Perspectives vaccinales

Odile Launay

Cours d'Automne en Chimiothérapie anti infectieuse et vaccinologie
Veyrier du Lac, 12 octobre 2021

Liens d’intérêt

- Recherches/essais cliniques : MSD, GSK bio, spmsd, Sanofi Pasteur, Janssen, Pfizer
- Advisory Boards : spmsd, Sanofi Pasteur, Janssen, Pfizer
- Cours, formations : Pfizer, MSD, Sanofi Pasteur
- Aides pour des recherches : MSD, GSK bio, spmsd, Sanofi Pasteur, Janssen, Pfizer

Histoire de la vaccination

Revue des Maladies Respiratoires (2019) 36, 74–81

ELSEVIER

Disponible en ligne sur ScienceDirect www.sciencedirect.com

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SÉRIE « VACCINATIONS » COORDONNÉE PAR E. BLANCHARD ET A. BERGERON (GREPI)

Histoire et principes de la vaccination

History and principles of vaccination

E. Canouï[a,*], O. Launay[a,b]

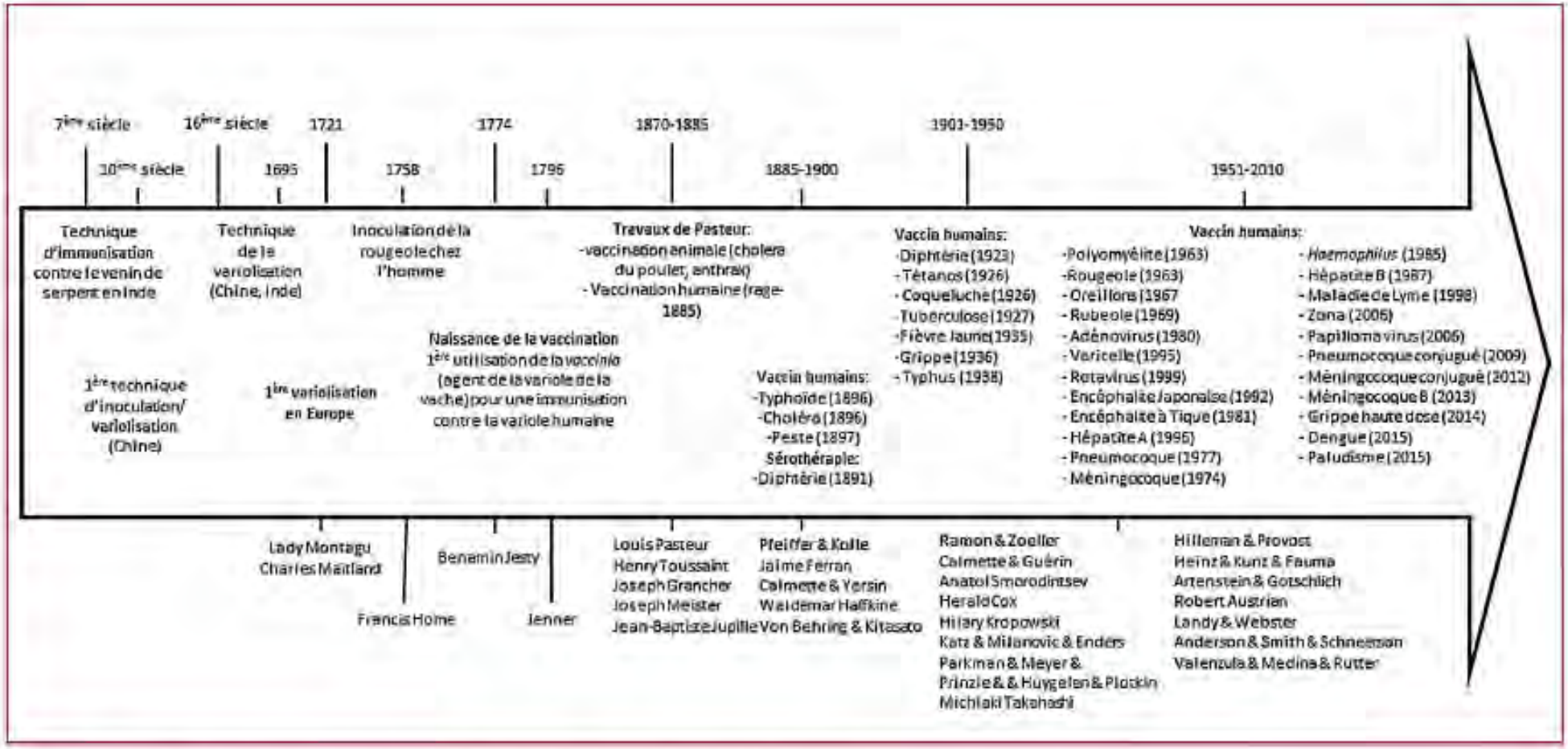

Figure 1. Histoire des découvertes et des grands noms de la vaccination.

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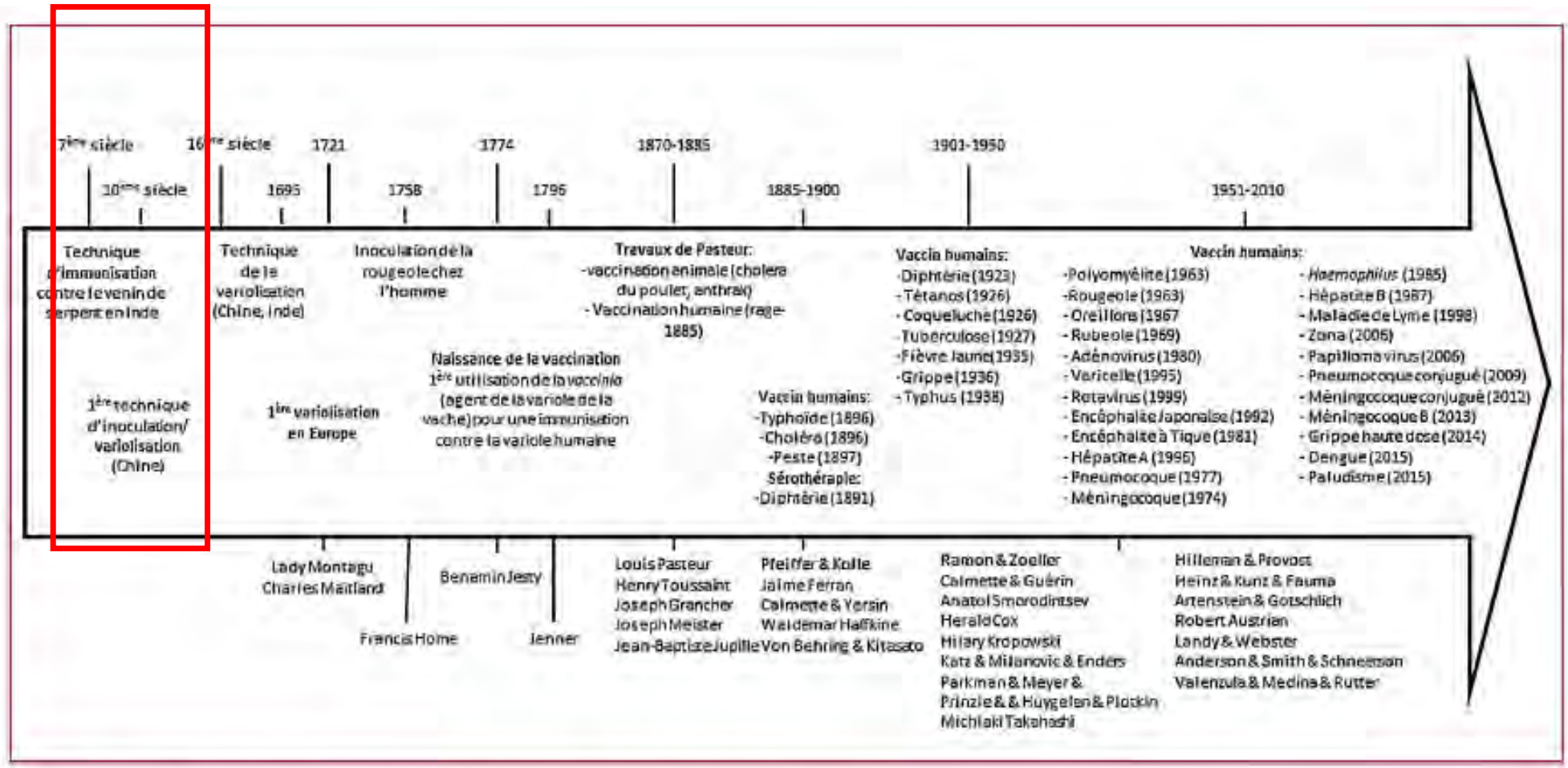

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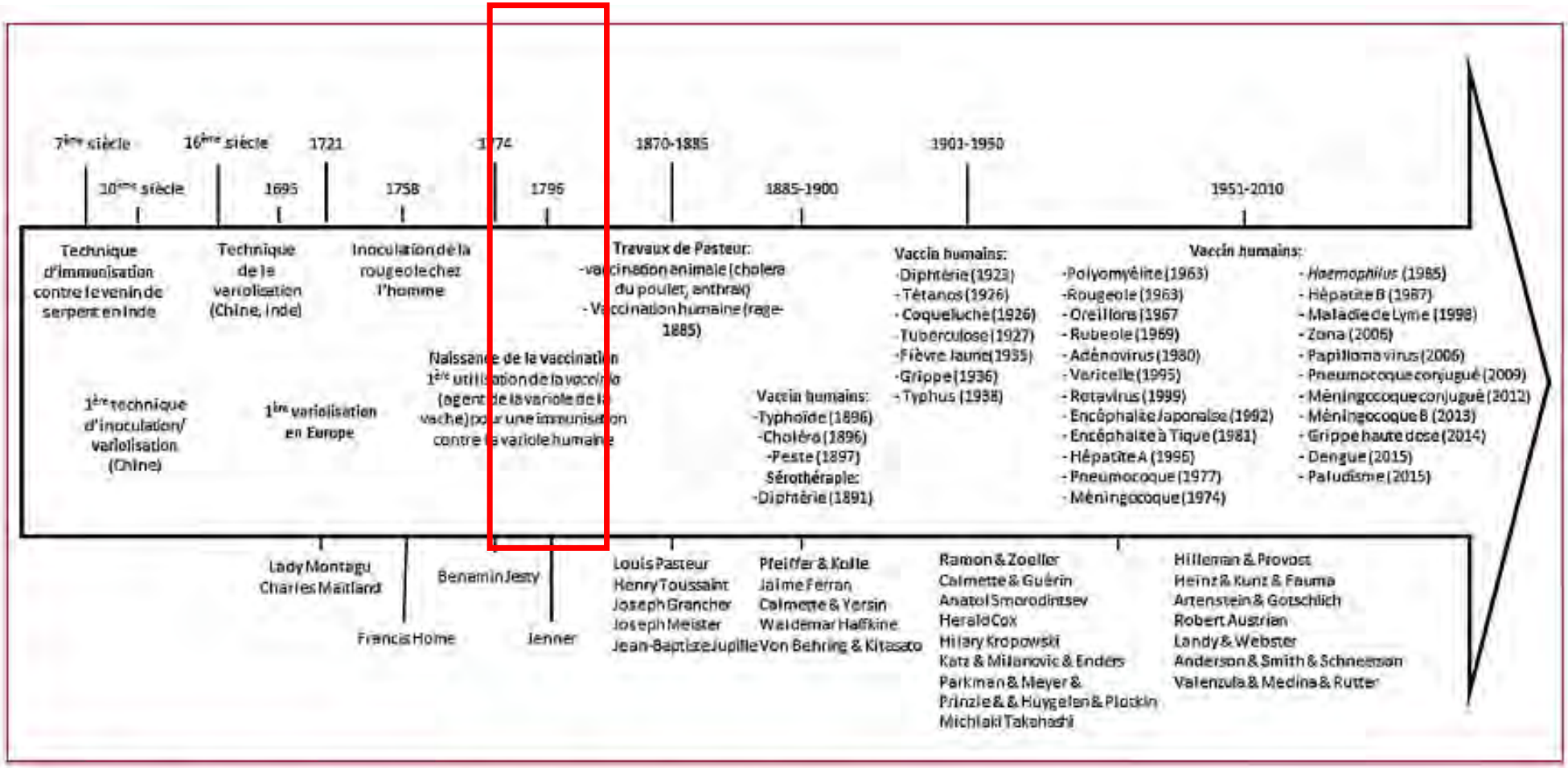

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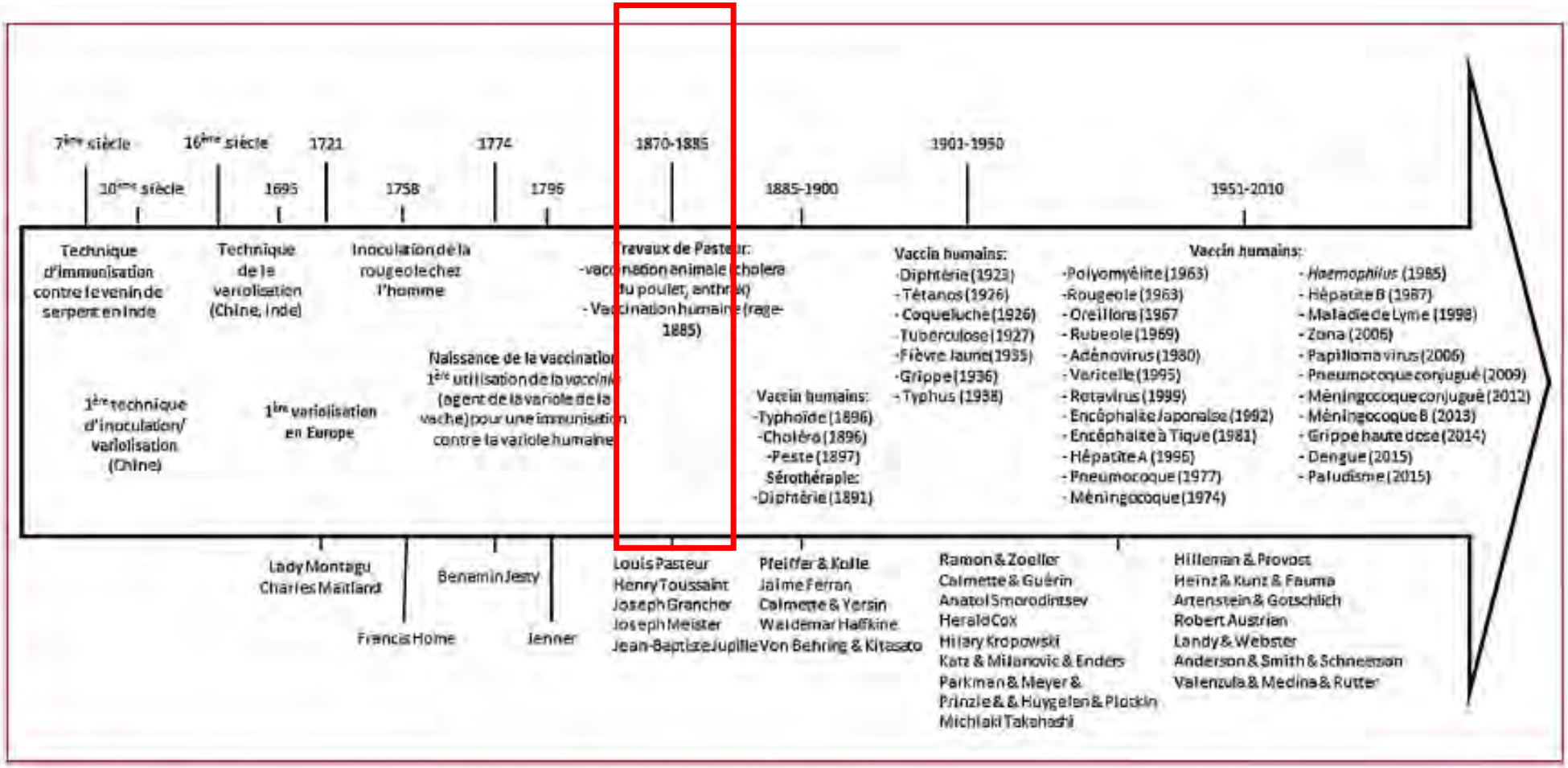

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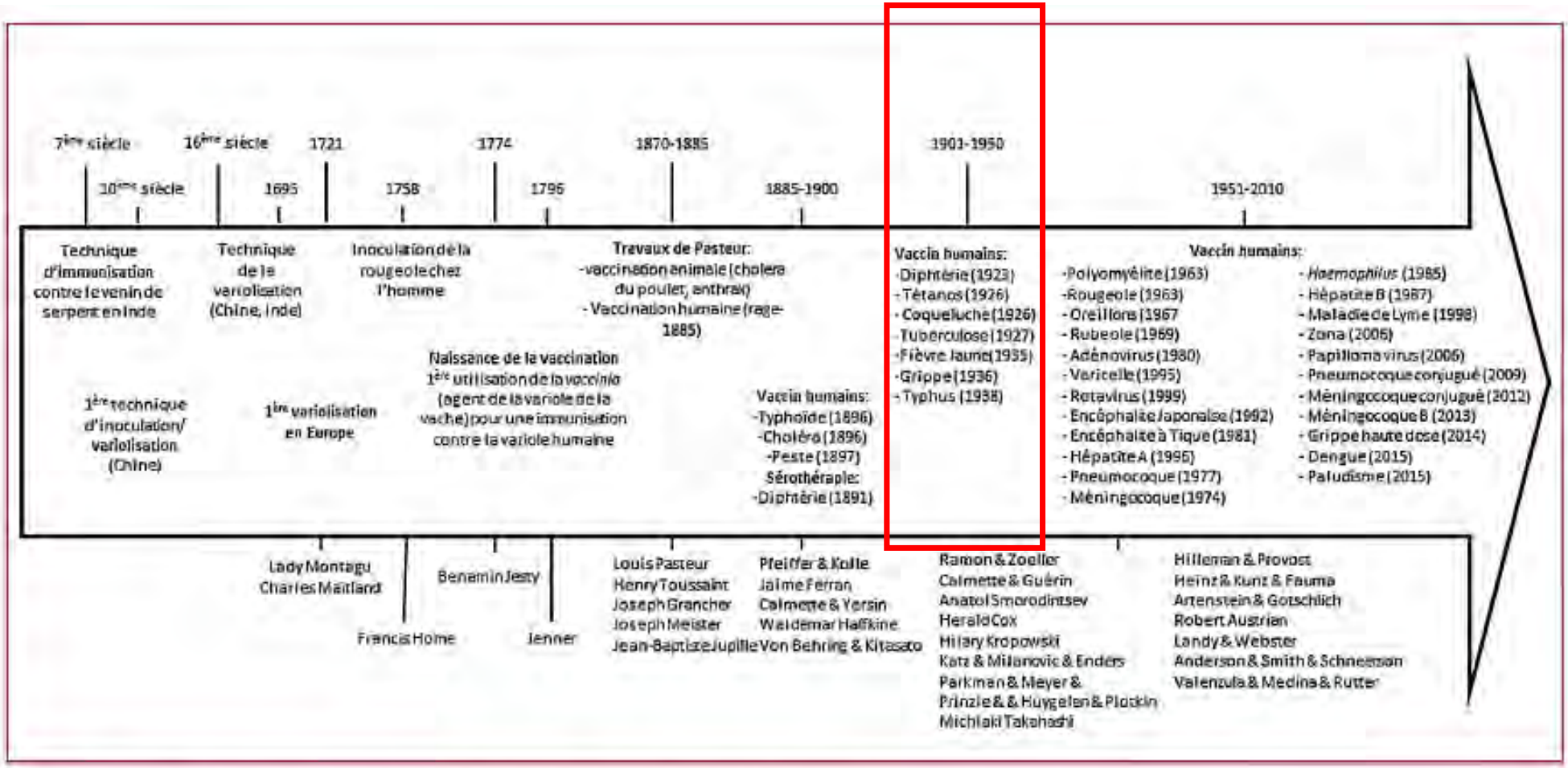

