

Disentangling patterns of community malaria transmission and burden using malaria prevalence among pregnant women attending antenatal care: a modelling study

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Summary

Background Malaria prevalence measured among pregnant women at the first antenatal care (ANC1) visit provides longitudinal estimates of malaria burden in pregnancy and correlates well with cross-sectional community prevalence, but additional analysis is required to estimate community incidence. We aimed to test whether ANC1-based malaria prevalence can, via an open-source, mechanistic, model-based framework, recover seasonal patterns of clinical incidence suitable for subnational programmatic decision making.

Methods We conducted a modelling study using monthly ANC1 malaria prevalence data from six previously published studies of malaria in pregnancy in six sub-Saharan African countries between May, 2010, and August, 2014. An extended, validated, age-structured malaria transmission model was fitted to monthly ANC1 malaria prevalence using particle Markov chain Monte Carlo (pMCMC) to infer monthly clinical incidence and seasonality metrics. Agreement between model-derived incidence and independently observed time series was assessed using the Markham Seasonality Index (MSI) and peak timing with concordance correlation coefficients (CCCs) and 95% CIs.

Findings Across the six intermittent screening and treatment in pregnancy (ISTp) datasets, total ANC1 sample sizes and positivity were Ghana, 622 (47.9%) of 1298; Burkina Faso, 592 (41.9%) of 1413; Mali, 284 (21.7%) of 1308; The Gambia, 105 (8.8%) of 1194; Kenya, 323 (21.1%) of 1528; and Malawi, 291 (15.9%) of 1825. Strong agreement was observed between model-derived incidence and independent cohort data for MSI (CCC 0.82 [95% CI 0.31–0.97]) and for peak timing (CCC 0.98 [95% CI 0.87–1.00]).

Interpretation A mechanistic pMCMC framework applied to routine ANC1 data can recover clinically relevant seasonality in incidence for the broader community, enabling subnational timing of seasonal interventions (such as seasonal malaria chemoprevention). These capabilities are especially valuable when high-quality case surveillance is scarce and household surveys are underfunded. Our work operationalises WHO guidance, highlighting ANC1 as an opportunity to strengthen malaria surveillance.

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Introduction

Worldwide, malaria continues to kill approximately 600 000 people annually.¹ Despite intensive efforts, global momentum towards malaria elimination has slowed, and funding since 2018 has consistently fallen short of what is needed to meet elimination goals.¹ Innovations that maximise the effect of malaria control measures are urgently required, with policy increasingly shifting from uniform national packages to subnational strategies aligned to heterogeneous local transmission.²

National and global burden estimation, including WHO approaches,¹ often relies on periodic, population-based surveys, such as Demographic and Health Surveys (DHS) and Malaria Indicator Surveys. These surveys provide high-quality prevalence estimates in children younger than 5 years and valuable contextual indicators, but their

logistical complexity restricts frequency and spatial resolution,³ and they are prone to disruption from external shocks, as seen during the COVID-19 pandemic⁴ and the 2025 pauses to the DHS Program.⁵ Consequently, the need for innovative and resilient data sources to monitor malaria transmission and burden is more urgent than ever.

Many countries have strengthened routine surveillance of passively detected clinical cases, yet such data are shaped by treatment-seeking behaviour⁶ and rates of non-malarial fever,⁷ both of which vary over time. Although the quality of passive surveillance data is improving, WHO uses survey-based data to provide national case estimates in 29 countries with less reliable surveillance data, which together represent 87% of the world's overall malaria burden.¹ Uncertain catchment populations further complicate interpretation at the subnational scale.⁶ Although routine case data remain

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See Online for appendix

Research in context

Evidence before this study

We searched Ovid Global Health and Ovid MEDLINE for studies published between Jan 1, 2010, and Dec 31, 2025, without language restrictions, using search terms for malaria and first antenatal care visit (ANC1) test positivity or prevalence, combined with terms indicating translation or comparison of ANC1 metrics with community transmission indicators or spatiotemporal risk patterns. To be included, studies needed to measure malaria prevalence at ANC1 or among pregnant women and compare this metric to indicators of malaria transmission or burden in non-pregnant populations. Of the six relevant studies identified, four compared malaria prevalence in children from household-based cross-sectional surveys with ANC1-based malaria prevalence. Across settings in sub-Saharan Africa, these studies generally reported a positive correlation between prevalence in pregnant women and prevalence in children younger than 5 years. This correlation suggests that pregnant women might serve as a sentinel population to estimate malaria prevalence in the community at large. The added benefit of malaria surveillance at ANC1 is the continuous collection of data from women attending ANC1 year-round, allowing the estimation of malaria prevalence more frequently than possible from cross-sectional surveys, and might be less sensitive to changes in care-seeking or the effect of other febrile illnesses than outpatient test positivity metrics. However, only two of the identified studies attempted to compare trends of ANC1-based malaria prevalence with trends in clinical incidence among children. None of the identified studies

used ANC1-based malaria prevalence to estimate trends in malaria transmission intensity.

Added value of this study

To the best of our knowledge, this study is the first to estimate trends in malaria transmission and incidence from monthly prevalence data collected at ANC1 visits using a mechanistic modelling framework. By considering known mechanisms of the interactions between mosquito populations, parasite infection, and immunity, we can rigorously reconstruct estimates of malaria transmission and incidence from parasite prevalence at ANC1. We provide an R package that performs this analysis and offers the opportunity to use these incidence estimates to assess the effectiveness of seasonal malaria chemoprevention activities.

Implications of all the available evidence

ANC1-based malaria surveillance can provide valuable information on malaria burden, particularly considering the 2025 interruptions in global household cross-sectional surveys. Using the presented framework, ANC1-based malaria surveillance data can help to inform malaria interventions, such as by monitoring chemoprevention effect within the general community at a subnational level. Collecting these data can facilitate decision making for pregnant women, health-care providers, and policy makers at all levels, ultimately combating the effects of malaria more effectively both during and outside of pregnancy.

essential for programme management, complementary data streams, especially those drawn from high-risk groups, could improve burden estimates.

