Malaria vaccines

World Health Organization

Summary of WHO Position Paper

WHO position paper on malaria vaccines

Weekly Epidemiological Record

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Executive summary

1. In 2022, **the global burden of malaria** was estimated to be **249 million cases** and **608 000 deaths annually**
   A. Approximately **95% of malaria cases and deaths occur in sub-Saharan Africa**, with the remainder occurring in South-East Asia and South America. Almost all malaria deaths are caused by *Plasmodium falciparum;* **most deaths occur in children under 5 years of age**
   B. **Morbidity due to *P. falciparum* can range from mild febrile illness to life-threatening disease** with coma, respiratory distress, severe anaemia or circulatory shock
2. The currently recommended **malaria vaccines are safe, efficacious and impactful** against uncomplicated or severe malaria and death
3. **WHO recommends the use of malaria vaccines for the prevention of *P. falciparum* malaria in children** living in malaria endemic areas, **prioritizing areas of moderate and high transmission**
   A. **Malaria vaccines** should be provided in a **4-dose schedule** in children **from around 5-months of age.** The minimum interval between any doses is 4 weeks; to achieve prolonged protection, the 4th dose should be given 6-18 months after the 3rd dose.
   B. **Malaria vaccines** should be provided as **part of a comprehensive malaria control strategy.** All malaria control interventions, including vaccines, provide partial protection; the highest impact is achieved when a mix of interventions is used.

1A Background of malaria

- **Malaria is a vector-borne disease** transmitted through the bite of infected anopheline mosquitoes
- **In 2022, the global burden of malaria** was estimated to be **249 million cases** and **608 000 deaths annually.** Approximately **95% of malaria cases and deaths occur in sub-Saharan Africa**, with the remainder in South-East Asia and South America.
- Almost all **malaria deaths** are caused by ***Plasmodium falciparum***, and **most occur in children under 5 years of age**
- **In many malaria-endemic areas, transmission occurs throughout the year**, often **with seasonal increases**. In areas of **highly seasonal malaria**, transmission may be **limited to several months a year**, influenced by rainfall patterns.
- **Factors contributing to the burden of malaria include** the efficiency of the vector in transmitting malaria, poor housing conditions that increase the exposure to mosquitoes, and weak health systems resulting in limited access to prevention and treatment services
- The **rate of progress in reducing malaria cases and deaths has slowed** since 2014, reflecting plateauing investment, suboptimal access to and use of interventions, and increasing insecticide and drug resistance

Key take-aways

The **global burden** of malaria is estimated to be **248 million cases** and **608 000 deaths annually**

95% of cases and deaths occur in **sub-Saharan Africa** and **most deaths occur in children**

1B Disease, diagnosis and treatment

- **Malaria morbidity** due to *P. falciparum* can range from **mild febrile illness to life-threatening disease** with coma, respiratory distress, severe anaemia or circulatory shock
- **Case fatality** rates in **severe malaria** have been estimated at **13-20% for hospitalized children** or **>90% if the children remains at home**
- **Severe malaria** may present **as life-threatening anaemia**. More frequently in **older children**, severe malaria may present as **cerebral malaria**
- The **contribution of malaria to increased childhood mortality due to common childhood illness** – such as pneumonia, diarrhoea and malnutrition (i.e. indirect malaria mortality) – is substantial. Malaria infection strongly predisposes children to bacteraemia and can account for more than half of all cases of bacteraemia in malaria endemic areas

Key take-aways

Malaria morbidity can range from **mild febrile illness to life-threatening disease**

Contribution of malaria to increased childhood mortality is substantial

1B Disease, diagnosis and treatment

- **Diagnosis** of malaria requires confirmation through microscopy, rapid diagnostic tests (RDTs) or polymerase chain reaction (PCR). **In most settings and facilities, RDTs are routinely used**
- The recommended **treatment** for uncomplicated *P. falciparum* malaria is **artemisinin-combination therapies (ACTs).** For severe malaria, the recommended treatment is intravenous or intramuscular artesunate followed by oral ACTs
- **Preventive interventions** include insecticide-treated nets (ITNs), indoor residual spraying (IRS) of insecticides, chemoprevention in pregnant women and children, and vaccines for children

Key take-aways

Malaria control tools include **insecticide-treated nets**, prompt **diagnosis and treatment**, **chemoprevention** for pregnant women and children, and **vaccines** for children