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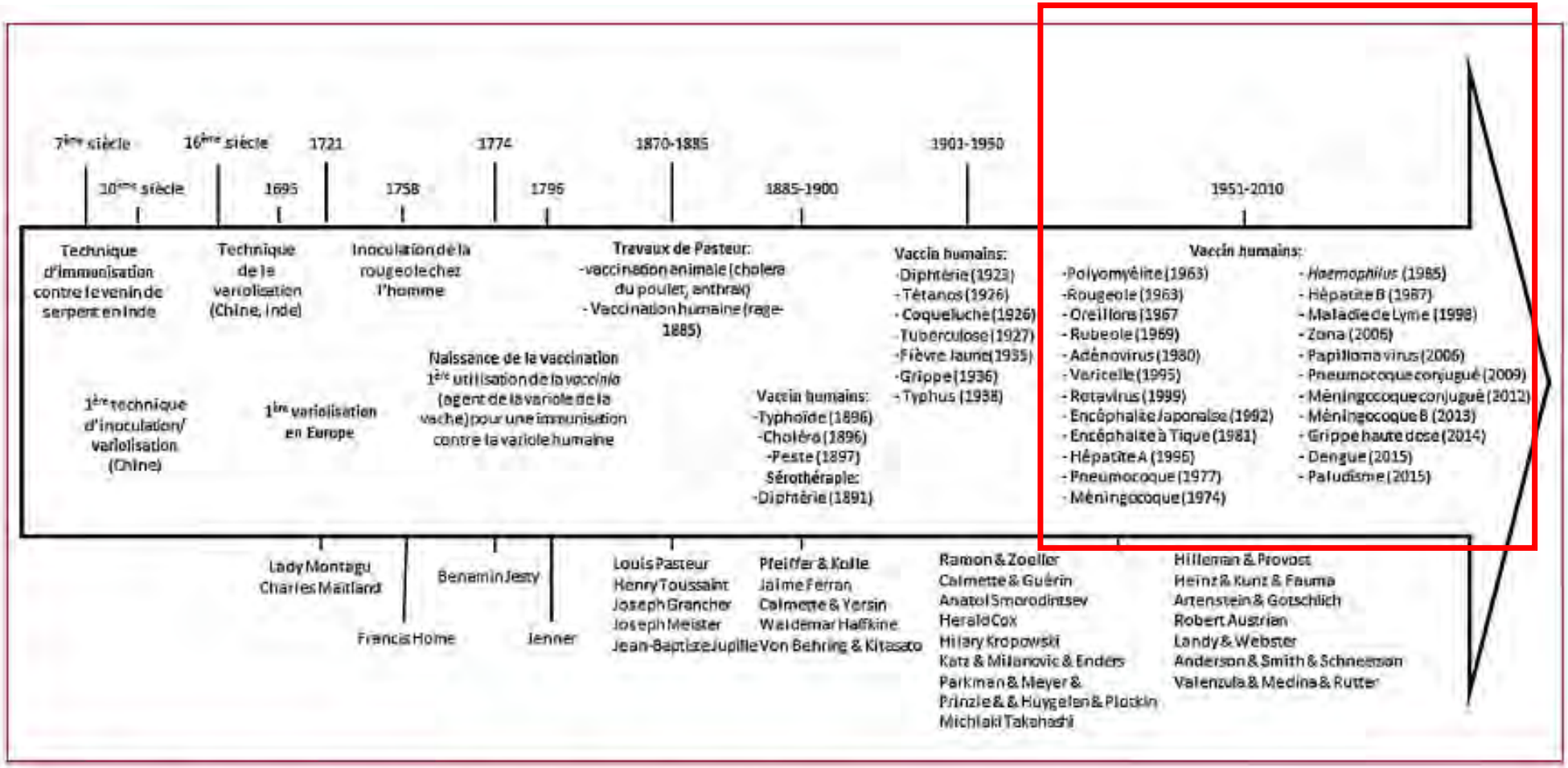
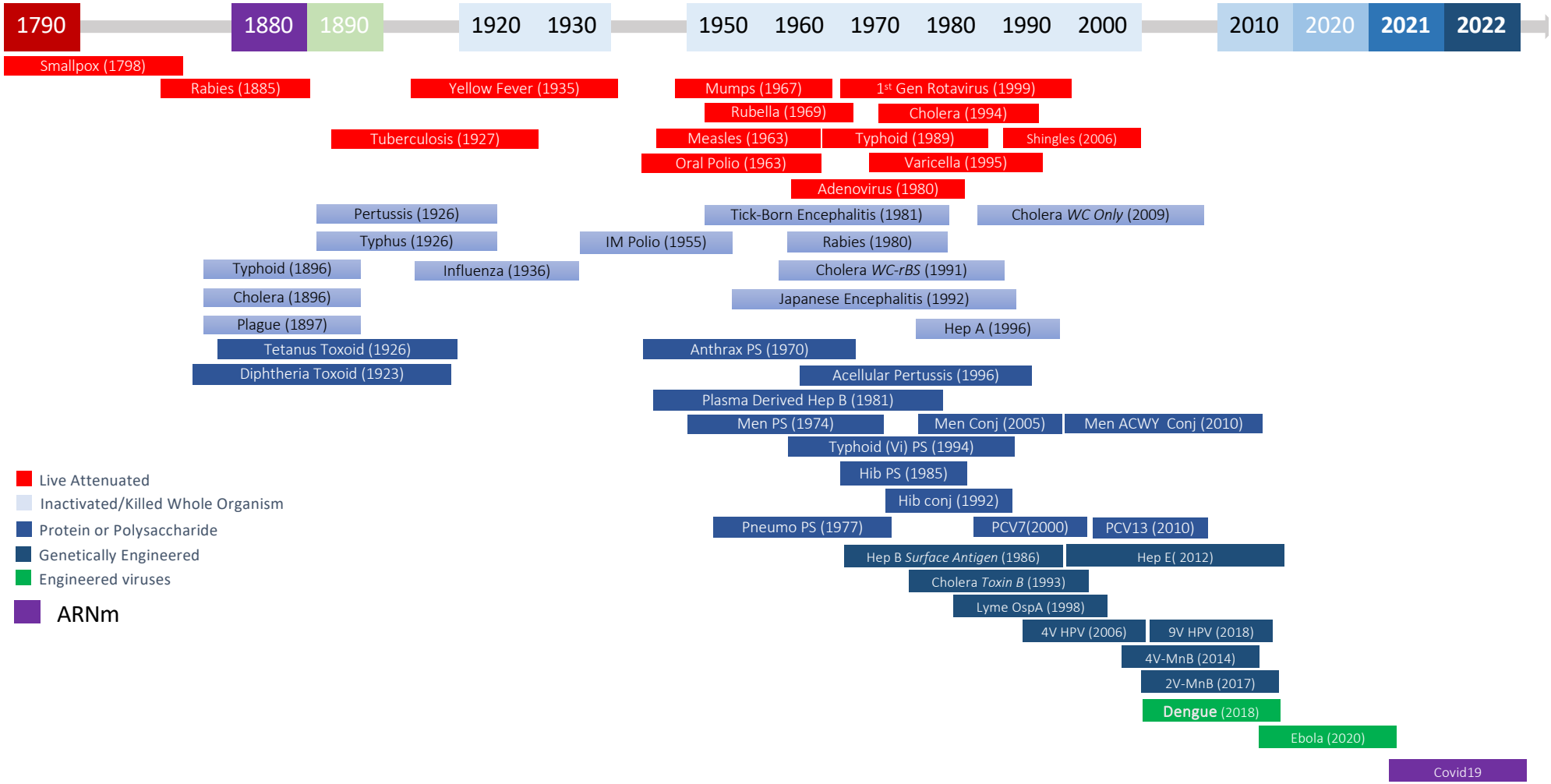


Figure 1. Histoire des découvertes et des grands noms de la vaccination.

Evolution des technologies vaccinales



Couvertures vaccinales

frontiers in Microbiology

REVIEW
published: 14 July 2020
doi: 10.3389/fmicb.2020.01526

Impact of Vaccines; Health, Economic and Social Perspectives

*Charlene M. C. Rodrigues[1,2] and Stanley A. Plotkin[3]**

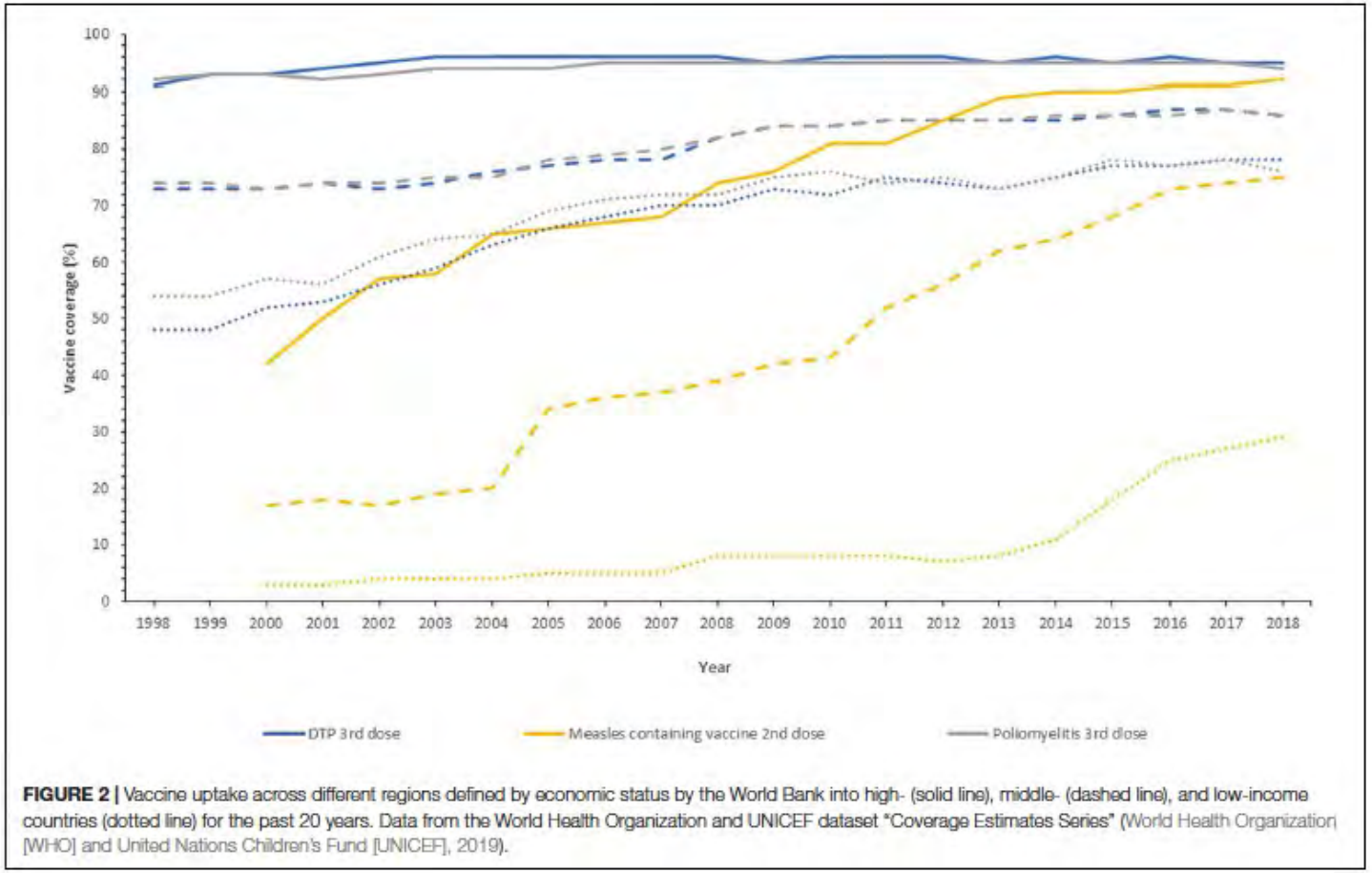
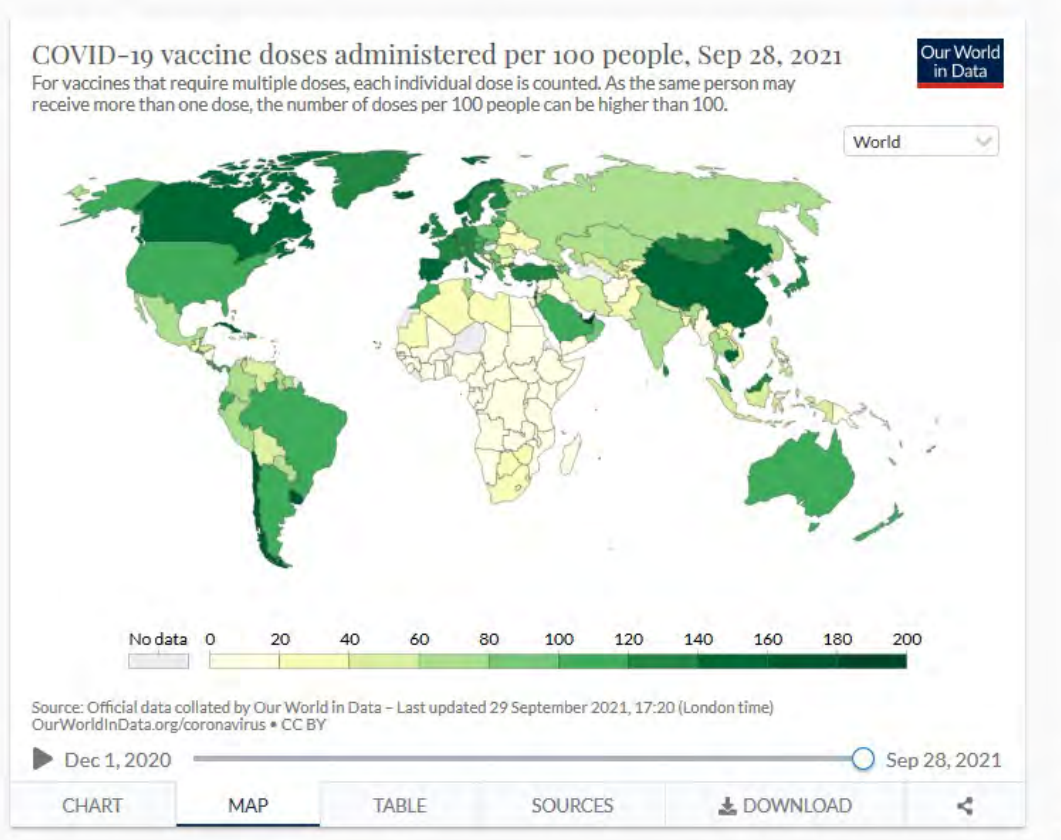


FIGURE 2 | Vaccine uptake across different regions defined by economic status by the World Bank into high- (solid line), middle- (dashed line), and low-income countries (dotted line) for the past 20 years. Data from the World Health Organization and UNICEF dataset "Coverage Estimates Series" (World Health Organization [WHO] and United Nations Children's Fund [UNICEF], 2019).

Vaccination COVID 19 dans le monde (au 29 septembre 2021)

- 45% de la population mondiale vaccinée 1 dose, MAIS seulement 2,3% dans les pays à faibles revenus
- Au total 6,2 milliards de doses administrées, actuellement 26,02 millions par jour



Impact des vaccins

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*Charlene M. C. Rodrigues[1,2] and Stanley A. Plotkin[3]**

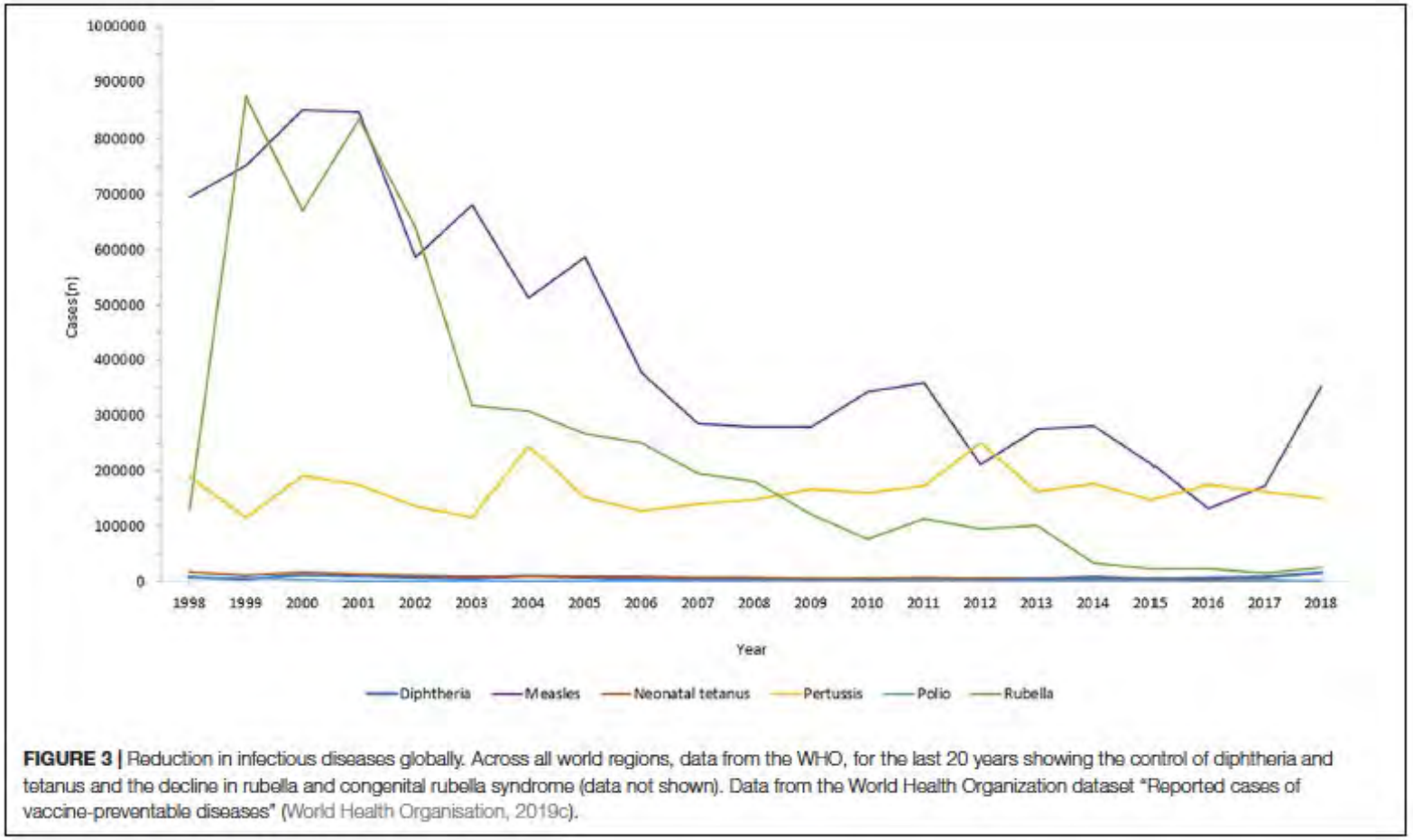
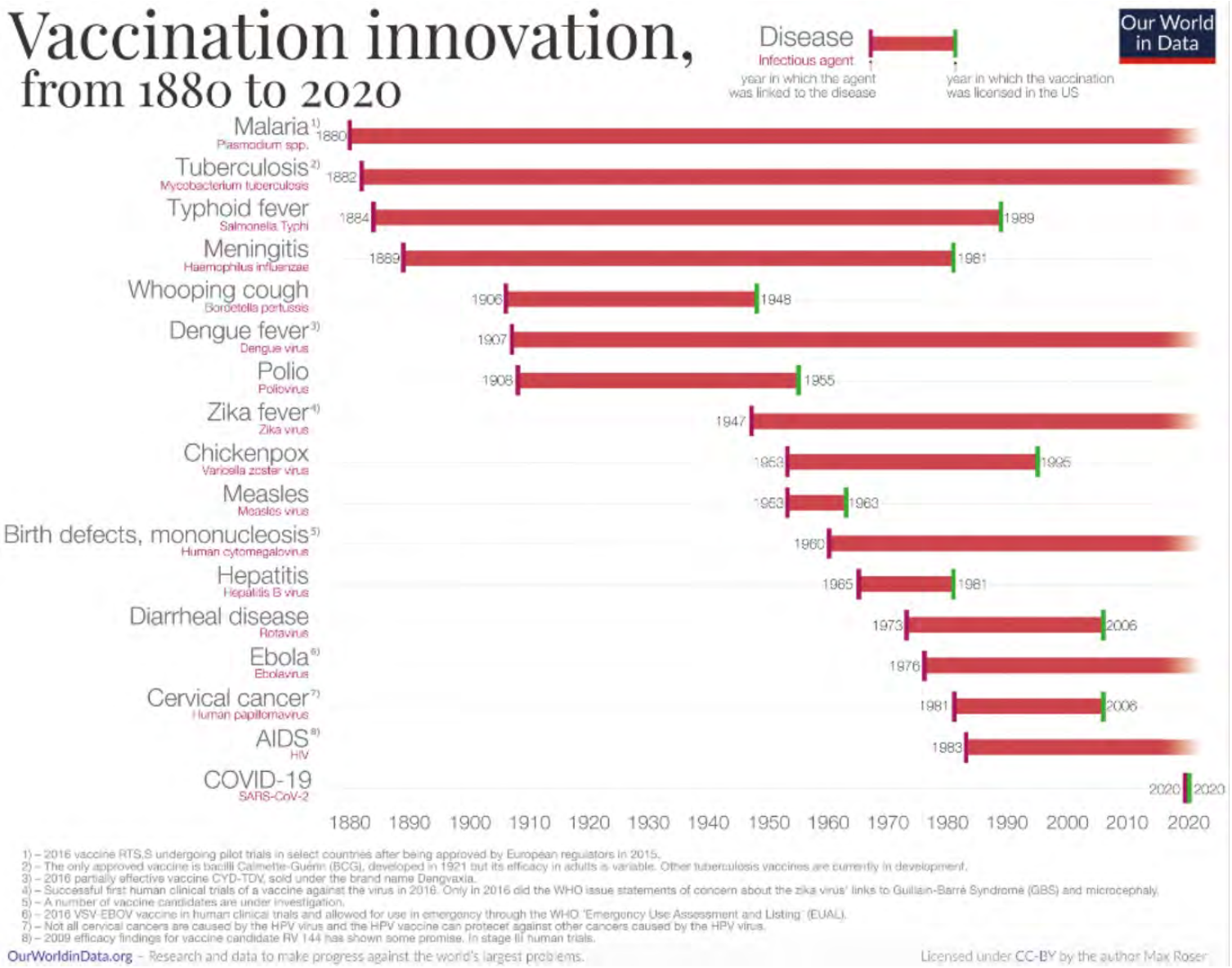
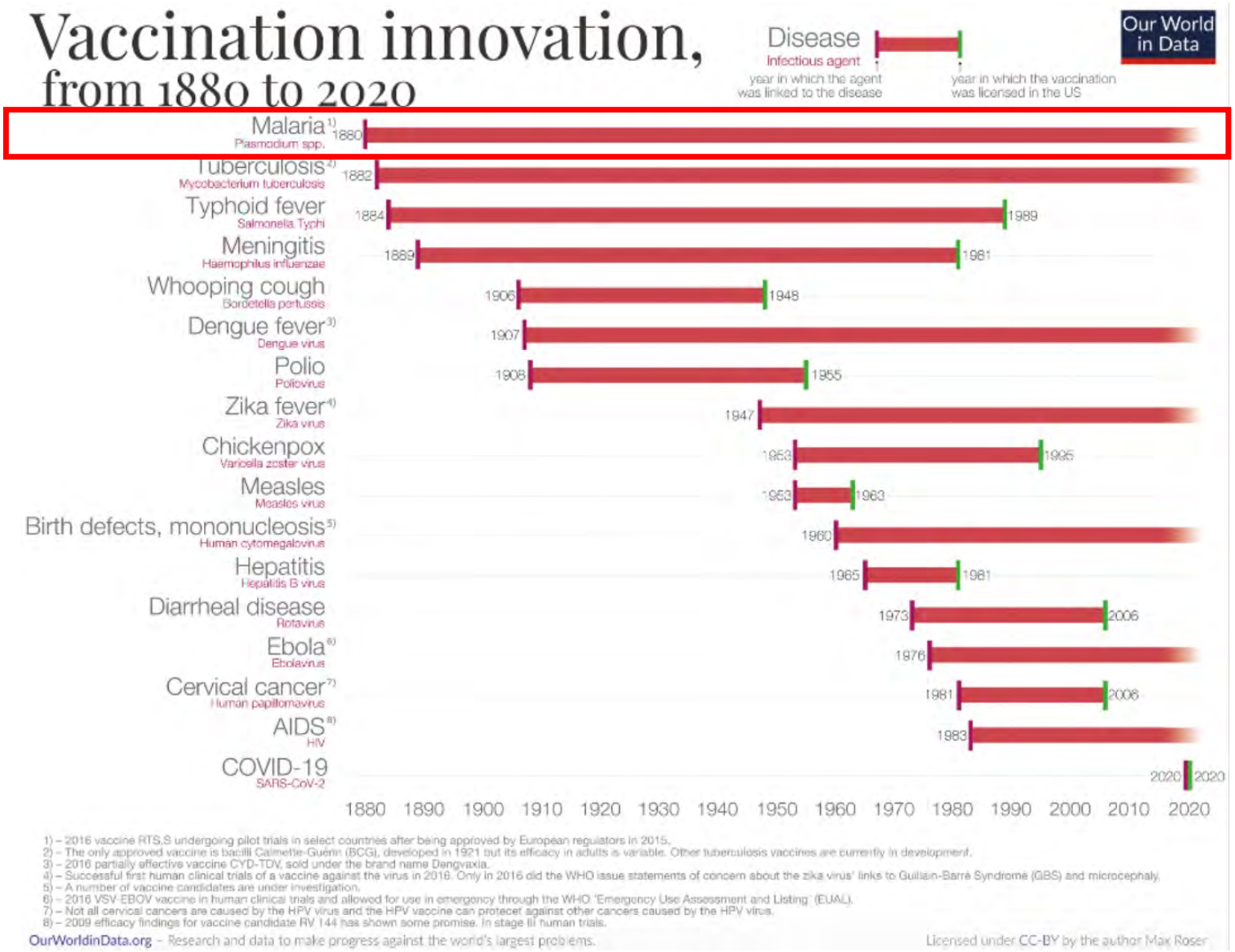


