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Conseil Supérieur de la Santé

What's new in Vaccines?

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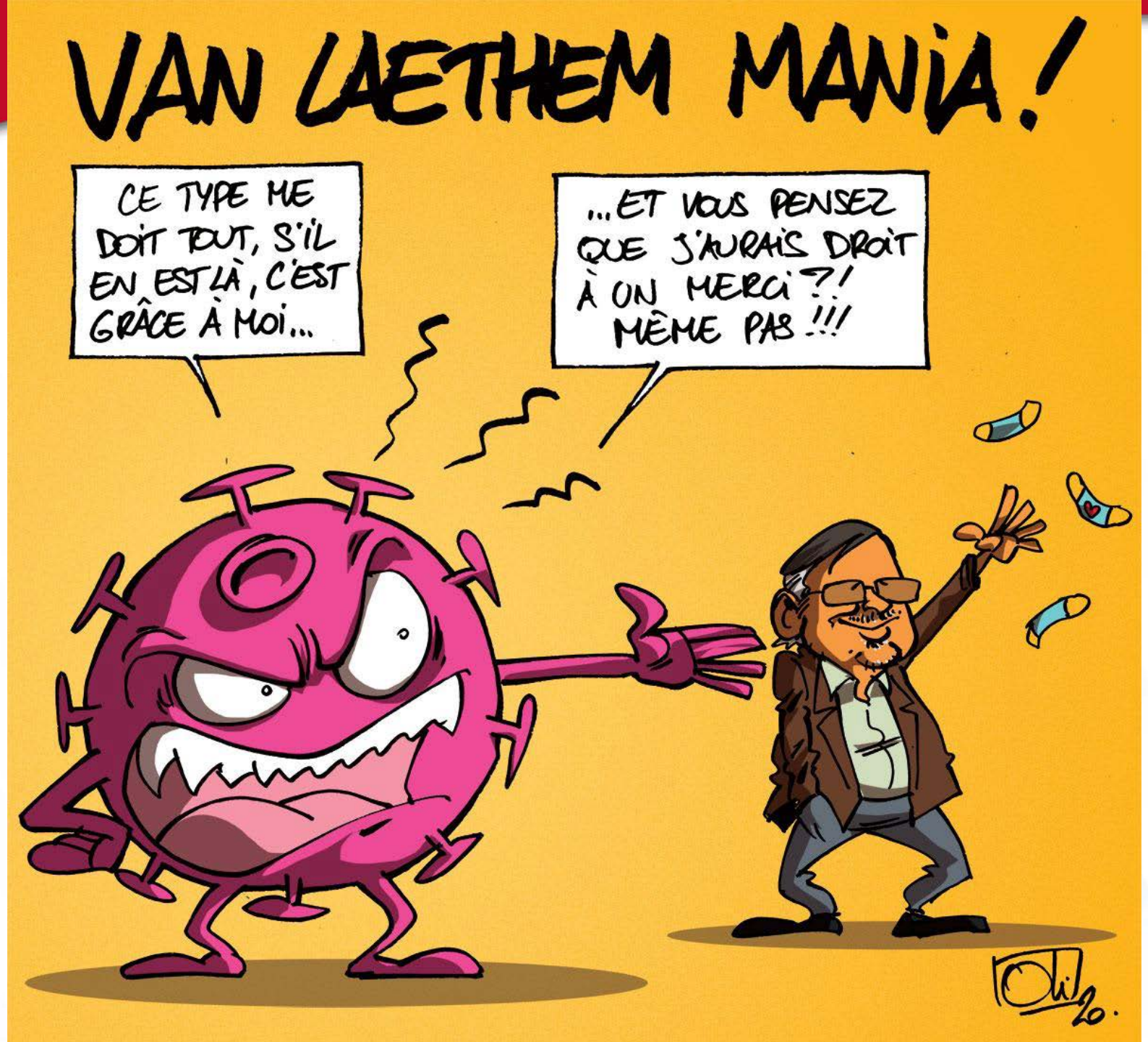
NITAG

National Immunization Technical Advisory Group

Co-presidents: Prof. S Callens /Prof. D Tuerlinckx
SHC secretariat: V Mertens / F Péters

VAN LAETHEM MANIA !



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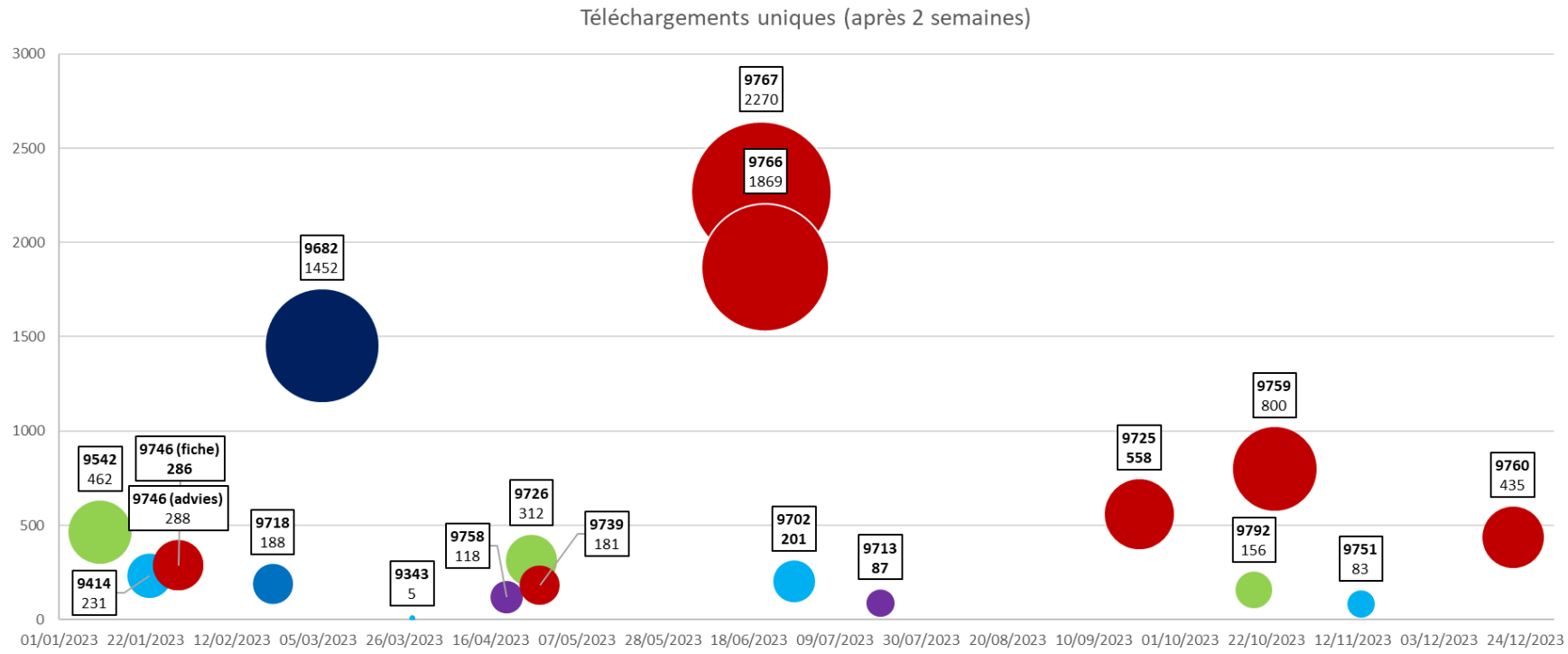
Published Advisory Reports

Published advisory reports 2023
Unique downloads / report

Adviesnummer	Titel
9760	RSV Kinderen
9759	Meningokokkenvaccinatie voor risicogroepen
9766	COVID-19 vaccinatie herfst-winterseizoen 2023-2024
9767	Vaccinatie seizoensgebonden griep: winterseizoen 2023-2024
9746	Vaccinatie van kinderen en adolescenten tegen pneumokokken
9725	Vaccinatie tegen RSV (volwassenen)
9739	Vaccinatie tegen dengue



Vaccination

Popular advisory reports CSS/HGR 2023

	N°	Sujet	Téléchargements uniques (01/01/-31/12)
1	9606	Basisvaccinatieschema	11 733
2	9766	COVID-19 booster 23-24	9224
3	9767	Seizoensgriep 23-24	2446
4	9674	Pneumo volwassen	1761
5	9682	Sterilisatie	1544
6	9768	OC RMG testing	1094
7	9759	Meningokokken	745
8	9284	FBDG	684
9	9725	RSV volwassenen	640
10	9746	Pneumo kinderen (advies+fiche)	557

