Highlights from the Strategic Advisory Group of Experts (SAGE) on Immunization meeting

11-13 March 2024

Geneva, Switzerland

https://www.who.int/news-room/events/detail/2024/03/11/default-calendar/sage_meeting_march_2024

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AGENDA


GLOBAL & REGIONAL REPORTS

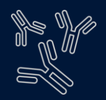

IMMUNIZATION AGENDA 2030


POLIOMYELITIS*


HEPATITIS E*


COVID-19


MPOX*


IMMUNE CORRELATES


RESPIRATORY SYNCYTIAL VIRUS

3 sessions (*) for recommendation

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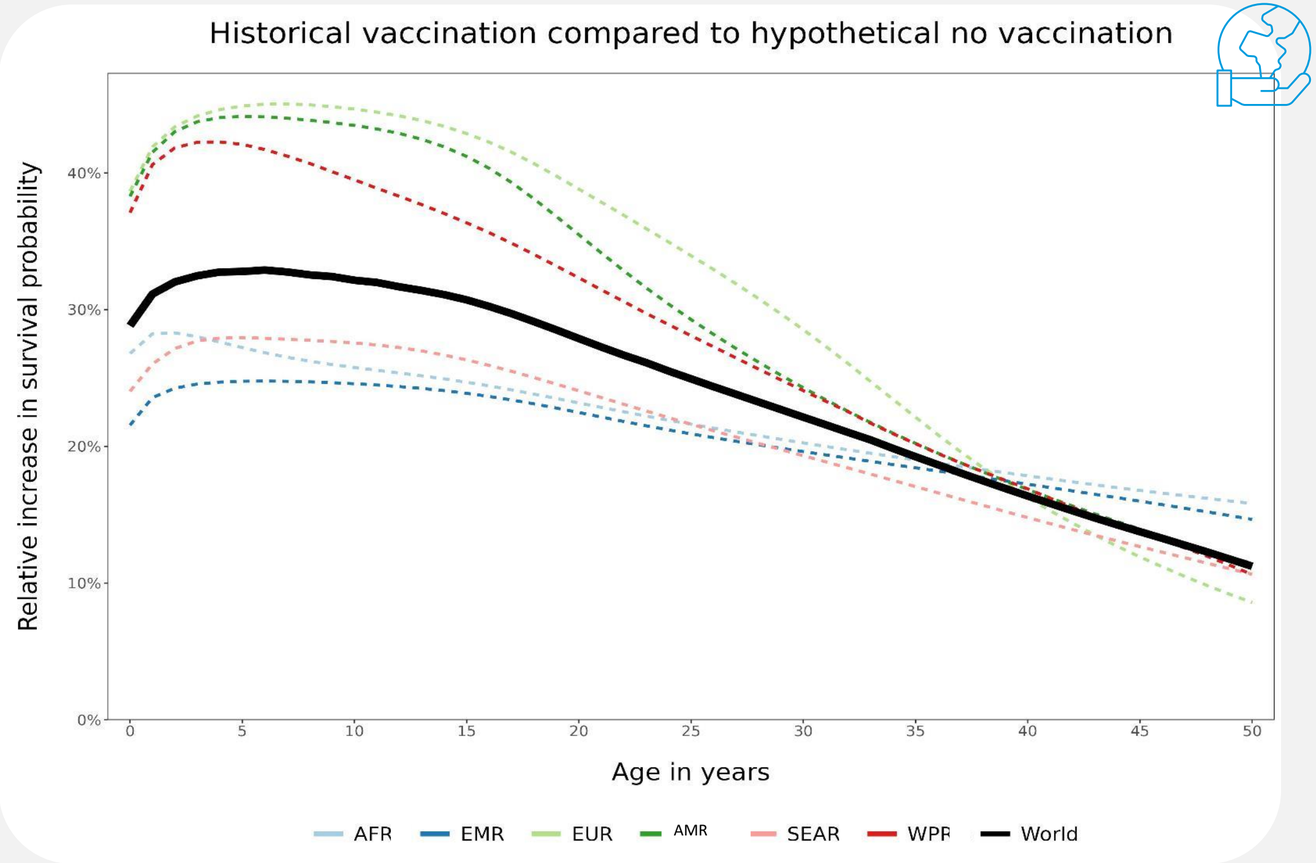
Global & Regional Reports

IVB report

On the 50th anniversary of the establishment of EPI the report reflected on the achievements over the past 50 years and aspirations for the next decades.

Immunization has improved child survival, controlled VPDs, and reduced inequities. It can serve as the backbone of PHC and can improve equity in access to all PHC services.



Source: Interim results of the global analysis estimating the impact of vaccination over 50 years.

Final estimates of deaths averted due to 50 years of vaccination will be released during World Immunization Week (24-30 April 2024)

EPI - Expanded Programme on Immunization
PHC – Primary Health Care

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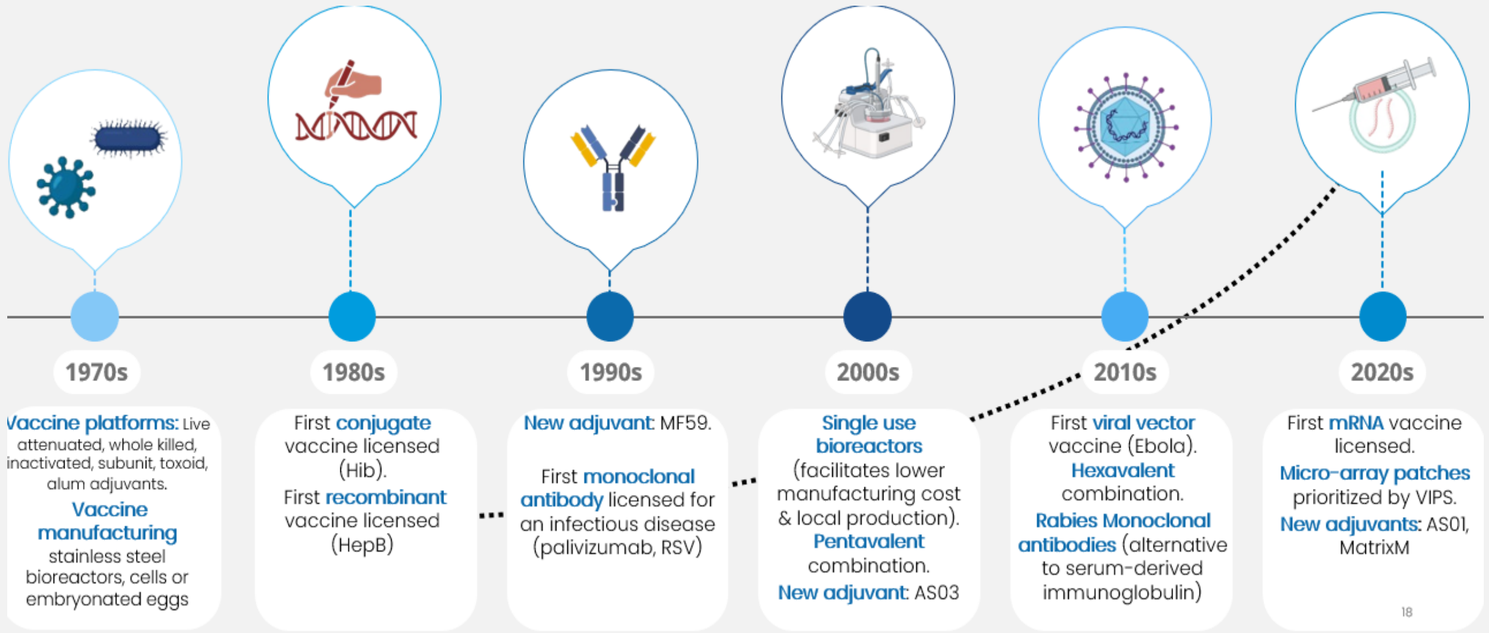
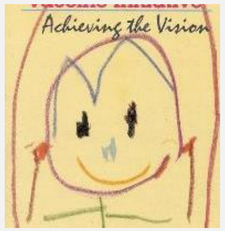
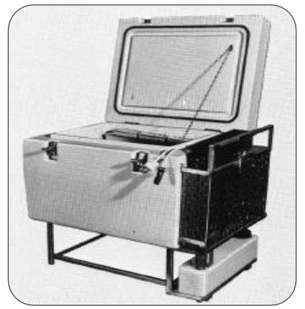
IVB report

Innovations in vaccines and technology has led to new and improved vaccines and facilitated their deployment & delivery; future innovations can surpass the ambitions established by CVI

The capacity for manufacturing vaccines in emerging economies has substantially increased and African regional vaccine manufacturing will be an additional step to vaccine equity and resilience.







Vaccine storage
From kerosene to ice-lined & solar direct-drive refrigerators/freezers

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Regional reports - SAGE observations

All regions experienced setbacks in vaccination during the COVID-19 pandemic though a recovery in vaccination coverage was observed in 2022 in all regions, except for the African region. Despite the progress, there is an accumulation of susceptible individuals that contributed to outbreaks of vaccine-preventable diseases (VPDs).

Many, though not all, countries across all regions have revised policies and established catch-up vaccination schedules, developed catch-up vaccination plans to fill immunity gaps using a variety of approaches, and many have started implementing their plans.

Regions reported major challenges in identifying children who missed vaccination doses and in delivering and monitoring vaccination to children older than 2 years of age.

Exemplary country initiatives in some countries have resulted in rapid progress. SAGE noted that close monitoring and robust accountability processes were key to success.

SAGE took note of the challenges with monitoring progress with catch-up vaccination related to weaknesses in health information systems, which will need to be strengthened to mainstream catch-up vaccination as part of routine immunization delivery.

SAGE noted the need for programme flexibility especially in fragile, conflict-affected, and vulnerable settings, and to establish linkages with other essential services and engage with local non-state actors to accelerate recovery.

Hepatitis E

Hepatitis E – topics reviewed

1 Background

2 Current WHO policy

3 Burden of disease and severity

4 GACVS review of safety of HEV in pregnancy

5 Reduced dose schedules of HEV

6 Recommendations

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Background

Hepatitis E, vaccination, regulatory status and ongoing activities

- Endemic and epidemic disease in low-resource areas; large outbreaks in Asia and Africa.
- High morbidity and mortality in pregnant women.
- Currently only one product available (Hecolin®).
- For use in individuals aged 16 years and over, schedule: 0, 1 and 6 months.
- Pre-filled syringe with an approved shelf life of at least 36 months (and up to 45 months under appropriate storage conditions).
- Very high vaccine efficacy 3 doses: 100% (95%CI: 72-100%); 2 doses: 100% (95%CI: 9–100%).
- WHO issued vaccine position in 2015
- No routine immunization recommendation, but use of the vaccine to mitigate or prevent outbreaks of hepatitis E.
- Registered in China and several other countries, no WHO prequalification yet.
- Remains an underused tool in fragile, conflict-affected and vulnerable settings, with timely access being one important barrier.
- Hepatitis E vaccine stockpile approved under International Coordinating Group (ICG) on Vaccine Provision in October 2023.

Safety of HEV during pregnancy

Conclusions

- Limited data on the use of HEV in pregnant women in China and South Sudan have not identified any safety signal to date.
- No safety concerns observed with other protein-based vaccines during pregnancy.
- The elevated risk of spontaneous abortions identified in a trial in Bangladesh needs to be investigated further.
- Risk-benefit in fragile, conflict-affected and vulnerable settings favours vaccination given the high hepatitis E-related morbidity and mortality in pregnant women.
- Important to generate much-needed evidence on the use of this vaccine during pregnancy given the substantial burden of Hepatitis E in pregnant women and the high risk of infection and subsequent complications.

Hepatitis E – SAGE recommendations

In fragile, conflict-affected and vulnerable (FCV) settings with documented hepatitis E virus circulation, where the **risk of severe disease during pregnancy is high, the benefits of vaccinating women of child-bearing age (≥16 years) outweigh potential harms.**

When implementing vaccination campaigns, SAGE stressed the importance of **accompanying HEV use with a learning agenda**, whenever possible.

SAGE **approved the use of a 2-dose schedule (0 and 1 month)** instead of the 3-dose schedule during campaigns in FCV settings.

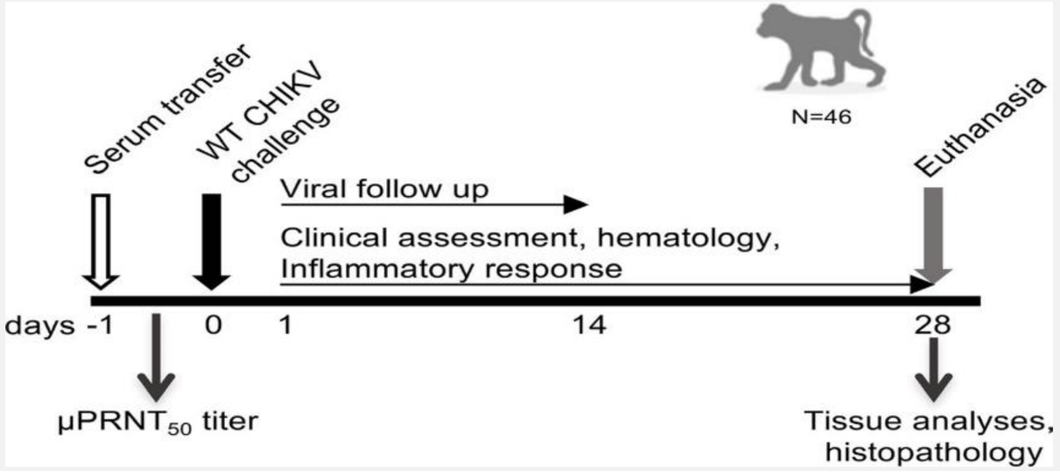
SAGE encouraged additional research on hepatitis E vaccination during pregnancy, in people living with HIV and in individuals under 16 years of age. In addition, SAGE asked to be informed of the outcomes of further analysis of the Bangladesh trial.