FIGURE 3 | Reduction in infectious diseases globally. Across all world regions, data from the WHO, for the last 20 years showing the control of diphtheria and tetanus and the decline in rubella and congenital rubella syndrome (data not shown). Data from the World Health Organization dataset "Reported cases of vaccine-preventable diseases" (World Health Organisation, 2019c).

Innovation vaccinale



Innovation vaccinale



Paludisme

- En 2019:
  - 229 millions de cas / an dans le monde
  - 409 000 décès/an
- Décès > 260 000 enfants africains < 5 ans chaque année

L'OMS recommande l'utilisation d'un vaccin antipaludique novateur destiné aux enfants exposés au risque de contracter la maladie

La recommandation historique d'utilisation du vaccin RTS,S/AS01 permettra de donner un nouvel élan à la lutte contre le paludisme

6 octobre 2021 | Communiqué de presse | Genève

« C'est un moment historique. Le vaccin antipaludique tant attendu pour les enfants représente une avancée pour la science, la santé de l'enfant et la lutte antipaludique », a déclaré **le Directeur général de l'OMS, le Dr Tedros Adhanom Ghebreyesus**.
« L'utilisation de ce vaccin parallèlement aux outils existants pour prévenir le paludisme pourrait sauver des dizaines de milliers de jeunes vies chaque année ».

Mosquirix™: RTS,S/AS01

- Mosquirix : vaccin développé par GSK et le Walter reed
- Vaccin actif à la phase pré erythrocytaire de l'infection
- **RTS,S**: vaccin de type VLP: vaccine like particule

Protéine de surface du sporozoïte de *Plasmodium falciparum (*circumsporozoïte), produite dans levures et AgHBs **adjuvanté avec AS01** (liposomes, QS21, saponine)
Protection contre le paludisme : 56% à un an, 36% sur une durée médiane de 48 mois

- Programme d'implémentation pilote (Malawi,Ghana, Kenya) en cours

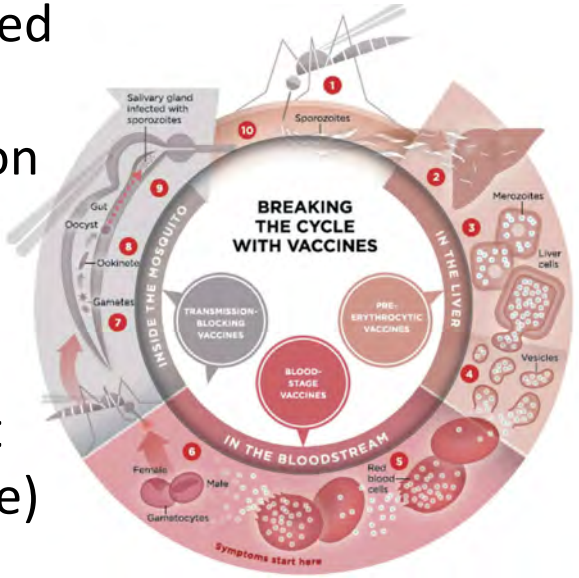


Table 1. RTS,S/AS01 Phase 3 efficacy results.

Age Group	6-12 weeks of age (n = 6537)	5-17 months of age (n = 8922)
Vaccine Efficacy against clinical malaria, 3-dose group (95% CI)	18.3% (11.7 to 24.4)	28.3% (23.3 to 32.9)
Vaccine efficacy against clinical malaria, 4-dose group (95% CI)	25.9% (19.9 to 31.5)	36.3% (31.8 to 40.5)
Vaccine Efficacy against severe malaria, 3-dose group (95% CI)	10.3% (−17.9 to 31.8)	1.1% (−23.0 to 20.5)
Vaccine efficacy against severe malaria, 4-dose group (95% CI)	17.3% (−9.4 to 37.5)	32.2% (13.7 to 46.9)

Mosquirix™: RTS,S/AS01

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

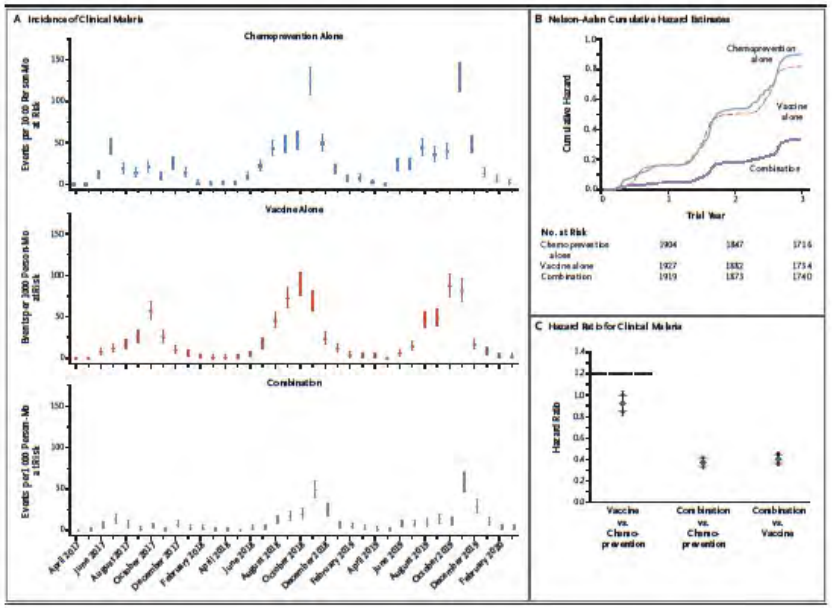
Seasonal Malaria Vaccination with or without Seasonal Malaria Chemoprevention

D. Chandramohan, I. Zongo, I. Sagara, M. Cairns, R.-S. Yerbanga, M. Diarra,

N ENGL J MED 385;11 NEJM.ORG SEPTEMBER 9, 2021

- 6861 nourrissons agés de 5-17 mois
- Mali et Burkina Faso

- 3 bras en dble aveugle:
  - Chimioprophylaxie (sulfadoxine–pyrimethamine and amodiaquine)
  - Vaccination une dose chaque année,
  - combinaison des 2
- **Suivi pendant 3 ans**
- Non infériorité du vaccin vs chimioprophylaxie seule
- Supériorité de la combinaison vs les 2 autres bras



Vaccin palu R21/Matrix-M

Efficacy of a low-dose candidate malaria vaccine, R21 in adjuvant Matrix-M, with seasonal administration to children in Burkina Faso: a randomised controlled trial

Mehreen S Datoo, Magloire H Natama*, Athanase Somé, Ousmane Traoré, Toussaint Rouamba, Duncan Bellamy, Prisca Yameogo, Daniel Valia, Moubarak Tegneri, Florence Ouedraogo, Rachidatou Soma, Seydou Sawadogo, Faizatou Sorgho, Karim Derra, Eli Rouamba, Benedict Orindi, Fernando Ramos Lopez, Amy Flaxman, Federica Cappuccini, Reshma Kailath, Sean Elias, Ekta Mukhopadhyay, Andres Noe, Matthew Cairns, Alison Lawrie, Rachel Roberts, Innocent Valéa, Hermann Sorgho, Nicola Williams, Gregory Glenn, Louis Fries, Jenny Reimer, Katie J Ewer, Umesh Shaligram, Adrian V S Hill, Halidou Tinto*

- Vaccin actif à la phase pré erythrocytaire de l'infection

- **R21**: vaccin VLP, protéine de surface du sporozoïte de *Plasmodium falciparum (*circumsporozoïte), produite dans *Hansenula polymorpha (Serum Institute of India)*, et AgHBs

adjuvanté avec Matrix M (adjuvant Novavax) (saponine)

- Nourrissons 5-17 mois
- 2 bras vaccins (Adjuvant a 25 et 50 microgrammes) vs vaccin rabique 3 doses et rappel à un an

- Protection contre le paludisme **à 6 mois** : **74% (95% CI 63–82) groupe 1,77% (67–84) groupe 2**
- **A 1 an, 77% (67–84) groupe 1.**

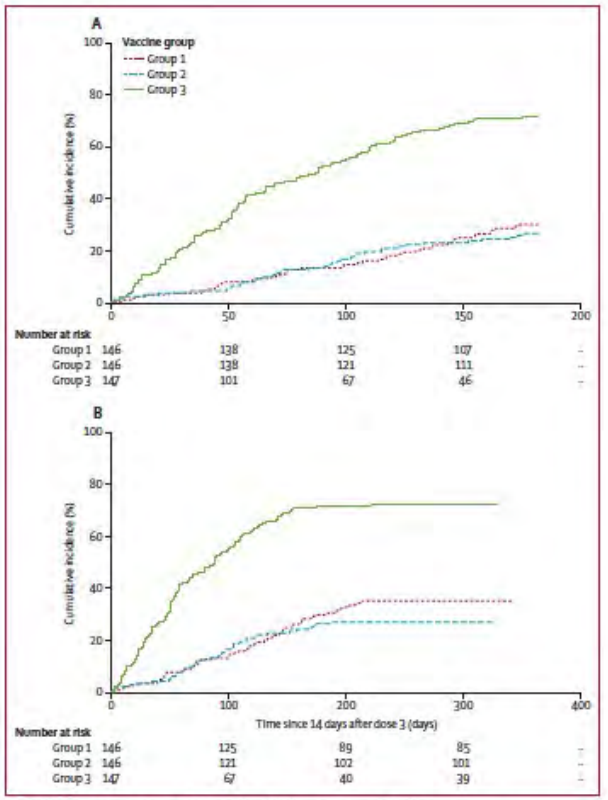


Figure 2: Kaplan-Meier estimates of the time to first episode of clinical malaria
The primary analysis was based on a modified intention-to-treat population. Group 1 received 5 µg R21/25 µg MM, group 2 received 5 µg R21/50 µg MM, and group 3, the control group, received rabies vaccinations (Rabivax-S). (A) Data beginning from 14 days to 6 months after third vaccination. (B) Data beginning from 14 days to 12 months after third vaccination. MM=Matrix-M.

Vaccin palu R21/Matrix-M

Efficacy of a low-dose candidate malaria vaccine, R21 in adjuvant Matrix-M, with seasonal administration to children in Burkina Faso: a randomised controlled trial

Mehreen S Datoo*, Magloire H Natama*, Athanase Somé, Ousmane Traoré, Toussaint Rouamba, Duncan Bellamy, Prisca Yameogo, Daniel Valia, Moubarak Tegneri, Florence Ouedraogo, Rachidatou Soma, Seydou Sawadogo, Faizatou Sorgho, Karim Derra, Eli Rouamba, Benedict Orindi, Fernando Ramos Lopez, Amy Flaxman, Federica Cappuccini, Reshma Kailath, Sean Elias, Ekta Mukhopadhyay, Andres Noe, Matthew Cairns, Alison Lawrie, Rachel Roberts, Innocent Valéa, Hermann Sorgho, Nicola Williams, Gregory Glenn, Louis Fries, Jenny Reimer, Katie J Ewer, Umesh Shaligram, Adrian V S Hill, Halidou Tinto

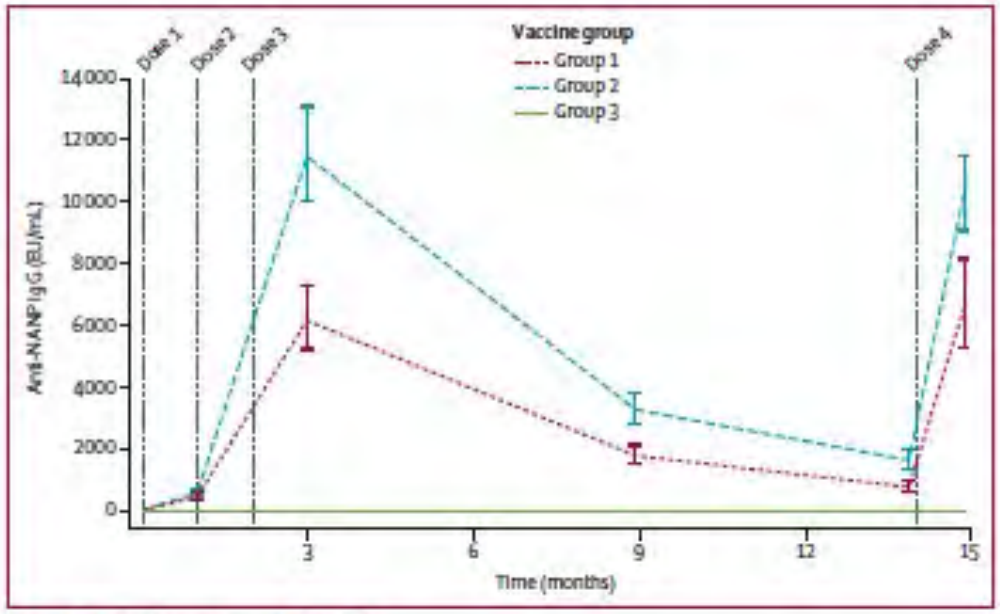
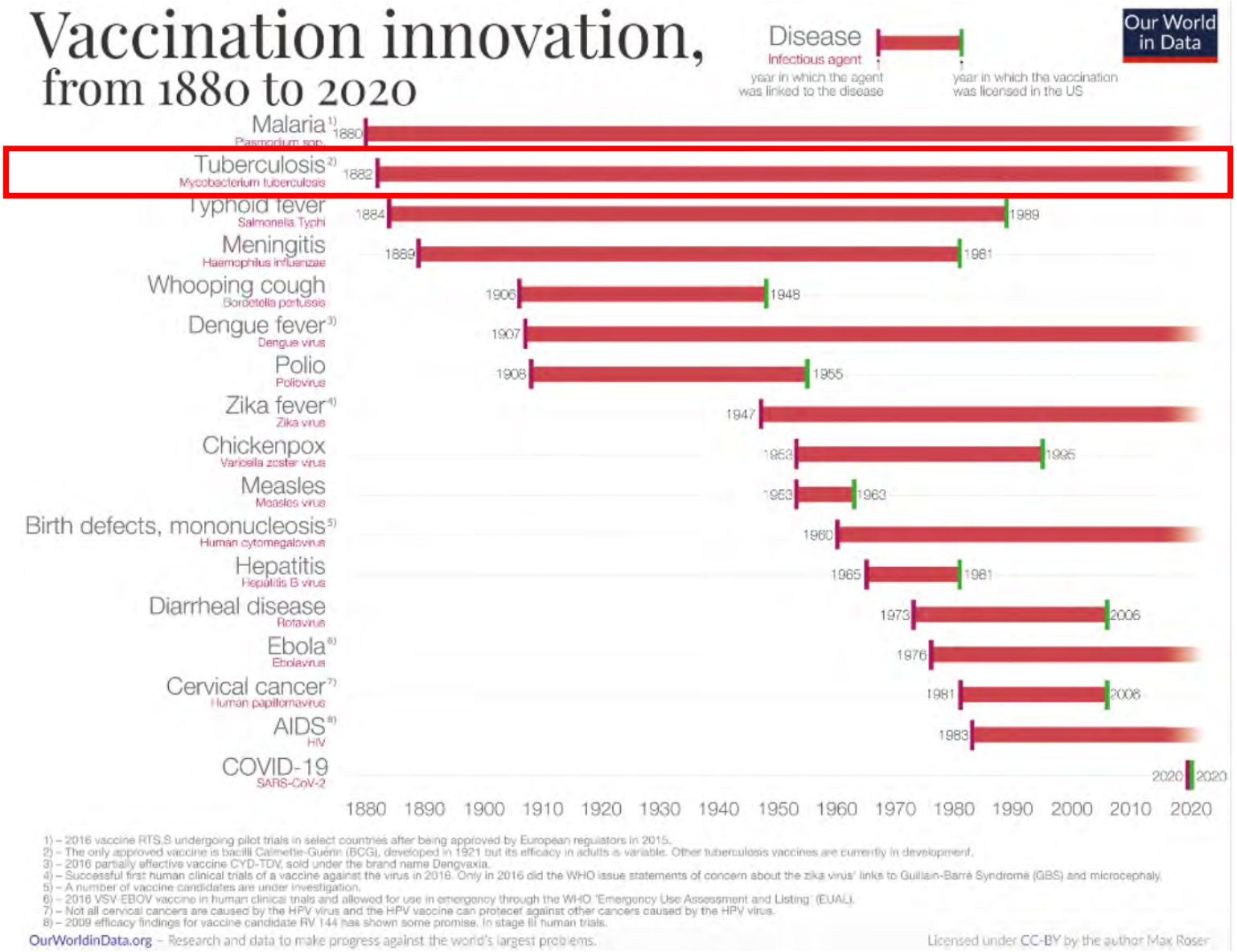


Figure 3: Antibody responses to R21/MM

(A) Geometric mean antibody titres (95% CI). Anti-NANP antibodies were measured by ELISA at baseline; 28 days after first vaccination; 28 days, 6 months, and 1 year after the third vaccination; and 28 days after the booster (fourth) dose administered 1 year after the third dose. Group 1 received 5 µg R21/25 µg MM, group 2 received 5 µg R21/50 µg MM, and group 3, the control group, received Rabivax-S. MM=Matrix-M. NANP=Asn-Ala-Asn-Pro.

