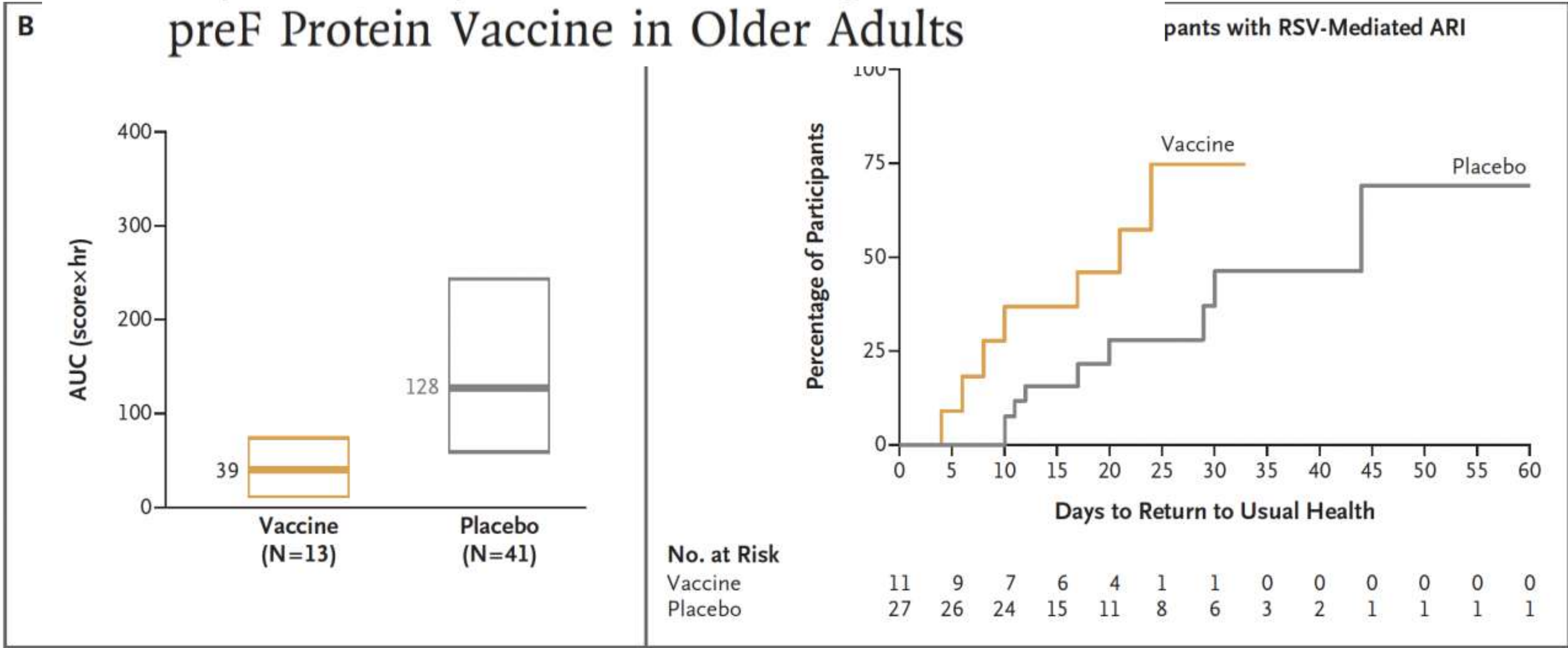
1. **Characteristics of the Participants at Baseline (Full Analysis Population).***

Characteristic	**Vaccine (N=2891)**	**Placebo (N=2891)**	**Total (N=5782)**
Median age (range) — yr	71 (65–94)	71 (65–98)	71 (65–98)
Age distribution — no. (%)			
65–74 yr	2126 (73.5)	2132 (73.7)	4258 (73.6)
75–84 yr	688 (23.8)	685 (23.7)	1373 (23.7)
≥85 yr	77 (2.7)	74 (2.6)	151 (2.6)
Sex — no. (%)			
Female	1640 (56.7)	1694 (58.6)	3334 (57.7)
Male	1251 (43.3)	1197 (41.4)	2448 (42.3)
Race or ethnic group — no. (%)†			
White	2658 (91.9)	2690 (93.0)	5348 (92.5)
Black	169 (5.8)	148 (5.1)	317 (5.5)
Asian	15 (0.5)	17 (0.6)	32 (0.6)
American Indian or Alaska Native	8 (0.3)	9 (0.3)	17 (0.3)
Native Hawaiian or other Pacific Islander	16 (0.6)	5 (0.2)	21 (0.4)
Multiple	9 (0.3)	14 (0.5)	23 (0.4)
Not reported, unknown, or missing data	16 (0.6)	8 (0.3)	24 (0.4)
Hispanic or Latino ethnic group			
Hispanic or Latino	84 (2.9)	97 (3.4)	181 (3.1)
Not Hispanic or Latino	2779 (96.1)	2773 (95.9)	5552 (96.0)
Not reported, unknown, or missing data	28 (1.0)	21 (0.7)	49 (0.8)
Smoking status — no. (%)			

