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Effect of seasonal malaria chemoprevention on incidence of malaria among children under five years in Kotido and Moroto Districts, Uganda, 2021: time series analysis

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Abstract

Background Seasonal malaria chemoprevention (SMC) refers to monthly administration of full treatment courses of anti-malarial medicine to children <5 years during high malaria transmission seasons. SMC has demonstrated effectiveness in Sahel and sub-Sahel countries in Africa. However, it was not implemented in Uganda until April 2021, when the country began SMC in the highly malaria-endemic Kotido and Moroto Districts. This study assessed the effect of SMC on malaria incidence among children <5 years of age in Kotido and Moroto Districts.

Methods An interrupted time-series analysis was conducted using monthly national health data from the Uganda Ministry of Health District Health Information System 2. The monthly data for outpatient (uncomplicated) malaria among children <5 years was extracted for the 52 months before SMC implementation (Jan 2017–Apr 2021) and 8 months during SMC implementation (May–Dec 2021). The monthly incidence of uncomplicated malaria per 1000 children <5 years was computed before and during SMC implementation.

Results In Kotido District, malaria incidence was 693/1000 during SMC implementation period, compared to an expected 1216/1000 if SMC had not been implemented. The mean monthly malaria incidence was 87/1000, compared to an expected mean of 152/1000 if SMC had not been implemented. This represents a statistically significant mean monthly change of −65.4 (95% CI = −104.6, −26.2) malaria cases/1000 during SMC implementation, or a 43.0% decline. In Moroto District, malaria incidence was 713/1000 during SMC implementation period, compared to an expected 905/1000 if SMC had not been implemented. The mean monthly malaria incidence was 89/1000, compared to an expected 113/1000 if SMC had not been deployed. This represents a statistically significant mean monthly change of −24.0 (95% CI = −41.1, −6.8) malaria cases/1000 during SMC implementation, or a 21.2% decline.

Conclusion Implementation of SMC substantially reduced the incidence of uncomplicated malaria among children <5 years in Moroto and Kotido Districts. Scaling up SMC in other districts with high malaria transmission could reduce malaria on a large scale across Uganda.

Keywords Malaria, High malaria transmission, Seasonal malaria chemoprevention, Uganda

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Background

Malaria is the leading cause of death and illness in Uganda and accounts for nearly 30% of all inpatient deaths among children under 5 years of age [1]. Interventions to reduce the transmission and burden of malaria in Uganda have intensified over the past 10 years, with increasing coverage of malaria control interventions, such as long-lasting insecticidal nets (LLINs), indoor residual spraying (IRS), and expanded treatment of malaria cases with artemisinin-based combination therapy (ACT) [1]. However, malaria prevalence in some areas, such as the Karamoja region, remains well above the Uganda Malaria Reduction Strategic Plan (UMRSP) target of 7% throughout the year [2]. To reduce the burden of malaria in children <5 years, the Uganda Ministry of Health implemented seasonal malaria chemoprevention (SMC) in Kotido and Moroto Districts in April 2021.

SMC is the intermittent administration of full treatment courses of an anti-malarial drug sulfadoxine-pyrimethamine (SP) and amodiaquine (AQ) [3]. The World Health Organization (WHO) recommends administering monthly courses of two anti-malarial drugs to children aged 3–59 months during the peak malaria transmission season. Each monthly SMC course involves one dose of SP and three daily doses of AQ, with SP and the first dose of AQ given under the supervision of the community distributor, and the remaining two doses of AQ given by the caregiver over the following two days, with flexibility in the duration of administration tailored to the length of the transmission season [3].

Initially piloted in the Sahel in 2010, SMC had been scaled up as a key malaria intervention in 12 countries by 2021 using community health workers and demonstrated effectiveness in this region [4]. Evidence from randomized control trials and modelling studies also showed that SMC was effective [5, 6]. However, it had not been implemented in Uganda until April 2021, when Uganda began SMC in Kotido and Moroto Districts. The effect of routine programme delivery of SMC by community health workers on the incidence of uncomplicated malaria among children under 5 years was assessed in Kotido and Moroto districts, Uganda.

