A decade of action: From PDVAC prioritization to SAGE recommendation for RSV immunization

PDVAC meeting, 9 December 2024

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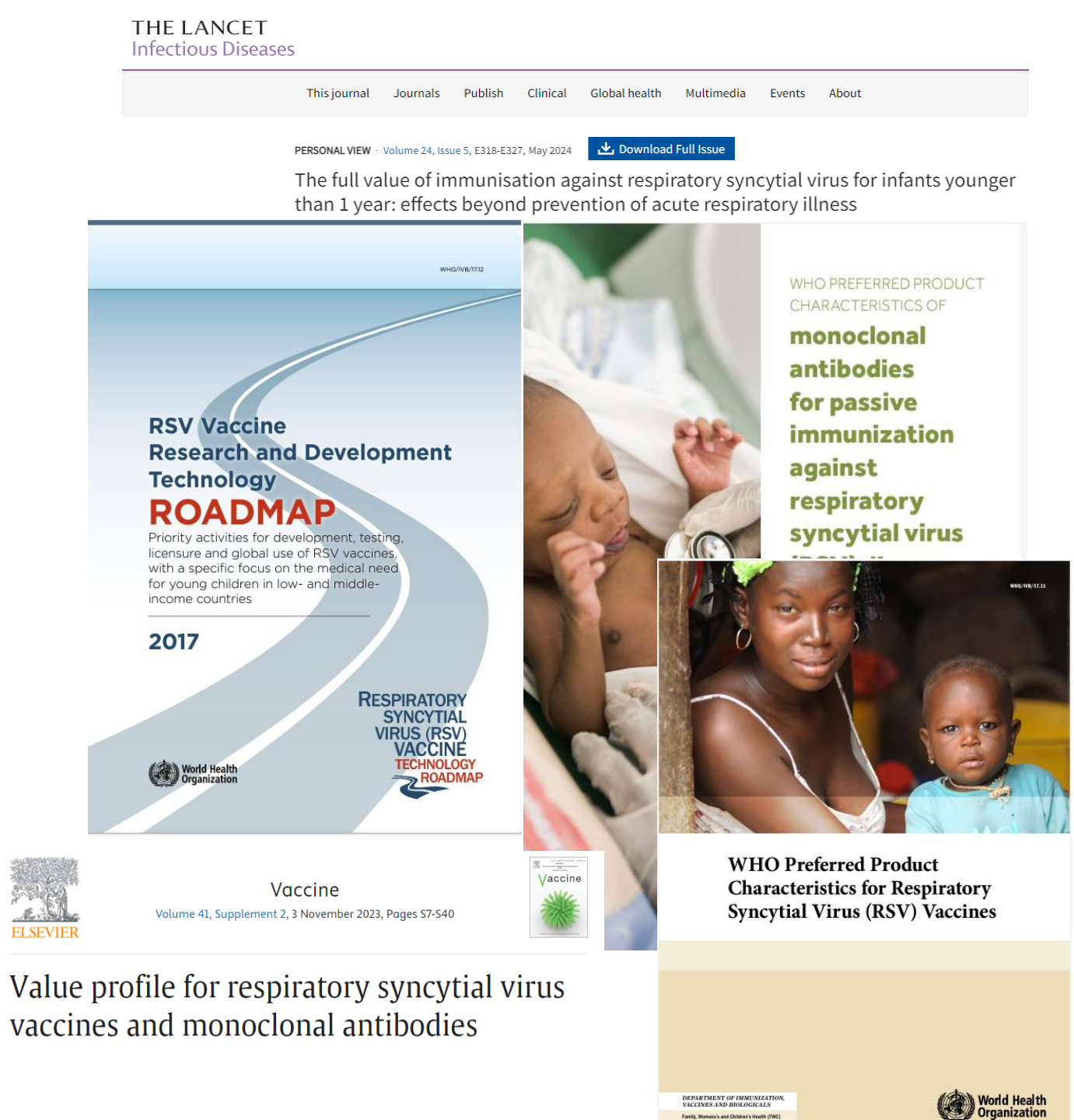
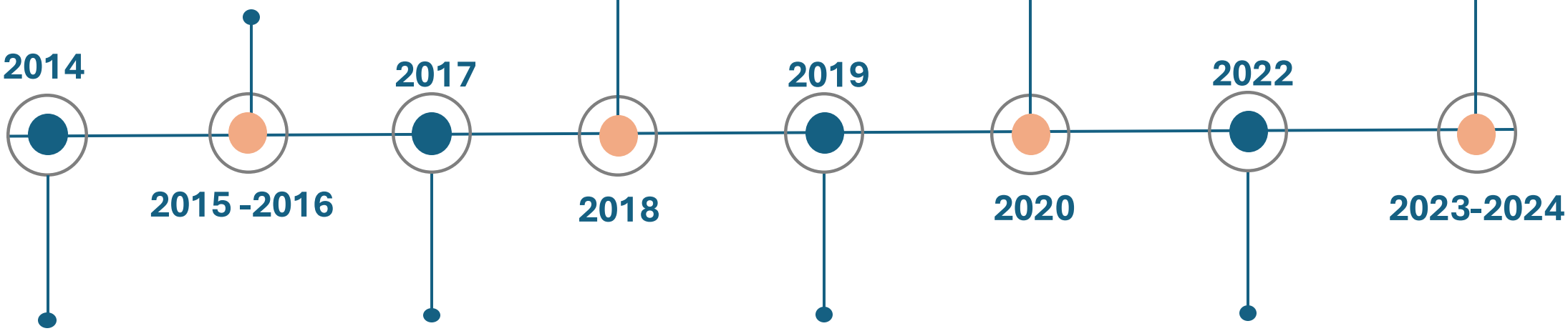
World Health Organization | IVB



