MALALTIES EMERGENTS

Rellevància de les vacunes

Javier Arranz Izquierdo

GMISBAL. IDISBA

GdT Infecciosas. semFYC

CS Escola Graduada. Palma de Mallorca. IBSALUT

Declaració d'interessos.

No rebo ingressos de la industria farmacèutica

Taula rodona sobre COVID a COFIB

Viatge a Madrid per a participar a grup focal EVALUA-COVID (Ministerio de Sanidad)

Definicions.

Emergents

Reconegudes a l'ésser humà per primera vegada

- VIH – SIDA
- SARS
- MERS
- Zika
- COVID
- Henipavirus

Re-emergents

Conegudes prèviament, però

Nous llocs:
West Nile, Chikungunya, Dengue, Crimea-Congo (CCHF), *Verola dels simis*

Noves formes:
SARM, Malària resistent, Influenza H5N1, TBC multirresistent

Resorgint:
Polio, Còlera, Dengue, Chikungunya

Factors.

Principals factors associats a l'emergència o re-emergència de patògens a humans	
1	Canvis a la utilització de la terra i practiques agrícoles
2	Canvis demogràfics i socials
3	Empitjorament de la salut humana (pobressa, malalties, etc.)
4	Sistema sanitari (hospitals, procediments)
5	Evolució dels patògens (Resistències, increment de virulència)
6	Contaminació de fonts d'aigua i aliments
7	Viatges internacionals
8	Manca o errades dels programes de salut
9	Comerç internacional (mercaderies)
10	Canvi climàtic

Woolhouse M, Gowtage-Sequeria S. Host Range and Emerging and Reemerging Pathogens. Em Inf Dis 2005; 16: 1842-7

Brots.

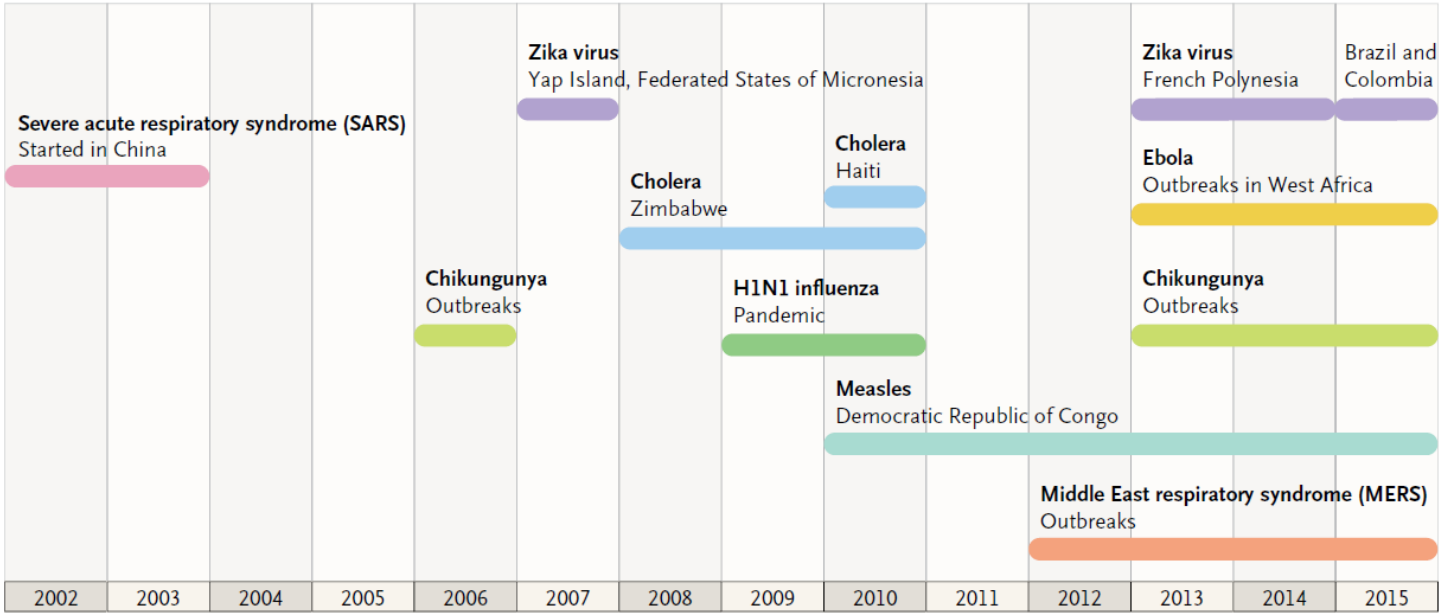

Figure 1. Major Emerging and Reemerging Infectious-Disease Outbreaks, Epidemics, and Pandemics, 2002 through 2015.

Sands P, Mundaca C, Dzau V. The Neglected Dimension of Global Security- A Framework for Countering Infectious Diseases Crises. N Engl J Med 2016; 374: 1281-7 DOI: 10.1056/NEJMsr1600236

Quines?

WHO Research and Development Blueprint

2018

- Arenaviral hemorrhagic fevers (including
- Lassa Fever)
- Nipah and related henipaviral diseases
- Chikungunya
- Emerging non-polio enteroviruses
- Cholera
- Plague
- Crimean-Congo Hemorrhagic Fever (CCHF)
- Rift Valley Fever (RVF)
- Filoviral diseases (including Ebola and Marburg)
- Severe Fever with Thrombocytopenia Syndrome (SFTS)
- Leishmaniosis
- West Nile Virus
- MERS-CoV
- Zika
- Other highly pathogenic coronaviral diseases (such as SARS)

WHO 2018 Annual review of diseases prioritized under the R&D Blueprint http://www.who.int/blueprint/priority-diseases/en/

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- MERS-CoV
- Zika
- Other highly pathogenic coronaviral diseases (such as SARS)

Prioritàries

- Crimean-Congo
- Ebola
- Lassa
- MERS and SARS
- Nipah and henipaviral diseases
- Rift Valley Fever
- Zika disease
- Disease X

WHO 2018 Annual review of diseases prioritized under the R&D Blueprint http://www.who.int/blueprint/priority-diseases/en/

Espanya

ETV	2016	2017	2018	2019	2020
Malària		829	853	783	115
Dengue	261	135	200	228	63
Hantavirus	0	0	0	0	0
Encefalitis CE	0	0	0	1	0
Chikungunya	105	53	27	516	59
Febre Q		481	456	332	170
West Nile	6	0	1	0	77
Crimea-Congo	2	0	2	2	3
Rift Valley	0	0	0	0	0
Zika	406	92	32		0

Annual Epidemiological Reports. ECDC. https://www.ecdc.europa.eu/en/publications-data/monitoring/all-annual-epidemiological-reports
Surveillance Atlas of Infectious Diseases. https://atlas.ecdc.europa.eu/public/index.aspx

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Annual Epidemiological Reports. ECDC. https://www.ecdc.europa.eu/en/publications-data/monitoring/all-annual-epidemiological-reports
Surveillance Atlas of Infectious Diseases. https://atlas.ecdc.europa.eu/public/index.aspx

1. Clínica emergents (poca)
2. Vacunes existents
3. Altres vacunes
4. mRNA

Clínica

CAMFiC
societat catalana de medicina familiar i comunitària

Anopheles | Aedes | Cullex | Flebotomo | Paparra

Febre

- MEG — Clínica molt variable
- Antecedents VIATGE - FAMÍLIA
  - Senegal
  - Nigèria
  - Guinea Eq
  - Malí
- Malària
- Artràlgies
- Conjunctivitis
- Dolor retroorbitari
- Rash
- Antecedent VIATGE
- VECTOR present
  - Dengue
  - Chikungunya
  - Zika
- Cefalea
- Confusió
- Somnolència
- Antecedent VIATGE
- VECTOR present
- Contacte ÈQUIDS
  - Nil Occ
  - Toscana
  - Encef CE
- Confusió
- MEG
- Sagnat
- Plaquetopènia
- Activitats aire lliure
- VECTOR present
- Picadura
  - Crimea - C

Clínica.