Immune correlates

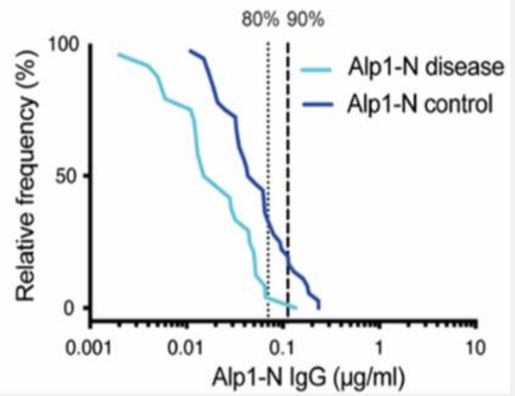
Immune correlates

- For some vaccines, the **Phase 3 trials with clinical outcomes are challenging** either because they require very **large sample sizes** or because of the **unpredictability of outbreaks** and regulatory approval may be issued based on immunological correlates of protection.
- SAGE was briefed on the proposed **regulatory pathways using this approach for chikungunya and Group B streptococcus (GBS) and vaccines** and the evidence in support of the proposed immunological correlates of protection.
- A chikungunya vaccine (live-attenuated) has been licensed based on immune correlates and GBS vaccines (protein-based and hexavalent glycoconjugate vaccines) are likely to use a similar pathway.

Chinkungunya



Group B streptococcus



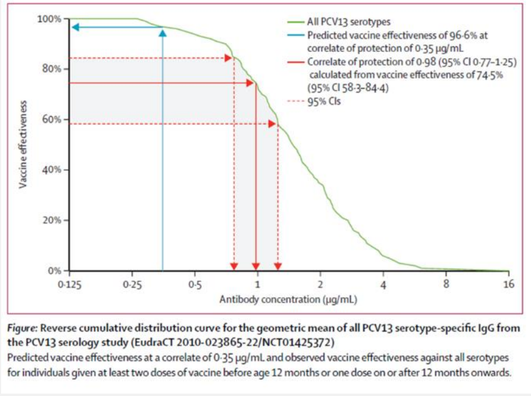


Figure: Reverse cumulative distribution curve for the geometric mean of all PCV13 serotype-specific IgG from the PCV13 serology study (EudraCT 2010-023865-22/NCT01425372)
Predicted vaccine effectiveness at a correlate of 0·35 μg/mL and observed vaccine effectiveness against all serotypes for individuals given at least two doses of vaccine before age 12 months or one dose on or after 12 months onwards.

Immune correlates – SAGE observations

- Since a chikungunya vaccine had received regulatory approval and there was interest in introducing this vaccine in several countries, **SAGE advised WHO to initiate a process to conduct a detailed review of the evidence and assess use case scenarios for the optimal use of this vaccine**.

- SAGE also noted that requiring evidence of clinical efficacy for GBS vaccines before issuing recommendations could delay registration and ultimately the use of the vaccine in LMICs. SAGE advised WHO to develop guidance on **evidence needed for policy** for vaccines where market authorization is provided in the absence of regulatory authorization.

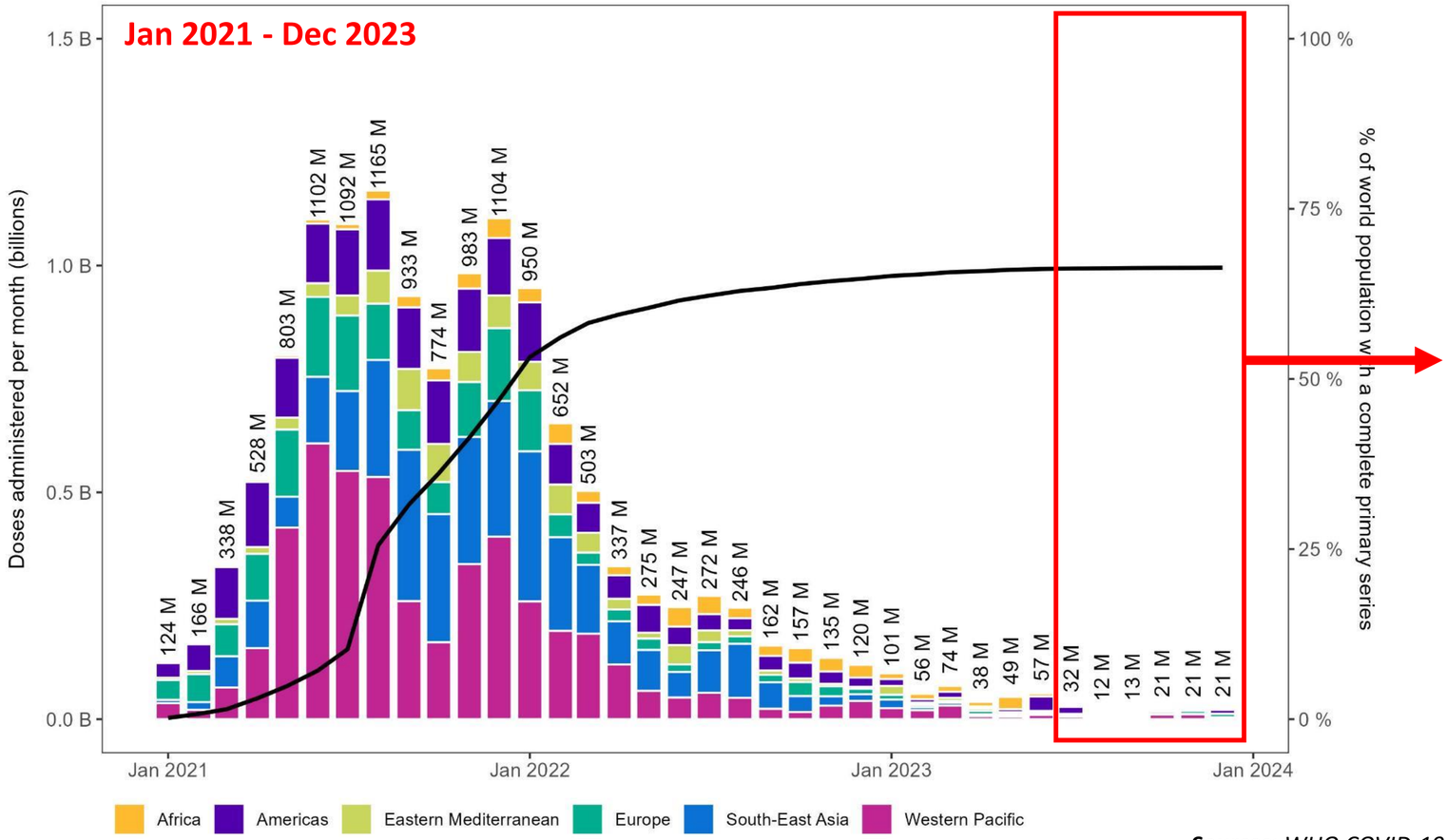
COVID-19

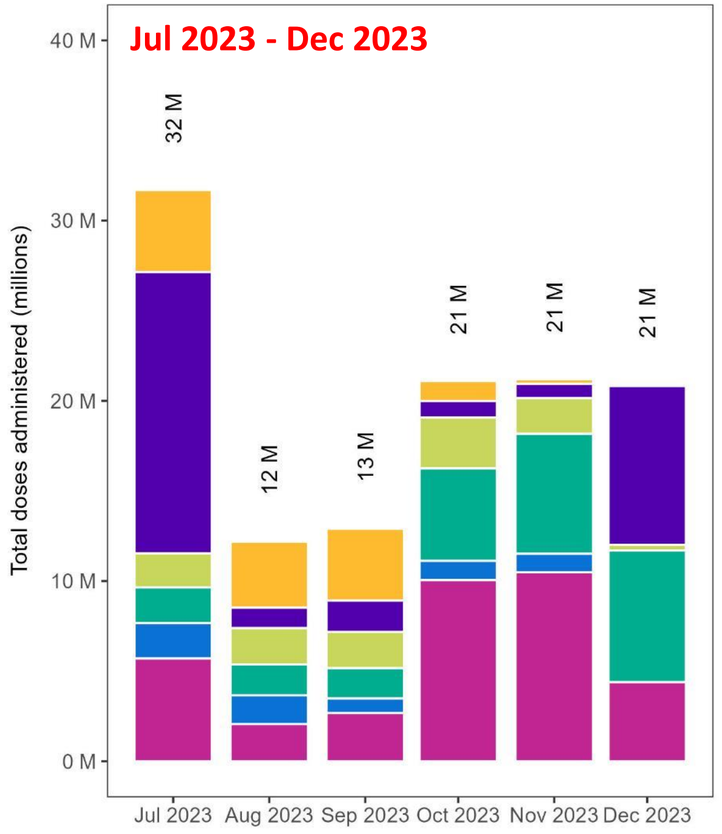
Summary – SARS CoV-2 epidemiology

- **COVID-19 continues to circulate widely across the globe**, as evidenced by sustained global test positivity rates around 10% and localized increasing trends in wastewater SARS-CoV-2 concentrations; **regional variations are worth noting**
- Wastewater trends suggesting increased activity in some Southeast Asia and Western Pacific countries sub national levels while trends of reported cases stayed stable –likely due to reduced testing.
- Weekly numbers of reported deaths are now consistently below 4 000 since mid-May 2023, reported from an average 50 countries. The number of countries sharing death data remain low; as such, **the actual number of deaths is unknown.**
- Limited reporting of hospitalization data and reporting delays make it difficult to draw strong conclusions from trends in hospitalizations, and **COVID-19 isn't the only pathogen circulating stressing health care systems**
- **JN.1. is the most prevalent variant;** it is currently evaluated to pose low public health risk. However, the virus continues to evolve, and we do not yet have seasonal/predictable temporal patterns
- **Seroprevalence** against SARS CoV-2 **is high, with some heterogeneity by age**
- **Declining and unrepresentative surveillance and sequencing is making it more difficult to rapidly assess known variants and detect new ones/recombinants**

DATA AS OF 31/12/2023

Vaccine uptake has declined substantially since its peak in late 2021 – 120 million doses were administered during the Jul – Dec 2023 period





Sources: *WHO COVID-19 vaccine administration data.*

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COVID-19 SAGE observations

The number of **cases, hospitalizations and deaths** of from COVID-19 continue to show a **declining trend**.

While **inequity in access to COVID-19 vaccines persists**, **demand has declined**, especially in LMICs.

Revaccination with Omicron-adapted bivalent vaccines continue to protect against symptomatic and severe disease during the XBB dominant period; there is a **moderate benefit of the monovalent XBB vaccines** over the bivalent or index virus vaccines.

SAGE reiterated that **monovalent XBB vaccines should be used when available**. However, countries should not delay administration of ancestral or bivalent vaccines to high priority-use groups if monovalent XBB vaccines are not available.

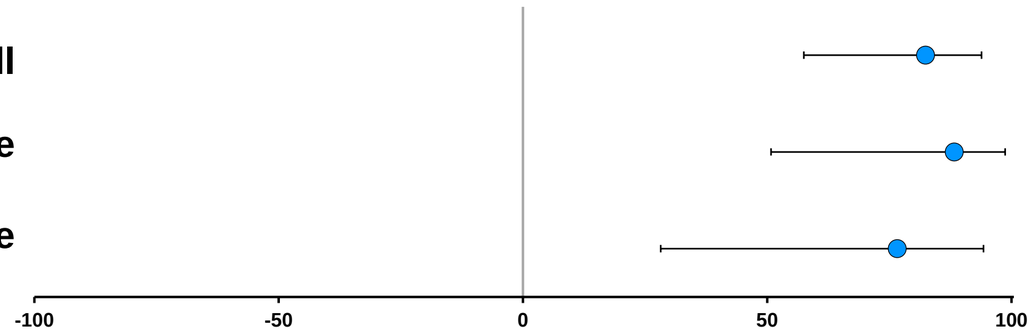
SAGE **reaffirmed the priority-use groups and frequency of re-vaccination** as outlined in the WHO SAGE Roadmap for prioritizing the use of COVID-19 vaccines

Respiratory Syncytial Virus (RSV)

Consistent Efficacy of the Pre-F vaccine in infants was Observed Across Country Income Categories: RSV Severe MA-LRTI

Slide provided by Pfizer

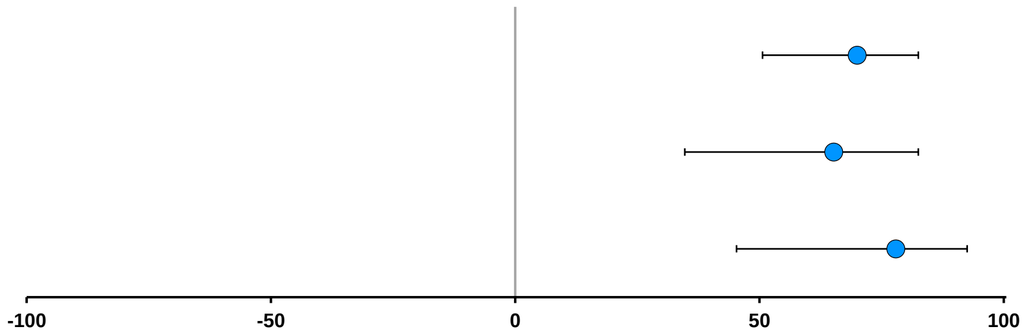
RSV Severe MA-LRTI 90 Days



Vaccine Efficacy (%) (95% CI)

	RSVpreF/Placebo N=3585/3563	VE
Overall	6:34	82.4%
High Income	2:17	88.3%
Low-Mid Income	4:17	76.6%

RSV Severe MA-LRTI 180 Days



Vaccine Efficacy (%) (95% CI)