RSV immunization products – 10 year timeline



2014

- PDVAC Prioritization of RSV

2015 -2016

- WHO consultation to identify key gaps, and 1st RSV review at SAGE
- WHO GISRS launches RSV surveillance pilot

2017

- PPC for RSV Vaccines (PDVAC recommends PPC for mAbs)
- First WHO international standard antiserum
- RSV TAG established

2018

- GAVI VIS 2018 – board approves RSV
- Ph3 Novavax maternal vaccine concludes – primary endpoint not met

2019

- PDVAC recommends CEA modelling for maternal immunization & mAbs

2020

- RSV TAG reviews Pfizer's maternal vaccine ph2 results & development plans
- TAG reviews ph2 results for nirsevimab

2022

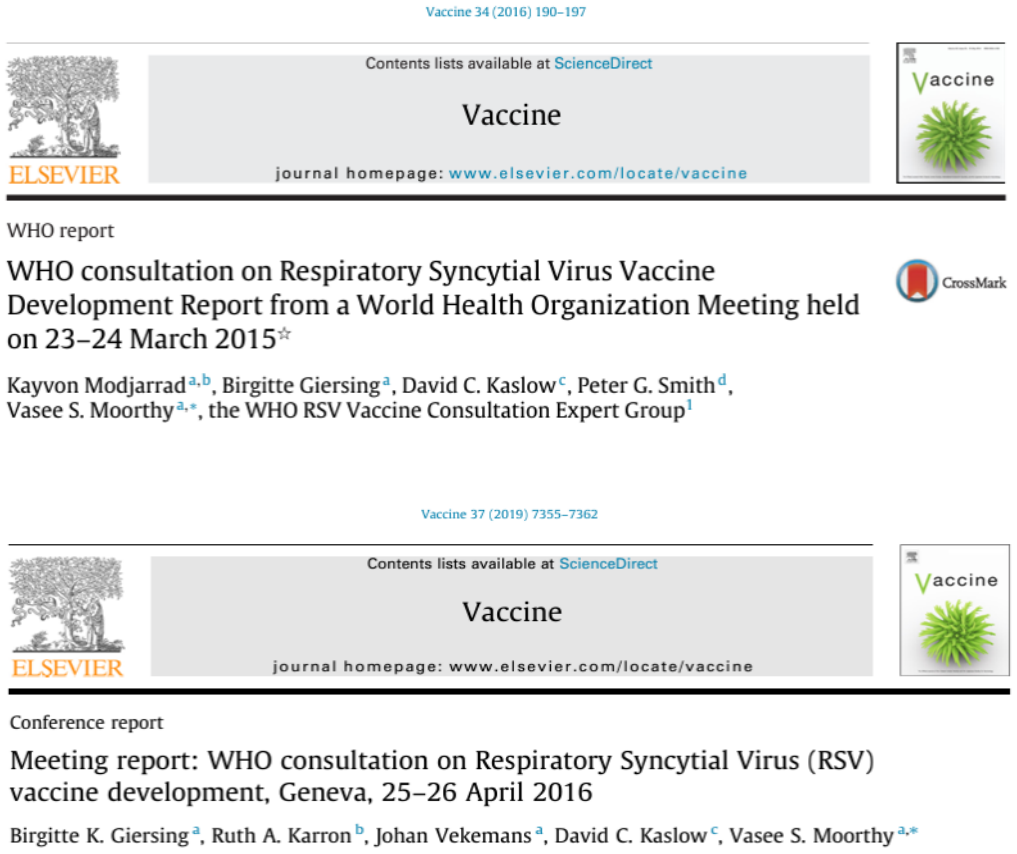
- PPC for mAbs
- GSK maternal Ph3 study stops due to safety signal
- SAGE recommends impact study
- Nirsevimab licensed