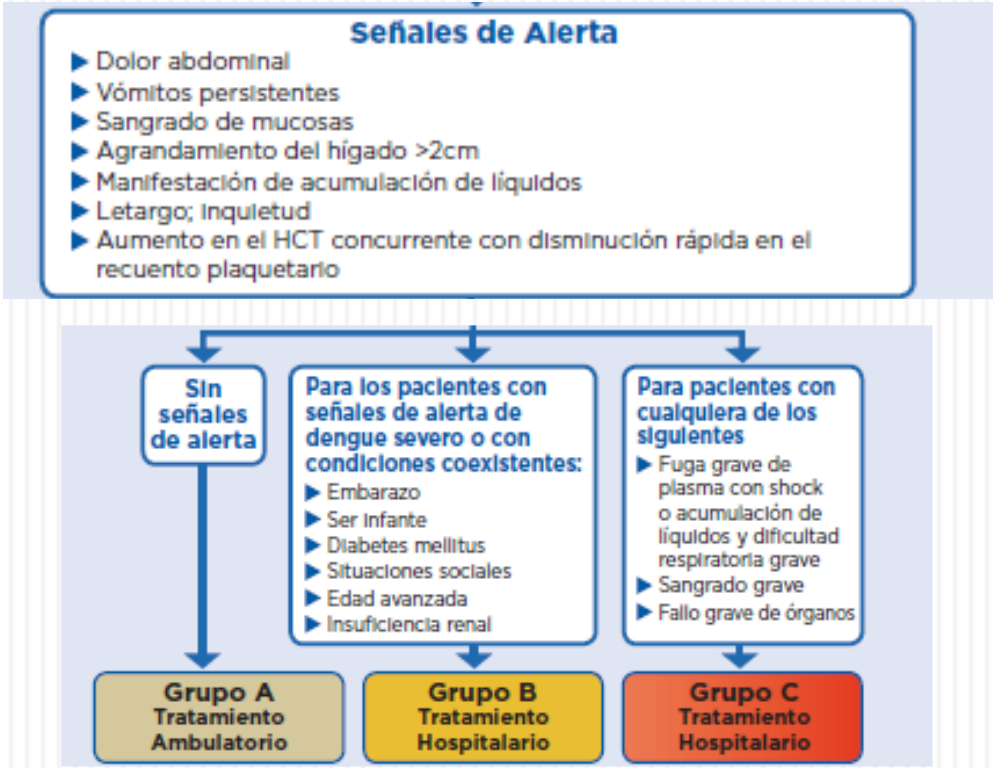
Febre	Clínica	Malalties	Viatges	Riscs	Vector
General	**Plurisimptomàtica**	**Malària**	Senegal Nigèria Malí Guinea Equatorial	Visita a família	Anopheles
Rash - Dolor	**Artràlgies** **Conjunctivitis** **Dolor retro-orbitari** **Rash**	**Dengue** **Chikungunya** **Zika**	Carib Àfrica Àsia "**NO** Viatges"		**Aedes**
Neurològic	**Cefalea** **Somnolència** **Confusió**	**Nil Occidental**	**NO** Viatges Sur d'Espanya Tarragona?	Èquids	**Cullex**
Coagulació	**Confusió** **MEG** **Sagnat** **Plaquetopènia**	**Crimea-Congo (CCHF)**	**NO** Viatges Extremadura, Àvila, Lleó Àsia central	Activitats aire lliure Caça **Sanitaris**	**Hyalomma**

Clínica.

EVALUACIÓN RÁPIDA DE RIESGO

Dengue autóctono en España
2ª actualización

31 mayo 2019



Clínica.

EVALUACIÓN RÁPIDA DE RIESGO

Meningoencefalitis por virus del Nilo occidental. Primeros casos detectados en Tarragona.

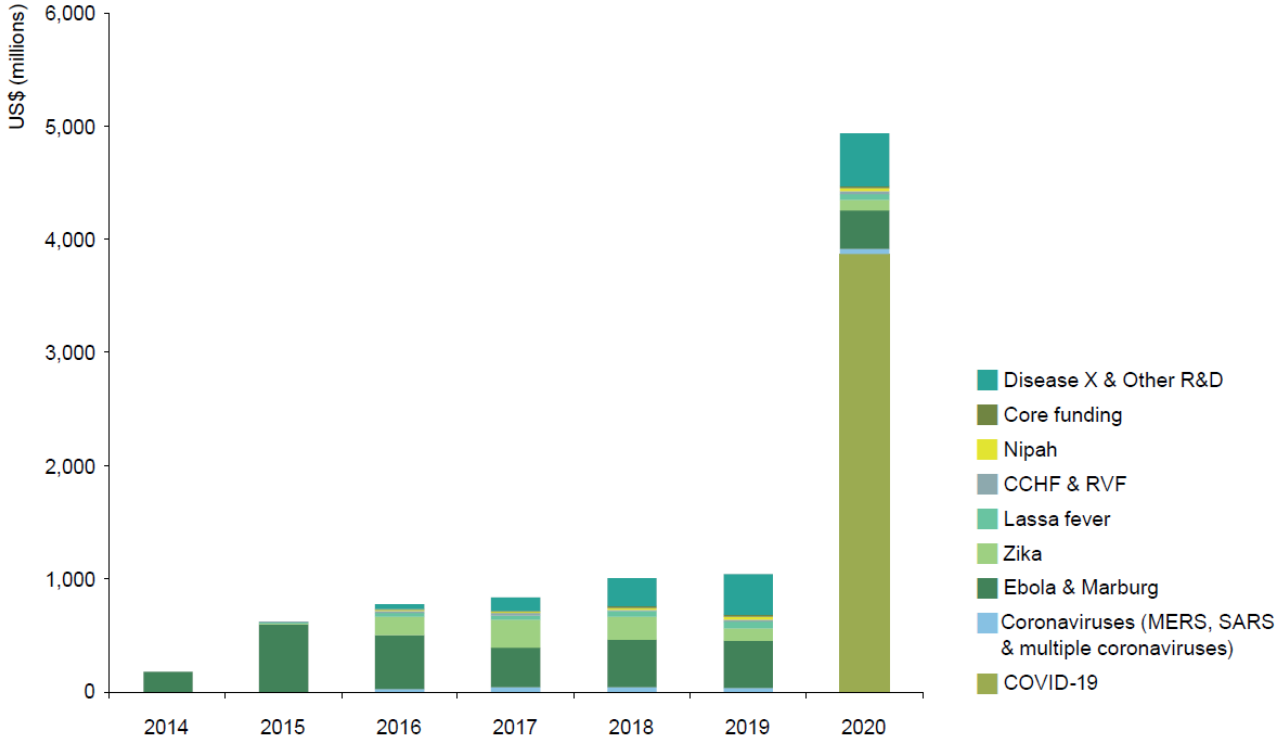
18 de octubre 2022

- Agost, 90 i 86 anys (Reus)
- Meningoencefalitis

- 2 casos a Càdis
- 6 brots en èquids

- 80% Assimptomàtics
- Febre, cefalea, artràlgies
- Neurològica (1/150)
- Mortalitat 4-14%
- Cavalls i cuidadors (Andalucia)

Vacunes.

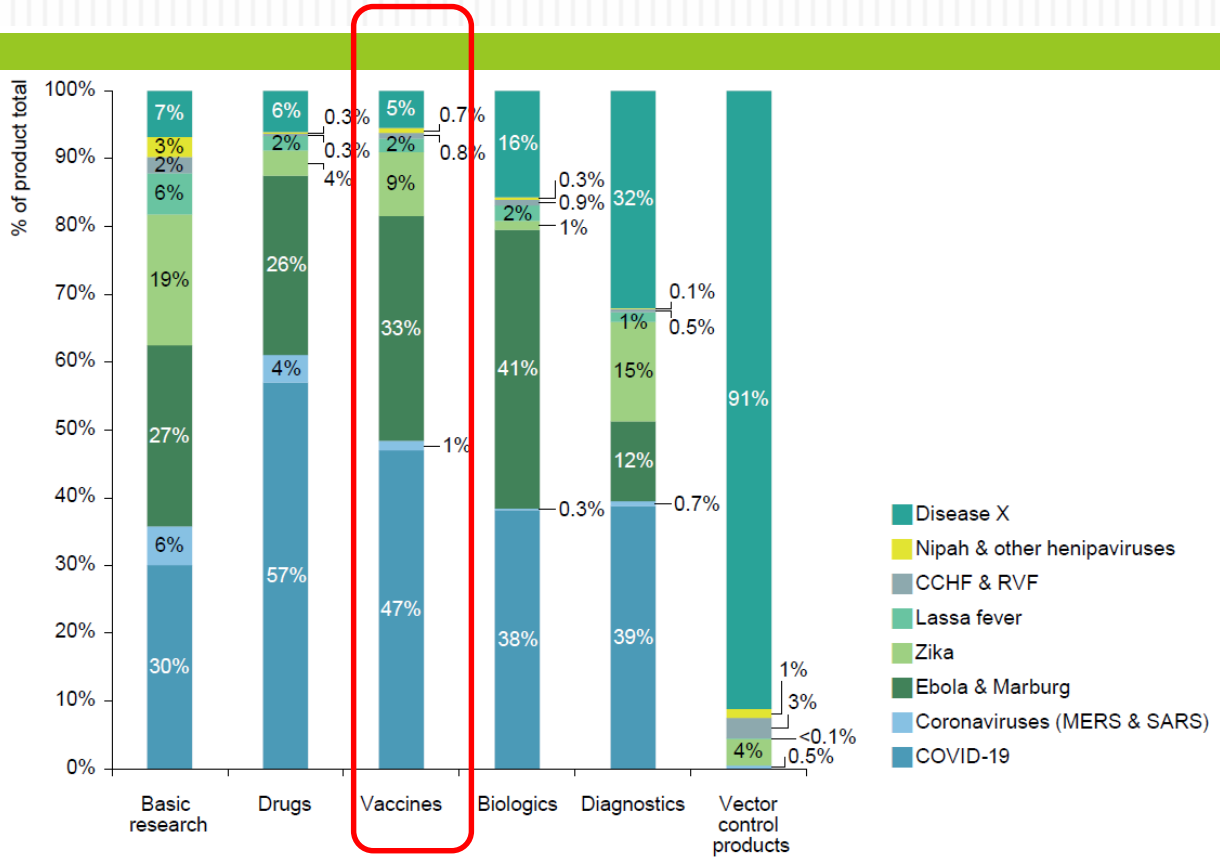


Prioritàries

- Crimean-Congo
- Ebola
- Lassa
- MERS and SARS
- Nipah and henipaviral diseases
- Rift Valley Fever
- Zika disease
- Disease X