Efficacy and Safety of an Ad26.RSV.preF–RSV preF Protein Vaccine in Older Adults



Efficacy and Safety of an Ad26.RSV.preF–RSV preF Protein Vaccine in Older Adults



No. at Risk

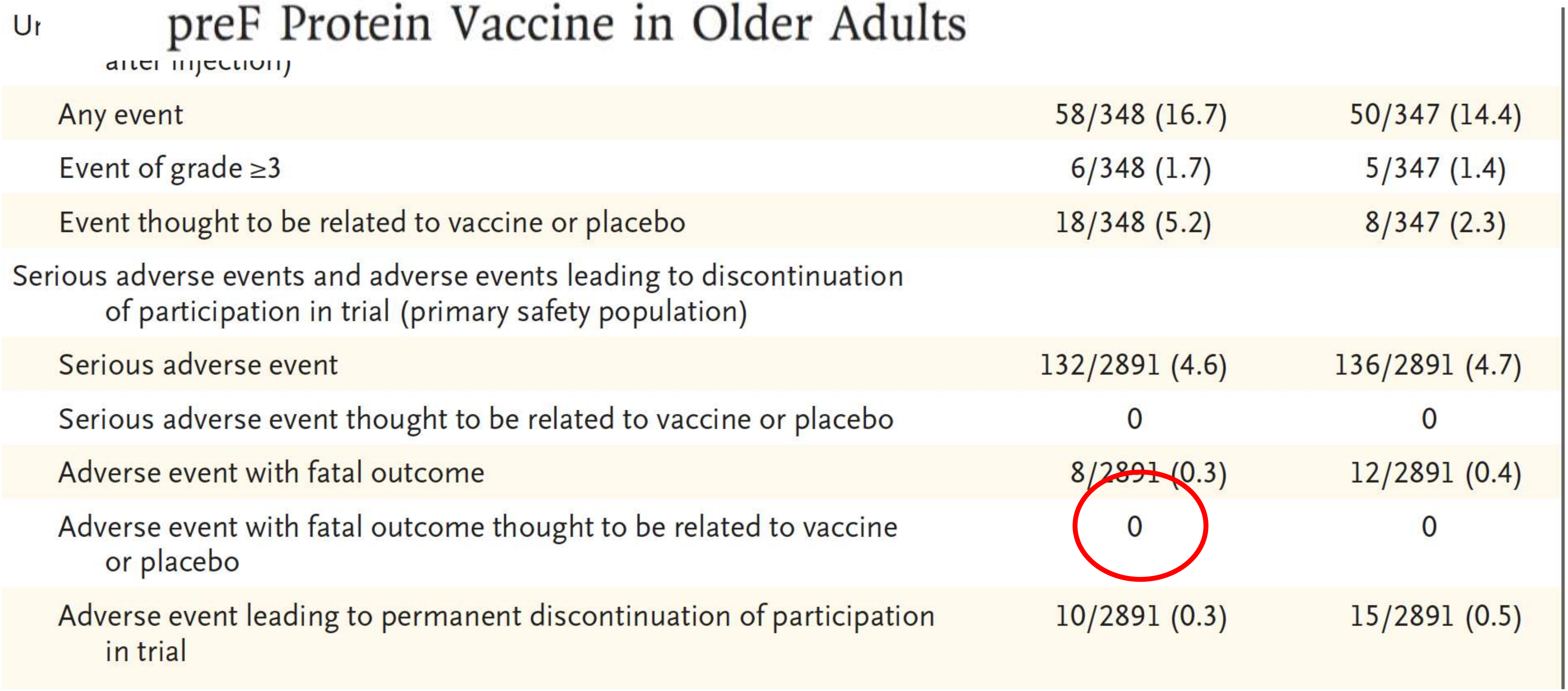
	0	5	10	15	20	25	30	35	40	45	50	55	60
Vaccine	11	9	7	6	4	1	1	0	0	0	0	0	0
Placebo	27	26	24	15	11	8	6	3	2	1	1	1	1

Figure 2. Vaccine Efficacy.

Efficacy and Safety of an Ad26.RSV.preF–RSV preF Protein Vaccine in Older Adults

5782 participants.
Une maladie des voies respiratoires inférieures a VRS répondant aux définitions de cas 1, 2 et 3 est survenue chez
6, 10 et 13 receveurs de vaccin et chez
30, 40 et 43 receveurs de placebo, respectivement.