Innovation vaccinale



Tuberculose

- Malgé vaccination universelle nnés et nourrissons dans les pays endemiques, la tuberculose est la 1ere case de décès par infection dans la monde:
- environ 1.4 millions de décès par an
- ¼ de la population mondiale est infecté 5-10% vontdevelopper la tuberculose maladie
- Cause majeure d'AB resistance: en 2019, 3.3% des nouveaux cas et 17,7% des cas prealablement traités

Vaccin Tuberculose

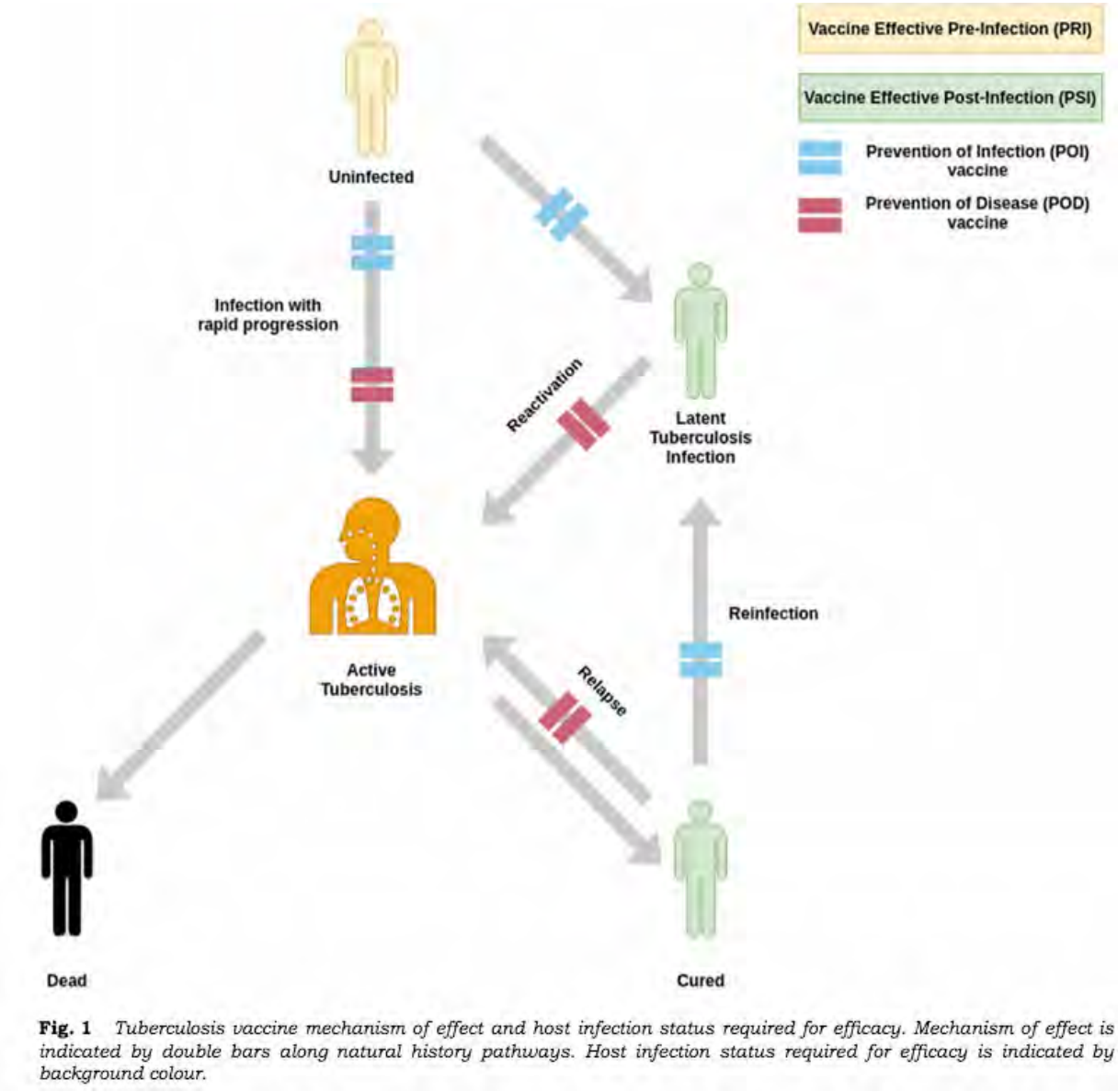


Fig. 1 *Tuberculosis vaccine mechanism of effect and host infection status required for efficacy. Mechanism of effect is indicated by double bars along natural history pathways. Host infection status required for efficacy is indicated by background colour.*

Vaccin Tuberculose

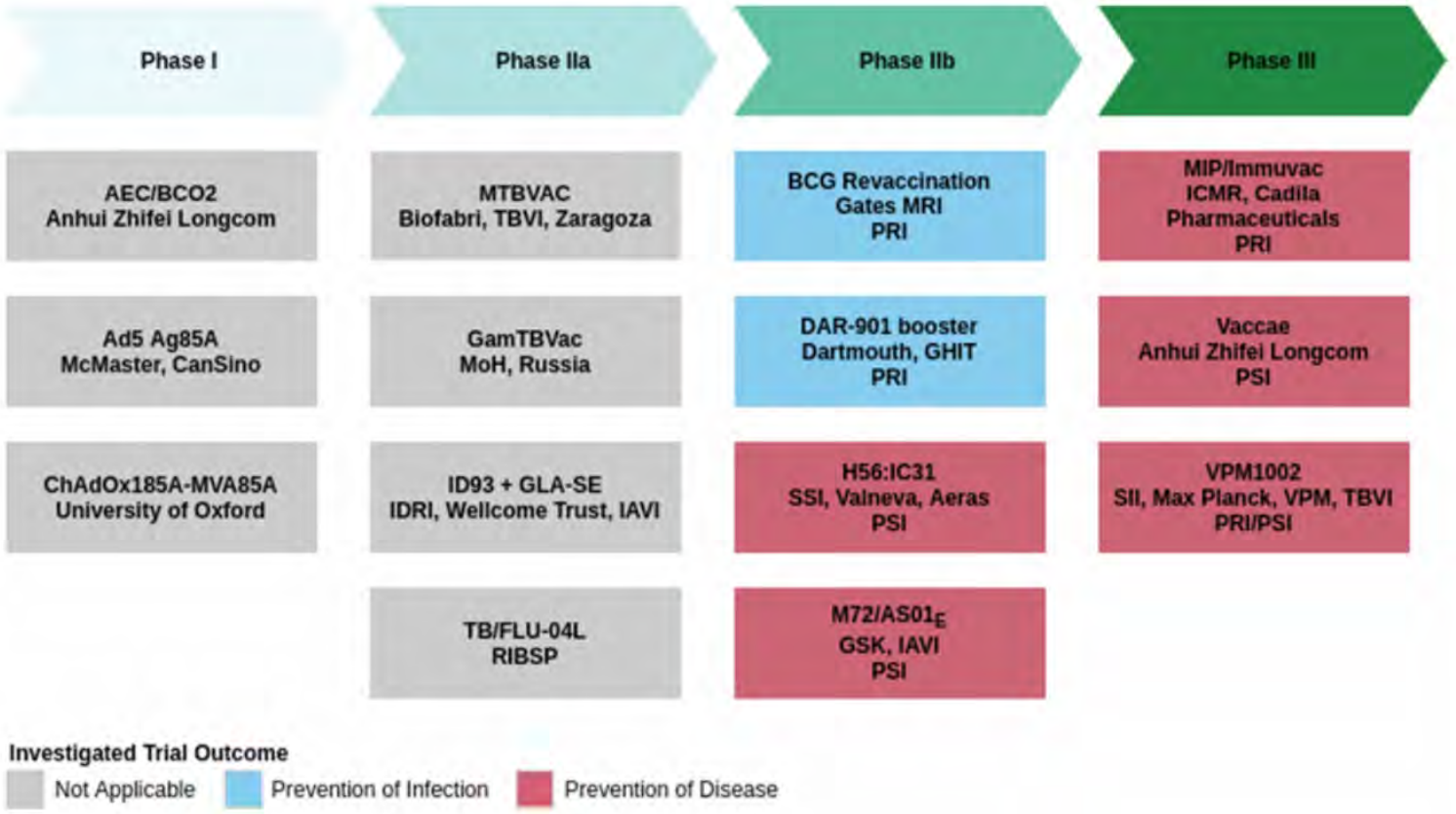


Fig. 2 *Classification of tuberculosis vaccines by trial phase, trial outcome (POI or POD) and population where vaccines were tested for efficacy (PSI, PRI or P&PI). The phase and trial outcome are based on the latest ongoing or completed clinical*

Vaccin tuberculose

ORIGINAL ARTICLE

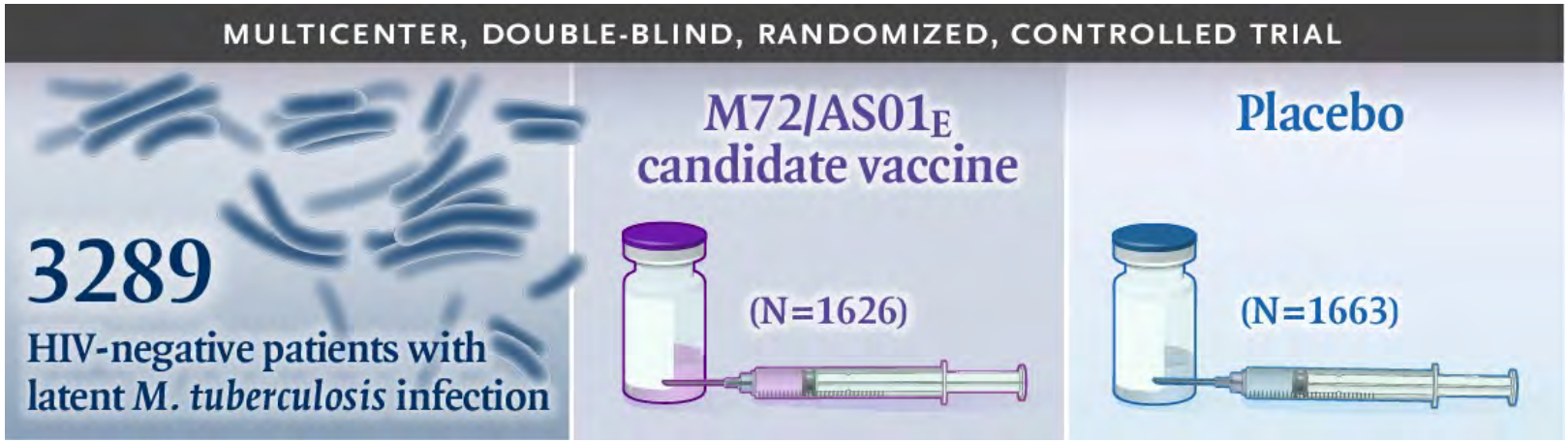
Final Analysis of a Trial of M72/AS01$_E$ Vaccine to Prevent Tuberculosis

Tait et al., NEJM 2019 PMID 31661198

Kenya, AFS, Zambie

Aout 2014 – Nov 2015

Financement GSK



Protéine de fusion recombinante M72

+

Adjuvant : AS01

Vaccin tuberculose

ORIGINAL ARTICLE

Final Analysis of a Trial of M72/AS01$_E$ Vaccine to Prevent Tuberculosis

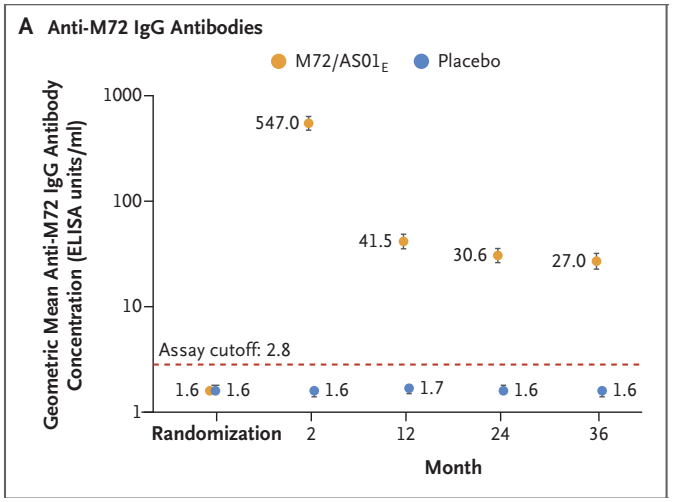
Tait et al., NEJM 2019 PMID 31661198

Efficacité

Definite pulmonary tuberculosis not associated with HIV infection at 3 yr	13 Participants	26 Participants
	Vaccine efficacy, 49.7% 90% CI, 12.1–71.2; 95% CI, 2.1–74.2	

Immunogénicité

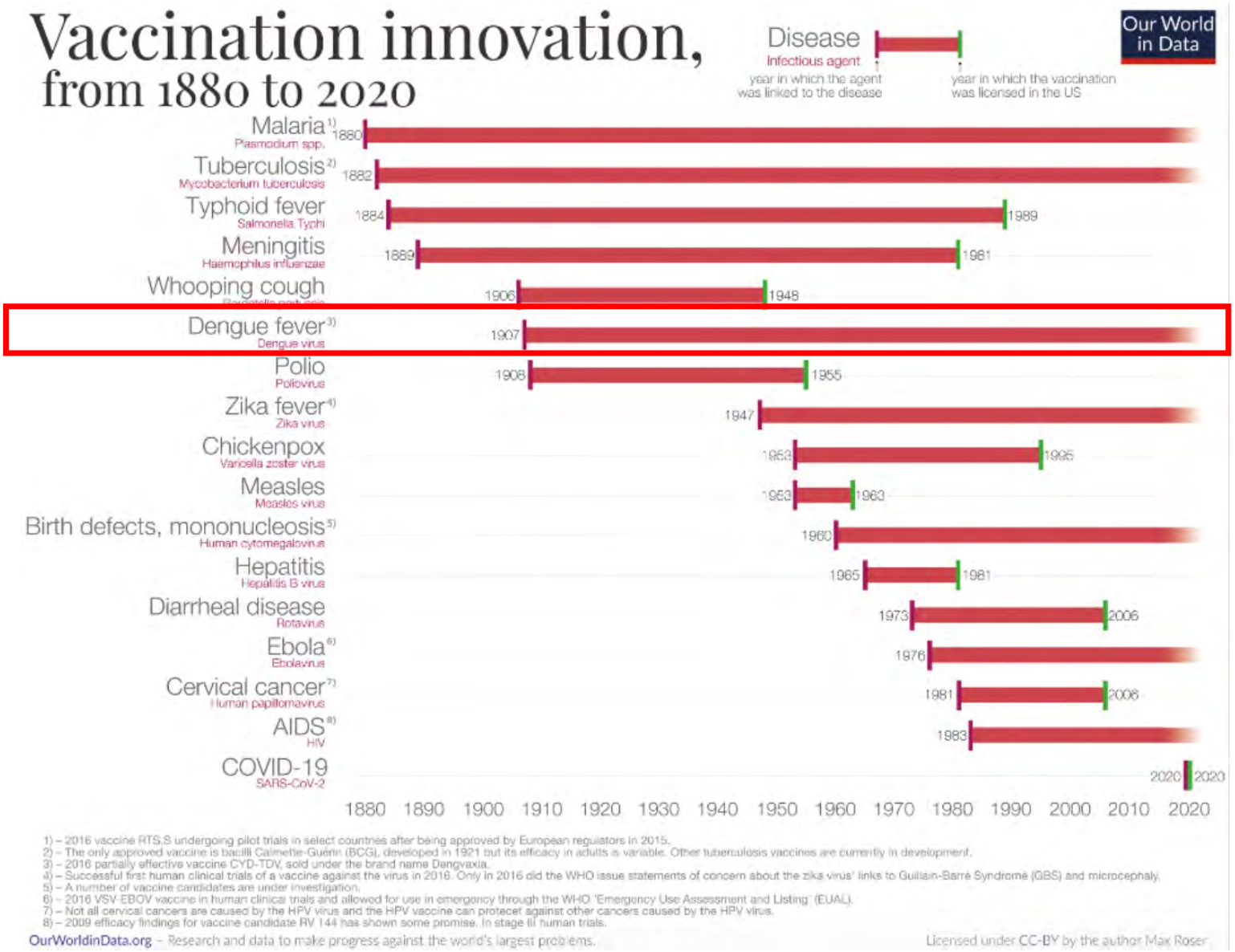
N = 244



Sécurité

Nombre EIG similaire dans les 2 groupes

Innovation vaccinale



Vaccin Dengue

- 390 millions de cas par an
- 500 000 hospitalisations
- Environ 20 000 deces

- Transmis par *Aedes aegypti* et *Aedes albopictus*

- 4 serotypes différents
- Les infections secondaires souvent plus graves

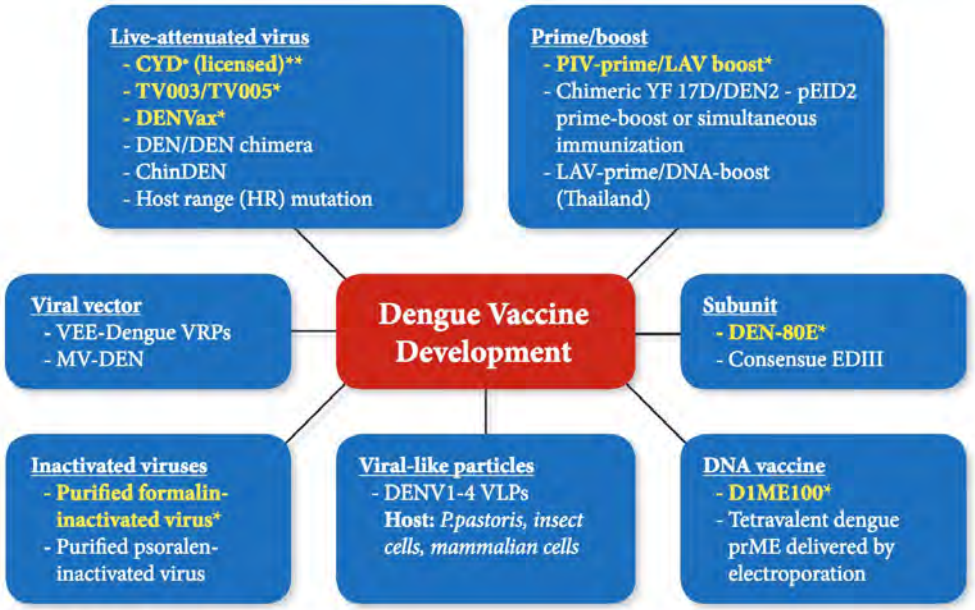
- 1 vaccin commercialisé Dengvaxia

APJAI Asian Pacific Journal of Allergy and Immunology

REVIEW ARTICLE

Dengue vaccine: Global development update

Eakachai Prompetchara,[1,2,3] Chutitorn Ketloy,[3,4] Stephen J. Thomas,[5] Kiat Ruxrungtham[4,6]



* Evaluating in clinical trials
** Licensed

Figure 2. Current dengue vaccine candidates and their evaluating status. Abbreviations: CYD; Chimeric Yellow Fever Dengue viruses, EDIII; envelope domain III, LAV; live-attenuated virus, MV; measles virus, PIV; purified inactivated virus, VEE; Venezuelan equine encephalitis, VRPs; virus replicon particles

Vaccin Dengue

APJAI Asian Pacific Journal of Allergy and Immunology

REVIEW ARTICLE

Dengue vaccine: Global development update

Eakachai Prompetchara,[1,2,3] Chutitorn Ketloy,[3,4] Stephen J. Thomas,[5] Kiat Ruxrungtham[4,6]

