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Médard Djedanem, Alkassoum Ibrahim, Mahaman Y. Nazibou, Mamane Salé Noura, Elhadji Y. M. Yacoudima, Abdoussalam Zakari, Hassani Omari Mbega, Zaneidou Mamane, Mody Issaka, Eric Adehossi, Jean Testa & Ronan Jambou

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Extension of seasonal malaria chemoprevention to older children: A pragmatic comparative study in two health districts in the Zinder region, Niger.

Médard DJEDANEM^{1,2}, Alkassoum IBRAHIM³, Mahaman Y NAZIBOU⁴, Mamane Salé NOURA⁵, Elhadji Y.M. YACOUDIMA^{2,5,6}, Abdoussalam ZAKARI¹, Hassani Omari MBEGA¹, Zaneidou MAMANE⁷, Mody ISSAKA⁷, Eric ADEHOSSI³, Jean TESTA^{2,8}, Ronan JAMBOU^{8,9}.

1 Epicentre Niger, BP13330 Niamey, Niger

2 Université Nazi Boni, Bobo Dioulasso, Burkina Faso

3 Faculté des Science de la Santé Université Abdou Moumouni, Niamey, Niger

4 Direction Régionale de la Santé Publique de Zinder, Zinder, Niger

5 Centre de Recherche Médicale et Sanitaire (CERMES), Niamey, Niger

6 Service de Santé de la Garde Républicaine, Niamey, Niger

7 Direction de la Surveillance et de la Riposte aux Epidémies, Ministère de la Santé Publique de la Population et des Affaires Sociales, Niamey, Niger

8 Laboratoire RETINES, Faculté de Médecine, Nice, France

9 Département de santé Globale Institut Pasteur, Paris, France

Corresponding author: Ronan Jambou, rjambou@pasteur.fr

SUMMARY

Context: Seasonal Malaria Chemoprevention (SMC) based on sulfadoxine-pyrimethamine (SP) and Amodiaquine (AQ) has been recommended by the WHO since 2012 for areas where malaria is endemic but seasonal. It consists of administering to healthy children under the age of five years a full three-day course of treatment every month for three to five months during the transmission season. However, in these areas, retrospective data on the burden of malaria among children aged 5 to 10 years could justify extending this strategy to this class of age. This study was conducted to evaluate the public health effectiveness of this extension in Niger.

Methods: We conducted a retrospective comparative observational study using routine DHIS2 data collected from two health districts in the Zinder region (Damagaram Takaya and Matameye) over a 36-month period (2021–2023). The study compared malaria trends between one district that implemented SMC extension to children aged 5–10 years (Damagaram Takaya) and another district where SMC remained restricted to children under 5 (Matameye).

In each district, five health facilities were selected using simple random sampling from the official list of operational health facilities provided by local health authorities. The selected facilities were used as sentinel sites for extracting data on fever episodes, uncomplicated malaria, severe malaria, and malaria-related deaths, stratified by age group. This design enabled the comparison of malaria incidence patterns before, during, and after

transmission seasons between districts with different SMC coverage strategies.

Results: From 2021 to 2023, children aged ≥ 5 years showed a higher incidence of uncomplicated malaria than younger children, particularly in 2021 when the incidence reached 33.34 per 1,000 compared with 12.45 per 1,000 in < 5 -year-olds in Damagaram Takaya

. In Damagaram Takaya, a significant decrease in both uncomplicated and severe cases occurred in 2023, following expansion of SMC to this age group. In Matameye, severe cases decreased as well, though there was no significant change in uncomplicated cases. In the same district, marked disparities were found between health facilities. Among children under five years, severe malaria cases were more frequent in Matameye, with peaks observed in 2021. Despite a slight decrease in 2023, there was no significant variation in uncomplicated cases during the study period in this district.

Extending SMC to children aged 5 years and older was associated with a gradual decline in the incidence of uncomplicated and severe malaria in the target district, but not in the control district. However, this new strategy did not result in a delay in the peak of transmission that would have been induced by the destruction of the parasite reservoir. There was also considerable variability in the data recorded by each health facility.

Conclusion: These results underscore the positive impact of expanding SMC to older children and the importance of adapting control strategies to local

circumstances. SMC is an effective, low-cost strategy for preventing malaria cases in children of all ages.

Keywords: SEASONAL MALARIA CHEMOPREVENTION, SAHEL, NIGER, COMPARISON STUDY, DHIS2, , ,.

I. INTRODUCTION

In sub-Saharan Africa and Sahelian countries, malaria in children under five remains the leading cause of mortality and morbidity, making this parasitic disease a major public health issue [1,2].

Indeed, WHO estimated that 282 million malaria cases and 610 000 malaria-related deaths were reported across 83 countries; of reported deaths, 94% were reported from Africa. [2]. Four countries were the largest contributors to new malaria cases in Africa: Nigeria (30.9%), the Democratic Republic of Congo (11.3%), Niger (5.9%), and Tanzania (4.3%) [3]. *Plasmodium falciparum* poses the greatest threat to human health in these regions, particularly among vulnerable groups such as children under five and pregnant women [4].

Since 2012, in an effort to prevent malaria in children under five, the World Health Organization (WHO) has recommended the use of Seasonal Malaria Chemoprevention (SMC) with Sulfadoxine-Pyrimethamine (SP) and Amodiaquine (AQ) in areas with high but seasonal malaria transmission, for three to five months each year among healthy, resident children. This is the case in the Sahel region, where 60% of cases occur during four to five

consecutive months of the year [5]. This strategy helps maintain therapeutic drug concentrations in the blood for about 28 days after administration to children. Since its implementation in malaria-endemic countries, SMC has helped save the lives of nearly 700,000 children under five and prevented approximately 160 million malaria infections [6]. Several West and Central African countries (Benin, Burkina Faso, Cameroon, The Gambia, Ghana, Guinea, Guinea-Bissau, Mali, Niger, Nigeria, Senegal, Chad, Togo) have adopted this strategy nationwide for children under five, and seven of these countries (Burkina Faso, Chad, Nigeria, Guinea, The Gambia, Mali, Niger) have expanded access to SMC through the ACCESS-SMC project [7,8,9]. Multiple studies [10-16] have reported that SMC is safe, cost-effective, and efficient in preventing malaria in children under five. However, in many countries implementing SMC, the first dose of AQ+SP is administered under the supervision of distributors from the National Malaria Control Program (NMCP); the second and third doses are given to the child's mother or guardian for home administration [7]. Many parents prefer thus to keep the last two doses to administer them when the child has a fever, which can reduce the effectiveness of the strategy [7].

In Niger, the malaria epidemiological profile is marked by a sharp increase in cases during the rainy season. Four epidemiological strata are identified in this Sahelian country : (i) a very low or sporadic transmission zone (fewer than 100 cases per 1,000 inhabitants) in the northern and northeastern parts; (ii) a low transmission zone (100-250 cases per 1,000); (iii) a moderate or

seasonal transmission zone over four months (250–450 cases per 1,000); and (iv) a very high transmission zone lasting four to six months (more than 450 cases per 1,000), located in the southwest [17]. Malaria is endemic throughout Niger and is the leading cause of outpatient visits. In 2023, the country recorded approximately 3,780,336 malaria cases in health facilities, with 29.62% of cases in the Zinder region, 23.39% in Maradi, 15.15% in Tahoua, and 14.27% in Tillabéri [18]. Niger ranks among the top eleven countries reporting the highest number of malaria cases [17,19], and SMC was first implemented there in 2013 [17]. In regions where annual rainfall is equal to or greater than 600 mm, about four to five SMC cycles are distributed to children under five [7,19].

Despite this strategy, malaria incidence increased from 209 to 237 cases per 1,000 inhabitants between 2021 and 2022 in Niger, with a prevalence of 29% in 2021 and 44.2% in 2022 [8,17,20]. Epidemiological data also show that the malaria burden among older children (up to 10 years old) continues to rise each year, especially in areas with many residual ponds and rice fields [19,21,22]. The burden of malaria in Niger is thus gradually increasing mainly among older children, which can be related to a slow acquisition of immunity. This could justify extending SMC coverage to this age group [7,19,23–25].

Currently in Niger, malaria prevention strategies include the use of Long-Lasting Insecticidal Nets (LLIN), Indoor Residual Spraying (IRS), SMC, and treatment of symptomatic cases. Malaria diagnosis and integrated case management are handled by Community Health Workers (CHW) in villages

located more than five kilometers from a health facility. Diagnosis is performed using Rapid Diagnostic Tests (RDTs) [10,17]. SMC is delivered door-to-door by CHW who assesses the child's health and administers the first dose of SP+AQ. The remaining doses (AQ) are given on the 2nd and 3rd days at home by the mother, parent, or guardian. A 28-day interval is maintained between each monthly treatment for four months.