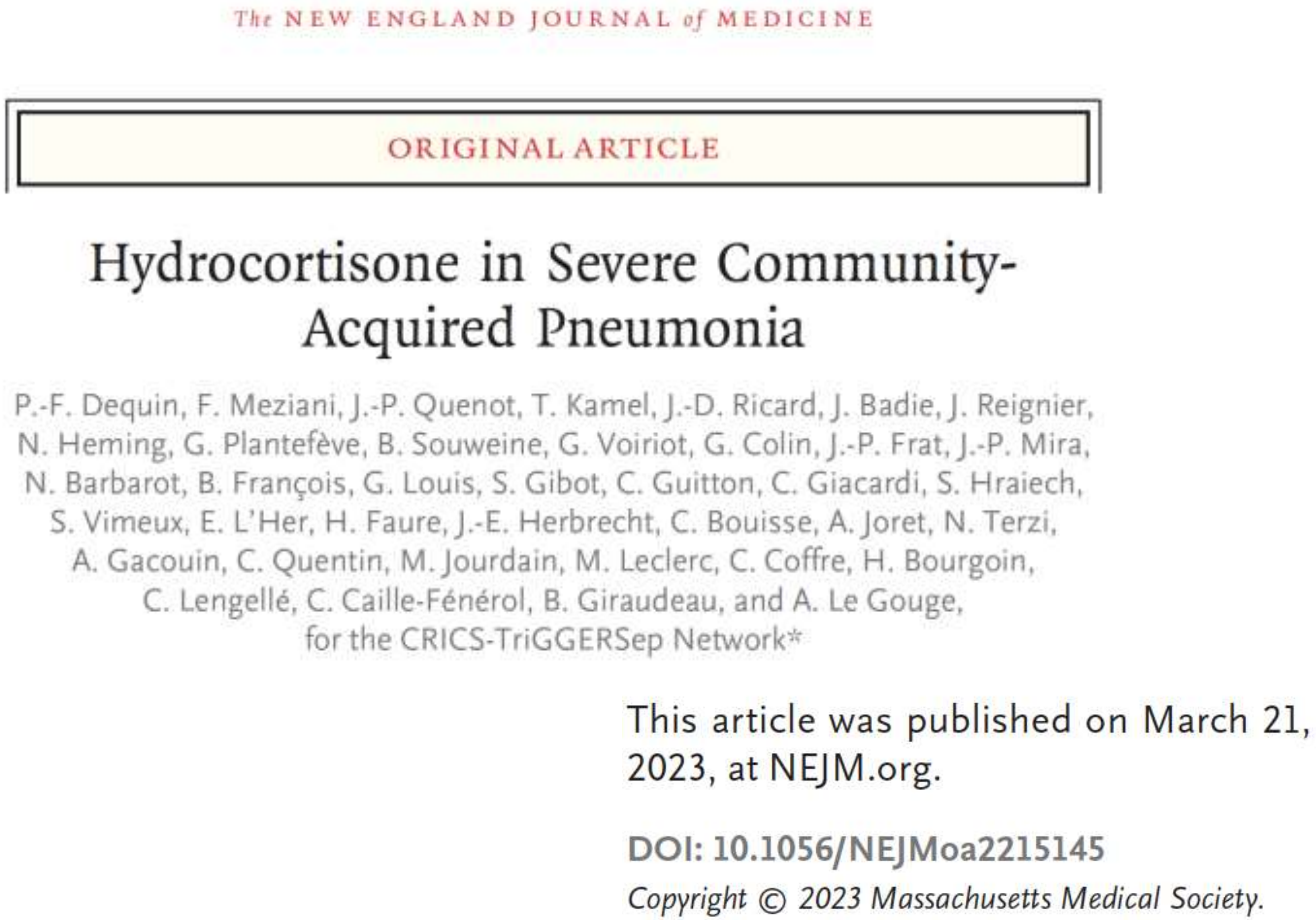
Efficacy and Safety of an Ad26.RSV.preF–RSV preF Protein Vaccine in Older Adults



Ur

after injection)

Any event	58/348 (16.7)	50/347 (14.4)
Event of grade ≥3	6/348 (1.7)	5/347 (1.4)
Event thought to be related to vaccine or placebo	18/348 (5.2)	8/347 (2.3)
Serious adverse events and adverse events leading to discontinuation of participation in trial (primary safety population)		
Serious adverse event	132/2891 (4.6)	136/2891 (4.7)
Serious adverse event thought to be related to vaccine or placebo	0	0
Adverse event with fatal outcome	8/2891 (0.3)	12/2891 (0.4)
Adverse event with fatal outcome thought to be related to vaccine or placebo	0	0
Adverse event leading to permanent discontinuation of participation in trial	10/2891 (0.3)	15/2891 (0.5)



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Hydrocortisone in Severe Community-Acquired Pneumonia

P.-F. Dequin, F. Meziani, J.-P. Quenot, T. Kamel, J.-D. Ricard, J. Badie, J. Reignier,
N. Heming, G. Plantefève, B. Souweine, G. Voiriot, G. Colin, J.-P. Frat, J.-P. Mira,
N. Barbarot, B. François, G. Louis, S. Gibot, C. Guitton, C. Giacardi, S. Hraiech,
S. Vimeux, E. L'Her, H. Faure, J.-E. Herbrecht, C. Bouisse, A. Joret, N. Terzi,
A. Gacouin, C. Quentin, M. Jourdain, M. Leclerc, C. Coffre, H. Bourgoin,
C. Lengellé, C. Caille-Fénérol, B. Giraudeau, and A. Le Gouge,
for the CRICS-TriGGERSep Network*

