

Relationship between nutritional status and malaria risk among children receiving routine seasonal malaria chemoprevention: evidence from a prospective cohort study in Mali

Soumba Keita,^a Mahamoudou Touré,^a Fousseyni Kané,^a Hamady Coulibaly,^a Daouda Sanogo,^a Ibrahim Sanogo,^{a,h} Drissa Konate,^a Idiatou Diallo,^b Moussa Keita,^c Sory Ibrahim Diawara,^c Amadou Sekou Traoré,^c Cheick Oumar Tangara,^a Issaka Guindo,^a Bourema Cissé,^a Abdoulaye Kassoum Koné,^d Hardy Williams,^e Aicha Monteiro,^e Niele Hawa Diarra,^f Mahamadou A Thera,^d Safiatou Niaré Doumbo,^d Nafomom Sogoba,^c Mahamadou Diakité,^{a,c} Jeffrey G Shaffer,^g and Seydou Doumbia^{a,c,*}



^aUniversity Clinical Research Center (UCRC), University of Sciences, Techniques and Technologies of Bamako, Bamako, Mali

^bGlobal Health and Population, Harvard TH Chan School of Public Health, Boston, MA, USA

^cInfectious Diseases and Medical Entomology Research and Training Center, University of Sciences, Techniques and Technologies of Bamako, Mali

^dParasites and Microbes Research and Training Center, University of Sciences, Techniques and Technologies of Bamako, Mali

^eDepartment of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

^fInternational Rescue Committee, Mali

^gCelia Scott Weatherhead School of Public Health and Tropical Medicine, Tulane University, New Orleans, LA, USA

Summary

Background Malnutrition and malaria remain major overlapping causes of morbidity among children in the Sahel, where seasonal malaria chemoprevention (SMC) is widely implemented. This study assessed the relationship between nutritional status and malaria outcomes, and whether SMC exposure influenced nutritional changes during routine implementation.

Methods A prospective cohort study was conducted among children aged 3–59 months during the 2024 malaria transmission season in Sirakorola, Mali. Children were enrolled before the first SMC round and followed monthly (July–October) for *Plasmodium* (*P.*) *falciparum* infection by microscopy, anthropometry, and SMC coverage. Clinical malaria incidence was measured through passive case detection (August–November), defined as fever (≥ 37.5 °C or within 48 h) with parasitological confirmation. Nutritional status was assessed using weight-for-age, height-for-age, and weight-for-height z-scores. Mixed-effects logistic and Poisson models estimated associations between nutritional status, *P. falciparum* infection, and clinical malaria incidence, adjusting for age, sex, SMC exposure, and follow-up period. Interaction terms assessed whether SMC modified the association between nutritional status and malaria risk. Nutritional changes were assessed using McNemar's test and longitudinal mixed-effects models for MUAC and weight.

Findings Of 425 enrolled children, 42.6% were malnourished at baseline. Malnutrition was independently associated with higher *P. falciparum* prevalence (6.5% vs. 2.6%; OR = 2.20, 95% CI 1.21–3.99), and increase clinical malaria incidence (9.1 vs. 6.0 per 100 person-months, adjusted incidence rate ratio = 1.82, 95% CI 1.11–2.97). Malaria incidence was higher during periods without SMC protection (>28 days since last dose). No evidence of interaction was observed between nutritional status and SMC exposure. MUAC and weight increased over the season across all nutritional groups, with no differential trajectories by baseline status.

Interpretation Malnutrition substantially increased malaria vulnerability despite high SMC coverage. Nutritional improvements observed during follow-up suggest potential synergistic benefits. Integrating nutrition interventions with SMC delivery could enhance child survival and accelerate malaria control in high burden regions.

Abbreviations: AQ, Amodiaquine; CHC, Community Health Center; CI, Confidence Interval; DHA-PQ, Dihydroartemisinin-Piperaquine; HRP2, Histidine-Rich Protein 2; IRR, Incidence Rate Ratio; LMIC, Low- and Middle-Income Countries; MUAC, Mid-Upper Arm Circumference; NIH, National Institutes of Health; OR, Odds Ratio; *P. falciparum*, *Plasmodium falciparum*; PCD, Passive Case Detection; RDT, Rapid Diagnostic Test; SD, Standard Deviation; SMC, Seasonal Malaria Chemoprevention; SP-AQ, Sulfadoxine-Pyrimethamine plus Amodiaquine; WAZ, Weight-for-Age Z-score; HAZ, Height-for-age Z-score; WHZ, Weight-for-Height Z-score; WHO, World Health Organization

*Corresponding author. University Clinical Research Center (UCRC), University of Sciences, Techniques and Technologies of Bamako (USTTB), Bamako, Mali.

E-mail address: sdoumbi@gmail.com (S. Doumbia).

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Keywords: Seasonal malaria chemoprevention; Malnutrition; Changes in nutritional status; Children under five

Research in context

Evidence before this study

We searched PubMed, Web of Science, Embase, the Cochrane Library, and Google Scholar for studies published between January 1, 2016, and December 31, 2024, without language restrictions. We used combinations of the terms “seasonal malaria chemoprevention” OR SMC AND malnutrition OR undernutrition OR stunting OR wasting OR underweight OR “nutritional status” AND “sub-Saharan Africa” OR Sahel AND “children under five”. We also screened reference lists of relevant articles.

We identified 11 eligible studies, including observational and interventional designs. Observational studies examining the associations between nutritional status and malaria during the SMC delivery period reported mixed findings: some studies reported no clear association, while others suggested higher infection risk or parasite density among undernourished children. Interventional studies evaluating nutritional supplementation alongside SMC also reported heterogeneous results, with several trials showing limited or no added benefit on malaria outcomes beyond SMC alone. Notably, few studies have formally assessed whether nutritional status modifies the effectiveness of SMC (i.e., interaction between nutritional status and SMC exposure). Overall, the available evidence remains sparse and methodologically diverse with limited capacity to draw firm conclusions.

Added value of this study

This prospective cohort study provides robust, real-world evidence from routine SMC implementation in Mali, with longitudinal assessment of both nutritional status and malaria outcomes. The study demonstrates that malnutrition is independently associated with increased malaria risk despite high SMC coverage, while higher SMC exposure provides strong protection against clinical malaria. By evaluating nutritional trajectories alongside malaria outcomes, the study also offers new insights into potential synergistic effects of repeated SMC rounds on child nutritional status.

Implications of all the available evidence

Taken together, these findings suggest that SMC alone may not fully protect children in settings with a high prevalence of malnutrition. Integrating targeted nutrition interventions into SMC delivery platforms could enhance child survival and strengthen malaria control efforts in high-burden settings. Further studies across diverse Sahelian settings, using designs better suited for causal inference, are needed to confirm these findings and guide policy on combined malaria-nutrition strategies.

