Swiss TPH

University of Basel

Accelerating malaria prevention through model-informed product selection and design

Insights from oral drugs, monoclonal antibodies, and vaccines

Lydia Braunack-Mayer

lydia.braunack-mayer@swisstph.ch

Acknowledgements

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Lydia Braunack-Mayer
Prof Melissa Penny
Dr Sherrie Kelly
Dr Josephine Malinga
Thiery Masserey
Dr Narimane Nekkab
Swapnoleena Sen

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Dr Jean-Luc Bodmer

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Dr Matthew Cairns

University of Basel
sciCORE | Center for Scientific Computing

Contact us

lydia.braunack-mayer@swisstph.ch

melissa.penny@unibas.ch

A need for new *Pf.* malaria prevention products

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Sources: https://www.forbes.com/sites/petersands/2023/05/05/felled-by-a-warming-world-will-malaria-be-the-next-pandemic/; https://www.lemonde.fr/en/le-monde-africa/article/2023/03/16/spread-of-a-new-mosquito-threatens-malaria-control-in-kenya_6019528_124.html; https://www.who.int/news/item/18-11-2022-tackling-emerging-antimalarial-drug-resistance-in-Africa; https://www.who.int/news/item/28-05-2021-statement-by-the-malaria-policy-advisory-group-on-the-urgent-need-to-address-the-high-prevalence-of-pfhrp2-3-gene-deletions-in-the-horn-of-africa-and-beyond

Traditional clinical development

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

Classical approach: growing body of evidence to reach impact

Accelerating development through modelling

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

Classical approach: growing body of evidence to reach impact

Modelling approach: shaping next-gen medical interventions

Vaccines, monoclonals, SMC drugs

Evidence generation and collaboration

Population-level health impact

Target Product Profile (TPP)