In 2022, the Damagaram Takaya health district was selected for a pilot study to extend SMC to children up to 10 years old. This district has one of the highest malaria rates in the country, with 57,429 cases and 39 deaths in 2020, 69,800 cases and 11 deaths in 2021, and 61,488 cases and 20 deaths in 2022 [18].

The present study was conducted to assess the effectiveness of extending the SMC age range to 10 years in reducing the malaria burden in this age group.

II. METHODS

Type and Site of the Study

The study was conducted as a retrospective comparative observational study using routine DHIS2 data collected from two health districts in the Zinder region (Damagaram Takaya and Matameye) over a 36 month period (2021-2023). The study compared malaria trends between one district that implemented Seasonal Malaria Chemoprevention (SMC) extension to children aged to 5-10 years (Damagaram Takaya) and another district where SMC remained restricted to children under 5 years (Matameye)

In each district, five health facilities were selected using simple random sampling from the official list of operational health facilities provided by local health authorities at the Regional Directorate of Public Health.. This method ensured that each facility had an equal chance of being included in the sample, guaranteeing representativeness and reproducibility of the selection. These facilities were used for collecting data on uncomplicated malaria, and severe malaria cases, and malaria related deaths, stratified by age group.

This design enabled the comparison of malaria incidence patterns before, during and after transmission seasons between districts with SMC coverage strategies.

Damagaram Takaya Health District is located in the southeast of the Zinder region, about 850 km east of Niamey. Its climate is semi-arid Sahelian, marked by a short rainy season lasting three months. Annual rainfall ranges between 400 and 600 mm, and temperatures during the dry season can reach or exceed 40°C. The district includes 1 District Hospital (DH), 20 Integrated Health Centers (IHC), and 41 Health Posts (HP), with an administrative health coverage of 29.53%. The population density is 34 inhabitants per km², with a total area of 1,826 km² and an altitude of 435 meters. The selected health facilities in Damagaram Takaya were: Urban IHC DTK, IHC Guidimouni, IHC Albakaram, IHC Baboul, and IHC Kanya Wani [26].

Matameye Health District is also located in the Zinder region, in the southeastern part of the country (Kantché department), about 900 km east of

Niamey. Its climate is Sahelian, characterized by a long dry season and a short rainy season. The average annual rainfall ranges between 400 and 600 mm, with year-to-year variations. The district covers an area of 2,381 km² and has a population density of 194 inhabitants per km². It includes 1 District Hospital (DH), 20 Integrated Health Center (IHC), and 40 Health Posts (HP). The selected health facilities for the study were: IHC Dangoudaou, IHC Kourni, Urban IHC Matameye, IHC Kantché, and IHC Tsaouni [27] (Figure 1).

Figure 1 : Map of the region of Zinder with the location of the ten dispensaries under study in the two districts

Both health districts are considered high-risk malaria transmission zones in Niger. In this region, two mosquito vectors are involved in malaria transmission: *Anopheles gambiae s.l.* (96%) and *Anopheles funestus* (2%) [28,29]. The risk of malaria transmission varies from north to south. In the southern part of the Zinder region, the number of bites per person ranges from 50 to 250, while in the northern part it is less than 20 [19]. Although the two districts are approximately 160 km apart, they share similar environmental and climatic conditions (Table I).

Table I Meteorological parameters of the two districts under survey
Study Population and Data Sources

The target population consisted of children aged 3 months to 10 years in the health districts of Damagaram Takaya and Matameye, who sought care at

randomly selected health facilities during the period from January 1, 2021 to December 31, 2023.

This study analyzed routine malaria data extracted from DHIS2 (District Health Information Software) for ten health facilities across the two districts. Consultations are recorded daily in three separate registers at each health facility: infant, child, and adult. For each patient, basic information was collected weekly. These data included: age group, area of residence, fever, malaria RDT/Thick drop results, diagnosis of uncomplicated and severe malaria, and deaths due to severe malaria. Children with fever related to an identified cause were registered in a separated register. The consultation data were then aggregated into monthly datasets for each health facility by age group and entered into DHIS2, then transmitted to the Directorate of Surveillance and Epidemic Response (DSRE) of the Ministry of Health and Public Hygiene (MS/HP).

DHIS2 is a modular, web-based software built using free and open-source Java frameworks for the collection, analysis, and presentation of aggregated statistical data. Final data were obtained in Excel format from the Notifiable Diseases (ND) reports for each health facility included in the study. The data collected included the number of recorded fever cases, the number of malaria tests performed, the number of positive tests, and among these, the number of confirmed uncomplicated and severe malaria cases, as well as the number of deaths due to severe malaria. These data were then related to the district population for the corresponding age groups.

In Niger, all health facilities—including those at the community level are equipped with Rapid Diagnostic Tests (RDTs) for malaria. Therefore, all malaria cases were confirmed either by RDT or Thick Blood Smear (THICK DROP) in facilities with medical laboratories. Severe malaria cases were defined according to World Health Organization (WHO) criteria [30]. RDT results are directly recorded in the consultation registers at health facilities. For District Hospitals (DH), Thick drop/RDT results are recorded in the laboratory register and matched with clinical data.

Inclusion and Exclusion Criteria

This study was based on secondary data, retrospectively extracted from weekly consultation report at health facilities. No primary data collection was conducted. No explicit inclusion and exclusion criteria were defined and applied to the data included in our analyses. Data entered and reported in DHIS2 follows consultation-based criteria applied by the head of dispensaries according to clinical case management and reporting guidelines from the Ministry of Health. No major change (e.g., change in clinical case management and reporting guidelines; change in dispensary staff) occurred in the local teams during the period of the study, local definitions were quite stable from one year to another.. However, as no major change occurred in the local teams during the period of the study, local definitions were quite stable from one year to another. The analysis focused exclusively on cases involving children aged 0-5 years and 5-10 years who presented for outpatient care with a febrile episode not clearly attributable to respiratory,

digestive, or viral causes. This selection corresponds to a retrospective exhaustive sampling of suspected malaria cases, as recorded in the health facility registers.

Statistical Analyses

Data analysis was performed using R software version 4.4.1. [31]). All analyses were based on unmodified DHIS2 routine data extracted into Excel Format. We first performed descriptive analyses to summarize yearly and monthly malaria indicators (fever cases, uncomplicated malaria, severe malaria, and deaths), grouped by district, health facility, and age group [32].

Data processing was conducted using the *deplyr* package, and visualizations were produced using *ggplot2*[33].

To compare seasonal malaria dynamics between districts, monthly values were normalized using the formula :
$$\text{Normalized value} = \frac{\text{monthly value} - \text{mean 36}}{\text{mean 36}},$$
 allowing comparison of relative patterns independent of absolute case numbers

This transformation produced a relative distribution of cases, allowing for comparison of seasonal profiles independently of absolute volumes and enabling unbiased principal component analysis (PCA).

Using these normalized data, a Principal Component Analysis (PCA) was conducted to reduce dimensionality and highlight key common or contrasting trends between districts. PCA was performed using monthly data from health

facilities (CSI), or aggregated by year, district, and facility. The variables included were: number of fever cases, uncomplicated malaria, severe malaria, and deaths (using the FactoMineR package [34]). Incidence rates were calculated by relating these totals to the district population at the same time and for the same age group.

PCA helped identify clusters of districts sharing similar seasonal profiles, providing insights into malaria dynamics. PCA on normalized data also yielded coordinates of points on the principal axes (PC1 and PC2). Euclidean distances between points were calculated using the formula: $\text{Distance} = \sqrt{(\text{PC1}_2 - \text{PC1}_1)^2 + (\text{PC2}_2 - \text{PC2}_1)^2}$; These distances ranged from 0.607 to 0.807 units, allowing for dimensionality reduction while preserving maximum information.

The PCA was performed as an exploratory visualization tool only. Because each health facility contributes only three annual aggregated observations (2021–2023), the number of data points is insufficient to support stable multivariate inference. Therefore, PCA outputs are descriptive and not intended for statistical generalization.

PCA results were visualized using the Factoextra package [34], with `fviz_pca_ind()` used to display individuals in the principal component space. The number of axes retained was determined by the cumulative percentage of explained variance. A cluster analysis was then performed using the coordinates of points on the PC1 and PC2 axes, applying the same Euclidean

distance range (0.607 to 0.807 units) to indicate proximity or separation between points (using the cluster package [35]).

No inferential statistical tests (regression) were applied, as the objective was exploratory comparison rather than causal estimation.

Ethical Considerations

This study did not involve any primary data collection. All data were anonymized prior to extraction from DHIS2. The study was conducted in collaboration with the Directorate of Statistics (DS) and the Directorate of Surveillance and Epidemic Response (DSRE), who granted access to the disaggregated raw data. The study was carried out in strict compliance with the Declaration of Helsinki for epidemiological research. The quantitative analysis relied solely on routine surveillance data collected at Integrated Health Centers (IHC) and posed no direct risk to the population studied through the analysis process itself. No modifications were made to the source data received.