2 Malaria vaccines

- **Two malaria vaccines are WHO recommended and prequalified.** Both are pre-erythrocytic vaccines that **prevent *P. falciparum* malaria in children**
  - The recommended malaria vaccines are not designed to interrupt malaria transmission and there is no known cross-protection with other non-*falciparum Plasmodium* species
- **The malaria vaccines have been shown to be safe and efficacious** for the prevention of *P. falciparum* malaria in children
  - In phase 3 clinical trials, the vaccines were shown to reduce clinical malaria by approximately 75% one year after dose 3, when provided in a **seasonal schedule**. When provided in an **age-based schedule**, the vaccines reduced clinical malaria by 51% (RTS,S/AS01) and 66% (R21/Matrix-M) one year after dose 3
- Pilot introduction of RTS,S/AS01 showed the **malaria vaccine to be impactful, reducing all-cause deaths** in children age-eligible for vaccine
  - RTS,S/AS01 has also been shown to be safe and impactful through pilot implementation, **reducing all-cause mortality** (excluding injury) by 13% **and severe malaria hospitalisations** by 22%
- Malaria vaccines are **administered intramuscularly in a 4-dose schedule**

Key take-aways

Currently available **malaria vaccines** are **safe** and **life saving.** Pilot introductions of the malaria vaccine **reduced all-cause mortality by 13%** in children age-eligible for vaccination

2 WHO Position along 6 dimensions

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- A Schedule & Product choice
- B Interchangeability
- C Safety & Co-administration
- D Vaccination of special populations
- E Role of the malaria vaccine among other prevention measures
- F Research priorities

2 Summary of WHO Position

- WHO recommends the use of malaria vaccines for the **prevention of *P. falciparum* malaria in children** living in malaria endemic areas, **prioritizing areas of moderate and high transmission**
- **Malaria vaccines should be provided as part of a comprehensive malaria control strategy**. All malaria control interventions, including vaccines, provide partial protection; the highest impact is achieved when a mix of interventions is used
- Both **recommended malaria vaccines are safe** and **efficacious**
- Malaria vaccines should be provided in a **4-dose schedule in children from 5 months of age**
  - The minimum interval between any doses is 4 weeks; however, to achieve prolonged protection, the 4th dose can be given 6-18 months after the 3rd dose

Key take-aways

Malaria vaccines are **recommended** for the **prevention of *P. falciparum* malaria in children** in **endemic areas, prioritizing** areas of **moderate and high transmission**

Source: Pneumococcal conjugate vaccines in infants and children under 5 years of age: WHO position paper – February 2019

2A WHO Position – Schedule & Product choice

Schedule

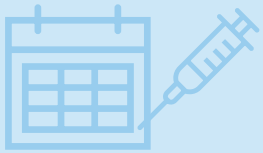
- Malaria vaccines should be provided in a **4-dose schedule in children from around 5 months of age**
  - Countries may choose to give the **first dose earlier than 5 months** of age to **increase coverage or impact**
  - The **minimum interval between any doses is 4 weeks**
  - However, to achieve prolonged protection, the **4th dose can be given 6-18 months after the 3rd dose**
- There can be **flexibility in the timing of the 4th dose,** including:
  - By aligning it with vaccines given in the **second year of life to improve coverage**
  - Giving it just **prior to seasonal peaks in malaria** transmission **to optimize vaccine efficacy**
- **A 5th dose, given one year after the 4th dose**, may be provided in areas of highly seasonal transmission or in other **areas where a significant malaria risk remains for children**

Key take-aways

Malaria vaccines should be provided in a **4-dose schedule from 5 months of age**

Minimum interval between doses is 4 weeks

There can be **flexibility in the timing of the 4th dose to improve coverage or efficacy**



2A WHO Position – Schedule & Product choice

Schedule (continued)

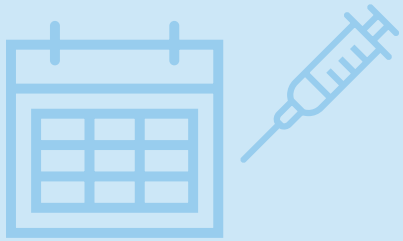
- **In areas with highly seasonal malaria transmission** or **perennial malaria transmission with seasonal peaks**, country may consider using an **age-based or seasonal approach, or a hybrid** of these approaches, giving the first 3 doses age-based and subsequent annual doses seasonally
- **At the time of vaccine introduction, catch-up vaccination can be considered in children up to 5 years of age**, subject to local epidemiology and age of high risk, feasibility, affordability and vaccine availability

Product choice

- The **choice of the product** used in a country should be based on the product characteristics and **programmatic considerations**, as well as **vaccine supply and long-term affordability**

Key take-aways

In areas with **highly seasonal malaria**, countries can use an **age-based or seasonal approach, or a hybrid** of the two approaches