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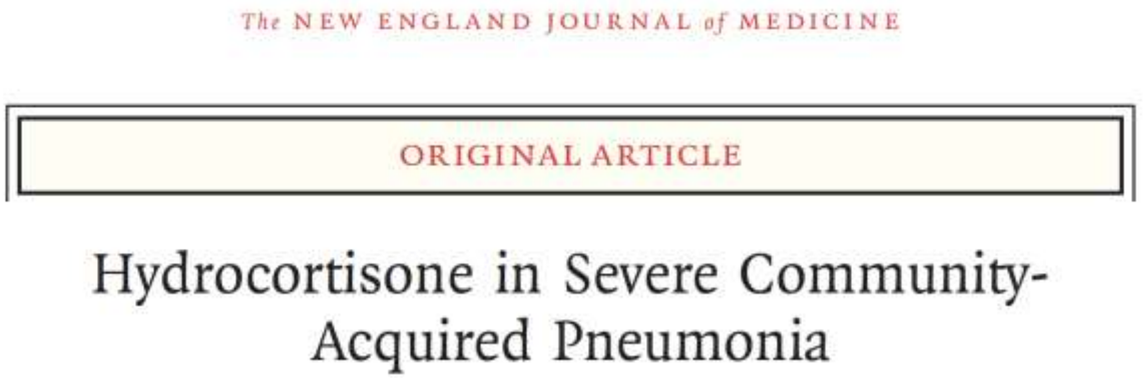


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Hydrocortisone in Severe Community-Acquired Pneumonia

Essai de phase 3, multicentrique, en double aveugle, randomisé et contrôlé, adultes admis en l'unité de soins intensifs (USI) pour une pneumonie communautaire grave

- hydrocortisone intraveineuse (200 mg par jour pendant 4 ou 8 jours, suivie d'une diminution progressive pendant un total de 8 ou 14 jours)
- ou un placebo.

Tous les patients ont reçu un traitement standard, y compris des antibiotiques et des soins de soutien.

Le résultat principal était le décès à 28 jours.

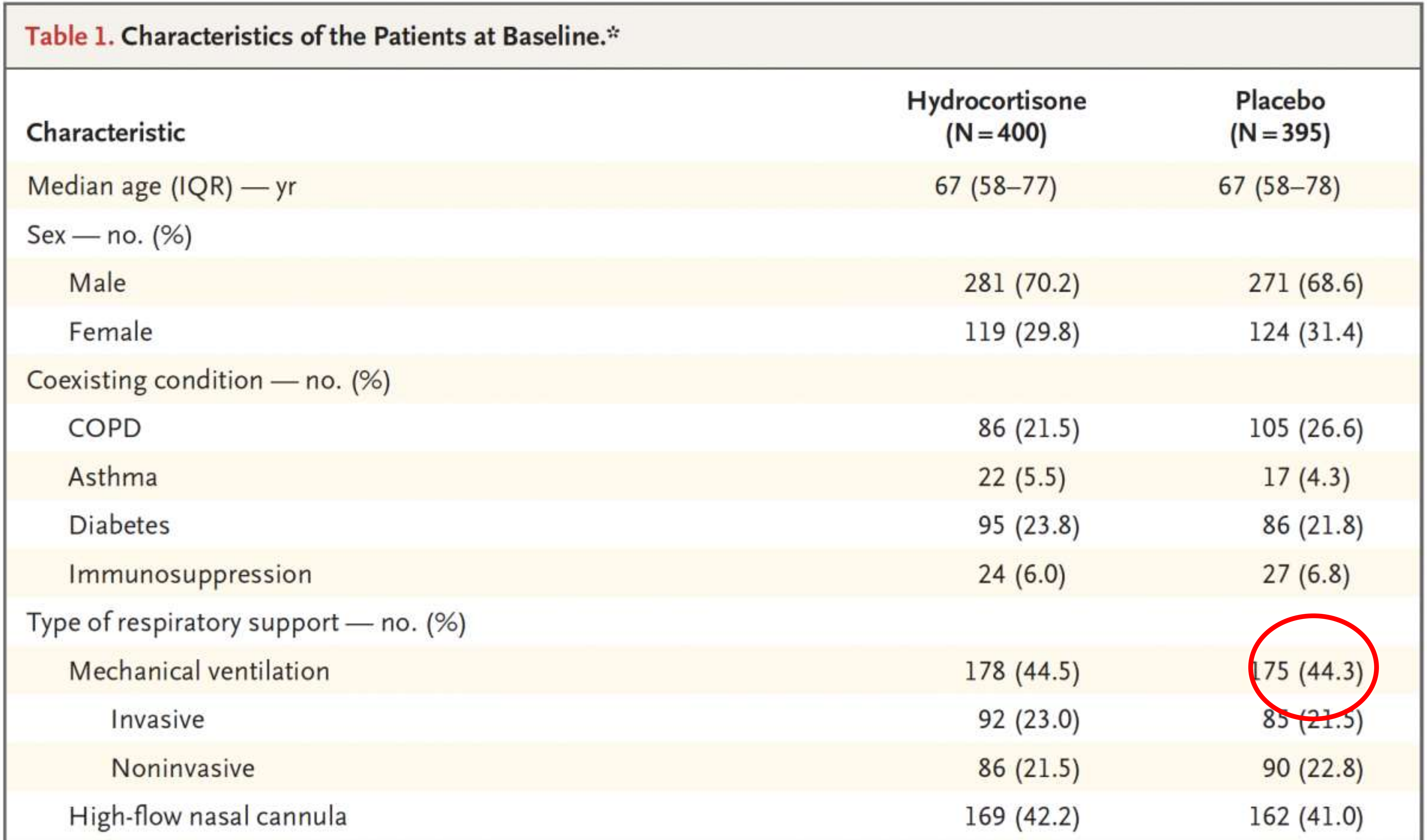
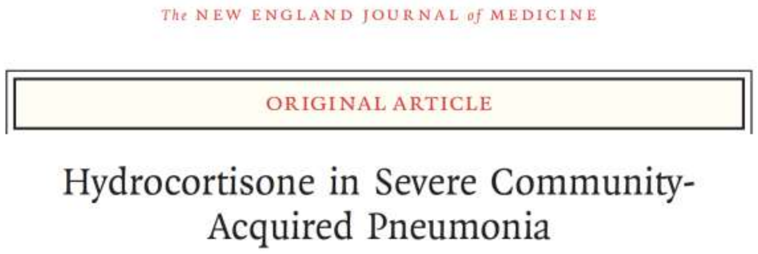