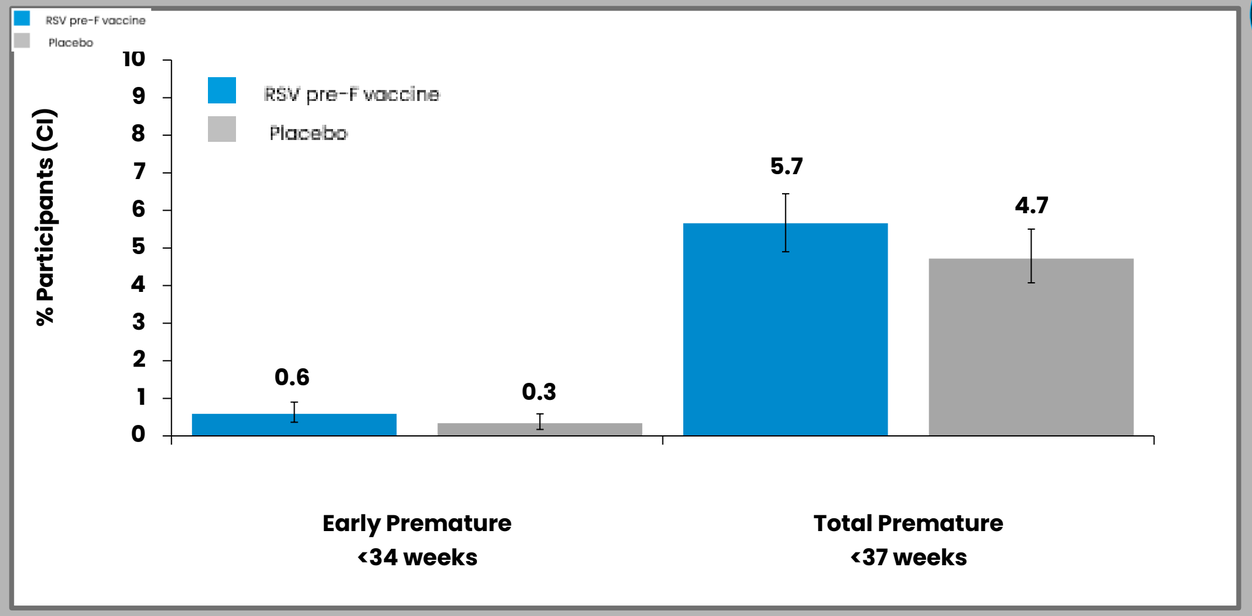
	RSVpreF/Placebo N=3585/3563	VE
Overall	21:70	70.0%
High Income	14:40	65.2%
Low-Mid Income	6:27	77.9%

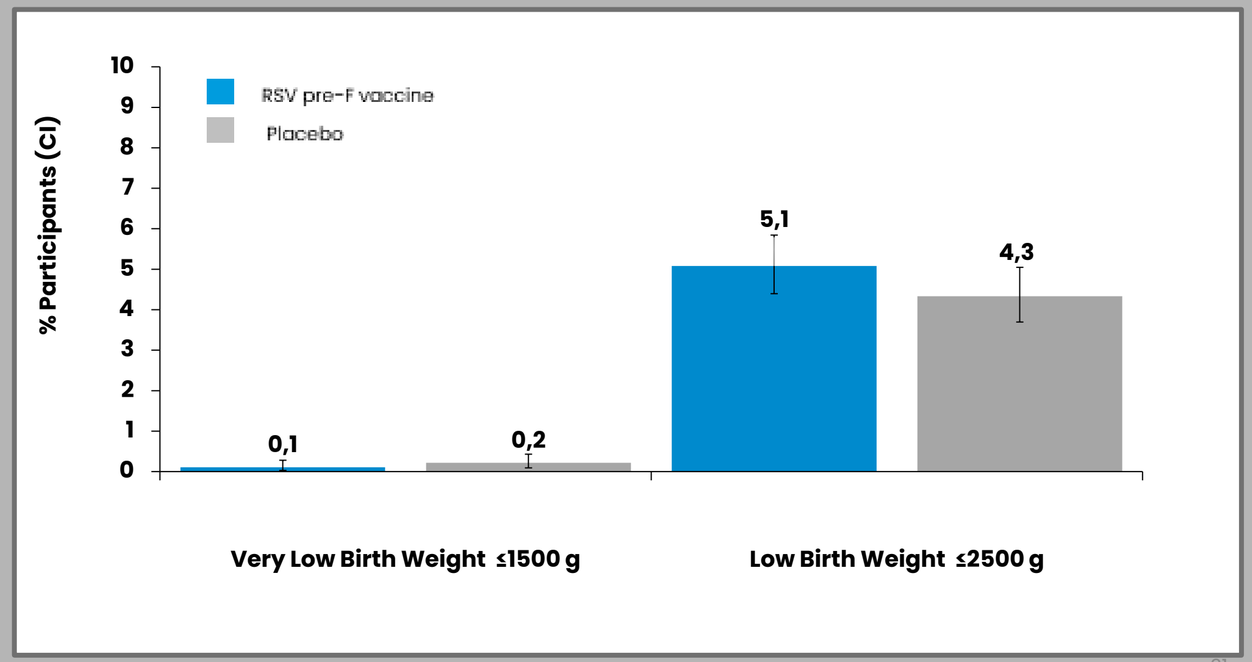
USA = 46% of evaluable participants in study. Other countries include South Africa, Argentina, Japan, Taiwan, Spain, Netherlands, Chile, The Gambia, Finland, New Zealand, Brazil, Mexico, Philippines, Australia, Canada, Denmark, Korea. High-income = USA (66% evaluable participants in category), Japan (9%), Taiwan, Spain (5%), Netherlands (4%), Chile, Finland (3%), New Zealand (2%) Australia, Canada, Denmark, Korea, (1% or less) Low/Middle income = South Africa (44% evaluable participants in category), Argentina (39%), The Gambia (7%), Brazil, Mexico, Philippines (3%)

RSV

SAGE was provided **data on products that recently received regulatory approval for prevention of RSV disease in infants and adults**. These included **RSV pre-F protein vaccines** for use in pregnant women to provide protection to young infants and to protect older adults, and **long-acting monoclonal antibodies** to protect young infants.

All products demonstrated **high efficacy** in protecting the target groups against medically-attended and severe RSV lower respiratory tract illness. However, **a numerical imbalance in preterm births was noted in pregnant women of the vaccine group in middle-income countries**. The products have been rolled out in a few countries.





Figures provided by Pfizer

RSV – SAGE observations

- A **SAGE Working Group has been established** to review the evidence on the use of these products and the findings of their **review will be presented to SAGE in September 2024**.

- SAGE recommended that products for the **prevention of RSV disease in infants be prioritised** for presentation in September 2024, followed by vaccines for the protection of older adults and articulated several issues that should be considered by the Working Group in their review of the evidence.

- SAGE highlighted the need for collecting adequate data on the safety of the vaccines during pregnancy in LMICs.

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IA2030 – Deep Dive

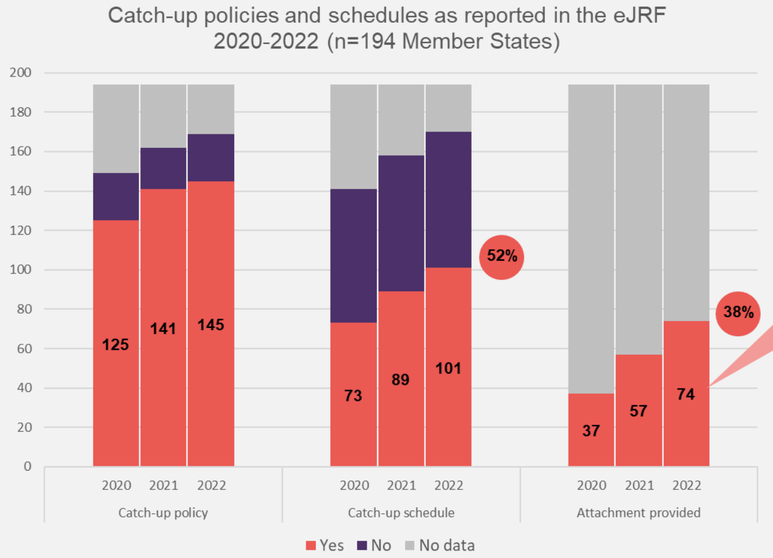
IA2030 – deep dive

SAGE was presented with an **overview of the Big Catch-up and progress with its implementation**. A country presentation from Cameroon exemplified the efforts made and challenges faced.

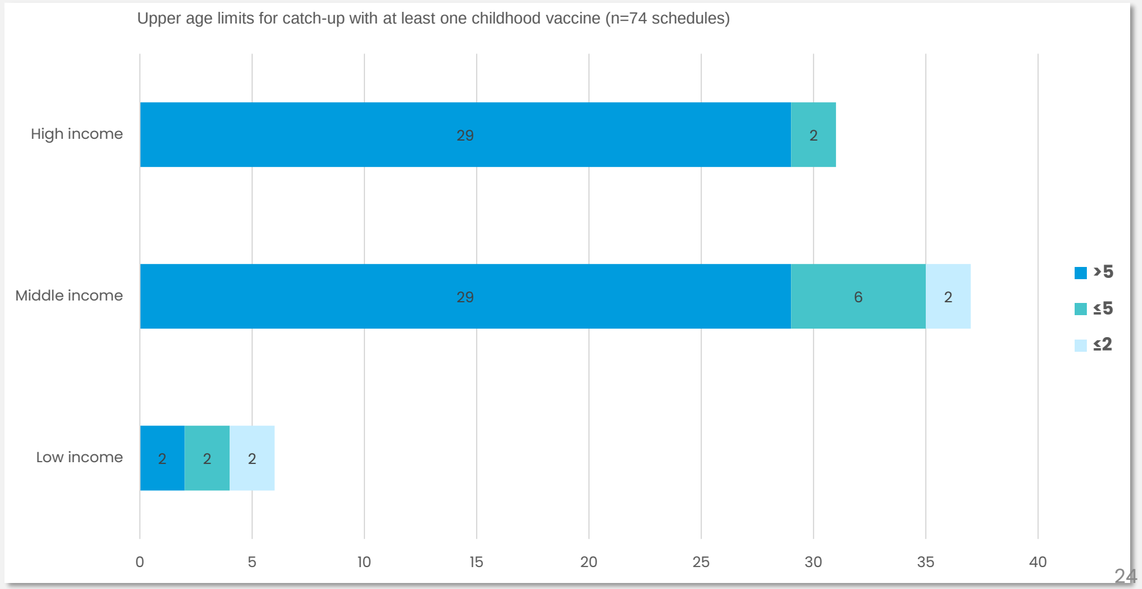
SAGE underscored the need for **political will, community engagement, and health worker capacity strengthening** and encouraged National Immunization Technical Advisory Groups (NITAGs) to guide the efforts.

Monitoring the Big Catch-Up is vital to document progress, learn lessons, inform future actions, and ensure accountability. **The IA2030 Data Strengthening and Use Working group has developed a guidance document laying out indicators** and suggested processes and tools to monitor and evaluate catch-up vaccination.

SAGE acknowledged that generating **granular data to fully monitor catch-up efforts** will not be feasible in the short term. During this period triangulated data from a combination of data sources using innovative analytic methods should be used to understand the impact of the BCU.



Of the 74 catch-up schedules provided for analysis, most (60, 81%) permit catch-up with at least one childhood vaccine* beyond 5 years of age. However, sample is still **mostly limited to high and middle-income countries**.



Big Catch-up – Key priorities for 2024

Tailored country response planning and implementation
Support countries to finalize and implement catch-up plans, aligned with health systems strengthening and zero-dose activity planning

Resource mobilization and mapping – Continue to mobilize financial and political investment for routine immunization; institutional support to Big Catch-up across Alliance partners

Policies and practices for long-term systems strengthening and change – Expand RI age-range policies, revise health information systems, and encourage investment in sustainable, integrated strategies for reaching missed children and communities

Strengthen linkages across programmes – Improve integration and coordination with measles, polio, and other disease-specific initiatives to leverage existing infrastructure, assets and opportunities and promote integration of activities

How will we monitor, evaluate and learn from the Big Catch-up (BCU)?

- **Contextual and adapted approaches and support for monitoring BCU efforts**
- **Multi-pronged approach for monitoring, evaluation and learning**
  - Readiness monitoring
  - Health information systems (admin data)
  - Real-time monitoring and targeted assessments
  - Case studies and surveys

See Yellow Book for current version of the guidance, or go to TechNet-21.org for English and French:

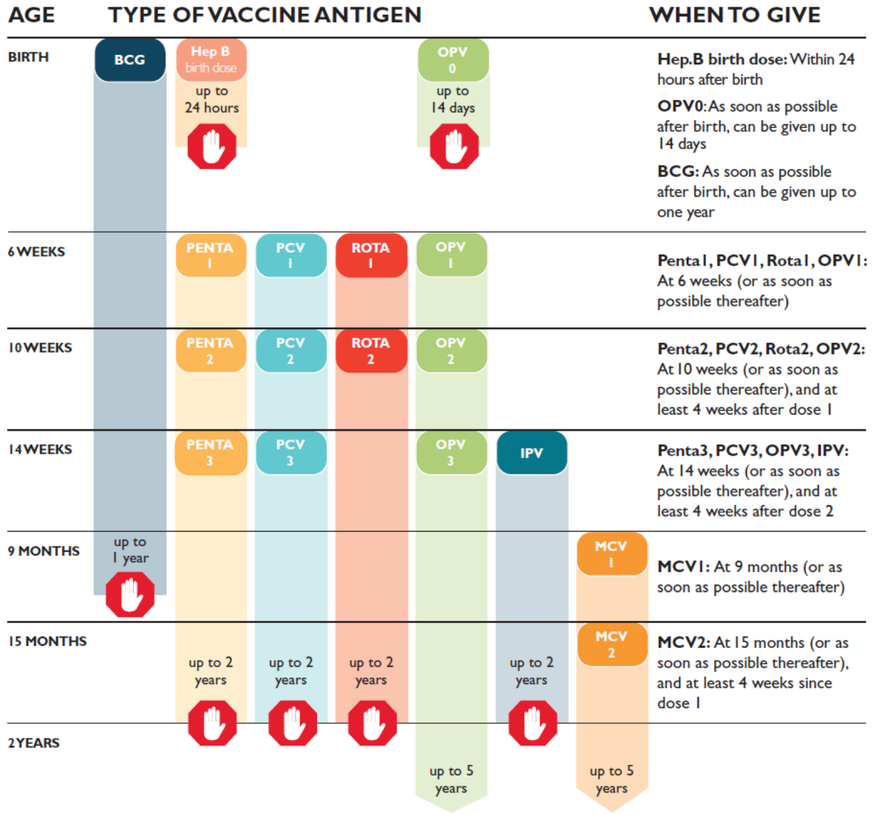
https://www.technet-21.org/en/resources/guidance/monitoring-and-reporting-of-essential-immunization-catch-up-in-the-context-of-the-big-catch-up