Table 1. Dengue vaccine candidates currently evaluate in clinical trials

Vaccine type	Vaccine name/Strategy	Developer	Clinical Trial Phase
Attenuated chimera	**CYD, Denvaxia®:** Yellow fever 17D vaccine virus backbone chimerized with prM and E proteins from DENV-1-4	Sanofi-Pasteur	Licensed, Post licensed evaluation is on-going
	TV003/TV005: Attenuated by deletion of 30 nucleotides from 3' UTR of DENV-1, DENV-3 DENV-4, and a chimeric DENV-2/DENV-4	US NIH	Phase III
	DENVax: Use attenuated DENV-2 PDK-53 as the backbone and replace with prM and E of other serotypes (DENV-2/-1, -2/-3, and -2/-4 chimeras)	US CDC/Inviragen/ Takeda	Phase III
Inactivated virus	**Purified formalin-inactivated virus (PIV)** formulated with adjuvants	WRAIR/GSK	Phase I
DNA vaccine	**Monovalent DENV-1** prME delivered by needle-free biojector **Tetravalent prM/E** formulated with Vaxfectin	US NMRC	Phase I
Subunit vaccine	**V180:** 80% of N-terminal E protein produced in insect cell formulated with ISOCOMATRIX and alhydrogel	Hawaii Biotech Inc. and Merck	Phase I
Heterologous prime/boost	**TLAV-prime/PIV-boost and *vice versa***	US Army Medical Research and Materiel Command	Phase I

Vaccin Dengue

APJAI Asian Pacific Journal of Allergy and Immunology

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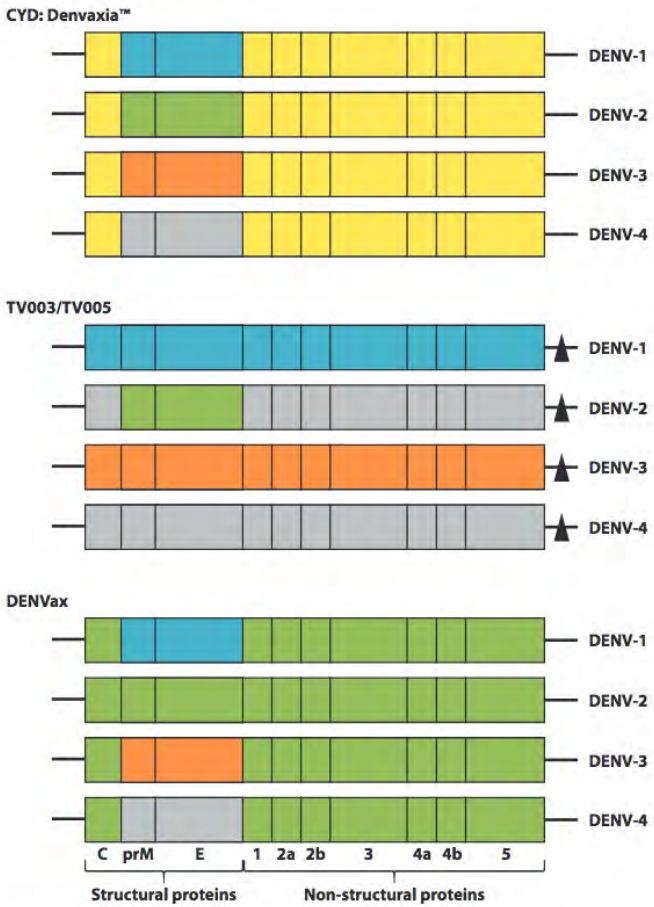

Figure 1. Schematic picture for comparison of developmental strategies of three live-attenuated dengue vaccines (CYD or Denvaxia™, TV003/TV005 and DENVax). Yellow = yellow fever 17D virus, blue = DENV-1, green = DENV-2, red = DENV-3, grey = DENV-4, triangle represents mutations at 3'UTR.

Vaccin Dengue

Efficacy of a tetravalent dengue vaccine in healthy children aged 4–16 years: a randomised, placebo-controlled, phase 3 trial

Shibadas Biswal, Charissa Borja-Tabora*, Luis Martinez Vargas, Hector Velásquez, Maria Theresa Alera, Victor Sierra, Edith Johana Rodriguez-Arenales, Delia Yu, V Pujitha Wickramasinghe, Edson Duarte Moreira Jr, Asvini D Fernando, Dulanie Gunasekera, Pope Kosalaraksa, Felix Espinoza, Eduardo López-Medina, Lulu Bravo, Suely Tuboi, Yanee Hutagalung, Pedro Garbes, Ian Escudero, Martina Rauscher, Svetlana Bizjajeva, Inge LeFevre, Astrid Borkowski, Xavier Saez-Llorens*, Derek Wallace*, for the TIDES study group†*

26 centres,

8 pays (47% Asie, 53 Am Latine)

N= 20 100, 2:1

2 doses TAK 003 ou Placebo (J1, M3)

Suivi 18 mois

Efficacité similaire en fonction statut sero +/- pour DENV1 et 2

EV IC95%	EV IC95%
Globale Dengue	73% [67-79]
Globale Dengue Grave	90% [83-95]
Séropositifs	76% [69-82]
Séronégatifs	66% [49-78]
DENV2	95% [90-98]
DENV1	70% [55-80]
DENV3	49% [27-64]
DENV4	51% [-69-86]

Biswal et al., Lancet 2020

Vaccin Dengue

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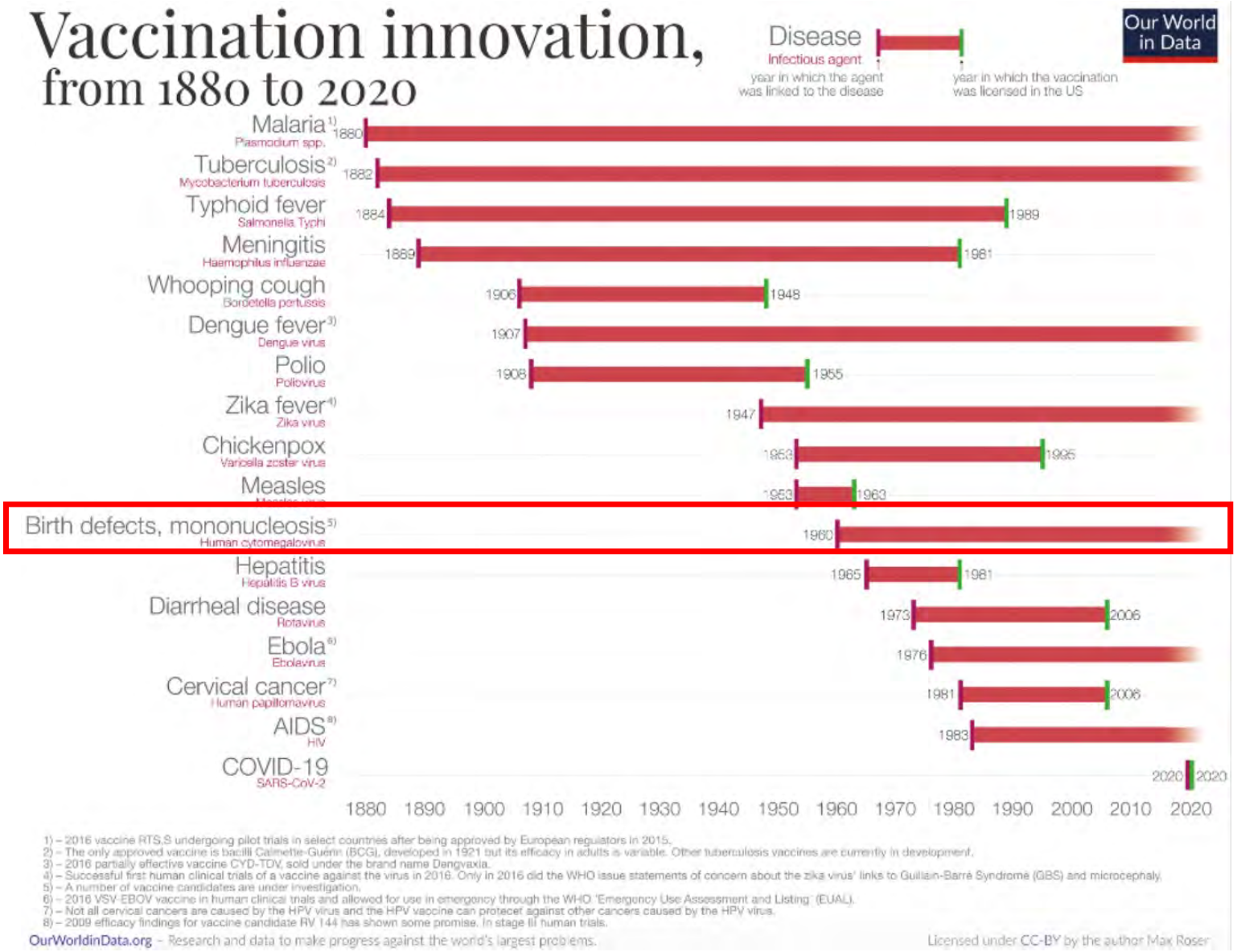
Potential Impact of Takeda's Dengue Vaccine Candidate Reinforced by Long-Term Safety and Efficacy Results

May 22, 2021

– Takeda's Dengue Vaccine Candidate (TAK-003) Prevented 83.6% of Hospitalizations and 62.0% of Dengue Illness Overall, With No Identified Important Safety Risks Through Three Years Following Vaccination in Ongoing Pivotal Phase 3 TIDES Trial

– Regulatory Filings for TAK-003 Progressing in European Union and in Many Dengue-Endemic Countries; Filing in United States Planned for Later This Year

Innovation vaccinale

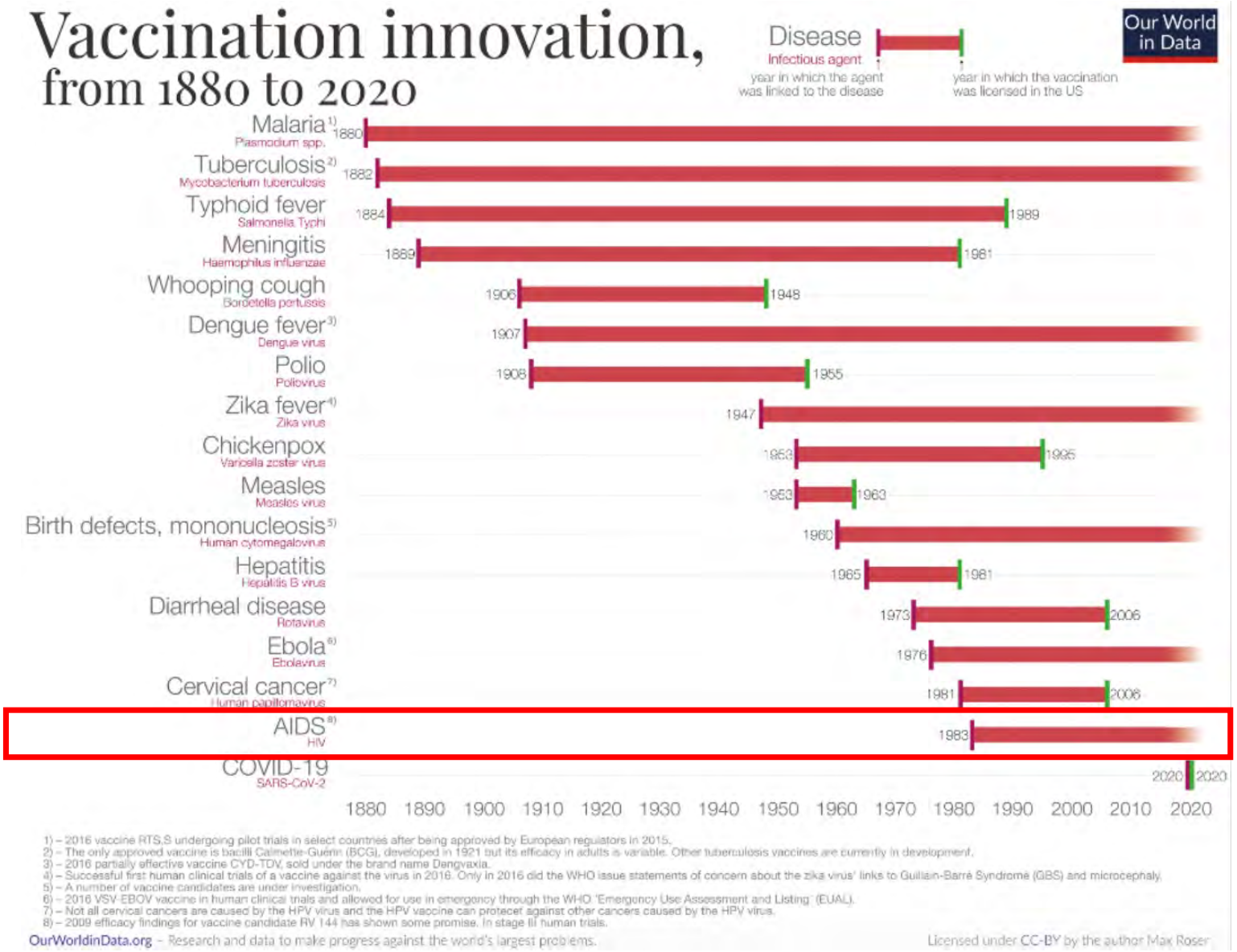


Vaccin CMV

Table 3
CMV vaccines in development.

Type of vaccine	Developer	Ref. #
Attenuated strain (Towne)	Wistar Inst./Med Coll VA	[41]
Recombinants with wild virus (Towne-Toledo)	Medimmune	[44]
Replication-defective virus	Merck	[51]
Vectored:		
Canary Pox	Sanofi	[52]
MVA	City of Hope	[57]
Adeno	Queensland Inst.	[58]
LCMV	Hookipa	[55]
VSV	Yale	[59]
Recombinant gB glycoprotein with adjuvant	Sanofi Pasteur, GSK	[45–47]
Soluble Pentamers	Redbiotech, GSK, Humabs	[49]
DNA plasmids	Astellas, Inovio	[61,63]
Self-replicating RNA	Moderna	[54,62]
Peptides	City of Hope	[64]
Dense bodies	Vaccine Project Management (Germany) and Serum Inst. India	[61]
Virus-like particles	Variations Bio	[56]

Innovation vaccinale



Vaccin VIH

vaccines

MDPI

Review

Preventive HIV Vaccines-Leveraging on Lessons from the Past to Pave the Way Forward

Parveen Sobia [1,†] and Derseree Archary [1,2,*,†]

[1] Centre for the AIDS Programme of Research in South Africa (CAPRISA), Nelson Mandela School of Medicine, University of KwaZulu-Natal, Durban 4001, South Africa; parveen.sobia@caprisa.org

Table 1. Major HIV vaccine trials past and current.

Name of Vaccine Trial	Vaccine (with or without Vector)	Phase of Trial	Number of Trial Participants and Trial Period	Virus and Immune Correlates Observed for Reduced or Increased Risk	Reasons for Trial Termination or Discontinuation
AIDSVAX B/E (VAX003)	Two rgp120 envs-Clade B and CRF01_AE Env antigens in alum	III	2546 1999–2003	Gp120 antibodies	No efficacy
AIDS VAX B/B (VAX004)	Clade B recombinant Env recombinant gp120 (rgp120) in alum	III	5417 1998–2003	Neutralizing gp120 antibodies and CD4 blocking antibodies	No efficacy
HVTN502 (STEP)	Merck Ad5 HIV-1 *gag/pol/nef*	IIb	3000 2004–2007	Pre-existing Ad5 antibodies, ex vivo IFN-γ and interleukin-2 secretion from CD4 and CD8 T cells [29]	Trial halted-No Efficacy-increased infections in vaccine group [14,34]
HVTN503 (Phambili)	Merck Ad5 Clade B *gag/pol/nef*	IIb	801 of 3000 February–September 2007	T cell-mediated virus pressure on infecting virus premised by vaccine proteins	Trial halted-No efficacy-unblinded analyses-increased infections-male vaccine group
HVTN505	DNA vaccine with Clade B *gag/pol/nef*, & recombinant Ad5 with Clade B *gag/pol* & Clades A/B/C *env*	III	2504 2009–2017	Virus Env mutations on CD4 binding site likely T cell-mediated Gp70 V1V2 antibodies were lower in HVTN 505 [46] than in RV144 [47]. The response to V3 CRF01_AE also inversely correlated with the risk of HIV infection in vaccine recipients with lower levels of Env-specific plasma IgA and neutralizing antibodies	Trial Halted Increased infections in vaccine group-no efficacy. MIT analyses showed no differences [36]
HVTN705 (Imbokodo)	Heterologous Prime/Boost Regimen Ad26.Mos4.HIV and with aluminum adjuvanted-clade C Env gp140	IIb	2637 2017–2022	Trial Ongoing	Trial Ongoing
HVTN706 (Mosaico)	Heterologous Regimen Ad26.Mos4.HIV and adjuvanted aluminum phosphate-clade C gp140 and Mosaic gp140	IIb	3800 2019–2024	Trial Ongoing	Trial Ongoing

HVTN—HIV Vaccine Trials Network, Env—envelope, MIT—Modified intention-to-treat.

Vaccin VIH

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 25, 2021 VOL. 384 NO. 12

Vaccine Efficacy of ALVAC-HIV and Bivalent Subtype C gp120–MF59 in Adults

G.E. Gray, L.-G. Bekker, F. Laher, M. Malahleha, M. Allen, Z. Moodie, N. Grunenberg, Y. Huang, D. Grove,

- Essai HVTN 702
- Combinaison vaccin vectorisé ALVAC M0, M1,+ protéine recombinante GP120 clade C adjuvanté MF59 M3, M6, M12, M18
- 5404 participants (70% femmes), phase 2b-3,
- Afrique du sud
- Analyse intermédiaire M24: inefficacité, 138 cas dans le groupe vaccin, 133 dans le groupe placebo
- Arret de l'essai

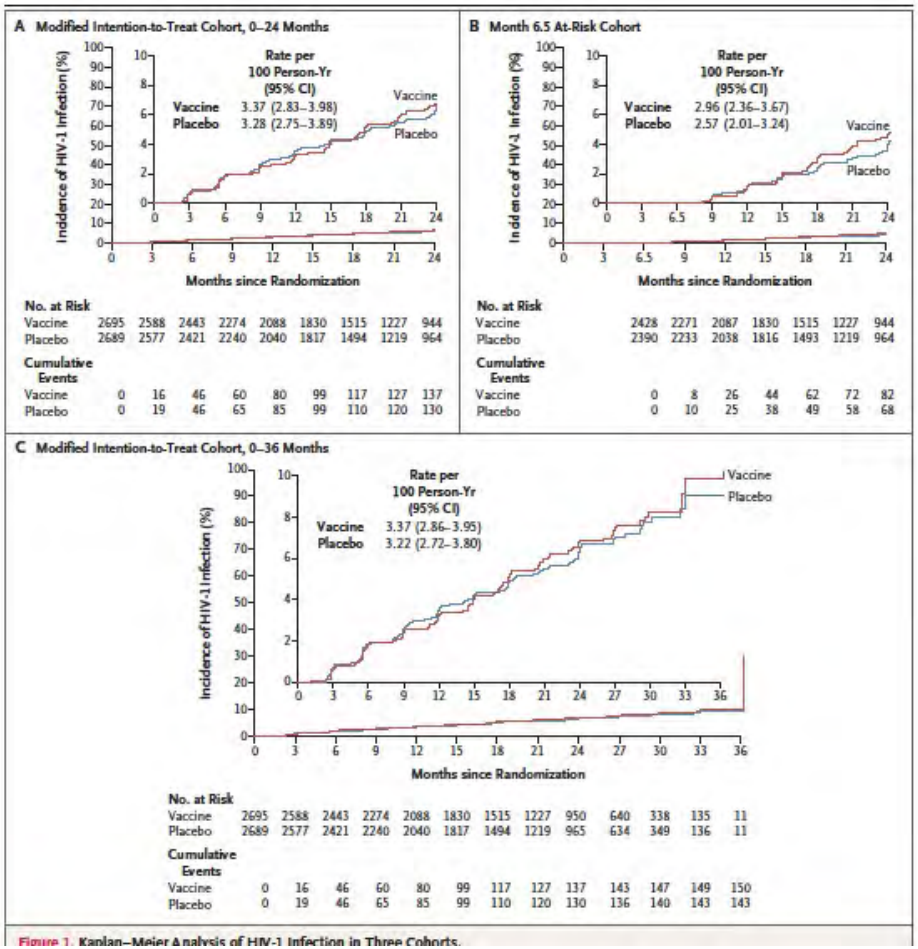


Figure 1. Kaplan–Meier Analysis of HIV-1 Infection in Three Cohorts.