Methods

Implementation of seasonal malaria chemoprevention in Uganda

In 2021, the Malaria Consortium, in partnership with the National Malaria Control and Elimination Programme in Uganda, implemented SMC in two districts: Moroto and Kotido (Fig. 1), both located in Karamoja region of north-eastern Uganda [7].

Karamoja region is largely inhabited by nomadic pastoralists [8]. This nomadic life style contributes to the unique health challenges in the region, as populations frequently move in search of water and pasture, making access to consistent healthcare difficult. Moroto has a population of approximately 103,344 people, while Kotido has about 219,296 [9]. The healthcare infrastructure in both districts includes district hospitals, health centres (levels II-IV), and community outreach programs via Village Health Teams (VHTs). Following household enumeration and SMC training, village health teams (VHTs, or volunteer community health workers who receive per diems) administered monthly therapeutic courses of anti-malarial drugs sulfadoxine-pyrimethamine and amodiaquine (SP+AQ) to approximately 83,300 children in Moroto and Kotido districts in the Karamoja region. Whereas SMC is implemented in the Sahel region and western Africa under a 4-month cycle [4], in Karamoja it was implemented 8 months during and after SMC implementation during one rainy season from May to October 2021, months during which the region normally records the highest numbers of malaria cases each year [10].

Description of other malaria interventions

Both Moroto and Kotido districts were part of national malaria control efforts that included LLIN distribution campaigns, conducted prior to the SMC pilot. By the time of SMC implementation in 2021, approximately 80% of households in these districts had access to LLINs [11]. Indoor residual spraying was also implemented in 2015 before the SMC intervention but had been discontinued by the time of this study [12]. Throughout the study period, no other major malaria control interventions were introduced, ensuring that the observed effects on malaria incidence could primarily be attributed to the SMC intervention.

Data source

Monthly data on outpatient (uncomplicated) malaria confirmed by either rapid diagnostic test (RDT) or microscopy among children under 5 years, were obtained from the Uganda Ministry of Health District Health Information System 2 (DHIS2) for 52 months before (January 2017–March 2021) and 8 months during SMC implementation (April–December 2021). The DHIS2 is an open-source platform in which all licensed public and private health facilities report monthly data on priority indicators. The platform allows for aggregation of these facility-level data across different administrative levels of the health system, i.e., from sub-location through national level. It does not cover care received in unlicensed facilities or in private pharmacies.

In Moroto and Kotido districts, data was reported from a network of health facilities. Moroto has 22 facilities,