3. RESULTS

3.1 Data Collected by District

Climatological data were obtained from local meteorological stations. Given the proximity of the two districts, rainfall recorded over the three years, as well as average weekly maximum and minimum temperatures, did not differ significantly between the two study sites (Table I). In total, the monitoring

covered five Integrated Health Centers (IHC) in each district over a 36-month period (from January 2021 to December 2023). The total populations of the two districts were different, with 388,736 inhabitants in Damagaram Takaya and 643,433 in Matameye, but with a similar age structure (data not shown). For each age group, ratios and incidence rates were calculated by dividing the sums of the events recorded for each variable by the population of the district in the same age group (Table II). Since the five selected IHC in each district do not serve the entire district population, the ratios calculated based on the total district population underestimate the actual results.

Table II Summary of data registered over the three years in the two districts

Over the three-year period, Damagaram Takaya recorded 63,568 positive Rapid Diagnostic Tests (RDT), of which 62,515 (98.34%) were uncomplicated malaria cases and 1,053 (1.65%) were severe malaria cases, with 1 death (0.01%). In Matameye, during the same period, 99,801 RDT were positive, including 98,273 (98.46%) uncomplicated malaria cases and 1,528 (1.54%) severe malaria cases, with no deaths recorded. The situation varied from year to year: in Damagaram Takaya, 22,515 uncomplicated malaria cases were detected in 2021, 20,801 in 2022, and 19,199 in 2023. Severe malaria cases were 499 in 2021, 317 in 2022, and 237 in 2023. In Matameye, 33,219 uncomplicated malaria cases were detected in 2021, 31,483 in 2022, and 33,571 in 2023. Severe malaria cases were 680 in 2021, 597 in 2022, and 251 in 2023 (Table II). Across all three years, for children (both under and over 5

years old), Damagaram Takaya showed lower incidence rates of fever, RDTs, uncomplicated malaria, and severe malaria compared to Matameye (Table II, Fig. 2 A-B-C). However, seasonality patterns were similar for the two districts (Fig. 2D).

Figure 2 Annual aggregated data on malaria collected in the two districts

A/ Total number of mild cases registered in the districts over the three years, for the two ages groups

B/ Total number of severe cases registered in the districts over the three years, for the two ages groups

C/ Monthly collection of data over the three years in the two districts, showing seasonal increase of transmission

D/ Weekly collection of data over the three years in the two districts, showing seasonal increase of transmission

In aggregated data, a non-significant decrease in uncomplicated malaria cases was observed in 2023 in Damagaram Takaya, which was not seen in Matameye (Fig 2A-B). Although, severe malaria decreased more markedly in Damagaram Takaya, a parallel decline was also observed in Matameye, despite the absence of SMC extension in this district. This shared downward trend suggests that factors unrelated to SMC such as variations in

transmission intensity, rainfall patterns, or health-seeking behaviour may have contributed to the reduction in severe malaria across the two districts.

3.2 Are the Two Districts Comparable for an Effectiveness Study?

Over the three-year period, for both districts children aged 5 years and older displayed a higher malaria burden, with incidence levels in 2021 nearly twice as high as in children under 5 years of age. When aggregating data over the three-year period (2021-2023), children under 5 years old had substantially fewer uncomplicated malaria episodes in the intervention district compared with the control district (28,645 vs 54,288 cases). A similar pattern was observed among older children ≥ 5 years, with lower malaria burden in the district implementing SMC extension (33,870 vs 43,983 cases). However, these differences are also related to the population of the districts and cannot be truly related to differences due to SMC.

3.2.1 Damagaram Takaya District (DTD)

In DTD, using normalized data over the three years, weekly data on uncomplicated malaria confirmed that children aged ≥ 5 years (DTK10) had a slightly higher number of cases ($p = 0.29$) than children under 5 years (Fig. 3A). However, for age group, the data also revealed a decline in uncomplicated malaria cases from 2021 to 2022 and 2023, coinciding with the introduction of SMC for older children (Fig. 3A), ($p = 0.02$). Seasonal trends in case numbers were similar for both age groups (Fig. 3A).

Figure 3 Monthly normalized data collected over the three years in the two districts

For each district data collected during a month are normalized according to the weekly mean calculated over the total data collected for this district over the three years. Some weeks with very high number of patients pike as out layer.

A-C/ Monthly normalized number of mild malaria cases collected

B-D/ Monthly normalized number of severe malaria cases collected

For the district of Daram Takaya a decrease of cases was observed over the three years

However, normalized weekly data for severe malaria (Fig 3B) showed that children under 5 still had a higher incidence of severe malaria (not statistically significant, $p = 0.29$) compared to those aged ≥ 5 . Among older children, seasonal fluctuations were less pronounced than in younger children and persisted throughout the period, highlighting their vulnerability to severe forms of the disease. The number of deaths was proportionally distributed across the health centers ($p = 0.40$) and between the two age groups ($p = 0.317$).

3.2.2 Matameye Health District (MHD)

In MHD, the number of fever cases differed between the two age groups ($p = 0.05$), but there was no significant annual variation ($p = 0.34$) (Table II).

Similarly, there was no interannual variation in uncomplicated malaria cases, despite a slight decrease in the total number of cases in 2023 ($p = 0.13$) (Fig 3C). However, significant differences were observed from one health centers to another ($p < 0.0001$).

For the same number fever attacks, children aged ≥ 5 years were tested more frequently for malaria than younger children and had, on average, a higher number of confirmed uncomplicated malaria cases. Older children remained a major contributor to the malaria caseload, especially in 2021 when their incidence was significantly higher than that of children under 5 in both districts

compared to younger children.

However, for severe malaria and deaths (Fig. 3D), no statistically significant difference was found between the two age groups ($p = 0.29$). A decrease in severe malaria cases was observed in 2023 ($p = 0.02$, Fig. 3D).

3.2.3 What about the Intra-District Heterogeneity?

The assessment of the impact of extending SMC to older children in the Damagaram Takaya district was based on aggregated district-level data. However, it was necessary to analyze the heterogeneity at the health facility (IHC) level to evaluate the relevance of this overall analysis.

The evolution of uncomplicated malaria across the ten randomly selected health facilities revealed significant variability between the different centers

(Fig 4A). The Urban IHC Matameye and Kourni (Matameye district), as well as Urban IHC DTK (Damagaram Takaya district), recorded the highest malaria rates over the three years. In contrast, Baboul, Albakaram, and Kanya Wané IHC in Damagaram Takaya and Dangoudaou IHC in Matameye reported much lower numbers (fewer than 2,000 cases over the three years).

Figure 4 Analyze of yearly data collected in each dispensary of the two districts

A/ total mild malaria cases collected for each dispensary during the three years , showing a large diversity of the number of cases

B/ Component principal analysis summarizing the normalized yearly data collected for the four variables (number of fever, number of mild malaria, number of severe cases and number of death) in each dispensary, for the three years in Takaya

C / Component principal analysis summarizing the normalized yearly data collected for the four variables(number of fever , number of mild malaria, number of severe cases and number of death) in each dispensary , for the three years in Matameye

Temporally, several IHCs Guidimouni (Damagaram Takaya), Kourni, Matameye, Tsaouni, and Kantché (Matameye) showed relative stability or slight decreases in case numbers from year to year (Fig. 4A).

In Damagaram Takaya, Baboul IHC recorded high morbidity, especially in 2021, with 118 severe malaria cases among children aged ≥ 5 years over the three years. Conversely, Albakaram IHC had a high number of uncomplicated cases among children ≥ 5 years, reaching 1,474 cases in 2023, along with 40 severe cases that same year. Urban IHC DTK recorded 87 severe cases among children < 5 years in 2021, but this number dropped to 2 in 2022 and 0 in 2023. Guidimouni IHC showed the opposite trend, with moderate numbers of uncomplicated and severe cases that increased among children ≥ 5 years in 2023 (57 cases). Kanya Wané IHC remained less affected, with fewer severe cases overall compared to other IHCs in the district.

Although district-level analyses showed an overall decline in malaria indicators in Damagaram Takaya in 2023, examination of each health facility revealed that this decrease was not fully homogeneous across the five selected health facilities.

For uncomplicated malaria, three facilities (Baboul, Guidimouni, and Kanya Wané) showed a progressive decline from 2021 to 2023 across most age groups. In contrast, Albakaram recorded an increase in 2023 after a temporary decrease in 2022, and health facility DTK showed a marked reduction only in 2023 after a peak in 2022. Among children aged ≥ 5 years, trends were similarly heterogeneous, with some facilities showing continuous declines and others showing fluctuations.

