Best of vaccins 2024

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Service d'Infectiologie, CHU de Saint-Etienne

Inserm CIC 1408- Axe Vaccinologie, I-Reivac, Covireivac

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Chaire Prévention, Vaccination, Contrôle de l'Infection PRESAGE

Contribution of vaccination to improved survival and health: modelling 50 years of the Expanded Programme on Immunization

Andrew J Shattock, Helen C Johnson, So Yoon Sim, Austin Carter, Philipp Lambach, Raymond C W Hutubessy, Kimberly M Thompson, Kamran Badizadegan, Brian Lambert, Matthew J Ferrari, Mark Jit, Han Fu, Sheetal P Silal, Rachel A Hounsell, Richard G White, Jonathan F Mosser, Katy A M Gaythorpe, Caroline L Trotter, Ann Lindstrand, Katherine L O'Brien, Naor Bar-Zeev

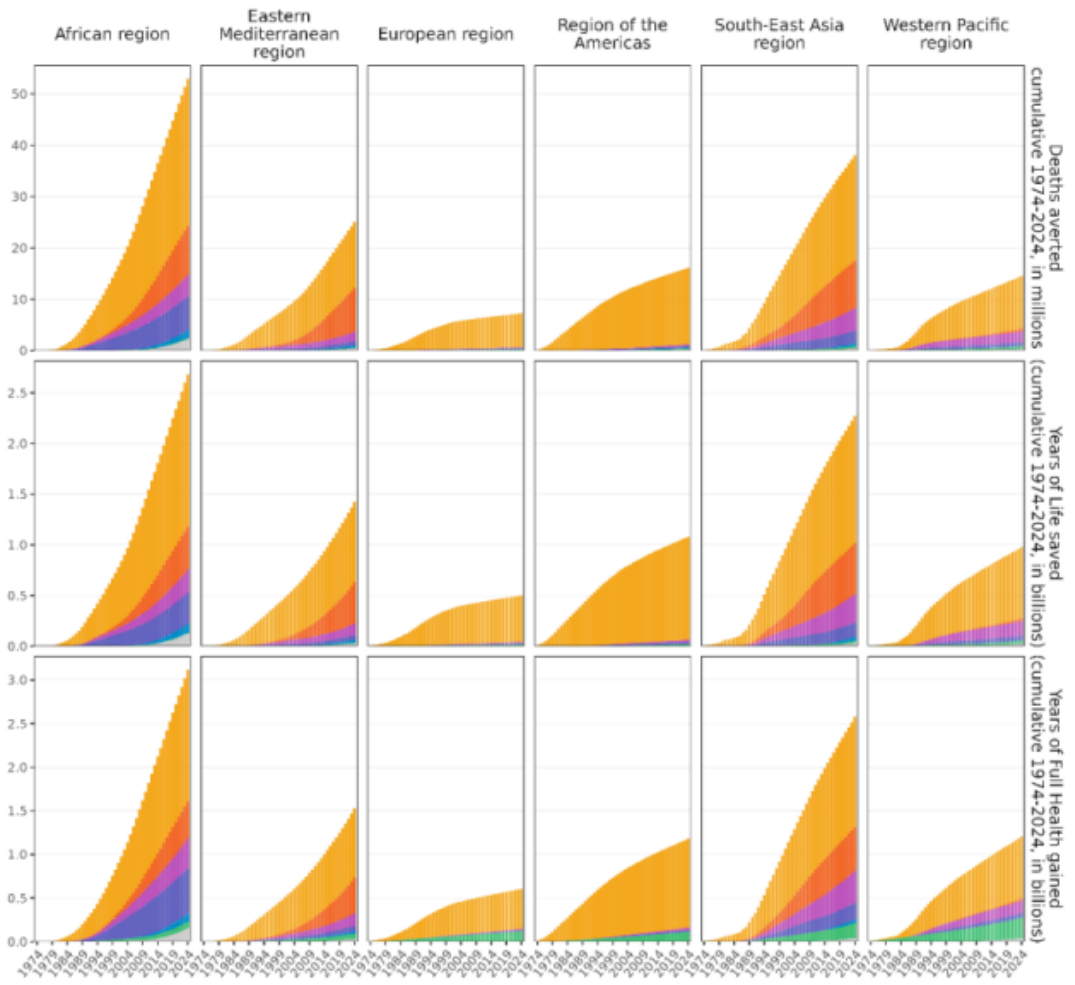


Figure S1 *Deaths averted, years of life saved, years of full health gained due to vaccination by WHO region.*

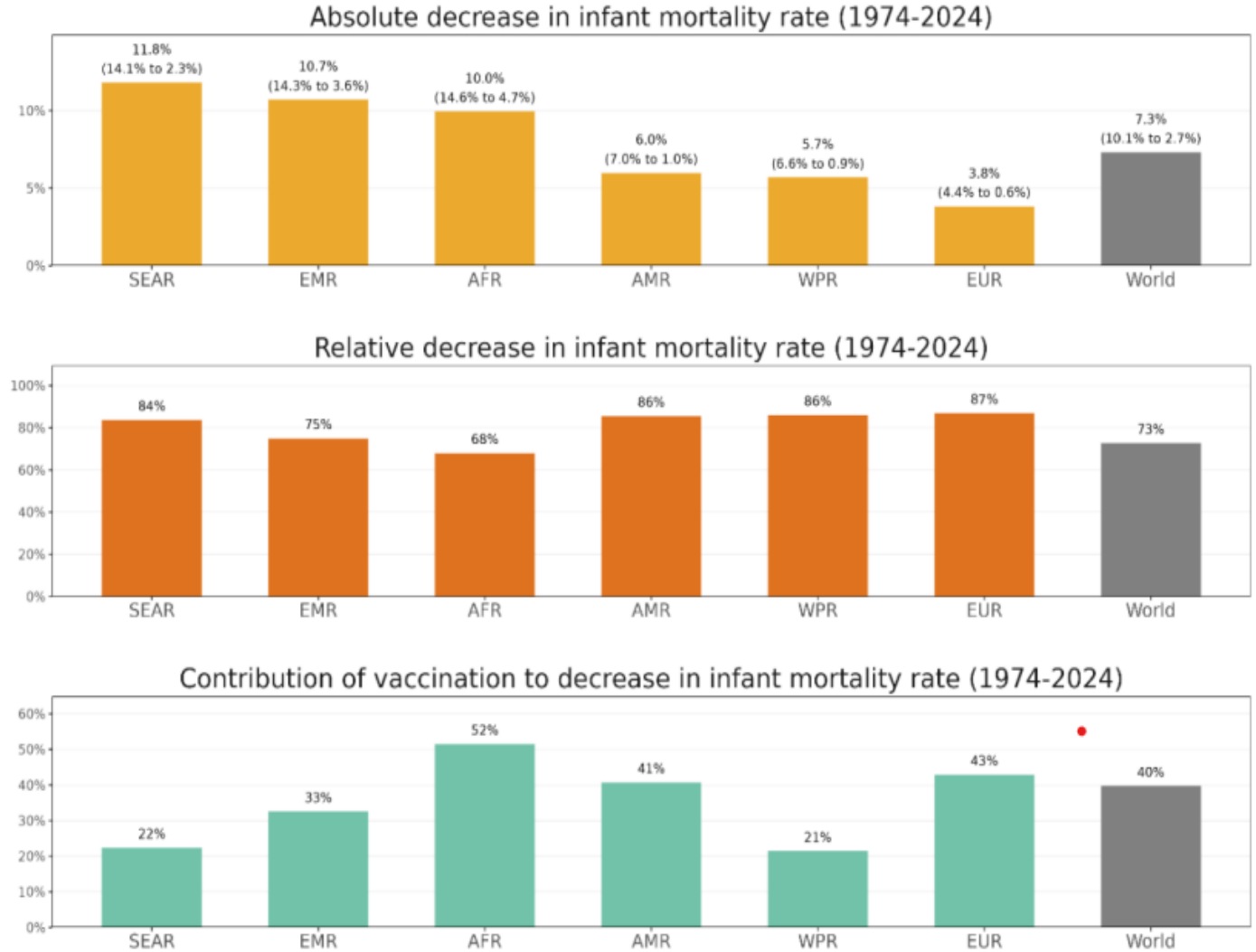
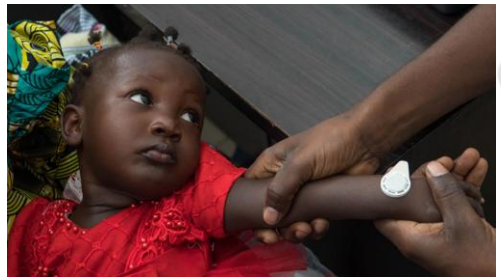
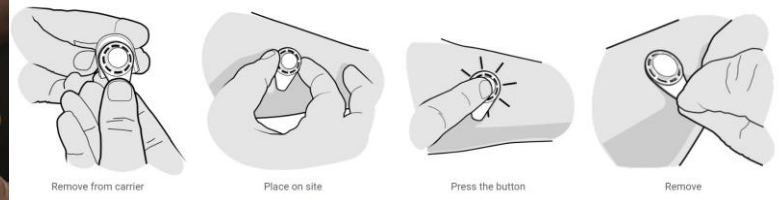


Figure S3 *Absolute and relative decrease in infant mortality and contribution of vaccination to the decrease in infant mortality, by region, 1974 – 2024. Regional acronyms: AFR = African region, AMR = Region of the Americas, EMR = Eastern Mediterranean region, EUR = European region, SEAR = South-East Asia region, WPR = Western Pacific region.*

A measles and rubella vaccine microneedle patch in The Gambia: a phase 1/2, double-blind, double-dummy, randomised, active-controlled, age de-escalation trial

Ikechukwu Adigweme, Mohammed Yisa, Michael Ooko, Edem Akpalu, Andrew Bruce, Simon Donkor, Lamin B Jarju, Baba Danso, Anthony Mendy, David Jeffries, Anne Segonds-Pichon, Abdoulie Njie, Stephen Crooke, Elina El-Badry, Hilary Johnstone, Michael Royals, James L Goodson, Mark R Prausnitz, Devin V McAllister, Paul A Rota, Sebastien Henry, Ed Clarke





May 18, 2021, and May 27, 2022, Monocentrique, Gambie. Bill & Melinda Gates Foundation
45 adultes (18-40 ans) (2:1) , 120 enfants (15-18 mois) et 120 nourrissons (9-10 mois) (1:1) ont été randomisés et vaccinés.
Double placebo. Immunogenicité J42, J180, safety (solicited jusqu'à J14, unsolicited jusqu'à J180)

	Toddlers		Infants	
	MRV-MNP and placebo-SC, n=60	MRV-SC and placebo-MNP, n=60	MRV-MNP and placebo-SC, n=60	MRV-SC and placebo-MNP, n=60
Acute allergic reaction	0	0	0	0
Local solicited adverse events				
MNP application site				
Any local solicited event*				
Total	50 (83%)	18 (30%)	46 (77%)	18 (30%)
Mild (grade 1)	50 (83%)	18 (30%)	46 (77%)	18 (30%)
Tenderness				
Total	1 (2%)	1 (2%)	0	0
Mild (grade 1)	1 (2%)	1 (2%)	0	0
Erythema				
Total	10 (17%)	9 (15%)		
Mild (grade 1)	10 (17%)	9 (15%)		
Induration				
Total	46 (77%)	9 (15%)		
Mild (grade 1)	46 (77%)	9 (15%)		
SC injection site				
Any local solicited event*				
Any reaction	8 (13%)	5 (8%)		
Mild (grade 1)	6 (10%)	5 (8%)	2 (3%)	4 (7%)
Moderate (grade 2)	2 (3%)	0	0	0
Systemic solicited adverse events				
Fever				
Total	5 (8%)	11 (18%)	8 (13%)	4 (7%)
Mild (grade 1)	1 (2%)	9 (15%)	5 (8%)	4 (7%)
Moderate (grade 2)	4 (7%)	1 (2%)	3 (5%)	0
Severe (grade 3)	0	1 (2%)	0	0
Any systemic solicited event†				
Total	27 (45%)	30 (50%)	31 (52%)	24 (40%)
Mild (grade 1)	24 (40%)	23 (38%)	28 (47%)	23 (38%)
Moderate (grade 2)	3 (5%)	7 (12%)	3 (5%)	1 (2%)

Data are n (%), where n=number of participants experiencing event by maximum severity grading. MRV=measles and rubella vaccine. MNP=microneedle patch. SC=subcutaneous. *Tenderness, erythema, and induration. †Vomiting, diarrhoea, irritability, drowsiness, reduced feeding, and rash.

Table 2: Solicited safety events from days 0 to 13—toddler and infant cohorts

Bonne tolérance:
Induration site d'administration
Décoloration cutanée

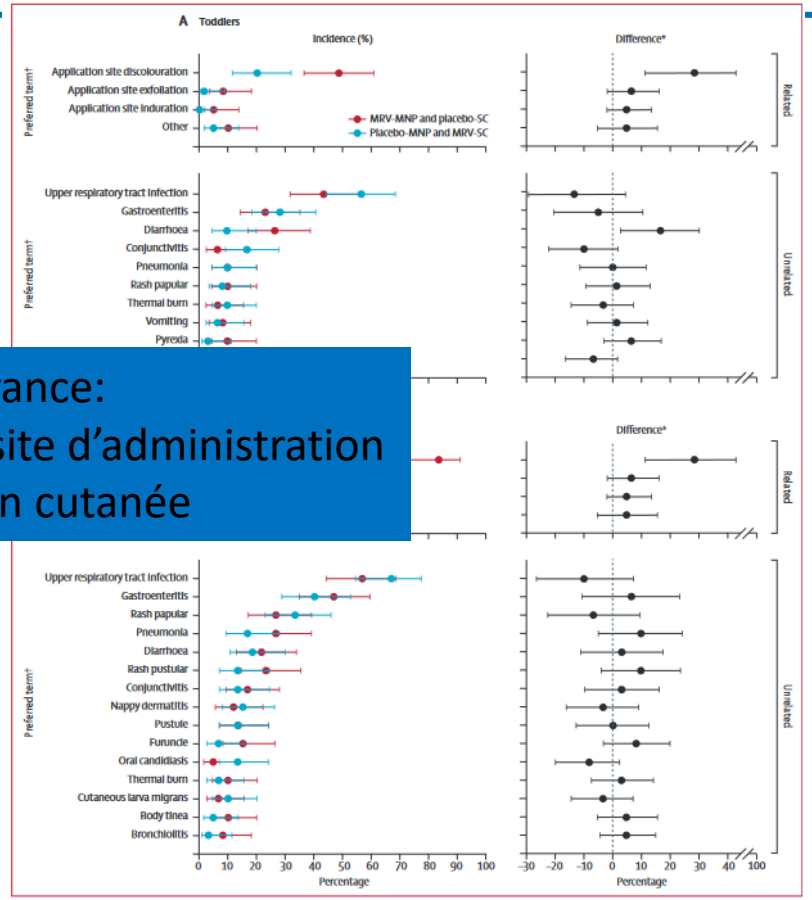


Figure 3: Unsolicited adverse events—toddler and infant cohorts

Bonne immunogénicité
Semble comparable vaccin SC

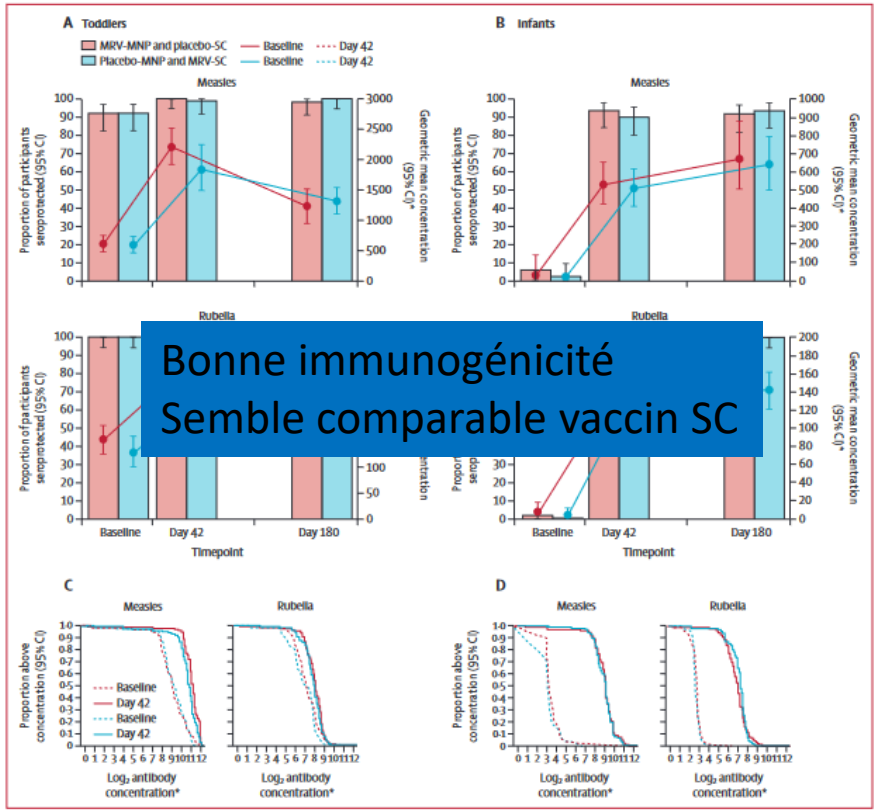


Figure 4: Serum neutralising antibody seroprotection levels, geometric mean antibody concentrations, and reverse cumulative distribution curves—toddler and infant cohorts

nature medicine

Brief Communication https://doi.org/10.1038/s41591-024-03201-5

The recombinant shingles vaccine is associated with lower risk of dementia

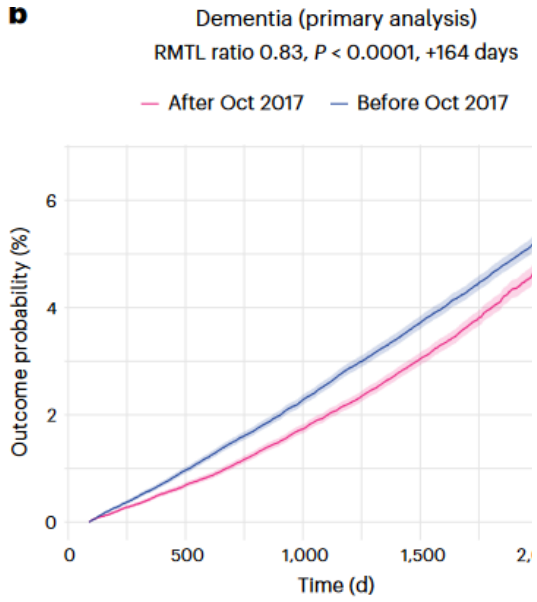
Received: 7 June 2024

Accepted: 17 July 2024

Maxime Taquet[1,2], Qu
Paul J. Harrison[1,2]