2023-2024

- Value Profile RSV
- Pfizer's maternal vaccine licensed
- SAGE WG review
- SAGE recommendation maternal immunization & mAbs
- RSV market study

PDVAC prioritization of RSV

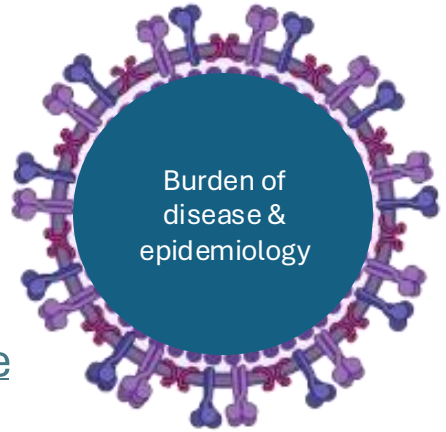
- RSV prioritized at first PDVAC meeting in 2014
  - Unmet public health need, particularly for infants in LMICs; significant clinical pipeline activity
- In 2015, WHO meeting on RSV vaccine development:
  - Included RSV experts (HICs & LMICs), regulators, vaccine developers, funders
  - Development of candidate case definitions for efficacy endpoints & clinical development
  - Proposal for development of R&D roadmap & preferred product characteristics (PPC)
  - Proposal for development of reference reagents for RSV
  - Called for inclusion of LMICs sites in clinical development and ensuring future access to LMICs
- In 2016:
  - SAGE reviewed RSV for the first time & recommended actions
  - 2nd WHO consultation on RSV vaccine development
  - RSV included in PDVAC's special issue on pipeline analyses



WHO RSV vaccine development consultations (2015 & 2016) at SAGE (2016) - identified RSV evidence gaps from regulatory, prequalification & policy perspectives & identified several areas for action to fill these gaps

Establishment of PDVAC Technical Advisory Group (**RSV-TAG**) in 2017 to guide WHO on technical products, data review (frequent meetings)

Burden of disease and epidemiology



WHO initiatives:

- WHO Global Influenza Surveillance Response System (GISRS) launched RSV surveillance
- 2019 WHO meeting on RSV in early life and recurrent wheeze and asthma
- 2020 WHO commissioned analysis: Assessing the strength of evidence for a causal effect of RSV LTRI on subsequent wheezing illness: a systematic review and meta-analysis
- Re-analysis of global burden of disease by WHO region (in response to WHO regional offices) – to be published
- WHO commissioned JHSPH to conduct a systematic review and meta-analysis of RSV proportion positive among ALRI hospital admissions in children in LMICs – to be published
- WHO commissioned LSHTM, Uni Edinburgh and Uni Nanjing to undertake finer age stratification of BoD in young children – to be published.