These results indicate that the district-level decline is not driven by a uniform reduction across all health facilities but rather by the combined effect of facilities following different trajectories. While the overall trend suggests a beneficial impact of interventions at the district level, the presence of strong intra-district heterogeneity highlights the importance of interpreting aggregated data with caution. Implementation of SMC could also have been very different from one part of a district to another. Because the study relies on routine aggregated DHIS2 data, a full facility-level causal assessment was not feasible.

In Matameye, disparities between health facilities were also significant. Urban IHC Matameye had the highest number of cases, with 5,103 uncomplicated cases in 2023 among children <5 years, and 1,255 severe cases in 2021 in the same age group. Kourni IHC also showed an upward trend in uncomplicated cases, peaking at 5,438 cases among children <5 years in 2023, and 128 severe cases in 2022. Kantché IHC followed a similar pattern, with consistently high uncomplicated cases, especially among children <5 years, and notable severe morbidity in 2022 (103 cases). In contrast, Dangoudaou and Tsaouni IHCs had more moderate levels of both uncomplicated and severe cases. No deaths were reported in this district in 2023.

Overall, Tukey's test confirmed homogeneity among health facilities ($p = 1.0$) for the number of deaths. The variable "year" had no effect on malaria occurrence ($p = 0.48$), and the interaction between health district and year

was not significant ($p = 0.39$), indicating that the impact of different years on malaria incidence was similar across districts. This suggests that the observed differences were mainly due to variations between health districts environments.

These results highlight marked intra-district heterogeneity, emphasizing the need to tailor interventions to the local dynamics specific to each region of the country (Table III).

Table III Data registered in the five dispensaries of each district summarized by year

Global Evolution of Health Centers Over Three Years

To conduct a comprehensive analysis of the evolution of health centers over the three-year period considering fever cases, number of tests performed, number of uncomplicated malaria cases, and number of severe malaria cases, annual data from each health center were normalized relative to the totals recorded for each variable across the entire district over the three years. A Principal Component Analysis (PCA) was performed separately for each district (Fig. 4, Table IV).

Table IV Coordinates of the variables on the two first axes of Principal Component Analysis

In the Damagaram Takaya district, the first axis (Dim 1) explained nearly 48% of the variance and was strongly correlated with fever and uncomplicated malaria (Fig. 4B). The second axis (Dim 2) captured variance related to severe malaria and deaths. The distribution of health centers on the factorial plane

revealed heterogeneity among certain facilities. Baboul and Albakaram IHC were strongly associated with uncomplicated malaria, while Urban IHC DTK showed a profile more oriented toward severe cases.

Most health centers showed a rightward shift in 2023, toward fever, indicating a decrease in malaria cases in favor of other causes of fever. The situation across health centers was fairly homogeneous over the three years (clustered points), except for Urban IHC DTK in 2021, which stood out (Fig 4B).

In the Matameye district, a similar situation was observed. Axis 1 (42.1% of variance) was dominated by fever and uncomplicated malaria, while Axis 2 accounted for severity of cases (Fig 4C). Again, health centers showed contrasting profiles, reflecting disparities in disease burden. In this district, the health centers most associated with malaria (both uncomplicated and severe) were Kantché, Kourni, Urban Matameye, and Tsaouni.

Although the PCA separates health facilities according to their annual malaria profiles, this pattern should be interpreted cautiously. Each facility has only three observations (one per year), which limits the statistical robustness of the PCA and may inflate apparent distances between facilities. The same Principal component analysis was conducted separately for the two groups of age showing the same profile. However, in 2023 for older children the shift to mild malaria and other causes of fever was observed which was not observed for younger ones. (data not shown)

3.3 Impact of extending SMC to children aged 5 to 10

Impact of treatment on uncomplicated malaria cases

Variance analysis revealed that the number of uncomplicated malaria cases recorded in the two health districts was significantly different ($p < 2e-16$, Table III).

Among children under 5 years of age in the Damagaram Takaya district, the number of uncomplicated cases recorded was relatively stable over the weeks (Fig. 3A), which is consistent with annual data showing a persistent incidence of malaria in this age group between 2021 and 2023. In Matameye, children also showed stability in recorded cases of uncomplicated malaria (Fig 3C), with moderate weekly fluctuations. The number of cases of severe malaria (Fig 3D) showed more marked variations, with an increase in 2022 (Tab II, Fig 3A).

For children aged ≥ 5 years in Damagaram Takaya, cases of uncomplicated malaria (Fig 3A) followed a similar trajectory to those of younger children, but with less intensity.

Impact of Treatment on Severe Malaria Cases

The incidence of severe malaria among children under five years was high, especially in the Matameye health district. In 2021, Matameye recorded more cases of severe malaria than Damagaram Takaya, in line with raw data. However, from 2022 to 2023, the number of severe malaria cases gradually

decreased in Damagaram Takaya while remaining stable in Matameye (Fig 3B), with a slight decrease in the standardized data (Fig 3D).

Among children aged 5 years and older, the number of severe malaria cases was also high, though slightly lower than among children under 5 years of age. In 2021, the number of cases was higher in Matameye than in Damagaram Takaya. In 2022, a moderate decline was observed in both districts. However, from 2021 to 2023, severe malaria and deaths showed significant decreases in the normalized number of cases in Damagaram Takaya but not in Matameye. This suggests a positive impact of targeted interventions for older children similar to that for younger children (Table II).

Impact of Treatment on Seasonality

The seasonal dynamics of uncomplicated malaria incidence in the health districts of Damagaram Takaya and Matameye between 2021 and 2023 (per 1,000 inhabitants) showed a clear increase during the rainy season months (June-October in Niger) (Fig 4). Values exceeded 20 cases per 1,000 inhabitants in both districts, with peaks above 30 cases per 1,000 observed in Matameye (Fig 4A). The number of uncomplicated malaria cases showed a sharp rise between weeks 30 and 45, with peaks occurring in both districts during the same period (Fig 2C). Matameye recorded higher peaks, reaching nearly 500 weekly cases, compared to 300 cases in Damagaram Takaya. During the dry season (November-May), incidence dropped below 5 cases per

1,000 inhabitants, reflecting the seasonal nature of uncomplicated malaria (Fig 3D).

Early systematic treatment of older children may reduce the parasite reservoir, potentially delaying the peak transmission period during the season. To detect this transmission peak delay induced by the implementation of SMC in older children, normalized data were analyzed using the SARIMA method. Four models were developed: DTK / Matameye ; >5 years / <5 years (Fig 5). Predicted data were plotted alongside actual non-normalized data.

Figure 5 SARIMA analysis of incidence of mild malaria in the two districts

Monthly incidence of mild malaria for the five dispensaries of the districts for children under (A-C) or more (B-D) than 5 years. Dark line: observed data; red line: estimated data; blue line: data forecasted for a fourth year. A-B/ Daram Takaya district. C-D/ Matameye district

The observed, estimated, and forecasted malaria incidence curves for Damagaram Takaya and Matameye, stratified by age group (<5 years and ≥ 5 years), revealed contrasting epidemiological profiles but showed a trend toward temporal synchronization. The observed incidence curves showed recurrent peaks in 2022, 2023, and early 2024 across all four subpopulations studied. These fluctuations suggest seasonal cycles, but no abrupt breakpoints were identified. Moderate time shifts were observed between the estimated and observed curves, especially during transitional phases

between high and low transmission seasons. These shifts may reflect delays in case detection or reporting. However, the consistency of peaks between the two districts and age groups does not suggest regional desynchronization of malaria epidemics (Fig 5).

4. DISCUSSION

This study was conducted to evaluate the impact of extending Seasonal Malaria Chemoprevention (SMC) to children aged 5 to 10 years on malaria-related morbidity and mortality under real-world conditions. Previous studies on this topic were mostly controlled clinical trials. In contrast, this study used routine data recorded by health centers between 2021 and 2023, from two neighboring health districts Damagaram Takaya, where the SMC strategy was extended to older children, and Matameye, where it was not. The real public health impact of this extension was therefore directly assessed. In each district, five health facilities were randomly selected for data collection.

A key limitation of this study is that the observed district-level decline in malaria indicators in 2023 was not completely consistent across all health facilities. Some health facilities showed clear reductions, while others exhibited fluctuations, indicating that intra-district heterogeneity may influence aggregated trends. As routine DHIS2 data do not allow for a detailed causal assessment at the facility level, the conclusions should be interpreted with caution.

Importantly, severe malaria declined not only in the district where SMC was extended but also in the control district. This parallel trend limits the attribution of the observed reductions solely to SMC extension. Other factors, such as broader malaria control activities, ecological variations, or temporal fluctuations in transmission, may also have influenced the observed outcomes.

