

Highlights from the Meeting of the Strategic Advisory Group of Experts (SAGE) on Immunization 25-29 September 2023

(The full report will be published in the Weekly Epidemiological Record on 1 December 2023, and only the wording of the full report should be considered final)

Session 1

Report from the Department of Immunization, Vaccines, and Biologicals.

- Climate change is accelerating the spread and burden of vaccine-preventable diseases and necessitating modifications in the strategy and implementation of immunization programmes; It has contributed to the backsliding in immunization coverage during the pandemic.
- WHO will be convening stakeholders to identify action necessary to adapt vaccines and immunization programmes for the growing climate threat.
- While there has been significant progress in restoring routine vaccination coverage to pre-pandemic levels, the progress has been uneven, especially in LMICs. Several countries have experienced large and disruptive outbreaks of measles and diphtheria in the last two years.
- Major progress has been made with the COVID-19 vaccination response. Starting in January 2024, the focus will shift to ensuring the annual uptake of vaccination in eligible populations.
- Despite the setbacks experienced during the pandemic, there are opportunities to build back better in the future. Several new vaccines, such as against respiratory disease (respiratory syncytial virus – RSV) or bacterial meningitis and sepsis (group B streptococcus – GBS) are likely to become available in the next five years, which will need to be prioritized for introduction and ensuring access to those most in need.
- Major progress has been made with the COVID-19 vaccination response, and it is critical to continue the progress particularly for those most at risk of disease, including with updates to reporting of coverage.

2024 will be the 50th anniversary of the founding of the Expanded Programme on Immunization (EPI) and a time to celebrate its successes.

Update from Gavi, the Vaccine Alliance.

- As part of the “Big Catch-up”, Gavi reviewed requests for support from 25 countries and will provide flexible financing and technical assistance.
- With the closure of the COVAX Facility in 2023, Gavi will transition to providing support for COVID-19 vaccination to the highest priority groups in eligible countries.
- Gavi is strengthening its role in pandemic prevention, preparedness, and response.

- To address shortfalls in oral cholera vaccine (OCV) supply to mitigate the risk of cholera outbreaks, an OCV market-shaping roadmap was agreed with partners and a UNICEF tender is ongoing for vaccine supply for the period 2024 to 2028.
- The pause in support for vaccines approved in the previous Gavi Vaccine Investment Strategy (VIS) has been lifted and their implementation is underway. The VIS 2024 is underway with a final decision expected by the Gavi Board in June 2024.

Session 2

Dengue

- Dengue poses a significant public health burden in endemic countries and is poised to increase further both in terms of incidence and geographic expansion, due to climate change and urbanization.
- The live-attenuated quadrivalent dengue vaccine developed by Takeda (TAK-003) has demonstrated efficacy against all four serotypes of the virus in baseline seropositive children (4-16 years) in endemic countries and against serotypes 1 and 2 in baseline seronegative children.
- In baseline seronegative children, the vaccine trial did not demonstrate efficacy against symptomatic disease against serotypes 3 and 4 and hospitalization due to serotype 3; there were too few cases of hospitalized serotype 4 cases to assess efficacy. The potential risk of enhanced disease due to serotypes 3 and 4 in seronegative vaccinated children cannot be ruled out.
- SAGE recommended that the vaccine be considered for introduction in settings with high dengue disease burden and high transmission intensity to maximize the public health impact and minimize any potential risk in seronegative persons.
- SAGE recommended that the vaccine be introduced to children aged 6 to 16 years of age. Within this age range, the vaccine should be introduced about 1-2 years prior to the age-specific peak incidence of dengue-related hospitalizations. The vaccine should be administered in a 2-dose schedule with a 3-month interval between doses.
- SAGE recommended that vaccine introduction should be accompanied by a well-designed communication strategy and community engagement.
- Post-authorization studies should be conducted to further study vaccine effectiveness and safety against serotypes 3 and 4.

Session 3

Antimicrobial resistance

- Modelling studies estimate almost 5 million deaths associated with resistant infections in 2019. However, vaccines remain an underrecognized tool to prevent antimicrobial resistance (AMR).

- WHO evaluated the value of existing and future vaccines on AMR. The analyses indicate that vaccines can have a significant impact on AMR-related health and economic burden and reduce antibiotic use.
- SAGE emphasized that AMR-related endpoints should be included in evaluating vaccines under development and that the evidence on the impact of vaccines on AMR should be considered in policy and investment decisions.