Other initiatives:

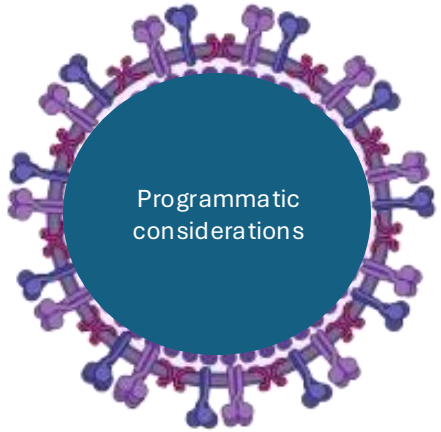
- BMGF community mortality studies, RSV GOLD, new BOD estimates in 2019 & others…

Regulation, Research & Development

WHO Initiatives:

- PPC for RSV pediatric and maternal vaccines published in 2017
- RSV vaccine research and development technology roadmap was published 2017
- Establishment of the first WHO International Standard for antiserum to RSV in 2017, developed in collaboration with 25 laboratories from 12 countries
- 2018 WHO Commissioned analysis: Informing RCTs of RSV vaccination during pregnancy to prevent recurrent childhood wheezing: a sample size analysis' (concludes: large RCT samples size needed therefore post-licensure studies needed)
- WHO Guidelines on the quality, safety and efficacy of respiratory syncytial virus vaccines for use by national regulatory authorities and vaccine manufacturers adopted by ECBS in 2020
- PPC for RSV monoclonal antibodies published in 2021
- 2022 WHO commissioned analysis on biological factors that may impair transplacental transfer of RSV immunization and implications for maternal immunization policy and research priorities for LMICs
- ECBS adopted WHO Guidelines on the clinical and non-clinical evaluation of monoclonal antibodies and related products intended for prevention of RSV disease in 2024

Programmatic considerations



SAGE called for: Linking RSV maternal immunization platform with other maternal vaccines and coordination with reproductive health

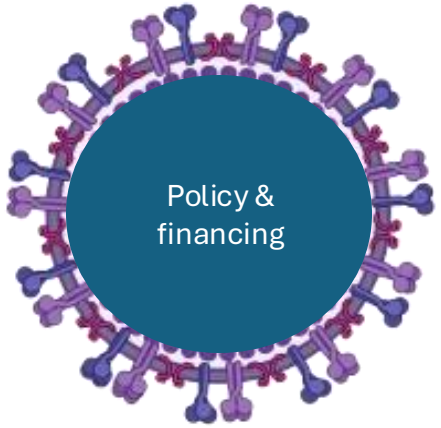
WHO Initiatives:

- Efforts in collaboration with maternal and child health colleagues at WHO
- Maternal Immunization and Antenatal Care Situation Analysis Report of the MIACSA project 2016–2019 (focus on understanding of the challenges and successes of ANC and EPI services in implementing maternal immunization maternal vaccines for tetanus toxoid, RSV and other conditions)
- 2021 WHO commissioned analysis on RSV seasonality and prevention strategy planning for passive immunization of infants in LMICs
- With PATH - PATH and WHO are assessing how current ANC visit timing and reach aligns with gestational age windows needed to optimize new maternal vaccines

Other Initiatives:

- Advancing Maternal Immunizarion (AMI, PATH), KAP surveys (JHPIEGO); Maternal Immunisation Readiness Network in Africa/Asia (MIRNAA, Wits universtiy)

Policy and Financing



WHO Initiatives:

- Updates to RITAGs, Global NITAG Network
- 2022 technical consultation on evaluation of RSV prevention cost effectiveness in LMICs
- 2023 Vaccine Value Profile for RSV vaccines and mAbs -intended to provide a high-level and holistic assessment of data that available to inform potential public health, economic and societal value
- 2024 Analysis on the full value of immunization against RSV for infants younger than 1 year, for consideration by policymakers aiming to use new RSV immunization products
- 2024 WHO Global Market Study on RSV Immunization Products

Other initiatives:

- Gavi approved the support of RSV immunization products under VIS 2018, contingent to availability of licensed products, SAGE recommendation and WHO prequalification. Gavi board June 2025 to confirm
- BMGF & Pfizer global access agreement to develop an MDV for LMICs