Introduction

Seasonal malaria chemoprevention (SMC) serves as a cornerstone intervention for reducing malaria morbidity and mortality, among children under five years of age during peak transmission seasons.¹ In Mali, SMC has been implemented nationwide since 2016 and is delivered during the rainy season, through monthly administration of sulfadoxine-pyrimethamine plus amodiaquine (SP-AQ) administered from July to October. Studies from the West Africa International Center of Excellence in Malaria Research (ICEMR) reported a substantial reduction in the prevalence of *Plasmodium falciparum* (*P. falciparum*) infection and clinical malaria incidence.^{2–5} Nevertheless, malaria infections and clinical malaria continue to be observed among some children during the SMC delivery period, including during the intervals between monthly treatment cycles.^{3,6–9} Findings from Burkina Faso and other

Sahelian settings are mixed: some studies suggest a higher malaria risk among malnourished children during SMC delivery,¹⁰ while others found no consistent association.¹¹ Factors that may be associated with malaria infections occurring during the SMC delivery period include antimalarial drug treatment,¹ adherence to the complete treatment regimen,¹² as well as host contextual factors such as nutritional status.¹³ Other potential contributors described in the literature include antimalarial drug resistance,⁷ and coexisting conditions that may affect both malaria risk and nutritional status. Both malaria and malnutrition are independent major causes of morbidity and mortality in malaria-endemic areas. Malnutrition and malaria morbidity often co-occur among children under five, the primary target of SMC,^{14–16} and children severely affected by one are often affected by both. Malnutrition is associated with multiple risk factors and displays

diverse clinical presentations, including acute malnutrition with wasting (low weight-for-height) and chronic malnutrition as stunting (low height-for-age). In Mali, the 2024 National Anthropometric, Nutritional, and Mortality Retrospective Survey¹⁷ showed that malnutrition remains a significant public health problem in all levels of severity, with a prevalence of 11.6% for global acute malnutrition (GAM), including 2.2% of severe acute malnutrition (SAM). The survey revealed that nearly 25% of children under 5 years old are affected by chronic malnutrition (stunting), and 21.1% are underweight. The relationship between malaria and malnutrition is complex and has been inconsistently described in the literature, with studies reporting heterogeneous associations depending on context, transmission intensity, and nutritional indicators assessed.¹⁸ In Sahelian countries, malaria transmission is highly seasonal and often coincides with the “lean season”, a period of heightened food insecurity, typically occurring between June and September, when household food stocks are depleted, food prices rise, and dietary diversity declines. This seasonal overlap may increase the concurrence of malaria exposure and malnutrition.¹¹ In this context, nutritional status may influence malaria risk through multiple pathways, including susceptibility to infection, or factors related to adherence to routine malaria preventive programs delivery, although causal mechanisms remain difficult to establish in observational settings. This study aimed to assess the association

between nutritional status and malaria outcomes, as well as to evaluate the impact of SMC exposure on nutritional indicators among children receiving routine SMC, taking into account both timing and the number of doses received. Additionally, the delivery of routine SMC provides opportunities for nutritional screening and targeted support to vulnerable children.

Findings from this research may inform strategies to integrate SMC delivery with nutritional screening or other nutritional-focused interventions, and to optimize resource allocation in areas of seasonal malaria transmission.

Methods

Study area

The study was conducted in Sirakorola located 120 km east of Bamako, in the health district of Koulikoro, Mali (Fig. 1). The population size is about 7000 inhabitants,³ with Bambara, Sarakolé, and Fulani representing more 90% of the ethnic groups. The climate is Sudan-Sahelian characterized by a long dry season (November–May), followed by the short rainy season (June to October). The average annual rainfall is 789.6 mm. Malaria transmission is highly seasonal, with most cases observed from June to October. The prevalence of *P. falciparum* infection ranges between 7 and 11%.^{3,19} The primary malaria vectors in the region are *An. gambiae*, *An. coluzzii*, and *An. Arabiensis*. Sirakorola has a Community Health Center (CHC) led by a physician and

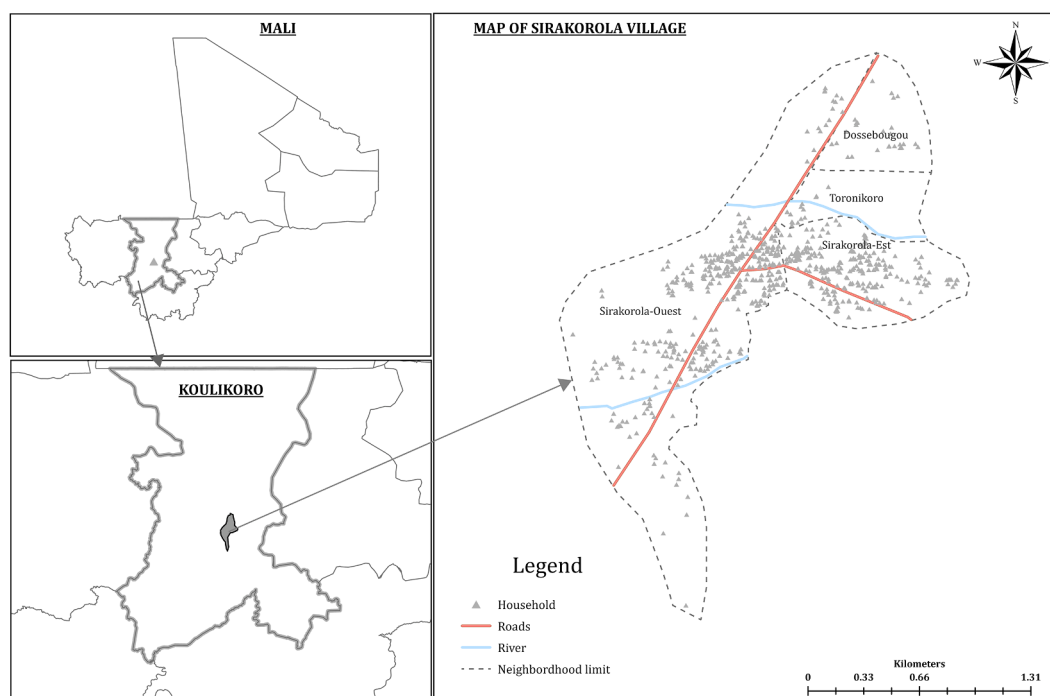


Fig. 1: Map showing the study area and the location of all households in Sirakorola.

provides primary health care to the community. The center has a nutritional support program implemented in accordance with the national Integrated Management of Acute Malnutrition (IMAM) guidelines. Children diagnosed with SAM are referred for appropriate medical and nutritional management, including ready-to-use therapeutic food (Plumpy'Nut®) or fortified blended flours, delivered through programs supported by the World Food Programme and other partners during the study period.

Study design and sampling

A prospective cohort study was conducted during the 2024 malaria transmission season (June to November) in Sirakorola. In June 2024, a complete population census identified all children aged 3–59 months residing in the study area, enumerating 771 children. Anthropometric measurements were collected for all enumerated children by trained field staff using standardized procedures, allowing classification of nutritional status according to WHO 2006 growth standards: weight-for-age (WAZ), height-for-age (HAZ), and weight-for-height (WHZ).

