# **Malaria Chemoprevention**

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SMC Annual Review & Planning Meeting 1 March 2022



#### Trends in malaria deaths – global and WHO African Region, 2000–2020

#### Global trends in malaria deaths, 2000–2020



**96%** of global malaria deaths in 2020 were in the WHO African Region.

> World Health Organization

#### Areas eligible for SMC and where SMC was implemented in 2019





## The 3 steps in the pathway to achieve impact



New recommendations implemented and achieve impact

#### Better anticipate

products or strategies that are likely to be key in future efforts to control and eliminate malaria

#### **2** Develop recommendations

for countries on "what to do" and what malaria control products to use based on the best available evidence

#### **3** Optimize uptake

of the recommendations by improving the way they are shared and updated

#### Feedback loop

 lessons from front-line workers and implementers feed back into the overall process

## Current recommendations – overly prescriptive?

- "In malaria-endemic areas, give sulfadoxine-pyrimethamine to all pregnant women in their first or second pregnancy monthly from the start of the second trimester."
- *"In areas of moderate-to-high malaria transmission where SP is still effective, provide intermittent preventive treatment* with SP to *infants* (< 12 months of age) (SP-IPTi) at the <u>time of the second and third rounds of vaccination against diphtheria, tetanus and pertussis (DTP) and vaccination against measles</u>."
- "In areas with highly seasonal malaria transmission in the sub-Sahel region of Africa, provide seasonal malaria chemoprevention (SMC) with monthly amodiaquine + SP for all <u>children < 6 years</u> during each transmission season."



#### **Overview of the Process of Guideline Development**



**Methodologist** 

#### Abbreviated PICO questions for Chemoprevention GDG

- 1. Should children living in settings with **perennial malaria transmission** be given anti-malarial medicines as chemoprevention?
- 2. Should children living in settings with **seasonal malaria transmission** be given anti-malarial medicines as chemoprevention?
- 4. Is mass drug administration (MDA) a safe and effective approach to reduce the burden of malaria in moderate and high transmission settings?
  - During emergencies or periods of health service disruption, should people living in malaria-endemic settings be given anti-malarial medicines for chemoprevention?
- 5. Should women be given anti-malarial medicines as chemoprevention during pregnancy?
- 6. Should school-age children living in settings with malaria transmission be given anti-malarial medicines as chemoprevention to reduce disease burden?
- 7. Should children hospitalized with severe anaemia in malaria-endemic settings be given antimalarial medicines as **chemoprevention post-discharge**?
- 8. In areas of moderate to high malaria transmission, should residents known to be at increased risk of clinical malaria, severe malaria, death, or other adverse effects of *P falciparum* infection, be given anti-malarial medicines as chemoprevention?



## Chemoprevention guideline timeline



Organization

# Planned changes to chemoprevention recommendations

- SMC and IPTi recommendations will no longer specify
  - Strict age groups
  - Transmission intensity thresholds
  - Numbers of SMC cycles or IPTi doses
  - Specific drugs
- Encourage use of local data to inform subnational tailoring of chemoprevention strategies
  - Ages at greatest risk of severe malaria / malaria admission
    - IPTi -> Perennial Malaria Chemoprevention (PMC)
  - Recognise that as transmission intensity decreases, disease burden decreases and value of chemoprevention strategies for burden reduction will also decrease
  - Duration of transmission season should determine the number of rounds of SMC; age-specific disease burden, feasibility and affordability of delivering PMC doses
  - Consider local data on costs, duration of protection of each treatment course\*, extent of seasonal variation, mix of interventions already deployed, etc



#### Global **Malaria** Programme

\* Use the standard Chemoprevention Efficacy Study (CPES) protocol

# Age-specific severe malaria admission rates and parasite prevalence



Age groups carrying the highest disease burden should be prioritized for malaria prevention

Global Malaria Programme

Paton et al., Science 373, 926–931 (2021)



## Revised recommendations – key points

- Underlying principle: a treatment course of an effective antimalarial will clear any existing, and prevent new, malaria infections for a period of time
- Updated chemoprevention recommendations reflect a paradigm shift to provide greater flexibility to NMPs to adapt control strategies to suit their settings
  - No longer specify strict age groups, transmission intensity thresholds, numbers of doses or cycles, or specific drugs
  - Local data should be used to inform subnational tailoring of chemoprevention strategies
- Each chemoprevention recommendation will be accompanied by a summary of available research evidence, an explanation of how this was used to inform the recommendation and key practical considerations to support implementation



# Chemoprevention efficacy studies (CPES)





# Drug efficacy

**Drug efficacy:** Capacity of an antimalarial medicine to achieve the therapeutic objective when administered at a recommended dose, which is well tolerated and has minimal toxicity



**Factors affecting efficacy** 



# **Efficacy studies**

METHODS FOR SURVEILLANCE OF ANTIMALARIAL DRUG EFFICACY	
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World Health Organization	

#### **Therapeutic Efficacy Studies (TES)**

- Follow-up and procedures in accordance with standard protocol
- Gold standard for monitoring treatment efficacy to inform treatment policy
- Follow-up group of patients with uncomplicated malaria to monitor treatment outcome
- WHO recommends that TES are done in sentinel sites at least once every 2 years
- Supplemented by information on molecular markers of resistance



- Information on treatment efficacy cannot be used as a surrogate for chemoprevention efficacy
- Molecular markers of drug resistance are a useful but imperfect tool of predicting the efficacy of chemoprevention strategies
  - Need to establish a standard protocol to monitor efficacy of chemoprevention

## **CPES** protocol



Key requirements of a protocol to study chemoprevention efficacy

- Provide information on the parasitaemia during follow-up period
- Collect data comparable across location and time of a good enough quality to inform policy
- Studies that can be done on a routine basis as for the TES without the need for a large external, clinical research team

**Study population** 

Main study outcome

Additional study outcomes include

- Individuals with no malaria symptoms eligible for a given chemoprevention as per the recommendations
- Study participants identified with asexual parasitaemia by microscopy during follow-up period from day 4 to day 28/42
- Days to reported failure
- Prevalence of molecular marker(s) of resistance to chemoprevention drug(s) at Day 0 and in any parasites detected after Day 4



# Key aspects of the draft CPES protocol



Clinical malaria	Study participant identified as having malaria at enrolment or during follow-up, must receive treatment as per the national treatment guidelines
Supervision of treatment	All medicine must be given under direct supervision
Follow-up period	28/42 days after start of chemoprevention administration with a drug with a short half-life
Days of participant follow- up	Weekly follow-up days (Days 7, 14, 21, 28) + any day that study participants have symptoms
Reinfection/ recrudescence markers	Blood collected on day 0 and day of failure to be analysed for markers of new infection /recrudescence
Drug resistance markers	Analysis of markers of drug resistance in DBS collected on day 0 for study participants with parasitaemia Analysis of markers of drug resistance in DBS collected for study participants with parasitaemia during follow-up

#### Next steps

- Partners are planning to implement studies of chemoprevention efficacy
- Lessons learned from these studies and work ongoing with statisticians will be used to adjust the protocol
- An updated document on surveillance of antimalarial drug efficacy is planned this year and will include:
  - Therapeutic efficacy studies
  - Integrated drug efficacy studies, and
  - Chemoprevention efficacy studies.





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