- Données issues de comparaison de cohortes vaccinés/non vaccinés ou issues d 'une étude de « randomisation » naturelle au Pays de Galles= réduction du risque de démence avec vaccin vivant atténué zona (Zostavax®)
- Zostavax® discontinué dans plusieurs pays

-Electronic health records (TriNetX US
-Cohorts included all patients who rec
October 2020 **(primary cohort)** and b
-Cohorts were matched for **60 covaria**
those associated with dementia), hist
-The primary outcome was a **first diag**
to 6 years post-vaccination in a time-



	n	RMTL ratio (95% CI)	P value	Additional time lived diagnosis-free among affected people, days (95% CI)
Propensity-score matched cohort studies				
Primary analysis	103,837	0.83 (0.79–0.87)	2.9×10^{-15}	164 (124–205)
Aligned follow-up horizons (cohort-wise)	103,837	0.83 (0.79–0.87)	4.3×10^{-15}	165 (121–209)
Predominant vaccine	100,532	0.82 (0.79–0.86)	7.5×10^{-16}	173 (131–214)
Adjusted for social deprivation	110,062	0.84 (0.80–0.88)	1.4×10^{-14}	157 (117–196)
Excluding those who received both vaccines	66,998	0.79 (0.74–0.83)	1.5×10^{-17}	214 (165–263)
Restricted exposure window (6 months)	20,243	0.83 (0.76–0.92)	0.00025	160 (74–246)
Females	54,846	0.78 (0.73–0.83)	2.3×10^{-15}	222 (168–276)
Males	43,990	0.87 (0.81–0.94)	0.00028	122 (56–187)
Other outcomes				
Mortality	103,837	0.98 (0.95–1.01)	0.22	18 (−11–47)
Composite endpoint of dementia or mortality	103,837	0.93 (0.91–0.96)	3.8×10^{-7}	64 (39–89)
Negative control outcome	103,837	0.97 (0.91–1.03)	0.29	32 (−27–90)
Herpes zoster infection	103,837	0.65 (0.61–0.69)	4.3×10^{-41}	381 (326–435)
Herpes zoster infection (females)	54,846	0.64 (0.59–0.69)	1.4×10^{-26}	393 (322–463)
Herpes zoster infection (males)	43,990	0.65 (0.58–0.72)	4.8×10^{-15}	387 (293–482)
Coarsened exact matched cohort studies				
Parametric estimates of variance	82,102	0.82 (0.77–0.87)	1.6×10^{-11}	192 (137–248)
Bootstrap estimates of variance	82,102	0.82 (0.79–0.86)	<0.001	192 (151–235)
Aligned follow-up horizons (pairwise)	82,102	0.85 (0.81–0.89)	<0.001	157 (111–203)

the bmj | BMJ 2024;385:e077341

Effect of the HPV vaccination programme on incidence of cervical cancer and grade 3 cervical intraepithelial neoplasia by socioeconomic deprivation in England: population based observational study

Milena Falcaro,[1] Kate Soldan,[2] Busani Ndlela,[3] Peter Sasieni[1]

DESIGN
Observational study.

SETTING
England, UK.

PARTICIPANTS
Women aged 20-64 years resident in England between January 2006 and June 2020 including 29 968 with a diagnosis of cervical cancer and 335 228 with a diagnosis of CIN3. In England, HPV vaccination was introduced nationally in 2008 and was offered routinely to girls aged 12-13 years, with catch-up campaigns during 2008-10 targeting older teenagers aged <19 years.

Table 5 | Estimated cohort specific numbers of invasive cervical cancers predicted and prevented by mid-2020 among women in the least and most deprived areas

	Predicted No of invasive cervical cancers* (95% CI)			Predicted rates per 100 000 women years			
	Scenario A: counterfactual	Scenario B: factual	Difference: scenarios A-B†	Scenario A: counterfactual	Scenario B: factual	Difference: scenarios A-B	% of cancers prevented: (A-B)/A
Cohort 5 (offered vaccine at age 16-18)							
Index of multiple deprivation (fifths):							
1st (most deprived)	331 (304 to 358)	234 (205 to 263)	97 (58 to 137)	14.8	10.4	4.3	29.4
5th (least deprived)	107 (98 to 116)	80 (63 to 96)	27 (9 to 46)	8.5	6.3	2.2	25.6
Cohort 6 (offered vaccine at age 14-16)							
Index of multiple deprivation (fifths):							
1st (most deprived)	105 (94 to 115)	33 (26 to 40)	71 (59 to 84)	11.0	3.5	7.5	68.3
5th (least deprived)	38 (34 to 42)	13 (9 to 16)	25 (20 to 30)	6.5	2.2	4.3	66.8
Cohort 7 (offered vaccine at age 12-13)							
Index of multiple deprivation (fifths):							
1st (most deprived)	27 (24 to 31)	4 (2 to 7)	23 (19 to 27)	3.0	0.5	2.6	84.6
5th (least deprived)	10 (9 to 12)	2 (1 to 3)	9 (7 to 10)	1.8	0.3	1.5	83.5

Results are reported under two scenarios: one as observed in the dataset (scenario B: factual) and one hypothetical where women had not been offered the HPV vaccination (scenario A: counterfactual).
CI=confidence interval; HPV=human papillomavirus.
*Numbers rounded to nearest integers.
†Difference may not equal scenarios A–B due to rounding.

Vaccine 42 (2024) S16–S21

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Evidence for an HPV one-dose schedule☆

Margaret Stanley[a], Anne Schuind[b], Kirthini K. Muralidharan[c,d,e,*], Dominique Guillaume[c,e,f], Victoria Willens[c,d,e], Hannah Borda[c,d,e], Marley Jurgensmeyer[c,d,e], Rupali Limaye[c,d,e,g,h]

Summary of ongoing and planned studies evaluating a single-dose HPV vaccine schedule.

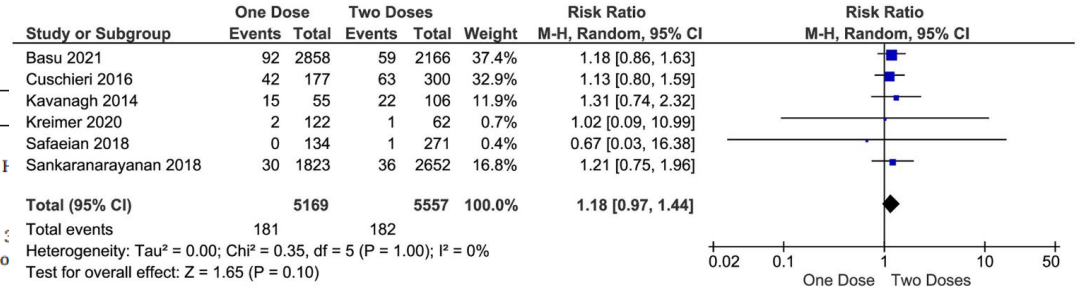
TRIAL/ COUNTRY	STUDY TYPE	VACCINE	AGE AT VACCINATION	RESULTS
Immunogenicity				
DoRIS/ Tanzania	Randomized Controlled Trial	2vHPV and 9vHPV	9–14-year-old girls	Seroconversion rates after 1-dose is non-inferior to 2 or 3 doses for H Non-inferiority not met for HPV 18 for one dose, but still high seropositivity.
India IARC/ India	Randomized now observational	4vHPV	10–18-year-old girls	Antibody titers to HPV 16/18 from one dose were inferior to 2 or 3 but still higher than those following natural HPV 16 or 18 infectio 10 years post-vaccination.
HANDS/The Gambia	Randomized Controlled Trial	9vHPV	4–8, 9–14, 15–26-year-old girls	Results expected.
ESCUDDO-PRIMAVERA/ Costa Rica	Randomized Controlled Trial	2vHPV and 9vHPV	9–14-year-old girls; 18–25 year old young women	Results expected.
CVT/ Costa Rica	Randomized now observational	2vHPV	18–25-year-old young women	Stable antibody levels through 16 years post-vaccination in all dose Levels at least 10-fold above natural infections.
Efficacy				
KEN SHE Kenya	Randomized Controlled Trial	2vHPV vs. 9vHPV	15–20-year-old girls	Very high vaccine efficacy with one dose of 9vHPV or 2vHPV up t months post-vaccination.
India IARC/ India	Randomized now Observational	4vHPV	10–18-year-old girls	Efficacy was similar at 12 years whether one, two, or three doses.
CVT/ Costa Rica	Randomized now Observational	2vHPV	18–25-year-old young women	Efficacy similar at 11 years whether one, two, or three doses.
PRISMA/ Costa Rica	Non-randomized Clinical Trial	2vHPV and 9vHPV	18–30-year-old young women	Results expected.
ESCUDDO/ Costa Rica	Randomized Controlled Trial	2vHPV and 9vHPV	12–16-year-old girls	Results expected.
Impact/Effectiveness				
Thailand Impact/ Thailand	Impact studies with repeat cross-sectional surveys	2vHPV	9–14-year-old girls	Results expected.
HOPE/ South Africa	Impact studies with repeat cross-sectional surveys	2vHPV	15–16-year-old girls	Results expected.

The UK, Ireland, Australia is giving a single dose of HPV vaccine,
Mexico and Tonga, Bolivia, Guatemala, and Peru are switching from a 2-dose to a single-dose
while Albania, Cape Verde, and Togo have recently introduced single-dose HPV vaccination

RESEARCH ARTICLE

The clinical effectiveness of one-dose vaccination with an HPV vaccine: A meta-analysis of 902,368 vaccinated women

Didik Setiawan[1,2]*, Nunuk Aries Nurulita[1], Sudewi Mukaromah Khoirunnisa[3,4], Maarten J. Postma[3,5,6]



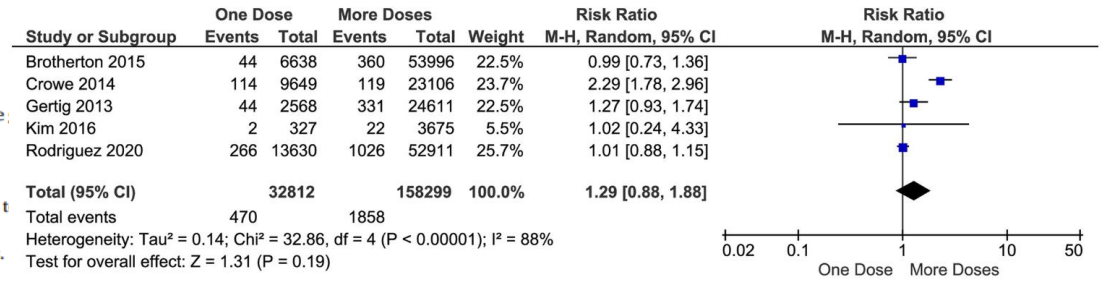


Fig 8. The effectiveness of one- and more-doses HPV vaccine on preventing HSIL or ASC-H incidence.

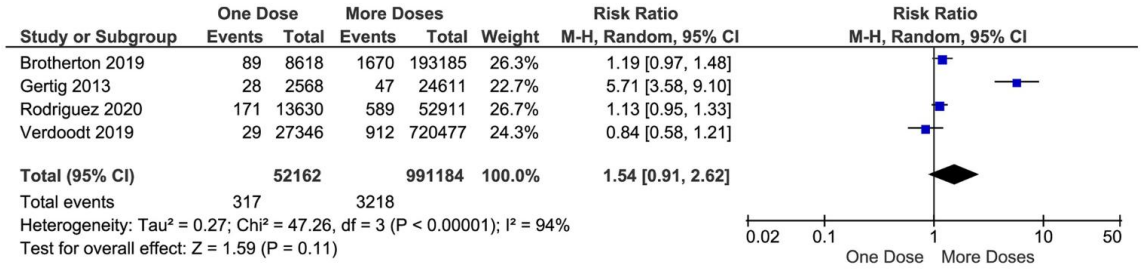


Fig 10. The effectiveness of one- and more-doses HPV vaccine on preventing CIN2/3 incidence.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Fractional Doses of Pneumococcal Conjugate Vaccine — A Noninferiority Trial

K.E. Gallagher, R. Lucinde, C. Bottomley, M. Kaniu, B. Suaad, M. Mutahi, L. Mwalekwa, S. Ragab, L. Twi-Yeboah, J.A. Berkley, M. Hamaluba, A. Karani, J. Shangala, M. Otiende, E. Gardiner, D. Mugo, P.G. Smith, C. Tabu, F. Were, D. Goldblatt, and J.A.G. Scott

Kenya,
-enfants recevant schéma 2+1 (6-8 sem, 14 sem puis 9 mois) soit de PCV 10, soit PCV 13 pleine dose, 40% ou 20%
-1 groupes recevant 3 doses pleine dose PCV 10
-swab nasopharyngé à 18 mois

Table 2. Carriage Prevalence at 9 and 18 Months of Age.*

Serotype	PCV13, Full Dose 2p+1 Schedule	PCV13, 40% Dose 2p+1 Schedule	PCV13, 20% Dose 2p+1 Schedule	PCV10, Full Dose 2p+1 Schedule	PCV10, 40% Dose 2p+1 Schedule	PCV10, 20% Dose 2p+1 Schedule	PCV10, Full Dose 3p+0 Schedule
	number/total number (percent)						
At 9 months of age							
PCV13 serotypes	37/207 (17.9)	49/210 (23.3)	43/206 (20.9)	49/198 (24.7)	49/203 (24.1)	61/209 (29.2)	52/206 (25.2)
PCV10 serotypes	10/207 (4.8)	16/210 (7.6)	13/206 (6.3)	10/198 (5.1)	12/203 (5.9)	18/209 (8.6)	9/206 (4.4)
3/6A/19A	27/207 (13.0)	33/210 (15.7)	30/206 (14.6)	39/198 (19.7)	37/203 (18.2)	43/209 (20.6)	43/206 (20.9)
6A/19A	20/207 (9.7)	28/210 (13.3)	25/206 (12.1)	33/198 (16.7)	26/203 (12.8)	38/209 (18.2)	35/206 (17.0)
Any serotype	174/207 (84.1)	173/210 (82.4)	168/206 (81.6)	158/198 (79.8)	167/203 (82.3)	178/209 (85.2)	173/206 (84.0)
At 18 months of age							
PCV13 serotypes	34/193 (17.6)	37/196 (18.9)	31/191 (16.2)	34/179 (19.0)	53/194 (27.3)	52/190 (27.4)	52/221 (23.5)
PCV10 serotypes	10/193 (5.2)	17/196 (8.7)	13/191 (6.8)	6/179 (3.4)	11/194 (5.7)	20/190 (10.5)	21/221 (9.5)
3/6A/19A	24/193 (12.4)	20/196 (10.2)	18/191 (9.4)	28/179 (15.6)	42/194 (21.6)	32/190 (16.8)	31/221 (14.0)
6A/19A	19/193 (9.8)	13/196 (6.6)	10/191 (5.2)	22/179 (12.3)	32/194 (16.5)	23/190 (12.1)	20/221 (9.0)
Any serotype	149/193 (77.2)	149/196 (76.0)	129/191 (67.5)	133/179 (74.3)	140/194 (72.2)	137/190 (72.1)	160/221 (72.4)

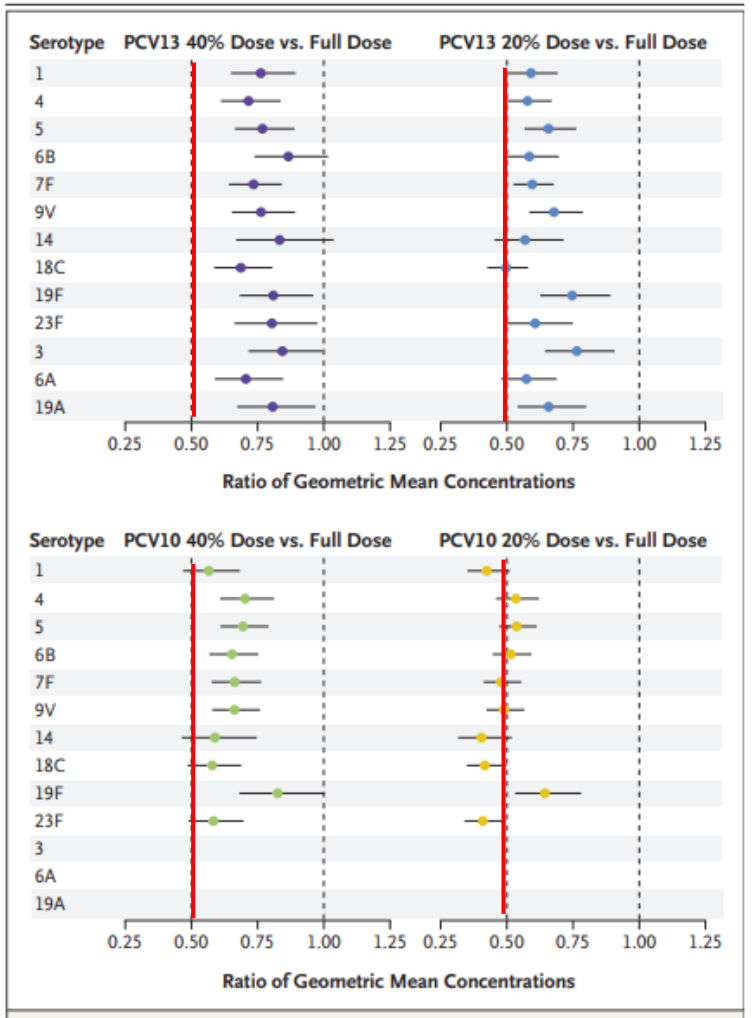
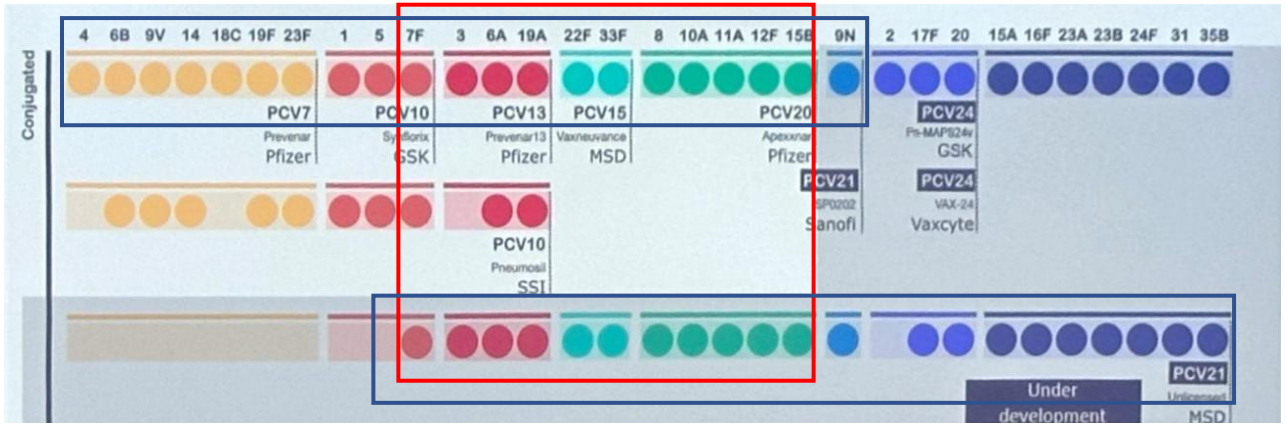


Figure 3. Ratio (Fractional Dose:Full Dose) of Geometric Mean Concentrations of IgG after the Booster.