(Arabic and Portuguese translations forthcoming)

Readiness monitoring

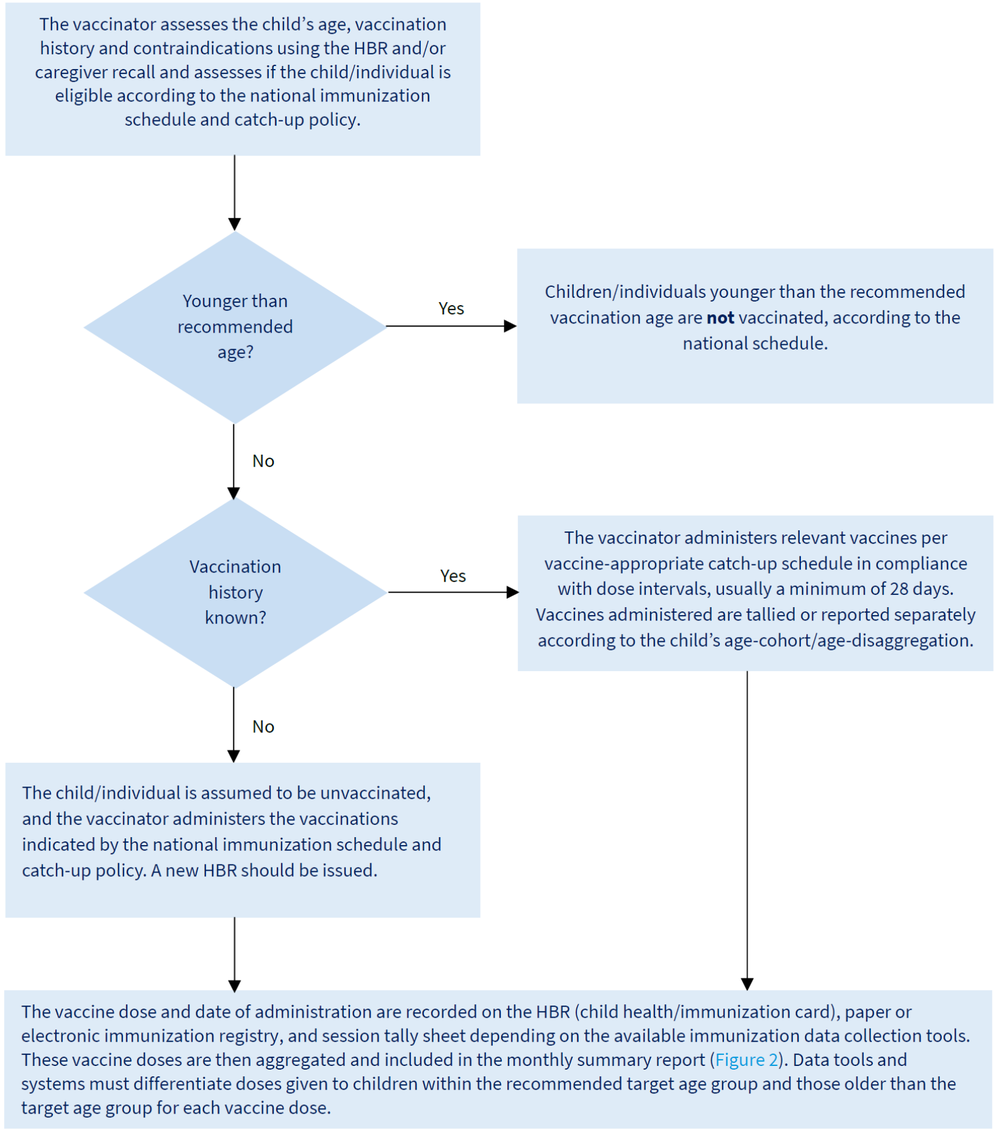
What indicators should be used to monitor country readiness?

- **Catch-up policy**, including **catch-up schedule**
- **Standard operating procedures (SOPs)**
- **Adapted data collection tools**
- **Updated information systems** to capture age-disaggregated vaccination data
- **Health workers oriented** on catch-up SOPs i.e. plans, tools etc.
- **Demand generation plan**
- **Supply and logistics readiness**



Source: MoH of Ethiopia / JSI, Inc.

How to determine eligibility for catch-up vaccinations?



Source: https://www.technet-21.org/en/resources/guidance/monitoring-and-reporting-of-essential-immunization-catch-up-in-the-context-of-the-big-catch-up

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Health information systems

What system strengthening measures are recommended?

As part of the BCU, several measures are recommended to **transform the admin information system to monitor catch up:**

1. Update **in-facility recording tools**
2. Emphasize **home-based records**
3. Enable recording of older-age catch-up in **health management information systems** (DHIS2 etc.)
4. Update **standard operating procedures** (SOP) and **training of health care workers, and strengthen supervision**

ANTIGENS/ ITEMS	0-11 MONTHS	TOTAL	12-23 MONTHS	TOTAL	24 MONTHS OR OLDER	TOTAL	TOTAL vaccinated
BCG							
Hep B BD							
OPV 0							
OPV 1							
OPV 2							
OPV 3							
IPV							
Penta 1							
Penta 2							
Penta 3							
Rota 1							
Rota 2							
Rota 3*							
PCV 1							
PCV 2							
PCV 3							
M/MR 1							
M/MR 2							
DTP4/Other*							
Vitamin A							
Long lasting insecticidal net*							

*depending on national health priorities and schedule of services

Source: https://www.who.int/publications/i/item/9789240016514

In-process monitoring:
Real-time monitoring and targeted assessments

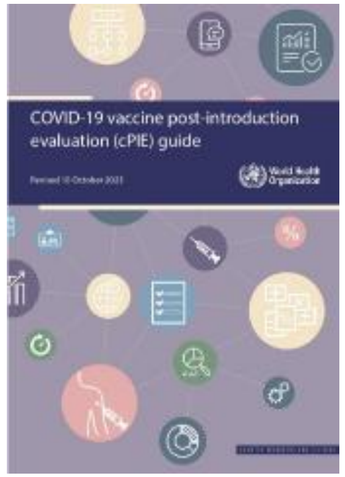
What additional assessments and monitoring should be carried out?

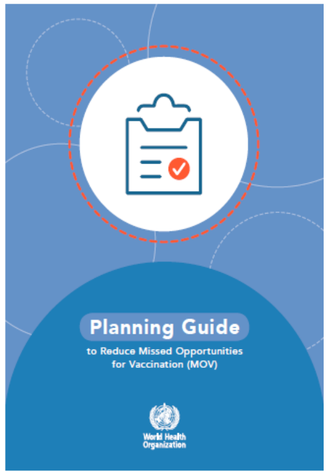
We recommend additional, targeted monitoring measures **during** catch-up activities to support rapid course corrections

1. **Rapid Convenience Monitoring (RCM):**
   - Conduct immediate post-Big Catch-Up activity rapid convenience assessments

2. **Include Behavioral and Social Drivers of Vaccination questions (BeSD, comparing different age groups)**

3. **Other existing rapid assessment tools**
   - Mini Post Introduction Evaluation (Mini-PIE) rapid assessment methodology
   - Missed Opportunities for Vaccination (MOV) methodology





Source: https://www.technet-21.org/en/resources/guidance/monitoring-and-reporting-of-essential-immunization-catch-up-in-the-context-of-the-big-catch-up

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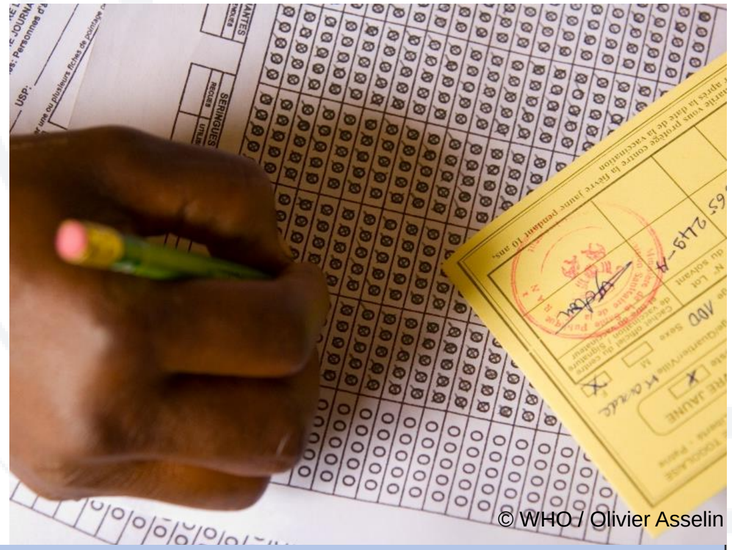
Results monitoring

What outcomes should be monitored?

These include the **number / proportion of catch-up target population vaccinated** with at least one vaccine dose:

- **DTP1**, by age cohort
- **DTP3**, by age cohort
- **IPV1** (and IPV2 as appropriate) by age cohort
- **MCV1**, by age cohort
- **MCV2**, by age cohort
- Any **other dose** prioritized (e.g., YF)



© WHO / Olivier Asselin

RESULTS					
2. To what degree has your country implemented or planned the following?					
a. Intensification of RI services such as periodic intensification of routine immunisation (PIRI), in relation to plan					*...partially/fully implemented planned PIRI services*
b. Supplementary immunisation activities (SIAs) (integrated with BCU) with targeting up to 59 months (in relation to plan)					*...partially/fully implemented planned SIAs*
c. Vaccination of older age children in routine immunisation service delivery, i.e. missed opportunities for vaccination (MOV) principles					*...partially/fully implemented planned vaccinations. In RI service delivery.*
BCU monitoring questions	**Responses**				
3. Based on national vaccination data for your country, how many additional children in each age group have been reached through BCU during this reporting period (note: "m" = months):					
a. DPT1	*<12m:*	*12–23m:*	*24–59m:*		*# of children reached with DPT1.*
b. DPT3	*<12m:*	*12–23m:*	*24–59m:*		*# of children reached with DPT3.*
c. (Any DTP: Only use this row if a breakdown of DPT1 and DPT3 is not possible.)	*<12m:*	*12–23m:*	*24–59m:*		*# of children reached with DTP.*
d. IPV	*<12m:*	*12–23m:*	*24–59m:*		*# of children reached with IPV.*
e. MCV1	*<12m:*	*12–23m:*	*24–59m:*		*# of children reached with MCV1.*
f. MCV2		*12–23m:*	*24–59m:*		*# of children reached with MCV2.*

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Case studies and surveys

What is the role of case studies and surveys?

Additional measures **after** catch-up activities to provide qualitative insight on coverage and learnings

1 Studies

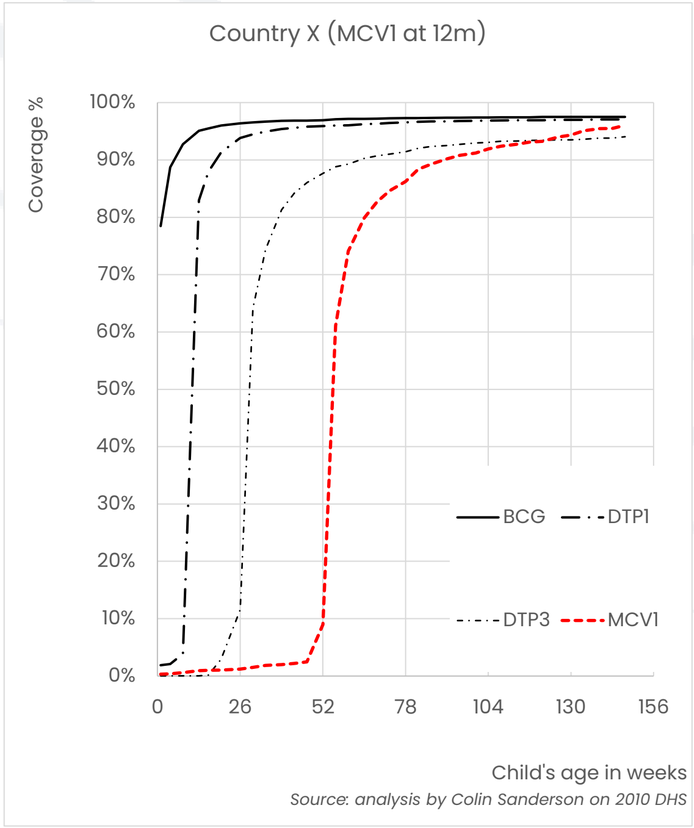
- Deep-dives to document lessons learned and long-term impact on health systems and behaviours (permanent changes, life course strategies for reducing zero dose and undervaccinated children)

2 Surveys

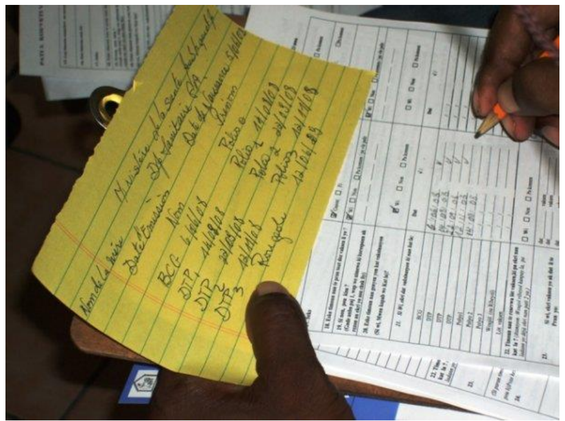
- Assess coverage and timeliness for older children (where dates available)

3 Other approaches

- Incorporate Big Catch-Up long-term impact questions into other existing program assessments (EPI reviews, etc)