G-FINDER. Landscape of Emerging Infectious Disease Research and Development: From Pandemic Response to Pandemic Resilience. Policy Cures Research Report 2022. www.policycuresresearch.org
Coalition for Epidemic Preparedness Innovations (CEPI) https://cepi.net/

Vacunes.



G-FINDER. Landscape of Emerging Infectious Disease Research and Development: From Pandemic Response to Pandemic Resilience. Policy Cures Research Report 2022. www.policycuresresearch.org

Vacunes.

Disease or R&D area	Basic research	Drugs	Vaccines	Biologics	Diagnostics	Vector control products	Unspecified	2019 total	2020 total
Coronavirus disease 2019 (COVID-19)	394.83	506.43	2,237.57	469.37	203.26	-	62.05		3,873.52
Coronaviruses (including MERS, SARS, and multiple coronaviruses)	15.84	8.08	13.69	0.52	0.54	0.33	1.24	38.56	40.24
Middle East Respiratory Syndrome (MERS)	5.52	2.95	8.50	0.52	0.49	0.33	0.43	29.46	18.73
Severe Acute Respiratory Syndrome (SARS)	4.66	1.67	1.18	-	0.05	-	-	6.79	7.56
Other coronaviral R&D in combination with MERS and/or SARS and/or COVID-19	5.66	3.46	4.01	-	<0.01	-	0.82	2.32	13.95
Filoviral diseases (including Ebola, Marburg)	26.59	22.67	138.76	145.42	3.38	-	3.81	410.65	340.63
Ebola	21.90	18.84	105.18	130.80	2.87	-	1.46	349.79	281.04
Marburg	1.91	2.88	17.62	12.21	0.21	-	-	37.79	34.83
Other filoviral R&D in combination with Ebola and/or Marburg	2.79	0.94	15.97	2.41	0.30	-	2.35	23.07	24.75
Zika	43.24	5.43	36.34	3.82	7.27	1.61	1.90	116.59	99.61
Arenaviral haemorrhagic fevers (including Lassa fever)	11.48	2.97	28.22	5.50	0.85	-	2.28	58.94	51.30
Lassa fever	11.07	1.75	27.11	4.66	0.85	-	2.28	56.29	47.72
Other arenaviral R&D in combination with Lassa fever	0.42	1.21	1.11	0.84	-	-	-	2.66	3.58
Bunyaviral diseases (including CCHF, RVF)	6.62	0.65	11.41	3.41	1.48	0.96	0.23	20.48	24.76
Crimean-Congo Haemorrhagic Fever (CCHF)	1.50	0.11	3.72	3.41	0.21	-	0.12	8.31	9.07
Rift Valley Fever (RVF)	2.43	0.24	7.39	-	0.43	0.96	0.11	8.85	11.57
Other bunyaviral R&D in combination with CCHF and/or RVF	2.69	0.30	0.30	-	0.85	-	-	3.31	4.13
Henipaviral diseases (including Nipah)	3.34	0.67	16.80	1.25	-	0.70	0.77	24.09	23.53
Nipah	2.59	0.67	16.80	1.25	-	0.70	0.77	23.19	22.78
Other henipaviral R&D including in combination with Nipah	0.75	-	-	-	-	-	-	0.90	0.75

Any	$
2015	72%
2019	43%
2020	38%

G-FINDER. Landscape of Emerging Infectious Disease Research and Development: From Pandemic Response to Pandemic Resilience. Policy Cures Research Report 2022. www.policycuresresearch.org

Malària

Malària.

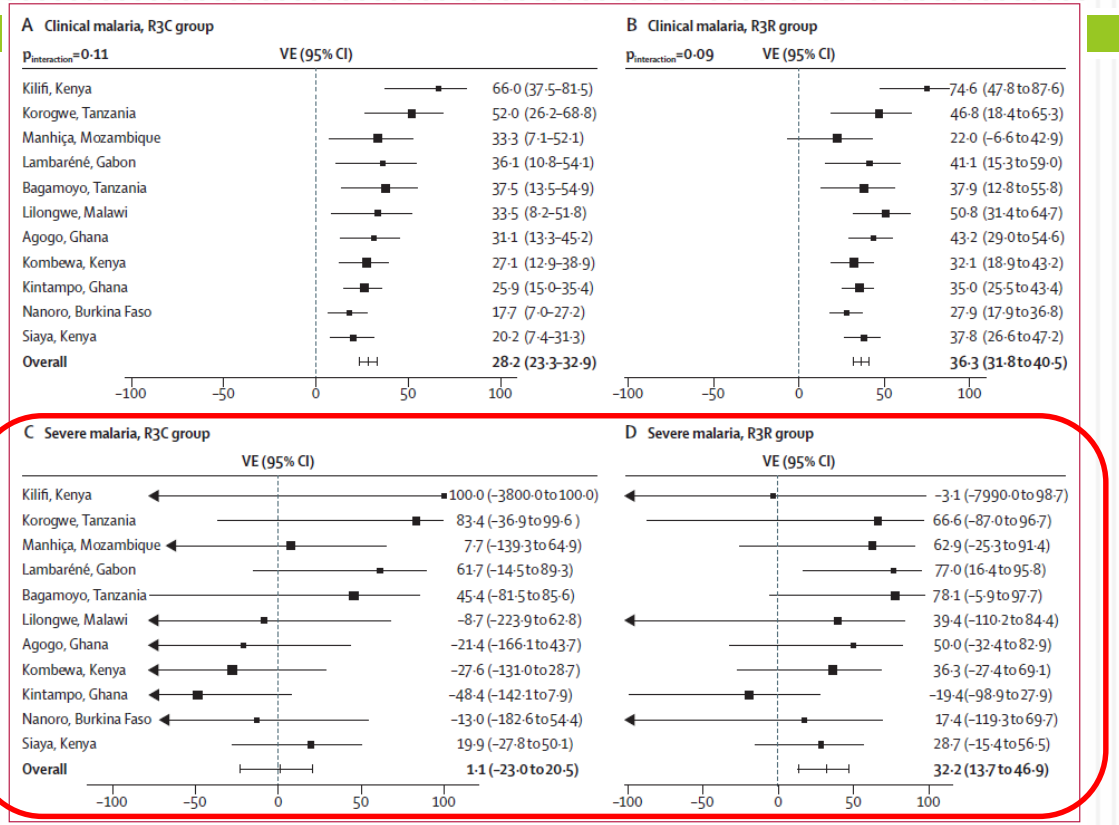
The World Health Organization recommends widespread use of the RTS,S/AS01 (RTS,S) malaria vaccine among children in sub-Saharan Africa and in other regions with moderate to high P. falciparum malaria transmission. The recommendation is based on results from the ongoing pilot programme in Ghana, Kenya and Malawi that has reached more than 1 million children since 2019.

The vaccine should be provided as a 3-dose primary series, starting from around 5 months of age and with a minimal interval between doses of 4 weeks.

A fourth dose should be given between about 12 and 18 months after the 3rd dose, just prior to the peak transmission season

WHO. Full Evidence Report on the RTS,S/AS01 Malaria Vaccine. Sept 2021

Malària.



RTS,S Clinical Trials Partnership Efficacy and safety of RTS,S/AS01 malaria vaccine with or without a booster dose in infants and children in Africa: final results of a phase 3, individually randomised, controlled trial. Lancet 2015; 386: 31–45

Malària.