Pas de différence de portage observé entre les groupes

Safety, tolerability, and immunogenicity of an adult pneumococcal conjugate vaccine, V116 (STRIDE-3): a randomised, double-blind, active comparator controlled, international phase 3 trial

*Heather L Platt, Christopher Bruno, Erik Buntinx, Enrique Pelayo, Diego Garcia-Huidobro, Elizabeth A Barranco-Santana, Folke Sjoberg, Joon Young Song, Carlos G Grijalva, Walter A Orenstein, Leslie Morgan, Doreen Fernsler, Weifeng Xu, Muhammad Waleed, Jianing Li, Ulrike K Buchwald on behalf of the STRIDE-3 Study Group**



	Cohort 1 (aged ≥50 years)		Cohort 2 (aged 18–49 years)	
	V116 (n=1179)	PCV20 (n=1177)	V116 (n=200)	PCV20 (n=100)
Sex				
Male	492 (41·7%)	507 (43·1%)	63 (31·5%)	36 (36·0%)
Female	687 (58·3%)	670 (56·9%)	137 (68·5%)	64 (64·0%)
Age	65 (57–69)	65 (57–69)	36 (26–43)	34 (28–42)
18–49 years	0	0	200 (100·0%)	100 (100·0%)
50–64 years	589 (50·0%)	587 (49·9%)	0	0
65–74 years	464 (39·4%)	464 (39·4%)	0	0
75–84 years	112 (9·5%)	113 (9·6%)	0	0
≥85 years	14 (1·2%)	13 (1·1%)	0	0
Race				
American Indian or Alaska Native	4 (0·3%)	4 (0·3%)	0	1 (1·0%)
Asian	148 (12·6%)	168 (14·3%)	38 (19·0%)	15 (15·0%)
Black or African American	116 (9·8%)	115 (9·8%)	13 (6·5%)	14 (14·0%)
Multiple	26 (2·2%)	30 (2·6%)	9 (4·5%)	6 (6·0%)
Native Hawaiian or Other Pacific Islander	17 (1·4%)	16 (1·4%)	1 (0·5%)	2 (2·0%)
White	867 (73·5%)	844 (71·7%)	139 (69·5%)	62 (62·0%)
Missing	1 (0·1%)	0	0	0
Ethnicity				
Hispanic or Latinx	259 (22·0%)	242 (20·6%)	58 (29·0%)	24 (24·0%)
Not Hispanic or Latinx	909 (77·1%)	922 (78·3%)	141 (70·5%)	76 (76·0%)
Not reported or unknown	11 (0·9%)	13 (1·1%)	1 (0·5%)	0
Pre-specified risk factors				
Alcohol use disorder	3 (0·3%)	3 (0·3%)	0	0
Chronic heart disease	25 (2·1%)	16 (1·4%)	0	0
Chronic kidney disease	26 (2·2%)	22 (1·9%)	0	1 (1·0%)
Chronic liver disease	21 (1·8%)	22 (1·9%)	3 (1·5%)	0
Chronic lung disease	135 (11·5%)	131 (11·1%)	19 (9·5%)	8 (8·0%)
Diabetes	212 (18·0%)	182 (15·5%)	7 (3·5%)	4 (4·0%)
Current smoking	139 (11·8%)	133 (11·3%)	23 (11·5%)	8 (8·0%)
Number of risk factors				
None	732 (62·1%)	768 (65·3%)	152 (76·0%)	81 (81·0%)
One	347 (29·4%)	328 (27·9%)	45 (22·5%)	18 (18·0%)
Two or more	100 (8·5%)	81 (6·9%)	3 (1·5%)	1 (1·0%)

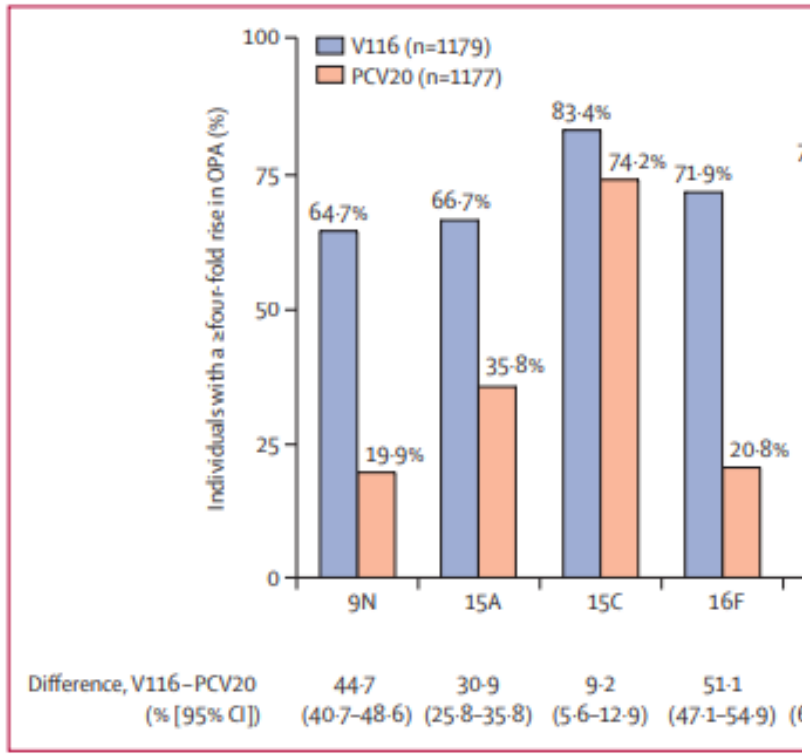


Figure 2: Analysis of OPA GMTs on day 30 in cohort 1 (adults ≥50 years)

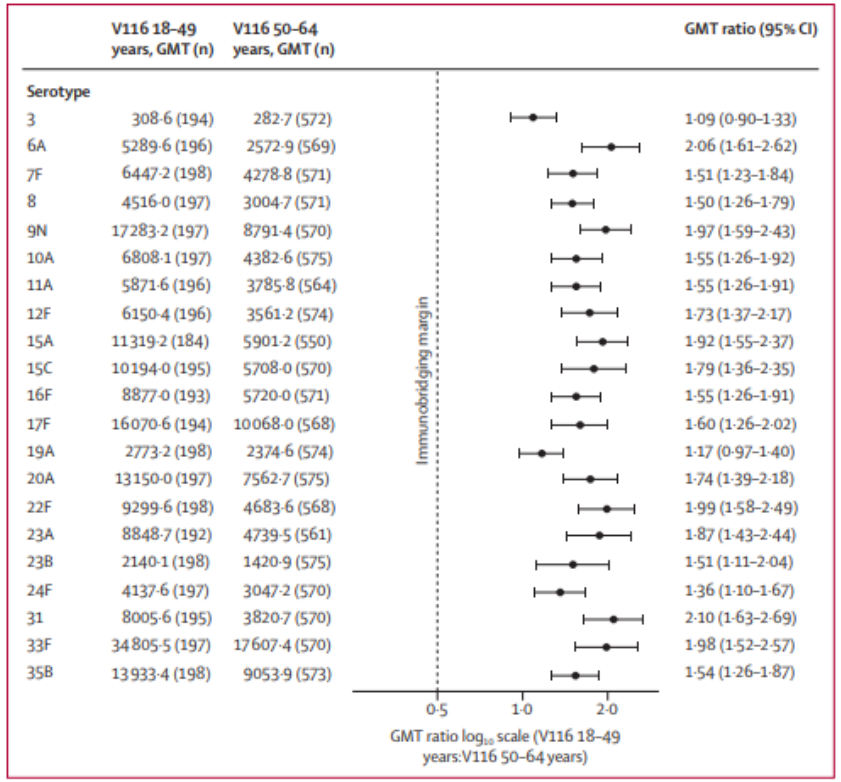


Figure 4: Immunobridging analysis of OPA GMTs on day 30 after vaccination with V116
OPA=opsonophagocytic activity. GMT=geometric mean titre.

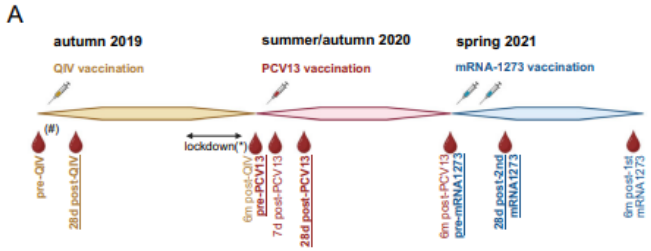
Immunobridging « vieux et jeunes »

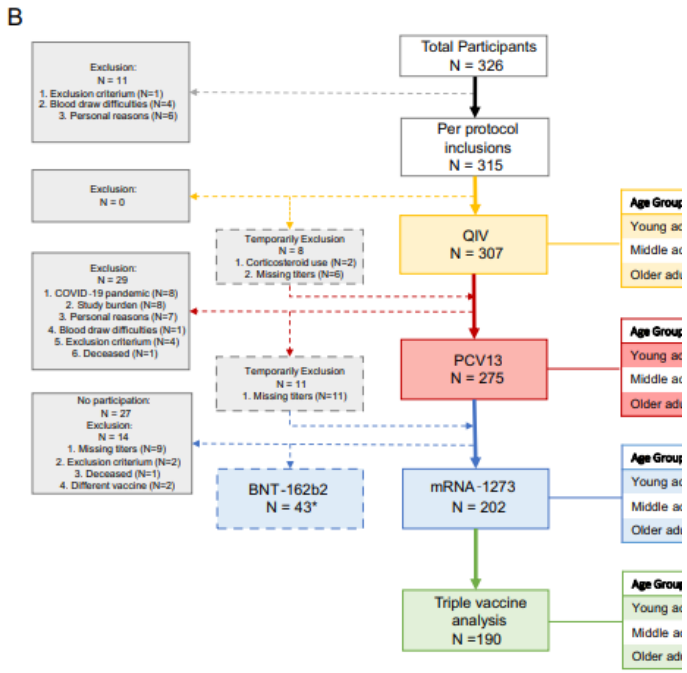
nature communications

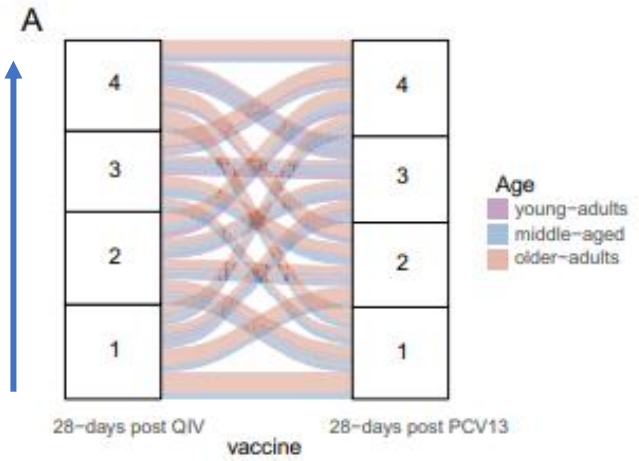
Article

https://doi.org/10.1038/s41467-024-50760-9

Multiple vaccine comparison in the same adults reveals vaccine-specific and age-related humoral response patterns: an open phase IV trial







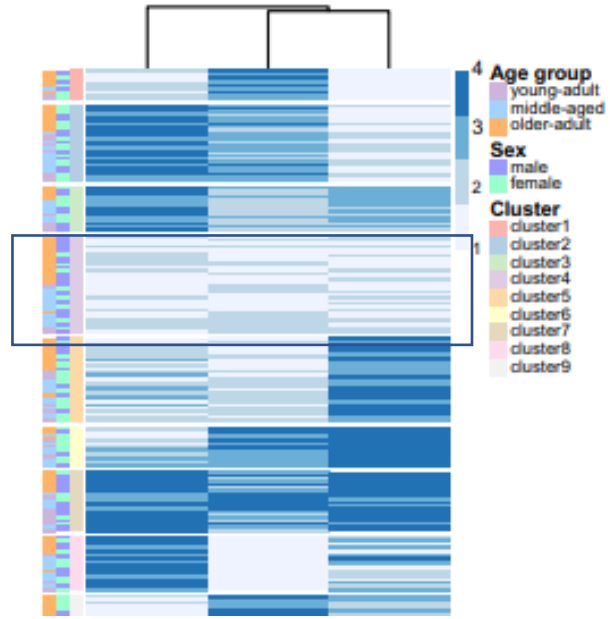


Table 2 | Demographic characteristics of the triple vaccine response clusters

	Cluster 1 n = 10	Cluster 2 n = 26	Cluster 3 n = 15	Cluster 4 n = 32	Cluster 5 n = 28	Cluster 6 n = 13	Cluster 7 n = 20	Cluster 8 n = 18	Cluster 9 n = 28
% Young adults	20	27	26.7	9.4	21.4	23.1	40	16.7	17.9
% Middle-aged	10	38.4	40	37.5	32.1	53.8	25	44.4	42.9
% Older adults	70	34.6	33.3	53.1	46.4	23.1	35	38.9	39.3
Age Mean (min-max)	60.9 (25–76)	56.6 (25–76)	56.9 (26–76)	64.2 (34–78)	60 (27–75)	58.8 (33–78)	54.7 (30–75)	55.9 (27–76)	58.6 (26–78)
% Males	50	42	46.7	68.8	42.9	30.8	70	44	32
BMI Mean (min-max)	26.2 (19–34.3)	24.3 (19.2–33)	25.2 (19.9–29.4)	25.5 (18.7–37)	25.5 (19.5–38.8)	25.5 (21.7–33.5)	25.2 (20.1–33)	26.2 (17.4–37)	24.8 (19.6–31.8)
H3N2 pre-vaccination titer median (min-max)	40 (5–160)	31.5*a (5–320)	20 (5–80)	5 (5–80)	5*b (5–40)	20 (5–320)	34 (5–320)	5 (5–80)	34 (5–320)
Frailty index median (min-max)	0.16 (0.03–0.39)	0.10 (0.0–0.34)	0.11 (0.03–0.27)	0.14 (0.03–0.31)	0.11 (0.0–0.36)	0.13 (0.03–0.27)	0.14 (0.0–0.36)	0.11 (0.0–0.25)	0.13 (0.03–0.24)
EQ-5D-3L median (min-max)	0.93 (0.72–1)	1 (0.72–1)	1 (0.30–1)	1 (0.30–1)	1 (0.72–1)	0.89 (0.69–1)	0.84 (0.33–1)	1 (0.65–1)	1 (0.68–1)
Number of medications median (min-max)	3.5 (0–9)	1 (0–8)	2 (0–9)	2 (0–7)	1 (0–10)	1 (0–8)	1.5 (0–11)	1 (0–5)	1 (0–8)

Optimisation of dose level and vaccination schedule for the VLA15 Lyme borreliosis vaccine candidate among healthy adults: two randomised, observer-blind, placebo-controlled, multicentre, phase 2 studies

Nicole Bézay, Laura Wagner, Vera Kadlecek, Michaela Obersriebnig, Nina Wressnigg, Romana Hochreiter, Martina Schneider, Katrin Dubischar, Ulla Derhaschnig, Anton Klingler, Julian Larcher-Senn, Susanne Eder-Lingelbach, Wolfgang Bender

- 3 lipidated fusion proteins, each linking the C-terminal domains of two OspA serotypes (1 and 2, 4 and 3; and 5 and 6)
- adjuvanted with aluminum hydroxid

Study one					Study two			
90 µg VLA15 (n=29)	135 µg VLA15 (n=214)	180 µg VLA15 (n=205)	Placebo (n=124)	All participants (n=572)	135 µg VLA15 (n=97)	180 µg VLA15 (n=98)	Placebo (n=51)	All participants (n=246)