Source: analysis by Colin Sanderson on 2010 DHS



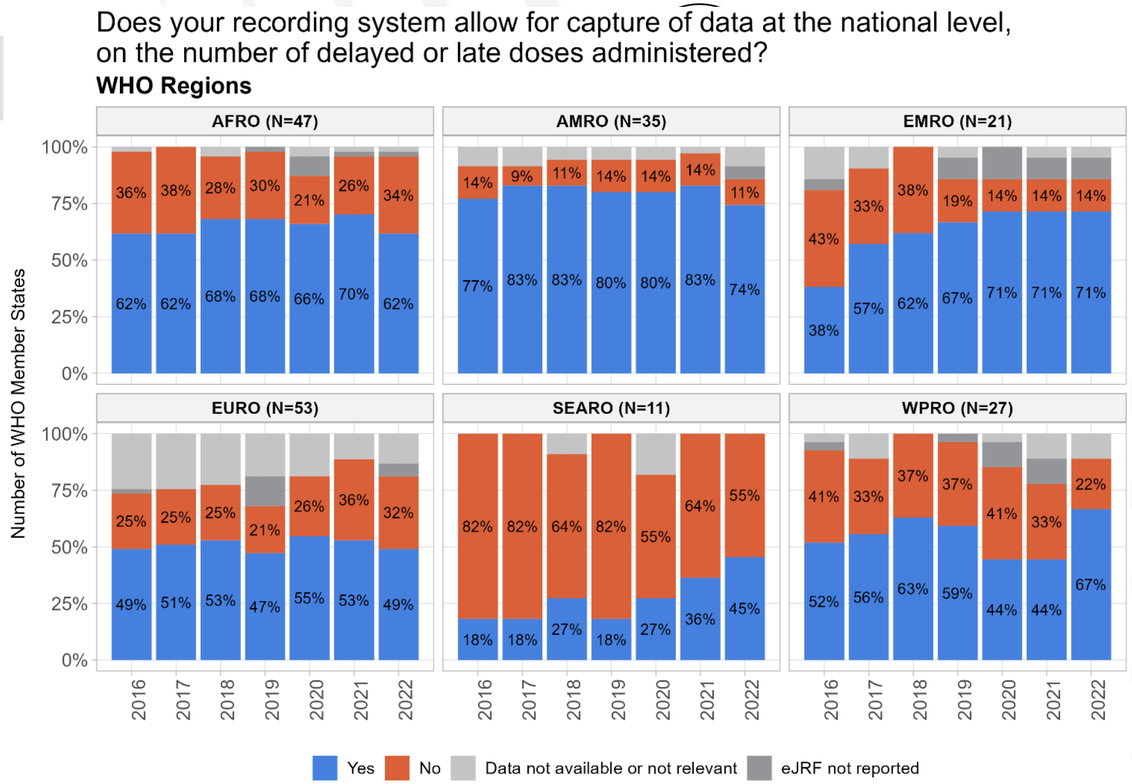
Summary: Common monitoring challenges

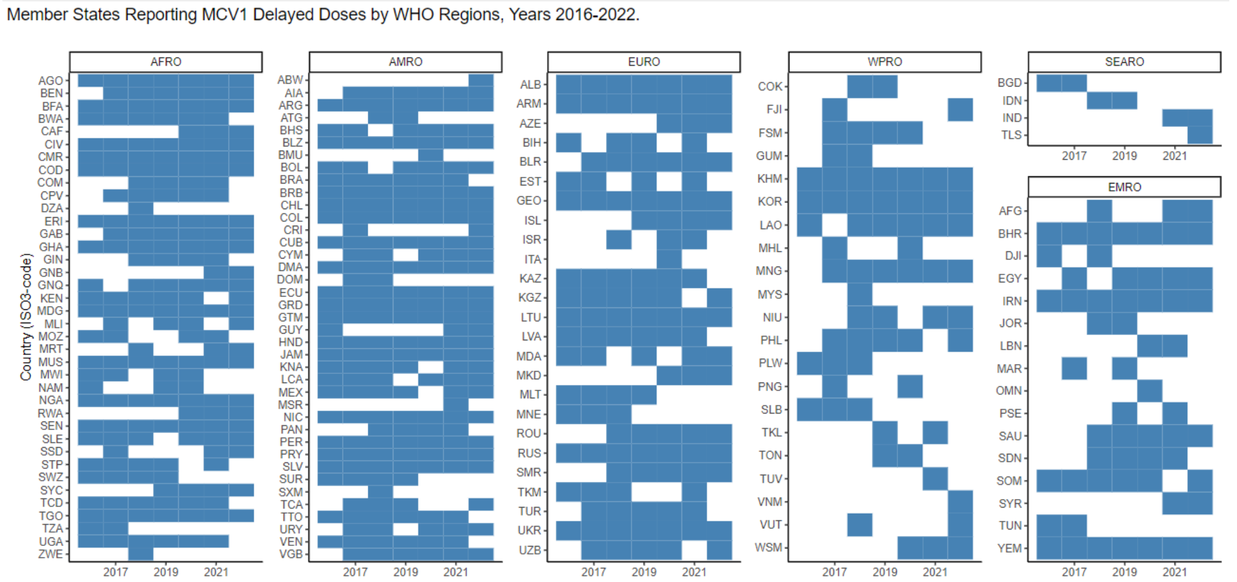
Country level:

- Determining eligibility for catch-up doses
- **Data tools and systems** in many countries not set up to capture catch-up doses by separating age groups: <12 m; 12-23 m, 24-59m.
- Home-based records not always available.
- Health workers not familiar with recording and aggregating data by age group
- **Administrative data** at risk of being “contaminated”, i.e., mixing doses given to infants with doses to children ≥12 months (or ≥24months)
- **Funding and time** needed to support catch-up M&E implementation

Global level:

- Big Catch-up is a heterogenous initiative
- Data collection is limited – **eJRF** is annual and historically collecting only MCV1 by age group (<12 m, 12-23m; (or ≥24m))
- **WHO/UNICEF estimates of national immunization coverage (WUENIC)** not designed to monitor catch-up





March 2024

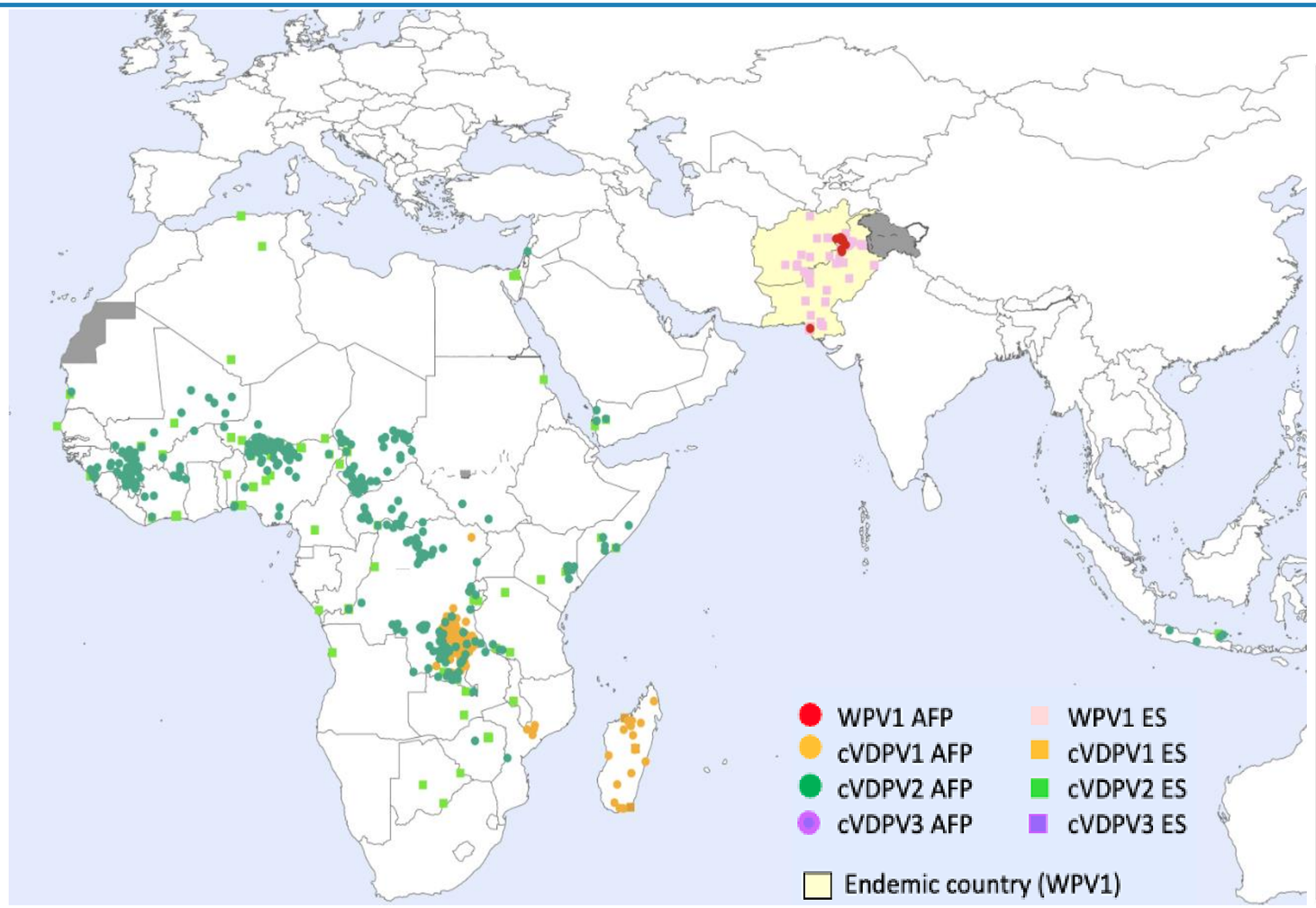
Poliomyelitis

Items for discussion/recommendation

1. To discuss the policy framework and triggers for bOPV cessation planning.

2. To recommend on use of fIPV administered intramuscularly.

Poliovirus Epidemiology: Global WPV1 & cVDPV Cases, 2023



Latest onset by country:

WPV1 cases (latest onset)		
Pakistan	6	24-Oct-23
Afghanistan	6	04-Sep-23
cVDPV1 cases (latest onset)		
DR Congo	105	24-Nov-23
Madagascar	24	16-Sep-23
Mozambique	4	11-Sep-23
cVDPV2 cases (latest onset)		
CAR	14	07-Oct-23
Nigeria	82	03-Dec-23
Guinea	46	28-Nov-23
DR Congo	118	19-Nov-23
Somalia	5	16-Sep-23
Chad	54	26-Nov-23
Côte d'Ivoire	6	12-Nov-23
Yemen	4	17-Nov-23
Mali	12	06-Nov-23
Kenya	8	21-Aug-23
Tanzania	3	16-Nov-23
Burundi	1	15-Jun-23
Burkina Faso	2	04-Jun-23
Zambia	1	03-Apr-23
Benin	3	15-Mar-23
Indonesia	6	06-Dec-23
Israel	1	13-Feb-23
Zimbabwe	1	02-Dec-23
Niger	2	11-Dec-23
Mauritania	1	17-Oct-23
South Sudan	2	07-Nov-23
Mozambique	1	22-Nov-23

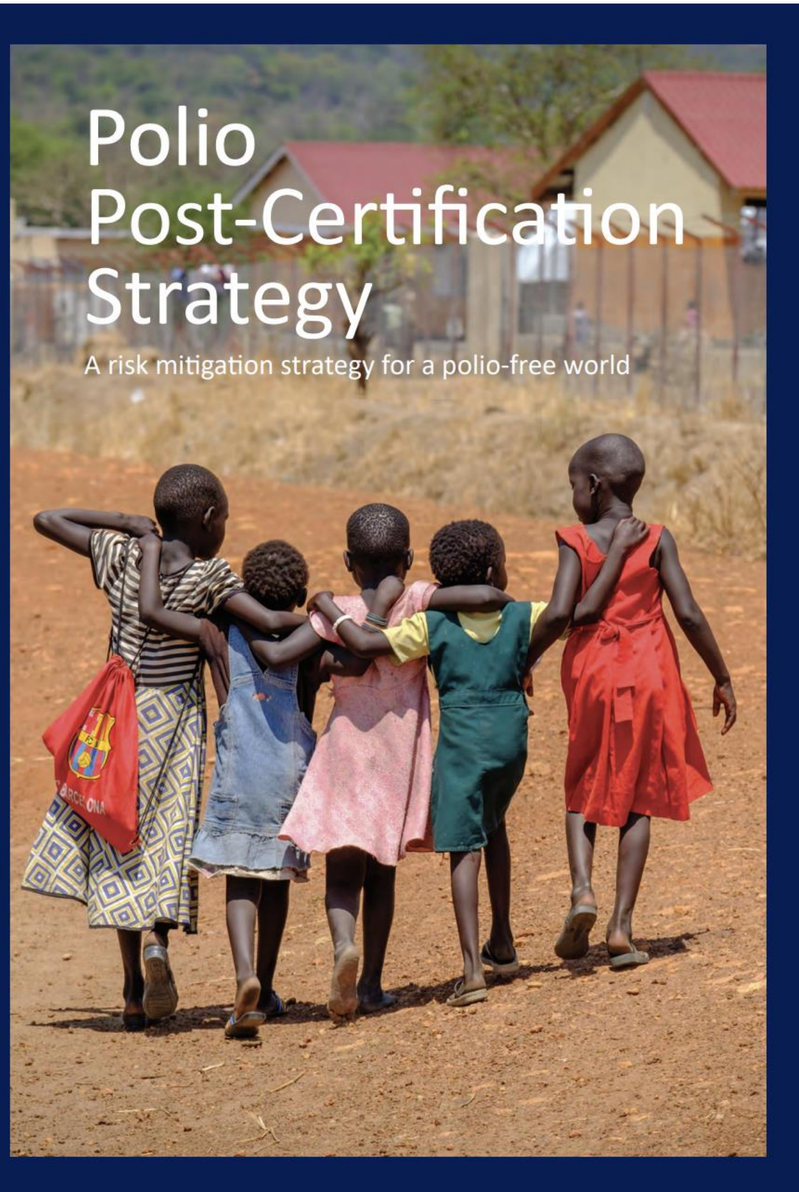
WPV1 isolates (latest collection)		
Pakistan	125	27-Dec-23
Afghanistan	62	23-Dec-23
cVDPV1 isolates (latest collection)		
Madagascar	91	31-Jul-23
cVDPV2 isolates (latest collection)		
Algeria	24	30-Oct-23
Nigeria	75	21-Dec-23
Côte d'Ivoire	33	05-Dic-23
DR Congo	37	07-Dic-23
Kenya	8	29-Sep-23
Mali	6	24-Oct-23
Zimbabwe	17	27-Dec-23
Somalia	9	21-Sep-23
Tanzania	6	20-Nov-23
Cameroon	13	28-Sep-23
Egypt	11	13-Sep-23
Guinea	11	24-Dec-23
Mauritania	2	18-Oct-23
Niger	4	19-Dec-23
Chad	3	10-Aug-23
Botswana	5	25-Jul-23
Burundi	13	13-Jun-23
Zambia	2	06-Jun-23
Yemen	10	25-Sep-23
CAR	1	19-May-23
Congo	2	07-Dic-23
Benin	4	05-Dic-23
Malawi	1	02-Jan-23
Sudan	5	20-Dic-23
Indonesia	1	07-Dic-23
Angola	1	05-Dic-23
Senegal	1	06-Nov-23