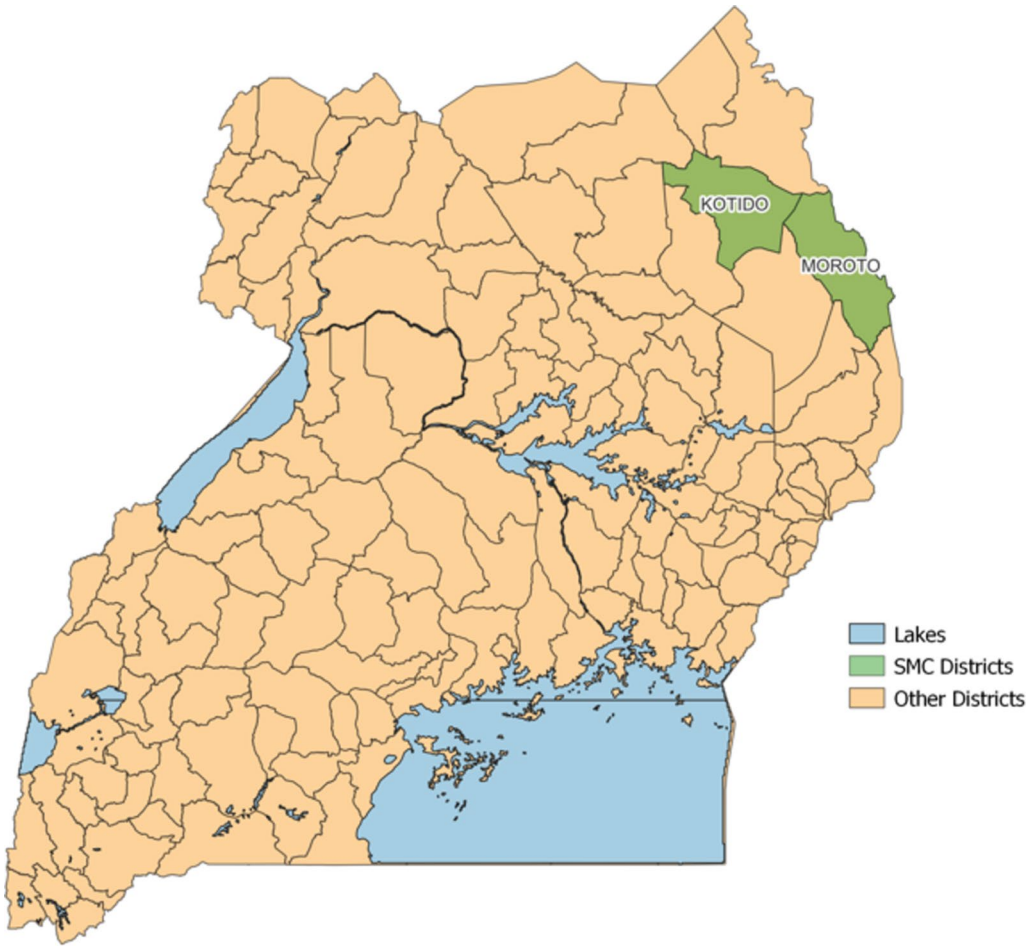

Fig. 1 Districts where seasonal malaria chemoprevention was implemented in Uganda

including 1 general hospital, 11 Health Centre IIs, and 10 Health Centre IIIs, while Kotido has 19 facilities, consisting of 1 regional referral hospital, 9 Health Centre IIs, and 9 Health Centre IIIs [13]. During the study period, the mean level of data completeness for reporting facilities in these districts was 92% [13]. For this analysis, district-level data were used because aggregated data smooths out random variations in health service use that can occur at the level of individual health facilities.

Statistical analysis

An interrupted time-series analysis (ITSA) model was used to compare trends in the incidence of uncomplicated malaria among children under 5 years before and during SMC implementation. The monthly incidence per 1000 children under 5 years was calculated. ITSA and other time series models assume that pre-intervention trends, seasonal variations, and levels would remain unchanged in the post-intervention period under a non-intervention counterfactual state [14]. The estimated intervention impact is the difference between the forecasted counterfactual state and observed data during the post-intervention period.

It was assumed that no competing events ('structural breaks') other than SMC implementation could affect the results. This assumption was verified using Supremum Wald tests for unknown structural breaks, and Wald tests for known structural breaks in the data, with none identified none.

Descriptive analyses were initially conducted, including an assessment of outcome distributions and identification of outliers. The data were decomposed to check for seasonality, trends, and random noise; and checks for autocorrelation and partial autocorrelation were perfomed. The unit root tests were conducted to estimate the number of lags required to make the data stationary. Outlier detection was conducted by visually inspecting the time-series data for any irregular spikes or dips in malaria case counts that deviated significantly from the expected trend based on historical data. Statistical

checks, such as z-scores, were applied to identify data points that exceeded ±3 standard deviations from the mean. Once outliers were detected, district biostatisticians were contacted to verify and correct these data points. The goodness-of-fit of the model by examining residuals for autocorrelation and confirmed that residuals exhibited no significant autocorrelation.

The ITSA model was specified as follows [15]:

$$Yt = \beta 0 + \beta 1t + \beta 2Dt + \beta 3[t - T1]Dt + \varepsilon t$$

where *Yt* represents the outcome. *TI* represents the interruption (SMC implementation) time. *Dt* is a dummy variable where 1 represents the post-intervention period. *t* is time from the start of the series. Note that under this formulation $[t-TI]$ will be zero for the pre-intervention period, and 1, 2, …, *n* for the post-intervention in equal time intervals. The error term, εt, uses Newey-West standard errors to account for serial εt correlation [16]

The interpretation of the estimates is as follows:

$\beta 0$ is the intercept; $\beta 1$ is the pre-intervention trajectory; $\beta 2$ is the immediate intervention effect; $\beta 3$ is the effect of the intervention over time i.e., the difference in the pre-shock and post-shock trajectories

The number of lags in this formulation is calculated for using the following formula [17]:

$$m = 0.75T1/3$$

The forecasts were compared with the actual observed values in the dataset.