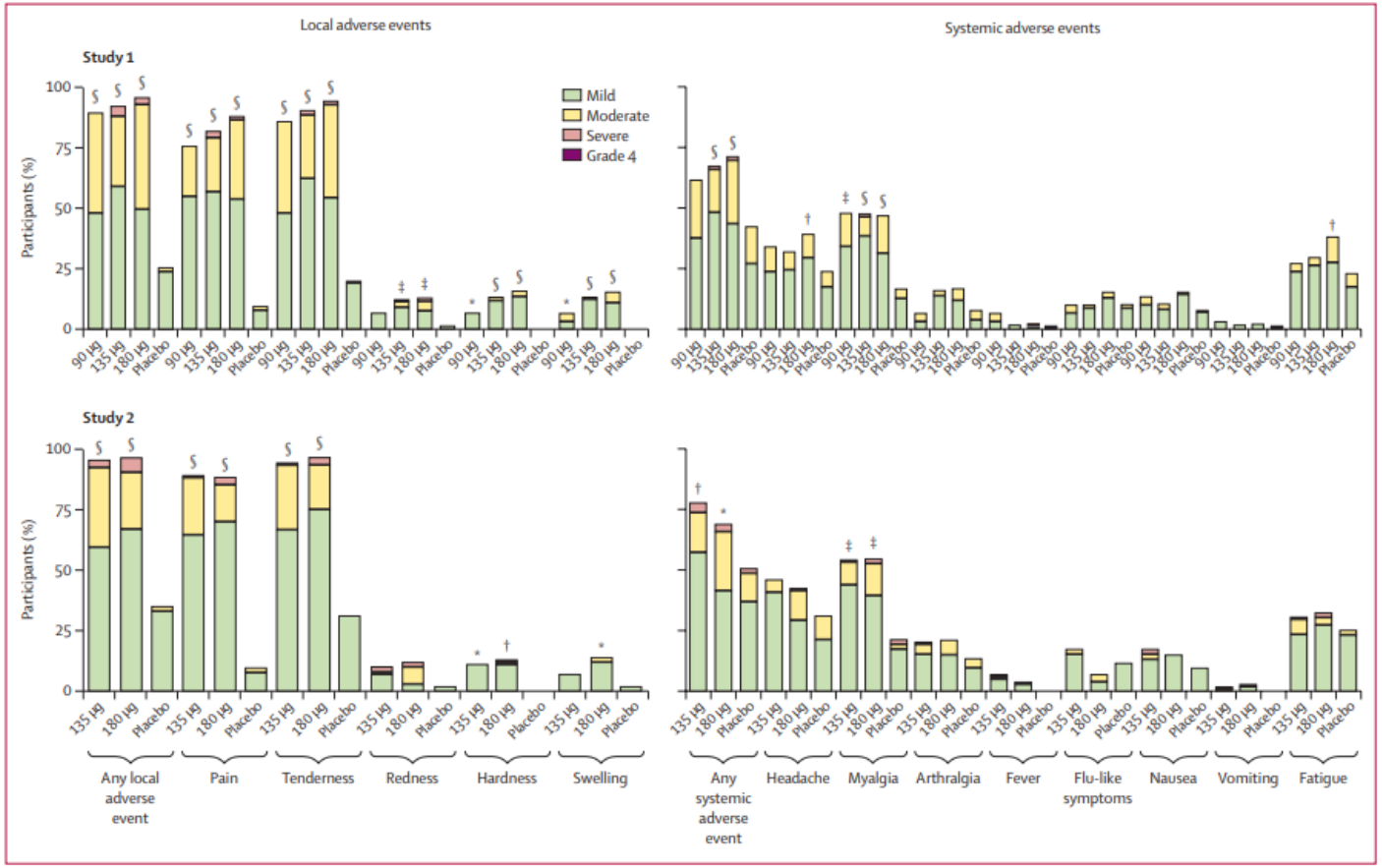
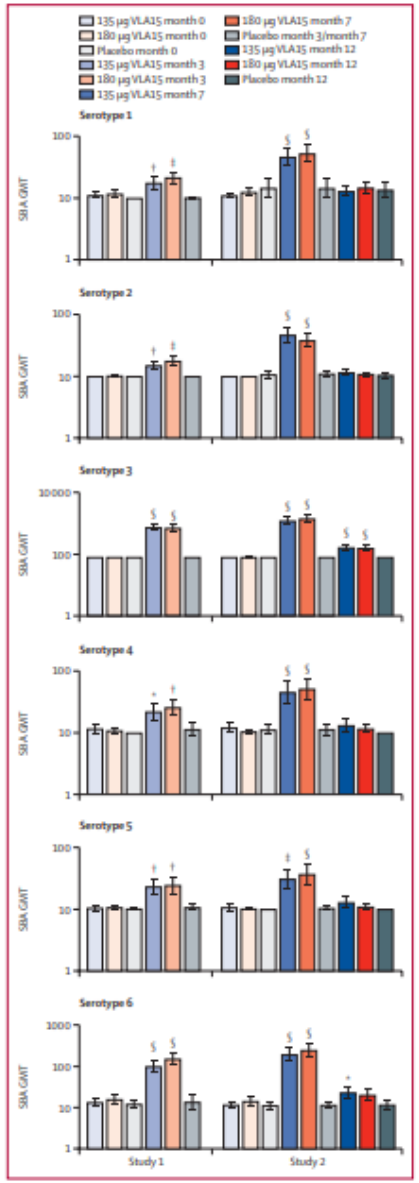


Figure 4: Percentages of participants with solicited local and systemic adverse events within 7 days after any vaccination in each study



OspA-specific serum bactericidal assay GMTs
at different timepoints in each study

180µg

Immunogenicity and safety of an 18-month booster dose of the VLA15 Lyme borreliosis vaccine candidate after primary immunisation in healthy adults in the USA: results of the booster phase of a randomised, controlled, phase 2 trial

Santhosh Kumar Ghadge, Martina Schneider, Katrin Dubischar, Laura Wagner, Vera Kadlecek, Michaela Obersriebnig, Romana Hochreiter, Anton Klingler, Julian Larcher-Senn, Ulla Derhaschnig, Wolfgang Bender, Susanne Eder-Lingelbach, Nicole Bézay

Open Forum Infectious Diseases

MAJOR ARTICLE

Preclinical Evidence for the Protective Capacity of Antibodies Induced by Lyme Vaccine Candidate VLA15 in People

Urban Lundberg,[1] Romana Hochreiter,[1] Yekaterina Timofoyeva,[2] Isis Kanevsky,[2] Andreas Meinke,[1] Annaliesa S. Anderson,[2] and Raphael Simon[2]

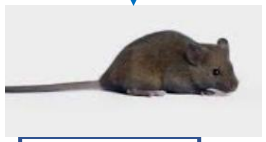


Table 1. Passive Transfer of Immune Sera Followed by *B burgdorferi* Tick Challenge

Human Serum Used For Transfer	Geomean Titer Post Transfer U/mL OspA ST1 IgG (Range)	Infected/Total[a]	*P* Value	Tick Colonization
Undiluted VLA15 immune serum pool	1196 (1043–1419)	0/9	.0090	6%
1:2 VLA15 immune serum pool	559 (507–655)	0/10	.0031	11%
1:4 VLA15 immune serum pool	256 (224–325)	1/8	.0498	19%
1:8 VLA15 immune serum pool	131 (106–152)	1/9	.0498	33%
Human nonimmune serum pool	20[b]	6/9	n/a	61%

Abbreviations: IgG, immunoglobulin G; n/a, not applicable; OspA, outer surface protein A.

[a]Infection was confirmed with at least 1 positive test (polymerase chain reaction, culture, serology).

[b]Enzyme-linked immunosorbent assay IgG titers measured below the lower limit of quantification of 40 U/mL were reported with 20 U/mL.

Table 2. Passive Transfer of Immune Sera Followed by *B Afzelii* Tick Challenge

Human Serum Used For Transfer	Geomean Titer Post Transfer U/mL OspA ST2 IgG (Range)	Infected/Total[a]	*P* Value	Tick Colonization
1:2 VLA15 immune serum pool	693 (599–745)	4/10	.0108	53%
1:4 VLA15 immune serum pool	352 (302–388)	4/9	.0294	75%
1:8 VLA15 immune serum pool	178 (168–191)	10/10	ns	94%
1:16 VLA15 immune serum pool	82 (71–95)	8/8	ns	100%
Human nonimmune serum pool	20[b]	9/9	n/a	67%

Abbreviations: IgG, immunoglobulin G; n/a, not applicable; ns, not significant; OspA, outer surface protein A.

[a]Infection was confirmed with at least one positive test (polymerase chain reaction, culture, serology).

[b]Enzyme-linked immunosorbent assay IgG titers measured below the lower limit of quantification of 40 U/mL were reported with 20 U/mL.

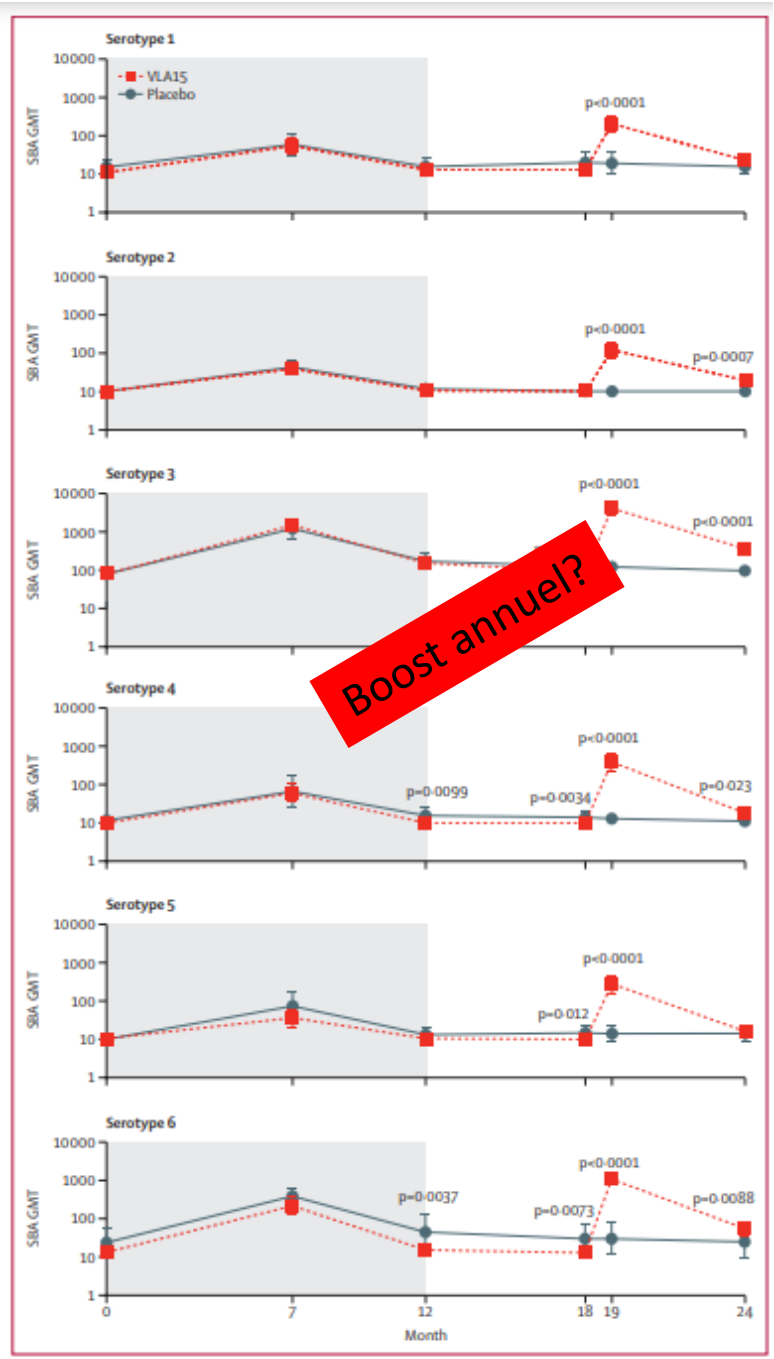


Figure 3: OspA-specific SBA GMTs by serotype over time (booster per-protocol population)

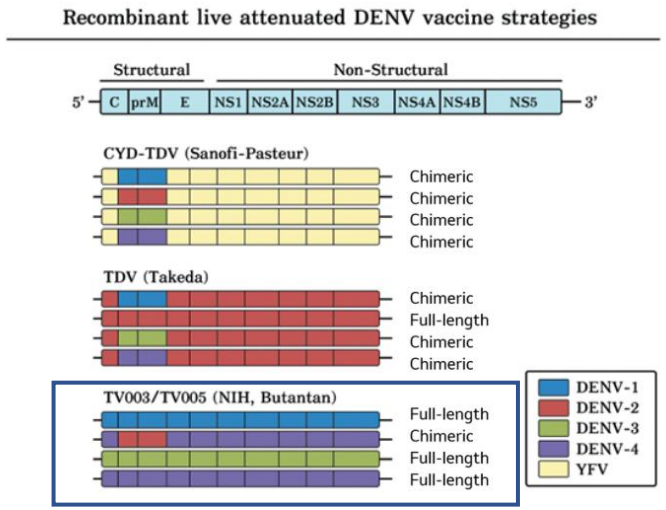
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 1, 2024 VOL. 390 NO. 5

Live, Attenuated, Tetravalent Butantan–Dengue Vaccine in Children and Adults

E.G. Kallás, M.A.T. Cintra, J.A. Moreira, E.G. Patiño, P.E. Braga, J.C.V. Tenório, V. Infante, R. Palacios, M.V.G. de Lacerda, D.B. Pereira, A.J. da Fonseca, R.Q. Gurgel, I.C.-B. Coelho, C.J.F. Fontes, E.T.A. Marques, G.A.S. Romero, M.M. Teixeira, A.M. Siqueira, A.M.P. Barral, V.S. Boaventura, F. Ramos, E. Elias Júnior, J. Cassio de Moraes, D.T. Covas, J. Kalil, A.R. Precioso, S.S. Whitehead, A. Esteves-Jaramillo, T. Shekar, J.-J. Lee, J. Macey, S.G. Kelner, B.-A.G. Coller, F.C. Boulos, and M.L. Nogueira

Essai contrôlé randomisé en double aveugle,
16 235 participants au Brésil (10 259 vaccins, 5976 placebo)



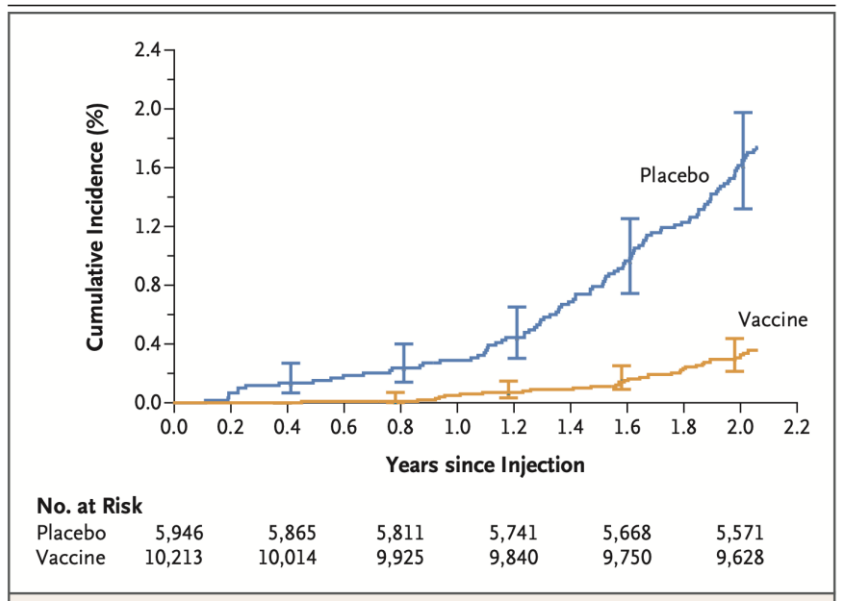


Figure 2. Cumulative Incidence of Virologically Confirmed Dengue through 2-Year Follow-Up.

Shown is the incidence of symptomatic, virologically confirmed dengue occurring more than 28 days after injection through the end of the 2-year follow-up period. Analysis excludes results that did not follow standard operating procedures for the reverse-transcriptase–polymerase-chain-reaction-assay. I bars indicate 95% confidence intervals.