Following the census and anthropometric assessment, children were screened for eligibility. Written informed consent was obtained from parents or legal guardians. Thirty-three children were excluded (25 with SAM per WHO criteria, five without consent, and three for other reasons), resulting in 738 eligible children.

From this eligible population, stratified random sampling was conducted based on nutritional status (malnourished vs. normal nutritional status) to ensure adequate representation of both groups. Caregivers of eligible but non-selected children were informed that selection was based on predefined sample size requirements and stratified random sampling procedures.

The sample size was calculated assuming an expected cumulative malaria incidence of 10%,⁹ a statistical power of 80% to detect a minimum risk ratio of 2.0 at a 95% confidence level, and a ratio of children with normal nutritional status to malnourished children of 1.5. The minimum required sample size was estimated at 395 children. This number was increased to 425 to account for potential loss to follow-up.²⁰ A detailed participant flow diagram is presented in Fig. 2.

Enrollment and sample collection procedure

At enrollment, each child was assigned a unique identification number. Baseline assessments included demographic characteristics, standardized anthropometric measurements, hemoglobin concentration, and parasitological testing. Children selected through stratified random sampling were enrolled in July 2024 after confirmation of eligibility criteria. Children with severe acute malnutrition, defined as a mid-upper arm circumference (MUAC) < 11.5 cm, and children presenting with febrile illness with confirmed

clinical malaria by rapid RDT at screening were excluded in accordance with WHO SMC guidelines.¹² Excluded children were referred for appropriate nutritional or clinical care through the CHC.

After obtaining informed consent from parents or legal guardians, 425 eligible children aged 3–59 months were enrolled in the study cohort in July 2024. The final cohort included 181 children classified as malnourished and 244 children with normal nutritional status. Because children with SAM were excluded, the “malnourished” group in this study children with moderate undernutrition (z-score < −2 SD).

Assessment of nutritional status and anemia

Anthropometric measurements (weight, height or length, MUAC) were obtained by trained research field staff using calibrated equipment, following standardized procedures. Data collection was led by the research team, with support from locally trained community health workers (CHWs). Prior to fieldwork, all personnel involved underwent standardized training, including both theoretical instruction and practical sessions to ensure accuracy and consistency of measurements. Quality assurance included routine supervision and periodic calibration of measurement equipment.

Age and sex were recorded as key demographic variables and used to compute anthropometric z-scores. WAZ, HAZ, and WHZ z-scores were calculated using the WHO 2006 Child Growth Standards.²¹ Overall malnutrition was defined as a composite indicator: children were classified as malnourished if at least one anthropometric index (WAZ, HAZ, or WHZ) was below −2 standard deviations (SD), and as having normal nutritional status if all three indices were ≥ −2 SD. Individual anthropometric indicators were also analyzed separately, including stunting (HAZ < −2 SD), wasting (WHZ < −2 SD), and underweight (WAZ < −2 SD).²² In addition, the number of concurrent deficits per child was assessed to characterize cumulative nutritional vulnerability.

Anemia status was assessed using HemoCue 301® to determine hemoglobin (Hb) concentration. Children were classified as non-anemic (Hb ≥ 11 g/dL), moderately anemic (Hb = 8–10.9 g/dL), or severely anemic (Hb < 8 g/dL), according to WHO guidelines.²³ All enrolled children were followed prospectively throughout the malaria transmission season.

Cross-sectional survey and SMC delivery

Four cross-sectional surveys were conducted from July to October (Fig. 2), each aligned with one SMC cycle.

Pre-SMC Administration Phase: Prior to the first SMC cycle, baseline assessments were conducted to determine *P. falciparum* infection and nutritional status. Nutritional status was evaluated using four indicators: overall nutritional status, WHZ, WAZ, and

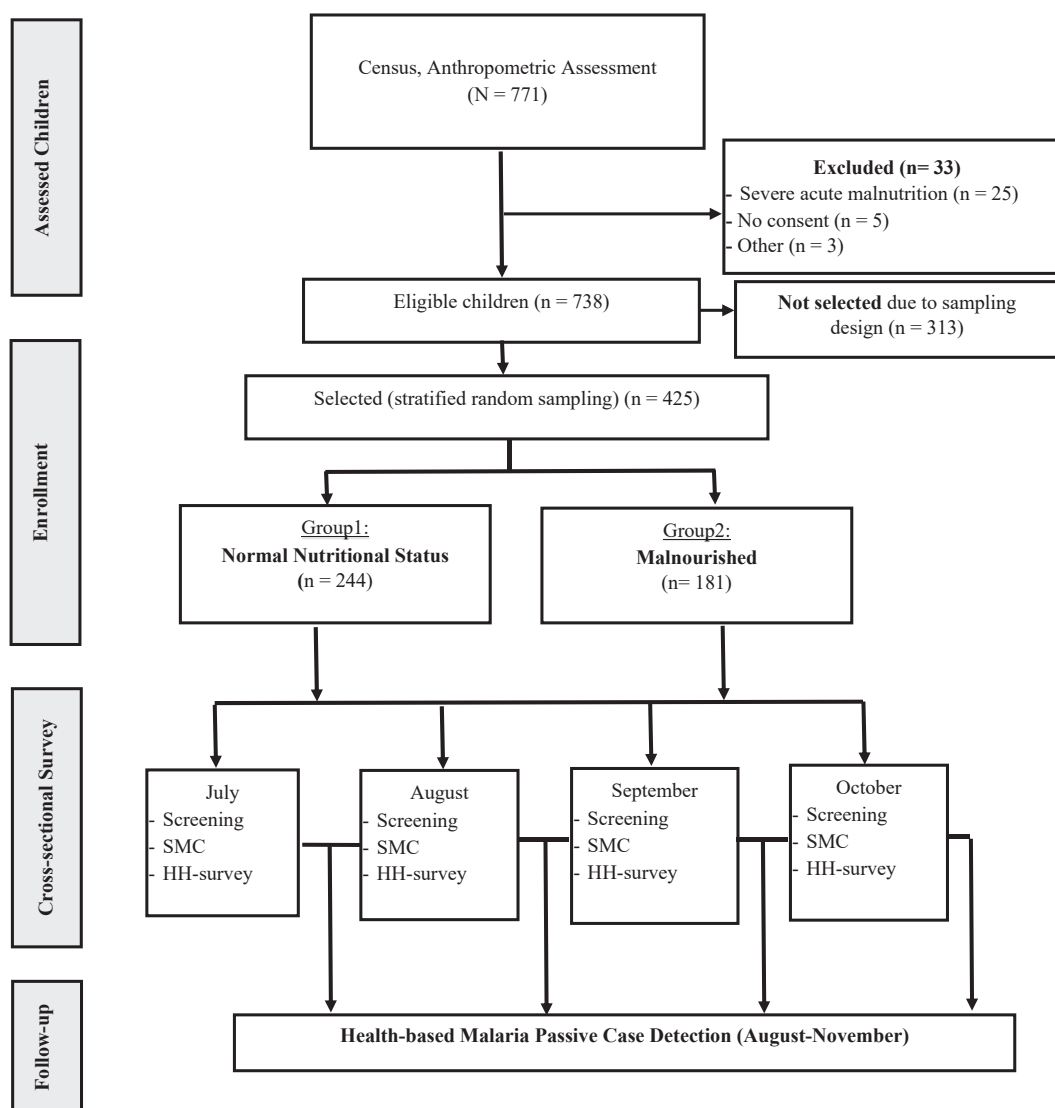


Fig. 2: Flow diagram of study design and sampling of study participants.