Table 1. **Characteristics of the Patients at Baseline.***

Characteristic	Hydrocortisone (N = 400)	Placebo (N = 395)
Median age (IQR) — yr	67 (58–77)	67 (58–78)
Sex — no. (%)		
Male	281 (70.2)	271 (68.6)
Female	119 (29.8)	124 (31.4)
Coexisting condition — no. (%)		
COPD	86 (21.5)	105 (26.6)
Asthma	22 (5.5)	17 (4.3)
Diabetes	95 (23.8)	86 (21.8)
Immunosuppression	24 (6.0)	27 (6.8)
Type of respiratory support — no. (%)		
Mechanical ventilation	178 (44.5)	175 (44.3)
Invasive	92 (23.0)	85 (21.5)
Noninvasive	86 (21.5)	90 (22.8)
High-flow nasal cannula	169 (42.2)	162 (41.0)



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

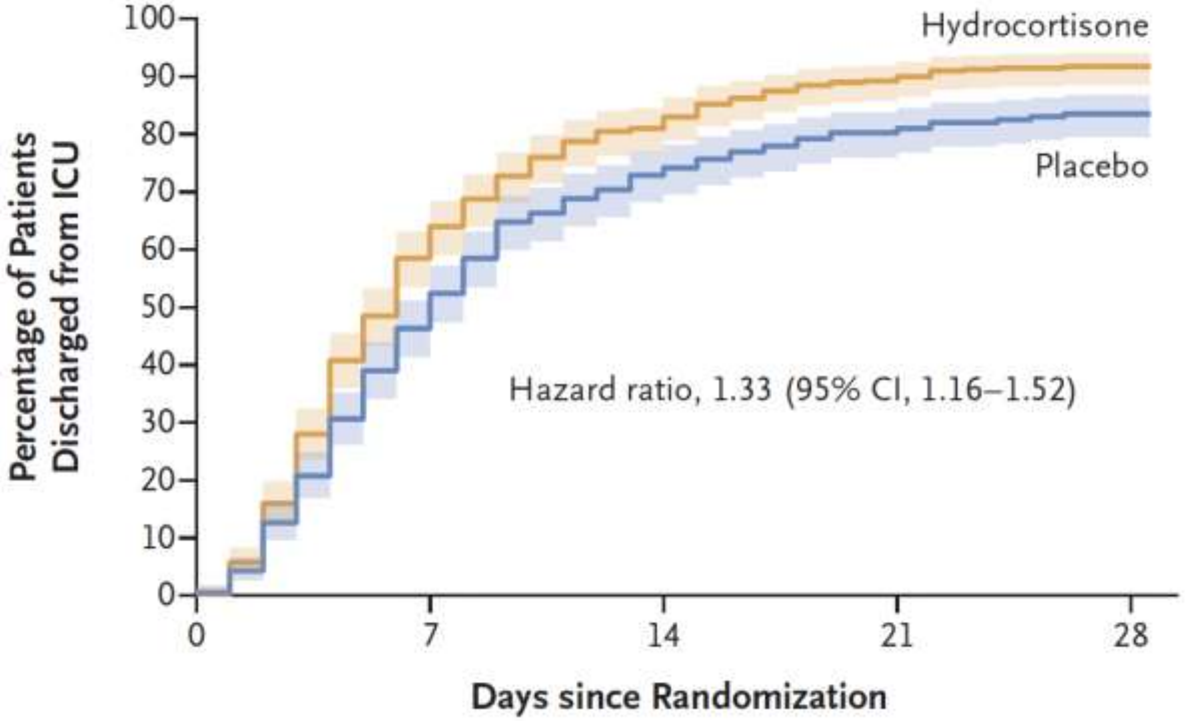
Hydrocortisone in Severe Community-Acquired Pneumonia

Au total, 800 patients ont été randomisés lorsque l'essai a été arrêté après la deuxième analyse intermédiaire prévue.

Les données de 795 patients ont été analysées.

Au jour 28, le décès était survenu chez

- 25 des 400 patients du groupe hydrocortisone et chez
- 47 des 395 patients du groupe placebo.