2B WHO Position – Interchangeability

- The malaria **vaccination series** for each child **should be completed with the same product whenever feasible**
- However, **if the product used for a prior dose is unavailable or unknown,** the series should be **completed with either of the available WHO-recommended malaria vaccines**
- **Restarting** the vaccine series is **not recommended**

Key take-aways

If a **prior dose is unavailable or unknown**, the **series can be completed with either vaccine**

Restarting vaccine series **not recommended**

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2C WHO Position – Safety & Co-administration

Safety

- Both vaccines are considered to be **safe and well tolerated**. There is a **small risk of febrile seizures** within 7 days **(mainly within 2–3 days) of vaccination**.
- As with any **vaccine introduction**, proper planning and training of staff to conduct **appropriate pharmacovigilance** should take place beforehand

Co-administration

- Malaria vaccines may be **administered simultaneously with other childhood vaccines**

Key take-aways

Recommended malaria vaccines are safe and well tolerated and may be administered with other childhood vaccines

2D WHO Position – Vaccination of special populations

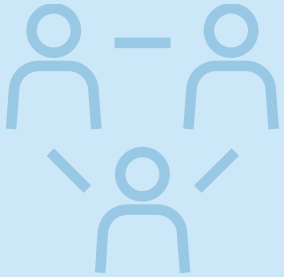
- **Malnourished children may be at particular risk of malaria infection and can be vaccinated with either vaccine**
- **RTS,S/AS01 can be given to children with HIV infection.** A trial of R21/Matrix-M in HIV-positive infants is ongoing
- The **malaria vaccine should be provided to infants and young children who relocated to an area of moderate or high transmission, including during emergency situations**
  - Countries are encouraged to consider strategies to improve coverage in populations with high need and at high risk of malaria burden and disease, including under-vaccinated children, hard-to-reach or marginalized populations, persons in areas of conflict of emergency, displaced populations, or those in other areas with poor access to health services. Some of these populations may benefit from delivery through campaigns.
- The vaccines are **not recommended for use in adults** (including health workers and pregnant persons). The vaccine is **not indicated for travellers**, who should **use chemoprophylaxis and vector control methods** to prevent malaria **when travelling to endemic settings**

Key take-aways

Both malaria vaccines can be used in **malnourished children**

RTS,S/AS01 can be given to **HIV-infected children**

Malaria vaccines are ***not* indicated for adults or travellers**



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2E WHO Position - Role of the malaria vaccine among other prevention measures

- **Malaria vaccines should be provided as part of a comprehensive malaria control strategy**
  - All malaria control interventions, including vaccines, provide partial protection; the highest impact is achieved when a mix of interventions is used
  - Appropriate mixes of interventions (ITNs, preventive chemotherapies, vaccines etc.) should be identified for different subnational settings
  - These mixes are defined by national malaria programmes on the basis of the local malaria epidemiology (e.g. intensity of transmission, age pattern of severe disease, vector species and vector behaviour, insecticide and drug resistance patterns) and contextual factors (e.g. structure and function of the health-care system)
- The additional **visits needed to administer malaria vaccine are opportunities to provide other integrated malaria control and preventive health services**, such as:
  - Missed vaccinations, vitamin A, deworming, ITNs, reminding of the importance of using an ITN and other preventive measures, and seeking prompt diagnosis and treatment for fever

Key take-aways

Malaria vaccines should be provided as **part of a comprehensive malaria control strategy**

Malaria vaccine visits are **opportunities to provide other health services**

2F WHO Position - Research Priorities

- For all WHO-recommended malaria vaccines, **operational research is needed, specifically in relation to the seasonal delivery approach**, including:
  - Annual pre-transmission season dosing after the first 3 doses are given through age-based delivery
  - How to best deliver the combination of seasonal malaria chemoprevention (SMC) and seasonal malaria vaccination
- **Countries are encouraged to document and evaluate their experience with vaccine introduction**, in particular the seasonal deployment of the vaccine, use of an expanded age range, or a 5-dose schedule
- **Research priorities identified for R21/Matrix-M include:**
  - Co-administration with childhood vaccines
  - Post-licensure studies on vaccine effectiveness in high perennial transmission settings
  - Impact on severe malaria and mortality
  - Monitoring of safety in infants and young children
  - Interchangeability studies to evaluate safety and effectiveness in children who receive different malaria vaccines in the same schedule

Key take-aways

Several research priorities are recommended for malaria vaccines

Countries are encouraged to document and evaluate their experience with vaccine introduction

Summary of WHO Position Paper on malaria vaccines – May 2024

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In case of additional questions, please reach out to the SAGE Secretariat at sageexecsec@who.int