Ethical approval and consent of participants

Permission from the Ministry of Health (MOH) was obtained to conduct this evaluation. The Office of Science, U.S. Centers for Disease Control and Prevention, determined that the primary intent of this evaluation was public health practice and not research. The study was conducted by using open access aggregate data in Uganda Ministry of Health DHIS2 and therefore consent to participate in this study is not applicable.

Results

Effect of seasonal malaria chemoprevention on malaria incidence among children under five years of age, Kotido District

Among children <5 years in Kotido District, malaria incidence was 693 per 1000 population during the SMC implementation period, compare to an expected 1216 per 1000 population if SMC had not been implemented. The mean monthly malaria incidence was 87 per 1000 population compared to an expected mean of 152 per 1000 population if SMC had not been implemented (Fig. 2). This represents a statistically significant mean monthly change of −65.4 (95% CI = −104.6, −26.2) malaria cases per 1000 population during SMC implementation.

A seasonality plot showed repeating patterns at similar months over the years (Fig. 3). There was no discernible pattern in the decomposition residual plot (Fig. 3). The series were stationary around a deterministic trend (KPSS statistic = 0.217, *p*-value = 0.1).

Effect of seasonal malaria chemoprevention on malaria incidence among children under five years of age, Moroto District

In Moroto District, incidence of uncomplicated malaria was 713 per 1000 population of children <5 years during the SMC implementation period, compared to an

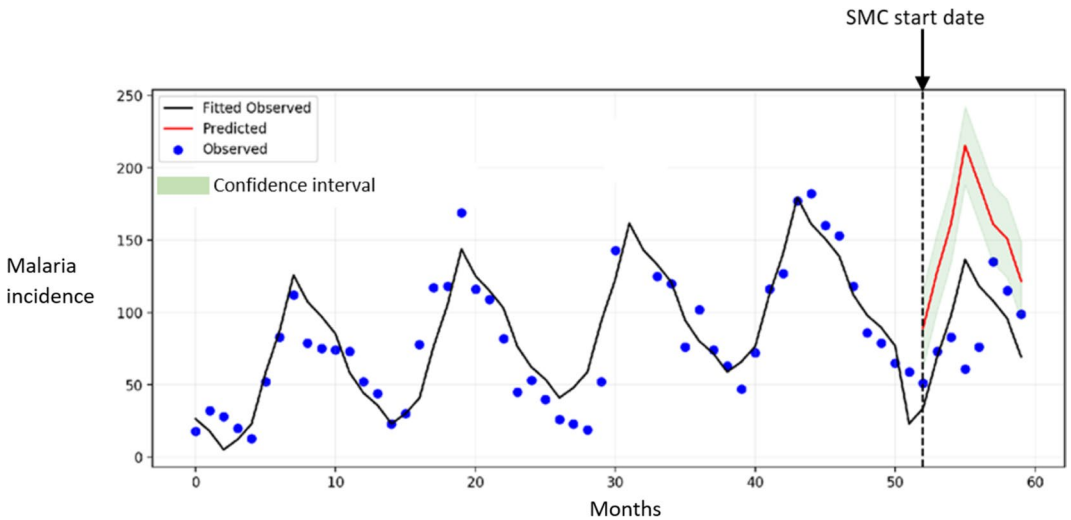

Fig. 2 Effect of seasonal malaria chemoprevention on malaria incidence among children under 5 years, Kotido District, Uganda, 2022