The 2025 WHO malaria surveillance manual⁸ proposes that malaria surveillance during antenatal care (ANC), in which women are tested for malaria at their first visit (ANC1), usually with a rapid diagnostic test, before treatment or prophylaxis (eg, intermittent preventive treatment in pregnancy [IPTp]), might offer such a stream. Because pregnancy increases susceptibility to severe and adverse birth outcomes, timely testing and treatment at ANC1 are beneficial for maternal–child health.³ Women in their first pregnancy are particularly susceptible, as placenta-binding antigen enables parasite accumulation in the intervillous space; immunity builds with successive pregnancies and in higher-transmission settings, so parasite positivity at ANC1 declines with gravidity at any given community prevalence.³ ANC attendance is high across much of sub-Saharan Africa (76% of pregnant women attend ANC1),⁹ and testing at ANC1 yields a continuous, near-real-time prevalence indicator with a clear case definition drawn year-round from a generally stable population. ANC1-based malaria prevalence correlates well with survey estimates,¹⁰ and WHO is reviewing evidence supporting the use of ANC1-based data as a surrogate for malaria prevalence surveys.⁸

However, given the complex relationships between indicators (figure 1A), translating longitudinal prevalence into continuous estimates of transmission and clinical incidence requires appropriate methods. Understanding seasonal variation in malaria burden is central to targeting interventions such as seasonal malaria chemoprevention (SMC), indoor residual spraying, mass drug administration, and vaccination. In west Africa, where mosquito breeding closely tracks rainfall,¹ seasonality is comparatively straightforward; in parts of east Africa, patterns reflect interacting influences of temperature, humidity, water balance, and perennial water sources.^{11,12} Even high-quality routine case data can blur these signals because not all fevers are caused by an incidentally detected malaria parasite.⁷ In places where seasonal tools are already deployed, re-assessing timing using case data alone is difficult.

Here, we introduce *anatembea*, an open-source R package, which translates monthly ANC1-based malaria prevalence into seasonal patterns of transmission and clinical incidence. The framework builds on a previously validated mechanistic malaria model used within the World Malaria Report ensemble.¹³ Using this extended version, we aimed to test whether ANC1-based malaria prevalence can recover community seasonality and incidence at decision-relevant scales.

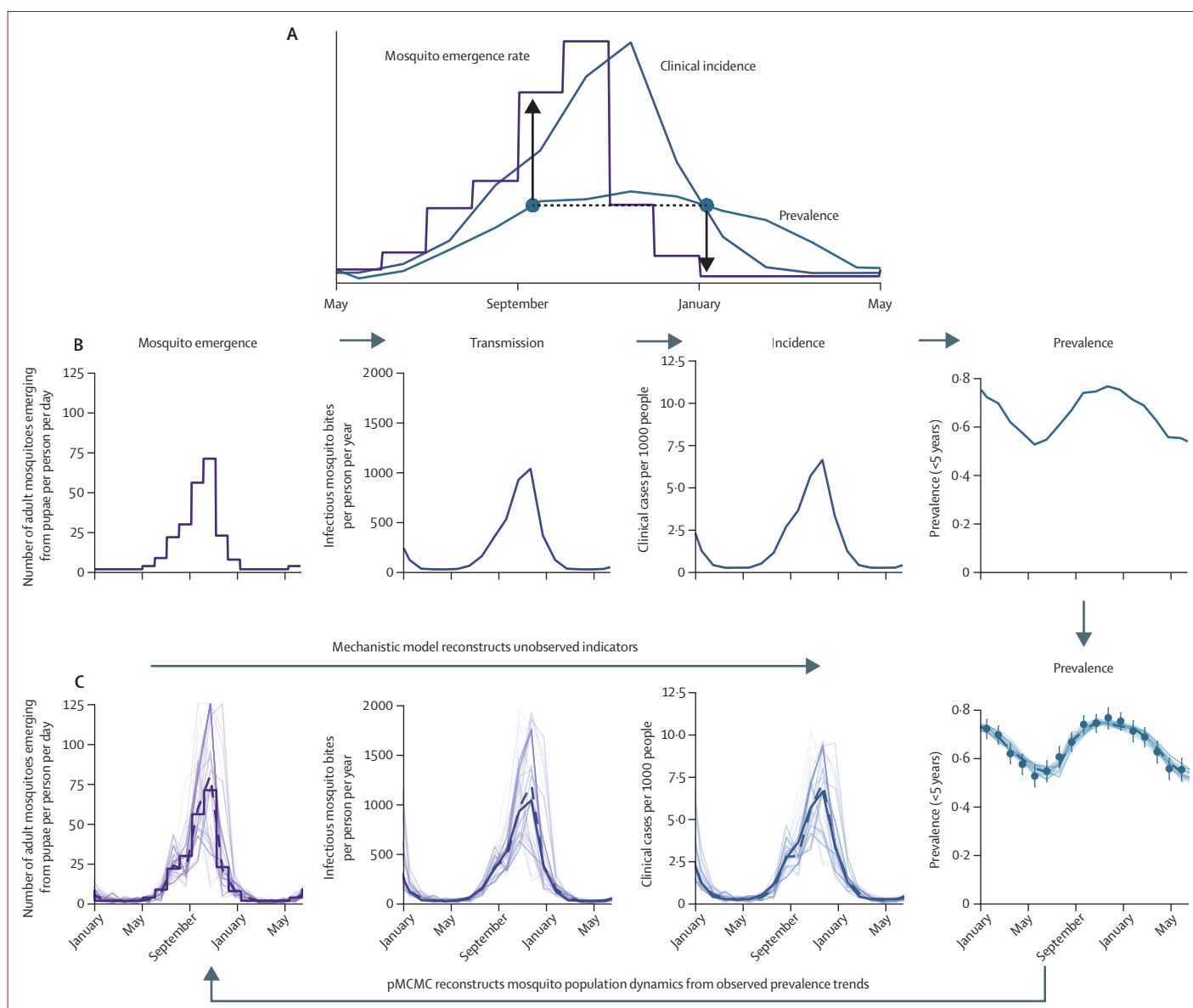


Figure 1: Using malaria prevalence as an indicator of transmission and burden

(A) Malaria prevalence is a lagged indicator of transmission and burden such that the same observed levels of prevalence at two different times of the year can correspond to vastly different stages of the transmission season. (B) The previously described and validated mechanistic malaria model (*malariasimulation*) describes the causal relationship between malaria indicators. Briefly, dynamics in mosquito vector populations partially determine seasonal variation in transmission intensity, which in turn drives trends in a community's incidence and prevalence. These trends are illustrated with solid lines. (C) In many settings, because entomological indicators are difficult to measure and clinical incidence measures can be difficult to interpret, malaria prevalence might be the most reliable source of data available to understand trends in malaria burden. Using the mechanistic model in conjunction with pMCMC, monthly prevalence estimates (blue points with error bars) can be used to back-calculate unobserved malaria indicators (ie, mosquito emergence, transmission intensity, and clinical incidence). Dark, solid lines represent the target values of these typically unobserved metrics, whereas lighter lines represent instances of the pMCMC model estimation. The dashed lines then represent the median value across the pMCMC posterior distribution. pMCMC=particle Markov chain Monte Carlo.