Poliovirus circulation (both of WPVs and cVDPVs) is the only currently declared Public Health Emergency of International Concern.

bOPV Cessation Planning

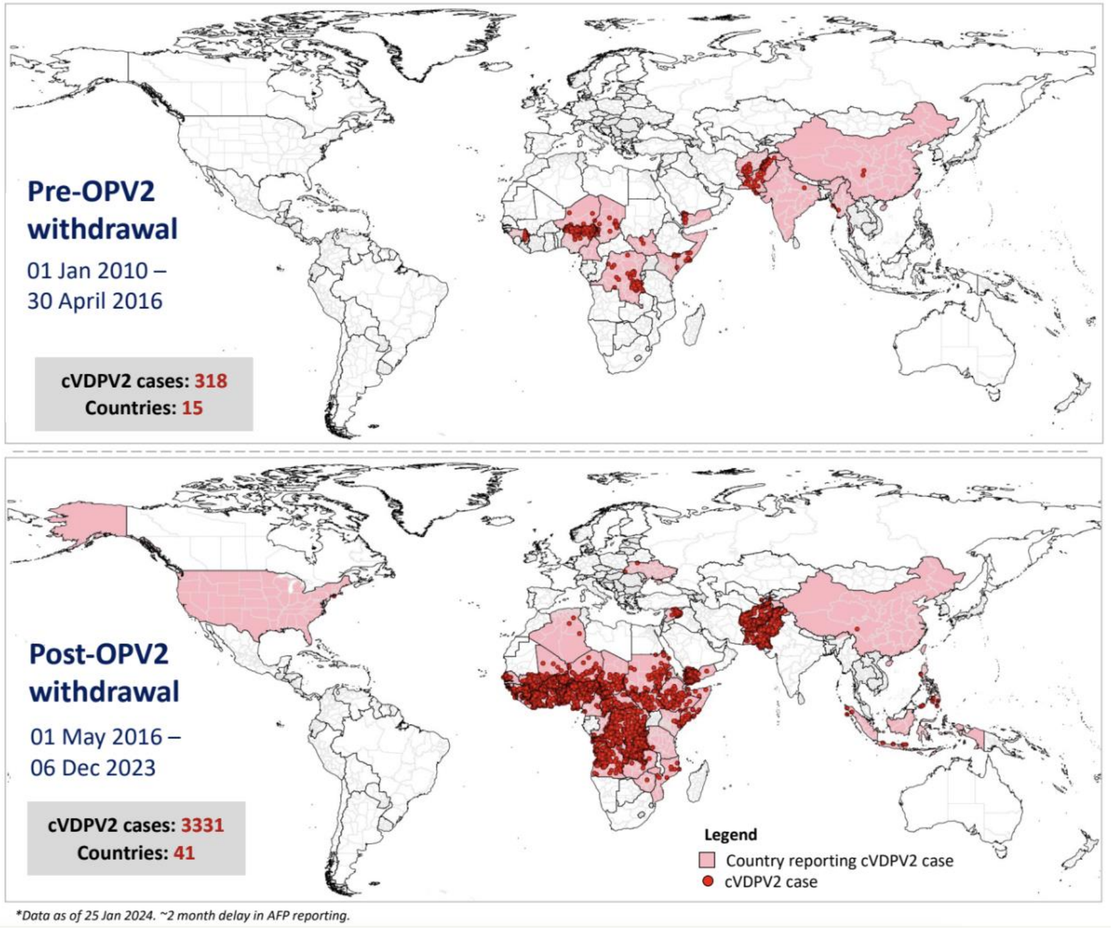
What is bOPV cessation?

- bOPV Cessation is a global withdrawal of bOPV from RI following certification of WPV eradication (all countries will become IPV-only)
  - There is consensus that the use of live poliovirus vaccines is incompatible with poliovirus eradication
  - The Global Certification Commission (GCC) will start process of certification of VDPV eradication only AFTER all OPVs are withdrawn from use
  - The first step in OPV cessation was the global switch from tOPV to bOPV in 2016
- The 2018 Post Certification Strategy[1] set the framework for bOPV Cessation one year after certification of WPV eradication (est. 2027)



bOPV Cessation Planning: Evaluation of the tOPV-bOPV Switch

- SAGE reviewed the key findings from an independent evaluation of the tOPV-bOPV switch
- The tOPV-bOPV switch was an unmitigated failure.
- The single overriding cause of the OPV2 cessation failure was/is the inability of the programme to close out outbreaks with timely, high-quality responses of an adequate scale



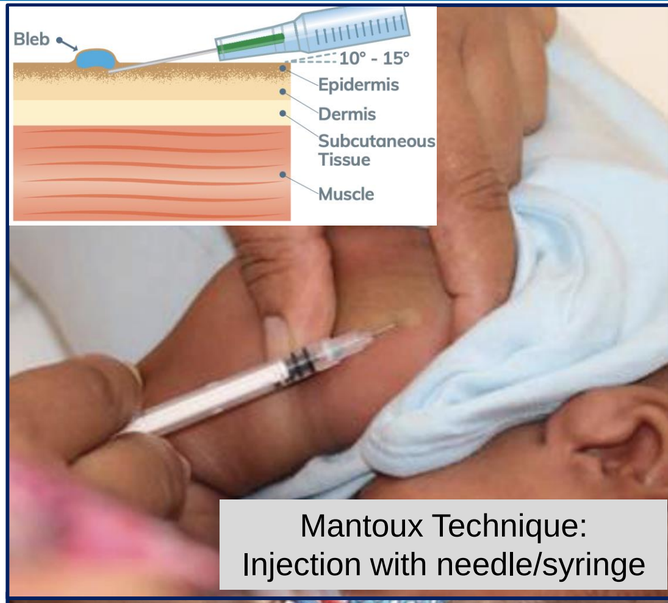
bOPV Cessation Planning: SAGE Deliberations

- SAGE concurred that the current timeline aimed for bOPV cessation in 2027 will not materialize given the uncertainty of WPV1 cessation and cVDPV1 and cVDPV2 interruption of transmission
- SAGE members strongly support that bOPV cessation should only be done after cVDPV2 outbreaks are stopped, including in the consequential geographies.
- SAGE recommended that low-polio-risk countries (as designated by each WHO region) with at least two IPV doses (full or fractional) attaining high coverage in RI should consider transitioning into IPV-only schedules ahead of planned synchronized bOPV cessation

- ***SAGE was supportive of the need for proposed programme enablers and triggers to guide cessation and highlighted that the specific and detailed criteria will need to be further elaborated by the bOPV Cessation Team (BOCeT) and presented for endorsement by SAGE in fall of 2024.***

Current options for fIPV intradermal administration

- Off-label fIPV administered intradermally with N/S is successfully given in the RI schedule of 6 countries – Sri Lanka[1], India[2], Bangladesh[3], Nepal[4], Cuba, and Ecuador[5].
- >10 intradermal fIPV campaigns with N/S or Tropis have been conducted from 2016-2023 in Pakistan, Nigeria and India (POLIS) as a response to either endemic transmission of WPV1 or outbreaks of cVDPVs
- Challenges with current methods of intradermal injection:
  - N/S requires training and skilled administration – improper administration may result in poor immunogenicity[6]
  - N/S entails complex operational logistics for outbreak response – requires fixed-station campaigns and a transient skilled workforce[7,8]
  - Cost of jet injectors makes the device less feasible for widespread integration into RI



Mantoux Technique:
Injection with needle/syringe

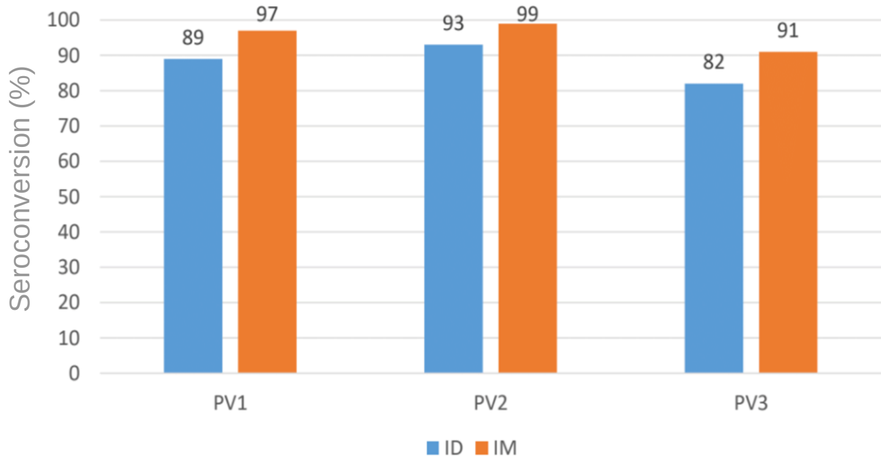
Pharmajet's Tropis:
Needle-Free Jet Injector

[1]DOI:10.4103/2224-3151.239418; [2]DOI:10.2471/BLT.18.218370; [3]DOI: 10.1093/infdis/jiw510; [4]UNICEF; [5]DOI:10.1016/j. lana.2022.100235; [6]DOI: 10.1016/j.vaccine.2012.11.021; [7]DOI: 10.15585/mmwr.mm6533a5; [8]DOI:10.15585/mmwr.mm6647a4e

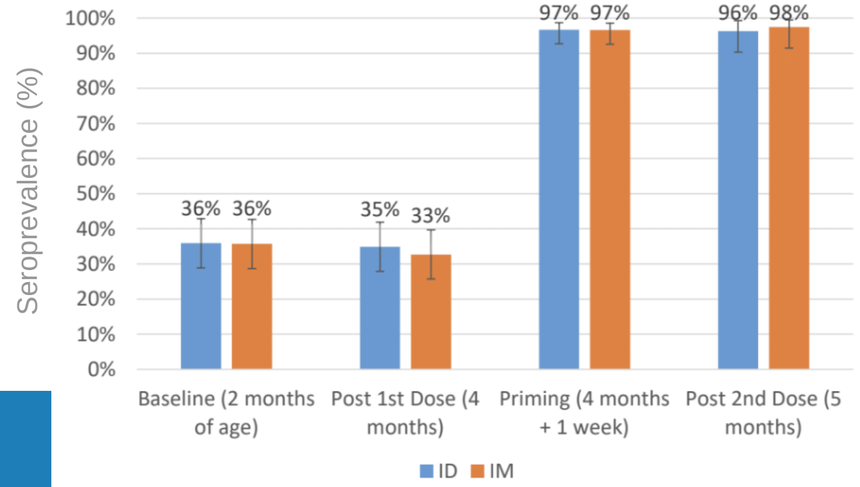
Fractional IPV intramuscular administration

There are now two studies from two different populations and age groups demonstrating non-inferiority of fractional IPV administered intramuscularly compared to intradermally

Two-Dose Seroconversion			
	IM	**ID**	**Difference**
Cuba at 4 and 8mo	98.7%	92.9%	5.8 (-4.1–15.7)
MOZ at 2 and 4mo	96.1%	92.2%	3.9 (-1.3–9.1)



Second dose seroconversion of fIPV administered at 4 and 8 months for three serotypes, Cuba



Type 2 poliovirus seroprevalence after fIPV administration at 2 and 4 months of age, Mozambique

SAGE Recommendation: Fractional IPV intramuscular administration

- SAGE previously recommended that an additional IPV or fIPV campaign can be added to outbreak response in areas with persistent poliovirus circulation after 2+ OPV campaigns.[1]

- Recognizing the non-inferiority in immunogenicity of intramuscular compared to intradermal administration of fIPV established via two different studies, SAGE recommends that countries responding to persistent poliovirus circulation may choose the mode of administration of fIPV (i.d. or i.m.) in outbreak response campaigns.

World Health Organization
Organisation mondiale de la Santé
Weekly epidemiological record
Relevé épidémiologique hebdomadaire
2 JUNE 2023, 97th YEAR / 2 JUIN 2023, 97e ANNÉE
No 22, 2023, 98, 239–256
http://www.who.int/wer

Meeting of the Strategic Advisory Group of Experts on Immunization, March 2023: conclusions and recommendations

SAGE was presented with evidence on the role of IPV in areas of persistent poliovirus transmission. On the basis of the evidence from clinical trials, observational studies, and field experience, SAGE recommended that, in areas where transmission continues after 2 or more OPV campaigns, an additional IPV (full or fractional dose) campaign (together with OPV whenever possible) should be conducted to enhance individual-level protection and reduce transmission by enhancing mucosal immunity. These campaigns should primarily target children under 5 years of age; however, older age groups may be considered if the epidemiological data warrant this. The focus should be on geographical areas at the highest risk for persistent poliovirus transmission. SAGE recommends paying particular attention to the Afghanistan-Pakistan border.