In both districts, among children under five, a marked seasonal pattern was observed, with malaria peaks occurring between July and September. SARIMA modeling confirmed the strong seasonality of transmission, with recurrent peaks during the rainy season. This regular seasonality highlights the strategic importance of planning and strengthening preventive measures ahead of this critical period. Seasonality is the key criterion used in West Africa to implement the SMC strategy [36]. The age criterion (<5 years) is not uniformly applied across countries for example, Mali has chosen to include its entire population, including older children, in the strategy [37,38].

Although the two districts are in the same geographically area and both implementing SMC for young children, comparative analysis of both raw and normalized data revealed different epidemiological trends between them during the 2021-2023 period. Matameye consistently showed higher incidence rates of fever, uncomplicated and severe malaria, and positive diagnostic tests compared to Damagaram Takaya.

In Mali, a study by Druetz et al. [39] evaluated the direct and indirect effects of SMC in a routine context. The results showed a significant reduction in malaria incidence among children exposed to SMC, including those older than 5 years. In Burkina Faso, a quasi-experimental study revealed that SMC administration under programmatic conditions reduced malaria incidence by 89% four weeks after administration and by 62% five to six weeks later, among both children under 5 and older children [40].

Nigeria and Senegal have also experimented with extending SMC to children aged 5 to 10 years. These initiatives were part of pilot projects aimed at evaluating operational feasibility, drug tolerance, and epidemiological impact of SMC. Early results indicate strong community acceptance and a notable reduction in malaria morbidity in these age groups [41].

Additionally, the study revealed significant intra-district heterogeneity in malaria morbidity, both in terms of the number of uncomplicated and severe cases, and test positivity rates. In Damagaram Takaya, Guidimouni IHC stood out with significantly higher rates of fever and uncomplicated malaria compared to other IHCs such as Albakaram, Baboul, or Kanya Wané. Similarly, in Matameye, Kantché IHC, despite conducting a large number of RDTs, paradoxically reported fewer confirmed malaria cases than other IHCs like Kourni.

Principal Component Analysis (PCA) confirmed this inter-facility variability, highlighting distinct profiles across health centers, despite similar seasonal

dynamics between the two districts. This underscores the need for targeted approaches that consider local specificities, adapting preventive interventions to local climatic contexts and transmission timing, as previously described [42].

Regarding severe malaria, both districts had similar but relatively low incidence rates, consistent with previous studies in Niger [21]. In Mali, a retrospective study conducted at CHU Gabriel Touré in Bamako between 2014 and 2018 evaluated the impact of SMC on cerebral malaria in children aged 0 to 15 years. Results showed a reduction in cerebral malaria frequency from 92.1% to 83.5% after SMC introduction ($p = 0.013$), a significant drop in case fatality ($p = 0.0001$), and an 8.6% decrease in cerebral malaria frequency post-SMC [43].

Another study [44] reported an 87% reduction in severe malaria cases at the end of the high transmission season (95% CI: 42%-99%, $p = 0.001$). In Burkina Faso, a quasi-experimental study in Kaya district compared data before (2014) and after (2015) SMC introduction among 2,523 children. Results showed a 51% reduction in malaria risk, a 32% decrease in moderate/severe anemia, and a 46% drop in febrile episodes [45].

Inter-district variance analysis showed that observed differences were mainly attributable to district-specific characteristics, rather than annual variation. PCA also revealed strong heterogeneity in health center profiles. Some facilities, like Urban IHC DTK or Tsaouni, reported higher normalized

numbers of severe cases, while others like Baboul or Albakaram were more associated with uncomplicated cases. These findings likely reflect health center performance more than transmission intensity, as the volume of RDTs performed was often lower in these facilities. This may indicate delayed care-seeking or limited accessibility during the rainy season.

Overall, Seasonal Malaria Chemoprevention (SMC) has proven effective in reducing malaria incidence among target children in Sahelian countries, as confirmed by several recent studies [45-39]. The extension of SMC to children over 5 years in Damagaram Takaya also appears to be associated with a progressive reduction in both uncomplicated and severe malaria cases in this age group—unlike Matameye, where trends remained more stable. Indeed, incidence dropped from 33.34 per 1,000 children in 2021 to 11.86 in 2022, confirming the likely effectiveness of this extension.

This improvement was not observed in Matameye, despite a downward trend. Similarly, results showed a measurable positive effect of SMC on mortality among children ≥ 5 years in Damagaram Takaya. These findings suggest a protective effect of the strategy, although further scaling studies are needed to confirm its effectiveness, taking into account other contextual factors such as bed net usage, socioeconomic status, etc.

However, several challenges hinder optimal implementation of this strategy, including accessibility in rural areas, insecurity, difficulty locating children for successive doses, and lack of reliable census data for target children.

While SMC is generally well accepted, some side effects such as vomiting, diarrhea, or skin rashes, often linked to amodiaquine can affect community adherence [39]. WHO recommends strengthening pharmacovigilance, monitoring adverse effects, and raising community awareness about the importance of completing treatment even if symptoms occur [34].

Furthermore, extending SMC to children aged 5 to 10 years should be considered in mesoendemic or hypoendemic areas of the country where malaria resurgence is observed, often linked to climate change affecting seasonality and transmission intensity [34,40]. Although this extension involves additional costs, it should be evaluated by each country based on local epidemiological data to better protect this under-covered age group.

In conclusion, the results of this study support a fine-tuned adaptation of malaria control interventions, integrating differentiated strategies based on districts, age groups, and local realities of health facilities. Extending SMC to older children, combined with targeted support for high-incidence health centers, could significantly improve the reduction of malaria-related morbidity and mortality in Niger.

5. Limitations of the Study

This study was conducted as a pragmatic comparison of evolution of malaria cases among older children with or without SMC. It is based on the analysis of the data collected in DHIS2. It aims to evaluate the global impact of the strategy on the burden of malaria among children. However, many limitations

are intrinsic of this design. No district can be truly compared to another in a large country like Niger. However, we focused on two districts as closed as possible in term of climate, ecology, population, economy etc. The comparison was also conducted among the same district (and not between districts) before and after implementation of the strategy which can be relevant to estimate this impact. The data before and after implementation can be of course impacted by change in meteorological fluctuations from one year to the other. However, as the two districts are only separated by 50km we can assume that the impact can be the same for both. In the same line data were collected retrospectively each year through the DHIS2 system. Each dispensary of the whole country is loading weekly aggregated data. The categorization of each medical consultation used for the weekly report can of course slightly varied from one dispensary to another despite clear recommendation of the health ministry. However, these slight variations can be assumed to be quite stable for a dispensary over the time, if no change occurred in the medical team. Global comparison can thus be relevant, but with a lower statistical power, assuming that statistically significant results can be due to a strong effect.

We were also unable to collect all the necessary information on the use of LLIN by parents at home as this information is not reported in DHIS2; there for all children were assumed to have received SMC . Therefore, all children were considered to have received treatment as in both districts reductions in malaria incidence in children over 5 years were reported.

CONCLUSION

During this study and despite very close ecological context of the two districts data revealed significant disparities in malaria dynamics between the Damagaram Takaya and Matameye districts, as well as substantial heterogeneity within each district. This can be considered as a limitation of this pragmatic approach.

However, these results underscore the impact of extension of SMC for older children. In a new step (in process) the impact on severe malaria and mortality should be evaluated at the hospital level. In the same line, these results pave the way to an extension of the strategy to districts in different areas of the country especially in those of low malaria transmission as the northern districts of the country..

List of Abbreviations

AQ: Amodiaquine

CHW: Community Health Workers

DHIS2: District Health Information Software 2

DSER: Direction of Surveillance and Epidemic Response

DTK: Damagaram Takaya

GE: Thick drop

HP: Health Post

IHC: Integrated Health Center

LLIN: Long-Lasting Insecticidal Net

MS/HP: Ministry of Health and Public Hygiene

ND: Notifiable Diseases

NMCP: National Malaria Control Program

PCA: Principal Component Analysis

PC1: First Principal Component

PC2: Second Principal Component

RDT: Rapid Diagnostic Tests

SARIMA: Seasonal Autoregressive Integrated Moving Average

SD: Statistics Direction

SMC: Seasonal Malaria Chemoprevention

SP: Sulfadoxine-Pyrimethamine

THICK DROP: Thick Blood Smear

WHO : World Health Organization

DECLARATIONS

- **Ethics approval and consent to participate:** Data were obtained from the National Central Health System of Niger (DHIS2), as CERMES

is a part of the Health Ministry. The data were anonymized and used under the national health surveillance mandate, in accordance with Niger's public health regulations. Ethical approval is thus unnecessary according to national regulations. This study as well as the management of data by the offices of the Health Ministry adhered to the Declaration of Helsinki.