7/10 => NITAG

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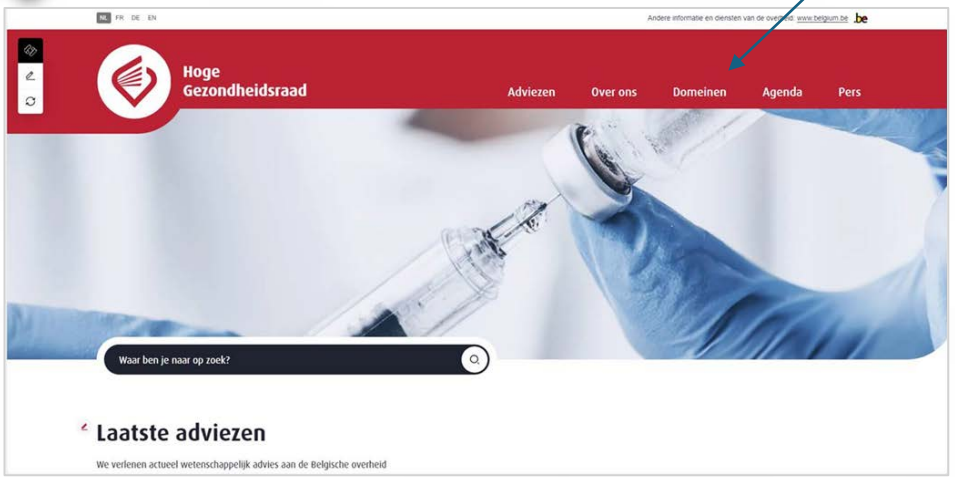
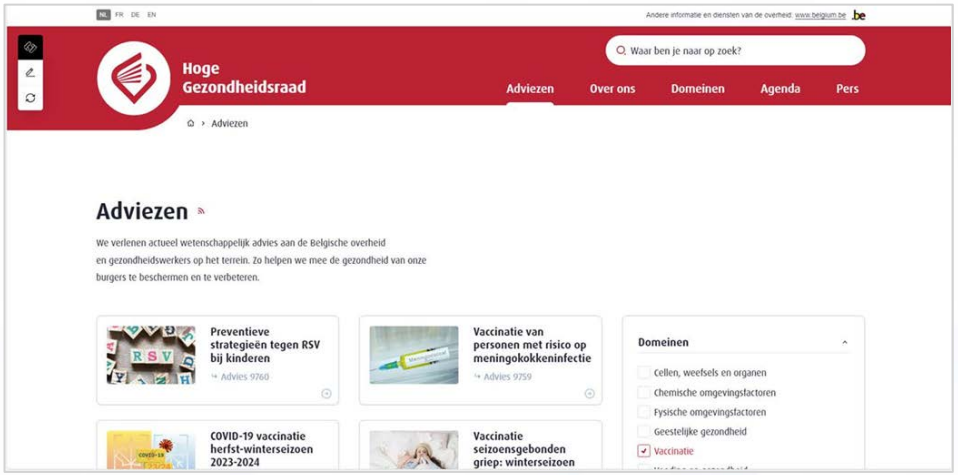
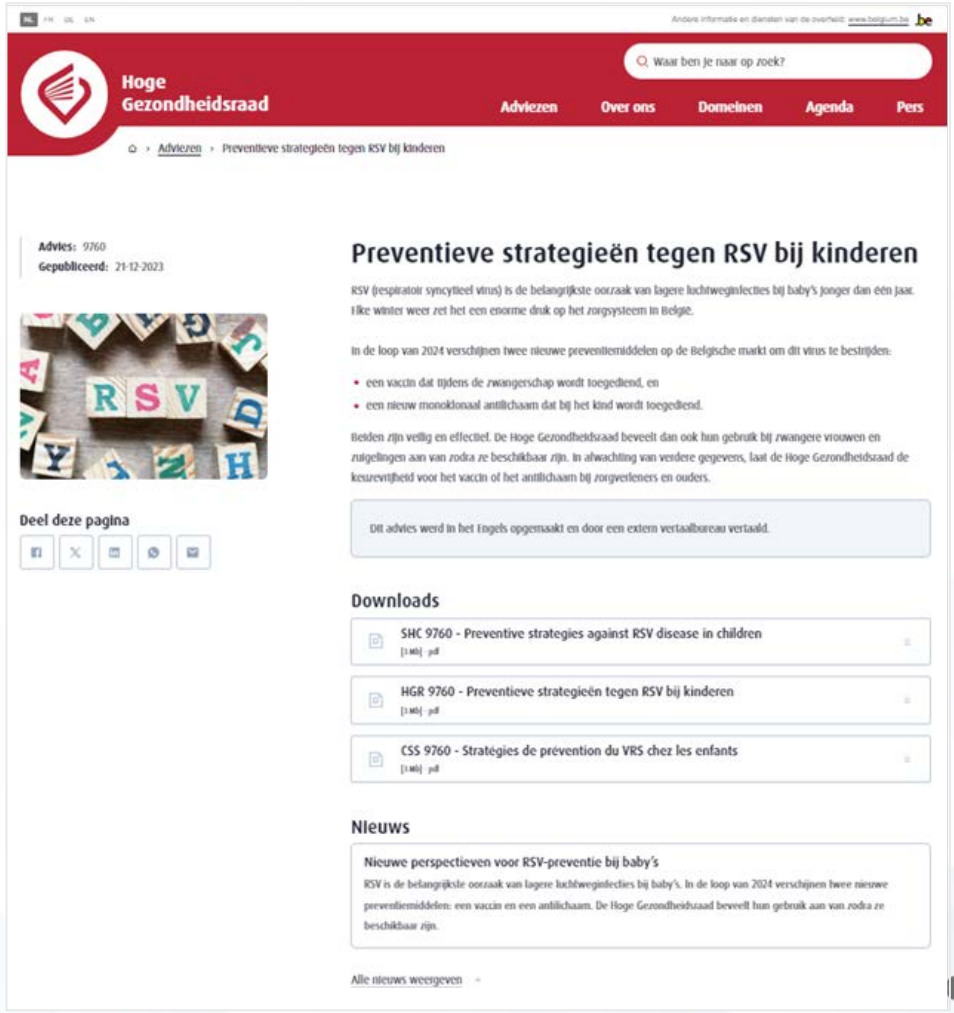
New Website and EU NITAG & GNN

New website CSS/HGR 2024 (mid May)







EU NITAG & GNN

EU NITAG: https://www.ecdc.europa.eu/en/about-us/partnerships-and-networks/national-immunisation-technical-advisory-groups-nitag

GNN: https://www.nitag-resource.org/network/map

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Progress and Plans for 2024

In progress/to start 2024

- Seasonal Influenza 2024-2025
- Mpox
- 2+1 Schedule
- Catch up vaccination
- COVID-19
- Revision RSV adult
- Revision RSV children
- Varicella
- MenABCWY
- Chikungunya
- Pneumococcal disease (children and adult)
- Vaccination of immunocompromised patients
- Vaccination of HCW

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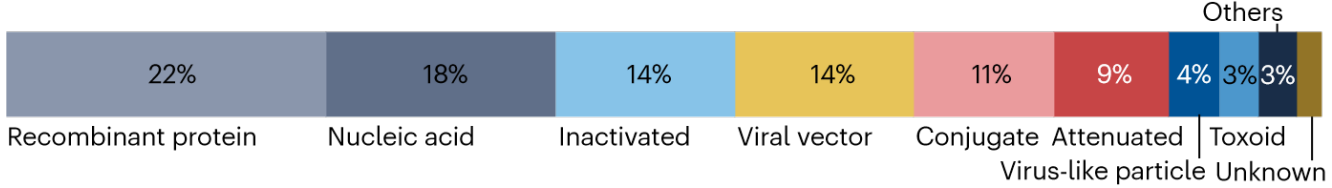
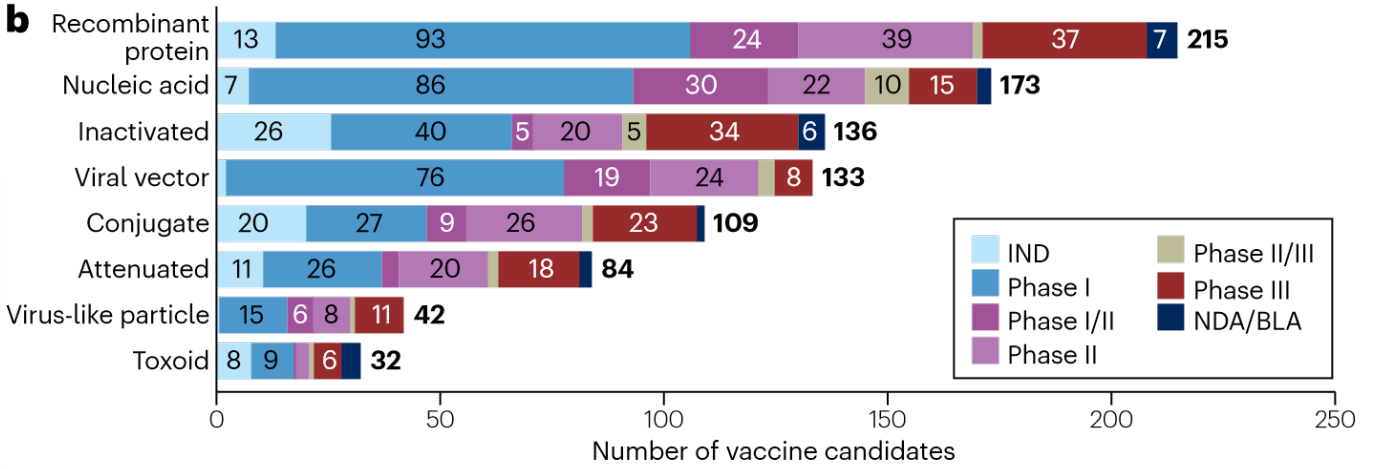
R&D Landscape for Infectious Disease Vaccines

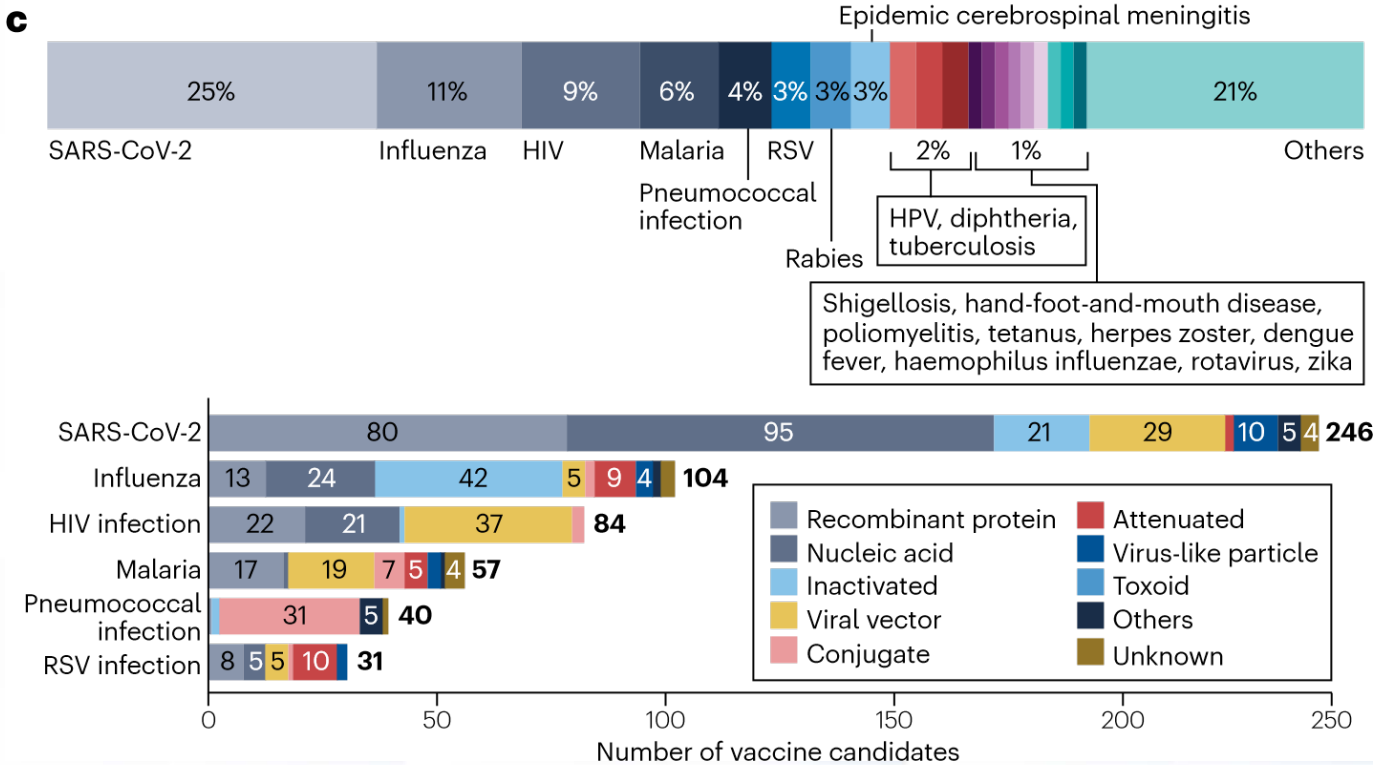
- The R&D landscape for infectious disease vaccines (nature.com)