[1]Meeting of the Strategic Advisory Group of Experts on Immunization, March 2023: conclusions and recommendations. 2023, 98, 239-256

Poliomyelitis
Summary of SAGE Observations & Recommendations from March 2024

SAGE was pleased to note that WPV1 circulation is confined to a small geographic area, and the genetic diversity of detected WPV1s is markedly decreased, however expressed **concern about the continued circulation of cVDPV2** in Africa and detections of cVDPV1 in several countries.

SAGE stressed the need for increased efforts to **improve routine immunization coverage, especially for IPV1.**

SAGE extended its **support to the bOPV Cessation Team in planning for the eventual cessation** of the use of Sabin bOPV and will review the triggers and pre-requisites developed by the bOPV cessation team to ensure a successful cessation.

SAGE reiterated that **only low-polio-risk countries with high coverage** with at least two IPV doses in the routine immunization schedule should **consider transitioning to IPV-only** vaccination schedules ahead of planned synchronised bOPV cessation.

SAGE recommended that to stop persistent poliovirus circulation, **countries opting for off-label fractional dose vaccination of IPV may choose either an intradermal or intramuscular route** of administration in outbreak response campaigns.

https://cdn.who.int/media/docs/default-source/immunization/sage/2024/march/sage-meeting-highlights_v3-march2024.pdf?sfvrsn=b7e9f570_2&download=true

Mpox

Standing recommendations for mpox issued by Director-General in accordance with IHR (2005)

States Parties are recommended to:

A. Have **national mpox plans** integrated into broader health systems. Capacities that have been built in resource-limited settings and among marginalized groups should be sustained.

B. Strengthen and sustain **testing and surveillance** capacity and ensure that new cases of mpox are notified nationally and to WHO.

C. Protect communities through **communication and engagement**; continue to build trust and fight stigma and discrimination.

D. **Invest in research** to better understand mpox disease and transmission patterns, and to develop improved vaccines, tests, and treatments.

E. **Provide travelers with information** to protect themselves and others before, during and after travel and refrain from implementing travel-related health measures, including mpox screening and testing for travelers.

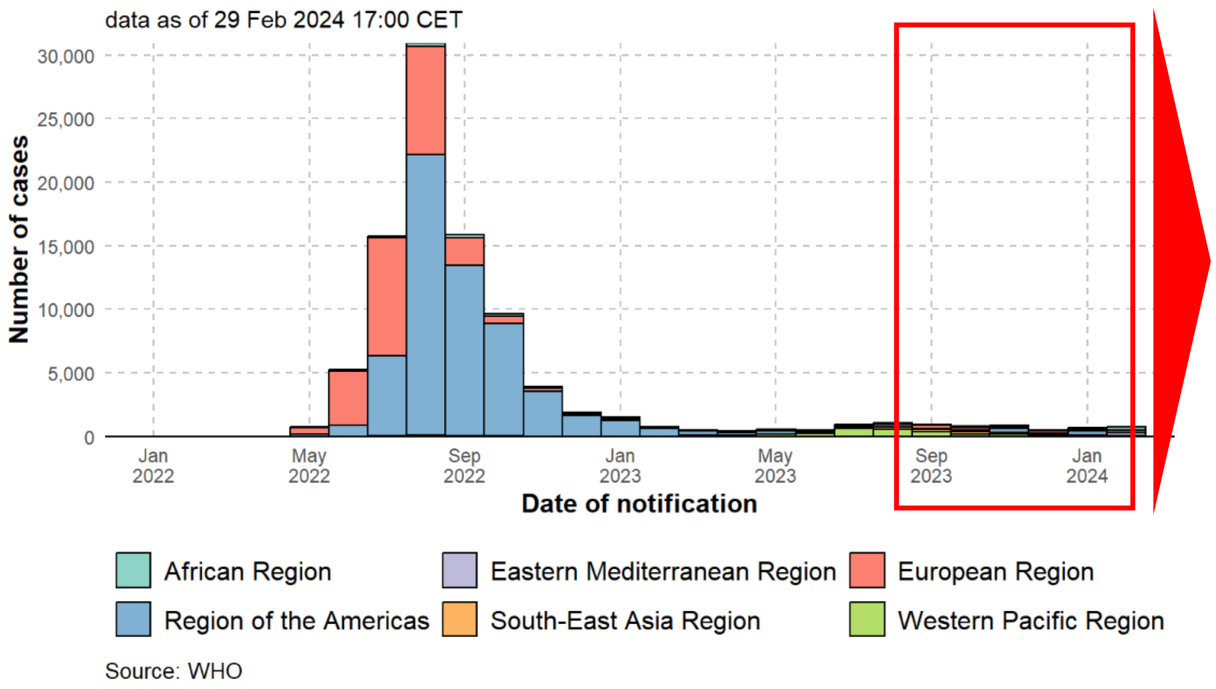
F. **Deliver optimal clinical care** for mpox patients, integrated within HIV and STI programmes, with access to treatments and measures to protect health workers and caregivers.

G. **Work towards equitable access to safe, effective and quality-assured vaccines,** tests and treatments for mpox.

World Health Organization

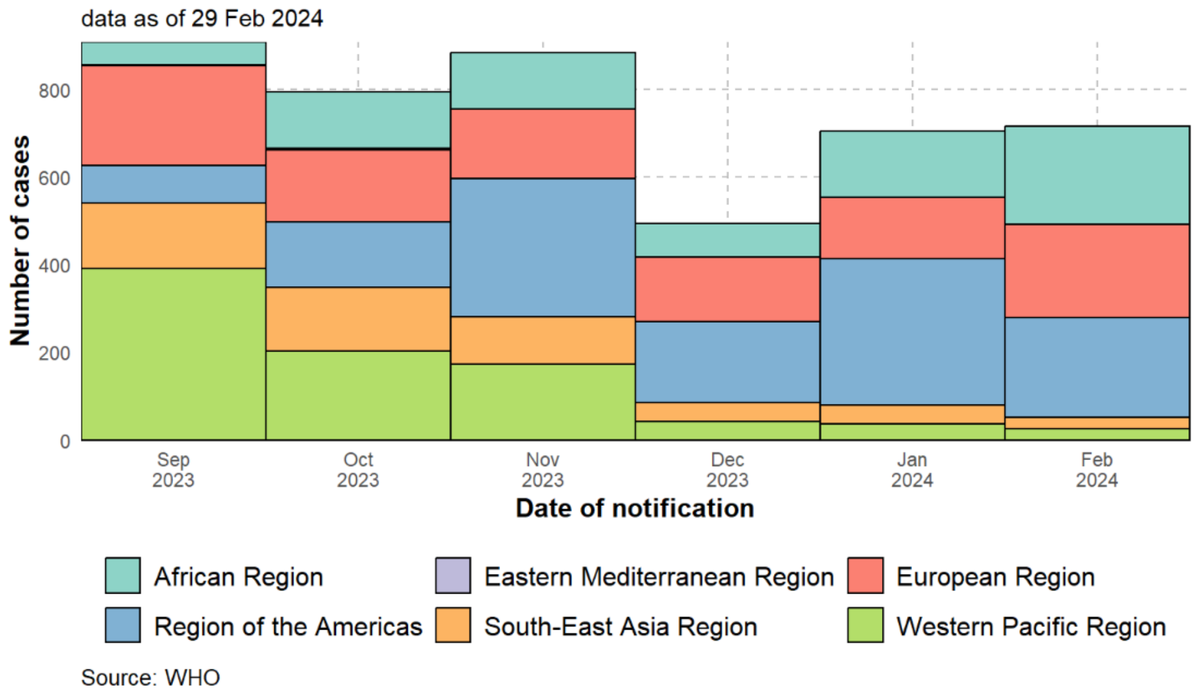
Mpox at the global level - epidemic curve over time and last 6 months, confirmed cases

01 Jan 2022 – 29 Feb 2024



Source: WHO

01 Sep 2023 - 29 Feb 2024



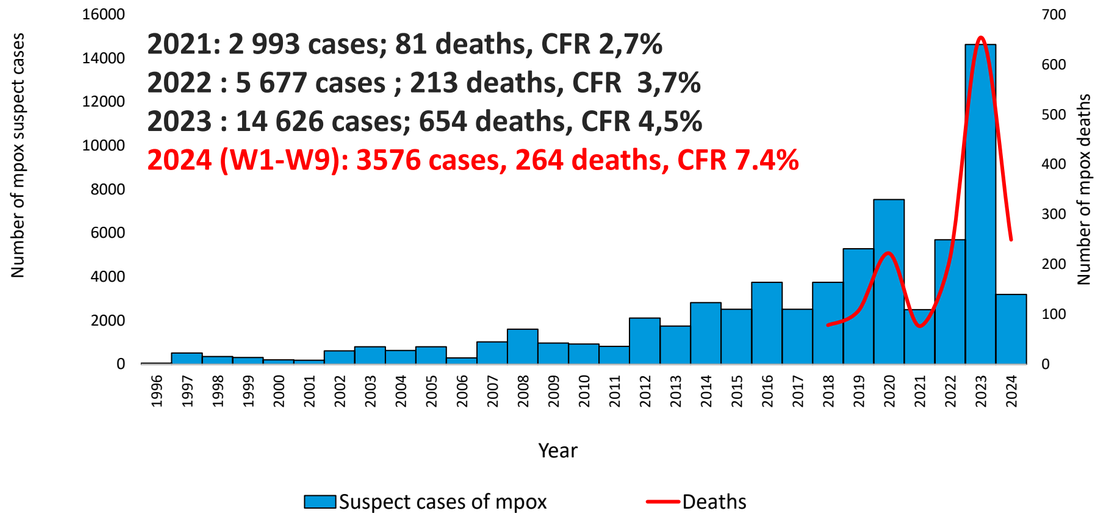
Source: WHO

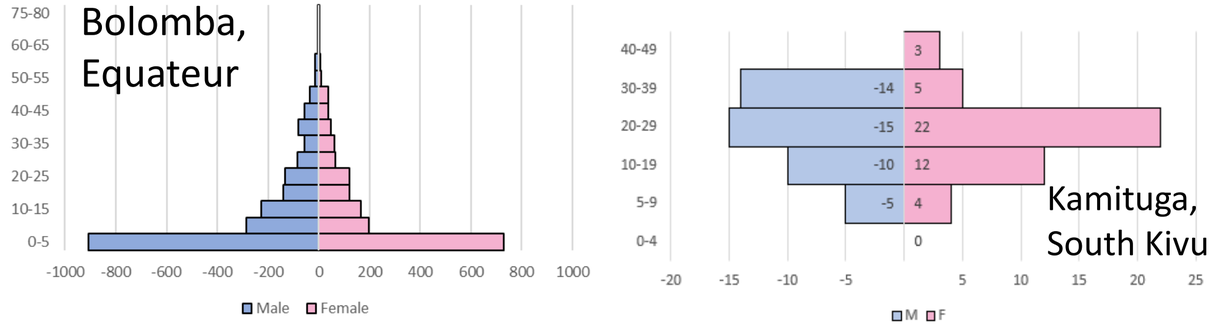
Notes: All data shown includes probable and confirmed mpox cases.

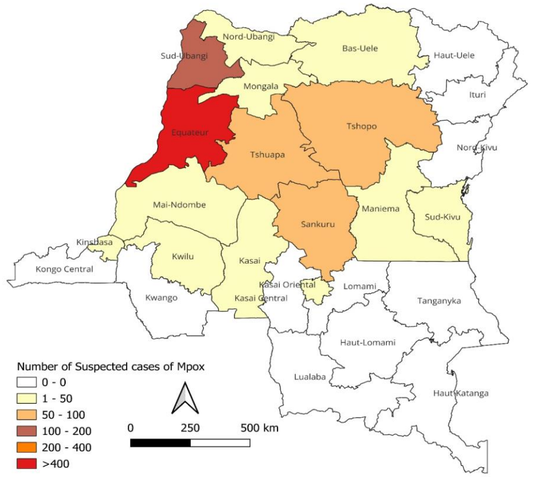
World Health Organization

Mpox in the Democratic Republic of the Congo – clade I

Suspected (clinically compatible) cases of mpox reported (1996 to W8-2024)