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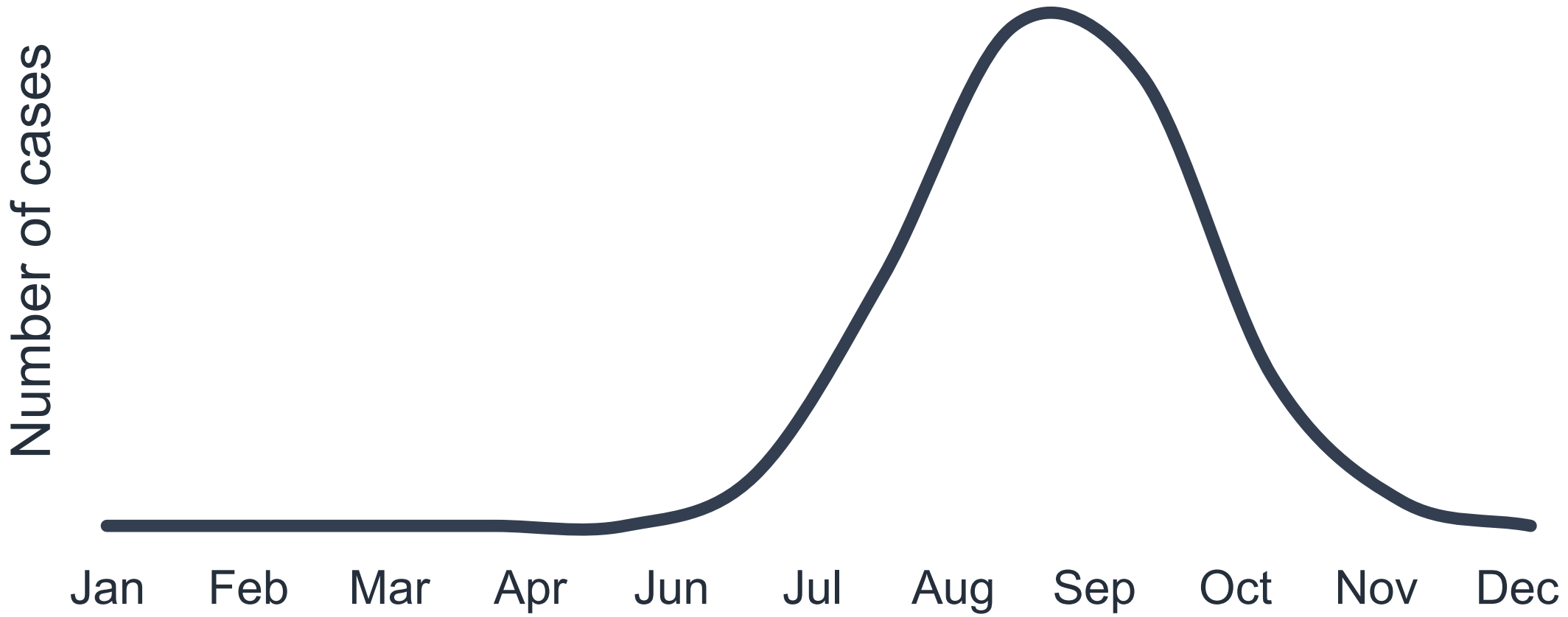