Candidate Vaccines

- 246 candidates for SARS-CoV-2
  - 25% of total candidates
- 104 candidates for influenza
  - 11% of total candidates
- 84 candidates for HIV
  - 9% of total candidates







R&D distribution

- Vaccine R&D is mainly concentrated in the USA, China, and western Europe
- Technology platform preferences differ in these regions
  - US pipeline features more nucleic acid vaccines
  - China pipeline has more inactivated vaccines and fewer viral vector vaccines
- 68% of candidates are being developed by private companies/industry
- 25% are being developed by academic or other non-profit organizations
  - Candidates against HIV and malaria are mostly developed by academic or other non-profit organizations

Region	Number of Candidates	Technology Platform Preferences
USA	355	More nucleic acid vaccines
China	271	More inactivated vaccines, fewer viral vector vaccines
Western Europe	144	

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Seasonal Influenza Vaccines

Influenza

- Return to trivalent vaccines
- Overcoming immunosensescence
  - Adjunvanted & High dose vaccines
- Pandemic avian influenza

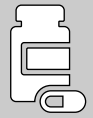
B/Yamagata antigen excluded from vaccines

[The End of B/Yamagata Influenza Transmission — Transitioning from Quadrivalent Vaccines | New England Journal of Medicine (nejm.org)]

- Initial influenza vaccines contained antigens from one type A and one type B virus.
- Post-1977: Introduction of trivalent vaccine including H1N1,H3N2, and one type B virus.
- Late 1980s: Discovery of two distinct type B lineages, B/Victoria and B/Yamagata.
- 1990s: B/Yamagata viruses predominated; decision to include in vaccines.
- 2000s: Reappearance of B/Victoria viruses, raising concerns about vaccine match.
- Development of quadrivalent vaccines in 2013 incorporating both B lineages.
- Continued cocirculation of both B lineages from 2011 to 2020.
- Disappearance of B/Yamagata lineage post-COVID-19 pandemic onset.
- **No confirmed global circulation of B/Yamagata viruses since March 2020**.

B/Yamagata antigen excluded from vaccines

B/Yamagata antigen excluded



FDA and global regulatory bodies lean towards returning to trivalent vaccines

WHO efforts to exclude B/Yamagata antigen as soon as possible

Enhanced Influenza Vaccines: Overcoming Immunosenescence

Immunosenescence: molecular mechanisms and diseases (nature.com)

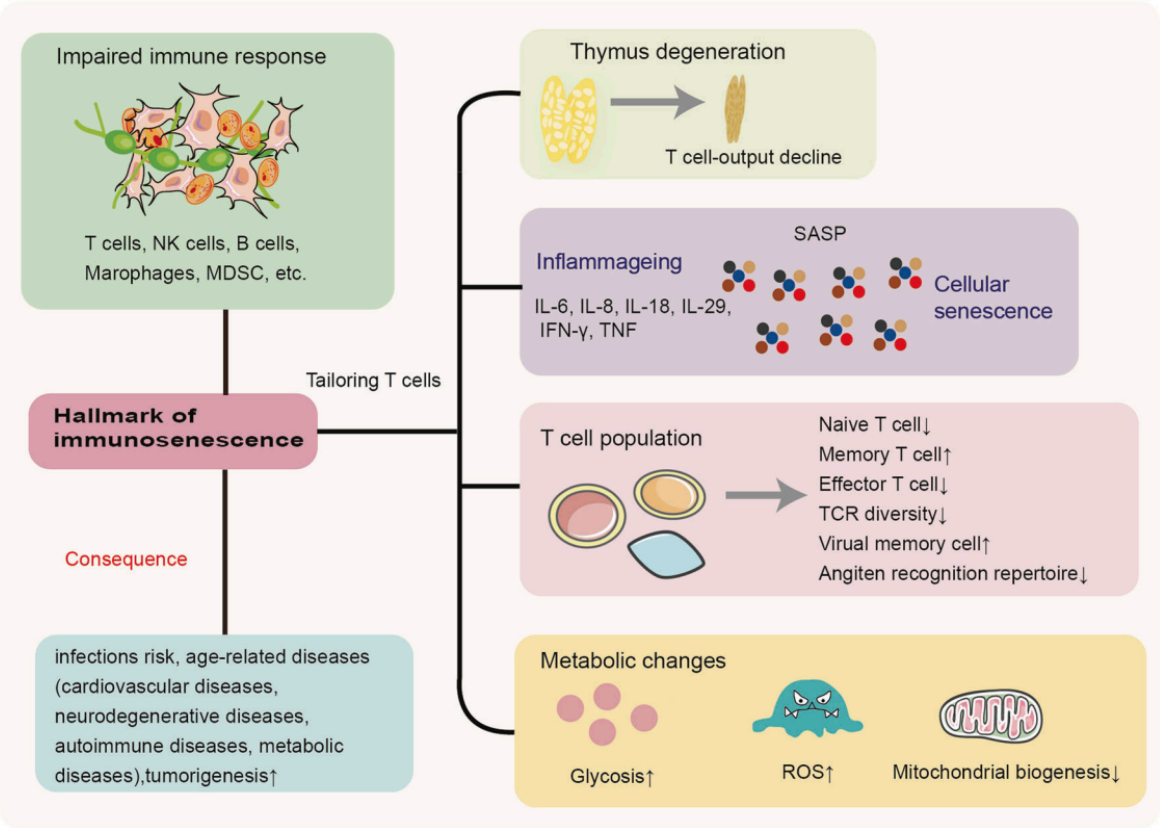


Fig. 2 Hallmarks of immunosenescence and related diseases. Various immune cell subsets changed during immunosenescence. There were significant changes in T-cell subpopulations, including a decline in T-cell production associated with age due to thymic degeneration, abnormal T-cell metabolism, changes in the proportion of T subpopulations, and an SASP-mediated chronic low-grade inflammatory environment. IFN-γ interferon-γ, IL-6 interleukin-6, IL-8 interleukin-8, IL-18 interleukin-18, IL-29 interleukin-29, MDSC myeloid-derived suppressor cells, NK cells natural killer cells, ROS reactive oxygen species, SASP senescence-associated secretory phenotype, TCR T-cell receptor, TNF tumor necrosis factor

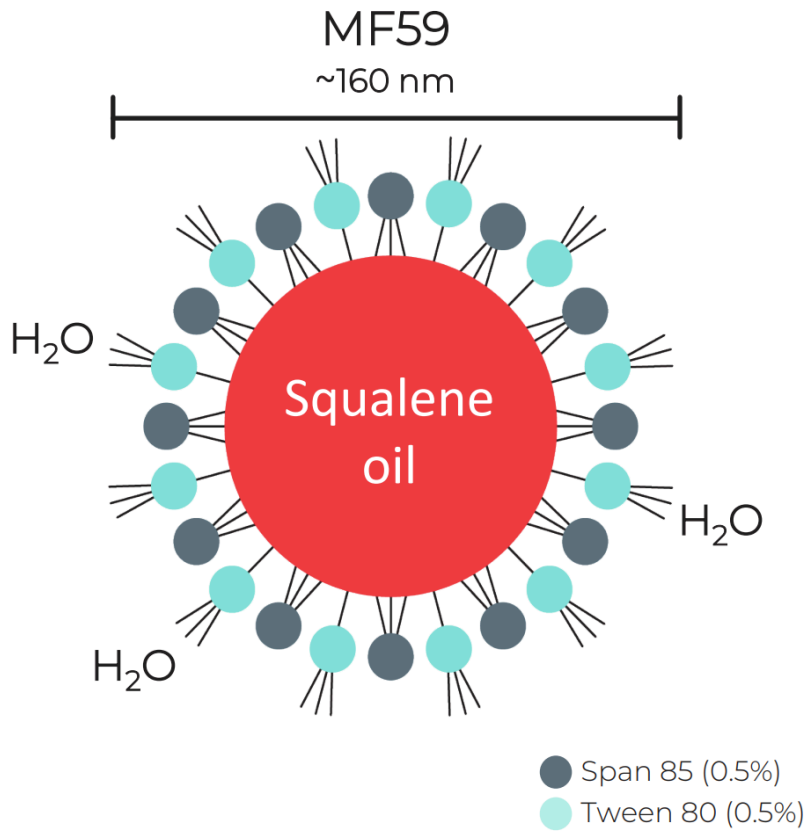
- Different technologies have been developed to overcome immunosenescence.
  - **Adjuvanted vaccines** designed for a more robust, durable and broader immune response.
  - **High-dose vaccines** contain more antigen to increase the size of the immune response.
  - …