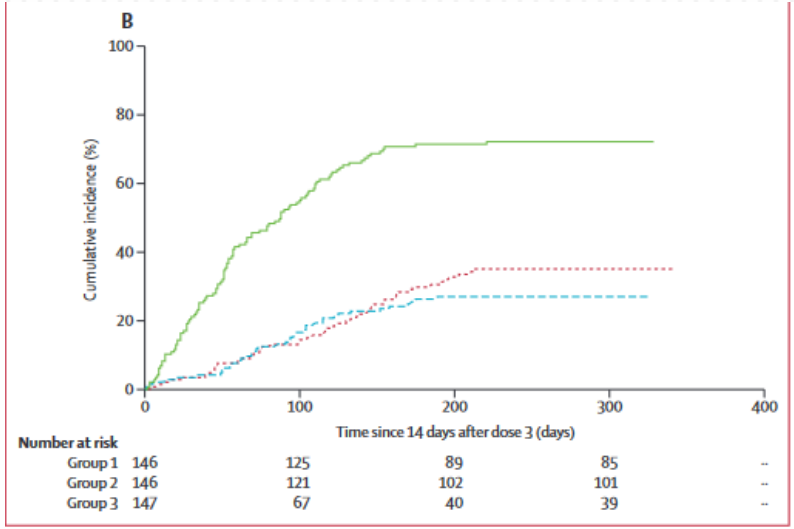


Figure 2: Kaplan-Meier estimates of the time to first episode of clinical malaria

Efficacy and immunogenicity of R21/Matrix-M vaccine against clinical malaria after 2 years' follow-up in children in Burkina Faso: a phase 1/2b randomised controlled trial

We previously reported high-level efficacy of R21 adjuvanted with 50 µg of Matrix-M, administered before the malaria season, reaching the WHO-specified goal of at least 75% efficacy over 1 year in the target population of African children. The administration of a booster dose 12 months following the primary series of R21/Matrix-M vaccinations shows the added benefit of a fourth dose when administered before the malaria season. Vaccine efficacy was maintained in the high-dose adjuvant group, at 80% following the booster vaccine over 12 months, and 75% over 24 months after the primary three-dose regimen. Furthermore, vaccine efficacy against multiple episodes of clinical malaria was similar (78%) over 2 years of follow-up. R21/Matrix-M has a favourable safety profile and also induces high levels of malaria-specific anti-NANP antibodies that correlate with the observed protection against clinical malaria.

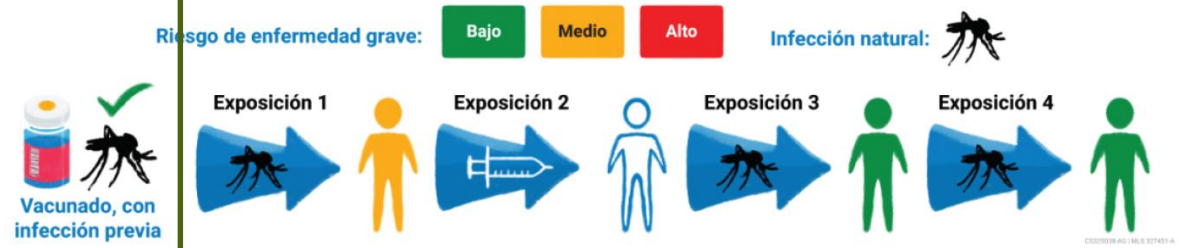
Mehreen S Datoo et al. Efficacy of a low-dose candidate malaria vaccine, R21 in adjuvant Matrix-M, with seasonal administration to children in Burkina Faso: a randomised controlled trial. Lancet 2021; 397: 1809–18
Mehreen S Datoo et al. Efficacy and immunogenicity of R21/Matrix-M vaccine against clinical malaria after 2 years' follow-up in children in Burkina Faso: a phase 1/2b randomised controlled trial. Lancet Infect Dis sept 2021. https://doi.org/10.1016/ S1473-3099(22)00442-X

Dengue.

Dengue.

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 70 / No. 6
December 17, 2021

Dengue Vaccine: Recommendations of the Advisory Committee on Immunization Practices, United States, 2021

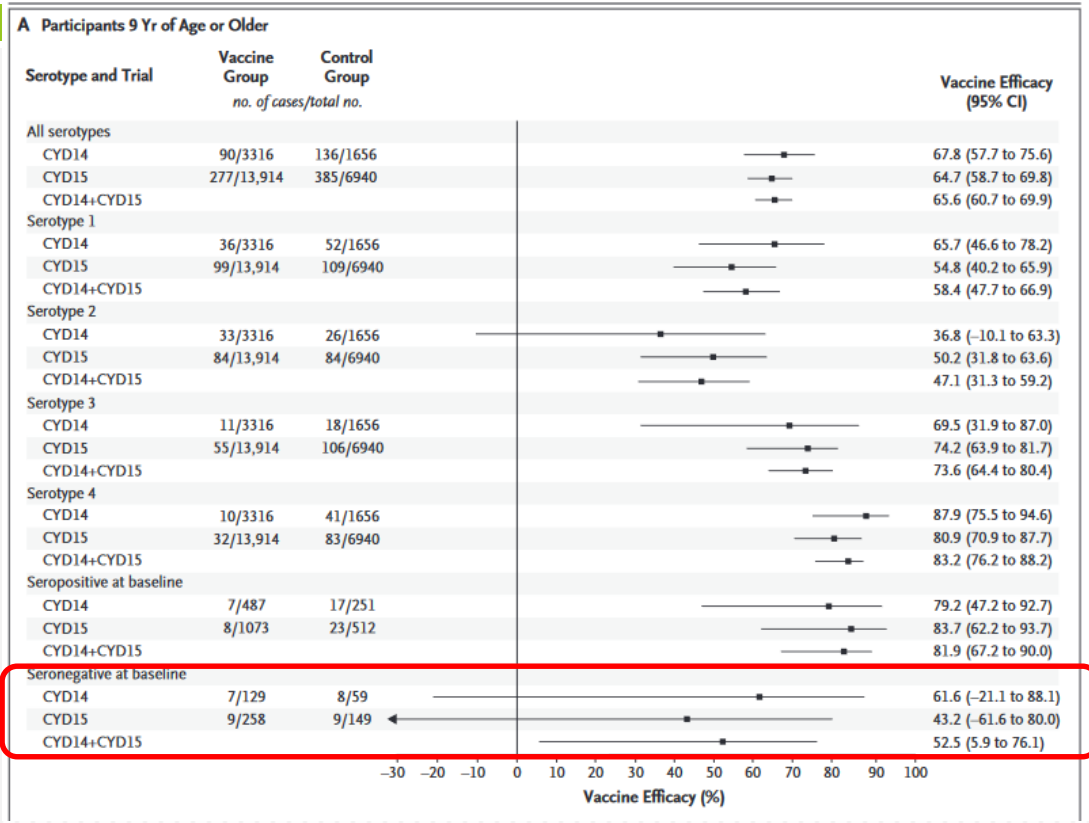


Test?

0-6-12 , subcutània, majors de 9 anys

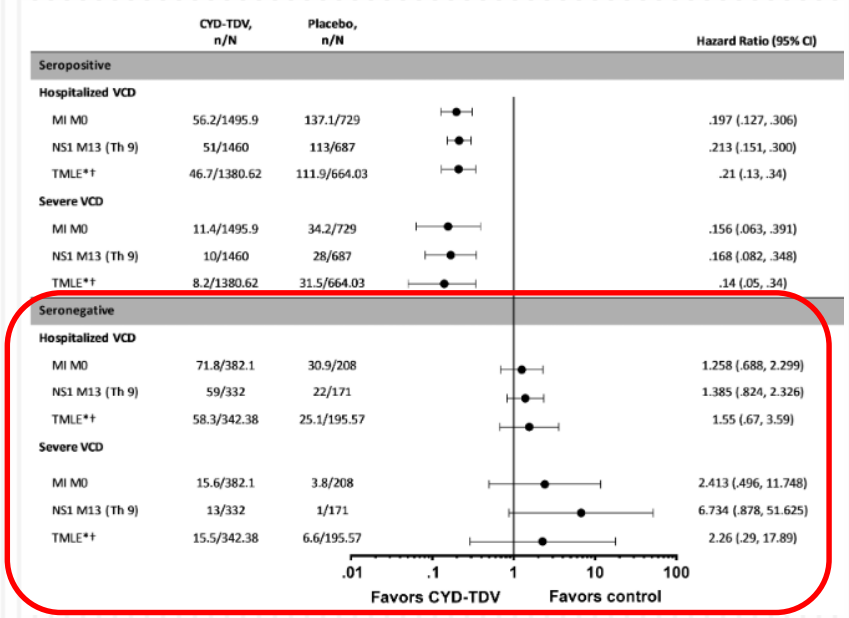
CDC. Dengue. Elegibilidad para la vacuna dengue https://www.cdc.gov/dengue/es/vaccine/hcp/eligibility/index.html

Dengue.