HAZ. Baseline infection prevalence was described by nutritional status. Parasitological assessments were subsequently performed monthly from July to October, immediately before each SMC cycle, to monitor changes in infection prevalence over the SMC delivery period. Children presenting with clinical signs suggestive of malaria were screened using a rapid diagnostic test (RDT). Those with confirmed clinical malaria were managed according to Mali's national guidelines and did not receive SMC during that cycle.

SMC Administration Phase: SMC was implemented through annual campaigns consisting of four monthly treatment cycles delivered from July to October, with each cycle comprising three consecutive daily doses. SP-AQ was delivered in collaboration with CHWs. The

first dose was administered door-to-door under directly observed therapy (DOT). Caregivers at home gave the second and third doses according to Mali's national SMC delivery strategy. Treatments were administered orally as age-appropriate portions of crushed tablets mixed with water. SP was dosed at 25 mg/kg sulfadoxine and 1.25 mg/kg pyrimethamine, and AQ at 10 mg/kg per day for three consecutive days. Details of the age-based dosing schedule are provided in [Supplementary Table_S1](#). At each SMC cycle, SP-AQ was administered through a monthly interval, providing approximately 28 days of prophylactic protection.

Post-SMC Administration Phase: A household survey was conducted 5 days after the first dose of each

SMC cycle to document treatment coverage, adherence, potential adverse events, and use of insecticide-treated nets (ITNs). Adherence to the full SMC regimen was defined as caregivers-reported completion in the three-day course (doses 1–3). SMC coverage was defined as administration of the first dose under DOT during each monthly cycle.

Health-based malaria passive case detection (PCD)

A study physician was based at the CHC and documented all clinical visits using standardized case report forms (CRFs). PCD began immediately after the first SMC round and continued from August to November, enabling a prospective monitoring of malaria incidence during periods of varying prophylactic coverage.

Parents were encouraged to bring their children to the CHC whenever malaria-related symptoms occurred, and CHWs conducted home visits to support care-seeking and identify symptomatic children. At each visit, clinical evaluation included axillary temperature measurement, RDT, and thick blood smear microscopy. Clinical malaria was defined as the presence of fever (axillary temperature ≥ 37.5 °C) or a history of fever within the preceding 48 h, in combination with parasitological confirmation by either a positive RDT or microscopy for *P. falciparum*.

To avoid double-counting, a new malaria episode was defined as one occurring ≥ 28 days after a previous episode in the same child. Children with symptoms suggestive of alternative causes of fever, such as respiratory, were clinically assessed and managed according to national guidelines, such cases were not classified as clinical malaria.

Malaria diagnosis

Paracheck[®] Rapid diagnostic test kit, recommended by the Malian National Malaria Control Program (NMCP), was used for diagnosing *P. falciparum* infection according to the manufacturer's instructions. The test detects histidine-rich protein 2 (HRP2) of *P. falciparum*. Thick smears were stained with Giemsa 3% and examined under oil immersion using an optical microscope (objectives 100) by experienced microscopists. Parasite density was calculated by counting the number of parasites per 300 white blood cells and multiplying by 25, assuming an average white blood cell count of 7500 per microliter of blood. A minimum of 100 fields were examined before a thick smear was deemed negative. Each slide was read independently by two certified microscopists. If discrepancies arose, a third microscopist reviewed the slide.

Data collection and management

Data was collected electronically using the REDCap[®] platform. Daily synchronization with the central database minimized entry errors, identified missing or inconsistent values, and ensured overall data quality.

Anthropometric data were checked for outliers using WHO Anthro criteria²⁴ before calculating z-scores in ENA for SMART (Emergency Nutrition Assessment for standardized monitoring and assessment of relief and transitions). All analyses were performed using R statistical software, version 4.4.3.

Statistical approaches

The statistical analysis addressed four predefined objectives: 1] Examine the association between nutritional status and *P. falciparum* infection prevalence at monthly follow-up visits; 2] Assess the relationship between nutritional status and clinical malaria incidence during the transmission season; 3] Identify factors associated with clinical malaria incidence, including the role of SMC exposure and its interaction with nutritional status; 4] Evaluate changes in nutritional status over the transmission season, including both overall changes between baseline and endline and longitudinal changes in anthropometric parameters.

Descriptive statistics were used to summarize demographic, nutritional, clinical, and parasitological characteristics, expressed as means with standard deviations or frequencies with proportions. Comparisons between children classified as malnourished and those with normal nutritional status at enrollment were conducted using appropriate descriptive methods.

To address the first objective, mixed-effects logistic regression models were fitted to cross-sectional monthly data to estimate the associations between nutritional status and *P. falciparum* infection prevalence. A random intercept for child ID accounts for repeated measurements within individuals. Results were presented as odds ratios (ORs) with 95% confidence intervals (CI).

For second objective, mixed-effects Poisson regression models were applied to passive case detection data to estimate incidence rate ratios (IRR) for clinical malaria, again incorporating a random intercept for child ID. Results are presented as IRRs with 95% CI.

The third objective was addressed using multivariable mixed-effects Poisson regression models based on individual-level longitudinal data with repeated measures. Exposure time was included as an offset to account for varying time at risk. SMC exposure was modeled as a time-varying variable, categorized as ≤ 28 days versus >28 days since the most recent dose to reflect the expected duration of chemoprophylactic protection. Nutritional status was treated as a time-updated exposure, measured at the beginning of each SMC cycle and carried forward to define risk periods. Models were adjusted for age group, sex and SMC period. An interaction term between SMC exposure and nutritional status was included to assess potential effect modification.

For the fourth objective, changes in binary nutritional indicators (overall nutritional status, WHZ, HAZ,

and WAZ) between baseline and endline were assessed using the McNemar chi-square test for paired outcomes, stratified by the number of SMC rounds received (1–2 vs. 3–4 rounds). Transitions were expressed as proportions within each stratum. Longitudinal changes in continuous measures (MUAC and weight) among children completing all four SMC rounds consecutively, were analyzed using linear mixed-effects models adjusted for age and sex, with child ID included as a random effect and SMC round as the main fixed effect. Analyses were stratified by baseline nutritional status, and an interaction term between SMC round and baseline nutritional status formally assessed differences in trajectories. Post-hoc comparisons with baseline (July) were performed using estimated marginal means with Bonferroni adjustment.