Methods

Extension of a validated malaria transmission model

We adapted a validated age-structured deterministic model of *Plasmodium falciparum* transmission (*malariasimulation*).¹⁴ In the original model, larval carrying capacity (and thus transmission intensity) varies seasonally via a Fourier series fitted to historical rainfall. To allow greater month-to-month

variation, we replaced this seasonal function with a user-defined stochastic process governing adult mosquito emergence from available habitats. In *anatembea*, this process is a Gaussian random walk on the log emergence rate, which then drives (figure 1B) entomological inoculation rate (EIR; the number of infectious bites per person per unit time), clinical malaria incidence (the number of new infections per unit

time that result in clinical disease), and malaria prevalence (the proportion of individuals who test positive for malaria by rapid diagnostic test or microscopy; that is, the number of symptomatic individuals and the number of asymptomatic individuals with detectable parasite levels divided by the total population size). Model-derived prevalence was fitted to monthly prevalence data (counts tested and positive) using a particle Markov chain Monte Carlo (pMCMC) algorithm¹⁵ (figure 1C), implemented using *odin*, *dust*, and *mcstate* R packages¹⁶ (appendix p 2). Conceptually, this inference mirrors COVID-19 approaches that reconstructed infection trends from death time series using known infection-to-death delays. Here, we analogously use the delay from infection to detection at ANC—driven primarily by the duration of detectable parasitaemia—to back-calculate underlying transmission (EIR).

To assess internal validity and identifiability of mosquito emergence rate, EIR, and clinical incidence from prevalence trends, we created synthetic prevalence data derived using the original *malariasimulation* seasonality (appendix p 1). We selected four archetypical settings—Equateur, Democratic Republic of the Congo (perennial); Tanga, Tanzania (bimodal); Upper East, Ghana (moderately seasonal); and Fatick, Senegal (highly seasonal)¹⁷—and simulated each at annual EIR of one, 50, and 100 infectious bites per person per year. We compared monthly pMCMC estimates to underlying target values using Pearson's R^2 , root-mean-square error (RMSE), and 95% credible interval (CrI) coverage.

Ethical approval

This study was a secondary analysis of previously collected data from published studies and did not involve recruitment of new participants, participant contact, or collection of new biological samples. All ANC1 and comparator datasets used in this analysis were aggregated or de-identified before analysis. Ethical approval and informed consent for the original clinical trials and observational studies were obtained by the investigators of those studies, as described in the original publications. For the West African ISTp trial,¹⁸ the protocol and amendments were approved by ethics committees in Burkina Faso, Ghana, Mali, The Gambia, and the UK, and participant records were anonymised and de-identified before analysis; participants consented for their clinical records to be used in the study. For the Malawi ISTp trial,¹⁹ ethical approval was obtained from the Liverpool School of Tropical Medicine and the Malawian National Health Science Research Committee, and written informed consent was obtained from all participants before randomisation. The Kenya ISTp trial²⁰ received ethical approval from the Kenya Medical Research Institute and the US Centers for Disease Control and Prevention.

Adaptation of the model to prevalence at antenatal care

We augmented an existing review¹⁰ of the relationship between malaria prevalence in children younger than

5 years (ie, aged 0–59 months) and malaria in pregnancy with 2023 studies,^{21,22} excluding observations with chemoprevention in children (SMC) or women (previous IPTp). We fitted a mixed-effects log-linear regression model stratified by gravidity to capture immunity history effects on diagnostic sensitivity¹⁰ and used the resulting coefficients to map modelled community prevalence to ANC gravidity-specific prevalence (appendix p 5).

Data analysis

We analysed ANC1 data from intermittent screening and treatment in pregnancy (ISTp) trials in six sub-Saharan African countries (Burkina Faso, The Gambia, Ghana, Malawi, Mali, and Kenya; table).^{18–20} For Kenya and Malawi, the model was fitted to primigravidae and multigravidae tested or positive counts; for the remaining countries, multigravidae was restricted to secundigravidae counts due to the original study inclusion criteria. Minimum user inputs for *anatembea* are monthly prevalence data. By default, in the absence of other contextual information, we used the first year's primigravidae prevalence to calibrate initial pre-observation transmission and immunity, minimising potential seasonal biases of a shorter calibration window (appendix p 5).

However, *anatembea* provides functionality for the user to adjust this assumption (see vignette). Meanwhile, other optional user parameters include pMCMC particles/step/chains, the maximum mosquito emergence rate, and treated proportion of clinical cases. No rainfall or other environmental data are required.

To cross-check seasonality against non-ANC1 sources, we collated location-specific clinical incidence and entomological datasets from the literature (appendix p 7). For the Malawi-based ISTp trial based in three health facilities across two regions (Blantyre and Chikwawa), a surveillance dataset of cerebral malaria cases in Blantyre, Malawi, was used.²³ Agreement between observed dataset-based and model estimated Markham Seasonality Index (MSI)²⁴ and seasonal peak timing was evaluated visually and via the concordance correlation coefficient (CCC) and associated 95% CI. We also compared estimates to observed Climate Hazards Group InfraRed Precipitation with Station data rainfall²⁵ and considered alignment with existing SMC practice for context only.