- **Consent for publication:** Not applicable
- **Consent to participate :** Not applicable
- **Availability of data and materials:** The dataset supporting the conclusions of this article is included within the article and its additional files
- **Competing interests:** The authors declare that they have no competing interests.
- **Funding Declaration:** this study was supported by institutional supports from EPICENTRE. The collection of data was supported by a grant EDCTP on SMC.
- **Authors' contributions**

DJEDANEM Médard: conducted the study, analyzed data and wrote the draft of the manuscript

Alkassoum IBRAHIM : collected data

Mahaman Y NAZIBOU : collected data

Mamane Salé NOURA : collected data

Yacoudima Yacoubou: collected data

ZAKARI Abdoussalam: collected data, analyzed data

Hassani Omari MBEGA : collected data

ZANEIDOU Mamane: conducted a part of statistical analysis

MODY Issaka: collected data

Eric ADEHOSSI : reviewed the final manuscript

TESTA Jean: reviewed the final manuscript

JAMBOU Ronan: defined the protocol, supervised the study analyzed data, co-wrote and corrected the manuscript

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Table I Meteorological parameters of the two districts under survey

Month	Matameye						Daram Takaya					
	High*	Temp*	Low*	Cloudie r	Clare r	Rain** *	High*	Temp*	Low*	Cloudie r	Clare r	Rain
Jan	84°F	72°F	60°F	31%	69%	0.0d	84°F	72°F	61°F	31%	69%	0.0d
Feb	90°F	77°F	65°F	38%	62%	0.0d	90°F	77°F	65°F	37%	63%	0.0d
Mar	98°F	85°F	73°F	51%	49%	0.1d	97°F	85°F	73°F	49%	51%	0.0d
Apr	102°F	91°F	79°F	59%	41%	0.6d	103°F	92°F	79°F	56%	44%	0.6d
May	102°F	92°F	81°F	60%	40%	3.4d	103°F	93°F	82°F	57%	43%	2.9d

Jun	98°F	89°F	79°F	54%	46%	8.4d	100°F	90°F	80°F	51%	49%	7.4d
Jul	92°F	84°F	76°F	56%	44%	18.6d	94°F	85°F	77°F	54%	46%	17.8d
Aug	90°F	81°F	75°F	59%	41%	20.3d	91°F	83°F	75°F	58%	42%	19.5d
Sep	93°F	84°F	75°F	55%	45%	10.0d	95°F	85°F	76°F	53%	47%	9.0d
Oct	97°F	85°F	74°F	50%	50%	1.2d	98°F	86°F	75°F	48%	52%	0.9d
Nov	92°F	80°F	68°F	47%	53%	0.0d	92°F	80°F	68°F	45%	55%	0.0d
Dec	86°F	73°F	61°F	39%	61%	0.0d	85°F	73°F	62°F	38%	62%	0.0d

* mean higher / lower temperature, **mean temperature, *** in decimeter

Table II Summary of data registered over the three years in the two districts

health district	Years	age groups	indidence fever	RDTs Completed	indicence RDTs+	indicence uncomplicated malaria	indicence Severe Malaria	indicence death	Fever cases
Damgaram Takaya	2021	< 5 years	21.78	21.78	12.77	12.45	0.31	0.001	18391
		≥ 5 years	48.22	48.22	33.98	33.34	0.65	0	17351
		total	29.68	29.68	19.11	18.69	0.41	0.0008	35742
	2022	< 5 years	69.52	69.48	36.86	36.32	0.5	0	16960
		≥ 5 years	16.25	16.24	12.05	11.86	0.19	0	16342
		total	26.65	26.64	16.89	16.64	0.25	0,00	33302
	2023	< 5 years	84.8	84.53	40.71	40.37	0.34	0	19450
		≥ 5 years	15.36	15.36	9.45	9.3	0.14	0	16410
		total	27.646	27.60	14.98	14.80	0.18	0,00	35860
Matameye	2021	< 5 years	20.13	20.13	14.02	13.79	0.22	0	26961
		≥ 5 years	33.79	33.79	25.46	24.84	0.62	0	20055
		total	24.32	24.32	17.54	17.18	0.35	0,00	47016
	2022	< 5 years	59.13	59.13	43.23	42.23	0.74	0	23165
		≥ 5 years	11.86	11.86	9.44	9.25	0.18	0	19143
		total	21.09	21.093	16.045	15.69	0.29	0,00	42308
	2023	< 5 years	64.2	64.2	48.03	47.69	0.34	0	25935
		≥ 5 years	11.4	11.4	8.6	8.52	0.06	0	19137
		total	21.64	21.64	16.25	16.12	0.12	0,00	45072

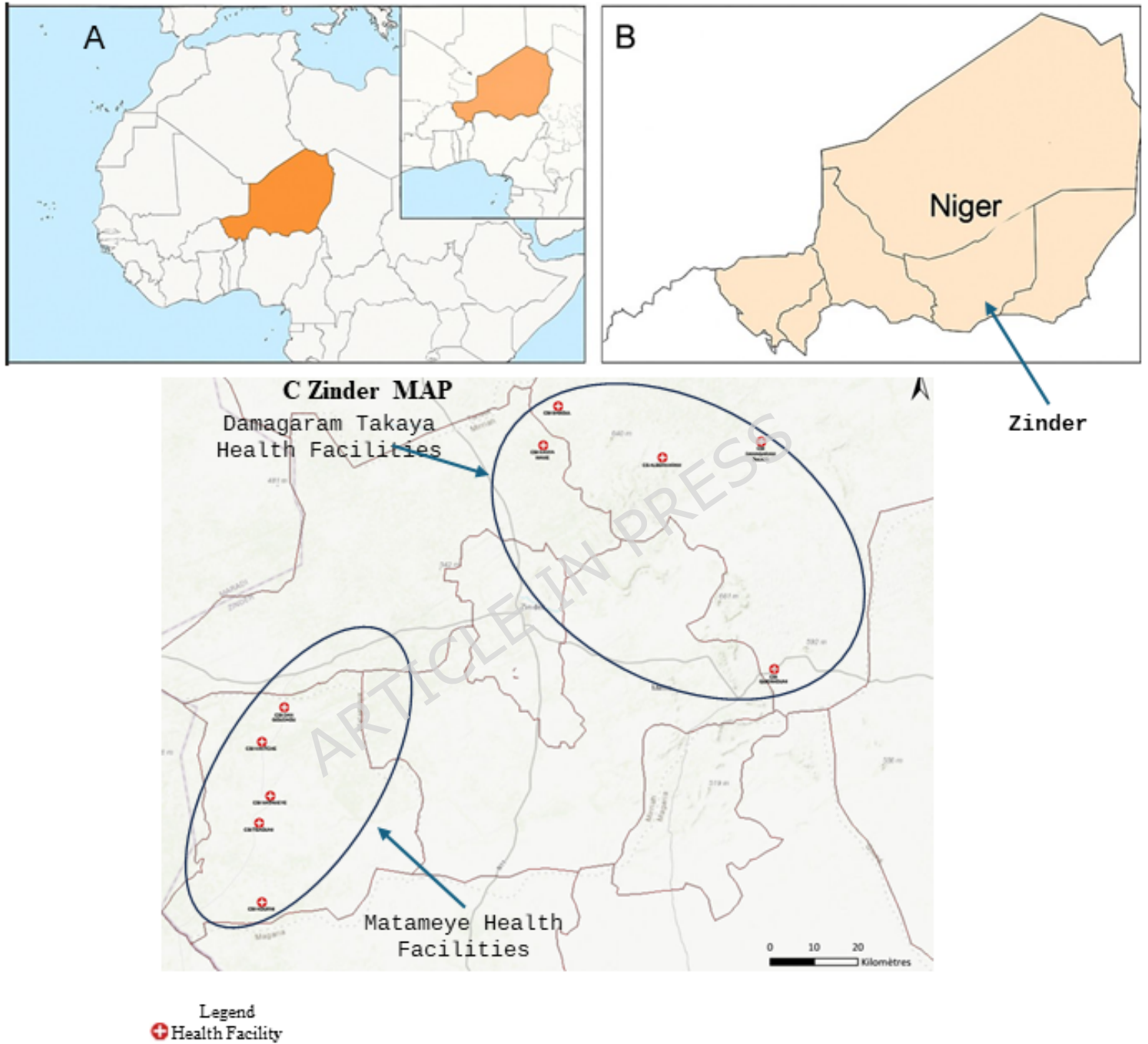
Table III Data registered in the five dispensaries of each district summarized by year

health district	CSI	age groups	2021			2022		
			Fever cases	uncomplicated total cases	total severe cases	Fever cases	uncomplicated total cases	total severe uncomplicated
Damgaram Takaya	Albakaram	< 5 years	979	489	3	693	365	0
		≥ 5 years	2066	1482	29	1210	1197	28
	Baboul	< 5 years	3132	1489	76	3079	1377	59
		≥ 5 years	2802	2052	118	2288	1887	91
	Guidimouni	< 5 years	6452	4681	35	5355	3791	39
		≥ 5 years	4654	3259	18	4348	3213	16
	Kanya wané	< 5 years	3935	2355	62	3864	2006	24
		≥ 5 years	3348	2505	41	3851	2804	24
	urbain DTK	< 5 years	3893	1503	87	3979	1328	2
		≥ 5 years	4481	2700	30	4842	2833	34
Matameye	Dangoudaou	< 5 years	5133	3118	31	2686	1709	15
		≥ 5 years	2898	1705	23	1449	1006	8
	Kantché	< 5 years	5448	3693	44	5244	3853	103
		≥ 5 years	5475	3806	55	4353	3418	89
	Kourni	< 5 years	6096	4912	22	6254	4729	128
		≥ 5 years	2578	1783	34	2663	1896	14
	urbain Matameye	< 5 years	5996	3195	1255	5734	3724	15
		≥ 5 years	4306	3255	186	5880	4422	121
	Tsaouni	< 5 years	4328	3560	85	3247	2531	32
		≥ 5 years	4798	4192	75	4798	4195	72