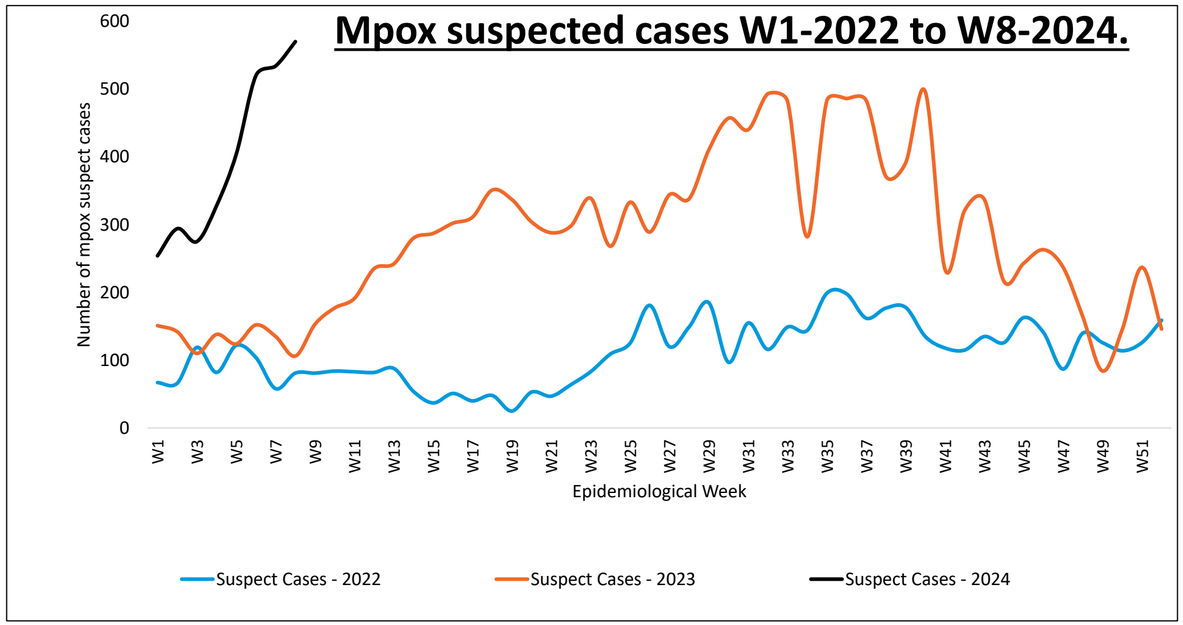


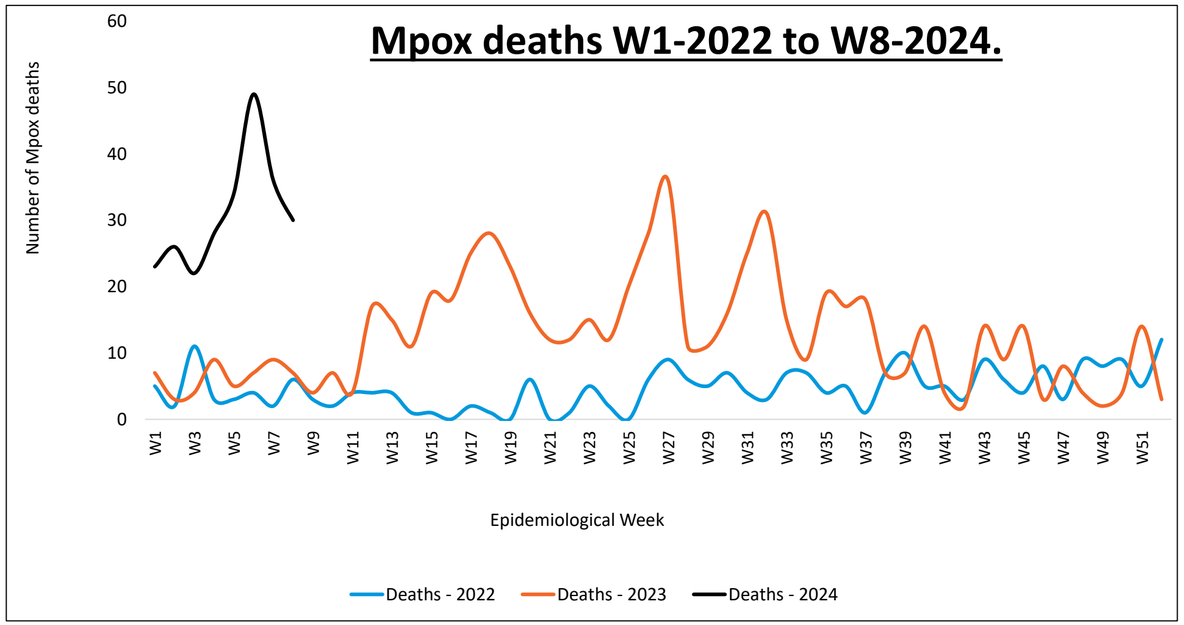
- **Rising number** of cases, deaths reported
- **Geographic expansion** – 23/26 provinces including Kinshasa
- **Sexual transmission**, sex workers, key populations, households
- **Rising case fatality** ratio
- Affecting mining areas, South Kivu
- Border countries at risk – civil unrest, population movements

DRC mission report

Mpox in the Democratic Republic of the Congo – 2022 to 2024

- **Cumulative W1 – W8 2024**:
  - 3576 suspected cases and 264 deaths reported (CFR=7.4%).
- **Epidemiological Week 8 2024**:
  - 570 suspected cases and 30 mpox deaths (5.3%)



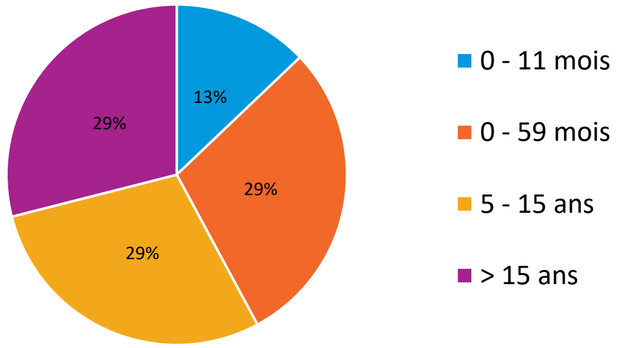


Source: Ministère de la santé, hygiène et prévention

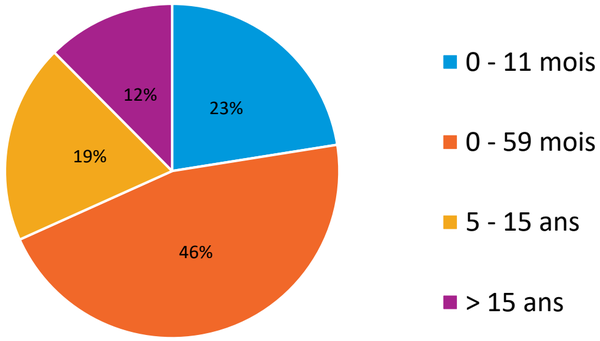
World Health Organization

Mpox in the Democratic Republic of the Congo – age and sex distribution

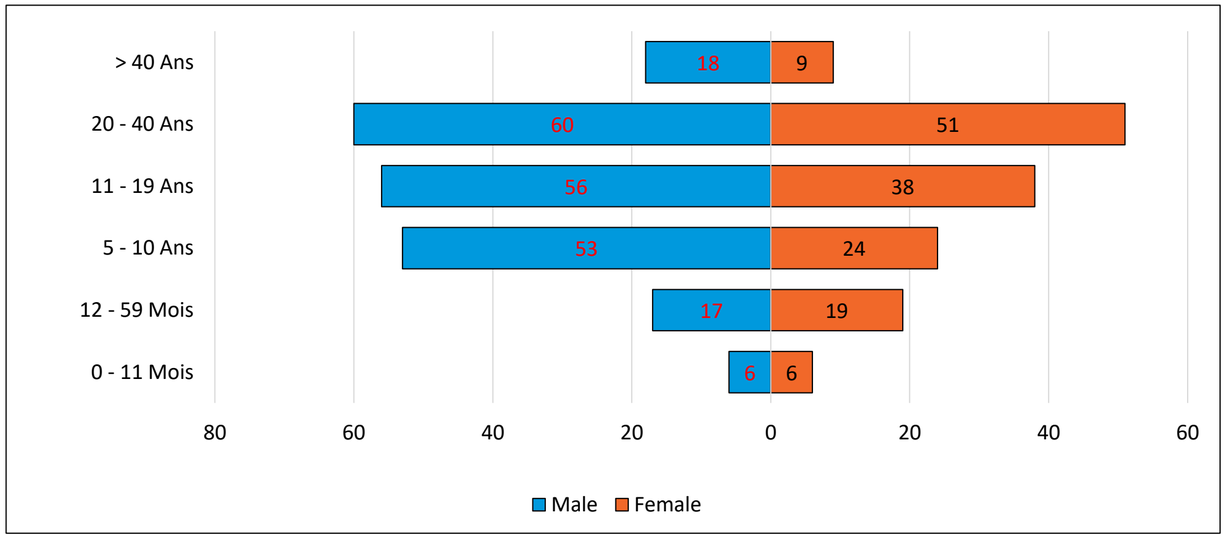
Age distribution of suspected cases of mpox W1-W8 2024 (n=3190)



Age distribution of mpox deaths W1-W8 2024 (n=246)



Age / sex distribution of laboratory-confirmed cases of mpox W1-W8 2024



Suspected cases from W1-W8 2024:

- Children <15 Years account for 71% of susp cases and 88% of deaths

Confirmed cases from W1-W8 2024:

- 58% are male (boys/men more affected across most age groups).
- Children <15 Years account for 57% of confirmed cases.

World Health Organization

Mpox in the Democratic Republic of the Congo – in summary

- **Continuing rise in reported cases, deaths**
  - One in five health zones already reporting >3500 cases in 2024
  - 9.5% laboratory-confirmed, nationally 76% of received specimens test + for mpox by PCR
  - mpox/HIV, mpox/HIV/syphilis co-infections now reported
  - **Equateur** – outbreak focus moved to Lotumbe HZ
  - **Kamituga**, South Kivu outbreak continues

- **Strain variations, gene deletions leading to diagnostic failure of clade I specific PCR**
  - review of diagnostic protocols
  - suggestion of enhanced human-to-human transmission of virus (APOBEC-related mutations)

- **Continuing enhanced studies in animals** (e.g. Sud Ubangi)

Mpox vaccine effectiveness: A systematic review and meta-analysis

- **VE Estimate PEP with MVA-BN: 20% (95%CI -24%-64%)**
  - *Challenging to measure VE and obtain appropriate control group*
  - *Low VE may in part be due to sexual transmission in study group*
  - *If PEP used, rapid access to vaccination recommended (<4 days)*
- **VE Estimate for 1-dose of MVA-BN: 76% (95%CI 65%-86%)**
  - *Relative stability of estimate with removal of poor-quality studies*
- **VE Estimate for 2-dose of MVA-BN: 82% (95%CI 72%-92%)**
  - *Relative stability of estimate with removal of poor-quality studies*
  - *Prioritize vaccination prior to exposure for at-risk individuals*
- GRADE with very low confidence for all estimates

Mpox systematic review on vaccine safety

- All mpox vaccines give local and systemic adverse events
- ACAM2000 (second generation vaccines) has a higher SAE and myocarditis risk compared to third generation vaccines (LC16, MVA-BN)
- LC-16 is approved for use in children in Japan with a good safety profile (use in 50,000 children, no serious adverse events).
- MVA-BN is licensed for persons 18 and older.
  - Limited data on MVA-BN use in children (studies in 159 children, use in a further 1003 children) show a good safety profile (no serious AE).
  - EBV vaccine (MVA-BN-filo) demonstrates a good safety profile (n= 52,229) and is licensed for use in children aged 1 and older.
- Graded certainty of evidence is low to very low

Recommendation mpox outbreak response[1]

- Vaccination is **recommended for persons at high risk of exposure to mpox in an outbreak**. The identification of populations at risk of exposure is limited in some settings by currently available epidemiological data. In studies involving men who have sex with men, pre-exposure vaccination with one or two doses of smallpox/mpox vaccine was demonstrated to be effective against mpox. Effectiveness of post-exposure vaccination is less certain, which may be linked to the predominantly sexual mode of transmission in available studies. To allow the greatest flexibility with respect to local risk assessment, varied modes of transmission and response options, populations to consider for vaccination may include:
    - **based on local epidemiology**, members of a geographically defined area or community (e.g. village), **including children**, with a documented high risk of exposure to mpox;
    - sex workers; gay, bisexual or other men who have sex with men (MSM) with multiple sexual partners; or other **individuals with multiple casual sexual partners**;
    - **health workers at risk of repeated exposure**; clinical laboratory and health care personnel performing diagnostic testing for mpox or providing care, and outbreak response team members (as designated by national public health authorities).
    - **contacts of persons with mpox**, ideally within four days of first exposure.[2] Contacts may include children, others in the household or in congregate settings (such as prisons, schools, health facilities or residential facilities)

1. Outbreak definition: occurrence of two or more laboratory confirmed (or one laboratory confirmed and one or more epidemiologically linked cases) of mpox in nationally or locally defined geographic areas

2. Criteria to define risk of exposure in this context include e.g. direct skin-to skin physical contact, contact with contaminated materials such as clothes or bedding. Vaccination ideally up to 14 days in the absence of symptoms.

Choice of vaccines for immunocompetent non-pregnant individuals

- WHO recommends that for immunocompetent non-pregnant individuals, non-replicating vaccine (MVA-BN), minimally replicating vaccines (LC16-KMB), replicating cell-culture derived vaccinia-based vaccines (e.g. ACAM2000) or equivalent vaccines that meet WHO standards for quality, are appropriate for use.
- Specific considerations, including potential off-label use, apply as to vaccine choice for special population groups (see recommendation on vaccine choice for special populations).

Choice of vaccine for special populations - infants, children and adolescents

- For infants, children and adolescents, where consideration is given to vaccination, non-replicating (MVA-BN) or minimally replicating (LC16-KMB) vaccines may be used.
    - LC16-KMB is approved for use in children in Japan.
    - While MVA-BN is currently not licensed for persons under 18 years old, this vaccine may be used in infants, children and adolescents when the benefits of vaccination outweigh the potential risks in the context of an mpox outbreak. The use of MVA-BN in children constitutes an “off-label” product use.
    - Replicating vaccine (such as ACAM2000) should not be used in infants.
    - WHO recommends further collection of data on vaccine safety and effectiveness for these populations.

Research priorities & call to action

- **Research priorities:**
  - In regions with endemic disease, there is urgent need for better understanding of modes of transmission; age-specific cases (incidence), deaths and seroprevalence; and characterization of risk factors for MPXV infection and severity of disease.
  - In particular, the reported high morbidity and mortality in children requires a dedicated effort to understand the epidemiology and vaccine effectiveness, safety and immunogenicity in this group.
  - Duration of vaccine protection based on route of administration and number of doses received must be defined.
- **Call to action:**
  - SAGE emphasizes the importance of **availability and access to vaccines** in mitigating the impact of mpox in regions with endemic disease and promoting equity
  - SAGE requests that immediate attention be given to **regulatory and procurement processes** that facilitate equitable vaccine access and deployment in low-and-middle income countries
  - SAGE strongly recommends **systematic on-going data collection during deployment of vaccines** to evaluate the effectiveness, safety and impact of vaccination strategies.
  - SAGE recommends **sustainable investment in research** institutions, research capacity and regulatory authorities **in the African region**

Global strategic framework for mpox (2024 – 2027)

Goal

Achieve sustained elimination of human-to-human transmission of mpox

Objectives

(1) Achieve control of mpox in every context

(2) Advance mpox research and access to countermeasures

(3) Minimize animal-human transmission

Elimination of human-to-human transmission is the absence of new cases (without defined travel history or zoonotic exposure) for ≥ three months in the presence of adequate surveillance. This goal applies to all countries and contexts.

World Health Organization

Thank you