Accelerating malaria prevention through model-informed product selection and design

Insights from oral drugs, monoclonal antibodies, and vaccines

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World Health Organization
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A need for new *Pf.* malaria prevention products

Tackling emerging antimalarial drug resistance in Africa

**WHO** is launching today a new strategy to respond to the urgent problem of antimalarial drug resistance in Africa. The strategy is being released during *World Antimicrobial Awareness Week*, a global annual campaign to improve awareness of the growing threat of resistance to antibiotics and other medicines.

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Sources:
Traditional clinical development

Classical approach: growing body of evidence to reach impact
Accelerating development through modelling

Classical approach: growing body of evidence to reach impact

Modelling approach: shaping next-gen medical interventions

Discovery -> Pre-clinical & early clinical testing -> Clinical trials -> Implementation

Vaccines, monoclonals, SMC drugs
Evidence generation and collaboration
Population-level health impact
Target Product Profile (TPP)
Therapeutics for prevention in children

Number of cases

Jan Feb Mar Apr Jun Jul Aug Sep Oct Nov Dec
Oral chemoprevention drugs are small-molecule drugs that provide ~1 month protection against clinical malarial. Sulfadoxine-pyrimethamine is widely used, but there is parasite resistance.
Pre-erythrocytic monoclonal antibodies are novel biologic drugs expected to provide 4+ months protection against clinical malaria.

The most advanced candidates are in phase II clinical development.
Pre-erythrocytic malaria vaccines provide partial protection against clinical malaria for 7+ months.

RTS,S was the first approved candidate, and R21 is in late clinical development.

There are many new candidates in clinical development.
Our simulation framework

DISEASE MODELLING

MALARIA PREVENTION SCENARIOS

INTERVENTION MODEL
including intervention coverage, initial efficacy, and effect decay

MODELLING AND SIMULATION
with OpenMalaria

SIMULATION DATABASE

DISEASE MODEL EMULATION
with Gaussian Process regression

EMULATION

ANALYSIS

OPTIMISATION identifies minimum requirements

GLOBAL SENSITIVITY ANALYSIS identifies drivers of effectiveness

Next-gen seasonal malaria chemoprevention

Lydia Braunack-Mayer, Melissa A Penny

Our results identified minimum product characteristics for a next-gen SMC drug

- We modelled multiple potential mechanisms of action for a range of potential chemoprevention drug profiles deployed as SMC, identifying minimum criteria for next-gen drugs

- Results have implications for chemoprevention candidate selection:
  - The ideal chemoprevention drug profile is not the same as the ideal treatment drug profile
  - We do not adequately understand SP’s activity:
    No time to lose - a roadmap for understanding sulfadoxine-pyrimethamine in malaria chemoprevention. Thiery Masserey, Lydia Braunack-Mayer, R Scott Miller, Jörg J Möhrle, Melissa A Penny

From: Design and selection of drug properties to increase the public health impact of next-generation seasonal malaria chemoprevention. Lydia Braunack-Mayer, Josephine Malinga, Thiery Masserey, Narimane Nekkab, Swapnoileena Sen, David Schellenberg, André-Marie Tchouatieu, Sherrie L Kelly, Melissa A Penny
Pre-erythrocytic monoclonal antibodies

Narimane Nekkab, Melissa A Penny

mAb modelling demonstrated the need for early evidence on effect decay from clinical trials

• Previous modelling for seasonal delivery (Burgert et al) showed the need for a **duration spanning the malaria season** to achieve non-inferiority to SMC

• Ongoing mAb modelling explores a **range of drug profiles** in the **absence of clinical trial data**, identifying considerations for clinical trial planning
  - Higher impact is predicted when delivered with a **treatment drug**
  - Existing trial data is not enough to estimate impact; data over **longer follow up** and with **low dosing regimens** is needed to identify the protective tail

Next-gen prevention vaccines

Josephine Malinga, Melissa A Penny

Modelling identified use-cases for pre-erythrocytic vaccines with longer duration than existing products

• We modelled multiple use-cases for the next-gen of pre-erythrocytic vaccines, quantifying public health impact administered with and without a treatment drug

• Early results show potential for long-term impact from a moderate improvement in vaccine duration
  • Improved vaccines can sustain impact into a 2nd year after vaccination
  • With a longer-duration vaccine, vaccinating adults may lead to transmission interruption in low prevalence settings and accelerate burden reduction elsewhere
  • These use-cases should be balanced by understanding vaccine duration and malaria disease patterns of age-burden and immunity
Outlook to intervention layering

Vector control layers
reduce the force of infection

Medical prevention layers
prevent clinical cases from occurring

Health system layers
detect and treat clinical malaria

Environmental
management

Long-lasting
insecticide treated
nets

Indoor residual
spraying

Chemoprevention
drug administration

Monoclonal antibody

Malaria vaccination

Routine treatment
(access to care)

Mass test and treat

Reactive case
detection

Transmission blocking
tools
Thank you for your attention

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