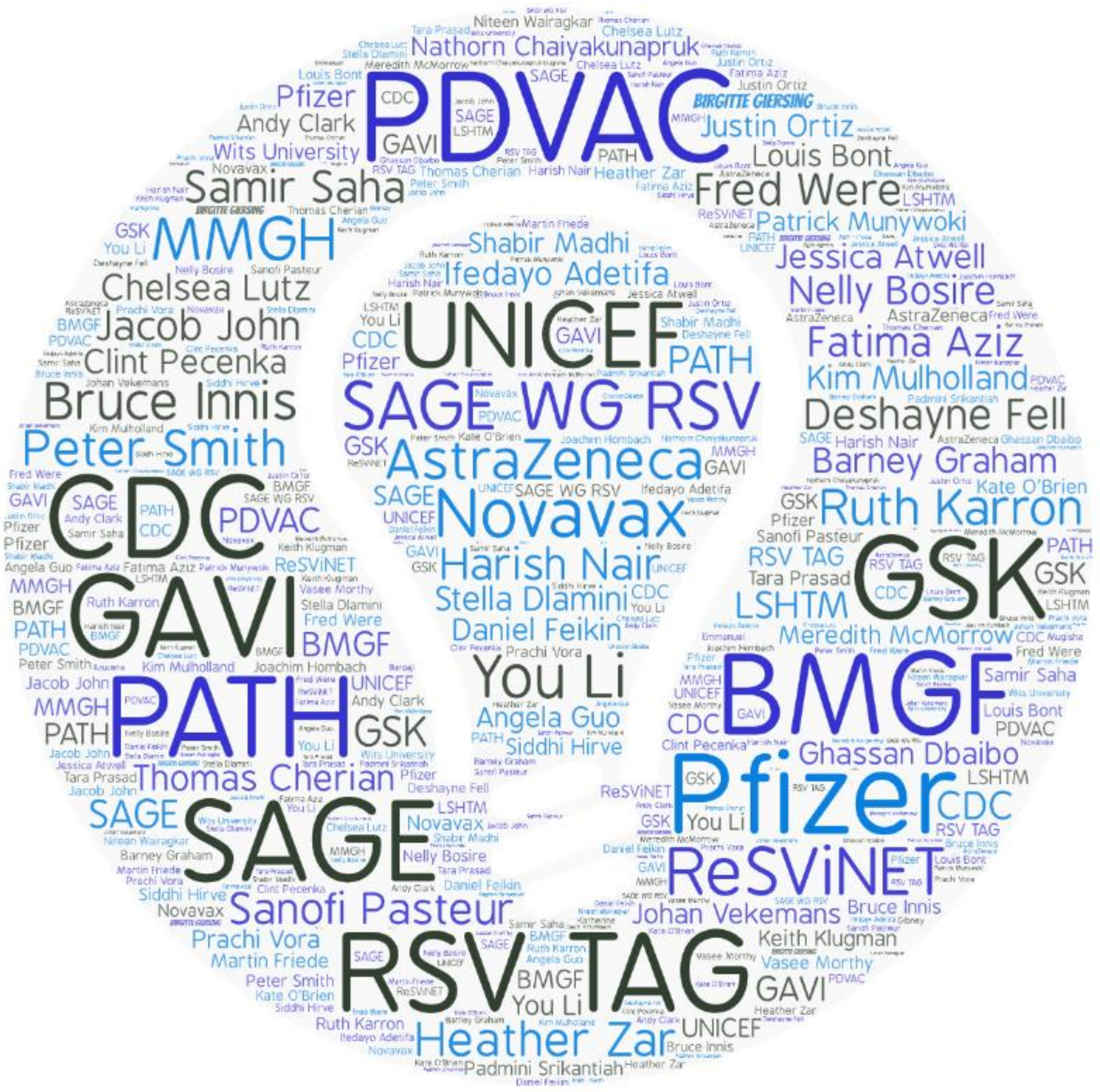
More recent SAGE input

- In October 2022, an update on RSV and product development was presented to SAGE, concerned that LICs has been largely absent from trials, SAGE called for: An adequately sized RCT to document the full potential public health impact of RSV immunization in LMICs – to support future country decision making
- In response to SAGE's call, WHO formed a subgroup of its RSV TAG to discuss the optimal study design and most important outcomes to measure in an RSV vaccine impact study.
- The impact study has two primary objectives:
    - Evaluate the efficacy of maternal immunization against severe RSV-LRTI through to 180 days of age.
    - Evaluate the safety of maternal immunization in relation to preterm births
- The Impact study is planned for 4 African countries : Ghana, Kenya, South Africa, the Gambia led by the Wits University and funded by BMGF
- SAGE called for the establishment of a SAGE working group in 2023