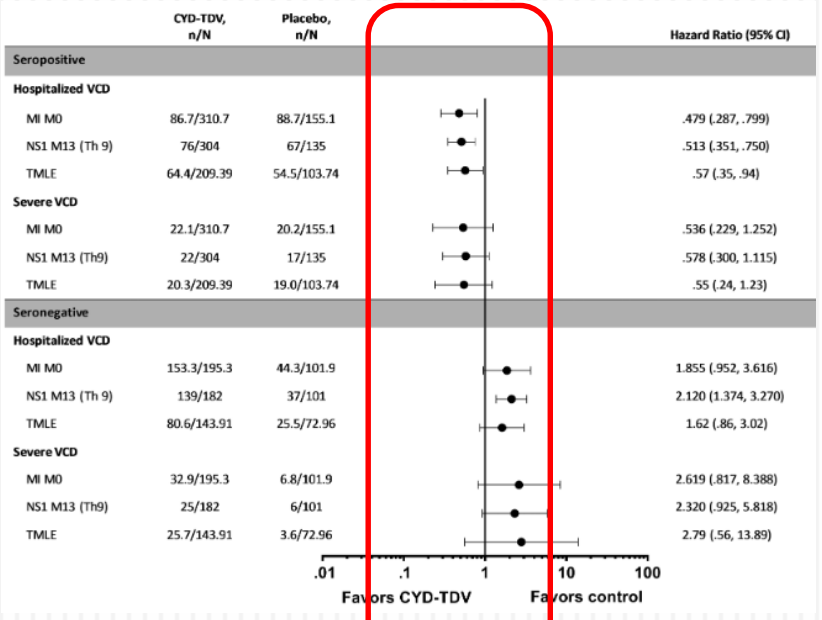


Hadinegoro S et al. Efficacy and Long-Term Safety of a Dengue Vaccine in Regions of Endemic Disease. N Engl J Med 2015;373:1195-206. DOI: 10.1056/NEJMoa1506223

Dengue.



> 9 anys



< 9 anys

Hadinegoro S et al. Efficacy and Long-Term Safety of a Dengue Vaccine in Regions of Endemic Disease. N Engl J Med 2015;373:1195-206. DOI: 10.1056/NEJMoa1506223

VACUNES. Dengue

	Placebo (n = 6687)	TAK-003 (n = 13 380)	Efficacy % (95% CI)
VCD			
Overall	494/6687 (2.4)	390/13 380 (0.9)	62.0 (56.6–66.7)
Seropositive	358/4854 (2.4)	262/9663 (0.9)	65.0 (58.9–70.1)
DENV-1	130/4854 (0.9)	114/9663 (0.4)	56.2 (43.7–66.0)
DENV-2	124/4854 (0.8)	42/9663 (0.1)	83.4 (76.4–88.3)
DENV-3	95/4854 (0.6)	94/9663 (0.3)	52.3 (36.6–64.2)
DENV-4	15/4854 (<0.1)	12/9663 (<0.1)	60.7 (16.0–81.6)
Seronegative	136/1832 (2.4)	128/3714 (1.1)	54.3 (41.9–64.1)
DENV-1	66/1832 (1.2)	77/3714 (0.7)	43.5 (21.5–59.3)
DENV-2	55/1832 (1.0)	9/3714 (<0.1)	91.9 (83.6–96.0)
DENV-3[a]	15/1832 (0.3)	36/3714 (0.3)	−23.4 (−125.3 to 32.4)
DENV-4	2/1832 (<0.1)	8/3714 (<0.1)	−105.5 (−867.5 to 56.4)

TAKEDA Vaccine: Manté eficacia als 3 anys, però amb una baixada prou important per alguns serotips (3 i 4). Sembla tenir major eficàcia a seronegatius que Dengvaxia.

Rivera L et al. Three-year Efficacy and Safety of Takeda's Dengue Vaccine Candidate (TAK-003) CID 2022:75

VACUNES. Dengue

Study Type:	Interventional (Clinical Trial)
Estimated Enrollment:	16944 participants
Allocation:	Randomized
Intervention Model:	Single Group Assignment
Masking:	Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)
Primary Purpose:	Prevention
Official Title:	Phase III Trial to Evaluate Efficacy and Safety of a Dengue 1,2,3,4 (Attenuated) Vaccine
Actual Study Start Date:	February 2016
Estimated Primary Completion Date:	August 2021
Estimated Study Completion Date:	August 2024

https://clinicaltrials.gov/ct2/show/NCT02406729

Febre Q.

CAMFiC
societat catalana de medicina familiar i comunitària

Febre Q.

Q fever vaccine is recommended for adolescents aged ≥15 years and adults who are at risk of infection with *C. burnetii*. These include:

- abattoir workers
- farmers
- stockyard workers
- shearers
- animal transporters (of high-risk animals such as cattle, camels, sheep, goats and kangaroos)
- veterinarians
- veterinary nurses
- veterinary students
- professional dog and cat breeders
- agricultural college staff and students
- wildlife and zoo workers who work with high-risk animals
- animal refuge workers (including those working in animal shelters and boarding facilities)
- laboratory workers who handle veterinary specimens or work with *C. burnetii*
- other people exposed to high-risk animals

People should have both serological and skin tests before vaccination.

Isken, L.D.; Kraaij-Dirkzwager, M.; Vermeer-de Bondt, P.E.; Rümke, H.C.; Wijkmans, C.; Opstelten, W.; Timen, A. Implementation of a Q fever vaccination program for high-risk patients in the Netherlands. Vaccine **2013**, 31, 2617–2622.

https://immunisationhandbook.health.gov.au/contents/vaccine-preventable-diseases/q-fever

Nil Occidental.

Nil Occidental.

Table 1. WNV vaccine candidates in clinical testing until today.

Candidate vaccine	Type	Key data to date	Most advanced clinical stage	References
Hydrovax-001	Inactivated using hydrogen peroxide	Neutralizing antibodies in 50% of individuals after two doses.	I	20
Inactivated WNV	Inactivated using formaldehyde	Neutralizing antibodies after three doses.	I/II	21
ChimeriVax-WN02	Recombinant yellow fever vaccine strain expressing the prM/E-fragment of WNV	Neutralizing antibodies (>90%) in younger and older age groups after one dose	II	22
rWN/DEN4Δ30	Recombinant attenuated DENV expressing the prM/E-fragment of WNV	Neutralizing antibodies in 89% of individuals after two doses.	I	23
HBV-002	Recombinant truncated E-protein	Neutralizing antibodies in all individuals after three doses	I	24–25
VRC WNV	DNA plasmid expressing the prM/E fragment	Neutralizing antibodies (>90%) in younger and older age groups after three doses	I	26

Ulbert S. West Nile virus vaccines – current situation and future directions HUMAN VACCINES & IMMUNOTHERAPEUTICS 2019, VOL. 15, NO. 10, 2337–2342
https://doi.org/10.1080/21645515.2019.1621149

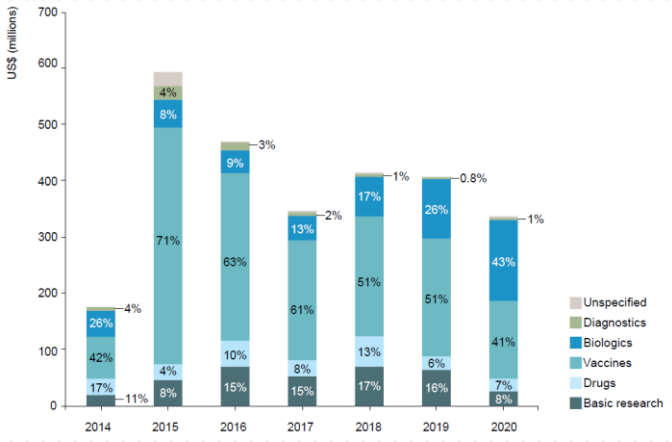
Chikungunya.

Chikungunya.

Vacuna	Tipus	Dosis	Sero+ (dies)	Sero+ (dies)	Obs.
MV-CHIK	Mediada per virus	2	50-96% (28)	18-90% (196)	NT_{50}
TSI-GSD-218	Atenuada	2	98% (28)	85% (365)	
PXVX0317	VLP	2	72-98% (7)	98% (760)	NT_{80}
Valneva (VLA1553)	Atenuada	1	30% (7) 100% (14)	100% (365)	NT_{50} **Fase III (pilot)**

Reisinger EC, Tschismarov R, Beubler E, et al. Immunogenicity, safety, and tolerability of the measles-vectored chikungunya virus vaccine MV-CHIK: a double-blind, randomised, placebo-controlled and active-controlled phase 2 trial. *Lancet* 2019; **392:** 2718–27.
Wressnigg N, Hochreiter R, Zoihsl O, et al. Single-shot live-attenuated chikungunya vaccine in healthy adults: a phase 1, randomised controlled trial. *Lancet Infect Dis* 2020; **20:** 1193–203.
Bennett S et al. Safety and immunogenicity of PXVX0317, an aluminium hydroxide-adjuvanted chikungunya virus-like paticle vaccine: a randomised, doublé blind, parallel-group, phase 2 trial. Lancet Infect Dis 2022; 22:134-55
Valneva Press release March 2022

Ebola.