Table IV Coordinates of the variables on the two first axes of Principal Component Analysis

	Dim.1	ctr	cos2	Dim.2	ctr	cos2	Dim.3	ctr	cos2
Daramtakaya									
Fever	0.933	48.026	0.871	-0.157	2.010	0.025	-0.116	1.755	0.013
uncomplicatedcases	0.930	47.741	0.865	-0.165	2.215	0.027	0.130	2.185	0.017
Severecases	0.186	1.902	0.034	0.770	48.242	0.593	0.607	47.997	0.369
Deaths	0.206	2.332	0.042	0.764	47.533	0.584	-0.608	48.063	0.369
Matameye									
Fever	0.963	42.134	0.927	-0.222	6.542	0.049	-0.153	51.324	0.023
uncomplicated cases	0.947	40.712	0.896	-0.286	10.871	0.082	0.148	48.417	0.022
Severe cases	0.614	17.155	0.378	0.789	82.587	0.622	0.011	0.258	0.000
Deaths	0.000	0.000	NaN	0.000	0.000	NaN	0.000	0.000	NaN

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**Figure n°1**

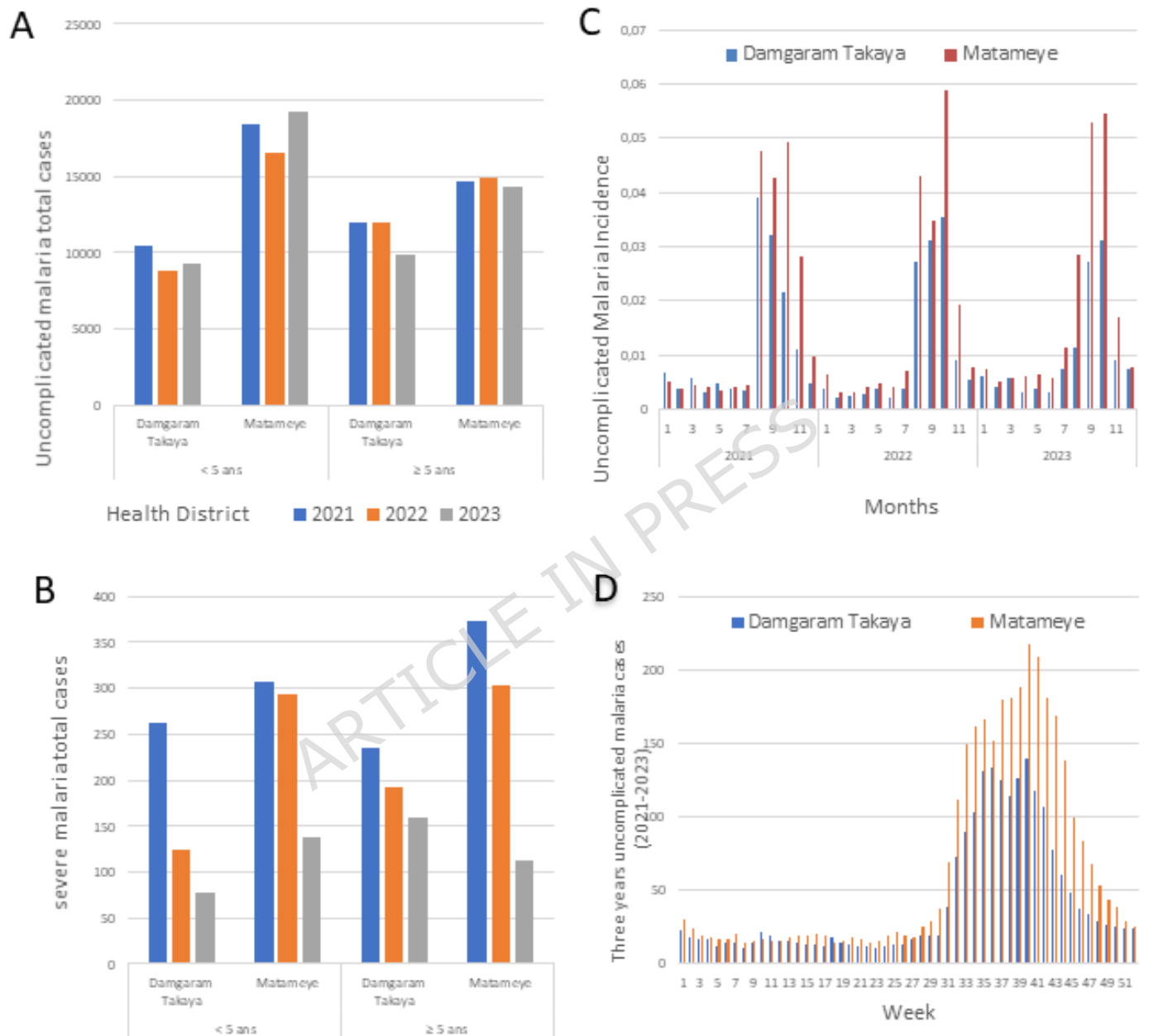


Figure n°2

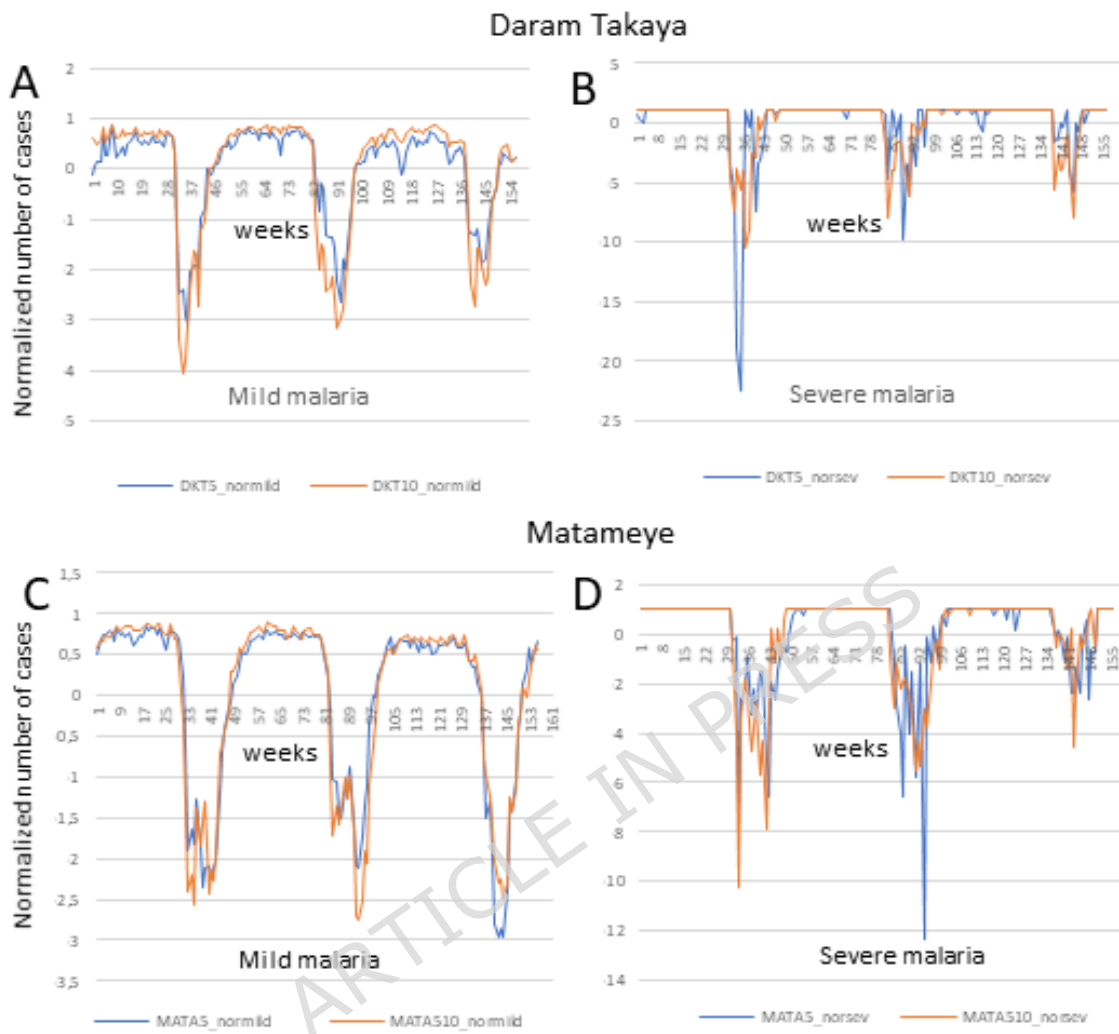


Figure n°3

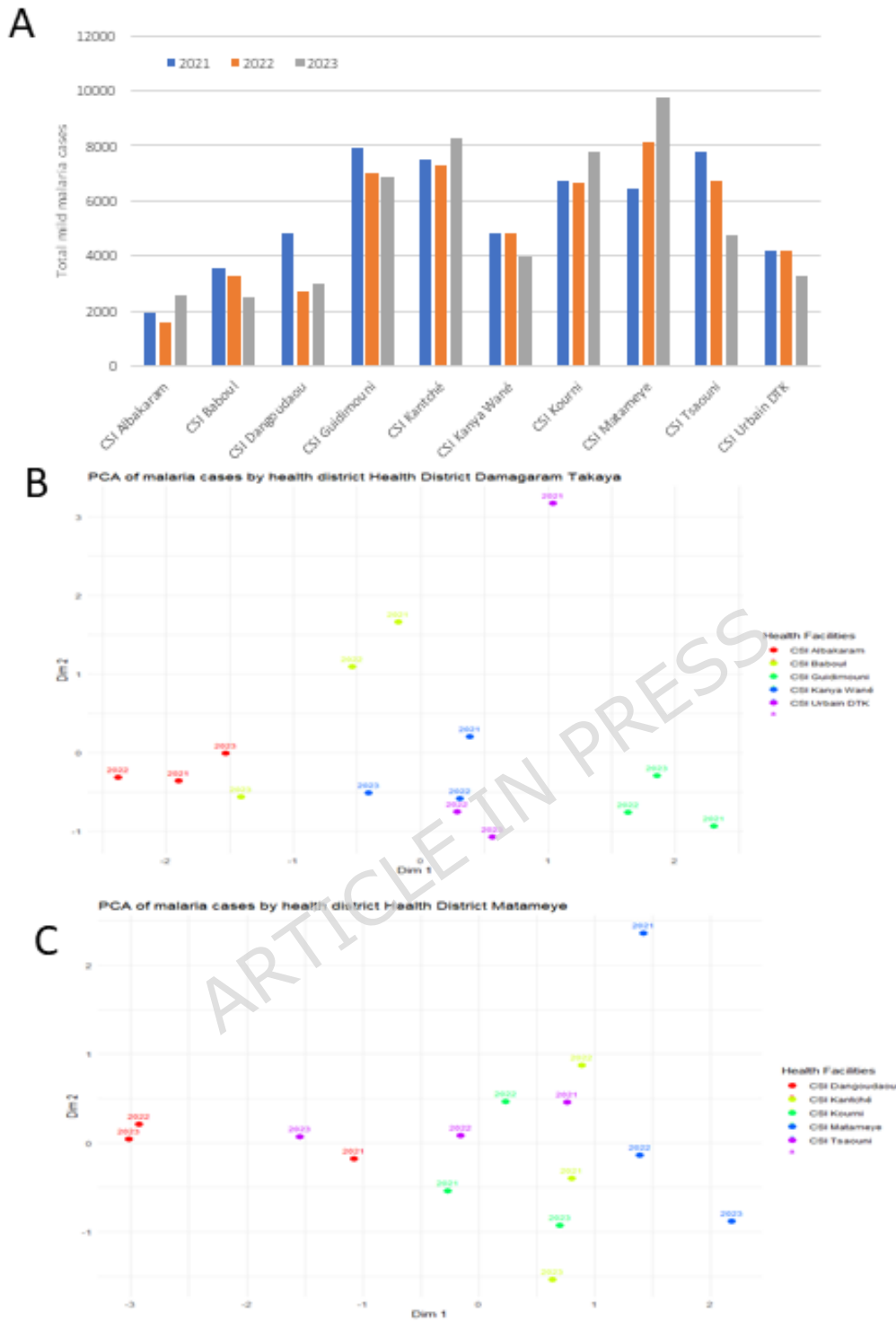
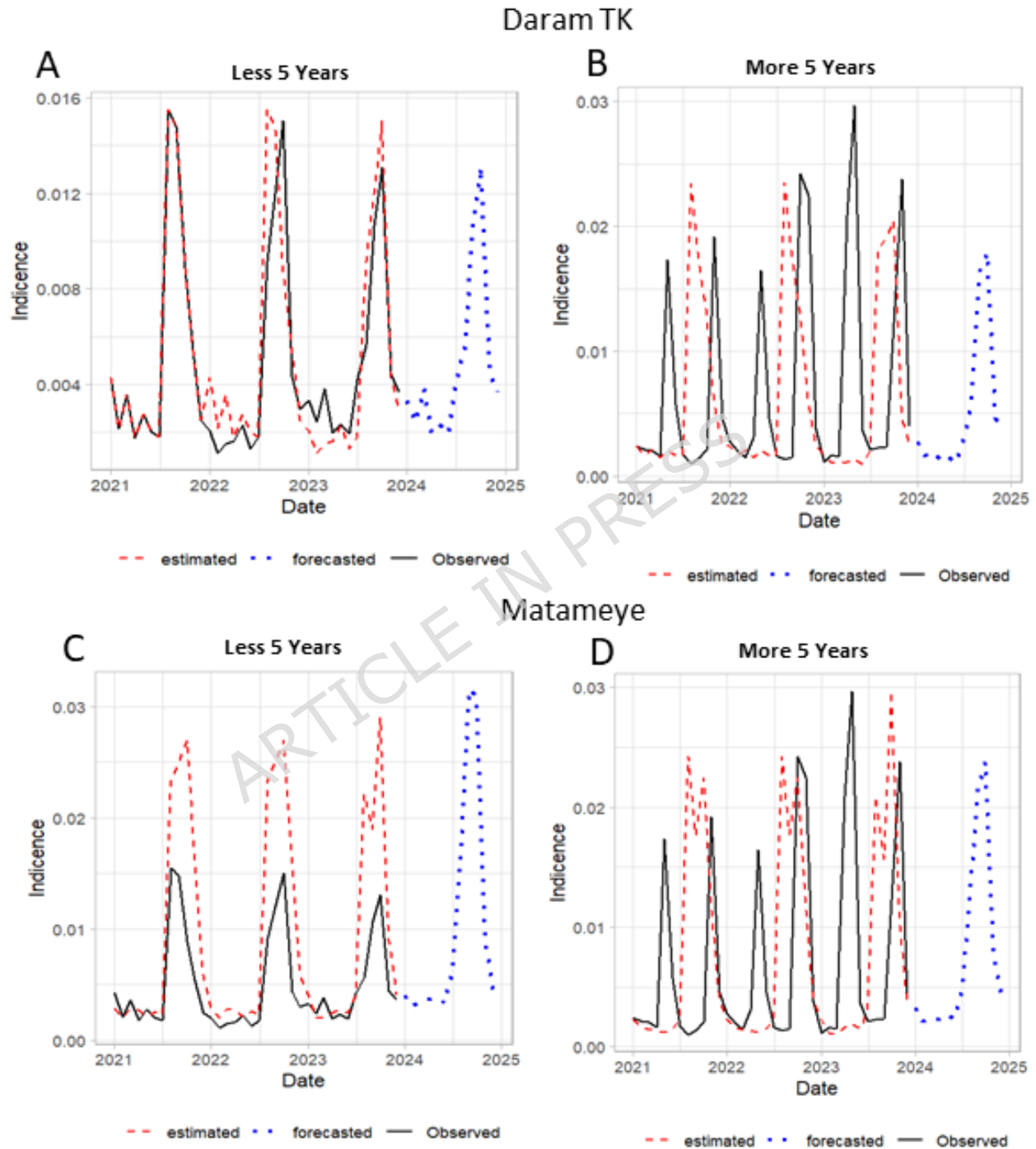


Figure n°4

**Figure n°5**