Vaccin VIH

- Analyse par sous groupe
- Pas d'efficacité selon le sexe
- Pas d'efficacité selon l'âge de vaccination

The NEW ENGLAND JOURNAL of MEDICINE

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Vaccine Efficacy of ALVAC-HIV and Bivalent Subtype C gp120–MF59 in Adults

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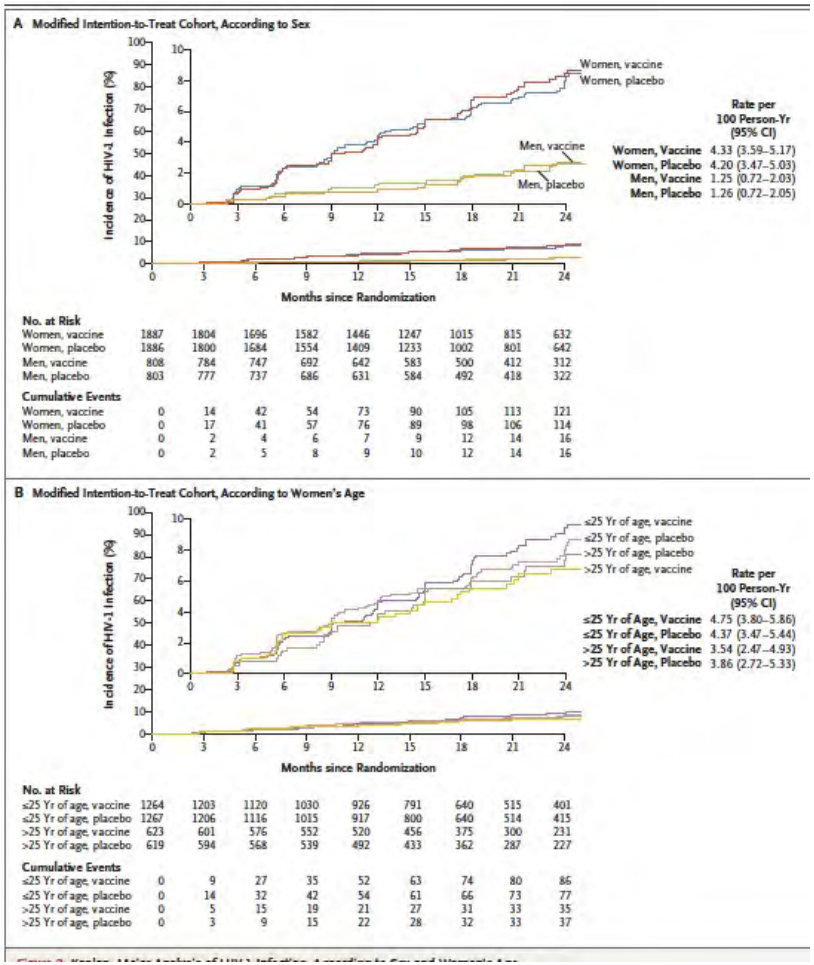


Johnson & Johnson and Global Partners Announce Results from Phase 2b Imbokodo HIV Vaccine Clinical Trial in Young Women in Sub-Saharan Africa

Investigational vaccine candidate did not provide sufficient protection against HIV infection

No vaccine-related safety signals identified

J&J HIV vaccine program continues with global Phase 3 Mosaico HIV study evaluating a different composition of the vaccine regimen in different populations

SMART NEWS

Moderna to Begin Human Trials for Two Experimental HIV Vaccines

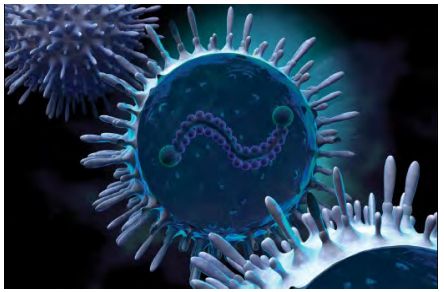
The vaccines are mRNA based, like the biotech company's Covid-19 vaccine

Elizabeth Gamillo

Daily Correspondent

August 26, 2021

VRS



- Principale cause virale d'infection respiratoire sévère et d'hospitalisation du jeune enfant
- > 60% des nourrissons avant l'âge de 1 an, 100% avant l'âge de 2 ans
- Pic d'hospitalisation chez le nourrisson entre 2 et 3 mois
- Risque d'infection sévère chez l'enfant jusqu'à l'âge de 5 ans
- Nourrissons à risque: prématurité, âge < 6mois, co morbidité cardiaque ou pulmonaire

- Pas d'immunité persistance, ré infection au cours de la vie tous les 3-5 ans
- Sévérité chez les personnes âgées et fragiles (co morbidités cardiaques ou pulmonaires) et en cas de déficit immunitaire portant sur l'immunité cellulaire CD8 (DCS, allogreffe de moelle, transplantation rénale ou sujets âgés)

VRS

Articles

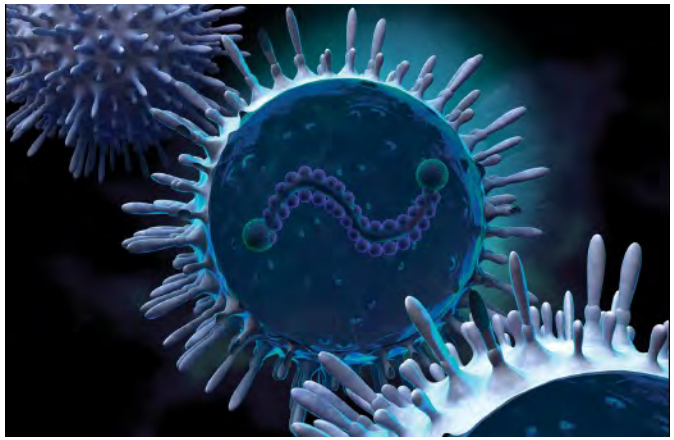
Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: a systematic review and modelling study

Ting Shi, David A McAllister, Katherine L O'Brien, Eric A F Simoes, Shabir A Madhi, Bradford D Gessner, Fernando P Polack, Evelyn Balsells, Sozinho Acacio*, Claudia Aguayo*, Issifou Alassani*, Asad Ali*, Martin Antonio*, Shally Awasthi*, Juliet O Awori*, Eduardo Azziz-Baumgartner*,

Chez l'enfant de moins de 5 ans dans le Monde en 2015

- 33 millions de cas
- 3,2 millions d'hospitalisations
- 118 200 décès

Lancet 2017; 390: 946-58



VRS

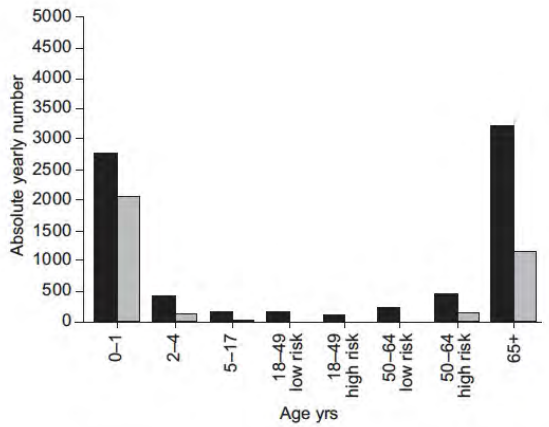


FIGURE 4. Respiratory syncytial virus-associated hospitalisation burden in the Netherlands. ■: *versus* summer baseline period; ■: *versus* peri-seasonal baseline period.

Eur Respir J 2007; 30: 1158–1166
DOI: 10.1183/09031936.00034407

Influenza- and respiratory syncytial virus-associated mortality and hospitalisations

A.G.S.C. Jansen*, E.A.M. Sanders#, A.W. Hoes*, A.M. van Loon¶ and E. Hak*

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 APRIL 28, 2005 VOL. 352 NO. 17

Respiratory Syncytial Virus Infection in Elderly and High-Risk Adults

Ann R. Falsey, M.D., Patricia A. Hennessey, R.N., Maria A. Formica, M.S., Christopher Cox, Ph.D., and Edward E. Walsh, M.D.

Clinical Microbiology and Infection 23 (2017) 253–259
Contents lists available at ScienceDirect
Clinical Microbiology and Infection
journal homepage: www.clinicalmicrobiologyandinfection.com

Original article

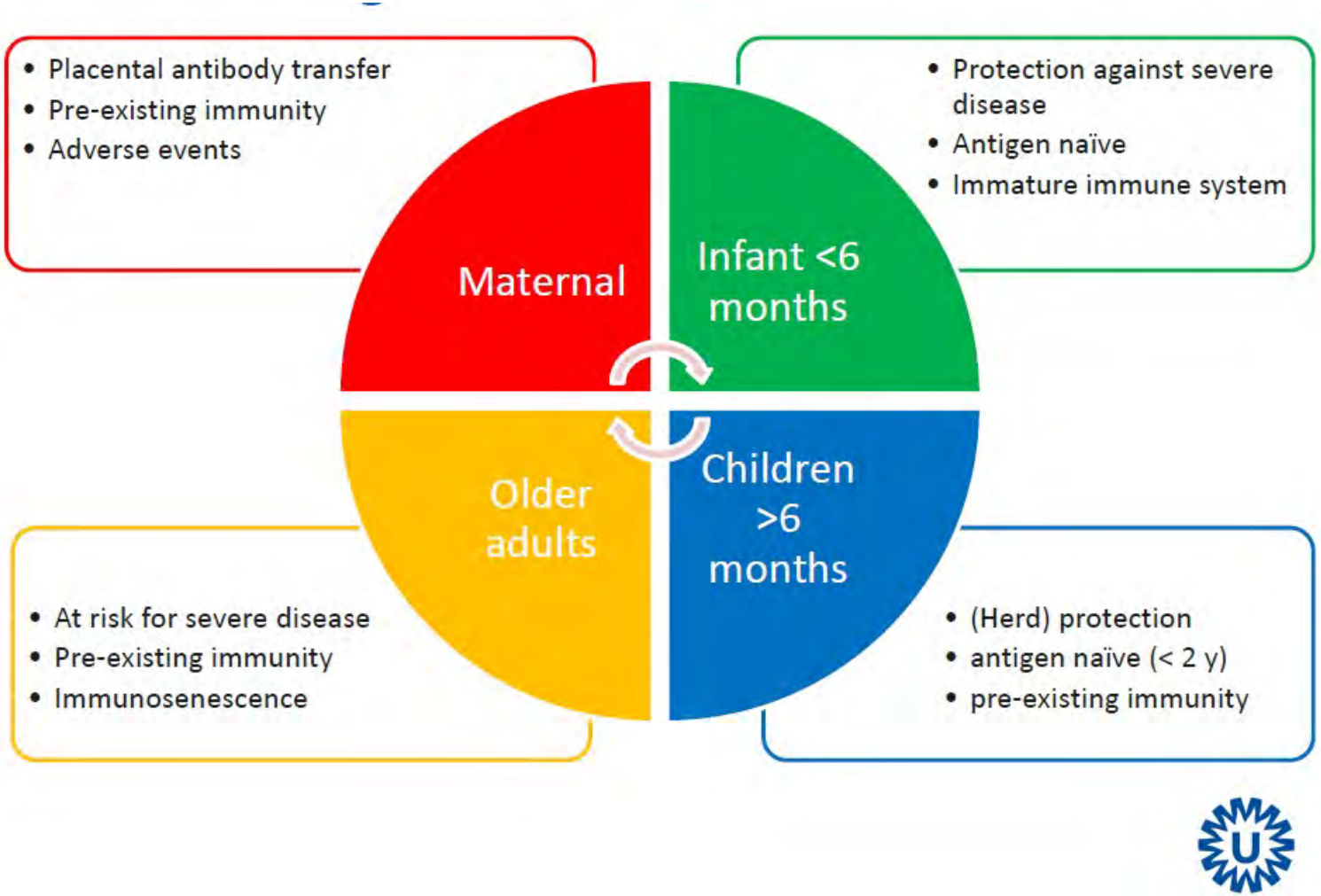
Clinical characteristics and outcome of respiratory syncytial virus infection among adults hospitalized with influenza-like illness in France

P. Loubet [1,2], N. Lenzi [3], M. Valette [4], V. Foulongne [5], A. Krivine [6], N. Houhou [7], G. Lagathu [8], S. Rogez [9], S. Alain [10], X. Duval [1,11], F. Galtier [3,12], D. Postil [13], P. Tattevin [14], P. Vanhems [15,16], F. Carrat [17,18], B. Lina [4,19], O. Launay [3,20,21,22,*], the FLUVAC Study Group

Chez l'adulte:

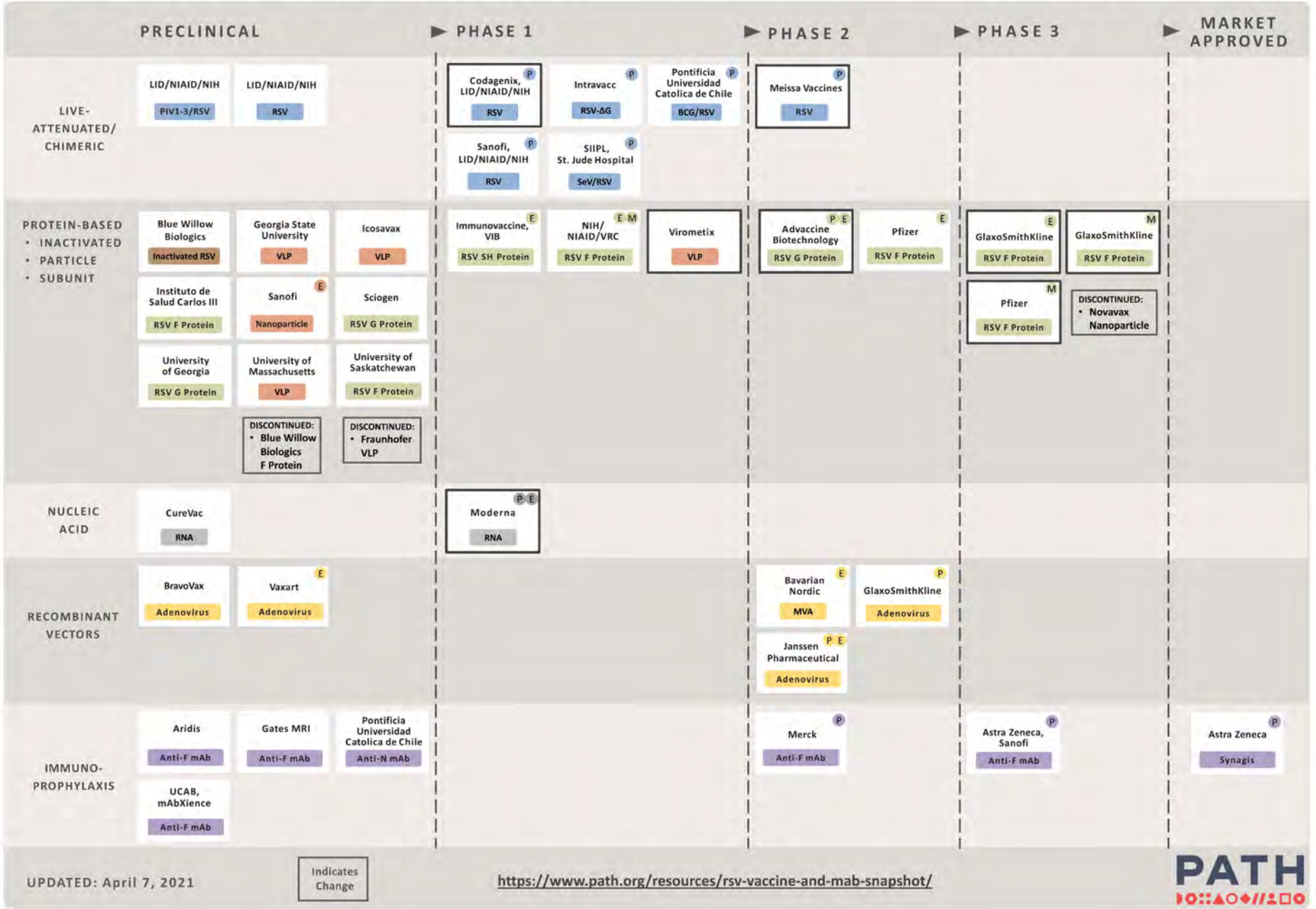
- 10 000 décès par an aux USA chez l'adulte de plus de 65 ans
- Autres terrains à risque:
  - Immunodéprimés
  - BPCO

Les cibles pour un vaccin anti VRS



RSV Vaccine and mAb Snapshot

TARGET INDICATION: P =PEDIATRIC M =MATERNAL E =ELDERLY



UPDATED: April 7, 2021

Indicates Change

https://www.path.org/resources/rsv-vaccine-and-mab-snapshot/

PATH

Vaccin VRS

- Vaccin nanoparticule (Novavax) Protein F VRS
- Vaccination 2:1 vs placebo
- Femmes enceintes 28SA et 36 SA

- Suivi enfants jusqu'à M6 pour l'efficacité

1 an pour la sécurité

- Critère principal: infection respiratoire basse avant 3 mois

4636 femmes incluses`
87 sites dans le Monde

Arret du developpement efficacité insuffisante

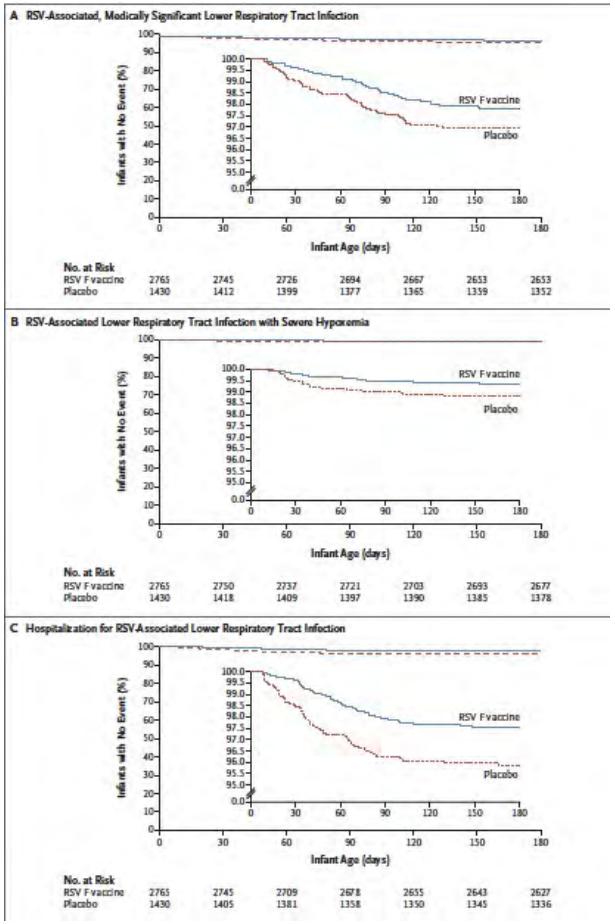
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Respiratory Syncytial Virus Vaccination during Pregnancy and Effects in Infants

S.A. Madhi, F.P. Polack, P.A. Piedra, F.M. Munoz, A.A. Trenholme, E.A.F. Simões, G.K. Swamy, S. Agrawal, K. Ahmed, A. August, A.H. Baqui, A. Calvert, I. Chen

N ENGL J MED 383;5 NEJM.ORG JULY 30, 2020



Ac monoclonaux VRS

- Nirsevimab (SP/AZ)
- IgG1 kappa monoclonale

- Proteine recombinante

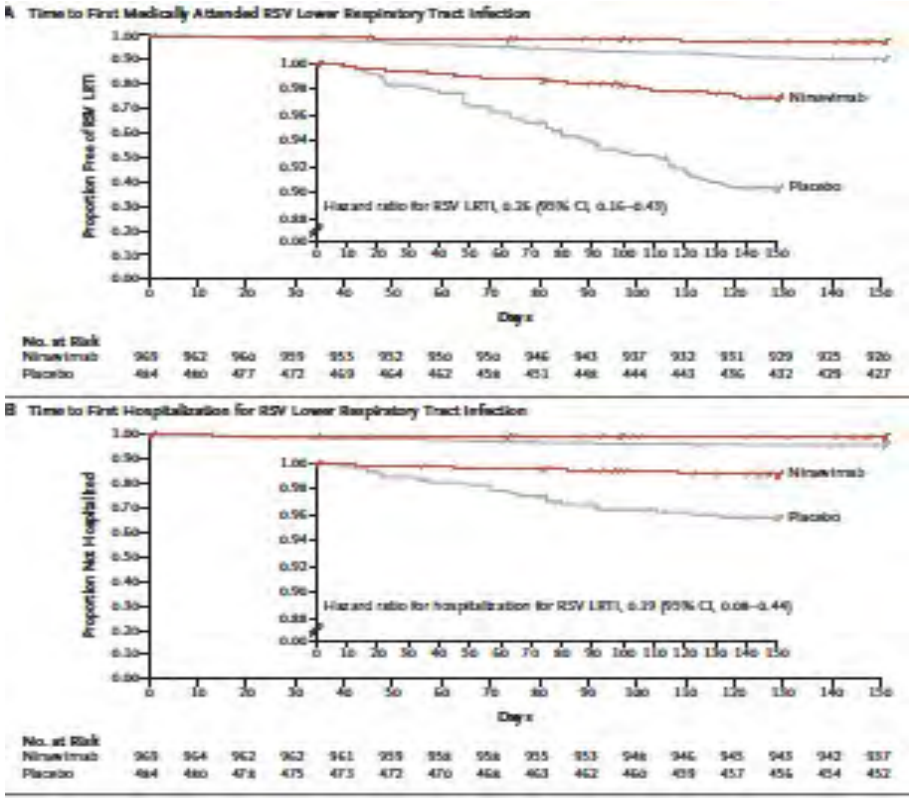
dirigée contre un épitope conservé présent sur la protéine de fusion du VRS
½ vie prolongée permettant une injection couvrant la période de circulation du VRS (5 mois)