1. Wong S-S & Webby RJ. Clin Microbiol Rev. 2013;26:476-92; 2. Wei C, et al. Nat Rev Drug Discov. 2020;19:239-52; 3. Scorza FB & Pardi N. Vaccines (Basel). 2018;6:20;

Systematic review update on the efficacy, effectiveness and safety of newer and enhanced seasonal influenza vaccines for the prevention of laboratory confirmed influenza in individuals aged 18 years and over (europa.eu)

The update included 59 studies, adding 17 new studies on effectiveness and safety

MF59-adjuvanted vaccine



- For the MF59-adjuvanted vaccine, the relative effectiveness (rVE) against lab-confirmed influenza ranged from -30% to 88%
- The rVE against hospitalization related to influenza was 59.2%
- There were no data on rVE against influenza-related mortality
- No increased risk of serious adverse effects was found for the MF59-adjuvanted vaccine

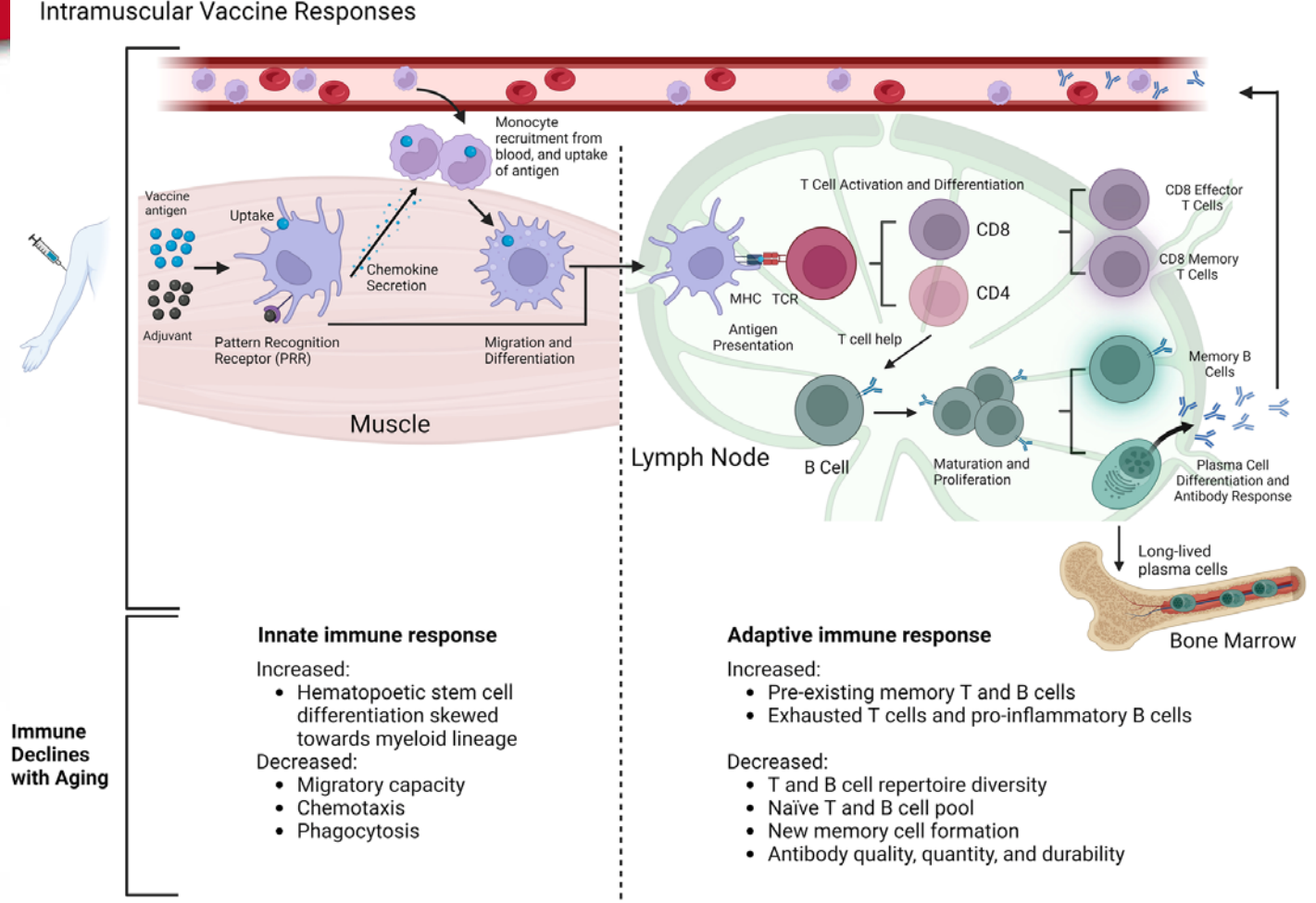
High-Dose Vaccine

The high-dose vaccine showed an rVE of 24.2% against lab-confirmed influenza

The rVE against hospitalization related to influenza was 27%

No increased risk of serious adverse effects was found for the high-dose vaccine

[Targeting the hallmarks of aging to improve influenza vaccine responses in older adults | Immunity & Ageing | Full Text (biomedcentral.com)]



Hallmark of Aging	Effect on Immune Response	Potential Effects on Vaccine Response
Inflammation	Increased exhausted/activated NK, T, & B cells Altered T cell differentiation Increased pro-inflammatory monocytes/macrophages	Improved antigen presentation Improved T cell differentiation, B cell responses, and antibody generation
Cellular Senescence	Accumulation of senescent cells in multiple tissues Increased inflammation due to senescence associated secretory phenotype (SASP)	Improved microenvironment within tissue to promote coordinated vaccine responses Improved regulation of immune cell differentaition
Mitochondrial Dysfunction	Decreased metabolic regulation (p38 MAPK, AMPK, p53), and antioxidant defense Increased activation of NLRP3 inflammasome	Improved T and B cell differentiation and function Reduced chronic inflammasome activation
Microbiome Disturbances	Increased gut permeability leading to increased systemic inflammation Altered immune signaling due to gut microbiota alterations	Reduced systemic inflammation from improved gut integrity Balanced microbiome to promote coordinated immune cell signaling and vaccine responses
Other Potential Targets	Decreased autophagy impacting immune cell responses Decreased stemness reducing proliferation and expansion Skewing towards myeloid lineage resulting in decreased naive lymphoid cell populations	Improved immune cell function, proliferation, and expansion Improved immune cell communication and coordinated vaccine responses to promote antibody responses

DaniFlu study

[A Pragmatic Randomized Feasibility Trial of Influenza Vaccines | NEJM Evidence]

Pragmatic, open-label, active-controlled, randomized feasibility trial	Conducted in Danish citizens aged 65 to 79 years during the 2021–2022 influenza season
Participants randomly assigned 1:1 to receive QIV-HD or QIV-SD	Randomization integrated into routine vaccination practice Trial relied solely on nationwide administrative health registries for data collection
Registry-based data collection was feasible	Complete follow-up data for 99.9% of participants
Lower incidence of hospitalization for influenza or pneumonia in QIV-HD group	rVE, 64.4%; 95% confidence interval, 24.4 to 84.6
Lower all-cause mortality in QIV-HD group	rVE, 48.9%; 95% confidence interval, 11.5 to 71.3

Conclusion of the ECDC systematic review

- The evidence base for vaccine effectiveness against lab-confirmed outcomes has not substantially improved
- There is a larger evidence base available on safety, showing a generally favorable safety profile
- Further research is needed, particularly regarding lab-confirmed outcomes and safety data
- The conclusion is that the evidence base for the relative effectiveness of newer and/or improved influenza vaccines remains limited

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Avian H5N1 Influenza

Avian H5N1 Influenza

- The outbreak of H5N1 avian influenza among American dairy cows has spread to at least 33 herds in eight states.
- There is only one confirmed human case, but experts warn that the situation could escalate rapidly.
- Questions remain about how the infection spreads, and there is a lack of transparency and consistency in testing cattle.

Human case: HPAI A(H5N1)

Human Case:

- An adult dairy farm worker in Texas contracted HPAI A(H5N1) in April 2024.
- The worker likely got infected from sick cows on the farm.
- Only experienced conjunctivitis (eye inflammation) and no other symptoms.
- The virus strain was similar to those found in other Texas dairy cattle farms.
- The worker recovered with antiviral medication and there were no further cases among their contacts.

HPAI A(H5N1) in Humans:

- Since January 2022, most human cases had contact with sick or dead poultry.
- Human-to-human transmission is not reported.
- Some cases, including children, experienced severe illness or death.
- The identified virus strains were susceptible to existing antiviral medications.

Genetic Changes and Mammalian Adaptation:

- HPAI A(H5N1) clade 2.3.4.4b virus can change within an infected mammal like a human.
- Some genetic markers linked to mammalian adaptation were found in recent human cases.
  - Change in PB2 E627K associated with viral adaptation to mammalian hosts
- Despite these changes, the virus still struggles to infect humans efficiently.
  - Lacked changes in hemagglutinin gene affecting receptor-binding specificity

Highly Pathogenic Avian Influenza A(H5N1) Virus Infection in a Dairy Farm Worker | New England Journal of Medicine (nejm.org)

AUDENZ | FDA

- STN: 125692
  Proper Name: Influenza A (H5N1) Monovalent Vaccine, Adjuvanted
  Tradename: AUDENZ
  Manufacturer: Seqirus, Inc.
  Indication:
  - AUDENZ is an inactivated vaccine indicated for active immunization for the prevention of disease caused by the influenza A virus H5N1 subtype contained in the vaccine.
  - AUDENZ is approved for use in persons 6 months of age and older at increased risk of exposure to the influenza A virus H5N1 subtype contained in the vaccine.