Extreme values were excluded using ± 3 standard deviations within each round prior to aggregation. Missing data were minimal (<5%), and complete-case analyses were conducted. Sensitivity analyses excluding observations with implausible values yielded consistent results. Model assumptions were assessed by examining residual distributions and homoscedasticity, with no major violations observed. Statistical significance was defined as a two-sided p -value < 0.05.

Ethical statement

This study was approved by the institutional ethics committee of the University of Sciences, Techniques and Technologies of Bamako (USTTB) under the reference number N°2024/203/CE/USTTB. Written informed consent was obtained from each participant's parents and/or legal guardians.

Results

Participant flow

Of the 771 children enumerated during the June 2024 census, 33 were excluded (25 with SAM, 5 whose parents did not provide consent, and 3 for other reasons), leaving 738 eligible children. Of these, 425 were selected through stratified random sampling and enrolled in the cohort, including 181 malnourished children and 244 children with normal nutritional status. The remaining 313 eligible children were not selected due to the sampling design.

Attendance at monthly follow-up visits was high overall. Some children missed individual visits but returned in subsequent rounds, reflecting intermittent participation rather than complete loss to follow-up. Participant flow is summarized in [Fig. 2](#).

Baseline sociodemographic, and clinical characteristics of the study cohort

Among the 425 children enrolled in the cohort, the prevalence of overall malnutrition defined as having at least one anthropometric indicator below -2 z-scores was 42.6% (181/425). The prevalence of underweight,

Characteristic	Category	Nutritional status		p-value
		Malnourished n (%)	Normal n (%)	
Age group (months)	<12	14 (7.7)	28 (11.5)	0.141
	12–23	18 (9.9)	14 (5.7)	
	24–59	149 (82.3)	202 (82.8)	
Sex	Male	95 (52.5)	120 (49.2)	0.565
	Female	86 (47.5)	124 (50.8)	
Fever	Temp ≥ 37.5 °C	2 (1.1)	6 (2.5)	0.476
Anemia (Hb, g/dL)	Moderate (8–10.9)	23 (12.7)	21 (8.6)	0.364
	Severe (<8)	2 (1.1)	3 (1.2)	
<i>P. falciparum</i> infection	Smear-positive	13 (7.2)	4 (1.6)	0.005

Table 1: Baseline characteristics by nutrition status.

stunting, and wasting was 24.2%, 25.1%, and 22.9%, respectively. Within the study population, 19.8% had a single anthropometric deficit, and 22.8% had two or more concurrent deficits. Detailed distributions are presented in [Supplementary Table_S2](#).

The [Table 1](#) presents the demographic and clinical characteristics at enrollment. The two study groups (children with normal nutritional status and malnourished children) had a similar age distribution, with more than 80% of children aged 24 months or older and a balance sex distribution, with nearly half of the participants being female. The prevalence of anemia was comparable in both groups, with 12.7% and 8.6% for moderate anemia, and 1.1% and 1.2% for severe anemia ($p = 0.4$). The prevalence of *P. falciparum* infection was significantly higher among malnourished children compared to their normal counterparts 7.2% vs. 1.6%; $p = 0.005$.

SMC coverage and adherence

SMC coverage and adherence were compared between malnourished and normal nutritional status children during the transmission season.

Most children attended three to four rounds of SMC ([Table 2](#)) with comparable coverage between malnourished (87.8%) and normal nutritional status (80.3%) groups ($p = 0.053$). Adherence to the three-day SMC regimen was high in both groups, with 98.3% of malnourished children and 96.3% of normal nutritional status children completing the full treatment course, with no significant difference between groups ($p = 0.340$).

Reported use of ITN remained high throughout the study period and did not differ significantly between nutritional groups. Cumulative side effects reported during SMC were comparable across groups ([Supplementary Table_S3](#)).

Relationship between nutritional indicators and malaria indicators

Prevalence of asymptomatic *P. falciparum* infection

The average monthly prevalence of *P. falciparum* infection was higher in malnourished children (6.5%

Variable	Nutritional status			p-value
	Malnourished	Normal	Overall	
	n (%)	n (%)	n (%)	
Number of SMC rounds received				
1–2	22 (12.2)	48 (19.7)	70 (16.5)	0.053
3–4	159 (87.8)	196 (80.3)	355 (83.5)	
Adherence to 3-day SMC regimen (Monthly SMC 3 dose received)				
No	3 (1.7)	9 (3.7)	12 (2.8)	0.340
Yes	178 (98.3)	235 (96.3)	413 (97.2)	

Table 2: SMC rounds received (coverage) and adherence by nutritional status.

over 555 person visits) than among those with normal nutritional status (2.6% over 896 person visits; $p = 0.006$), with peaks in October for both groups (Supplementary Table_S4).

Among smear-positive children, median parasite density was 551 parasites/ μL (IQR: 160–4791) in malnourished children and 320 parasites/ μL (IQR: 80–920) in children with normal nutritional status, with no significant difference between groups ($p = 0.180$).

Malnourished children had higher odds of *P. falciparum* infection compared to those with normal nutritional status (Fig. 3a). The association was consistent when overall malnutrition was considered (OR = 2.20, 95% CI 1.21 to 3.99) as well as by individual indicators: WHZ (OR = 3.20, 95% CI 1.63 to 6.27), and WAZ (OR = 2.85, 95% CI 1.49 to 5.47). No significant association was observed for HAZ (OR = 1.38, 95% CI 0.70 to 2.71).

Incidence of clinical malaria

During the PCD at the CHC, the incidence rate of clinical malaria was 9.1 per 100 person-months (84/905) among malnourished children, and 6.0 per 100