- Une injection chez des nourrissons nés prematurés
- Randomisation 2:1 (969:484)
- Efficacité:
  - réduction de 70% des infections respiratoires basses
  - 78% des infections respiratoires basses hospitaliées

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 JULY 30, 2020 VOL. 383 NO. 5

Single-Dose Nirsevimab for Prevention of RSV in Preterm Infants

M. Pamela Griffin, M.D., Yuan Yuan, Ph.D., Therese Takas, B.S., Joseph B. Domachowske, M.D., Shabir A. Madhi, M.B., B.Ch., Ph.D., Paolo Manzoni, M.D., Ph.D., Eric A.F. Simões, M.D., Mark T. Esser, Ph.D., Anis A. Khan, Ph.D., Filip Dubovsky, M.D., Tonya Villafana, Ph.D., and John P. DeVincenzo, M.D., for the Nirsevimab Study Group*



Vaccin typhoïde

- Essai de **phase 2b 'challenge'**

- Volontaires randomisés en 3 groupes :
- vaccin typhoide Vi polysaccharides (n=37)
- vaccin Vi conjugué (tétanos toxoid) (n=41)
- vaccin méningo conjugué ACYW (n=34)
  1 dose 25 microgrammes
- A M1: challenge oral par 1-5 10^4 CFU *S typhi* Quailes strain
- Hémoculture tous les jours pdt 2 semaines après challenge
- Antibiothérapie systématique à J14

- Critère ppal: proportion de participants développant une typhoïde (fièvre > 38°C pdt plus de 12h ou bactériémie)

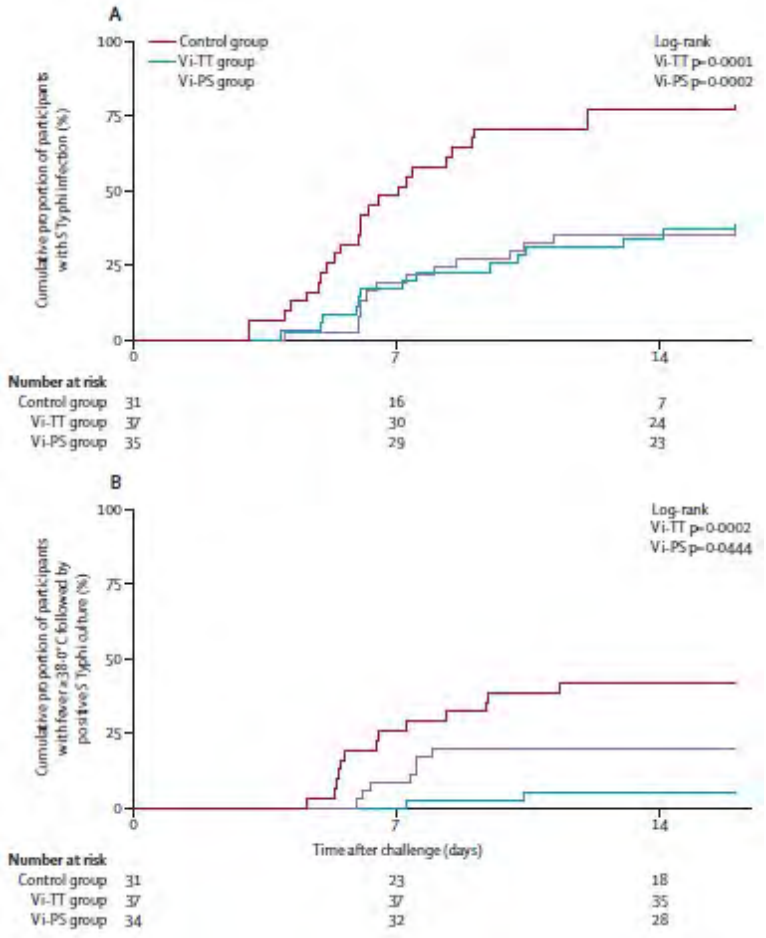
- **Résultats en terme d'efficacité:**
  54.6% (95%CI: 26.8-71.8) vaccin conjugué
  52.0% ((95%CI: 23.2-70.0): non conjugué

En analyse post hoc: fièvre + bactériémie, supériorité du vaccin conjugué 87.1% vs 42.7%

Articles

Efficacy and immunogenicity of a Vi-tetanus toxoid conjugate vaccine in the prevention of typhoid fever using a controlled human infection model of *Salmonella* Typhi: a randomised controlled, phase 2b trial

Celina Jin, Malick M Gibani, Maria Moore, Helene B Juel, Elizabeth Jones, James Meiring, Victoria Harris, Jonathan Gardner, Anna Nebykova, Simon A Kerridge, Jennifer Hill, Helena Thomaides-Brears, Christoph J Blohmke, Ly-Mee Yu, Brian Angus, Andrew J Pollard



Vaccin typhoïde conjugué

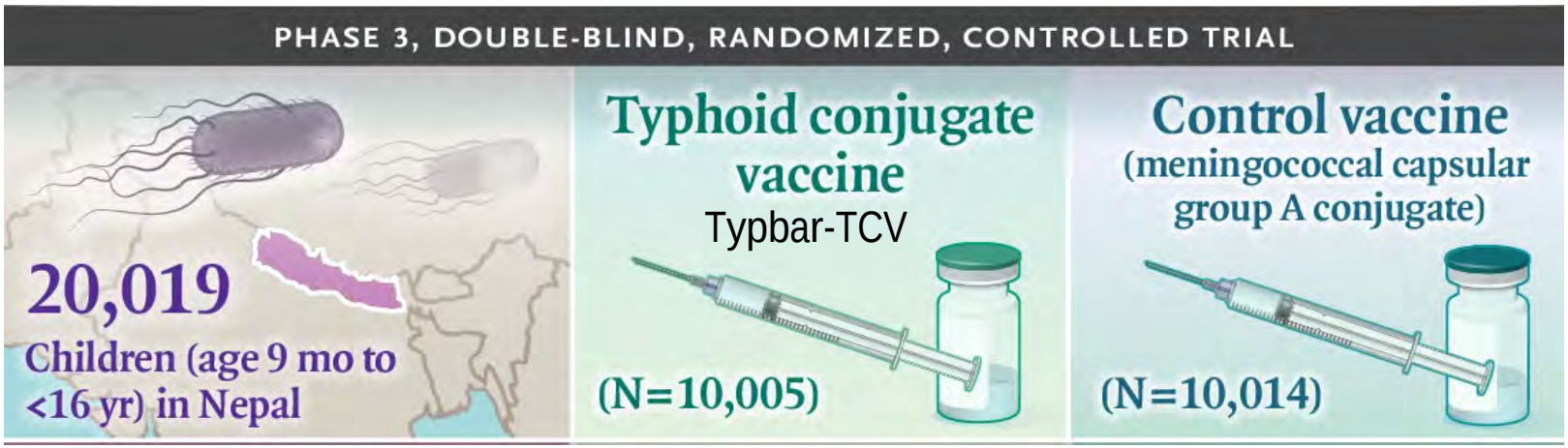
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Phase 3 Efficacy Analysis of a Typhoid Conjugate Vaccine Trial in Nepal

Mila Shakya, M.P.H., Rachel Colin-Jones, M.A., Katherine Theiss-Nyland, Ph.D.,

Shakya M et al. N Engl J Med. 2019 Dec 5;381(23):2209-2218.



Népal

Nov 2017 – Avril 2018

Financement : Gates Foundation

Vaccin typhoide conjugué phase 3

- Essai de phase 3, randomisé, contrôlé réalisé au Népal, en double aveugle
- Enfants âgés de 9 mois et 16 ans, ratio 1:1 vaccin typho¨de conjugué vs Men A conjugué
- Objectif ppal: fièvre typhoïde confirmée (hémoculture+)
- 20 019 enfants: 10,005 TCV; 10,014 MenA vaccine
- Fièvre typhoïde confirmée: 7 (79 cas/ 100,000 personne-années) vs 38 (428 cas / 100,000 personne-années)
- Efficacité vaccinale :

  81.6% (IC95%: 58.8; 91.8; P<0.001)

The NEW ENGLAND JOURNAL of MEDICINE

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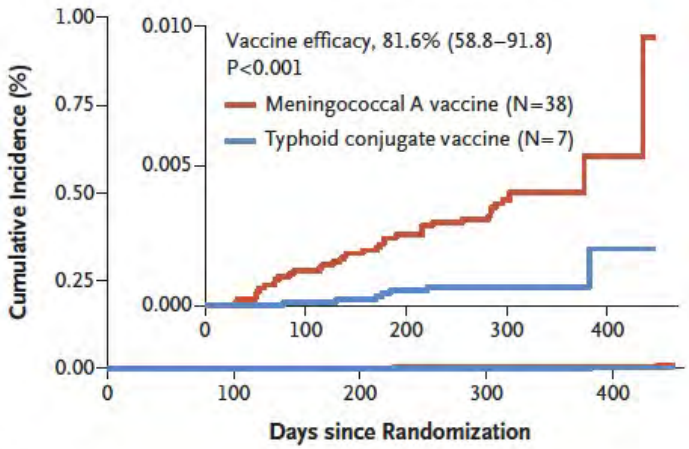


No. at Risk					
Meningococcal A vaccine	10,013	9536	9072	7233	649
Typhoid conjugate vaccine	10,005	9541	9120	7316	645

Figure 1. Kaplan–Meier Estimates of the Cumulative Incidence of Blood Culture–Positive Typhoid Fever, According to Trial Group.

Vaccin typhoide conjugué phase 3

- Essai de phase 3, randomisé, contrôlé réalisé au Malawi, en double aveugle
- Enfants âgés de 9 mois et 12 ans, ratio 1:1 vaccin typhoïde conjugué vs Men A conjugué
- Objectif ppal: fièvre typhoïde confirmée (hémoculture+)
- 28 130 enfants
- Fièvre typhoïde confirmée: 12 (46,9 cas/ 100,000 personne-années) vs 62 (243 cas / 100,000 personne-années)
- Efficacité vaccinale ITT :

  83.7% (IC95%: 68,1; 91.6)

The NEW ENGLAND JOURNAL of MEDICINE

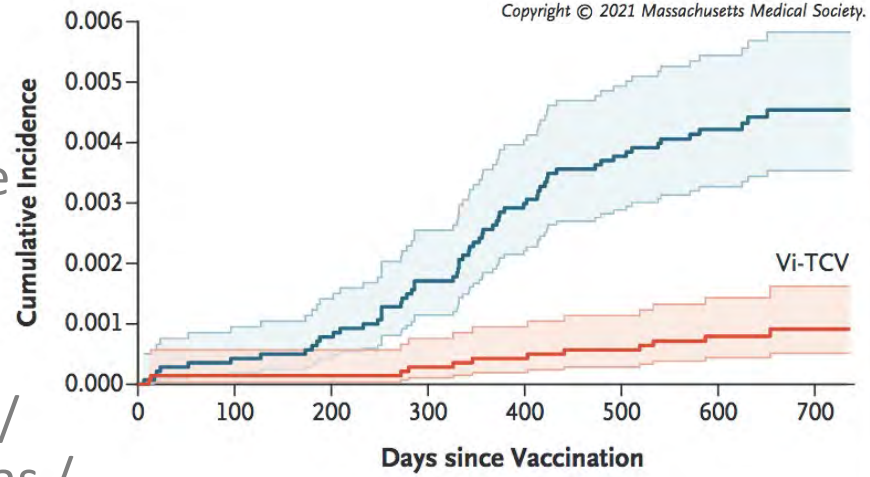
ORIGINAL ARTICLE

Safety and Efficacy of a Typhoid Conjugate Vaccine in Malawian Children

Priyanka D. Patel, M.B., B.S., Pratiksha Patel, M.B., B.S., Yuanyuan Liang, Ph.D.,

This article was updated on September 16, 2021, at NEJM.org.

N Engl J Med 2021;385:1104-15.
DOI: 10.1056/NEJMoa2035916



No. at Risk								
MenA vaccine	14,061	14,048	14,036	14,021	14,002	13,989	11,517	4769
Vi-TCV	14,069	14,061	14,057	14,052	14,050	14,047	11,606	4830

Figure 2. Kaplan–Meier Estimates of the Cumulative Incidence of Blood Culture–Positive Typhoid Fever in the Intention-to-Treat Population.

The intention-to-treat population included all participants who underwent randomization and received a dose of a vaccine. Shaded areas indicate 95% confidence intervals. Blood culture–confirmed typhoid fever occurred in 62 children in the MenA group and in 12 children in the Vi-TCV group.

Vaccins et antibioresistance

Table 2 Vaccine candidates in clinical development with the potential to prevent diseases caused by pathogens highlighted in this review

Vaccine	Composition	Latest trials
C. difficile		
PF-06425090 (Pfizer)[58]	Genetically/chemically inactivated *C. difficile* toxins A and B ClinicalTrials.gov identifier NCT03090191	Phase 3
ACAM-CDIFF (Sanofi)[86]	Formalin-inactivated wild-type toxoid (A and B) ClinicalTrials.gov identifier NCT01887912	Phase 3
VLA84 (Valneva)[87]	Recombinant fusion protein consisting of truncated toxin A and B ClinicalTrials.gov identifier NCT02316470	Phase 2
S. aureus		
SA4Ag (Pfizer)[88]	CP5/CP8-CRM_{197}, P-Y variant ClfA, MntC ClinicalTrials.gov identifier NCT02388165	Phase 2b
4C-Staph (GSK)[89]	Csa1A (Sur2), FhuD2, EsxA/EsxB, HIAH35L ClinicalTrials.gov identifier NCT01160172	Phase 1
Group B *Streptococcus*		
Trivalent GBS vaccine (GSK)[90]	Capsular epitopes of GBS serotypes Ia, Ib and III conjugated to CRM197 ClinicalTrials.gov identifier NCT02270944	Phase 2
Bivalent GBS protein vaccine (Minervax)[91]	N-terminal domains of the Rib and alpha C surface proteins	Phase 1
E. coli		
EcoXyn-4V (GlycoVaxyn)[92]	*E. coli* bioconjugate vaccine ClinicalTrials.gov identifier NCT02289794	Phase 1
FimH adhesin vax[93] (Sequoia)	Protein-based vaccine	Phase 1
JNJ63871860 (Janssen)[94]	*E. coli* bioconjugate vaccine	Phase 2

Maladies infectieuses émergentes et développement vaccinal

Table 2 The Coalition for Epidemic Preparedness Innovations (CEPI) funded projects (as of November 2019)

Partner	Disease	CEPI funding	Technology platform	Development phase
Janssen Vaccines and University of Oxford	Lassa	US$19.0 million	Recombinant virus	Preclinical
	MERS-CoV			Phase I
	Nipah			Preclinical
Profectus BioSciences, Emergent BioSolutions, and PATH	Lassa	US$36.0 million	Recombinant virus	Preclinical
	Nipah	US$25.0 million	Protein subunit	Preclinical
International AIDS Vaccine Initiative (IAVI)	Lassa	US$54.9 million	Recombinant virus	Preclinical
IDT Biologika	MERS-CoV	US$36.0 million	Recombinant virus	Phase I
Themis Bioscience	Lassa	US$58.5 million	Recombinant virus	Phase I
	MERS-CoV			Preclinical
	Chikungunya			Phase III
University of Tokyo	Nipah	US$31.0 million	Recombinant virus	Phase I
Inovio Pharmaceuticals	Lassa	US$56.0 million	DNA	Preclinical
	MERS-CoV			Phase II
Colorado State University	Rift Valley fever	US$9.5million	Attenuated virus	Preclinical
Wageningen Bioveterinary Research	Rift Valley fever	US$12.5 million	Attenuated virus	Phase I
Valneva	Chikungunya	US$23.4 million	Attenuated virus	Phase I
Public health vaccines	Nipah	US$43.6 million	Recombinant virus	Preclinical
Imperial College London	Marburg	US$8.4 million	RNA	Preclinical
	Influenza			
	Rabies			
CureVac	Lassa	US$34.0 million	RNA	Preclinical Phase I
	Rabies			
	Yellow fever			
University of Queensland	MERS-CoV	US$10.6 million	Recombinant protein	Preclinical
	Influenza			
	Respiratory syncytial virus			

- CEPI: vaccins prioritaires : Ebola, Lassa, MERS Cov, Nipah , fièvre de la Vallée du Rift, Chikungunya
- Soutien pour le développement de plateformes technologiques pouvant être utilisées rapidement en cas d'émergence

Bernasconi V et al, 2020

Vaccins COVID-19 de ’première génération’: données des essais de phase 3

- Efficacité précoce (souche originale, formes symptomatiques)
  - > 90% pour les vaccins ARNm après 2 doses :
    - 95% (vaccin Pfizer BioNtech)
    - 94,1% (vaccin Moderna)
    - *48% (vaccin Curevac)*

Publications scientifiques des essais de Phase 3

Vaccins COVID-19 de ’première génération’: données des essais de phase 3

- Efficacité précoce (souche originale, formes symptomatiques)
  - > 90% pour les vaccins ARNm après 2 doses :
    - 95% (vaccin Pfizer BioNtech)
    - 94,1% (vaccin Moderna)
    - *48% (vaccin Curevac)*
  - 70% pour les vaccins vectorisés adénovirus
    - 74% (vaccin Astra Zeneca)
    - 67% (vaccin Janssen, 1 dose)
    - 91,6 (vaccin Gamaleya)

Publications scientifiques des essais de Phase 3

Etat de lieux au 4 septembre 2021

Virus (inactivé, atténué)

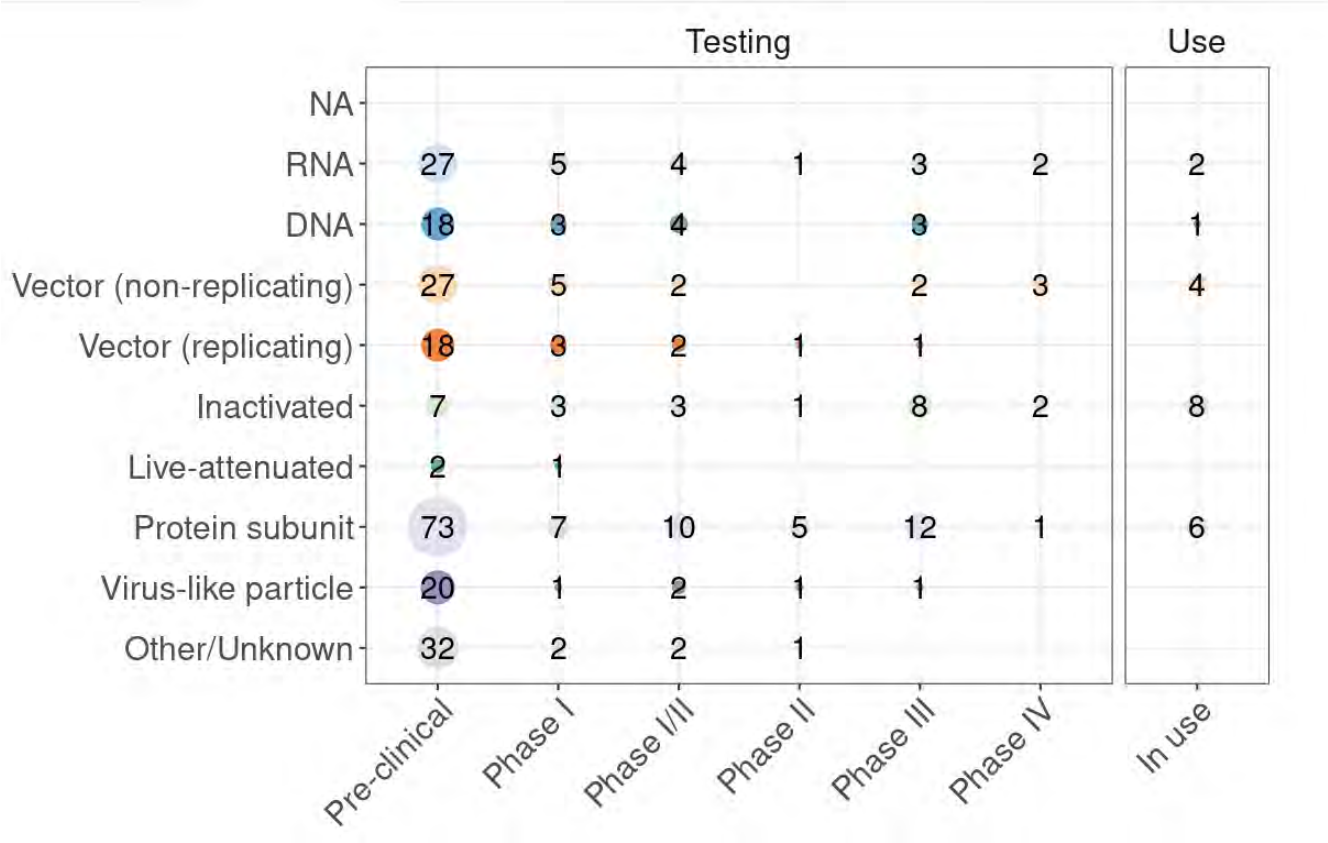
Vecteur viral (réplicatif, non réplicatif)