Because comparator data for the ISTp population in southern Malawi were scarce, we identified additional clinical incidence datasets from both surveillance and research study sources in the Blantyre and Chikwawa regions^{23,26–28} (appendix p 8). Monthly malaria prevalence data were also extracted from two additional studies in Blantyre and Chikwawa regions^{29,30} and used to fit the model to examine fine-scale seasonality and implications for intervention timing. Finally, we illustrated one programmatic app by simulating SMC: we applied published prophylactic profiles for sulphadoxine-pyrimethamine and amodiaquine (SP-AQ)³¹ to model-derived clinical incidence for each Malawi prevalence dataset (appendix p 5).

	Country	Sites	Dates	Gravidity	Gestational age	Total prevalence	Average monthly sample size (primigravid/multigravid)*
Tagbor et al (2015) ¹⁸	Ghana	Navrongo	June, 2010–October, 2011	Primigravidae and secundigravidae	16–30 weeks	622/1298 (47.9%)	42.5/33.8
Tagbor et al (2015) ¹⁸	Burkina Faso	Ziniaré	June, 2010–September, 2011	Primigravidae and secundigravidae	16–30 weeks	592/1413 (41.9%)	41.4/46.9
Tagbor et al (2015) ¹⁸	Mali	Kita, Yirimadjo, and San	May, 2010–October, 2011	Primigravidae and secundigravidae	16–30 weeks	284/1308 (21.7%)	46.7/30.1
Tagbor et al (2015) ¹⁸	The Gambia	Bassé	June, 2010–July, 2011	Primigravidae and secundigravidae	16–30 weeks	105/1194 (8.8%)	51.4/40.0
Desai et al (2015) ²⁰	Kenya	Siaya County	April, 2012–August, 2014	All	16–32 weeks	323/1528 (21.1%)	25.4/50.7
Madanitsa et al (2016) ²⁹	Malawi	Southern Malawi	July, 2011–March, 2013	All	16–28 weeks	291/1825 (15.9%)	30.4/60.2

Data are n/N (%) unless otherwise specified. *Multigravid women in Ghana, Burkina Faso, Mali, and The Gambia are restricted to secundigravidae.

Table: Study details of six trials of intermittent screening and treatment for malaria in pregnancy across sub-Saharan Africa

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

To test our algorithm's performance and to verify the identifiability of transmission trends from monthly time series data, we first applied our approach to simulated malaria prevalence data in children younger than 5 years before extending the framework to ANC1-derived data. From this simulated younger than 5 years' prevalence data alone—providing no information about rainfall patterns or other dynamic variables—we accurately captured the pre-specified seasonal shape of transmission within each archetypal setting (appendix p 9). As prevalence drives the pMCMC fitting, agreement between target and estimated values was strong ($R^2=1$, RMSE=0.02 for all four sites; appendix p 10). Agreement between target and estimated clinical incidence and EIR was generally high ($R^2>0.9$), except for clinical incidence in the perennial setting of the Democratic Republic of the Congo ($R^2=0.75$), wherein the pMCMC did not detect minor fluctuations. Agreement between target and estimated values of mosquito emergence was generally lower than the other metrics ($R^2=0.66$ – 0.96), possibly due to overestimation at low target values. These differences possibly do not severely affect the model, as large differences in low mosquito emergence rates result in similar values in EIR and clinical incidence. The proportion of months in which the estimated 95% CrI captured the target value of transmission metrics was more than 75% for seasonal locations but much lower in the Democratic Republic of the Congo (20–40%), again due to the tendency for the model to ignore minor fluctuations (appendix p 11). For example, in the Democratic Republic of the Congo, at an EIR of 100 infectious bites per person per year, transmission troughs were overestimated by 0.0016 cases per person per month and peaks underestimated by 0.0011 cases per

person per month. To ensure proper starting conditions for the model, the average prevalence of the first year of observed data was provided, setting an expectation on the initial level of community immunity and transmission levels (appendix p 12). We also found that initiating the semistochastic process 12 months before the beginning of the observation window typically provided the tool enough flexibility to optimise the information provided by the observed prevalence data about dynamics before the observation window. However, the first 3 months of data are typically subject to a high degree of uncertainty (appendix p 13).

The data used to augment the review of van Eijk and colleagues¹⁰ (appendix p 6) support observations from the original analysis that prevalence—here, the detection of malaria parasites of any species by microscopy, or rapid diagnostic test irrespective of the presence of symptoms—from primigravidae is similar to that within children younger than 5 years, but that prevalence in multigravidae progressively underestimates both as prevalence increases (figure 2; appendix pp 10, 14). Coefficients estimated from the log-linear regression summarising this relationship were used to translate the pregnancy-naïve estimates in prevalence in children younger than 5 years generated by the mechanistic model into estimates of prevalence among pregnant women, allowing comparison of the model with the observed prevalence measured at ANC1. This is the default process in *anatembea*.

We applied our pMCMC framework to real-world ANC1 data from ISTp trials across sub-Saharan Africa. Across the six ISTp datasets, total ANC1 sample sizes and positivity were Ghana, 622 (47.9%) of 1298 during June, 2010–October, 2011; Burkina Faso, 592 (41.9%) of 1413 during June, 2010–September, 2011; Mali, 284 (21.7%) of 1308 during May, 2010–October, 2011; The Gambia, 105 (8.8%) of 1194 during June, 2010–July, 2011; Kenya, 323 (21.1%) of 1528 during April, 2012–August, 2014; and Malawi, 291 (15.9%) of 1825 during July, 2011–March, 2013.