Table 2. Vaccine Efficacy at 2 Years after Injection.*

Confirmed Dengue	Vaccine			Placebo			Cumulative
	Cases	Person-Yrs at Risk	Estimated Incidence (95% CI)	Cases	Person-Yrs at Risk	Estimated Incidence (95% CI)	Vaccine Efficacy (95% CI)
	no. (total no.)			*no. (total no.)*			%
Any serotype							
Regardless of serostatus	35/10,215	20,452	0.17 (0.12 to 0.24)	100/5,947	11,927	0.84 (0.68 to 1.02)	79.6 (70.0 to 86.3)
With previous exposure	8/4,994	10,063	0.08 (0.03 to 0.16)	45/3,023	6,092	0.74 (0.54 to 0.99)	89.2 (77.6 to 95.6)
Without previo						1.03 (0.77 to 1.34)	73.6 (57.6 to 83.7)
DENV-1							
Regardless of s						0.42 (0.31 to 0.55)	89.5 (78.7 to 95.0)
With previous						0.31 (0.19 to 0.49)	96.8 (81.0 to 99.8)
Without previo						0.58 (0.39 to 0.82)	85.6 (69.1 to 94.0)
DENV-2							
Regardless of serostatus	26/10,215	20,458	0.13 (0.08 to 0.19)	50/5,947	11,967	0.42 (0.31 to 0.55)	69.6 (50.8 to 81.5)
With previous exposure	7/4,994	10,063	0.07 (0.03 to 0.14)	26/3,023	6,107	0.43 (0.28 to 0.62)	83.7 (63.1 to 93.5)
Without previous exposure	18/4,826	9,579	0.19 (0.11 to 0.30)	24/2,690	5,376	0.45 (0.29 to 0.66)	57.9 (20.8 to 78.1)

2-6 ans= VE 80,1% (95% CI 77,6-95,6%)
7-17 ans= VE 77,8% (95% CI 55,6-89,6%)
18-59 ans= VE 80,1% (90% CI 68,2-97,5%)

* Vaccine efficacy was estimated on the basis of the exact binomial method proposed by Chan and Bohidar,[27] and 95% confidence intervals were estimated with the use of Blaker's exact confidence interval.[28] The person-years at risk was the cumulative time (in years) until the participant received a diagnosis of the first symptomatic episode of virologically confirmed dengue or until the end of the 2-year follow-up period for each participant, whichever came first. Incidence (per 100 person-years at risk) was calculated as the number of symptomatic, virologically confirmed dengue cases (the number of participants with at least one symptomatic virologically confirmed dengue episode more than 28 days after injection until the end of the follow-up period) divided by the cumulative person-years at risk. Vaccine efficacy according to previous dengue exposure was calculated for participants with dengue serostatus at baseline (those who had preinjection $VRNT_{50}$ results). Only DENV-1 and DENV-2 were detected during the 2-year follow-up.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Safety and Efficacy of Immunization with a Late-Liver-Stage Attenuated Malaria Parasite

O.A.C. Lamers, B.M.D. Franke-Fayard, J.P.R. Koopman, G.V.T. Roozen, J.J. Janse, S.C. Chevalley-Maurel, F.J.A. Geurten, H.M. de Bes-Roeleveld, E. Iliopoulou, E. Colstrup, E. Wessels, G.-J. van Gemert, M. van de Vegte-Bolmer, W. Graumans, T.R. Stoter, B.G. Mordmüller, E.L. Houlder, T. Bousema, R. Murugan, M.B.B. McCall, C.J. Janse, and M. Roestenberg

In this trial, researchers assessed the use of mosquito bites for immunization with GA2 — a *mei2* single knockout *Plasmodium falciparum* NF54 parasite (sporozoite form) with extended development into the liver stage — in healthy adults who had not had malaria.

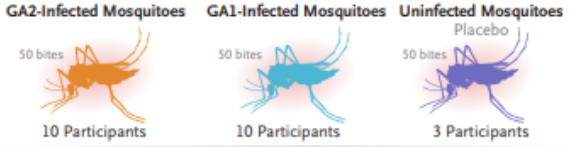
Progress in the **eradication of malaria** has slowed, and there is a need for new tools.

WHY WAS THE TRIAL DONE?

The malaria vaccines currently approved by the World Health Organization are subunit vaccines that result in protection that is modest and short-lived. Alternative vaccination strategies based on whole, genetically attenuated plasmodium parasites might improve protection. GA1, a genetically attenuated plasmodium parasite with short intrahepatic development, resulted in low protective efficacy in a previous trial. Whether late-arresting GA2 can induce better protection than GA1 is unclear.

HOW WAS THE TRIAL CONDUCTED?

After an open-label dose-escalation stage (stage A), adults who had not had malaria were randomly assigned to receive 50 bites from GA2-infected mosquitoes, 50 bites from GA1-infected mosquitoes, or 50 bites from uninfected mosquitoes (placebo), in three immunization sessions at 28-day intervals (stage B). Three weeks after the last immunization, participants underwent controlled human malaria infection with 5 bites from mosquitoes infected with unattenuated *P. falciparum* strain 3D7. The primary end point was the number and severity of adverse events and blood-stage parasitemia indicating breakthrough infection after GA2 mosquito-bite immunization.



PARTICIPANTS

WHO	43 adults: 20 in stage A and 23 in stage B
	Age: 19–35 years; median, 23 years
	Women: 51%; Men: 49%
CLINICAL STATUS	Had not had malaria
	In good health, as assessed by medical history, physical examination, and general laboratory evaluation

TRIAL DESIGN

- MULTISTAGE
- DOSE-ESCALATED (STAGE A)
- DOUBLE-BLIND (STAGE B)
- RANDOMIZED
- PLACEBO-CONTROLLED (STAGE B)
- LOCATION: THE NETHERLANDS

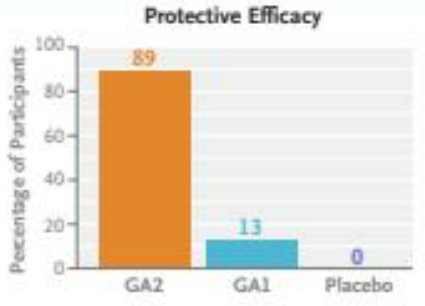
3 semaines après la dernière immunisation CHIM pour 20 volontaires

P. FALCIPARUM STRAIN

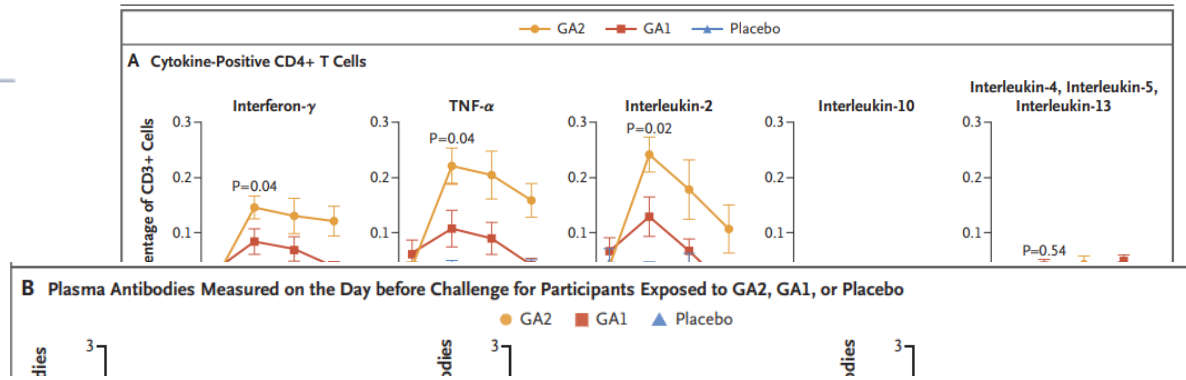
P. falciparum strain 3D7, used in the trial for controlled human malaria infection, is an unattenuated clone of the parental parasite strai *P. falciparum* NF54, which was used to generate the attenuated strains GA2 and GA1.

RESULTS

Protective efficacy after controlled human malaria infection was greater in the GA2 group than in the GA1 and placebo groups.



Adverse events were similar in the three groups. No serious adverse events occurred. In addition, there were no breakthrough infections after immunization with GA2.

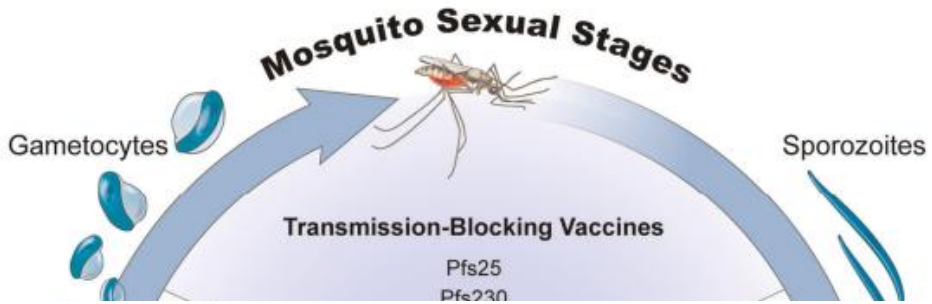


LIMITATIONS AND REMAINING QUESTIONS

- Conclusions from this trial are limited by the small sample size and the large number of immunologic analyses. More trials with greater numbers of participants are required to better understand the safety profile of GA2.
- The immunogenicity of GA2 needs to be assessed for durability and against heterologous *P. falciparum* strains in regions where malaria is endemic.

CONCLUSIONS

The findings of this small trial suggest that a late-arresting parasite (GA2) offers higher protective efficacy against *P. falciparum* controlled human malaria infection than an early-arresting parasite (GA1), without known safety concerns.



Safety and efficacy of PfSPZ Vaccine against malaria in healthy adults and women anticipating pregnancy in Mali: two randomised, double-blind, placebo-controlled, phase 1 and 2 trials

Halimatou Diawara, Sara A Healy*, Agnes Mwakingwe-Omari, Djibrilla Issiaka, Aye Diallo, Seydou Traore, Ibrahim H Soumbounou, Santara Gaoussou, Irfan Zaidi, Almahamoudou Mahamar, Oumar Attaher, Michal Fried, Blair J Wylie, Rathy Mohan, Viyada Doan, Justin Y A Doritchamou, Amagana Dolo, Robert D Morrison, Jing Wang, Zonghui Hu, Kelly M Rausch, Amatigue Zeguime, Tooba Murshedkar, Natasha KC, B Kim Lee Sim, Peter F Billingsley, Thomas L Richie, Stephen L Hoffman†, Alassane Dicko†, Patrick E Duffy†, for the PfSPZ Vaccine Study Team‡*

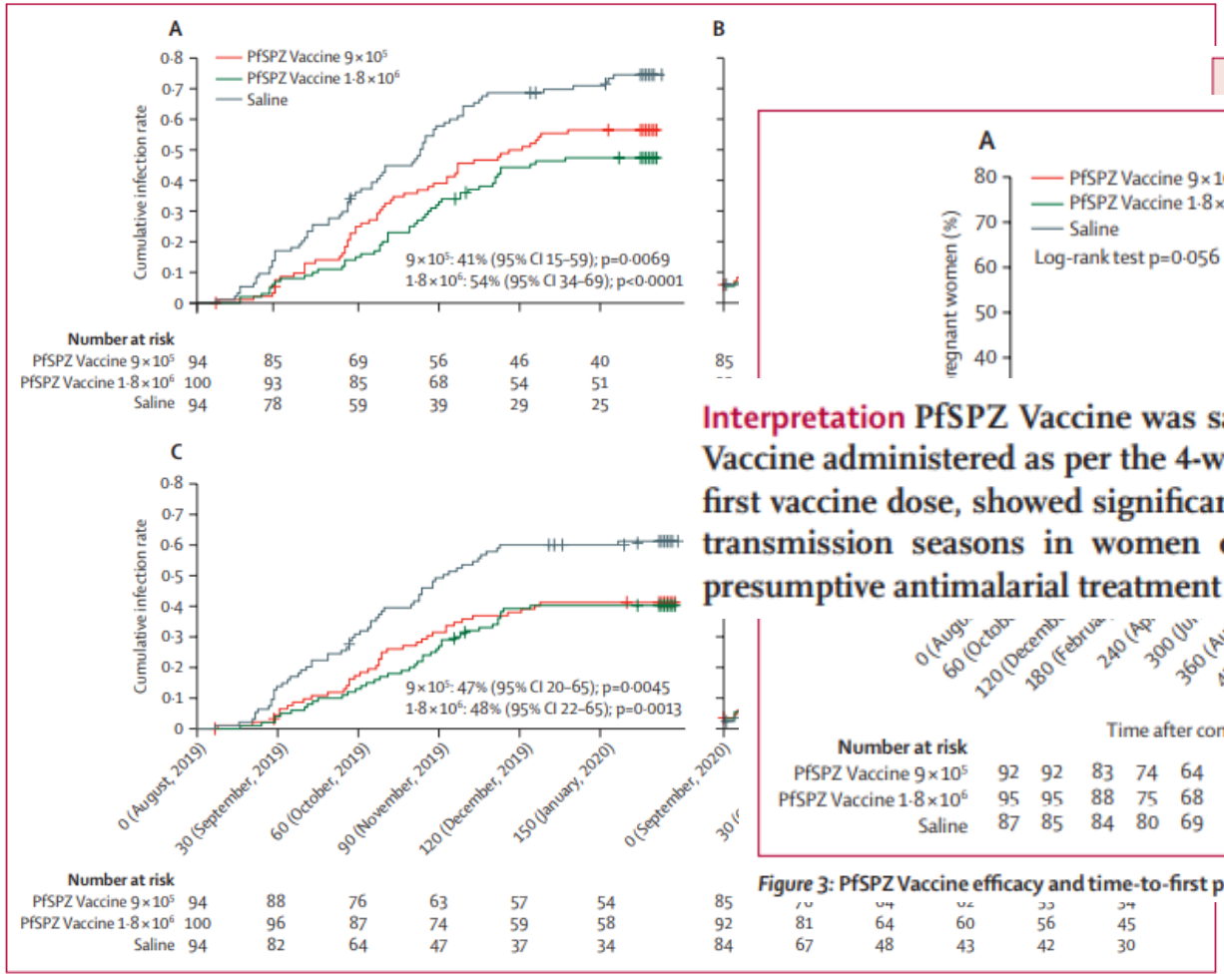
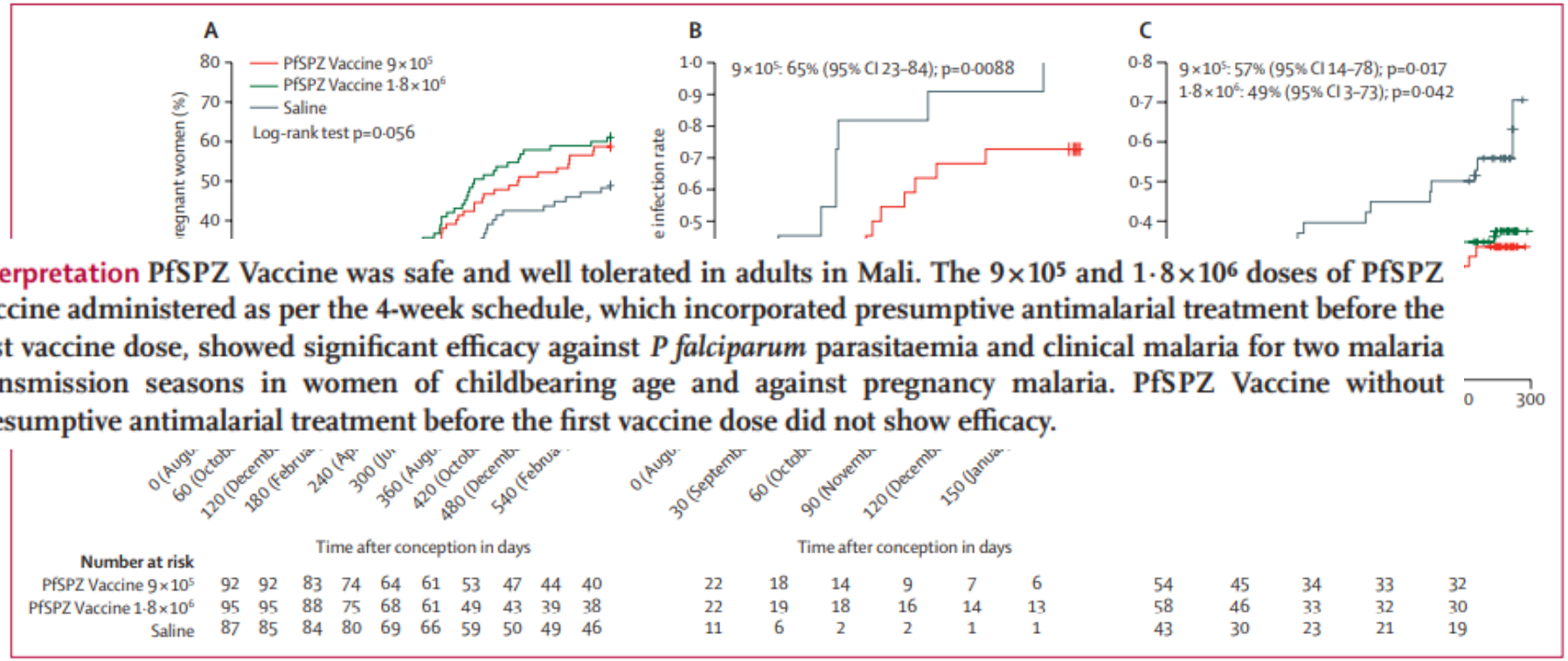


Figure 2: PfSPZ Vaccine efficacy against parasitaemia and clinical malaria in MLSPZV4

MLSPZV4 trial (2019–21) MLSPZV3 trial (2018–19)



Interpretation PfSPZ Vaccine was safe and well tolerated in adults in Mali. The 9×10^5 and $1{\cdot}8\times10^6$ doses of PfSPZ Vaccine administered as per the 4-week schedule, which incorporated presumptive antimalarial treatment before the first vaccine dose, showed significant efficacy against *P falciparum* parasitaemia and clinical malaria for two malaria transmission seasons in women of childbearing age and against pregnancy malaria. PfSPZ Vaccine without presumptive antimalarial treatment before the first vaccine dose did not show efficacy.