Session 4

Meningitis

- SAGE recommended that all countries in the African meningitis belt introduce the novel pentavalent meningococcal conjugate vaccine targeting serogroups A, C, Y, W and X (Men5CV) into their routine immunization programmes in a single-dose schedule at 9 to 18 months of age.
- In high-risk countries, and countries with high-risk districts, a catch-up campaign should also be conducted at the time of the introduction of Men5CV, targeting all individuals aged 1 to 19 years.
- Countries in the meningitis belt that have already introduced a monovalent meningococcal A conjugate vaccine (MenACV) into their routine programme should switch to Men5CV.
- Countries that have not yet introduced MenACV should do so now and not wait until Men5CV is available, to avoid the risk of a resurgence of *Neisseria meningitidis* serogroup A (NmA).
- Before the planned introduction of Men5CV in immunization programmes, reactive vaccination campaigns may be extended to areas assessed to be at increased risk of an epidemic during the upcoming season.
- The implementation of the recommendation will be instrumental in eliminating epidemic meningitis epidemics in the meningitis belt as envisioned in the 2030 global WHO road map.

Session 5

Immunization Agenda 2030 (IA2030)

- SAGE was presented with the technical progress report, which was developed through a collaborative, multi-stakeholder process and reviewed and endorsed by the Immunization Agenda Coordination Group.
- Progress against the IA2030 indicators was stalled due to the impact of the COVID-19 pandemic and was off-track for six of the seven impact goal targets; progress against the target for the introduction of new vaccines is on track driven by the introduction of new vaccines in low-income countries in 2022.

- While there are promising signs of recovery, it is uneven; recovery is especially slow in low-income countries and vulnerable populations living in fragile and conflict-affected settings.
- Low coverage of measles-containing vaccines has increased the risk of large, disruptive outbreaks.
- Beyond the time-limited campaigns as one part of the “Big Catch-up”, sustained efforts to fill immunity gaps are required in the immediate and long term through strengthening of immunization programmes within primary health care and along the life-course. The aim is to restore immunization programme performance to pre-pandemic levels (2nd objective of the Big Catch-up) and to do more to get onto the trajectory needed to achieve the 2030 goals (3rd objective of the Big Catch-up).
- A shared action agenda for 2023-2024 that sets out a series of short-term and high-level priorities to align the efforts of countries, regions, global partners, and other stakeholders has been developed and SAGE was invited to provide feedback on this action agenda.
- The action agenda has six trajectories, which are catch-up and strengthening of immunization programmes, equity promotion, regaining control of measles, making the case for investment into immunization, accelerating the introduction of WHO-recommended vaccines, and advancing vaccination in adolescence.

Session 6

Poliomyelitis

- SAGE was pleased to note that wild poliovirus type 1 (WPV1) circulation is confined to a small geographic area at the border between Afghanistan and Pakistan and with lower genetic diversity between isolates.
- SAGE expressed concern about the continued detection of circulating vaccine-derived poliovirus (cVDPV) type 2 (cVDPV2) in Africa and increasing detection of cVDPV type 1 in several countries and stressed the need for efforts to improve routine immunization coverage; routine immunization is the means by which most polio vaccines are delivered and hereby establish individual and population-based immunity.
- SAGE recommended that to minimize the risk of seeding new cVDPV2 outbreaks, the novel oral poliovirus vaccine type 2 (nOPV2) should be used in high-quality campaigns with a maximum interval of 4 weeks between campaign rounds.
- SAGE recommended that in areas of type 1 and 2 poliovirus cocirculation, sequential vaccination campaigns with nOPV2 and bivalent OPV (bOPV) should be implemented; short intervals between homologous vaccines should be considered.

Session 7

Malaria

- In a joint session, SAGE and the Malaria Policy Advisory Group (MPAG) reviewed the available evidence on the novel malaria vaccine R21/Matrix-M.
- The R21/Matrix-M vaccine is similar to the RTS,S/AS01 malaria vaccine and there is no evidence that one vaccine performs better than the other.
- SAGE and MPAG recommended that either the R21/Matrix-M or RTS,S vaccine be used for the prevention of *P. falciparum* malaria in children living in malaria-endemic areas, prioritizing areas of moderate and high transmission but also considering vaccination in low transmission settings.
- Vaccine introduction should be done in the context of comprehensive malaria control efforts.
- The R21/Matrix-M vaccine should be administered in a 4-dose schedule from 5 months of age, as recommended for RTS,S; a 5th dose may be considered in areas where there is a significant malaria risk remaining in children who have received four doses.
- The availability of this second malaria vaccine is expected to close the gap between supply and demand, enabling broader and possibly unconstrained access; malaria vaccines introduced widely have the potential to save tens of thousands of young lives each year.