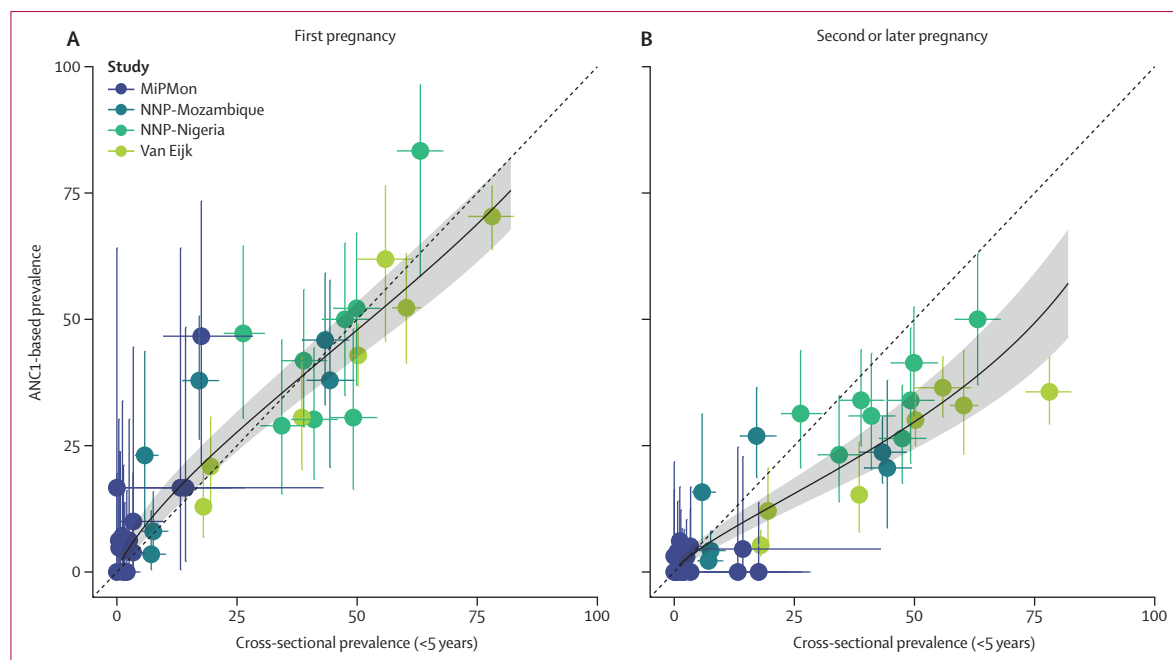


Figure 2: Correlation of malaria prevalence between children younger than 5 years and women at their ANC1 visit

Correlation of malaria prevalence between children younger than 5 years and women at their ANC1 visit during their first (A) and second or later pregnancy (B) across multiple sites in sub-Saharan Africa. Children younger than 5 years are defined as children aged 0–59 months. The black line shows model fit with associated 95% credible intervals (grey shaded areas). MiPMon: Pujol and colleagues.¹⁹ NNP: Gutman and colleagues.¹⁸ Van Eijk: van Eijk and colleagues.¹⁰ ANC1=first antenatal care visit.

Figure 3 shows model fits to prevalence in primigravida and multigravida women from ISTp trials across sub-Saharan Africa, with associated estimates of daily clinical incidence in children younger than 5 years for each location across the study period. In west Africa, the model translated peaks in prevalence occurring in the first months of the dry season into peaks of transmission occurring during the rainy season. The model interpreted subsequent steady declines in prevalence from the middle of the dry season onwards as being indicative of sustained periods of near-zero transmission, before transmission increases again soon after the rains resume. These seasonal peaks coincide with the timing of SMC campaigns within the region.

To help with corroborating model accuracy, we identified longitudinally collected measures of clinical case incidence (appendix p 7). For study settings in Burkina Faso, Ghana, Kenya, and Mali, clinical trial data that used case definitions suitable for assessment of seasonality (ie, symptoms with parasitaemia above a high-density threshold or when the individual was test-negative in the previous month) were identified. Our estimates showed strong agreement with these data in terms of MSI (CCC 0.82 [95% CI 0.31–0.97]) and timing of peak (CCC 0.98 [95% CI 0.87–1.00]), accurately capturing the wider transmission season in Navrongo, Ghana (figure 3). In The Gambia, the identified comparison data source did not take place over a 12-month period, although our results also showed close agreement with the timing and shape of the transmission season. Similarly, when comparing our seasonality estimates to those of rainfall seasonality (appendix p 15), the magnitude of the

MSI strongly agreed (CCC 0.96 [95% CI 0.85–0.99]), whereas estimated incidence consistently peaked after rainfall (CCC 0.83 [95% CI 0.40–0.96]).

Although we could not find equivalent data to compare with estimates from Madanitsa and colleagues,¹⁹ which comprised sites straddling Chikwawa and Blantyre districts in southern Malawi, we found several datasets from routine data and research settings in the area (appendix p 8). Clinical case burden, including severe and cerebral malaria, was available from Queen Elizabeth Central Hospital (QECH) in the city of Blantyre between 2001 and 2010.²³ Malaria cases with severe anaemia were also available from the Chikwawa District Hospital, one of the health facilities used in Madanitsa and colleagues.¹⁹ In addition, two Chikwawa-based research datasets were also identified, which included EIR and clinical incidence collected during the Majete Malaria Project, a 5-year community-based malaria control project.^{27,29} The locations of QECH, the three health facilities from Madanitsa and colleagues,¹⁹ and the three communities of the Majete Malaria Project are shown in figure 4A.

Based on incidence estimates from ANC1 malaria prevalence collected from Blantyre and Chikwawa health facilities as presented by Madanitsa and colleagues,¹⁹ malaria incidence peaked on Jan 31 (95% CrI: Dec 28 to Feb 28), corresponding to peak rainfall in these two districts, which, between 1997 and 2022, typically peaked in mid-to-late January (range: Dec 30 to Feb 8; figure 4B). Other data sources reveal a more complex picture of malaria seasonality within southern Malawi. Data from QECH in Blantyre