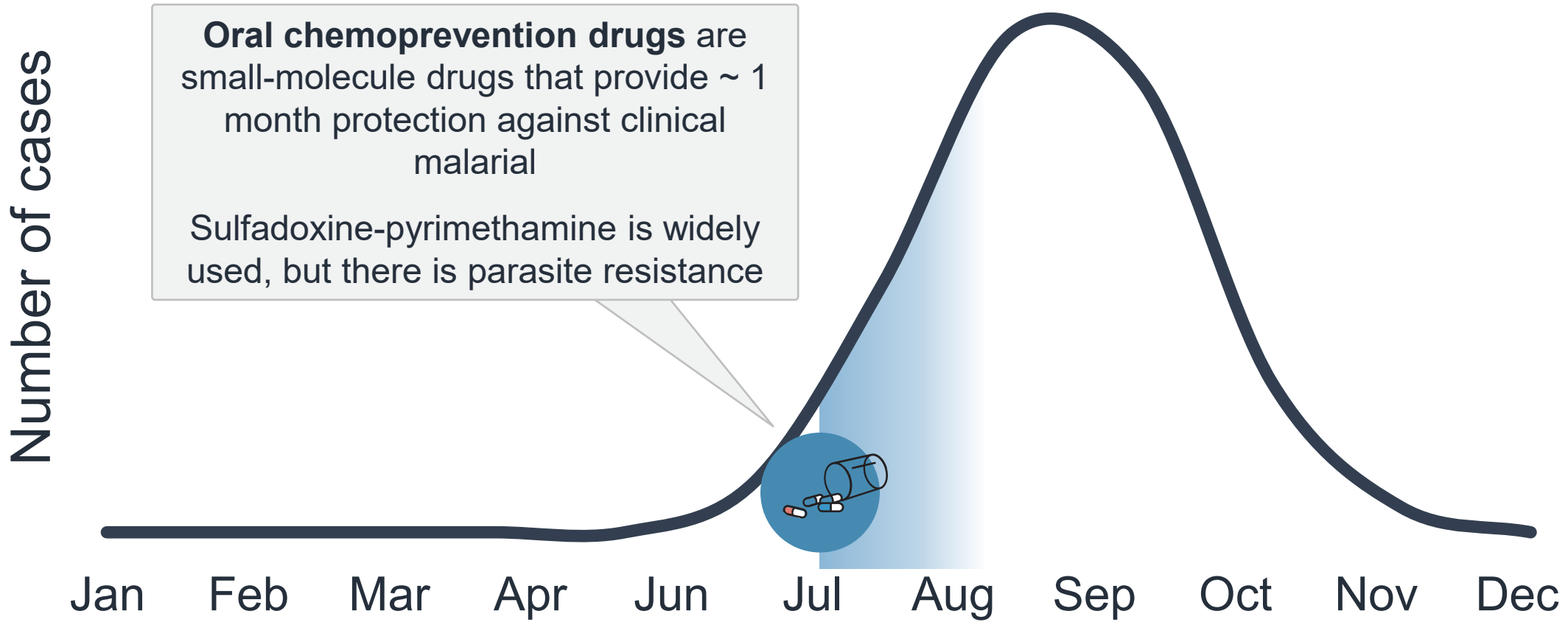
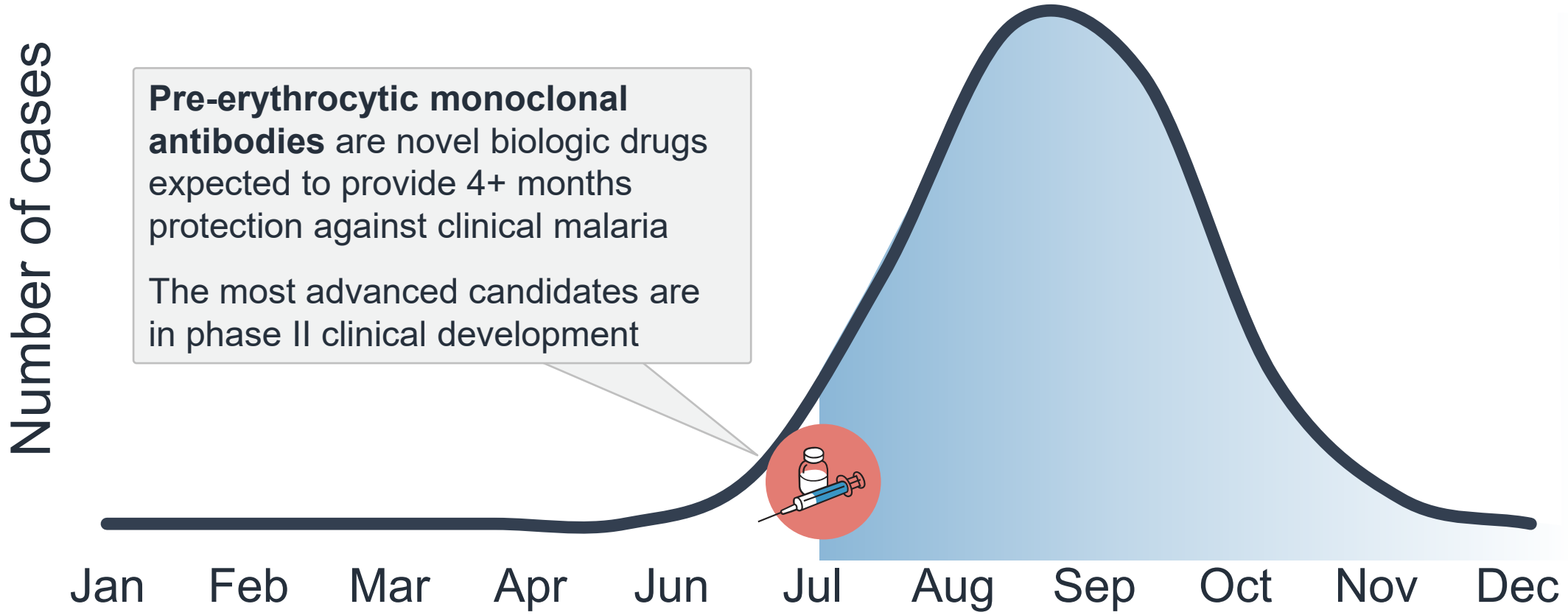
Therapeutics for prevention in children