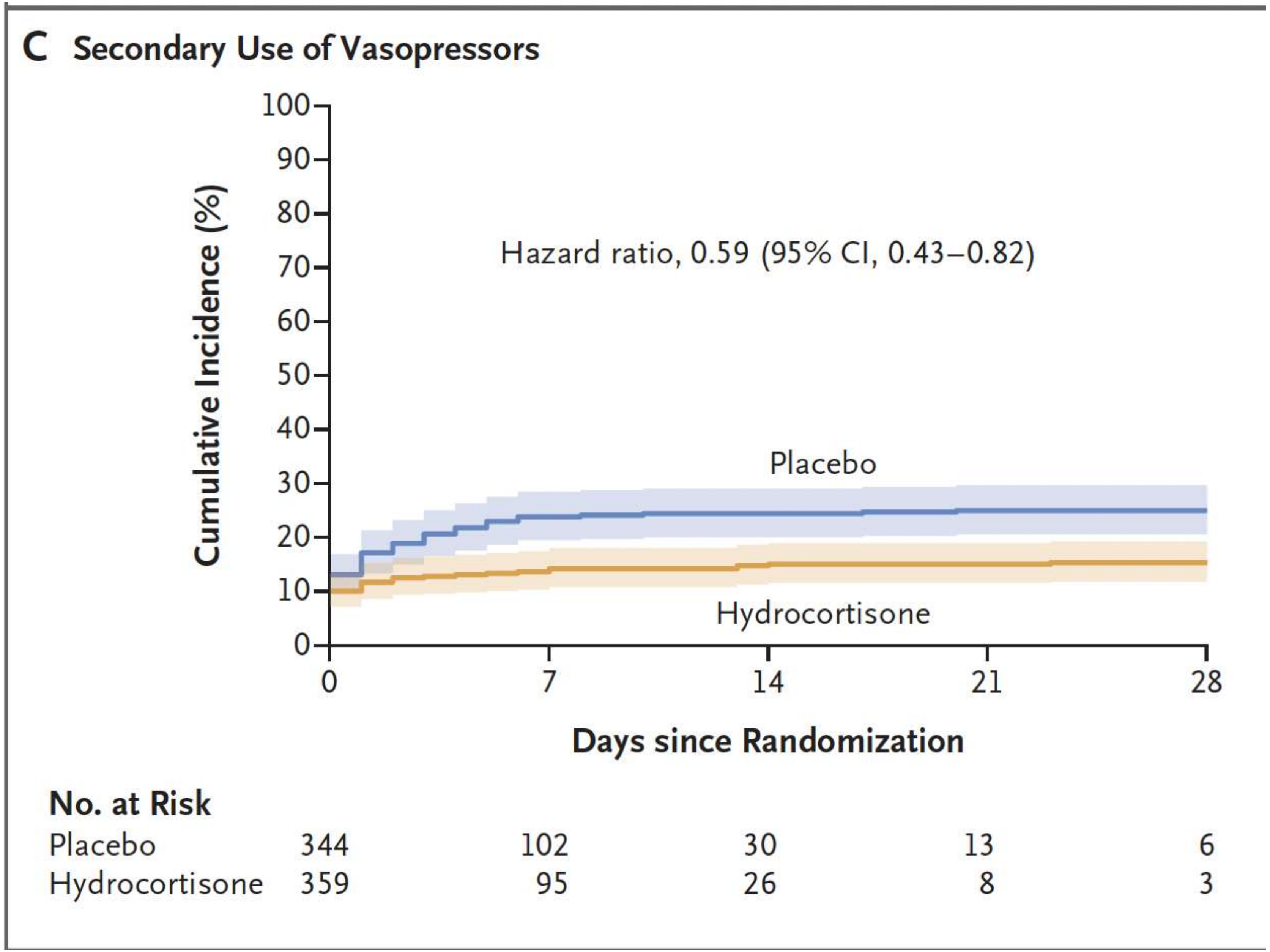


No. at Risk

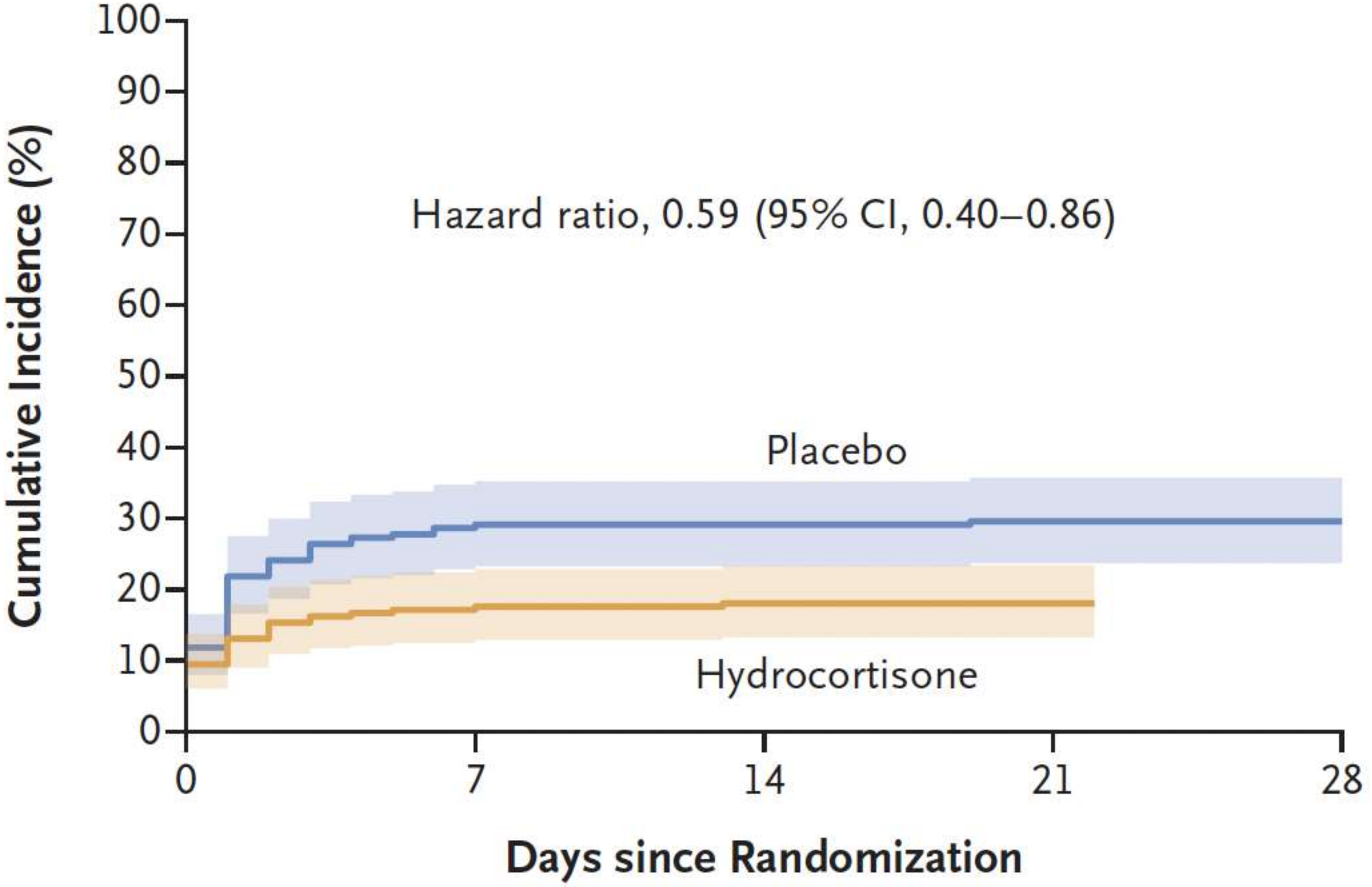
Hydrocortisone	400	160	67	31	17
Placebo	395	198	85	48	27

Figure 2. Discharge from ICU by Day 28.

Shown is the cumulative percentage of patients who were discharged from the ICU by day 28 (a secondary outcome in the trial). The length of ICU stay was compared in the framework of a competing-risk model, with death considered as a competing event. For secondary outcomes, the widths of the confidence intervals have not been adjusted for multiplicity and may not be used in place of hypothesis testing.