Figure 3: PfSPZ Vaccine efficacy and time-to-first pregnancy and risk of malaria in pregnancy

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 2, 2024 VOL. 390 NO. 17

Subcutaneous Administration of a Monoclonal Antibody to Prevent Malaria

K. Kayentao, A. Ongoiba, A.C. Preston, S.A. Healy, Z. Hu, J. Skinner, S. Doumbo, J. Wang, H. Cisse, D. Doumtabe, A. Traore, H. Traore, A. Djiguiba, S. Li, M.E. Peterson, S. Telscher, A.H. Idris, W.C. Adams, A.B. McDermott, S. Narpala, B.C. Lin, L. Serebryannyy, S.P. Hickman, A.J. McDougal, S. Vazquez, M. Reiber, J.A. Stein, J.G. Gall, K. Carlton, P. Schwabl, S. Traore, M. Keita, A. Zéguimé, A. Ouattara, M'B. Doucoure, A. Dolo, S.C. Murphy, D.E. Neafsey, S. Portugal, A. Djimdé, B. Traore, R.A. Seder, and P.D. Crompton, for the Mali Malaria mAb Trial Team*

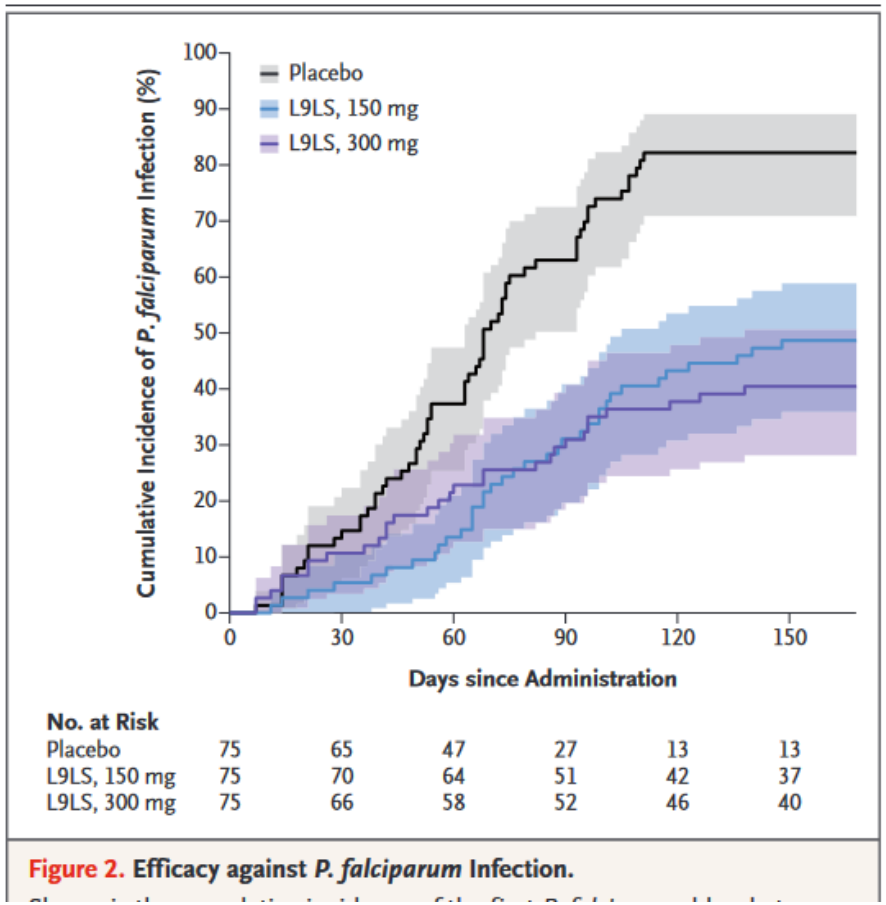


Figure 2. Efficacy against *P. falciparum* Infection.

Dose escalation trial,
225 enfants entre 6-10 ans
75 par bras
Mali

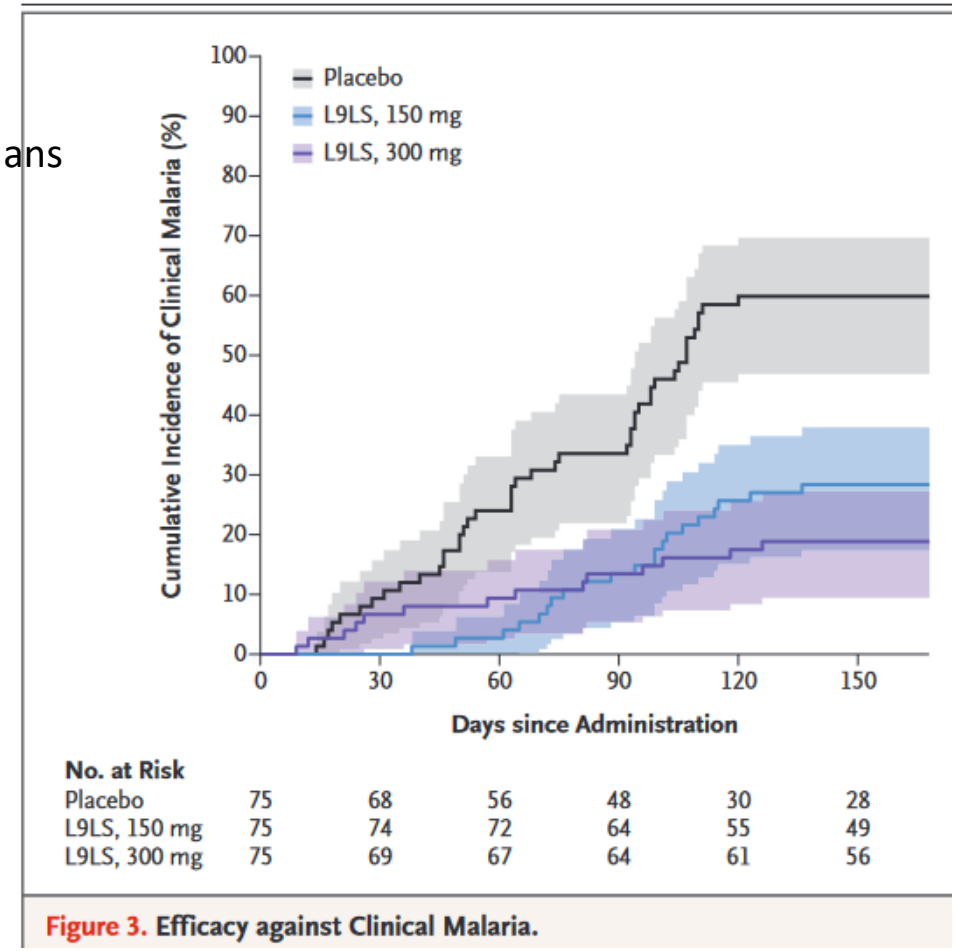


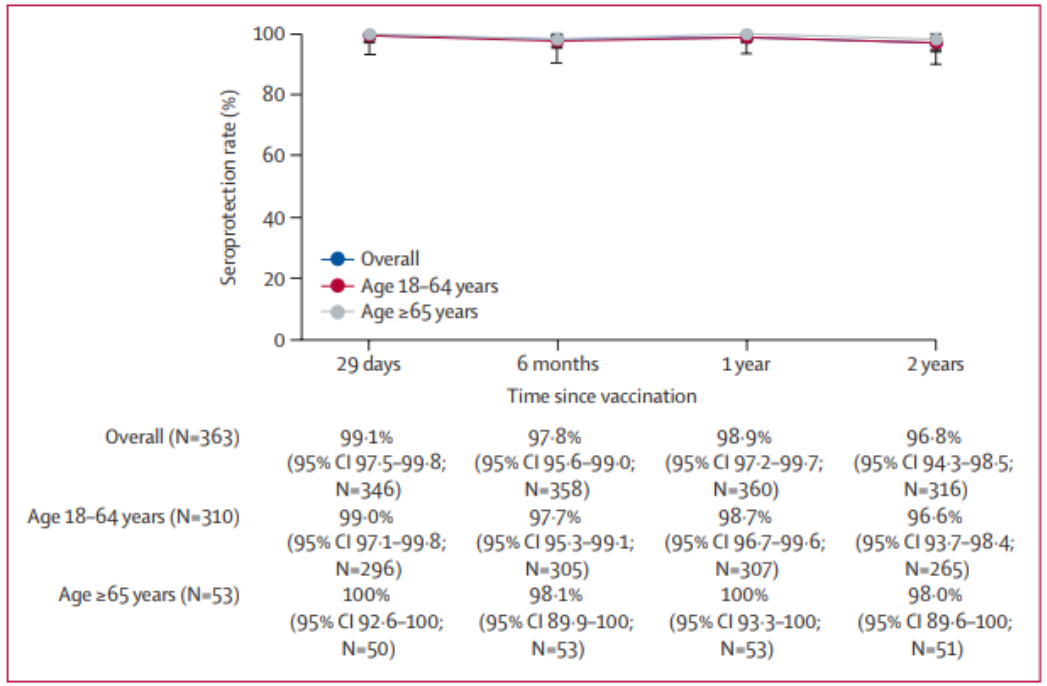
Figure 3. Efficacy against Clinical Malaria.

RESULTS

No safety concerns were identified in the dose-escalation part of the trial (part A). In part B, 225 children underwent randomization, with 75 children assigned to each group. No safety concerns were identified in part B. *P. falciparum* infection occurred in 36 participants (48%) in the 150-mg group, in 30 (40%) in the 300-mg group, and in 61 (81%) in the placebo group. The efficacy of L9LS against *P. falciparum* infection, as compared with placebo, was 66% (adjusted confidence interval [95% CI], 45 to 79) with the 150-mg dose and 70% (adjusted 95% CI, 50 to 82) with the 300-mg dose ($P<0.001$ for both comparisons). Efficacy against clinical malaria was 67% (adjusted 95% CI, 39 to 82) with the 150-mg dose and 77% (adjusted 95% CI, 55 to 89) with the 300-mg dose ($P<0.001$ for both comparisons).

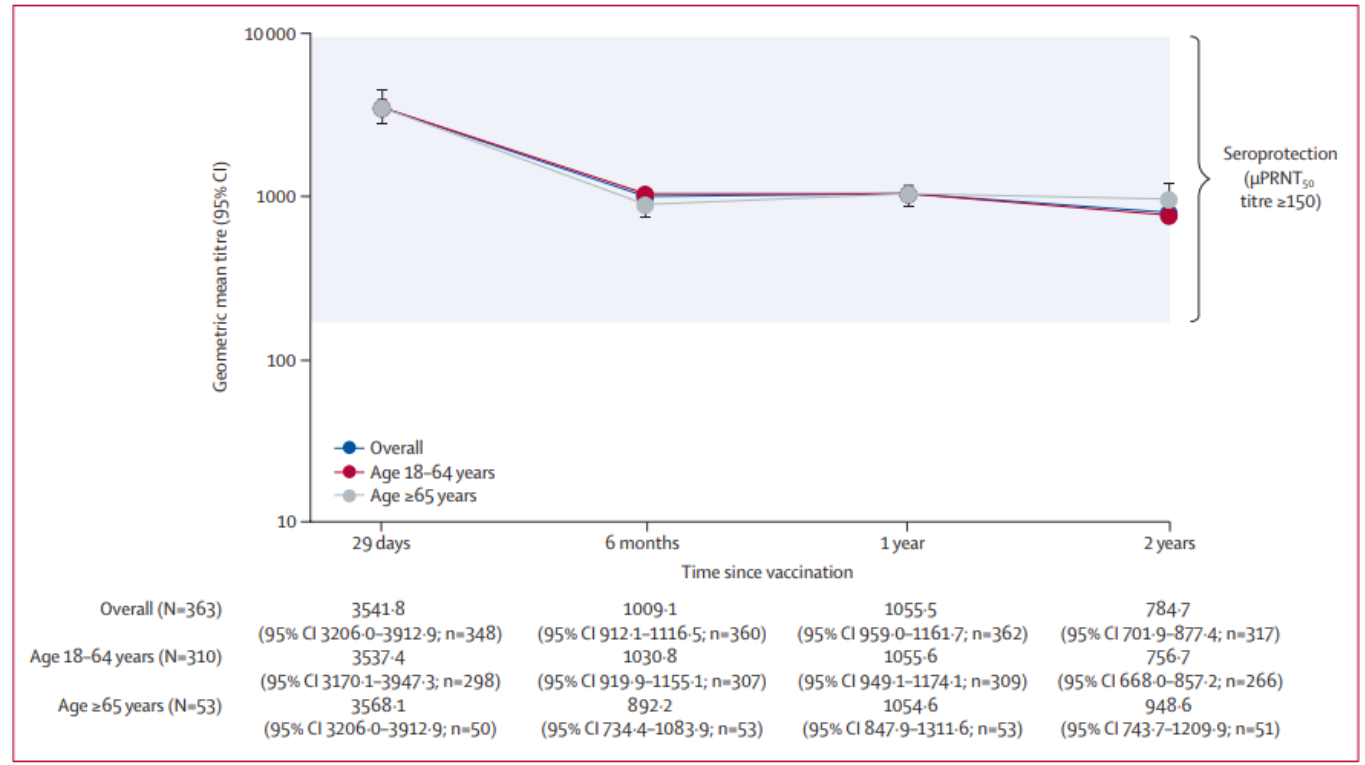
Antibody persistence and safety of a live-attenuated chikungunya virus vaccine up to 2 years after single-dose administration in adults in the USA: a single-arm, multicentre, phase 3b study

Robert McMahon, Sebastian Toepfer, Natascha Sattler, Martina Schneider, Marivic Narciso-Abraham, Sandra Hadl, Romana Hochreiter, Karin Kosulin, Robert Mader, Oliver Zoihsl, Nina Wressnigg, Katrin Dubischar, Vera Buerger, Susanne Eder-Lingelbach, Juan-Carlos Jaramillo



	29 days	6 months	1 year	2 years
Overall (N=363)	99·1% (95% CI 97·5–99·8; N=346)	97·8% (95% CI 95·6–99·0; N=358)	98·9% (95% CI 97·2–99·7; N=360)	96·8% (95% CI 94·3–98·5; N=316)
Age 18–64 years (N=310)	99·0% (95% CI 97·1–99·8; N=296)	97·7% (95% CI 95·3–99·1; N=305)	98·7% (95% CI 96·7–99·6; N=307)	96·6% (95% CI 93·7–98·4; N=265)
Age ≥65 years (N=53)	100% (95% CI 92·6–100; N=50)	98·1% (95% CI 89·9–100; N=53)	100% (95% CI 93·3–100; N=53)	98·0% (95% CI 89·6–100; N=51)

Figure 2: **Seroprotection rate for chikungunya virus-specific neutralising antibodies until 2 years after single-dose vaccination of VLA1553**



	29 days	6 months	1 year	2 years
Overall (N=363)	3541·8 (95% CI 3206·0–3912·9; n=348)	1009·1 (95% CI 912·1–1116·5; n=360)	1055·5 (95% CI 959·0–1161·7; n=362)	784·7 (95% CI 701·9–877·4; n=317)
Age 18–64 years (N=310)	3537·4 (95% CI 3170·1–3947·3; n=298)	1030·8 (95% CI 919·9–1155·1; n=307)	1055·6 (95% CI 949·1–1174·1; n=309)	756·7 (95% CI 668·0–857·2; n=266)
Age ≥65 years (N=53)	3568·1 (95% CI 3206·0–3912·9; n=50)	892·2 (95% CI 734·4–1083·9; n=53)	1054·6 (95% CI 847·9–1311·6; n=53)	948·6 (95% CI 743·7–1209·9; n=51)

Figure 3: **Geometric mean titres for chikungunya virus-specific neutralising antibodies up to 2 years after single-dose vaccination of VLA1553**

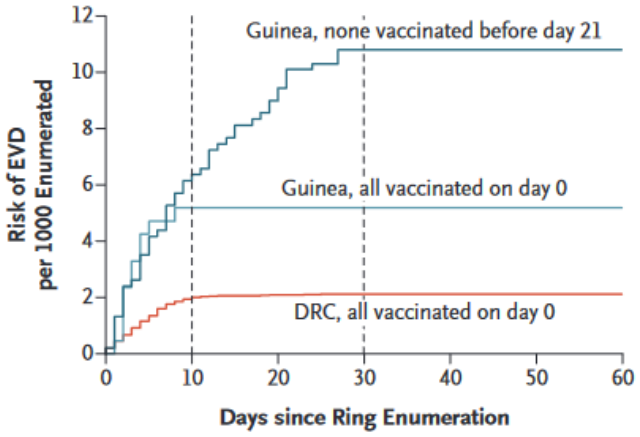
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Ebola Outbreak Response in the DRC with rVSV-ZEBOV-GP Ring Vaccination

J.-J. Muyembe, H. Pan, R. Peto, A. Diallo, A. Touré, P. Mbala-Kingebene, S.H. Bateyi Mustafa, N. Tambwe, S. Mulangu, S. Ahuka-Mundeke, E. Mukamba Musenga, G. Enwere, P.-S. Gsell, I.M. Longini, X. Riveros Balta, C.H. Roberts, M. Marks, M.N.K. Yao, A.S. Gueye, I.-S. Fall, P. Salama,* M.J. Ryan, and A.M. Henao-Restrepo, for the Ebola Ring Vaccination Team in the DRC

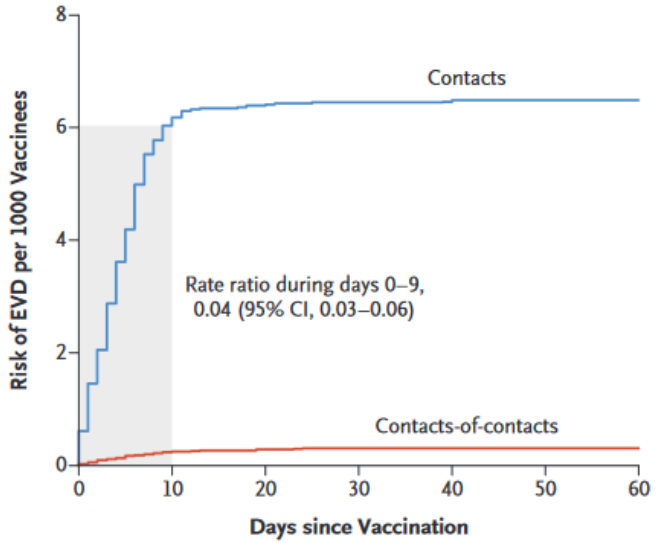
Vaccination was performed with one dose of rVSV-ZEBOV-GP, an attenuated, genetically engineered, replication-competent live vaccine. (Ervebo®, MSD)



No. Enumerated	
Guinea, none before day 21	4,556
Guinea, all on day 0	2,119
DRC, all on day 0	194,399

No. with Onset of EVD (risk per 1000)	Days 0–9	Days 10–29	Day 30 or later
Guinea, none before day 21	28 (6.15)	21 (4.64)	0
Guinea, all on day 0	11 (5.19)	0	0
DRC, all on day 0	380 (1.95)	32 (0.16)	22 (0.11)

Figure 3. EVD Onset in Guinea and DRC Rings among Contacts or Contacts-of-Contacts of EVD Cases.