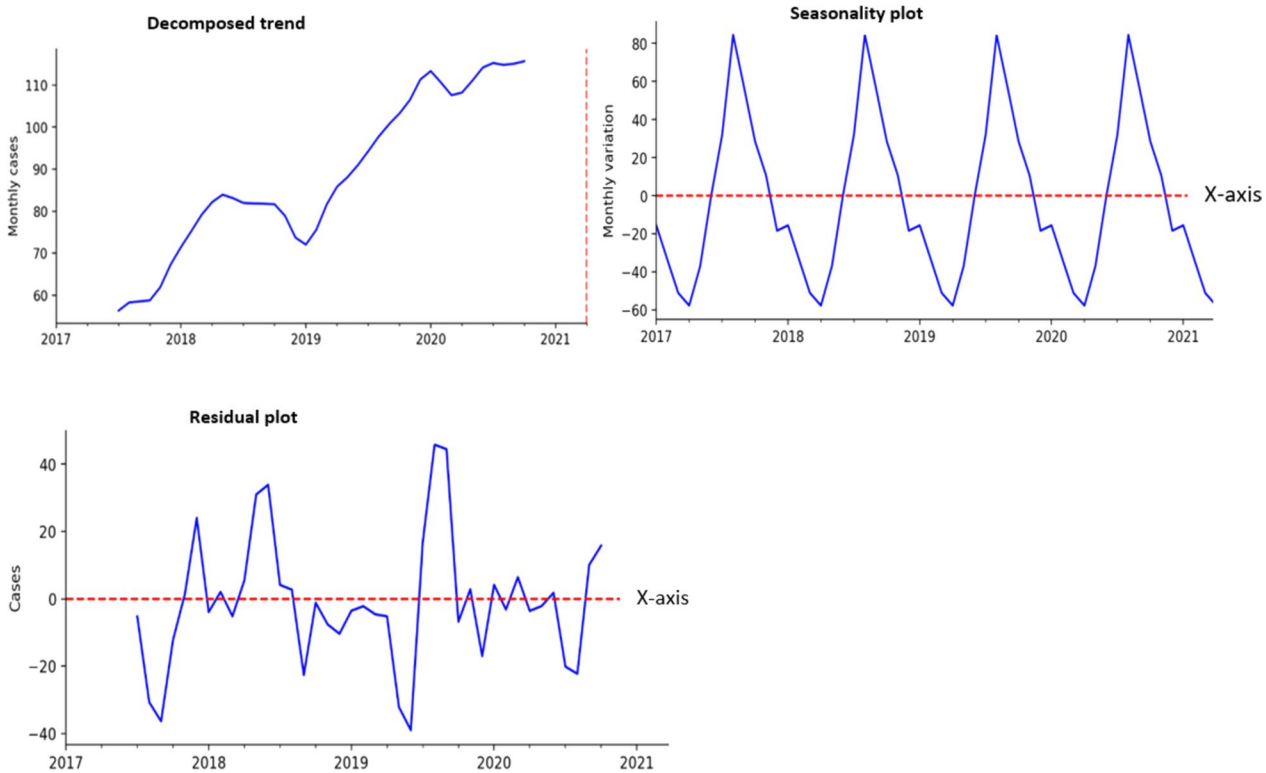

Fig. 3 Series decomposition trend, seasonality, and residual plot of malaria incidence in Kotido District, Uganda, January 2017–December 2021

expected 905 per 1000 if SMC had not been implemented. The mean monthly malaria incidence was 89/1000, compared to an expected 113 per 1000 if SMC had not been deployed (Fig. 4). This represents a statistically significant mean monthly change of −24.0 (95% CI = −41.1, −6.8) malaria cases per 1000 during SMC implementation.

Seasonality plot showed repeating patterns at similar months over the years (Fig. 5). There was no discernible pattern in the decomposition residual plot (Fig. 5). The series were stationary around a deterministic trend