Session 8

Smallpox

- SAGE was presented with the results of a systematic review of the available data on the safety and efficacy of Smallpox vaccines, including the second and third-generation vaccines; no data were available for the fourth-generation orthopoxvirus vaccine.
- First-generation vaccines have higher rates of serious adverse events and myocarditis.
- SAGE recommended the addition of the third-generation MVA vaccine to the WHO reserve in addition to the existing vaccines.
- Primary prevention through vaccination is recommended for laboratory personnel handling orthopoxviruses, and outbreak response teams. Revaccination may be administered as often as every 3 to 5 years for laboratory workers at the highest risk. The need and frequency of re-vaccination of other high-risk groups need to be determined.
- In the case of outbreak response, targeted vaccination is recommended for contacts and other persons at risk of infection. Second and third-generation vaccines are recommended for outbreak response. When these are not available, first-generation can be considered. Vaccination should not be withheld from previously vaccinated persons. Large-scale mass vaccination is not recommended.
- Immunocompromised or pregnant persons and caregivers or close contacts of such persons should receive non-replicating vaccines.

Session 9

COVID-19

- SAGE was presented with updated data on the epidemiology of COVID-19, including death rates among priority-use groups; vaccine effectiveness data during Omicron XBB sub-lineages circulation; and pre-clinical and clinical data on novel monovalent XBB vaccines.
- Based on the data reviewed, SAGE recommended a simplified single-dose regime for primary immunization for most COVID-19 vaccines which would improve acceptance and uptake and provide adequate protection at a time when most people have had at least one prior infection.
- Available data suggest the monovalent Omicron XBB vaccines provide modestly enhanced protection compared to bivalent variant-containing vaccines and monovalent index virus vaccines.
- When monovalent XBB vaccines are not available, any available WHO emergency-use listed or prequalified vaccine, bivalent variant-containing or monovalent index virus vaccines, may be used since they continue to provide benefits against severe disease in high-risk groups.
- SAGE approved an updated roadmap for COVID-19 vaccination that reflects the simplified schedule, updated recommendations on revaccination and the currently available COVID-19 vaccines.

Session 10

Mumps

- Most countries have introduced mumps vaccination through the use of the measles-mumps-rubella combination (MMR) vaccine.
- While associated with significant short-term morbidity, the most severe complication – encephalitis – occurs with a similar frequency and at a similar age as measles. Mumps is a significant cause of long-term hearing loss.
- The available evidence indicates that the mumps vaccines in use are safe and effective and that mumps is well controlled in all countries with sustained high coverage.
- In low- and middle-income countries, data on the burden and epidemiology of mumps is scarce and the incremental cost of the MMR vaccine over the measles-rubella (MR) vaccine is substantial.
- SAGE therefore recommended a careful review of the uncertainties, risks and programmatic implications when considering the introduction of mumps-containing vaccines in LMICs.
- Countries that introduce the mumps vaccine should provide it in combination with measles and rubella as MMR vaccine delivered using the same schedule as for MR vaccines and

maintain high coverage as recommended for MR vaccines which will mitigate the risk of a shift in age-specific incidence of infection.

- Countries that introduce the mumps vaccine should enhance surveillance to demonstrate the impact of the vaccine and monitor epidemiological shifts.

Session 11

Cholera

- Since 2021, cholera outbreaks have become more frequent, larger and more deadly with a strong link to climate change.
- SAGE reinforced its 2017 recommendation that all relevant target groups for vaccination in OCV campaigns, including pregnant women, be considered for vaccination.
- SAGE expressed its deep concern about the continuing supply constraints of the oral cholera vaccine (OCV) and asked that strategies for mitigating the impact of these supply shortfalls be accelerated.
- Based on an assessment of evidence, SAGE acknowledged the public health benefit of the use of the killed whole cell bivalent (O1, O139) OCV (EuBiologics) under controlled temperature chain (CTC) conditions of not more than 10 days at ambient temperatures not exceeding 40°C.