No. Vaccinated	
Contacts	57,563
Contacts-of-contacts	136,836

No. with Onset of EVD	Days 0–9	Days 10–29	Day 30 or later
Contacts	347	24	9
Contacts-of-contacts	33	8	13

Figure 2. Risk of EVD among Vaccinees during Eastern DRC Outbreak (2018–2020).

Shown is the rate of EVD per 1000 contacts and contacts of contacts who re

Table 1. EVD Onset in Contacts of Index Cases, According to Timing of Vaccination and of EVD Onset among Vaccinees.*

Interval between EVD Onset in Index Case and in Contacts	Rate of EVD Onset in Contacts, According to Time from Index-Case Onset to Vaccination				Rate Ratio (95% CI)
	Day 0 to 8† (N=31,027)		Day ≥9† (N=26,536)		
	no. of contacts	*EVD rate/ 1000 contacts*	*no. of contacts*	*EVD rate/ 1000 contacts*	
Day 0 to 11	138	4.45	NA	NA	NA
Day 12 to 17	68	2.19	103	3.88	0.55 (0.40–0.76)
Day 18 to 23	2	0.06	53	2.00	0.03 (0.01–0.11)
Day 24 to 29	4	0.13	3	0.11	—
Day 30 to 59	0	0	2	0.08	—
Day ≥60	3	0.10	4	0.15	—

Efficacy of typhoid conjugate vaccine: final analysis of a 4-year, phase 3, randomised controlled trial in Malawian children

Priyanka D Patel, Yuanyuan Liang, James E Meiring, Nedson Chasweka, Pratiksha Patel, Theresa Misiri, Felistas Mwakiseghile, Richard Wachepa, Happy C Banda, Florence Shumba, Gift Kawalazira, Queen Dube, Nginache Nampota-Nkomba, Osward M Nyirenda, Tsion Girmay, Shrimati Datta, Leslie P Jamka, J Kathleen Tracy, Matthew B Laurens, Robert S Heyderman, Kathleen M Neuzil, Melita A Gordon* on behalf of the TyVAC team†*

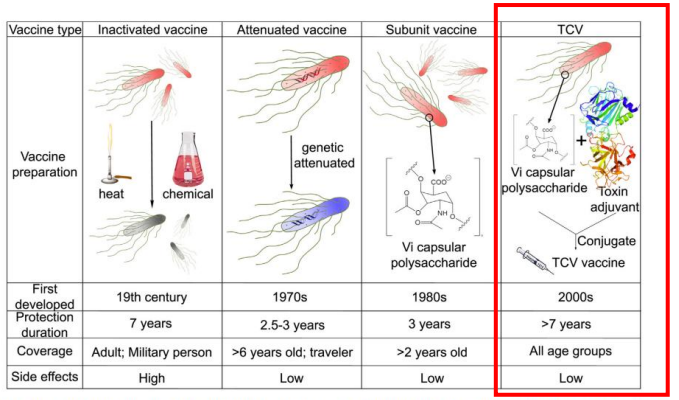


Figure 2. Comparison of typhoid vaccines. Method of preparation, protective efficacy, coverage, and side effects of different typhoid fever vaccines over time. TCV, typhoid conjugate vaccine.

healthy children aged 9 months to 12 years were randomly assigned (1:1) by an unmasked statistician to receive a single dose of Vi polysaccharide conjugated to tetanus toxoid vaccine (Vi-TT, Typbar TCV, Bharat Biotech International) or meningococcal capsular group A conjugate (MenA) vaccine.

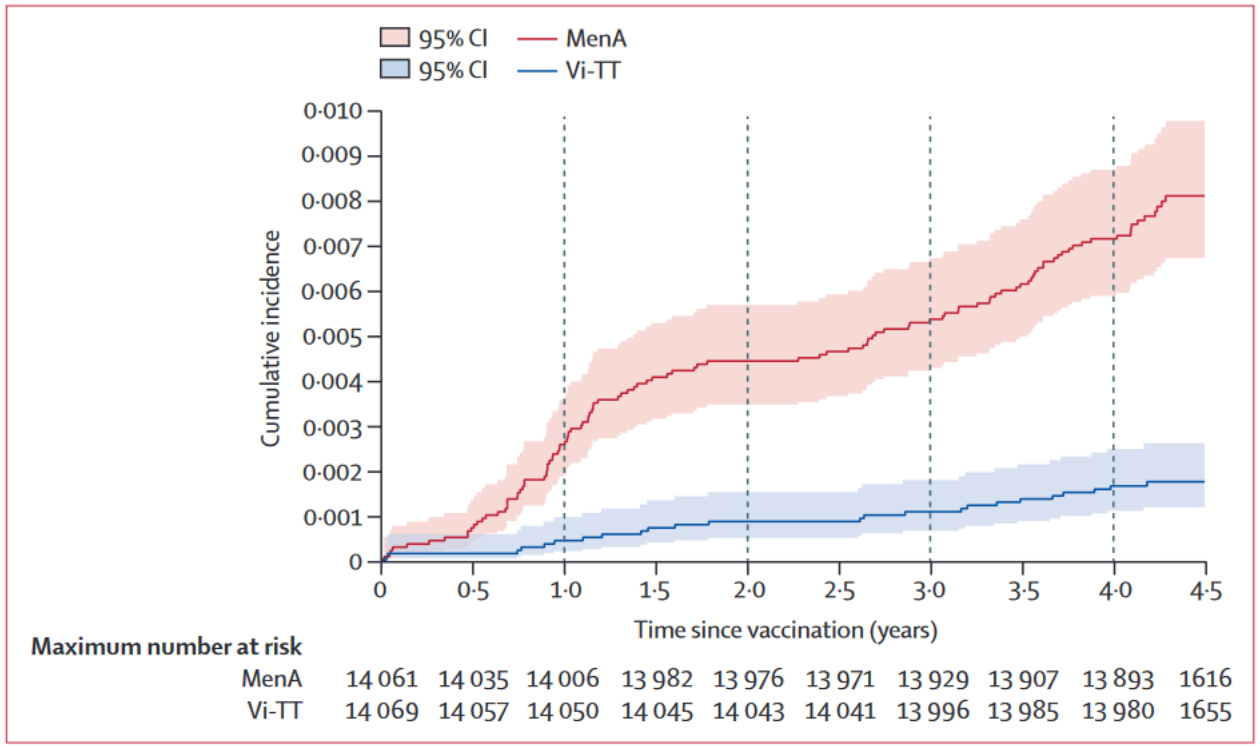
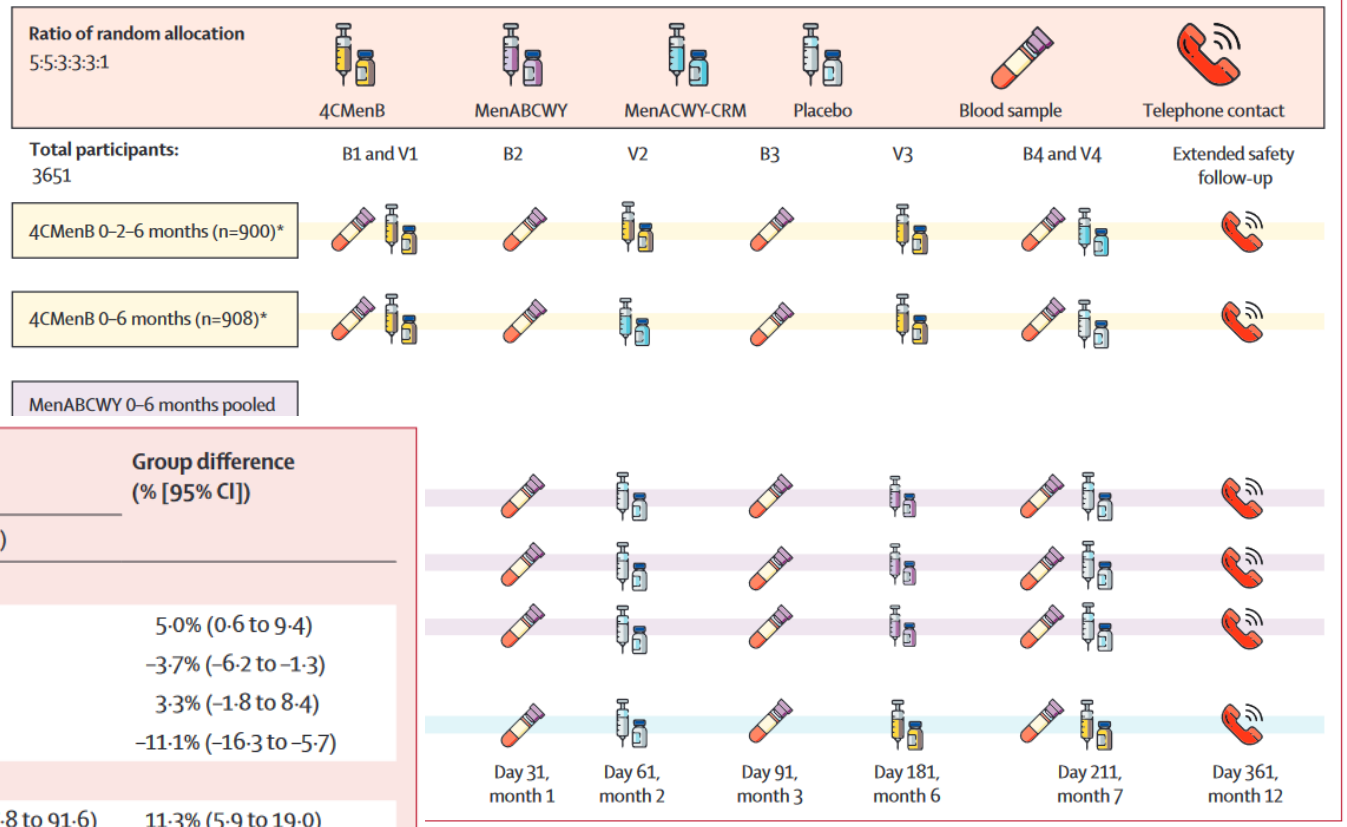


Figure 3: **Kaplan-Meier estimates of the cumulative incidence of blood-culture positive typhoid fever**

	Number at risk	Total follow-up time (person-years)	Number of cases of blood-culture-confirmed typhoid fever	Incidence rate (per 100 000 person-years; 95% CI)	Protective efficacy of Vi-TT (95% CI)
Cumulative time since vaccination					
0–1 years					
Vi-TT	14 069	14 058	6	42·7 (19·2–95)	83·4% (60·1–94·3)
MenA	14 061	14 036	36	256·5 (185·0–355·6)	Ref
0–2 years					
Vi-TT	14 069	28 104	12	42·7 (24·2–75·2)	80·7% (63·8–90·5)
MenA	14 061	28 021	62	221·3 (172·5–283·8)	Ref
0–3 years					
Vi-TT	14 069	42 135	15	35·6 (21·5–59·1)	80·1% (65·0–89·4)
MenA	14 061	41 983	75	178·6 (142·5–224·0)	Ref
0–4 years					
Vi-TT	14 069	56 121	23	41·0 (27·2–61·7)	77·1% (63·7–86·1)
MenA	14 061	55 889	100	178·9 (147·1–217·7)	Ref
0–4·61 years					
Vi-TT	14 069	60 500	24	39·7 (25·4–59·0)	78·3% (66·3–86·1)
MenA	14 061	60 220	110	182·7 (150·1–220·2)	Ref

Breadth of immune response, immunogenicity, reactogenicity, and safety for a pentavalent meningococcal ABCWY vaccine in healthy adolescents and young adults: results from a phase 3, randomised, controlled observer-blinded trial

Terry Nolan, Chiranjiwi Bhusal*, Jiří Beran, Mark Bloch, Benhur Sirvan Cetin, Ener Cagri Dinleyici, Daniel Dražan, Satu Kokko, Susanna Koski, Outi Laajalahti, Joanne M Langley, Mika Rämet, Peter C Richmond, Peter Silas, Bruce Tapiero, Florence Tiong, Mary Tipton, Benita Ukkonen, Betul Ulukol, Maria Lattanzi, Mauro Trapani, Arnold Willemsen, Daniela Toneatto, on behalf of the QUINTET study group†*



	MenABCWY group		4CMenB 0–2 group		MenACWY group		Group difference (% [95% CI])
	n/N	% (95% CI)	n/N	% (95% CI)	n/N	% (95% CI)	
Serogroup B antigen indicator strain*							
fHbp	538/675	79·7% (76·5 to 82·7)	537/719	74·7% (71·3 to 77·8)	NA	NA	5·0% (0·6 to 9·4)
NadA	622/671	92·7% (90·5 to 94·5)	691/717	96·4% (94·7 to 97·6)	NA	NA	−3·7% (−6·2 to −1·3)
NHBA	420/678	61·9% (58·2 to 65·6)	421/718	58·6% (54·9 to 62·3)	NA	NA	3·3% (−1·8 to 8·4)
PorA	271/642	42·2% (38·4 to 46·1)	375/704	53·3% (49·5 to 57·0)	NA	NA	−11·1% (−16·3 to −5·7)
Serogroups A, C, W, and Y†							
MenA	1135/1170	97·0% (95·9 to 97·9)	NA	NA	96/112	85·7% (77·8 to 91·6)	11·3% (5·9 to 19·0)
MenC	1156/1189	97·2% (96·1 to 98·1)	NA	NA	57/114	50·0% (40·5 to 59·5)	47·2% (38·1 to 56·3)
MenW	1150/1185	97·0% (95·9 to 97·9)	NA	NA	71/115	61·7% (52·2 to 70·6)	35·3% (26·9 to 44·5)
MenY	1157/1196	96·7% (95·6 to 97·7)	NA	NA	83/119	69·7% (60·7 to 77·8)	27·0% (19·4 to 35·8)

Non-inferiority of MenABCWY compared with 4CMenB was measured by percentages of participants with a four-fold rise in hSBA titres against four meningococcal serogroup B indicator strains one month after two MenABCWY doses and two 4CMenB doses (the 0–2 schedule was evaluated within the 4CMenB 0–2–6 group). Non-inferiority of MenACWY-CRM was measured by percentages of MenACWY-naive participants with a four-fold rise in hSBA titres against serogroups ACWY one month after two MenABCWY doses and one MenACWY-CRM dose. Analyses were done in the per-protocol set. Non-inferiority was demonstrated if the lower limit of two-sided 95% CI for group differences for all four indicator strains or serogroups were above −10%. The MenABCWY group were administered the meningococcal serogroups ABCWY vaccine at study months 0 and 6; the 4CMenB 0–2 group were administered two doses of 4CMenB at study months 0 and 2; and the MenACWY group were administered meningococcal serogroups ACWY-CRM glycoconjugate vaccine at study month 0. 4CMenB=four component meningococcal serogroup B. fHbp=factor H binding protein. hSBA=human serum bactericidal antibody. Men=meningococcal serogroup. n=number of participants with four-fold rise in hSBA titres. NA=not applicable. NadA=*Neisseria* adhesin A. NHBA=neisserial heparin-binding antigen. PorA=Porin A. *MenACWY group not included because it did not have an administered vaccine containing serogroup B antigen. †4CMenB 0–2 group not included because it did not have an administered vaccine containing serogroups A, C, W, and Y antigens.

Table 3: **Non-inferiority of investigational MenABCWY vaccine compared to 4CMenB and MenACWY-CRM**

nature medicine

Article

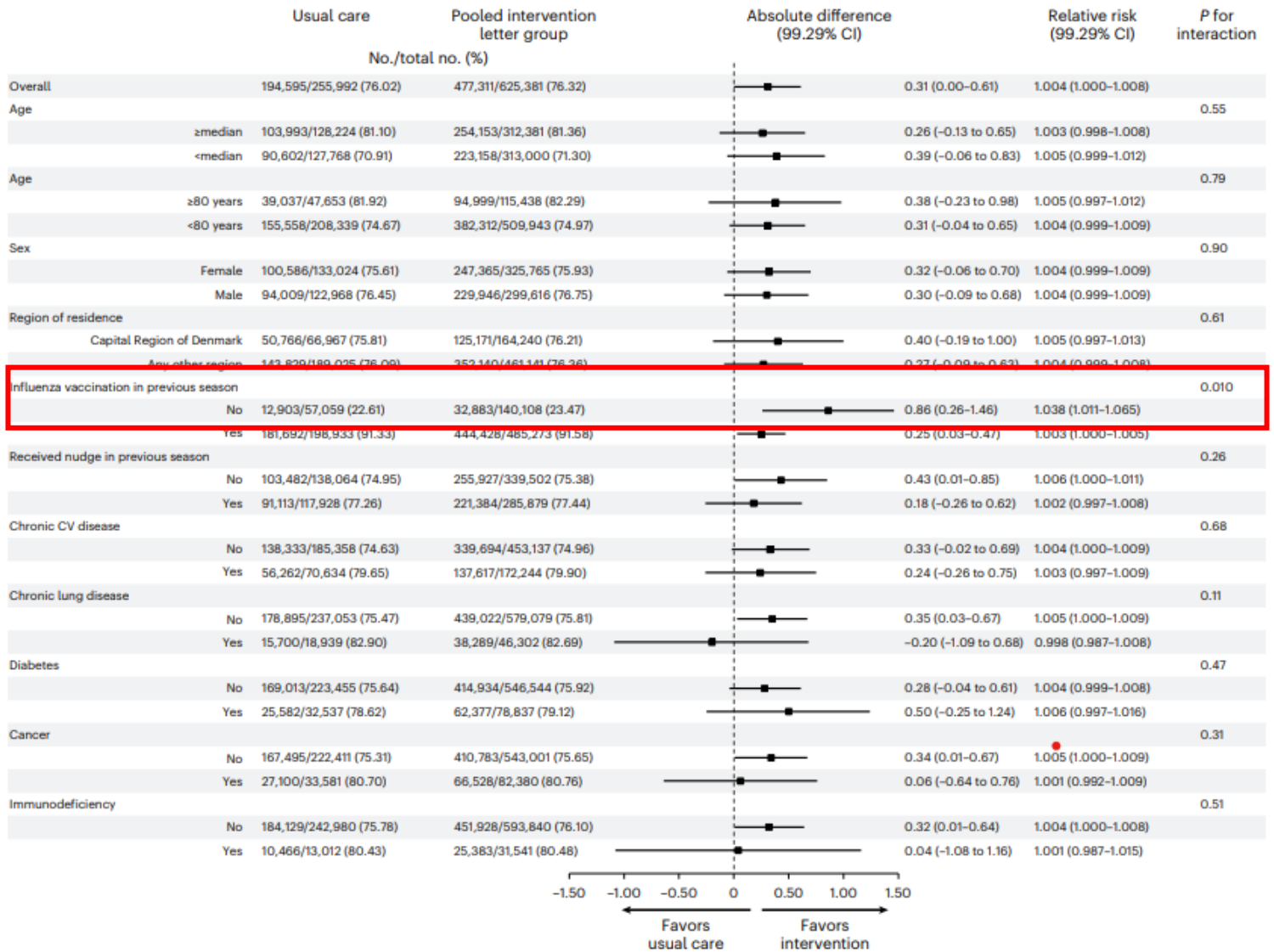
https://doi.org/10.1038/s41591-024-03202-4