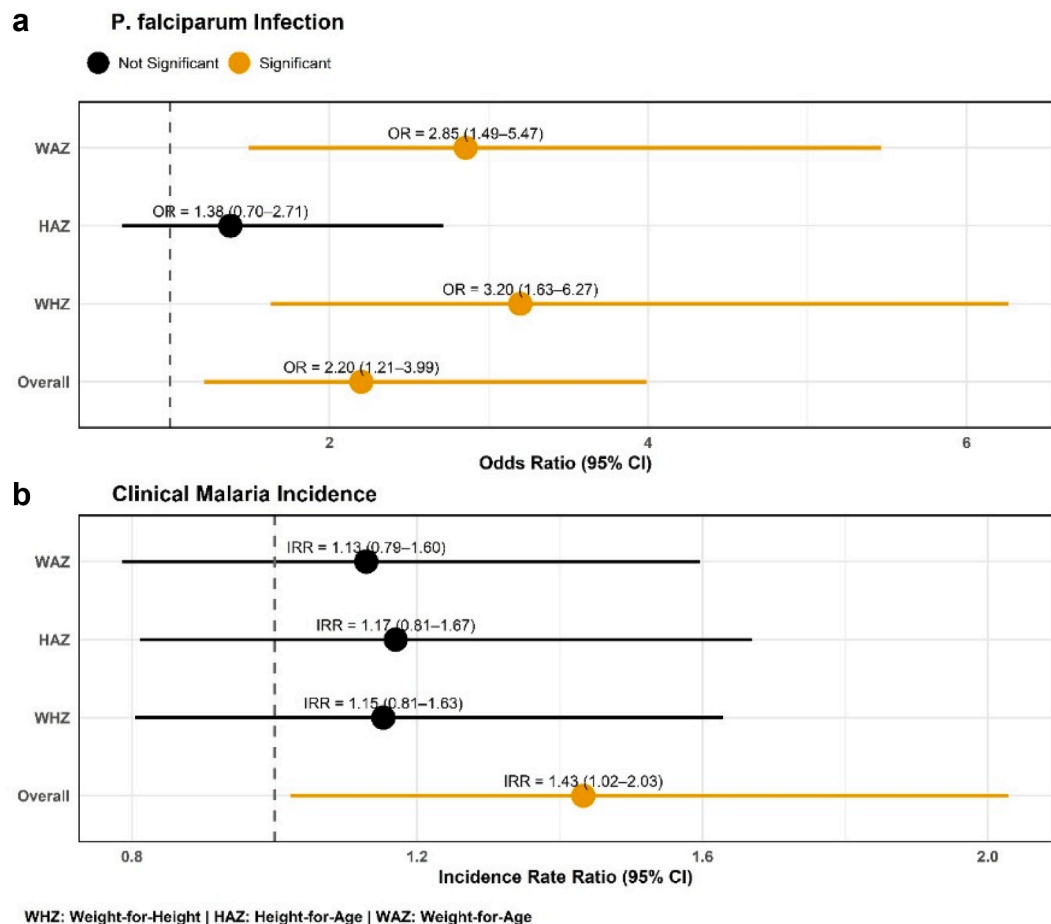


Fig. 3: Association between nutritional status and malaria outcomes among children in Sirakorola, July to October 2024. Panel (a) shows the odds (ORs) for *P. falciparum* infection estimated using mixed-effects logistic regression models. Panel (b) shows adjusted incidence rate ratios (IRRs) for clinical malaria estimated using mixed-effects Poisson regression models. The reference category was children with normal nutritional status. Points represent effect estimates (OR or IRR), and horizontal bars indicate 95% confidence intervals. The dashed vertical line indicates the null value (OR or IRR = 1).

person-months (73/1220) among children with normal nutritional status (IRR = 1.52; 95% CI, 1.13 to 2.12).

The mean follow-up time was similar between groups, with 3.64 months among children with normal nutritional status and 3.66 months among malnourished children. Median follow-up time was identical in both groups (4.07 months), indicating comparable person-time across groups.

Overall, 46.4% (84/181) of malnourished children experienced at least one episode of malaria between July and November, compared with 29.9% (73/244) of children of normal nutritional status ($p < 0.001$). Monthly cumulative incidence remained higher among malnourished children, peaking in September (18.2%) and October (13.3%), whereas the normal group peaked at 13.1% in October and declined to 4.9% in November ([Supplementary Table S5](#)).

In [Fig. 3b](#), individual anthropometric indicators (WHZ, HAZ, and WAZ) were not significantly associated with clinical malaria incidence, whereas overall malnutrition was associated with a higher incidence of clinical malaria (IRR = 1.43, 95% CI 1.02 to 2.03).

Multivariable analysis of the risk factors for clinical malaria among children under SMC

We used a multivariable mixed-effects Poisson regression model including an interaction term between nutritional status and SMC exposure to assess risk factors for malaria incidence during the SMC period.

In the mixed-effects Poisson regression model including an interaction between nutritional status and time-varying SMC exposure, several factors were independently associated with malaria incidence ([Table 3](#)). After adjustment, malnourished children had a significantly higher risk of developing clinical malaria compared with children of normal nutritional status (aIRR = 1.82, 95% CI: 1.11 to 2.97; $p = 0.017$). Periods without SMC exposure were associated with a markedly higher incidence of clinical malaria compared with periods under chemoprophylaxis (aIRR = 8.26, 95% CI: 2.87–23.84; $p < 0.001$). Malaria incidence also increased as the transmission season progressed, with significantly higher rates observed in August (aIRR = 8.77, 95% CI: 1.85–34.04), September (aIRR = 7.93, 95% CI: 1.85–34.04), and October (aIRR = 17.43, 95% CI: 4.26–71.42) relative to July. The interaction term between nutritional status and SMC exposure was not statistically significant (aIRR = 0.50, 95% CI: 0.03–8.96; $p = 0.640$), indicating no evidence that the protective effect of SMC differed by nutritional status. Thus, malnourished and well-nourished children benefited similarly from SMC, and the increased malaria risk associated with malnutrition did not vary according to SMC exposure. The interaction term between nutritional status and SMC exposure was not statistically significant (aIRR = 0.50, 95% CI: 0.03 to 8.96; $p = 0.640$).

Characteristic	IRR	95% CI	p-value
Nutritional status			
Normal	1	–	–
Malnourished	1.82	1.11–2.97	0.017
Exposure to SMC treatment			
Exposure (≤ 28 days)	1	–	–
No Exposure (> 28 days)	8.26	2.87–23.84	< 0.001
Age group			
< 12 months	1	–	–
12–23 months	1.00	0.33–3.06	0.996
24–59 months	0.87	0.37–2.06	0.753
Sex			
Male	1	–	–
Female	0.84	0.51–1.37	0.477
SMC period			
July	1	–	–
August	8.77	2.07–37.06	0.003
September	7.93	1.85–34.04	0.005
October	17.43	4.26–71.42	< 0.001
Interaction term			
Malnourished $\times$ No Exposure	0.50	0.03–8.96	0.640

IRR, incidence rate ratio; CI, confidence interval.

Table 3: Factors associated with malaria incidence among children under five years in Sirakorola: a multivariable Poisson mixed effects model analysis.

To further explore whether SMC coverage modified the association between nutritional status and malaria incidence, stratified analyses were conducted by the number of SMC rounds received (1–2 vs. 3–4) ([Supplementary Table S6](#)). Incidence rates were consistently higher among malnourished children across both strata. The association was not statistically significant among children receiving 1–2 rounds (aIRR = 1.37; 95% CI: 0.33–5.70) but was statistically significant among those receiving 3–4 rounds (aIRR = 1.76; 95% CI: 1.02–3.02).

These findings do not provide evidence that SMC coverage modified the association between nutritional status and malaria incidence, as effect estimates were consistent across strata despite differences in statistical precision.

Nutritional status transitions across SMC rounds

About 355 out of 425 participants (83.5%) attended three to four SMC rounds, while 70 (16.5%) attended only one to two rounds.