Therapeutics for prevention in children



Therapeutics for prevention in children



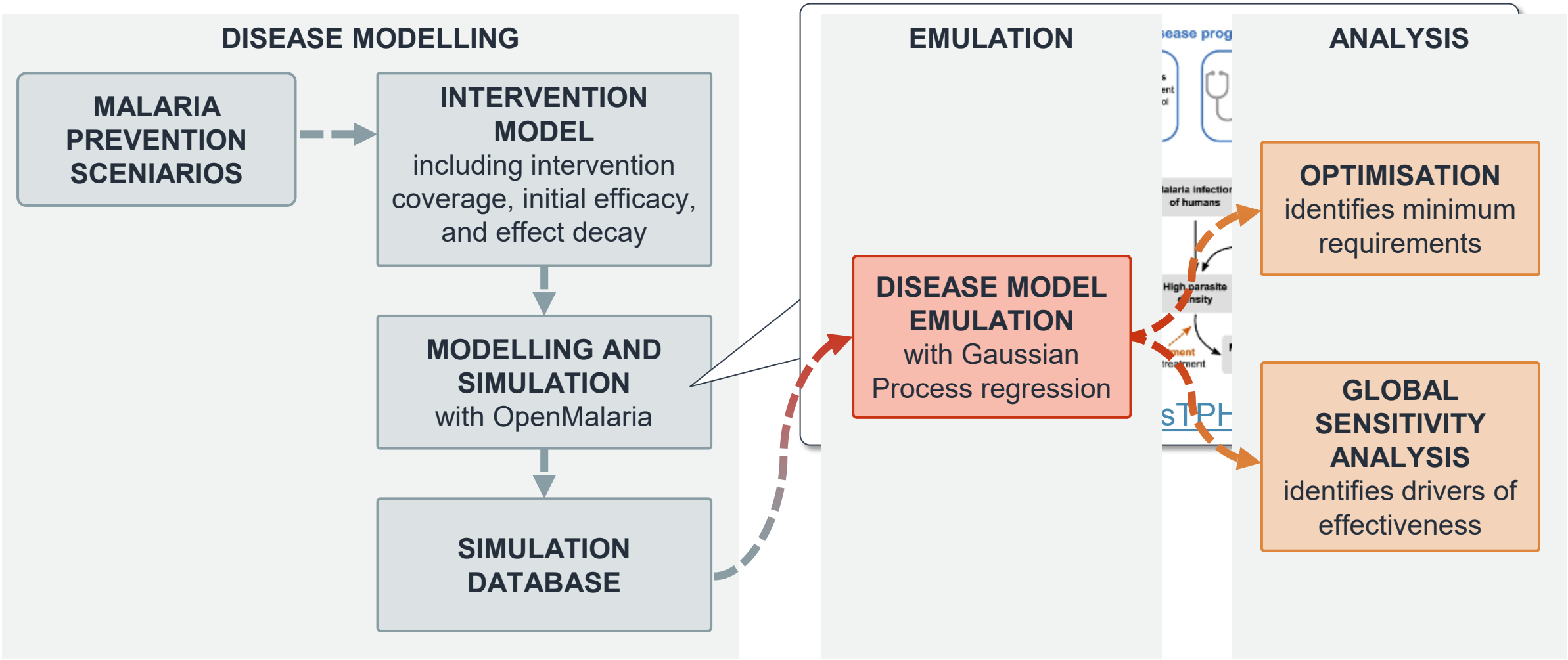
Therapeutics for prevention in children

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



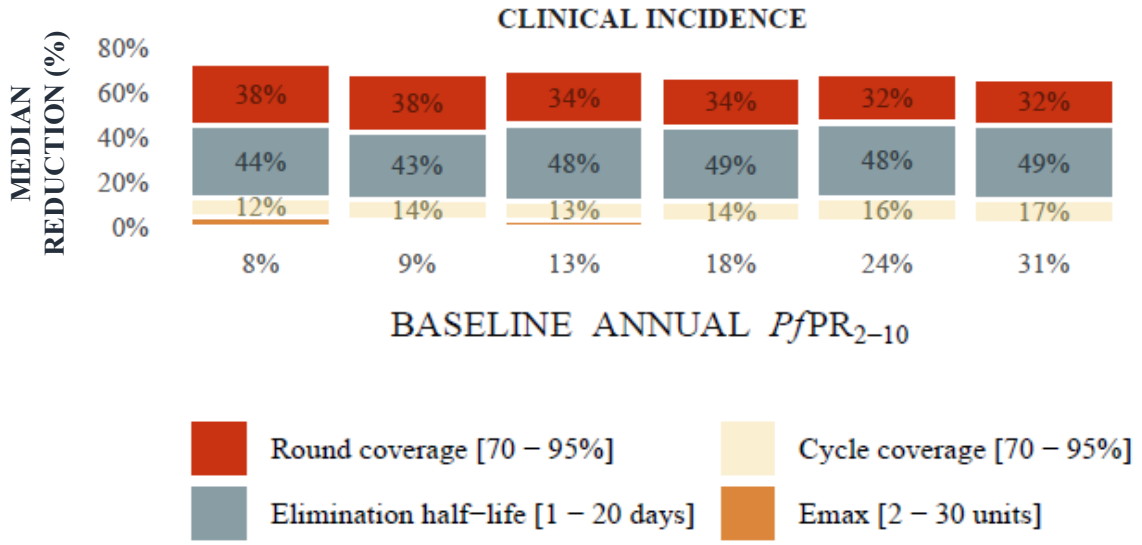
Golumbeanu, M., Yang, GJ., Camponovo, F. *et al.* Leveraging mathematical models of disease dynamics and machine learning to improve development of novel malaria interventions. *Infect Dis Poverty* **11**, 61 (2022). https://doi.org/10.1186/s40249-022-00981-1

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*



Drivers of impact on SMC effectiveness