First FDA-approved vaccine for the prevention of Ebola virus disease, marking a critical milestone in public health preparedness and response

For Immediate Release:

December 19, 2019

Ebola.

- Més de 350.000 dosis administrades des de 2019
- Coalició entre MSF i WHO

Table 1. Advantages and disadvantages of post-Phase I clinical trial vaccines for EBOV disease.

Vaccine	Manufacturer	Advantages	Disadvantages	Status
Ervebo (rVSV-ZEBOV-GP; V920; rVSVΔG-ZEBOV-GP) Monovalent, expresses EBOV GP (Kikwit variant)	Merck NewLink Genetics PHAC (National Microbiology Laboratory in Winnipeg, Manitoba)	• Only vaccine with proven clinical efficacy • Rapid immunostimulatory properties enable its use in an outbreak setting or as an emergency postexposure prophylactic • Single-dose approach eliminates the need for patient follow-up • Good safety profile, 2 SAEs reported deemed related to the vaccine (febrile reaction and anaphylaxis) that later resolved • Durable humoral immunity, strong immune responses reported at least 2 years after vaccination • Lower doses of vaccine needed than adenovirus-based vaccines	• Only targets EBOV, which was responsible for the 2013–2016 outbreaks and more recent flare-ups • Only licensed for adults ≥18 years of age • Reports of arthritis in a subset of vaccinees associated with increasing age and increased IgG titers beyond 6 months • Infectious virus found in synovial joints of vaccinees suggests unlikely but possible vaccine shedding/secondary transmission • Requires ≥60°C storage temperature; −60°C to −80°C stability is 36 months, 2°C to 8°C for no more than 2 weeks, room temperature for no more than 4 hours	• Licensed by US FDA and EMA • Granted Breakthrough Therapy • Designation by the US FDA and PRIME status by the EMA • Phase III trials completed in Africa, the US, Canada, and Europe • Expanded access protocols used in Guinea and in the DRC • Tested in children older than or equal to 1 year (PREVAC), women that later became pregnant, and HIV–positive individuals; appears immunogenic and safe but still examining its suitability in these populations • Durability, antibody threshold of protection? • Safety and immunogenicity in the immunocompromised and pregnant/lactating women?
Zabdeno/Mvabea (Ad26.ZEBOV + heterologous MVA-BN-Filo boost) Multivalent after second dose, Zabdeno expresses EBOV GP (Mayinga) Mvabea expresses EBOV GP, SUDV GP, TAFV NP, and MARV GP	Johnson & Johnson (Janssen division) Bavarian Nordic	• Approved for individuals 1 year and older • Good safety profile, 2 SAEs reported deemed related to vaccine (Miller Fisher syndrome and small fiber neuropathy) that later resolved • Multivalent after second dose; targets EBOV, SUDV, and TAFV as well as MARV (although, only indicated for EBOV) • Replication deficiency eliminates vaccine shedding concerns • Multiple storage options: Ad26.EBOV: −20°C to −60°C for 48 months and +2 to +8°C for 12 months; MVA-BN-Filo: 20°C to −60°C for 42 months and +2 to +8°C for 6 months	• Lower predicted vaccine efficacy than Ervebo (approximately 53%) based on stringent nonhuman primate bridging data • Requires 2 doses (patient follow-up cause for concern) • Not ideal for outbreak settings as 8 weeks must pass before the second dose is administered • High doses of vaccine required for immunogenicity compared to Ervebo • Booster vaccination recommended 4 months post second dose • Mvabea does not include immunogen targeting *Bundibugyo* or *Bombali ebolaviruses* • Data on cross-protection against non-EBOV or MARV does not exist • Preexisting immunity to vector may reduce the effectiveness of the vaccine	• Licensed by EMA under exceptional circumstances • Phase I/II/III trials completed in Europe, the US, and Africa • Submitted dossier to the US FDA to request licensure using the Animal Rule • Submitting to WHO for EUAL • Other vaccine combination/variants are being explored to enhance immunogenicity/efficacy of Zabdeno and Mvabea • Durability, antibody threshold of protection? • Safety and immunogenicity in the immunocompromised and pregnant/lactating women?

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Ebola.

Vaccine	Manufacturer	Advantages	Disadvantages	Status
ChAd3-EBOZ with or without Mvabea (cAd3-ZEBOV; ChAd3-EBO-Z) Monovalent, expresses EBOV GP (Mayinga variant) Mvabea expresses EBOV GP, SUDV GP, TAFV NP, and MARV GP	GlaxoSmith Kline Okairos NIAID	• Single-dose and/or optional multivalent boost • Good safety profile, no SAE reports, mild-to-moderate reactogenicity • Can be administered to children (1 year and older) and adults • Uses chimpanzee-specific adenovirus to circumvent preexisting immunity to vector • Replication deficiency eliminates vaccine shedding concerns • At high dose (1e11 particles), can be used for reactive vaccination	• Lower predicted vaccine efficacy than Ervebo (approximately 60%–90% protection with high 1e11 dose no Mvabea boost based on nonhuman primate bridging data) • chAd3-EBOZ only targets EBOV • Optional Mvabea targets more virus species but is only indicated for EBOV • Higher doses of vaccine required for immunogenicity compared to Ervebo • Requires ≥60°C storage temperature for single-dose vials (stability at ≤60°C is 24 months), currently evaluating stability at other storage conditions • Antibody responses decreased by roughly half at 180 days after vaccination; booster recommended	• Not yet licensed by the US FDA or EMA • Phase II trials completed in Europe, the US, and Africa • Ongoing trials to explore safety and immunogenicity of other vaccine variations including multivalent, homologous, and heterologous combinations as well as shorter dosing intervals • Completed randomized, double-blind Phase II trial in adults: immediate vs. placebo + delayed (6 months) vaccination for adults • Completed randomized, observer blind Phase II trial in children: immediate Vx + Placebo (Meningococcal Vx) at 6 mo vs. Immediate placebo + Vx at month 6 for children • Durability with booster, antibody threshold of protection? • Immunogenicity in immunocompromised and HIV populations?
Ad5-EBOV Monovalent, expresses EBOV GP (Makona variant)	BIT CanSino (China)	• Single dose • Good safety profile, no SAE reports; adverse reactions mild and self-limiting • Storage at +2°C to +8°C for 12 months (2 vials of lyophilized powder + 1 vial of diluent)	• Only targets EBOV • Preexisting immunity to Ad5 vector may reduce the effectiveness of the vaccine • Only indicated for 18 to 60 years of age • No clinical efficacy data, only immunogenicity data • GP-specific antibodies decreased 85% at day 168	• Not licensed in the US, UK, or EU • Licensed in China based on Animal Rule by the Chinese Food and Drug Administration • Submitting to WHO for Emergency Use • Phase II—Assessment and Listing (EUAL) • Durability, antibody threshold of protection? • Immunogenicity in immunocompromised and HIV populations?
GamEvac-Combi and GamEvacLyo Heterologous prime-boost w/ rVSV and Ad5 expressing EBOV GP (Makona)	Gamaleya Research Institute of Epidemiology and Microbiology (Russia)	• Combo approach to take advantage of benefits of each platform (consists of rVSV and Ad5 expressing EBOV GP) • Stable at –16°C to –20°C for 12 months	• Only targets EBOV • 2 doses (prime + boost at 21 days) • Only indicated for 18 to 55 years • Preexisting immunity to Ad5 vector may reduce the effectiveness of the vaccine • No published clinical efficacy data, only immunogenicity data • Preexisting neutralizing Ad5 antibodies negatively influenced GP responses in half-dose but not the full-dose group	• Not licensed in the US, UK, or EU • Licensed by the Ministry of Health of the Russian Federation for emergency use in December 2015 based on Phase I and II safety and immunogenicity data • Completed Phase III trial in Guinea (Kindia) • Completed Phase IV trial in Russia • Durability, antibody threshold of protection? • Immunogenicity in immunocompromised and HIV populations?

Ebola.

The University of Oxford have begun recruiting for a Phase I trial to test an Ebola vaccine in human volunteers – with the first vaccinations having already taken place.

The study will assess the immune response and safety of the new vaccine against the Zaire and Sudan species of Ebola.

3 minute read · October 17, 2022 5:07 PM GMT+2 · Last Updated 5 days ago

Serum Institute to produce Ebola vaccine for use in Uganda outbreak

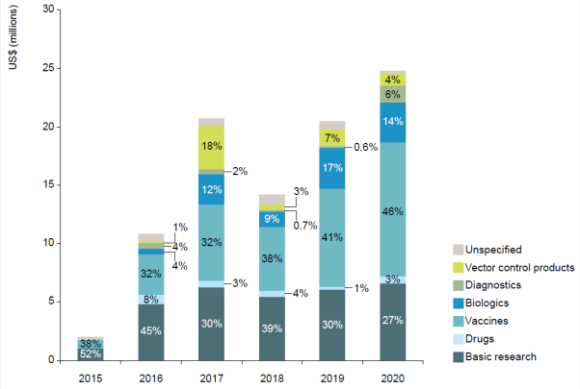
Crimea – Congo.