A total of four possible transitions were analyzed to characterize changes or stability in nutritional status, across SMC rounds ([Table 4](#)). For overall nutritional status, children who received 3–4 SMC rounds were significantly more likely to improve from malnourished to normal nutritional status than those who received only 1–2 rounds (21.1% vs. 11.4%; $p = 0.004$). In contrast, the proportion of children transitioning from normal to malnourished was similar between the two

Status/SMC rounds	Total	Malnourished n (%)	Maln. to Norm. n (%)	Norm. to Maln. n (%)	Normal n (%)	p-value
Overall						
1–2 rounds	70	14 (20.0)	8 (11.4)	9 (12.9)	39 (55.7)	0.808
3–4 rounds	355	84 (23.7)	75 (21.1)	44 (12.4)	152 (42.8)	0.004
WAZ						
1–2 rounds	58	0 (0.0)	7 (12.1)	8 (13.8)	43 (74.1)	0.796
3–4 rounds	323	34 (10.5)	50 (15.5)	36 (11.1)	203 (62.8)	0.131
HAZ						
1–2 rounds	65	9 (13.8)	5 (7.7)	7 (10.8)	44 (67.7)	0.564
3–4 rounds	318	51 (16.0)	27 (8.5)	26 (8.2)	214 (67.3)	0.891
WHZ						
1–2 rounds	55	2 (3.6)	5 (9.1)	7 (12.7)	41 (74.5)	0.564
3–4 rounds	310	23 (7.4)	59 (19.0)	31 (10.0)	197 (63.5)	0.003

Note. Malnourished = remained Malnourished; Maln. to Norm. = Malnourished at baseline to Normal at the end; Norm. to Maln. = Normal at baseline to Malnourished at the end; Normal = remained Normal.

Table 4: Changes in nutritional status from baseline to endline among children by SMC rounds received.

groups (12.4% vs. 12.9%; $p = 0.808$), indicating no differential risk of deterioration. Among individual indicators, improvements in WHZ were more frequent among children completing 3–4 rounds compared with those receiving 1–2 rounds (19.0% vs. 9.1%; $p = 0.003$). No statistically significant differences were observed for

WAZ or HAZ. Taken together, these findings suggest that repeated SMC contact may be associated with modest short-term improvements in acute nutritional status, particularly weight-for-height, while chronic indicators such as stunting remain largely unchanged over the study period.

Changes in MUAC and weight over four SMC rounds

As shown in Fig. 4, panels (a) and (b) both MUAC and body weight increased over the four SMC rounds among children with malnourished and normal baseline nutritional status. Among children who were malnourished at baseline, adjusted mean MUAC rose from 14.89 cm (95% CI 14.65–15.13) in July to 15.32 cm (95% CI 15.08–15.55) in September, with values stabilizing thereafter. Their adjusted mean weight increased from 13.68 kg (95% CI 13.23–14.13) in July to 14.18 kg (95% CI 13.73–14.62) in September, followed by a plateau in October.

Children with normal baseline nutritional status showed similar patterns. MUAC increased from 15.05 cm (95% CI 14.85–15.24) in July to 15.33 cm (95% CI 15.13–15.52) in September, with little change thereafter. Weight increased from 13.45 kg (95% CI 13.09–13.82) in July to 14.10 kg (95% CI 13.74–14.47) in September, followed by a slight decline in October. There was no evidence that MUAC or weight trajectories differed by baseline nutritional status (MUAC interaction $p = 0.329$; weight interaction $p = 0.788$), indicating that both malnourished and well-nourished children experienced comparable short-term gains over the SMC delivery period.

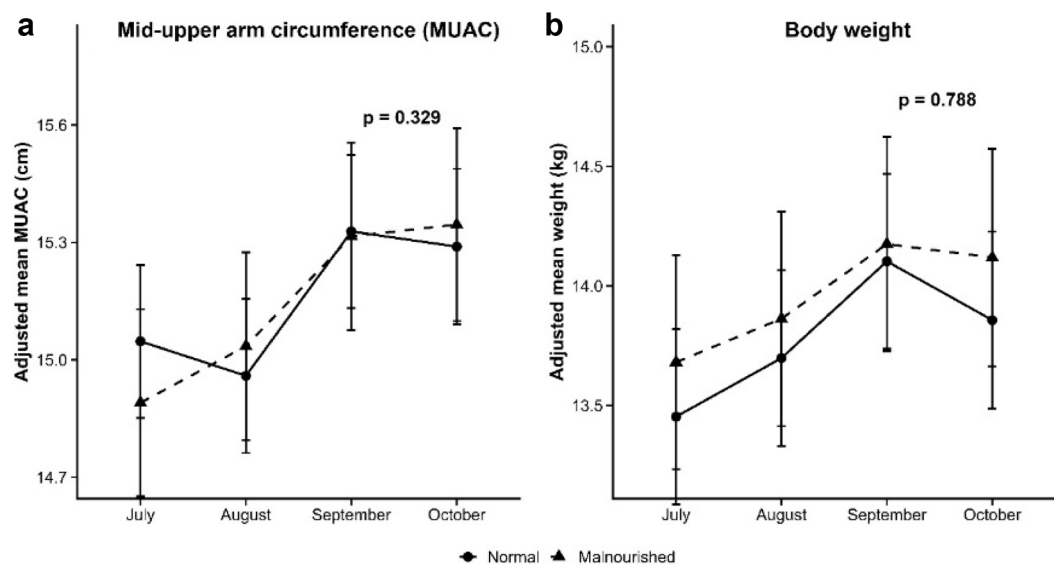


Fig. 4: Anthropometric changes over four SMC rounds between malnourished vs. normal children assessed at baseline in Sirakorola, (July to October 2024). Panel (a) shows mid-upper arm circumference (MUAC) and panel (b) body weight among malnourished children at baseline. Panel (c) shows MUAC and panel (d) body weight among children with normal nutritional status at baseline.

Discussion

This prospective cohort study examined the relationship between nutritional status and malaria risk among children under five receiving routine SMC in a high transmission setting in Mali. Malnutrition was highly prevalent at the start of the malaria transmission season, and nutritional status assessed longitudinally was independently associated with increased malaria risk, including higher *P. falciparum* prevalence, parasite density, and clinical malaria incidence. Although SMC coverage was high, malaria incidence was substantially greater during periods without SMC exposure (>28 days since the last dose), regardless of nutritional status. Nutritional improvements were most evident among children with higher SMC attendance, likely reflecting increased engagement with health services rather than a direct pharmacological effect of SP-AQ. Together, these findings highlight the importance of addressing nutritional vulnerability alongside efforts to optimal SMC adherence.

The longitudinal prospective cohort design allowed a temporal assessment of nutritional status in relation to subsequent malaria outcomes, among children enrolled prior to any SMC treatment, including *P. falciparum* infection, parasite density, and clinical malaria incidence. High and comparable SMC coverage across nutritional groups reduces the likelihood of confounding related to differential exposure to chemoprevention, although residual confounding by unmeasured factors cannot be excluded.

At baseline, 42.6% of children were classified as malnourished using a composite indicator, highlighting the substantial burden of undernutrition in the study population. Nearly one-quarter of children exhibited multiple concurrent deficits, indicating a gradient of vulnerability relevant to malaria risk. This finding is consistent with reports from other Sahelian countries, including Burkina Faso,^{11,16} where malnutrition peaks during the food-insecure “lean season”, coinciding with the SMC campaign in malaria transmission season. The coexistence of this risk aligns with our observation of an independent association between malnutrition and increased malaria incidence (aIRR = 1.82, 95% CI: 1.11–2.97).