Electronic nudges for sustained influenza vaccination uptake in older adults: the nationwide randomized NUDGE-FLU-2

Table 2 | Description of study arms

Study arm	Description	Behavioral science concep
Usual care	The usual care group received no letter on influenza vaccination but was subject to other standard public health vaccination campaigns.	-
Standard letter	Standard informational letter (displayed in Extended Data Fig. 3)	-
Repeated letter	Standard letter sent at baseline and repeated after 10 d	Priming and hot state activa
CV gain	Text added to standard letter	Gain framing (CV)
Respiratory gain	Text added to standard letter	Gain framing (respiratory)
Implementation prompt	Text added to standard letter, including highlighted booking link	Active choice/implementat intention prompt
Loss framing	Text added to standard letter	Loss framing

An English translation of the standard letter is shown in Extended Data Fig. 3. All letters were written in the Danish langua



JAMA | Original Investigation

Electronic Nudges to Increase Influenza Vaccination in Pa… With Chronic Diseases

A Randomized Clinical Trial

Niklas Dyrby Johansen, MD, PhD; Muthiah Vaduganathan, MD, MPH; Ankeet S. Bhatt, MD, MBA, ScM; Daniel Modin, …
Brian L. Claggett, PhD; Kira Hyldekær Janstrup, PhD; Carsten Schade Larsen, MD, DMSc; Lykke Larsen, MD, PhD; Loth…
Michael Dalager-Pedersen, MD, PhD; Lars Køber, MD, DMSc; Scott D. Solomon, MD; Pradeesh Sivapalan, MD, PhD; Je…
Cyril Jean-Marie Martel, PhD; Tyra Grove Krause, MD, PhD; Tor Biering-Sørensen, MD, MSc, MPH, PhD

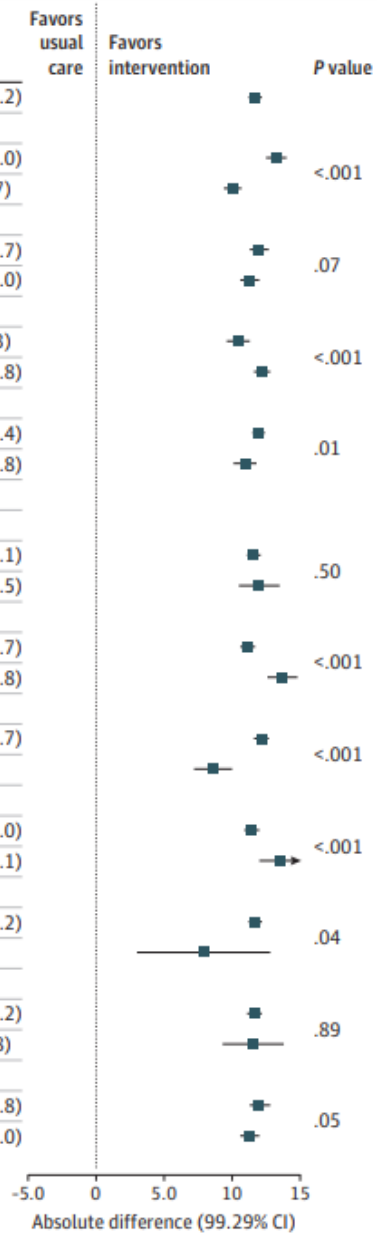
DESIGN, SETTING, AND PARTICIPANTS Nationwide pragmatic registry-based randomized clinical implementation trial conducted between September 24, 2023, and May 31, 2024, enrolling all Danish citizens aged 18 to 64 years who met criteria for free-of-charge influenza vaccination in light of preexisting chronic disease. All trial data were sourced from nationwide administrative health registries.

INTERVENTION Randomized in 2.45:1:1:1:1:1:1 ratio to no letter (usual care) or 6 different behaviorally informed electronic letters.

Figure 2. Results for Primary End Point of Influenza Vaccination Receipt

Comparison type	No./total No. Intervention	Usual care
Individual comparisons		
Loss-framing letter vs usual care	13 748/35 385 (38.9)	24 289/87 059 (27
Implementation prompt letter vs usual care	14 067/35 701 (39.4)	24 289/87 059 (27
Respiratory gain letter vs usual care	13 728/35 320 (38.9)	24 289/87 059 (27
CV gain letter vs usual care	14 028/35 271 (39.8)	24 289/87 059 (27
Repeated letter vs usual care	14 906/35 649 (41.8)	24 289/87 059 (27
Standard letter vs usual care	13 705/35 496 (38.6)	24 289/87 059 (27
Pooled comparison		
Any intervention letter vs usual care	84 182/212 822 (39.6)	24 289/87 059 (27

Variable	No./total No. Intervention	Usual care	Relative risk (99.29% CI)	Absolute difference (99.29% CI)	P value
Overall	84 182/212 822 (39.6)	24 289/87 059 (27.9)	1.42 (1.39-1.44)	11.7 (11.2-12.2)	
Age, y					
≥52.0	52 823/106 340 (49.7)	15 856/43 577 (36.4)	1.37 (1.34-1.39)	13.3 (12.5-14.0)	<.001
<52.0	31 359/106 482 (29.5)	8433/43 482 (19.4)	1.52 (1.47-1.56)	10.1 (9.4-10.7)	
Sex					
Female	47 145/113 017 (41.7)	13 810/46 437 (29.7)	1.40 (1.37-1.43)	12.0 (11.3-12.7)	.07
Male	37 037/99 805 (37.1)	10 479/40 622 (25.8)	1.44 (1.40-1.48)	11.3 (10.6-12.0)	
Region of residence					
Capital Region of Denmark	26 137/67 599 (38.7)	7800/27 653 (28.2)	1.37 (1.33-1.41)	10.5 (9.6-11.3)	<.001
Any other region	58 045/145 223 (40.0)	16 489/59 406 (27.8)	1.44 (1.41-1.47)	12.2 (11.6-12.8)	
Influenza vaccination in previous season					
No	30 542/145 048 (21.1)	5397/59 354 (9.1)	2.32 (2.23-2.40)	12.0 (11.5-12.4)	.01
Yes	53 640/67 774 (79.1)	18 892/27 705 (68.2)	1.16 (1.15-1.17)	11.0 (10.1-11.8)	
Disease-specific eligibility criteria					
Chronic lung disease					
No	72 201/186 822 (38.6)	20 696/76 518 (27.0)	1.43 (1.40-1.45)	11.6 (11.1-12.1)	.50
Yes	11 981/26 000 (46.1)	3593/10 541 (34.1)	1.35 (1.30-1.41)	12.0 (10.5-13.5)	
Chronic cardiovascular disease					
No	65 628/169 019 (38.8)	19 160/69 155 (27.7)	1.40 (1.38-1.43)	11.1 (10.6-11.7)	<.001
Yes	18 554/43 803 (42.4)	5129/17 904 (28.6)	1.48 (1.43-1.53)	13.7 (12.6-14.8)	
Type 1 or 2 diabetes					
No	70 732/181 942 (38.9)	19 900/74 512 (26.7)	1.46 (1.43-1.48)	12.2 (11.6-12.7)	<.001
Yes	13 450/30 880 (43.6)	4389/12 547 (35.0)	1.24 (1.20-1.29)	8.6 (7.2-10.0)	
Immunodeficiency					
No	73 835/189 222 (39.0)	21 331/77 295 (27.6)	1.41 (1.39-1.44)	11.4 (10.9-12.0)	<.001
Yes	10 347/23 600 (43.8)	2958/9764 (30.3)	1.45 (1.38-1.52)	13.5 (12.0-15.1)	
Impaired breathing due to muscular weakness					
No	82 883/210 260 (39.4)	23 843/86 017 (27.7)	1.42 (1.40-1.45)	11.7 (11.2-12.2)	.04
Yes	1299/2562 (50.7)	446/1042 (42.8)	1.18 (1.06-1.32)	7.9 (3.0-12.8)	
Kidney or liver disease					
No	79 556/201 977 (39.4)	22 929/82 689 (27.7)	1.42 (1.40-1.44)	11.7 (11.1-12.2)	.89
Yes	4626/10 845 (42.7)	1360/4370 (31.1)	1.37 (1.28-1.47)	11.5 (9.3-13.8)	
Other chronic conditions with increased risk of severe influenza					
No	40 502/100 137 (40.4)	11 635/40 968 (28.4)	1.42 (1.39-1.46)	12.0 (11.3-12.8)	.05
Yes	43 680/112 685 (38.8)	12 654/46 091 (27.5)	1.41 (1.38-1.44)	11.3 (10.6-12.0)	



JAMA Network Open

Original Investigation | Infectious Diseases

Safety of Simultaneous Vaccination With Adjuvanted Zoster Vaccine and Adjuvanted Influenza Vaccine

A Randomized Clinical Trial

Kenneth E. Schmader, MD; Emmanuel B. Walter, MD, MPH; Kawsar R. Talaat, MD; Wes Rountree, MPH; Marek Poniewierski, MD, MS; Emily Randolph, MBA; Sean X. Leng, MD, PhD; Bettina Wunderlich, PhD; Michael M. McNeil, MD, MPH; Oidda Museru, MSN, MPH; Karen R. Broder, MD

MF59-QIV vs HD QIV

Figure 1. CONSORT Diagram

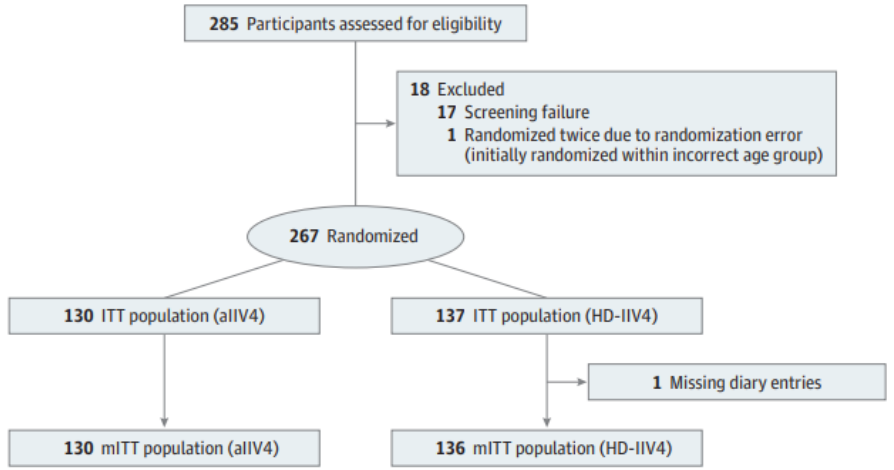
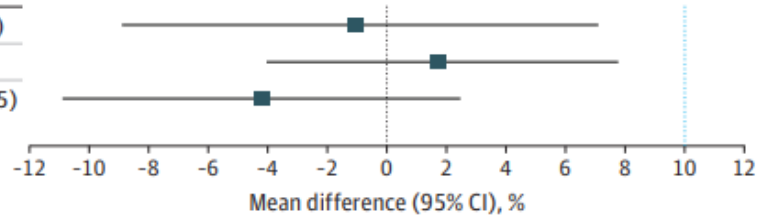


Figure 2. Difference in Proportions for Any Severe, Local, or Systemic Reactions From Recombinant Zoster Vaccine (RZV) Dose 1 and Quadrivalent Adjuvanted Inactivated Influenza Vaccine (aIIV4) vs RZV Dose 1 and Quadrivalent High-Dose Inactivated Influenza Vaccine (HD-IIV4)

Severe reaction	Mean difference (95% CI), %
Any severe reaction	-1.0 (-8.9 to 7.1)
Any local severe reaction	1.7 (-4.0 to 7.8)
Any systemic severe reaction	-4.2 (-10.9 to 2.5)

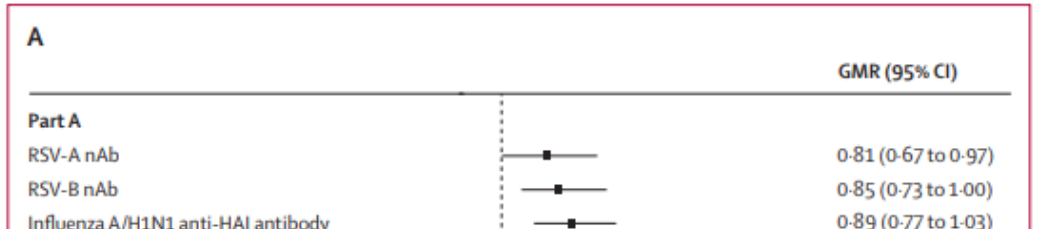


Conclusions

In this randomized clinical trial of simultaneous administration of RZV dose 1 and aIIV4 in older adults, the proportion of participants with at least 1 severe reaction was not higher after RZV dose 1 and aIIV4 compared with RZV dose 1 and HD-IIV4. There were no significant differences between the groups in the occurrence of SAEs after RZV dose 1 and adjuvanted or nonadjuvanted influenza vaccine. The postvaccination effect on HRQOL was similar between the 2 groups. From a safety standpoint, the simultaneous administration of RZV and aIIV4 was an acceptable option for vaccine delivery among older adults.

Safety and immunogenicity of mRNA-1345 RSV vaccine coadministered with an influenza or COVID-19 vaccine in adults aged 50 years or older: an observer-blinded, placebo-controlled, randomised, phase 3 trial

Jaya Goswami, Jose F Cardona, Denise C Hsu, Alana K Simorellis, Lauren Wilson, Rakesh Dhar, Joanne E Tomassini, Xiaowei Wang, Archana Kapoor, Avi Collins, Vinicius Righi, Lan Lan, Jiejun Du, Honghong Zhou, Sonia K Stoszek, Christine A Shaw, Caroline Reuter, Eleanor Wilson, Jacqueline M Miller, Rituparna Das, on behalf of the study investigators*



Clinical Infectious Diseases

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IDSA Infectious Diseases Society of America

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OXFORD

Safety and Immunogenicity of Bivalent RSVpreF Vaccine Coadministered With Seasonal Inactivated Influenza Vaccine in Older Adults

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Clinical Infectious Diseases

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IDSA Infectious Diseases Society of America

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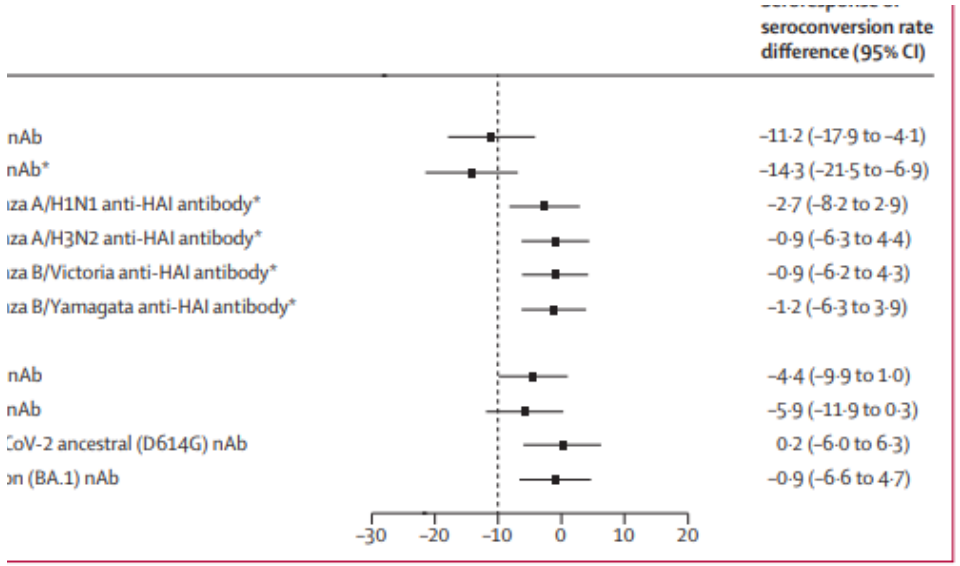
Immunogenicity, Reactogenicity, and Safety of AS01$_E$-adjuvanted Respiratory Syncytial Virus (RSV) Prefusion F Protein-based Candidate Vaccine (RSVPreF3 OA) When Co-administered With a Seasonal Quadrivalent Influenza Vaccine in Older Adults: Results of a Phase 3, Open-Label, Randomized Controlled Trial

Reynaldo Chandler,[1] Nathali Montenegro,[2] Cecilia Llorach,[3,4] Lorena Noriega Aguirre,[5] Sophie Germain,[6] Sherine O. Kuriyakose,[7] Axel Lambert,[6] Dominique Descamps,[6] Aurélie Olivier,[6] and Veronica Hulstrøm[6]



GMRs of antibody responses (A) and seroresponse or seroconversion differences (B) after
nistration of mRNA-1345 with SIIV4 (part A) or mRNA-1273.214 (part B) versus individual vaccines