Incellipan | European Medicines Agency (europa.eu) (conditional)

- Incellipan is a pandemic influenza vaccine (H5N1).
  - It is a surface antigen, inactivated, adjuvanted, and prepared in cell cultures.
- It is authorized for use in the European Union.
- Effective against H5N1 subtype of influenza A virus

Study	Participants	Doses	Antibodies after 3 weeks	Antibodies after 6 months
Main Study	3,200 adults	2 doses, 3 weeks apart	67%	12%
Children Study	330 children	2 doses, 3 weeks apart	96%	N/A

Celldemic | European Medicines Agency (europa.eu)

- Celldemic suspension for injection in pre-filled syringe
  - Zoonotic influenza vaccine (H5N1)
  - Surface antigen, inactivated, adjuvanted, prepared in cell cultures
- Influenza virus surface antigens: haemagglutinin and neuraminidase
  - Inactivated strain: A/turkey/Turkey/1/2005 (H5N1)-like strain (NIBRG-23) (clade 2.2.1)
  - 7.5 micrograms per 0.5 ml dose
  - Propagated in Madin Darby Canine Kidney (MDCK) cells
  - Expressed in micrograms haemagglutinin

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COVID19

Persbericht bij het advies COVID-19-vaccinatie in 2024 | Persbericht | Gezondheidsraad (Nederland)

- **Vaccination advice for 2024:**
  - People over the age of 60, medical risk groups and healthcare workers who have direct contact with vulnerable patients.
- **No vaccination offer for pregnant women:**
  - The risk of severe illness and premature birth is very low due to the built-up immunity of the population against the current virus variants.
- **More efforts to reach target audiences:**
  - These should be able to choose whether or not to make use of the offer. In 2023, the participation rate among certain groups was relatively low.
- **No vaccination to prevent post-COVID:**
  - The Council does not think this is desirable because it is unclear how many cases of post-COVID can be prevented with vaccination.

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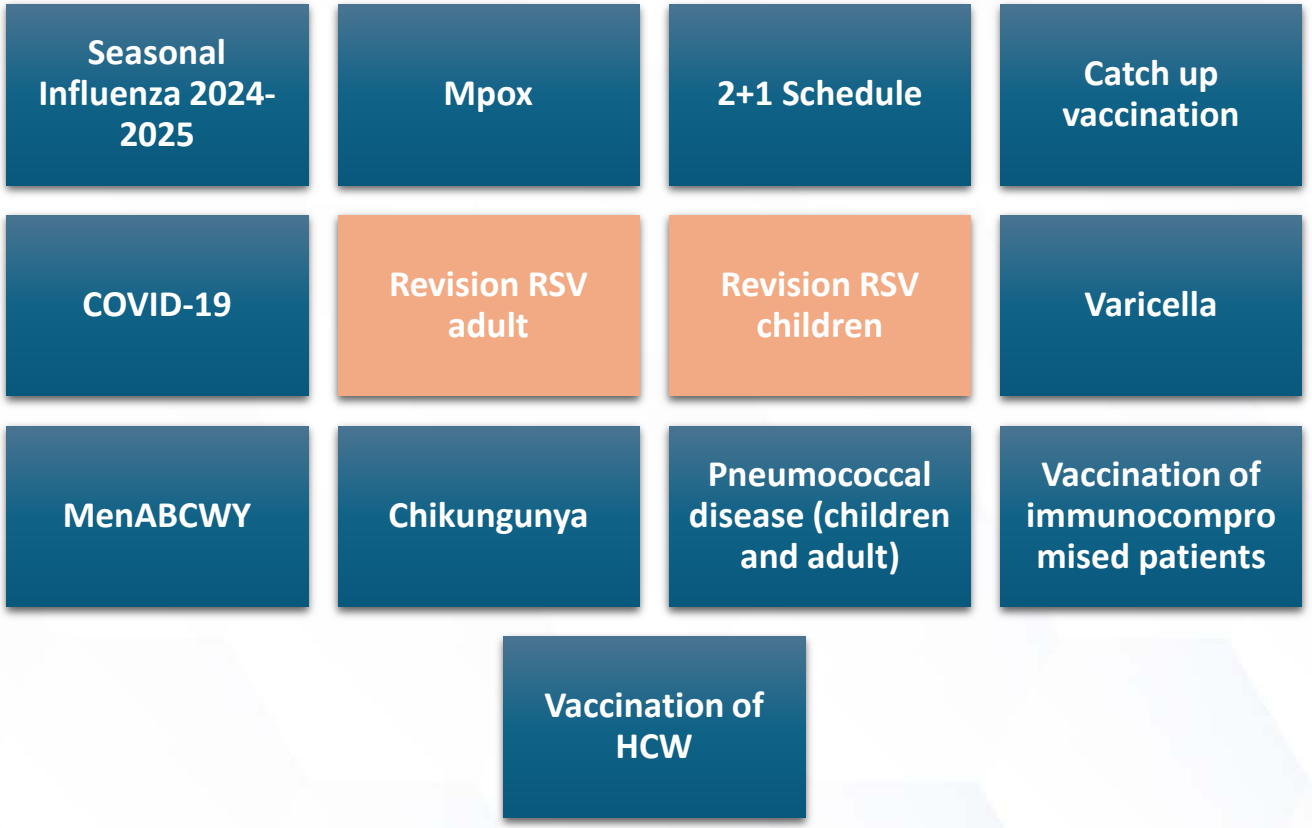
RSV

In progress/to start 2024

Update on RSV



RSV

- Neonates :Advisory 9760 - Prevention against RSV in children
- Adults: Season 2 data available

RSV neonates

Nirsevimab (Beyfortus®)

Vaccin (Abrysvo®)

- RSV is a leading cause of morbidity and death in babies worldwide.
- In Belgium, approximately 14,500 RSV infections lead to 3,200 to 3,600 hospital admissions each year.
- Prevention has been limited to Palivizumab, but new options such as Nirsevimab and Abrysvo® offer hope.
- Nirsevimab provides five months of protection with one dose, while Abrysvo® provides protection to babies through vaccination of pregnant women.
- Both products were recommended for the 2023-2024 winter season, with freedom of choice for caregivers and parents.

Nieuwe hoop

Nirsevimab (Beyfortus®)

Vaccin (Abrysvo®)

- Vaccin voor zwangere vrouwen
- 1 prik tussen 28-36 weken zwangerschap
- Minimum 6 maanden bescherming na geboorte
- Effectiviteit: ↓ risico op RSV-
  - Ernstige infectie met 69 %
  - ziekenhuisopname met 57 %

Nieuwe hoop

Nirsevimab (Beyfortus®)

Vaccin (Abrysvo®)

- Nieuw langwerkend monoklonaal antilichaam voor zuigelingen
- 1 prik bij de geboorte tijdens of net voor het RSV-seizoen
- Minimum 5 maanden bescherming na prik
- Effectiviteit: ↓ risico op RSV-
  - infectie met 75%
  - ziekenhuisopname met 79%

Use of Respiratory Syncytial Virus Vaccines in Older Adults: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023 | MMWR (cdc.gov)

TABLE 1. Efficacy of 1 dose of GSK respiratory syncytial virus RSVpreF3 vaccine against respiratory syncytial virus–associated disease among adults aged ≥60 years — multiple countries, 2021–2023

Efficacy evaluation period	Vaccine efficacy against outcome*	
	RSV-associated LRTD†	RSV-associated medically attended LRTD§
Season 1¶	82.6 (57.9–94.1)**	87.5 (58.9–97.6)††
Season 2§§	56.1 (28.2–74.4)††	—¶¶
Combined seasons 1 and 2 (interim)* **	74.5 (60.0–84.5)†††	77.5 (57.9–89.0)††

TABLE 3. Efficacy of 1 dose of Pfizer respiratory syncytial virus RSVpreF vaccine against respiratory syncytial virus–associated disease among adults aged ≥60 years — multiple countries, 2021–2023

Efficacy evaluation period	Vaccine efficacy against outcome, % (95% CI)*	
	RSV-associated LRTD†	RSV-associated medically attended LRTD§
Season 1¶	88.9 (53.6–98.7)	84.6 (32.0–98.3)
Season 2 (interim)**	78.6 (23.2–96.1)	—††
Combined seasons 1 and 2 (interim)§§	84.4 (59.6–95.2)	81.0 (43.5–95.2)

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Pneumococcal Disease

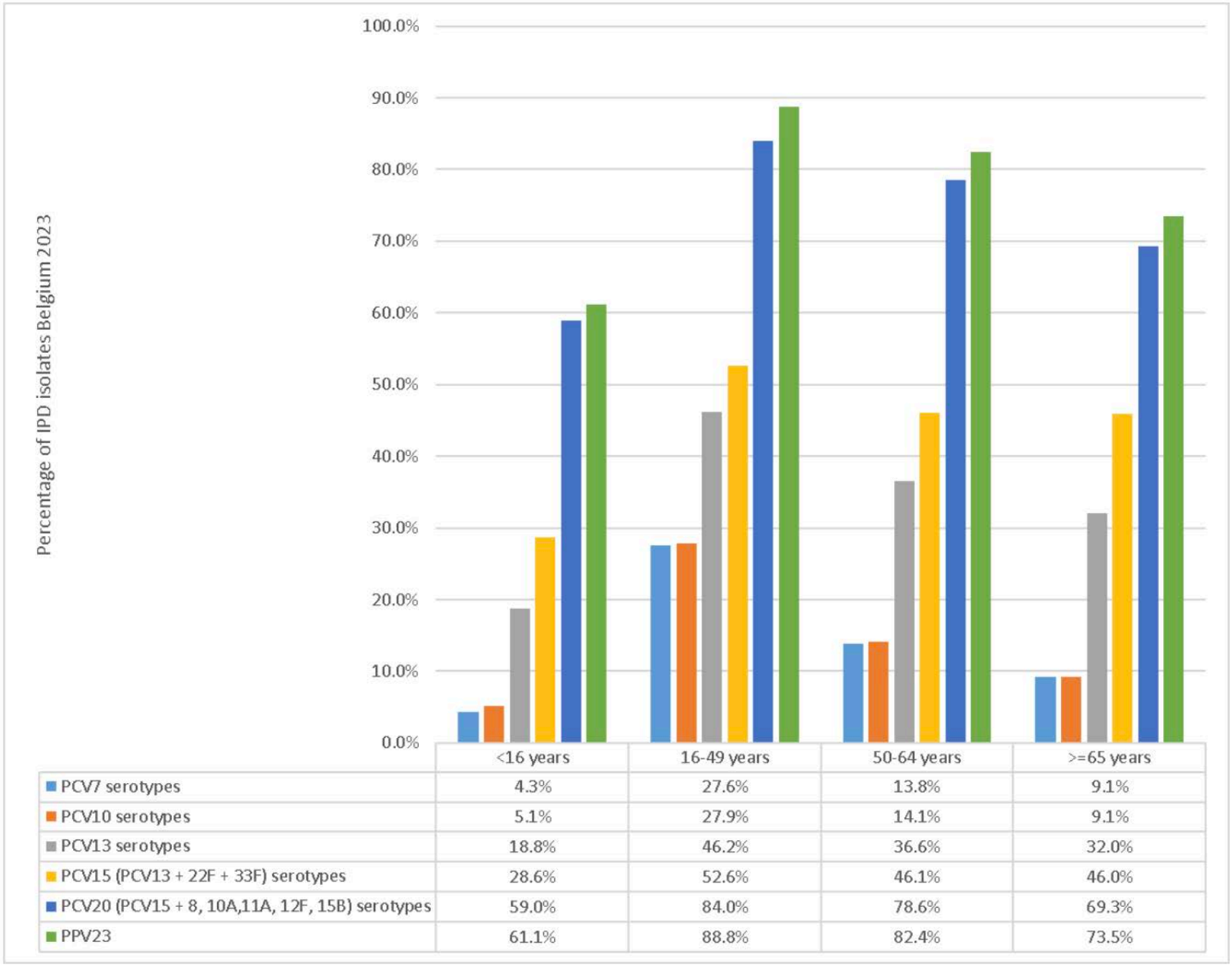
Pneumococcal Vaccines

- The recent approval of PCV20 by the EMA for children
- The use of PCV13 in a 1+1 schedule in the UK
- The development of a new complementary vaccine for adults (PCV21-VII6)
- Other pneumococcal vaccines in the pipeline