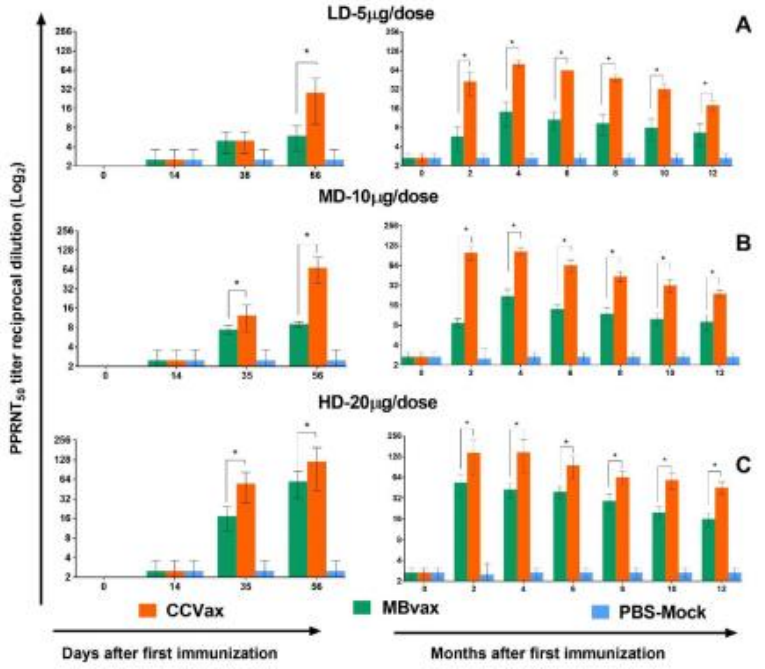
Crimea – Congo.

- L'única vacuna comercialitzada és la V42/81 a Bulgària.
- Inactivada, derivada de cervell de ratolí.
- 0 – 30d – 1 any i records cada 5 anys
- Recomenada a militars, personal sanitari, granjers, o persones que visquin o treballin en regions endèmiques de Bulgària

Papa A, Papadimitirou E, Crhistova I. Sthe Bulgarian vaccine Crimean-Congo haemorragic fever virus strain. can J Infect Dis, 2011; 43: 225-229

Crimea – Congo.





- La investigación sobre vacunas en cultivos celulares parece prometedora
- De igual forma el uso de plásmidos DNA i VLP

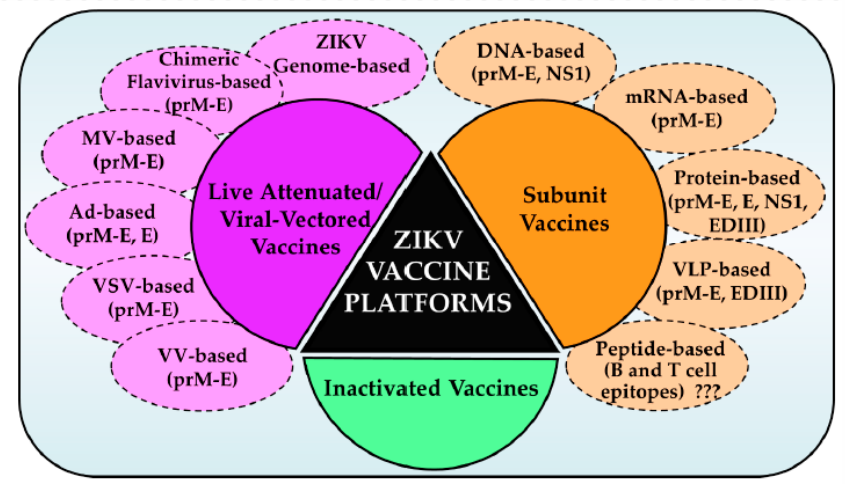
Berber E, Çanakoglu N, Tonbak S, Ozdarendeli A. Development of a protective inactivated vaccine against Crimean–Congo hemorrhagic fever infection. Heliyon 7 (2021) e08161. https://doi.org/10.1016/j.heliyon.2021.e08161

G-FINDER. Landscape of Emerging Infectious Disease Research and Development: From Pandemic Response to Pandemic Resilience. Policy Cures Research Report 2022. www.policycuresresearch.org

Zika.

Zika.

- Dificultats per assaijos clinics.
  - Transmisió heterogènia
  - Epidèmia difícil de pre-veure
  - Clínica amplia (objectiu?)?
  - Tests diagnòstics
- Investigació > 45 vacunes. Fase I - II



Pattnaik A, Sahoo B, Pattnaik A. Current Status of Zika Virus Vaccines: Successes and Challenges. Vaccines 2020, 8, 266; doi:10.3390/vaccines8020266

VACUNES

Zika.

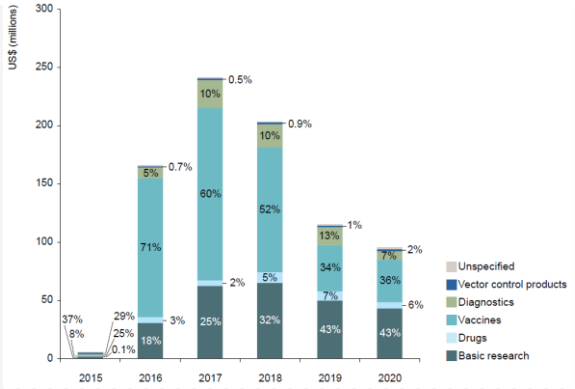


Table 1. ZIKV vaccine candidates and their status in clinical trials.

Platform	Vaccine Name	Sponsor	Antigen	Status in Clinical Trials	
				Phase 1	Phase 2
DNA	VRC5283	NIAID/VRC	prM-E	NCT02996461	NCT03110770
	VRC5288		prM-E	NCT02840487	
	GLS-5700	GeneOne Life Science, Inc./ Inovio Pharmaceuticals	prM-E	NCT02809443/ NCT02887482	
RNA	mRNA-1325	Moderna Therapeutics	prM-E	NCT03014089	
	mRNA-1893			NCT04064905	
Live Attenuated Viral Vectored	rZIKV/D4Δ30-713	NIAID	prM-E	NCT03611946	
	MV-ZIKV	Themis Bioscience GmbH	prM-sE	NCT02996890	
	MV-ZIKV-RSP		prM-E	NCT04033068	
	ChAdOx1 Zika	University of Oxford	prM-E	NCT04015648	
Inactivated Virus	ZPIV	NIAID/WRAIR/BIDMC	Whole virion	NCT02963909 NCT02952833 NCT02937233 NCT03008122	
	PZIV (TAK-246)	Takeda Pharmaceuticals	Whole virion	NCT03343626	
	BBV121	Bharat Biotech	Whole virion	CTRI/2017/05/ 008539	
	VLA1601	Valneva Austria GmbH/ Emergent Biosolutions	Whole virion	NCT03425149	

Platform | Vaccine Name | Sponsor | Antigen | Status in Clinical Trials | Phase 1 | Phase 2

Pattnaik A, Sahoo B, Pattnaik A. Current Status of Zika Virus Vaccines: Successes and Challenges. Vaccines 2020, 8, 266; doi:10.3390/vaccines8020266

Nipah.

Henipavirus

Virus Langya

- 2022
- Infecció respiratòria
- Xina
- 35 casos

Henipavirus

Virus Hendra

- 1994
- Infecció respiratòria i neurològica
- Cavalls i cuidadors (Austràlia)
- 7 casos humans

Virus Nipah

- 1998
- Infecció respiratòria i neurològica
- Porcí i cuidadors (Surest asiàtic)
- 600 casos (mortalitat 70%)

Virus Mojiang

- 2014
- Infecció respiratòria
- Xina
- 3 casos (morts)

Virus Langya

- 2022
- Infecció respiratòria
- Xina
- 35 casos

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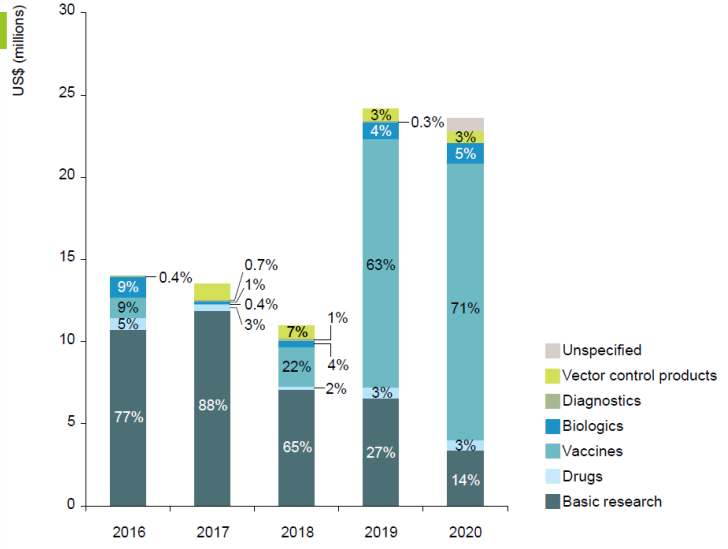
Nipah.