SAGE RSV Working Group, formed in Dec 2023

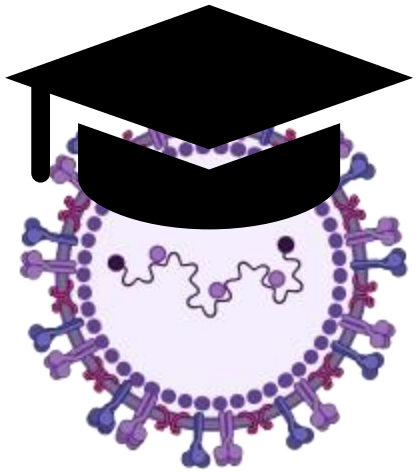
- 14 members (2 SAGE)
- All 6 WHO regions
- Various backgrounds (e.g. clinical pediatrics and OB/GYN, epidemiology, clinical trials, health economics, NITAG membership)
- 13 virtual meetings and a 3-day in-person meeting
- **Recommendations by SAGE in Sept 2024** (later presentation)

Name	Organization	Expertise/Role	Country/ WHO region
Kathy Neuzil	U. Maryland/NIH	SAGE member, Chairperson	USA/AMRO
Kim Mulholland	Murdoch Children's Research Institute/LSHTM	SAGE member	Australia/WPRO
Clint Pecenka	PATH USA	Health economics	USA/AMRO
Emmanuel Mugisha	PATH Uganda	Uganda NITAG	Uganda/AFRO
Fatima Aziz	Infectious Disease Research Laboratory, Aga Khan Uni	Molecular epidemiology of RSV	Pakistan/EMRO
Harish Nair	University of Edinburgh	RSV global burden & epi	India and UK; SEARO/EURO
Azucena Bardají	ISGlobal, Spain CISM, Mozambique	Maternal & child health in Africa RSV burden & maternal immunization	Spain, EURO
Katherine Gibney	University of Melbourne	Chair of the Aus NITAG WG on RSV. ID & vaccine policy expertise	Australia/WPRO
Meredith McMorrow	US CDC	RSV epi expert (ACIP RSV support)	USA/AMRO
Patrick Munywoki	Kenya CDC	RSV epi expert	Kenya/AFRO
Ruth Karron	BSPH, Johns Hopkins U	PDVAC chair; RSV clinical trials & epi expertise	USA/AMRO
Jacob John	CMC Vellore	Pediatrics, Epidemiology & Clinical Trials.	India/SEARO
Ghassan Dbaibo	American University of Beirut	Paediatrican, EMRO RITAG member, PDVAC member	Lebanon/EMRO
Nelly Bosire	Kenya Paediatric Research Consortium	Practicing OB/GYN with interests in health policy and practice	Kenya/AFRO



It takes a village

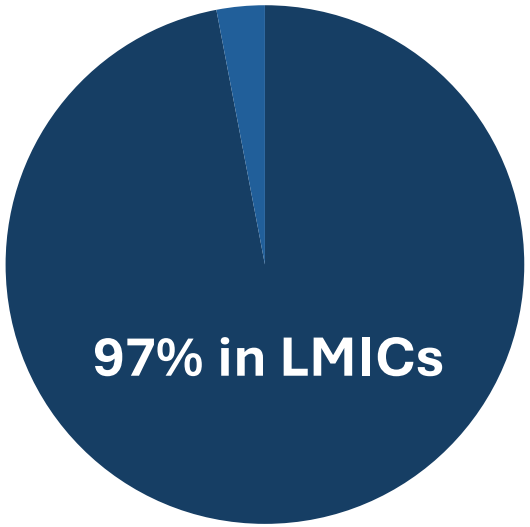
RSV infant immunization is a PDVAC graduate



SAGE Recommendations

But this is not the end of the journey

101,000
deaths



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Stakeholder panel: reflections

Moderator: Ruth Karron

Panelists:

- Tonya Villafana, Vice President Franchise. Medical & Scientific Affrairs, AstraZeneca
- Julie Skinner, Vice President of bacterial vaccines and technology, Pfizer
- Jules Millogo, Director, Public Health Partnerships, Merck Vaccines
- Sonali Kochhar, Clinical Associate Professor, Global Health, University of Washington (SAGE member)