PCV20 Approved by EMA for Children

- PCV20 is now approved by the EMA for children aged 2-23 months. (3+1 schedule)
- In Belgium, 45% of all IPD cases in children under 2 years of age in 2023 were caused by PCV20-non-PCV13 serotypes.

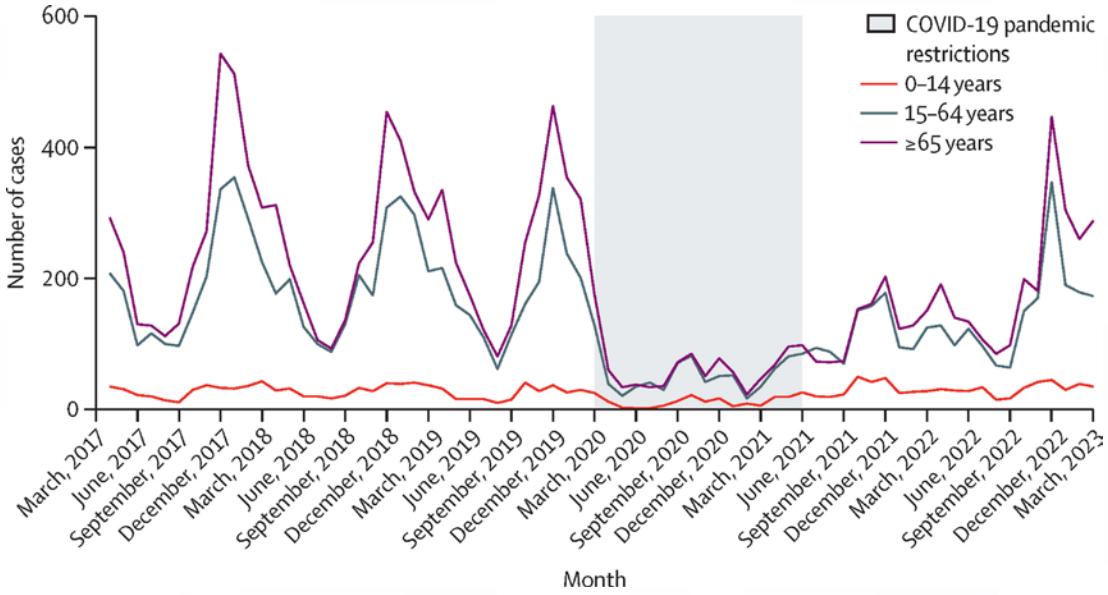
Serotype coverage of the current authorized pneumococcal vaccines per age group based on the invasive pneumococcal disease isolates received at the National Reference Centre in 2023



	<16 years	16-49 years	50-64 years	>=65 years
PCV7 serotypes	4.3%	27.6%	13.8%	9.1%
PCV10 serotypes	5.1%	27.9%	14.1%	9.1%
PCV13 serotypes	18.8%	46.2%	36.6%	32.0%
PCV15 (PCV13 + 22F + 33F) serotypes	28.6%	52.6%	46.1%	46.0%
PCV20 (PCV15 + 8, 10A,11A, 12F, 15B) serotypes	59.0%	84.0%	78.6%	69.3%
PPV23	61.1%	88.8%	82.4%	73.5%

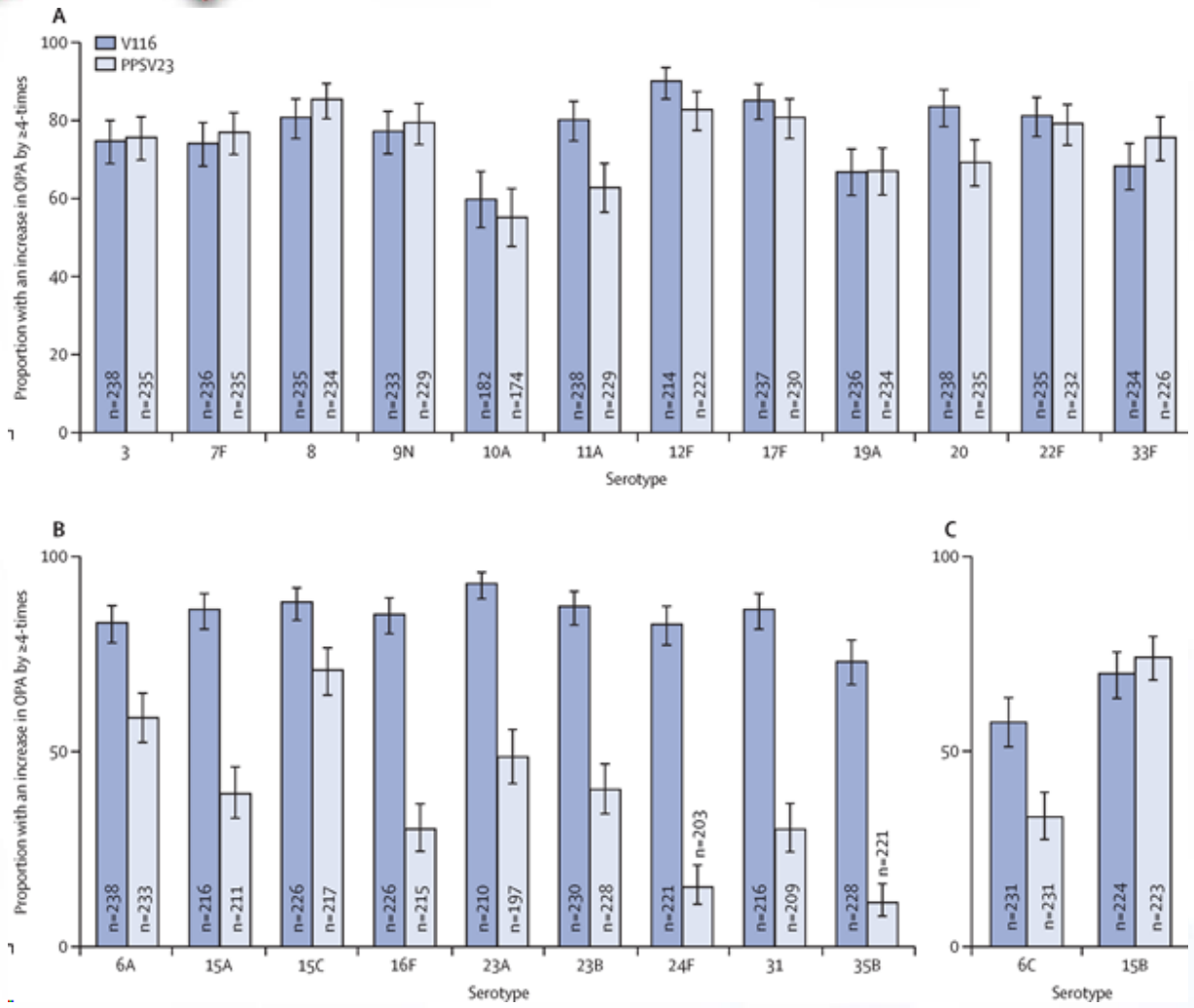
[Invasive pneumococcal disease 3 years after introduction of a reduced 1 + 1 infant 13-valent pneumococcal conjugate vaccine immunisation schedule in England: a prospective national observational surveillance study - The Lancet Infectious Diseases]

Invasive pneumococcal disease cases by month and age group, 2017–18 to 2022–23



- The UK was the first country worldwide to implement a reduced 1 + 1 PCV immunisation schedule nationally on Jan 1, 2020.
- Children receive two doses of PCV13: one at 2 months of age and one at 12-15 months of age.
- Early data suggests that this schedule is as effective as the 2+1 schedule, which was previously used in the UK.

Safety, tolerability, and immunogenicity of a 21-valent pneumococcal conjugate vaccine, V116, in healthy adults: phase 1/2, randomised, double-blind, active comparator-controlled, multicentre, US-based trial - The Lancet Infectious Diseases



- A new complementary vaccine for adults, PCV21-VII6, is in development
- Specifically designed to protect against serotypes of pneumococcus that are common in adults.
- PCV21-VII6 is expected to be available in the next (few) year(s).

V116 is an **adult specific** pneumococcal conjugate vaccine (PCV)

- Includes **21 pneumococcal serotypes**, 4µg/PnPs individually conjugated to CRM197 formulated without an adjuvant
- Single dose, 0.5mL **pre-filled syringe**, intramuscular injection for adults 18+
- The serotypes in V116 accounted for **~85% of IPD** and the **8 unique serotypes accounted for ~30%** of IPD in US adults ≥65 years in 2019
- V116 is currently under **Priority Review** by the FDA for the prevention of IPD and pneumonia in adults ≥18 years of age with target action date of June 17, 2024.