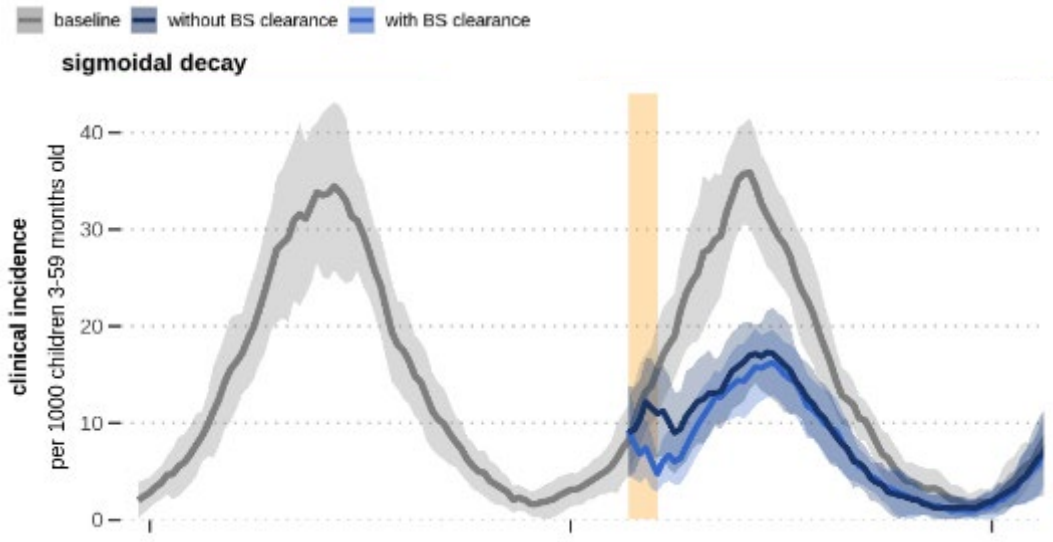
From: **Design and selection of drug properties to increase the public health impact of next-generation seasonal malaria chemoprevention.** *Lydia Braunack-Mayer, Josephine Malinga, Thiery Masserey, Narimane Nekkab, Swapnoleena Sen, David Schellenberg, André-Marie Tchouatieu, Sherrie L Kelly, Melissa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



Burgert L, Reiker T, Golumbeanu M, Möhrle JJ, Penny MA. Model-informed target product profiles of long-acting-injectables for use as seasonal malaria prevention. PLOS Global Public Health 2022; 2(3): e0000211.