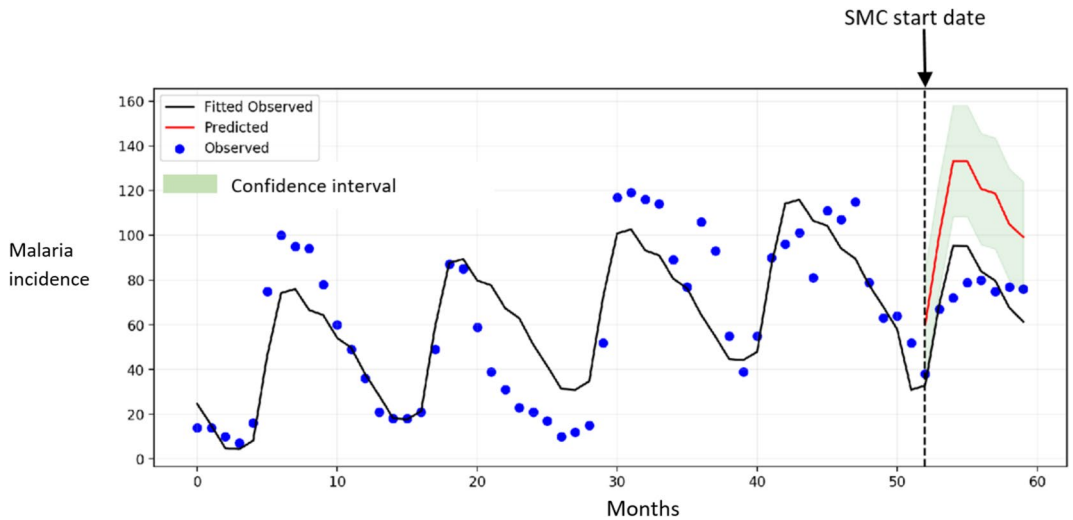

Fig. 4 Effect of seasonal malaria chemoprevention on malaria incidence among children under 5 years, Moroto District, Uganda, 2022