	Serotype Composition																												
PCV13	4	6B	9V	14	18C	19F	23F	1	3	5	6A	7F	19A																
PCV15	4	6B	9V	14	18C	19F	23F	1	3	5	6A	7F	19A	22F	33F														
PPSV23	4	6B	9V	14	18C	19F	23F	1	3	5		7F	19A	22F	33F	2	8	9N	10A	11A	12F	15B	17F	20					
PCV20	4	6B	9V	14	18C	19F	23F	1	3	5	6A	7F	19A	22F	33F		8		10A	11A	12F	15B							
V116									3		6A	7F	19A	22F	33F		8	9N	10A	11A	12F		17F	20A	15A	15C	16F	23A	23B	24F	31	35B

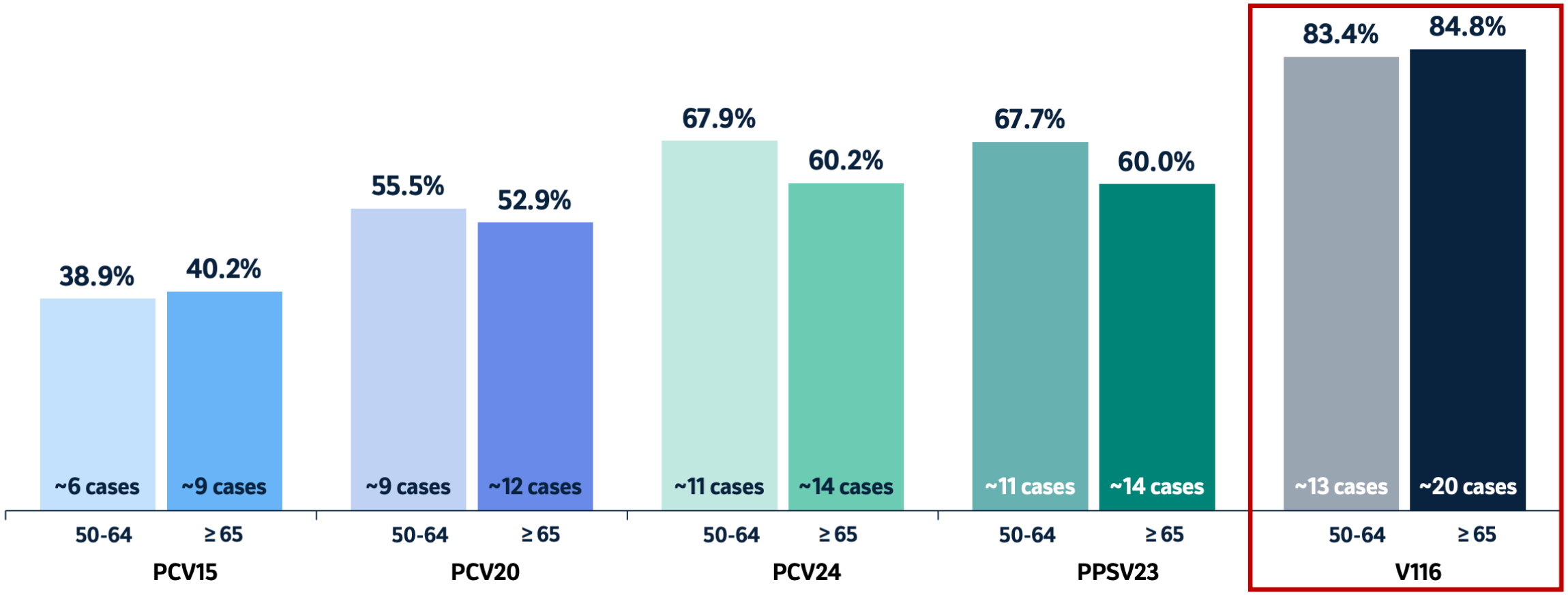
IPD, invasive pneumococcal disease; PCV, pneumococcal conjugate vaccine; PCV13, pneumococcal conjugate vaccine, 13-valent; PCV15 pneumococcal conjugate vaccine, 15-valent, PCV20, pneumococcal conjugate vaccine, 20-valent.

1. **CDC**, IPD Serotype Data 2019, as compiled from data provided through Active Bacterial Core surveillance (ABCs).
2. 2. **Platt H**, Omole T, Cardona J, Fraser NJ, Mularski RA, Andrews C, Daboul N, Gallagher N, Sapre A, Li J, Polis A, Fernsler D, Tamms G, Xu W, Murphy R, Skinner J, Joyce J, Musey L. Safety, tolerability, and immunogenicity of a 21-valent pneumococcal conjugate vaccine, V116, in healthy adults: phase 1/2, randomised, double-blind, active comparator-controlled, multicentre, US-based trial. Lancet Infect Dis. 2023 Feb;23(2):233-246. https://pubmed.ncbi.nlm.nih.gov/36116461/

15C is denoted here to represent the serotype protection proposed with deOAc15B as the molecular structures for deOAc15B and 15C are similar (Jones C, Lemercinier X. 2005. Full NMR assignment and revised structure for the capsular polysaccharide from Streptococcus pneumoniae type 15B. *Carbohydr Res* 340:403-409.)

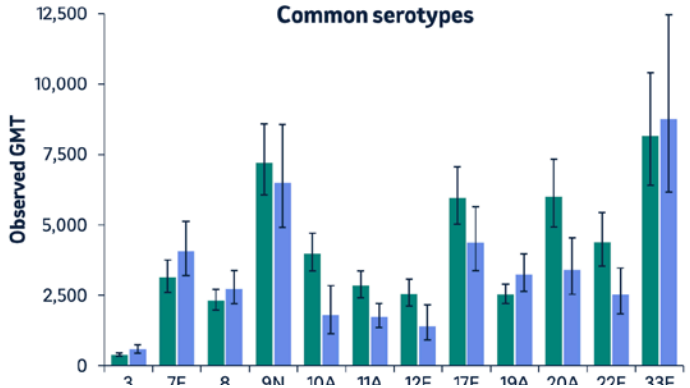
In adults 50–64 and ≥65 years of age, serotypes in V116 are responsible for the majority of residual IPD in adults

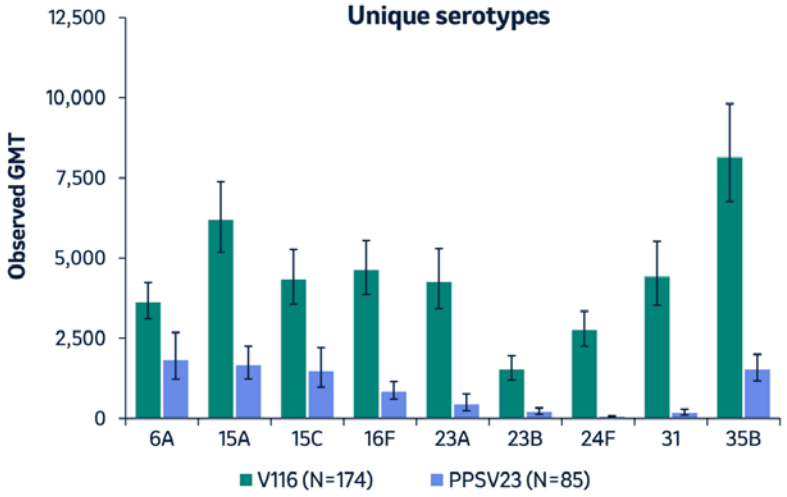
IPD coverage (% of serotypes and cases per 100,000) in US Adults 50–64 and ≥65 years of age, 2019



Source: US Centers for Disease Control and Prevention, IPD serotype data 2019, as compiled from data provided through Active Bacterial Core surveillance (ABC).

STRIDE-6 (NCT05420961): V116 Pneumococcal Vaccine Trial in "Pre-vacinated" adults





- **Investigated V116 in adults 50+ previously vaccinated with pneumococcal vaccine** (n=712)
- **Participants received:**
  - V116 (investigational vaccine)
  - PCV15 (existing vaccine)
  - PPSV23 (existing vaccine)
- **V116 immunogenic across all groups, measured 30 days post-vaccination**
- **V116 response comparable to PCV15/PPSV23 for shared serotypes**
- **V116 generated higher response for serotypes it uniquely targets**
- **V116 effective regardless of time since prior vaccination**
  - Including >10 years since PPSV23 (n=56)
  - 5-9 years since PPSV23 or other pneumococcal vaccines (n=208)
- **V116 safety profile similar to PCV15 and PPSV23**

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Dengue

WER Dengue: WHO guidance

- **Travellers and Dengue Vaccine TAK-003:**
  - **Who benefits most:**
    - Travellers with previous dengue infection (seropositive) visiting endemic areas again.
  - **Benefit:**
    - Reduces risk of severe dengue infection (especially DENV2 or DENV1).
  - **Lower benefit:**
    - Travellers without previous infection (seronegative), may not protect against all serotypes and could increase risk for severe dengue with DENV3/DENV4.
  - **Transmission:**
    - Dengue risk varies by location and time (epidemics).
  - **Pre-vaccination screening:**
    - Not required, but helpful if available to assess risk-benefit.
  - **Vaccination schedule:**
    - First dose: Up to 14 days before travel.
    - Second dose: Minimum 3 months after first dose.
  - **Age limits (current recommendation):**
    - 6 to 60 years old.