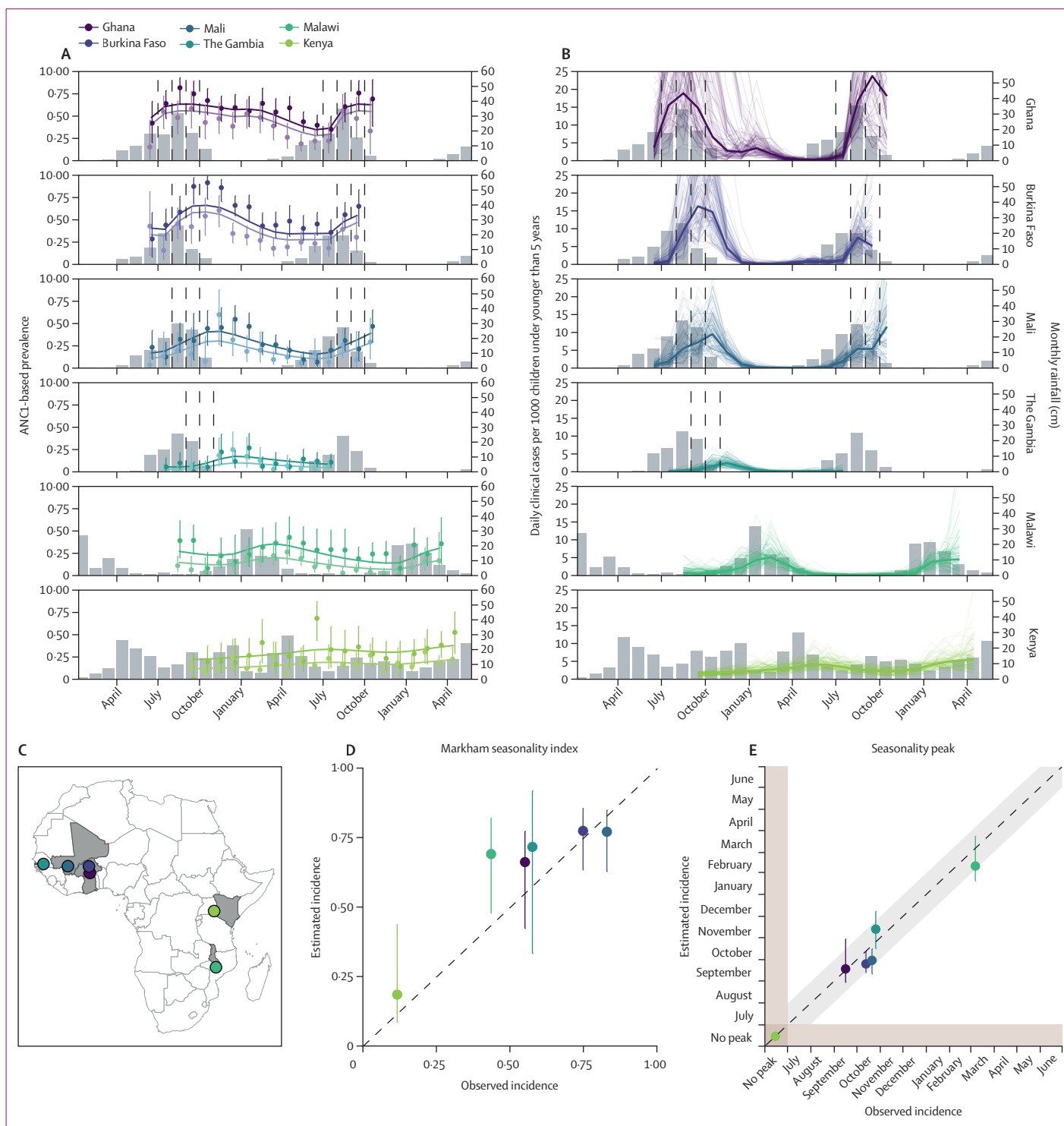


Figure 3: Reconstructing clinical incidence from ISTp trial data using the *anatembea* framework

(A) Model fits (solid line) to prevalence in primigravid (dark colour) and secundigravid (four west Africa locations) or multigravid (east Africa locations; light colour) women from the six ISTp trials. Points with error bars represent the monthly observed ANC1-based prevalence and associated 95% CIs. (B) Associated estimates of daily clinical case burden for each location across the study period. The dark, thick line represents the median trend, while faint, thin lines represent individual model iterations in the pMCMC process. In both (B) and (C), grey bars represent observed rainfall (in cm), while dashed black lines mark reported SMC trials for context. (C) Study locations for six trials of intermittent screening and treatment in pregnancy (ISTp) across sub-Saharan Africa from 2010 to 2014. (D) Comparison of the MSI between observed and estimated trends in clinical incidence. MSI measures the degree of annual seasonality of a given monthly indicator. (E) Comparison of the timing of the seasonal peak between observed and estimated trends in clinical incidence. In locations with MSI < 0.25, the timing of the peak was not calculated (represented by tan bars). In both (D) and (E), the black dashed line represents the 1:1 agreement line ($x=y$), while (E) shows a ± 30 -day deviation tolerance around this agreement. ANC1=first antenatal care visit. CI=confidence interval. ISTp=intermittent screening and treatment in pregnancy. MSI=Markham Seasonality Index. pMCMC=particle Markov chain Monte Carlo. SMC=seasonal malaria chemoprevention.