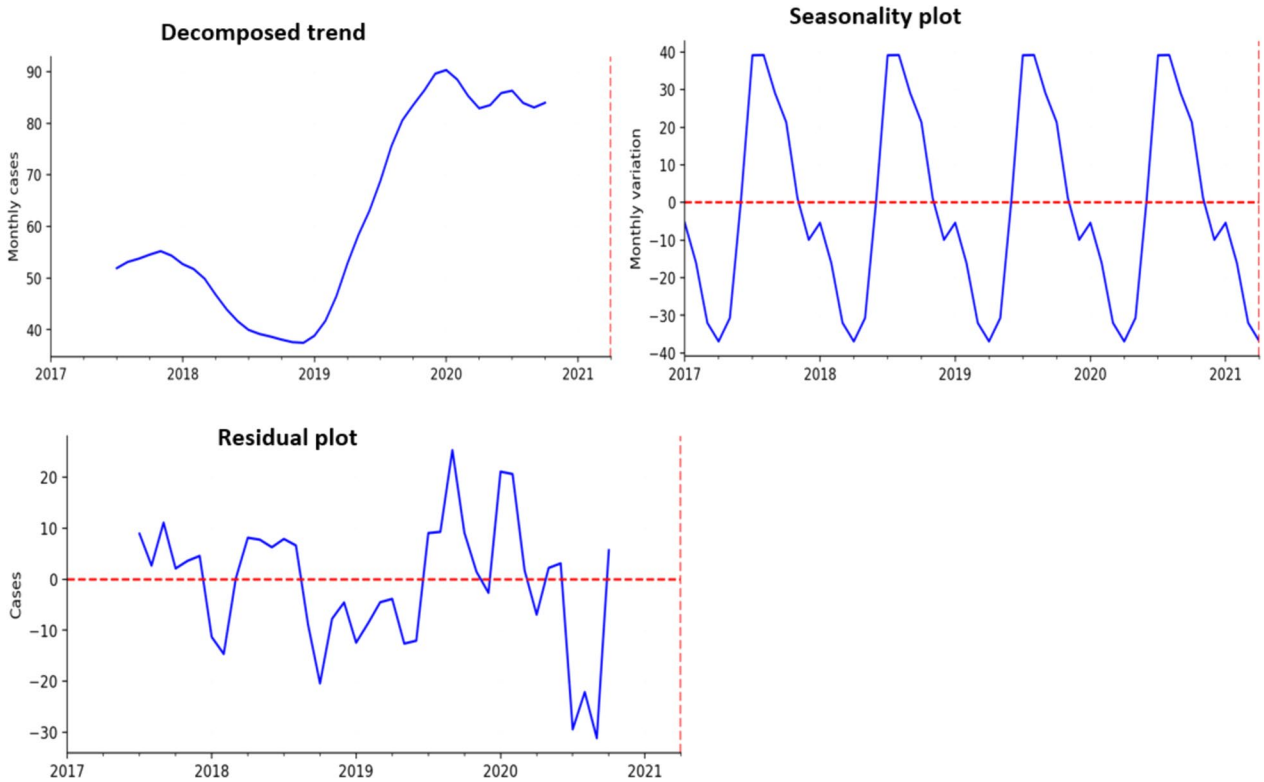

Fig. 5 Series decomposition trend, seasonality and residual plot of malaria incidence in Moroto District, Uganda, January 2017–December 2021

[Kwiatkowski–Phillips–Schmidt–Shin (KPSS) statistic = 0.236, *p*-value = 0.1].

Discussion

Seasonal malaria chemoprophylaxis is thought to be an important adjunctive intervention to reduce malaria in children in addition to other, well-established anti-malarial interventions such as indoor residual spraying, use of long-lasting insecticidal nets, and integrated community case management (iCCM) [18–20]. Despite being evaluated in clinical trials, there are few data on the impact of its field implementation. In Uganda, SMC administered by volunteer community health workers substantially reduced incidence of uncomplicated malaria among children <5 years in two high-malaria-burden districts.

SMC reduced malaria incidence by 43 and 21% in Kotido and Moroto districts respectively. This is a smaller effect than what was observed when SMC was delivered by a similar approach using community health workers in Burkina Faso (69%) [21] and Mali (65%) [22]. The observed difference may be partly due to changes in supervision of SMC implementation during the COVID-19 pandemic in Uganda. Intensive supportive supervision is recommended in the early stages of SMC implementation to identify and resolve challenges [23]. However, a report from Malaria Consortium indicated that supportive supervision was compromised during the COVID-19 pandemic period due to travel restrictions and other issues [24]. In addition, disruptions of other routine malaria interventions, such as distribution of LLINs at health facilities could have negatively impacted malaria control [25], and reduced the overall additive impact of SMC on malaria control in Uganda, compared to the conditions under which studies elsewhere were conducted.

The reduction in malaria incidence following SMC implementation in Moroto District was half that observed in Kotido District. Since SMC was implemented at the same time (during high transmission season) and given that the two neighbouring districts have similar local epidemiological conditions [10], this is difficult to explain. A review of the experiences of implementing SMC in these districts could highlight possible reasons for the observed differences to inform scale up of SMC in other districts.

The study showed that non-experimental population-level implementation of SMC by community health workers has promise in supplementing the effect of other antimalarial interventions. However, this study has limitations. First, DHIS2 data are often incomplete and subject to recording error which could lead to

either overestimation or under estimation of the effect of the intervention. Following data abstraction, outlier data points were identified and contacted district biostatisticians to correct any outliers in DHIS2. It was verified that there were no drops in data reporting rates during SMC implementation period, compared with the pre-implementation period. This process helped mitigate the impact of reporting errors and ensured the integrity of the data used in the analysis.

Conclusion

Implementation of SMC significantly reduced incidence of uncomplicated malaria among children <5 years in Moroto and Kotido districts in Uganda. Scaling up SMC in other districts with high malaria transmission could reduce malaria on a large scale across Uganda.

Abbreviations

ACTs	Artemisinin-based combination therapy
AQ	Amodiaquine
DHIS2	District Health Information Software System version 2
HMIS	Health management information system
IPD	In-patient department
LLINs	Long-lasting insecticidal nets
OPD	Out-patient department
SMC	Seasonal malaria chemoprevention
SP	Sulfadoxine-pyrimethamine

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Author contributions

A,K developed the study protocol. A.K analyzed the data and contributed to interpretation. A.K drafted the manuscript. B.K, R.M, D.R, L.B, D.K, J.R.H, A.R.A supervised the study and contributed to interpretation of findings. All authors contributed to the write up, and all read and approved the final manuscript.

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Availability of data and materials

No datasets were generated or analysed during the current study.

Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the US Centers for Disease Control and Prevention, Uganda Public Health Fellowship Program, and the National Institute of Public Health.

Declarations

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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