Despite high SMC coverage, malnourished children consistently exhibited higher *P. falciparum* prevalence throughout the transmission season. These findings suggest that although SMC remains effective, it may not fully offset the increased vulnerability associated with poor nutritional status. This residual risk may reflect biological mechanisms, including impaired both innate and adaptive immune responses and reduced ability to control parasitemia.²⁵ Residual confounding by socioeconomic status, living conditions, and access to care cannot be excluded. Similar observations have been reported in Burkina Faso, where malnourished

children were more likely to experience breakthrough infections during SMC campaigns,¹¹ and in Malawi, where lower WAZ and WHZ scores were associated with asymptomatic malaria infections.²⁶ These findings reinforce the notion that nutritional vulnerability independently heightens malaria risk.

While overall malnutrition was significantly associated with malaria incidence, individual anthropometric indicators (WHZ, WAZ, HAZ) alone were not. This supports the use of a composite nutritional indicator, which better captures multidimensional deficits and have been shown to more sensitively identify children at highest risk.²⁷ However, composite measures conflate heterogeneous nutritional phenotypes, warranting cautious interpretation.

In multivariable analysis, nutritional status remained independently associated with malaria incidence after adjusting for age, gender, SMC exposure, and follow-up period. Exposure to SMC treatment strongly protective, consistent with its effectiveness when delivered according to the recommended schedule.¹² Although statistical power may have limited detection of subtle interaction, the consistency of effect estimates across strata suggest that malnourished and normal nutritional status children benefit similarly from SMC. The absence of evidence of interaction should be interpreted cautiously, as limited statistical power may have reduced our ability to detect effect modification.

Both malnutrition and lower SMC exposure were independently associated with higher malaria risk, with no evidence that the effect of one depended on the other. This aligns with the pharmacological mechanism of SP-AQ, suppresses blood-stage parasitemia through pathways unlikely to differ substantially in moderately malnourished children. While reduced drug bioavailability has been reported in severely underweight populations,²⁸ evidence in moderately malnourished children, who comprised the majority of our cohort, remains limited. Current age-based dosing of SP-AQ is generally considered adequate, although further pharmacokinetic studies are warranted. Malaria incidence increased as the season progressed, with peaks in September–October reflecting the well-described seasonal transmission patterns in the sahel.²⁹ Although clinical trials have demonstrated enhanced SMC effectiveness when paired with lipid-based nutrient supplements,^{13,16} our prospective cohort design allowed assessment of whether monthly routine SMC delivery was associated with changes in nutritional status. Improvements in nutritional indicators were observed, particularly among children malnourished at baseline. However, these changes are unlikely to be attributable to SMC alone and may reflect seasonal recovery, concurrent nutritional care, and increased contact with health services during the transmission season.

Therapeutic nutritional support was minimal ($n = 2$), suggesting limited direct influence on population-level trends.

Among children who completed all four SMC rounds, both MUAC and body weight demonstrated consistent increases across season, with similar trajectories in both nutritional status groups. These patterns suggest that nutritional recovery was driven by contextual and programmatic factors rather than chemoprevention itself. The relative stability of MUAC and weight among children with normal nutritional status further supports the interpretation. Repeated household and health service contact during SMC delivery may have facilitated routine nutritional screening, early identification of at-risk children, and timely referral to nutrition programs, highlighting the potential of SMC campaigns as a platform for integrated child health interventions.

Limitations

The observational design of the study precludes causal inference regarding the effect of SMC on nutritional outcomes, and the associations observed may be influenced by residual confounding or unmeasured factors. Although loss to follow-up was relatively low (<20%) and SMC coverage was high (>80%), selection bias cannot be excluded. High participation in SMC campaigns facilitated systematic screening for malnutrition and referral for nutritional care, which may have influenced both exposure and outcomes. Differences in healthcare-seeking behavior and contact with health services may also have contributed to residual confounding.

Adherence to SMC treatment relied partly on caregiver reports for non-observed doses, which may introduce reporting bias. However, adherence assessment was strengthened through triangulation with objective measures including drug blister pack checks, DOT for first doses, random home visits verification. In addition, socioeconomic variables such as household income, assets, parental education, household food security, and distance to health facility were not systematically collected as data were derived from routine programmatic activities. These factors may have influenced both nutritional status and malaria risk, although socioeconomic conditions are relatively homogeneous within the study area and may therefore have had limited impact on between-group comparisons. Malaria diagnosis relied on RDTs confirmed by microscopy, consistent with routine practice in this setting. However, these methods have limited sensitivity compared with molecular techniques such as PCR, particularly for detecting low-density parasitemia.³⁰ As a result, asymptomatic submicroscopic infections may have been under-ascertained, and our findings are likely to reflect clinically detectable malaria. Finally, as the study was conducted in a single rural setting, the generalizability of findings to other contexts may be limited. Further studies

in diverse Sahelian settings across Mali and similar high-transmission areas are needed to confirm these results.

Conclusion

This study demonstrates that malnutrition remains a major and independent driver of malaria vulnerability among young children in the Sahel, even in the context of high SMC coverage. While SMC substantially reduced malaria incidence during periods of chemoprophylactic protection, it did not eliminate the excess risk associated with poor nutritional status. Modest improvements in acute nutritional indicators were observed over the transmission season, but these likely reflect broader seasonal and programmatic influences rather than a direct effect of chemoprevention. These findings underscore the need for integrated strategies that pair effective malaria prevention with strengthened nutritional support, leveraging SMC delivery platforms as an opportunity to reach vulnerable children with complementary interventions to improve child health outcomes in high-burden settings.

Contributors

SK conceived the study and drafted the manuscript with support from SD and MT. SD, FK, IS, and JGS developed the modeling framework, and SK performed the analyses. SK, DS, and IG were responsible for field data collection. HC managed the data. BC prepared the study area map. HW, ID, AM and JGS reviewed and edited the manuscript for English language and grammar. SD, MD, NS, MAT, SN, ID, DK, MK, SID, AST, SK, NHD, and AKK contributed to the revision and critical review of the manuscript.

SK, HC, DS, FK, and IG verified the underlying data. SD, MT, SK, HC, FK, DS, JGS, and IG had access to the raw data used in the study. SK had final responsibility for the decision to submit the manuscript for publication.

IS reviewed and approved the manuscript prior to his passing on April 25, 2026. All remaining authors have read and approved the final version of the manuscript.

Data sharing statement

Data supporting the findings of this study are available from the corresponding author upon reasonable request.

Editor note

The depiction of boundaries and territories on this map does not imply any judgement on the part of The Lancet Regional Health Africa or its affiliated institutions regarding the legal status of any country, territory, or area, or the endorsement of any such boundaries.

Declaration of interests

The authors declare that they have no conflicts of interest related to the content of this manuscript.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.lanafr.2026.100102>.

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