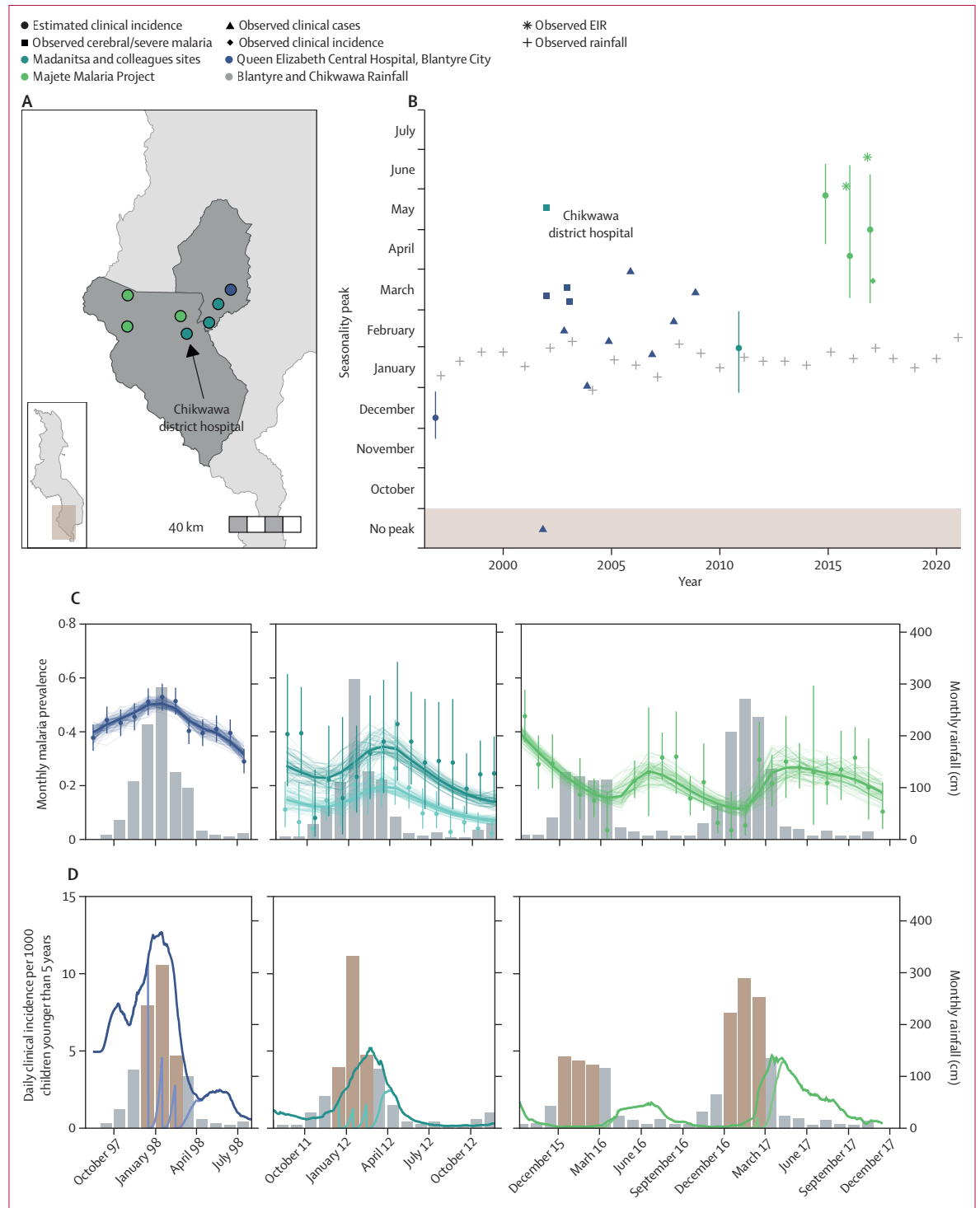


Figure 4: Capturing complex seasonality patterns of malaria burden in southern Malawi

(A) The regions of Blantyre and Chikwawa (dark grey shading) are centres of several malaria studies across multiple sites. To the furthest east is Queen Elizabeth Central Hospital in Blantyre City, with several time series of clinical, severe, or cerebral malaria cases, and malaria prevalence among pregnant women at their ANC1 visit. In northern Chikwawa regions are the locations of three villages that comprise the Majete Malaria Project, where malaria prevalence, EIR, and clinical incidence were collected between 2015 and 2019. Straddling the border of the two regions are three health facilities used to recruit participants in the Madanitsa and colleagues²⁰ ISTp trial. The westernmost of these (marked Chikwawa District Hospital) contributed an additional time series of severe malaria cases. (B) Timing of peak malaria burden varies over time and geography and by data source. Points with error bars represent peak timing as measured using ANC1-modelled estimates of clinical incidence using

the *anatembea* framework. Cross marks indicate peak mean rainfall total across both Chikwawa and Blantyre regions. The tan bar indicates measures with an MSI below 0.25 and therefore lack an annual seasonal peak. (C) In addition to the Madanitsa and colleagues²⁰ ISTp trial ANC1 prevalence data (middle panel), the *anatembea* framework was fit to ANC1-based prevalence from Queen Elizabeth Central Hospital, Blantyre City, and prevalence among children younger than 5 years from Majete Malaria Project, Chikwawa. Observed prevalence estimates and 95% CIs are shown by the points with error bars. Median estimated prevalence trend (thick, dark line) and a sample of model iterations (pale, thin lines) demonstrate the model fits to the prevalence trends. As the data from the ISTp trial were disaggregated by the pregnant woman's gravidity, two sets of prevalence fits are displayed. Grey bars represent monthly rainfall in Blantyre and Chikwawa regions. (D) Fitting the model to monthly prevalence data revealed an increasing lag (from east to west) between peaks in observed rainfall (bars) and estimated clinical incidence (dark lines). Implications of this observation on intervention implementation are illustrated with the simulated impact (pale lines) of a hypothetical seasonal malaria chemoprevention (SMC) campaign in which timing was defined by rainfall patterns. Months of SMC implementation are indicated by the tan bars. ANC1=first antenatal care visit. EIR=entomological inoculation rate. ISTp=intermittent screening and treatment in pregnancy. MSI=Markham Seasonality Index. SMC=seasonal malaria chemoprevention.

suggest highly variable timing of malaria transmission peaks ranging from Jan 2 to March 30, including 1 year with an MSI below 0.25, suggesting no discernible peak. Incidence estimates from ANC1 prevalence data collected at QECH in 1997–98, however, suggest an earlier peak of Dec 9 (95% CrI: Nov 23 to Dec 29) (figure 4B, C). In contrast, in Chikwawa, entomological and case data from the Majete Malaria Project in 2015–19 suggest a later peak in transmission between March and June (figure 4B). Similarly, severe malaria cases at the Chikwawa District Hospital, which is the ISTp health facility furthest west and closest to the Majete sites, peaked on May 18. Fitting to trends in infection prevalence also collected in the Majete study results in estimated incidence peaks that overlap with the Majete or Chikwawa District Hospital estimates (2015: May 27, 95% CrI: April 20 to June 20; 2016: April 11, 95% CrI: March 10 to June 19; 2017: May 1, 95% CrI: March 6 to June 12; figure 4B, C). To show the potential implication of these seasonality differences, we simulated the effect of SMC timed to coincide soon after the beginning of the rainy season, as typically performed in the Sahel. We estimated that such an approach would have reduced malaria burden in communities served by the QECH in 1997–98 and during the ISTp trial in 2011–12, but not during the Majete study (figure 4D).