Acide nucléique (ADN, ARN)

Protéines recombinantes

331 vaccine candidates

107 in clinical testing



https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/

Vaccination COVID hétérologue

Une vaccination hétérologue

AZ – Pfizer BNT est plus immunogène que

- la vaccination homologue

  AZ-AZ

  Ou Pfizer BNT-Pfizer BNT

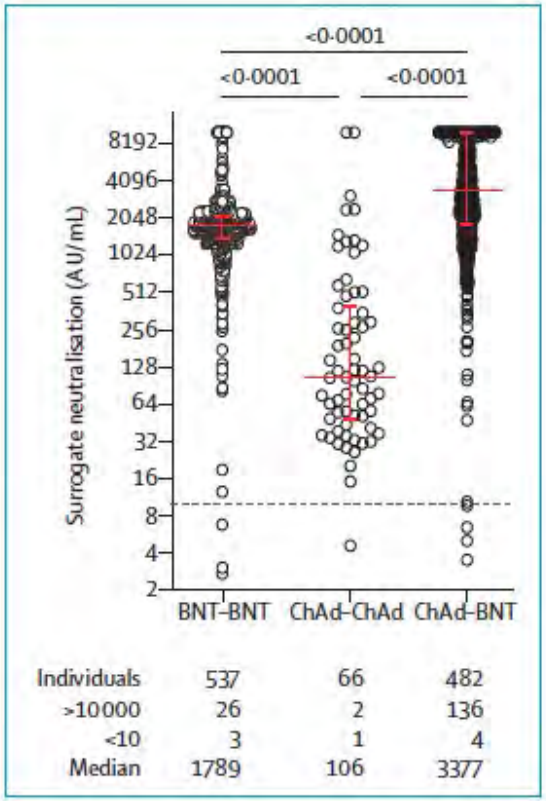


Figure: **Comparison of surrogate neutralisation activity induced by homologous and heterologous COVID-19 vaccine regimens**

Heterologous prime–boost vaccination with ChAdOx1 nCoV-19 and BNT162b2

Lancet Infect Dis 2021
Published Online
July 29, 2021
https://doi.org/10.1016/
S1473-3099(21)00420-5

Matthias Tenbusch†,

Vaccination COVID

Vaccin Novavax

Nanoparticule: Protéine recombinante protéine Spike 5µg

+ adjuvant Matrix M

2 doses à 3 semaines d'intervalle

EV: 89.7% (IC95% 80.2 to 94.6)

- 86.3% (IC95%, 71.3 - 93.5) variant
  96.4% (IC, 73.8 -99.5)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

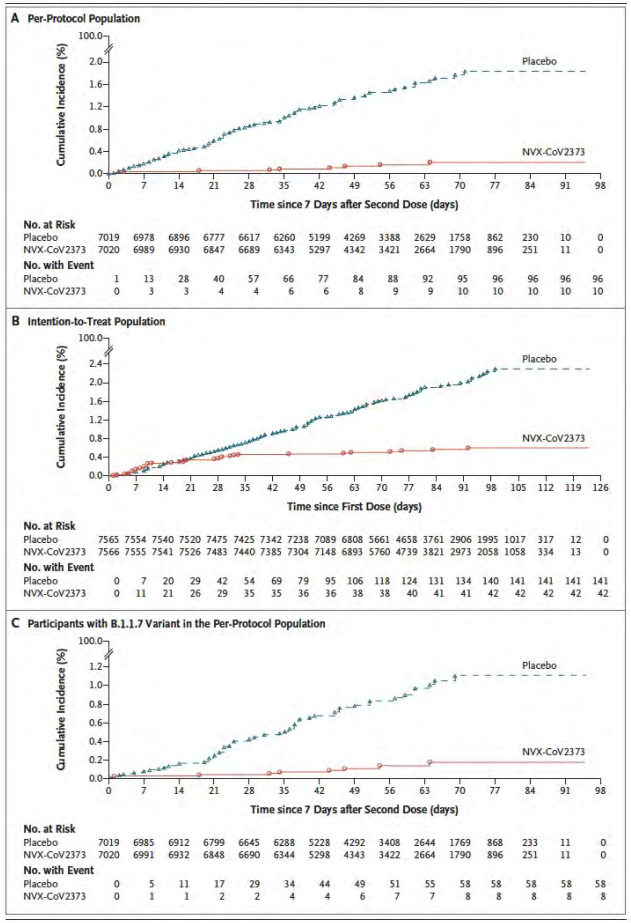
Safety and Efficacy of NVX-CoV2373 Covid-19 Vaccine

P.T. Heath, E.P. Galiza, D.N. Baxter, M.

This article was published on June 30, 2021, at NEJM.org.

N Engl J Med 2021;385:1172-83.
DOI: 10.1056/NEJMoa2107659

The NEW ENGLAND JOURNAL of MEDICINE



Vaccination COVID

Safety and immunogenicity of a SARS-CoV-2 recombinant protein vaccine with AS03 adjuvant in healthy adults: interim findings from a phase 2, randomised, dose-finding, multi-centre study

Saranya Sridhar MBBS[1], Arnel Joaquin MD[2], Matthew I Bonaparte PhD[3], Agustin Bueso MD[4], Anne-

- Essai de phase 2 randomisé
- Protéine recombinante PreS

produite dans baculovirus

- 3 doses : 5,10 et 15µg
- 2 injections a 3 semaines d'intervalle
- Adjuvanté avec AS03 (GSK)

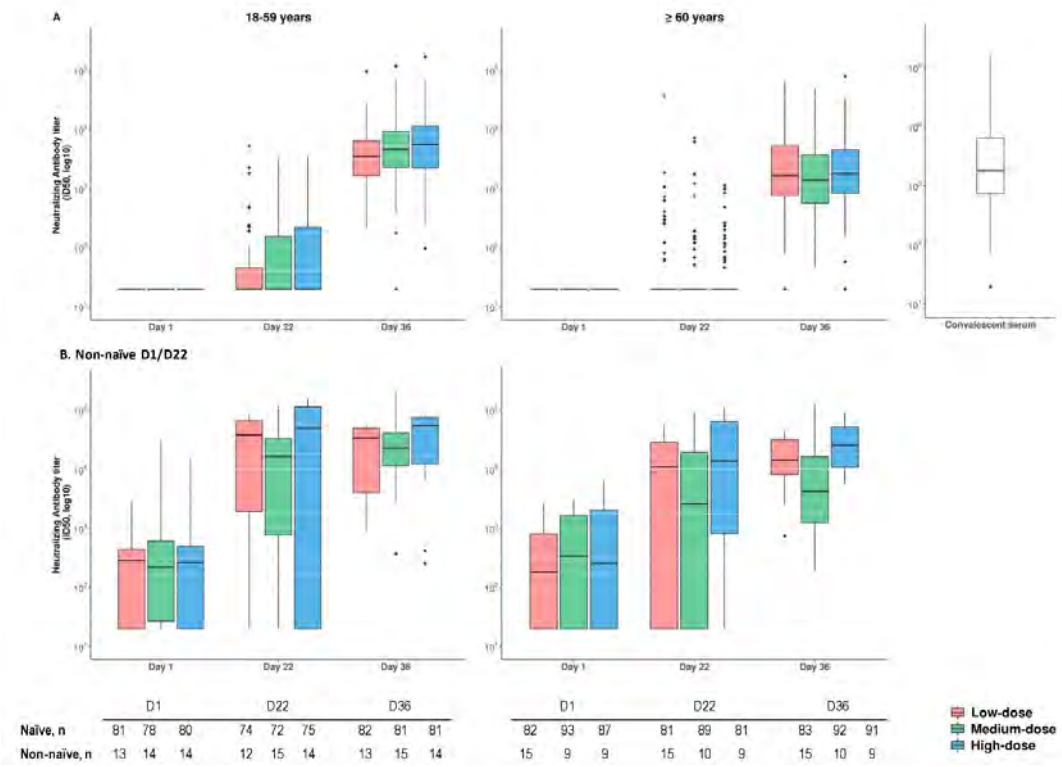
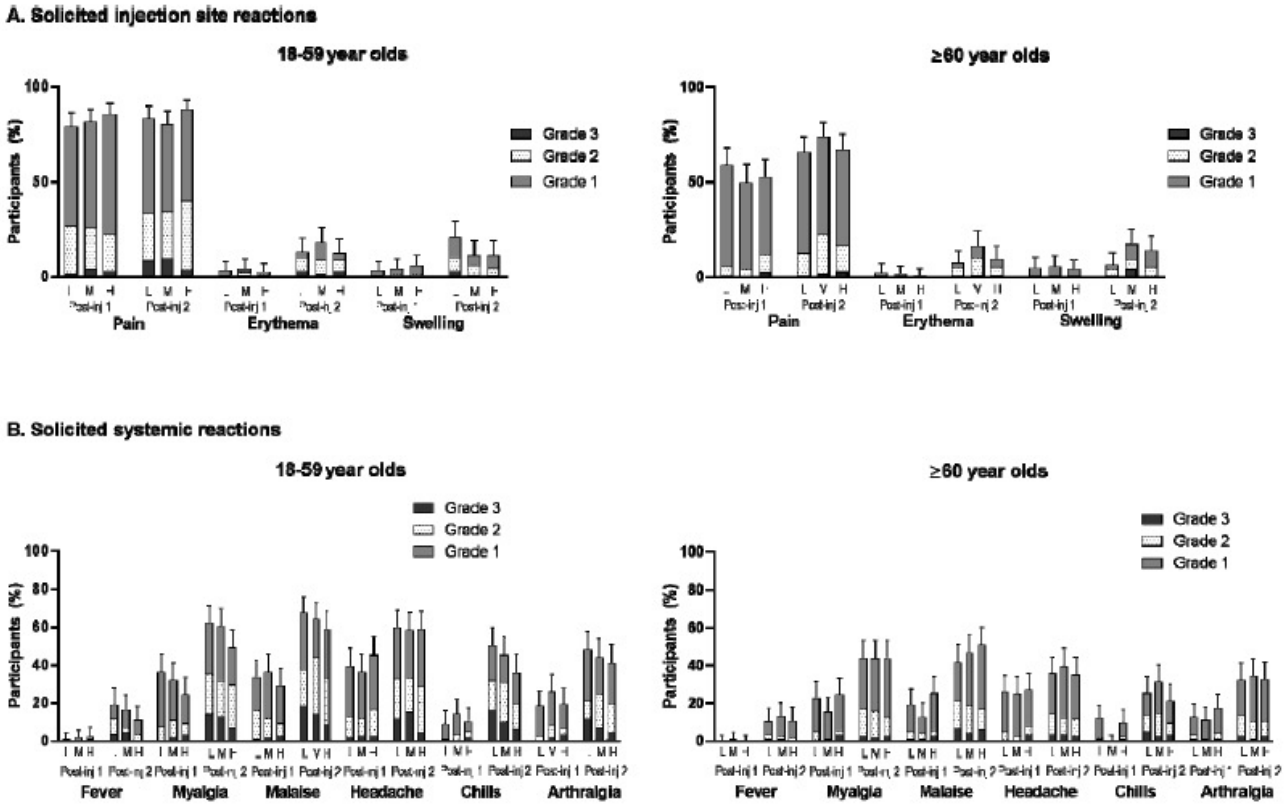


Figure 2: Neutralising antibody response to D614G, after each injection of low-, medium- and high-dose CoV2 preS dTM-AS03 formulations, by SARS-CoV-2 naïve status (PPAS). Footnote: Boxes indicate median and quartile ranges. Outliers are plotted as individuals points. D, study day; n, number of participants available for each endpoint are shown in the table. For the panel of convalescent sera, n=79

Vaccination COVID

Safety and immunogenicity of a SARS-CoV-2 recombinant protein vaccine with AS03 adjuvant in healthy adults: interim findings from a phase 2, randomised, dose-finding, multi-centre study

Saranya Sridhar MBBS[1], Arnel Joaquin MD[2], Matthew I Bonaparte PhD[3], Agustin Bueso MD[4], Anne-



L = low-dose group (5 µg). M = medium-dose group (10 µg). H = high-dose group (15 µg). Post-inj = post-injection.

Vaccination COVID 19 par voie nasale

- **Vaccination nasale:**

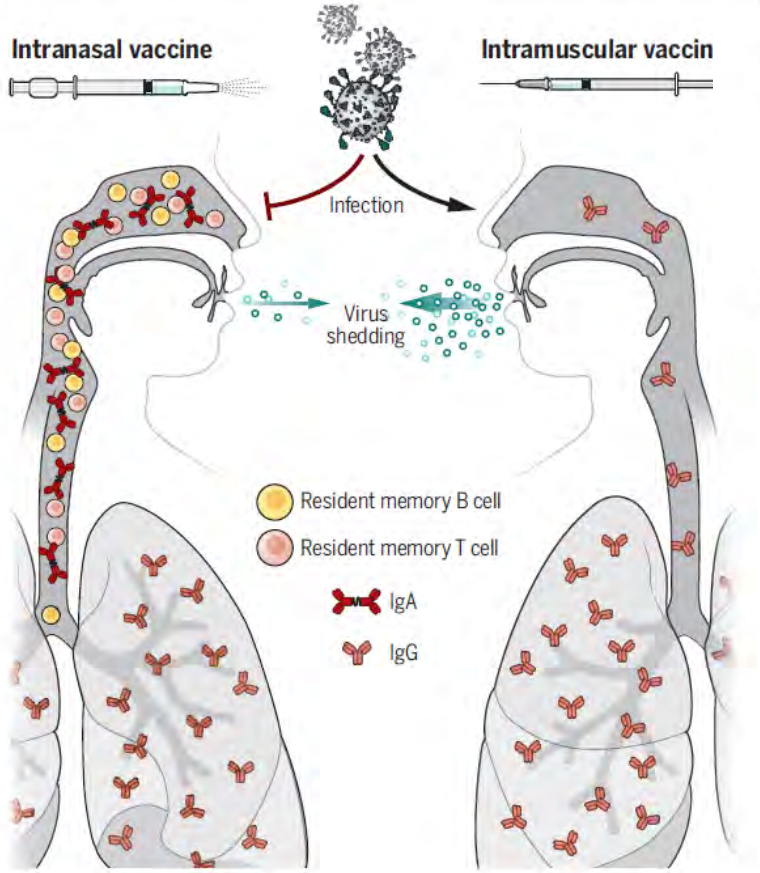
Ig A et cellules T et B mémoires dans le nez et les voies aériennes supérieures

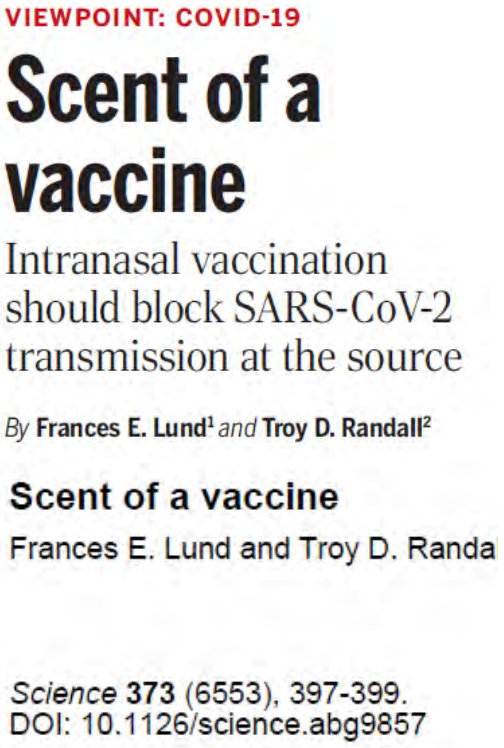
Prevention de l'infection et reduction de l'excrétion virale

- **Vaccination IM:**

igG seriques,

protection infection pulmonaire par transsudation au niveau pulmonaire mais n'empeche pas l'infection nasale et l'excretion virale




VIEWPOINT: COVID-19

Scent of a vaccine

Intranasal vaccination should block SARS-CoV-2 transmission at the source

By Frances E. Lund[1] and Troy D. Randall[2]

Scent of a vaccine

Frances E. Lund and Troy D. Randa

Science **373** (6553), 397-399.
DOI: 10.1126/science.abg9857

Vaccination ARNm
une nouvelle ère en vaccinologie

REVIEWS

Check for updates

mRNA vaccines for infectious diseases: principles, delivery and clinical translation

Namit Chaudhary[1], Drew Weissman[2] and Kathryn A. Whitehead[1,3]✉

REVIEWS | DRUG DISCOVERY

Table 1 | **Clinical trials of mRNA vaccines against infectious diseases beyond COVID-19**

Funding source	Name	Target	Vaccine type	Route of administration	Clinical trial phase	Clinical trial identifier
Moderna	mRNA-1647	CMV	Nucleoside-modified mRNA–LNP	Intramuscular	Phase II	NCT04232280, NCT03382405
Moderna	mRNA-1443	CMV	Nucleoside-modified mRNA–LNP	Intramuscular	Phase I	NCT03382405
Moderna	mRNA-1893	Zika	Nucleoside-modified mRNA–LNP	Intramuscular	Phase I	NCT04064905
Moderna	mRNA-1325	Zika	Nucleoside-modified mRNA–LNP	Intramuscular	Phase I	NCT03014089
Moderna	mRNA-1653	hMPV/PIV3	Nucleoside-modified mRNA–LNP	Intramuscular	Phase I	NCT04144348, NCT03392389
Moderna	mRNA-1345	RSV	Nucleoside-modified mRNA–LNP	Intramuscular	Phase I	NCT04528719
Moderna, Merck	mRNA-1777 (V171)	RSV	Nucleoside-modified mRNA–LNP	Intramuscular	Phase I	Unregistered
Moderna, Merck	mRNA-1172 (V172)	RSV	Nucleoside-modified mRNA–LNP	Intramuscular	Phase I	Unregistered
Moderna	mRNA-1851 (VAL-339851)	Influenza A (H7N9)	Nucleoside-modified mRNA–LNP	Intramuscular	Phase I	NCT03345043
Moderna	mRNA-1440 (VAL-506440)	Influenza A (H10N8)	Nucleoside-modified mRNA–LNP	Intramuscular	Phase I	NCT03076385
Moderna	mRNA-1010	Influenza A (H1N1, H3N2), influenza B (Yamagata lineage, Victoria lineage)	Unknown	Intramuscular	Phase I/II	NCT04956575
Translate Bio, Sanofi	MRT5400	Influenza A (H3N2)	Unknown	Intramuscular	Phase I	Unregistered
Translate Bio, Sanofi	MRT5401	Influenza A (H3N2)	Unknown	Intramuscular	Phase I	Unregistered
Moderna	mRNA-1944	Chikungunya	Nucleoside-modified mRNA–LNP	Intramuscular	Phase I	NCT03829384
Moderna	mRNA-1388 (VAL-181388)	Chikungunya	Nucleoside-modified mRNA–LNP	Intramuscular	Phase I	NCT03325075
CureVac	CV7201	Rabies	Unmodified mRNA complexed in RNActive	Intradermal, intramuscular	Phase I	NCT02241135
CureVac	CV7202	Rabies	Unmodified mRNA–LNP	Intramuscular	Phase I	NCT03713086
GSK	GSK3903133A	Rabies	Self-amplifying mRNA in cationic nanoemulsion	Intramuscular	Phase I	NCT04062669

CMV, cytomegalovirus; GSK, GlaxoSmithKline; HIV, human immunodeficiency virus; hMPV, human metapneumovirus; LNP, lipid nanoparticle; PIV3, parainfluenza virus type 3; RSV, respiratory syncytial virus.

Merci pour votre attention