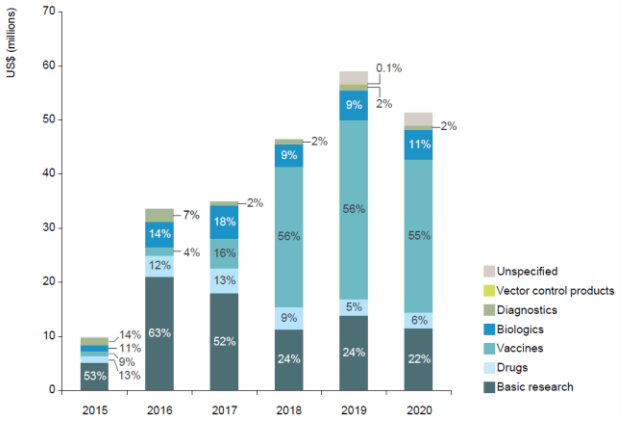


Study Type:	Interventional (Clinical Trial)
Estimated Enrollment:	60 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)
Masking Description:	Double-blind
Primary Purpose:	Prevention
Official Title:	A Phase 1 Randomized, Single Center, Double-Blind, Placebo-Controlled, Dose-Response Study to Evaluate the Safety and Immunogenicity of rVSV-Nipah Virus Vaccine Candidate PHV02 in Healthy Adult Subjects
Actual Study Start Date:	January 10, 2022
Estimated Primary Completion Date:	January 2023
Estimated Study Completion Date:	January 2024

Lassa

VACUNES

Lassa



IAVI announces first vaccinations at Liberia site in Phase I clinical trial of Lassa fever vaccine candidate

The trial is designed to evaluate the candidate's safety, tolerability, and immunogenicity

NEW YORK – AUGUST 31, 2022 – IAVI, a nonprofit

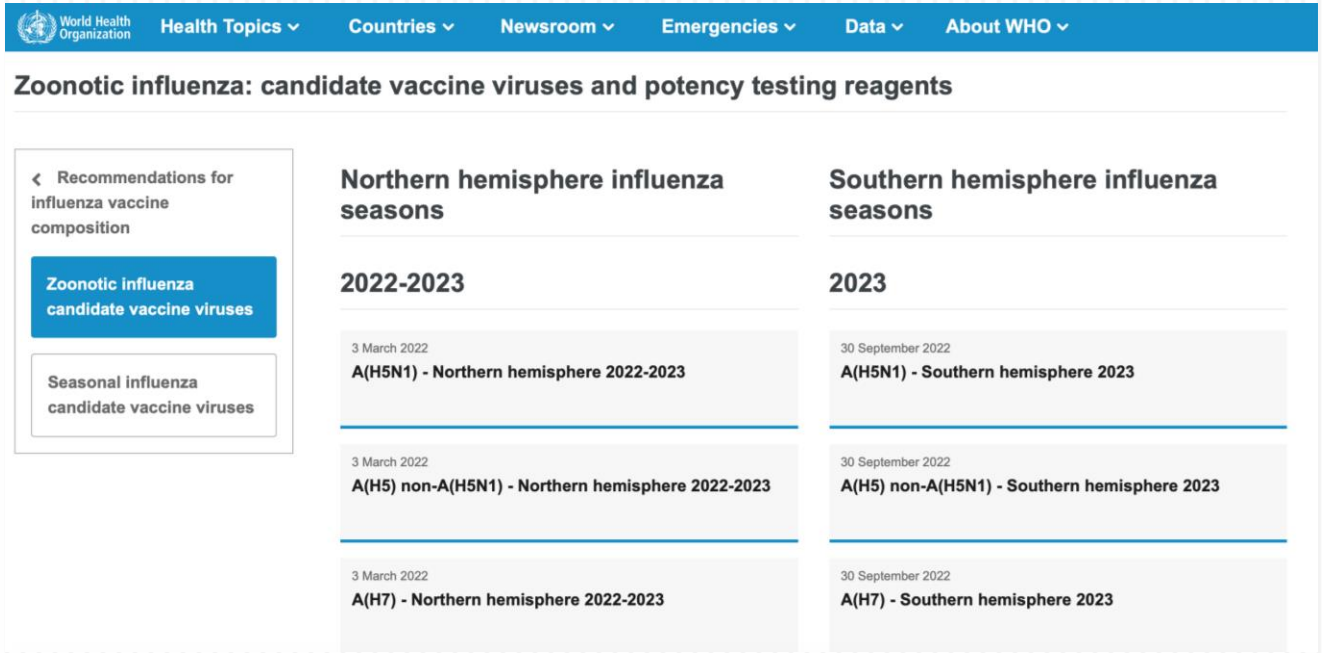
Gripe aviar.

EVALUACIÓN RÁPIDA DE RIESGO

Primera detección de gripe aviar A(H5N1) en humanos en España

4 de octubre de 2022

Gripe aviar.



https://www.who.int/teams/global-influenza-programme/vaccines/who-recommendations/zoonotic-influenza-viruses-and-candidate-vaccine-viruses

VACUNES

mRNA

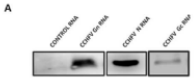
mRNA. Crimea-Congo

GA No. 732732: Start Date: 01/01/2017 End Date: 31/12/2022	CCHFVaccine

Nucleic acid based vaccines are emerging as promising alternatives to conventional live attenuated or subunit vaccines approaches. mRNA is rapid to produce, cannot integrate into the host genome, and generate protection at low doses.

We have designed mRNA molecules based on the genomic information generated within this project. Modified mRNAs encoding different CCHFV proteins have been synthesized in collaboration with the Weissman lab (University of Pennsylvania, USA). The modified mRNA has been packaged into lipid nanoparticles, transfected into mammalian cells and protein expression in cell lysate was analyzed by western blot (figure 1A).

To monitor the immunogenicity and productivity of the CCHFV mRNA particles, IFNAR KO mice have been immunized and challenged with CCHFV (Figure 1B). Our results show that all mRNA-vaccinated mice survived the viral challenge, while all control mice died within 4 days post challenge (figure 4 B)-(manuscript under preparation). This platform will be followed up by additional experiments and will be applied on other animal models.



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VACCINES AND ANTIVIRAL A

Nucleoside-Modified mRNA Vaccines Protect IFNAR$^{-/-}$ Mice against Crimean-Congo Hemorrhagic Fever Virus Infection

mRNA. Zika

VIROLOGY

Development of a potent Zika virus vaccine using self-amplifying messenger RNA

Article

mRNA Vaccine Protects against Zika Virus

mRNA. Malària

Hunting the ‘perfect protein’ for malaria mRNA vaccine

Scientists are working to establish the safety and efficacy of mRNA-based malaria vaccines. Clinical trials on the first mRNA-based malaria vaccine are set to start this year. Experts are optimistic of success but

Can mRNA Make a Difference in the Fight Against Malaria?

Evelina Angov, Chief, Laboratory of Molecular Parasitology, Walter Reed Army Institute of Research, believes mRNA vaccines could play an

mRNA. Dengue i Chikungunya

ARTICLES
https://doi.org/10.1038/s41591-021-01573-6
nature medicine
Check for updates

OPEN

A phase 1 trial of lipid-encapsulated mRNA encoding a monoclonal antibody with neutralizing activity against Chikungunya virus

Moderna scraps lead mRNA chikungunya candidate after phase 1, slowing push beyond prophylactic vaccines

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VACCINES AND ANTIVIRAL AGENTS

Check for updates

A Dengue Virus Serotype 1 mRNA-LNP Vaccine Elicits Protective Immune Responses

mRNA. Lassa, Nipah, Peste

Title: Development of a Modified mRNA-Based Vaccine for Lassa Virus

Descriptive Note: [Technical Report, Annual Report]

Corporate Author: University of Texas Medical Branch

Moderna has dosed the first participant in a Phase 1 trial of its Nipah virus vaccine candidate, mRNA-1215, that has been developed in collaboration with the US National Institutes of Health (NIH).

An Effective mRNA-LNP Vaccine Against the Lethal Plague Bacterium 1

CAMFiC
societat catalana de medicina familiar i comunitària

Moltes gràcies

javier.arranz@ibsalut.es