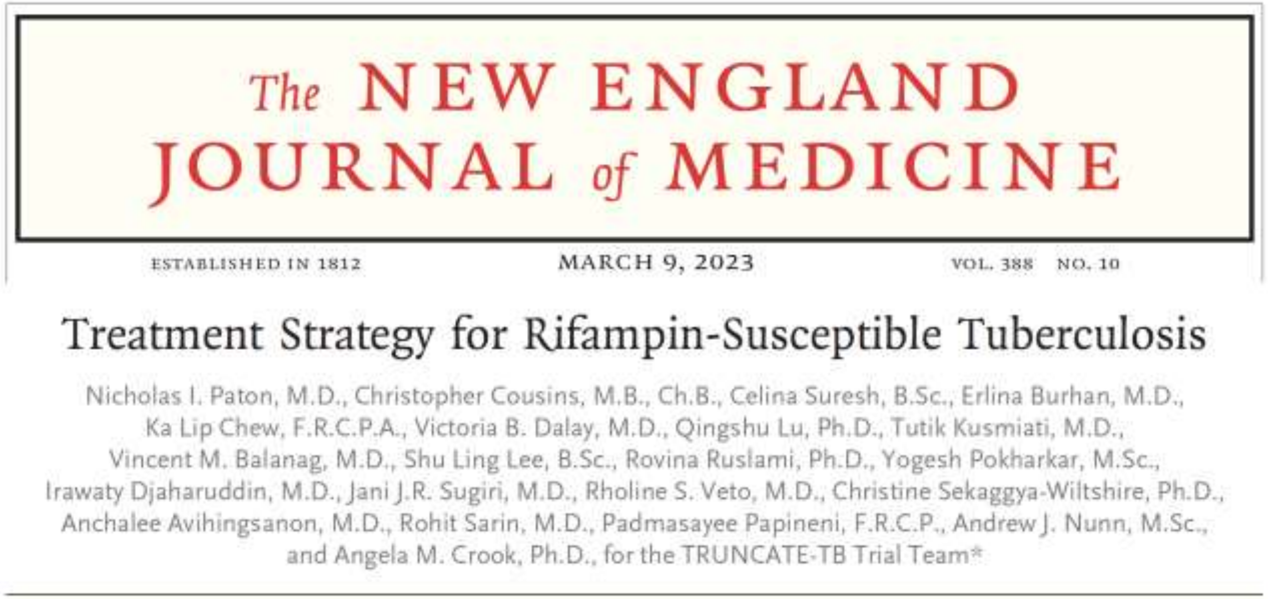

C Secondary Use of Vasopressors
Cumulative Incidence (%)
100
90
80
70
60
50
40
30
20
10
0
Hazard ratio, 0.59 (95% CI, 0.43–0.82)
Placebo
Hydrocortisone
0
7
14
21
28
Days since Randomization
No. at Risk
Placebo 344 102 30 13 6
Hydrocortisone 359 95 26 8 3

A Intubation in Patients Who Did Not Receive Any Mechanical Ventilation at Baseline



No. at Risk

Placebo	220	45	8	2	1
Hydrocortisone	222	49	6	1	0



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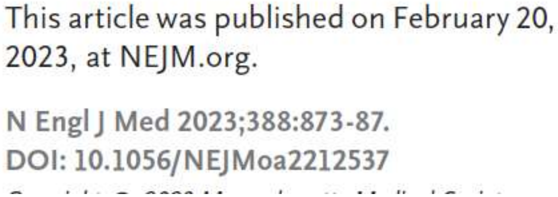
Treatment Strategy for Rifampin-Susceptible Tuberculosis

Nicholas I. Paton, M.D., Christopher Cousins, M.B., Ch.B., Celina Suresh, B.Sc., Erlina Burhan, M.D., Ka Lip Chew, F.R.C.P.A., Victoria B. Dalay, M.D., Qingshu Lu, Ph.D., Tutik Kusmiati, M.D., Vincent M. Balanag, M.D., Shu Ling Lee, B.Sc., Rovina Ruslami, Ph.D., Yogesh Pokharkar, M.Sc., Irawaty Djaharuddin, M.D., Jani J.R. Sugiri, M.D., Rholine S. Veto, M.D., Christine Sekaggya-Wiltshire, Ph.D., Anchalee Avihingsanon, M.D., Rohit Sarin, M.D., Padmasayee Papineni, F.R.C.P., Andrew J. Nunn, M.Sc., and Angela M. Crook, Ph.D., for the TRUNCATE-TB Trial Team*



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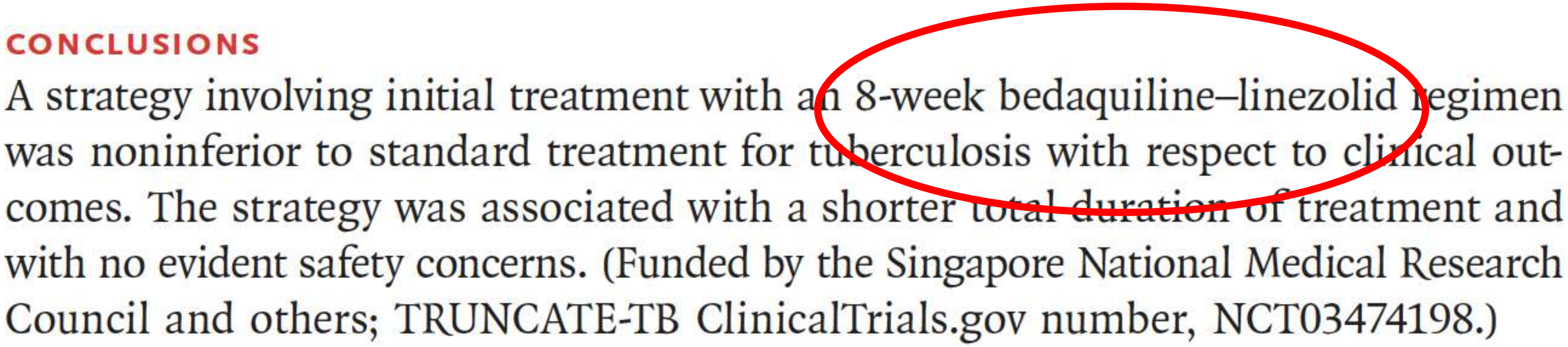

CONCLUSIONS

A strategy involving initial treatment with an 8-week bedaquiline–linezolid regimen was noninferior to standard treatment for tuberculosis with respect to clinical outcomes. The strategy was associated with a shorter total duration of treatment and with no evident safety concerns. (Funded by the Singapore National Medical Research Council and others; TRUNCATE-TB ClinicalTrials.gov number, NCT03474198.)

Conclusion

- Conséquences dramatiques du Covid sur la prise en soin des personnes agées.
- Pas de fermeture systématique des EHPAD
- Surmortalité évidente par Covid vs. grippe
- Intérêt de l’Interferon dans la Covid et du Paxlovid
- Inefficacité des médicaments autre que ceux recommandé dans la Covid.
- Attention au retour de la diphtérie
- Augmentation des décès par pneumonie dans le monde
- Bientôt plus de VRS?
- Bientôt les traitements court pour la tuberculose