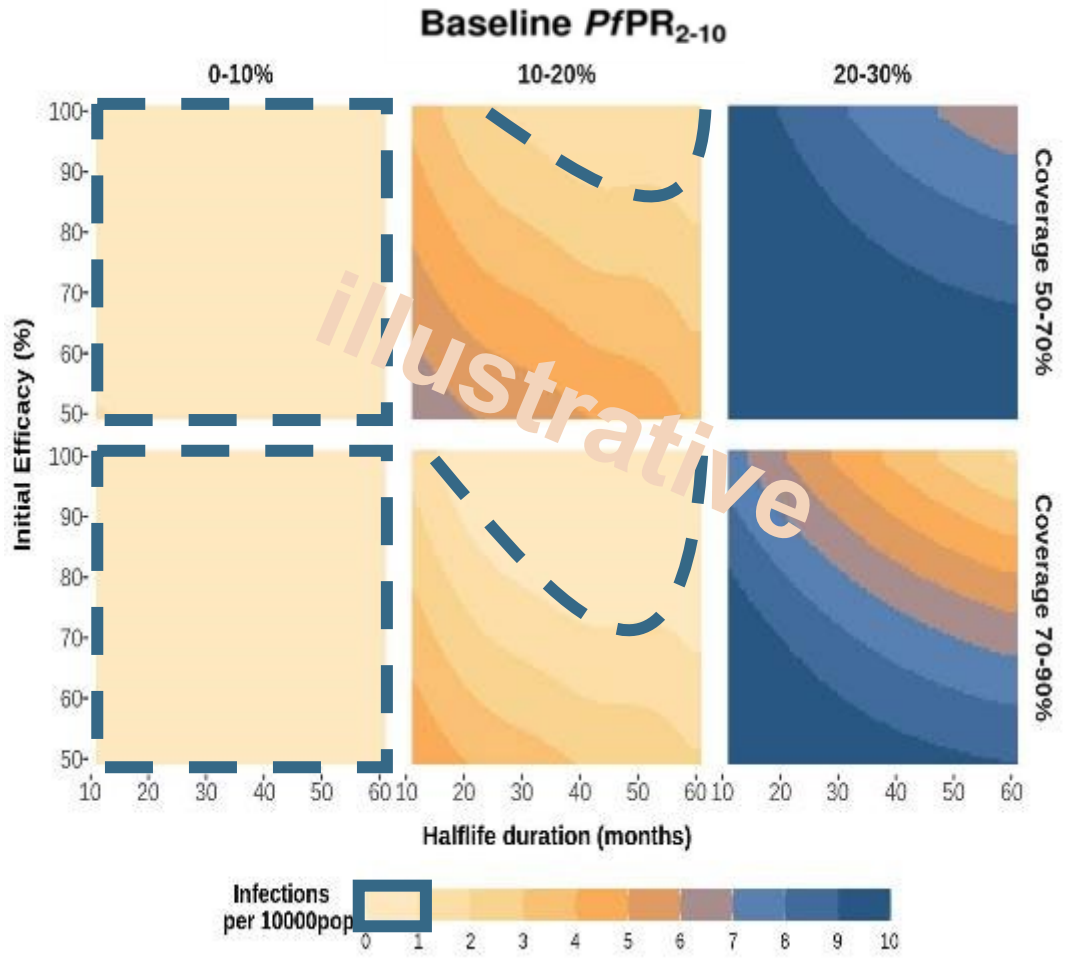
Next-gen prevention vaccines

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

Exemplar elimination scenarios



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

Thank you for your attention

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