Novel vaccines

- Dengue: Butantan trial just published
- Chikungungya vaccin advice in the making

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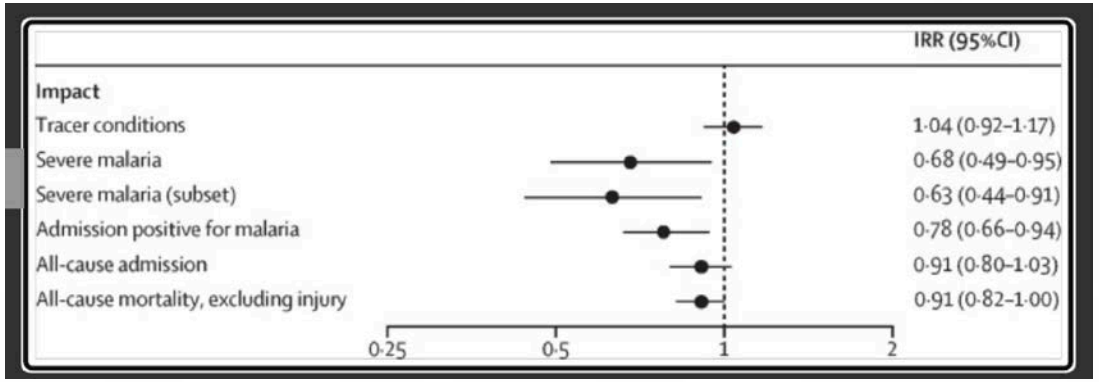
Malaria

Malaria

- RTS,S : real world data available
- Monoclonal AB

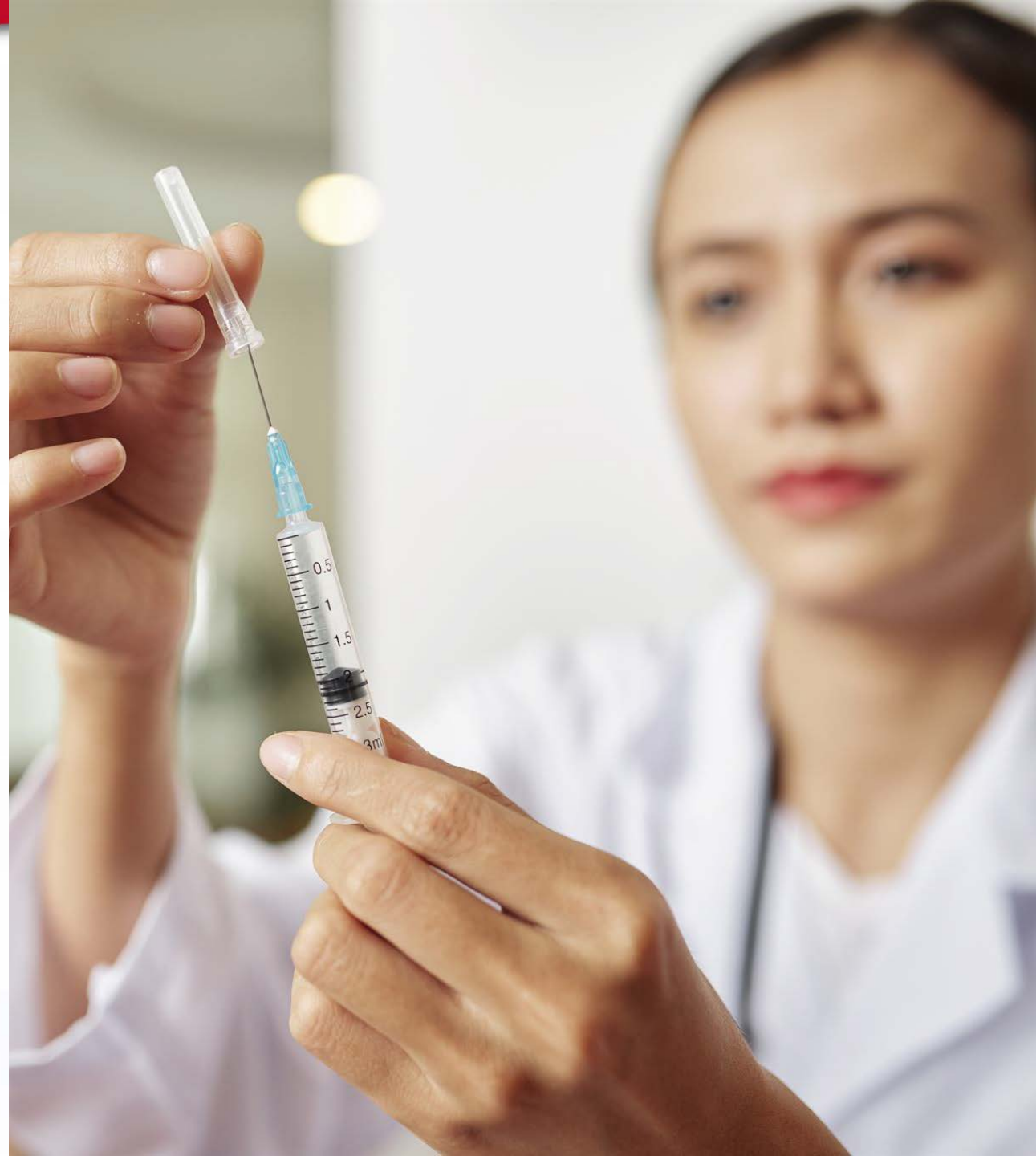
Feasibility, safety, and impact of the RTS,S/AS01E malaria vaccine when implemented through national immunisation programmes: evaluation of cluster-randomised introduction of the vaccine in Ghana, Kenya, and Malawi - The Lancet



- More than 650,000 children received at least one dose and about 490,000 children received three doses. The first dose had a 75% vaccination rate and the third dose had a 63% vaccination rate.
- Introduction of the RTS,S vaccine reduced severe malaria hospital admissions by 32% and all-cause mortality (except injury) by 9%.
- The results show that the RTS,S vaccine can be effectively deployed through national immunization programs and can offer significant public health benefits.

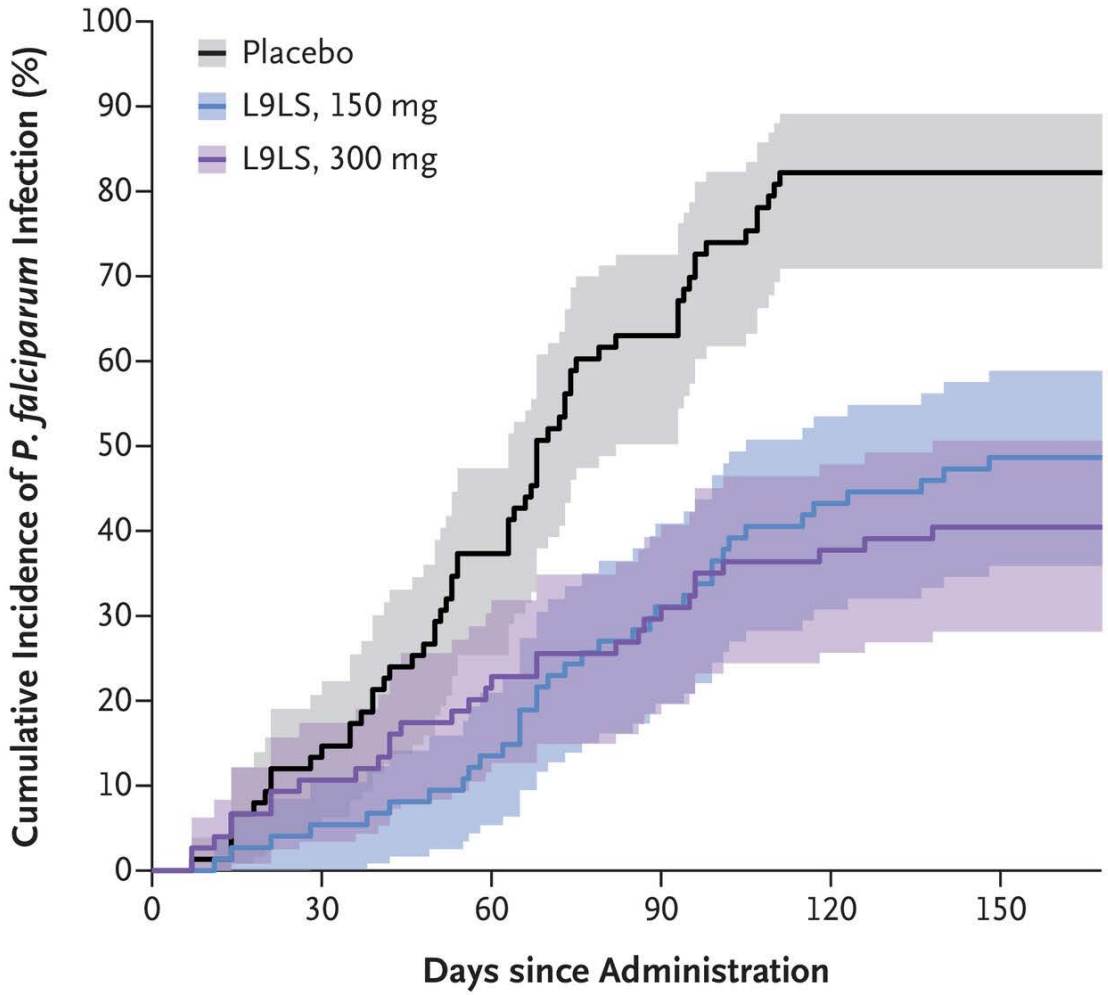
[Subcutaneous Administration of a Monoclonal Antibody to Prevent Malaria | New England Journal of Medicine (nejm.org)]

- Design of Trial
  - Double-blind, randomized, placebo-controlled
  - Part of a phase 2 trial
- Assessment of L9LS
  - Single subcutaneous dose
  - Preventing P. falciparum infection
- Target Population
  - Children in Mali
- Duration
  - 6-month malaria season



Clinical Trial: Intervention

- 225 healthy children aged 6-10 participated in the study
  - Randomly assigned to receive 150mg or 300mg of L9LS or placebo
- Artemether-lumefantrine administered 7-12 days prior to L9LS or placebo
  - Clears possible preexisting P. falciparum blood-stage infection
- Primary efficacy end point: P. falciparum blood-stage infection
  - Determined by blood smear performed at least every 2 weeks for 24 weeks



No. at Risk

Placebo	75	65	47	27	13	13
L9LS, 150 mg	75	70	64	51	42	37
L9LS, 300 mg	75	66	58	52	46	40

P. falciparum Infection with Onset between Weeks 1 and 24

Group	Number of Participants	Efficacy in Preventing P. falciparum Infection
L9LS, 150 mg	75	66%
L9LS, 300 mg	75	70%
Placebo	75	N/A

- Study conducted on healthy children aged 6 to 10 years
  - Three groups: L9LS 150 mg, L9LS 300 mg, and Placebo
  - Each group had 75 participants
- L9LS 150 mg showed 66% efficacy in preventing P. falciparum infection
- L9LS 300 mg showed 70% efficacy in preventing P. falciparum infection

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I was unable to tackle in detail many more suggestions such as the therapeutic use of HPV, single-dose HPV, Mpox etc…