Discussion

By extending a validated mechanistic model, our framework shows that malaria prevalence measured at ANC1 can inform transmission dynamics and clinical burden, reliably capturing seasonality and peak timings. Using six ISTp trial datasets, we recovered known geographical nuances in west Africa, such as later season onset from east to west and broader seasons from north to south in the Sahel. This ability to capture patterns in which transmission and rainfall are well-correlated suggests that the same approach can help to interrogate settings where such relationships are less predictable. By applying the model to clustered communities in southern Malawi, we showed how ANC1 can reveal shifts in seasonal patterns with direct implications for seasonal intervention strategies. Together, these findings provide key evidence to support the 2025 updated WHO malaria surveillance manual⁸ that proposes the use of ANC1-based malaria prevalence data to understand a community's transmission dynamics and to cross-validate with other data sources.

Translating ANC1-based prevalence data into transmission is complex.^{3,32} For example, because parasite

prevalence reflects infections accumulated over preceding months, seasonal peaks in prevalence peaks can occur after transmission has begun to decline, marking the transition from high-transmission to low-transmission periods rather than the true transmission maximum.³² Similar prevalence values can, therefore, occur under different transmission intensities.

The *anatembea* package effectively analyses the entire time series, explicitly learning from both prevalence levels and trends to overcome the inherent lagging nature of prevalence measures, enabling robust estimation of seasonality and timing. This capability is important in high-asymptomatic prevalence contexts, when routine passive case detection might understate seasonal transmission signals because fevers in children reflect both malaria and non-malarial illness with coincidental parasitaemia.⁷

In southern Malawi, we found that appropriately timed seasonal interventions (eg, SMC or seasonal vaccination) could substantially reduce burden in children despite concerns that rainfall alone might be an unreliable guide. However, marked heterogeneity was evident over small distances: in Majete, transmission peaks lagged rainfall by much longer than expected compared with areas near Blantyre less than 50 km away. Even with multiple research datasets spanning two decades, the degree, timing, and drivers of malaria seasonality in this small area remain uncertain. Beyond rainfall, incorporating other environmental and ecological factors might improve subnational stratification of intervention timing and suitability, but research-level data alone is unlikely to achieve the scale required for such analysis. Additionally, as climate variability increases, routine data with higher spatiotemporal resolution will be essential.^{1,2} Building on this proof-of-concept, we will collaborate with the Tanzanian National Malaria Control Programme to use ANC1 data to investigate environmental drivers of seasonality and to support decision making on seasonal interventions.

Beyond the identification of seasonality patterns, the framework also supports programmatic evaluation through counterfactual simulations based on realistic contemporary local burden patterns. This application is particularly relevant when interventions in young children (eg, SMC and vaccination) suppress clinical case counts in that age group without proportionally reducing adult infection or transmission.³³ In such settings, routine paediatric case counts alone will be insufficient to reassess seasonal intervention timing. Applying our approach when these interventions are already in place can help separate

intervention-driven declines from broader changes in transmission.

Several uncertainties and technical challenges remain. Our current translation from ANC1-derived prevalence to community prevalence uses fixed coefficients by gravidity and transmission intensity based on a few datasets—especially for secundigravidae at higher prevalence—and might require refinement to include emerging data and allow for changing immunity patterns. Accurately representing background immunity to clinical disease also remains difficult, although its effect on burden estimates seems to diminish within the first 2 years of observation. Future updates will allow incorporation of external priors (eg, population-based surveys and Malaria Atlas Project estimates) and local programme information (eg, vector control) to stabilise early inference and improve calibration. Additionally, to address the limitation of relying on one mechanistic structure from the World Malaria Report ensemble,¹ future work will explore the incorporation of alternative models that can be feasibly executed in the computationally intensive pMCMC framework. Although *anatembea* reproduced intra-annual features across synthetic scenarios, it smoothed small, regular fluctuations under perennial transmission due to the current random walk proposal. We will explore locally adaptive volatility or machine learning-based approaches to capture these undulations while maintaining computational feasibility.

Data availability and quality are practical constraints. Despite the recognised risks of malaria in pregnancy, routine ANC malaria screening is not yet universal, sometimes due to cost concerns or perceptions that testing does not improve outcomes under IPTp-SP guidelines.³⁴ Nonetheless, tracking infection in pregnant women fills an important gap as resources increasingly focus on childhood interventions and as ANC attendance remains high and stable across sub-Saharan Africa. Routine ANC data face the usual concerns—selection bias from differential access and data quality issues—and knowing changes to ANC1 screening procedures is crucial to appropriate trend interpretation.⁸ However, the stability of the ANC1 population can aid error detection and correction. Strengthening access to early ANC, particularly in rural and socio-economically disadvantaged areas, would improve both representativeness and maternal–child health. In future iterations of *anatembea*, residual bias can be formally incorporated into the inference framework by adjusting likelihood calculations according to ANC coverage.

As national cross-sectional surveys become less frequent or delayed, ANC1-based malaria surveillance offers a cost-effective complement to existing systems, bolstering nationally owned burden estimates. Although not a substitute for the breadth of data in the DHS Program, ANC1 surveillance—analysed with a mechanistic framework—could sharpen subnational decisions on the timing and targeting of seasonal tools, support monitoring of intervention effect, and improve resource allocation for both pregnant women and the broader community.

Contributors

PGTW and JTH conceived and designed the study. SG, PD, CG, GM, AP, AMa, AMo, AMu, JW, MM, CK, Li-P, VM, SK, MD, KM, KSP, JS, SMT, DW, SRM, AMvE, DC, KK, JEW, SOC, KB, FC, KM, SA, SL, HT, BG, FoTK, and JRG contributed data or aided with data interpretation. JTH, PGTW, AH, ESK, MB, and RGF developed methods and software for the analysis of the data. PGTW and JTH verified the underlying data of the study. PGTW, JTH, AMu, AMo, and MEC conducted analyses and prepared figures. All authors contributed to drafting and revising the manuscript. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

We declare no competing interests.

Data sharing

The package *anatembea* is available at GitHub. Data for individual studies can be requested from the original cited author and can be coordinated by the corresponding author. Synthetic data and all code for the current analysis are available at GitHub.

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For more on **Malaria Atlas Project**, see <https://malariaatlas.org/>

For more on the ***anatembea* package code**, see <https://github.com/mrc-ide/anatembea>

For more on **synthetic data and analysis code**, see https://github.com/jt-hicks/anc_pmc_mcmc_analysis

For more on the **DHS Program**, see <http://www.dhsprogram.com>

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