Spatio-temporal variation of malaria hotspots in central Senegal, 2008-2012

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Abstract

Background In malaria endemic areas, identifying spatio-temporal hotspots is becoming an important element of innovative control strategies targeting transmission bottlenecks. The aim of this work was to describe the spatio-temporal variation of malaria hotspots in central Senegal, and to identify the meteorological, environmental, and preventive factors that influence this variation.

Methods The weekly incidence of malaria cases recorded from 2008 to 2012 in 575 villages of central Senegal (total population 523,908) during a trial of Seasonal Malaria Chemoprevention (SMC), were analysed. Data on weekly rainfall and annual vegetation types were obtained for each village from remote sensing data. The time series of weekly malaria incidence for the entire study area was divided into periods of high and low transmission using change-point analysis. Malaria hotspots were detected during each transmission period with the SaTScan method. The effects of rainfall, vegetation type, and SMC intervention on the spatio-temporal variation of malaria hotspots were assessed using a General Additive Mixed Model.

Results The malaria incidence rate for the entire area ranged from 0 to 115.34 cases/100,000 person weeks during the study period. During high transmission periods, the cumulative malaria incidence rate varied between 7.53 and 38.1 cases/100,000 person-weeks, and the number of hotspot villages varied between 62 and 147. During low transmission periods, the cumulative malaria incidence rate varied between 0.83 and 2.73 cases/100,000 person-weeks, and the number of hotspot villages varied between 10 and 43. Villages with SMC were less likely to be hotspots (OR=0.48, IC95%: 0.33-0.68). The association between rainfall and hotspot status was non-linear and depended on vegetation type and the amount of rainfall. The association between village location in the study area and the hotspot status was also showed.

Conclusion In our study, malaria hotspots varied over space and time according to a combination of meteorological, environmental, and
preventive factors. Knowing the similar environmental and meteorological particularities of hotspots, surveillance on these factors could lead targeted public health interventions in local context. Moreover, the issue of spatial hotspots and foci of malaria persistence during LTPs needs to be further addressed.

Background

Of the 435,000 deaths attributed to malaria worldwide in 2017, 93% were recorded in sub-Saharan Africa [1]. In Senegal, annual malaria incidence rose from 14 to 25.94 cases/1,000 person-years between 2009 and 2017, despite the strengthening of control strategies. In 2017, malaria incidence ranged from 0.4 (Saint-Louis) to 473.9 cases/1,000 person-years (Kedougou) across the country's 72 health districts [2]. It is now known that spatial heterogeneity of Malaria distribution reduce the effectiveness of malaria control programme. Thus, this spatial heterogeneity may contribute to the persistence of transmission at a significant level[3] . The detection of heterogeneity patterns in malaria endemic areas is therefore becoming an important element of recent approaches that seek to identify transmission bottlenecks [4–13]. Variations in heterogeneity have been observed even at a very local scale—for example, within 8-km radius areas in Kenya [7], at the village level in Senegal (KeurSocé) [14]and at the household level in Tanzania (Korogwe District) and Mali (Bandiagara) [9, 15]. Central Senegal is covered by the country’s 2 largest Health and Demographic Surveillance Systems (HDSS), which provide data on malaria cases and population at the village level [16]. Moreover, the heterogeneous distribution of malaria has been shown to depend on a series of environmental factors that favour vectors development and host-vector interactions [17, 18].

In view of these findings, the WHO recommends developing targeted strategies aimed at accelerating the malaria elimination process [5, 19]. The first step to ensure the
effectiveness of these strategies is to accurately identify geographical areas of greatest risk, called hotspots, where they are expected to exert a stronger impact on malaria transmission. Indeed, hotspots can maintain transmission during the dry season, and they can be the source of epidemic episodes during the rainy season [5].

However, while certain locations exhibit a constant hotspot status, certain hotspots can be unstable over time [8]. This instability adds a layer of complexity to the process of malaria transmission, and may consequently hinder the effectiveness of prevention strategies.

Yet, while a number of studies on malaria have explored the environmental factors that may influence spatial hotspot distribution [5, 7, 8, 20, 21], few have attempted to explain the spatio-temporal dynamics of malaria hotspots [22].

The aim of this work was to describe the spatio-temporal variation of malaria incidence hotspots in villages of central Senegal, and to identify the meteorological, environmental, and preventive factors that influence this variation.

Methods

Study area and dataset

The study area included 575 villages (linked to 38 health posts) that spanned 2 health districts—Bambey and Fatick—located in west-central Senegal [16]. The total population of the study area was approximately 500,000. The median population of the villages was 499 with interquartile range [233; 1029]. Each village was linked to a health post. The median number of villages linked to each health post was 11, with interquartile range [8; 19].

In 2017, 1.2 cases/1,000 person-years were recorded in the Bambey health district and 2.1 cases/1,000 person-years were recorded in the Fatick health district [2].

Seasonal malaria chemoprevention (SMC) trial was implemented in this area from 2008 to 2010 [16, 23–25]. The SMC protocol consisted in administering a combination of sulfadoxine-pyrimethamine and amodiaquine to children (under 5 years in 2008 and under
10 years of age 2009-2010), in each month from September to November. The SMC trial [16, 25] had established a surveillance system in each health post of the study area since 2008. For each health post, a list of GPS positioned villages has been established. For each village, from January 2008 to December 2012, a census of the population was undertaken annually, malaria cases (detected by rapid diagnostic test) were reported daily with the village name and collected at the health post level. For this study malaria cases were aggregated on week.

For the same period, vegetation data were derived from MODIS (Moderate-Resolution Imaging Spectroradiometer) rasters [26]. Four MODIS-derived vegetation types were present in the area: open shrublands, grasslands, croplands, and mixed vegetation. The latter consisted of a mosaic of croplands, forests, shrublands, and grasslands in which no single component represented more than 60% of the landscape. For each village, the proportion surface area of vegetation types within a 0.55 km radius buffer zone was calculated annually (Additional file 1), and the vegetation type covering the largest surface area was retained as the modal type.

Total weekly rainfall was calculated for each village using daily rainfall amounts (mm) derived from the Tropical Rainfall Measuring Mission (TRMM) and extracted from the NASA Goddard Earth Sciences website with a 0.25 degree resolution [27].

**Statistical methods**

First, we conducted a change-point analysis of the time series of weekly malaria incidence rate over the entire study area in order to detect High Transmission Periods (HTPs) and Low Transmission Periods (LTPs). As per this method, we identified the dates (called change-points) associated with significant changes in the mean and variance of malaria incidence rate. We chose to use the PELT (Pruned Exact Linear Time) algorithm and the MBIC (Modified Bayes Information Criterion) penalty criterion for convergence and
optimization reasons [28–30].

Second, for each identified period, we searched for high-risk clusters (hotspots) using the SaTScan method developed by Kulldorff [31]. Following this approach, neighbouring villages were aggregated into groups with similar incidence using an elliptical window with variable size, centre, and rotation. Kulldorff’s statistics based on the likelihood ratio (Poisson model with a purely spatial analysis) were tested using a Monte Carlo algorithm (999 replicates). Then, a hotspot was selected when the incidence inside the window was significantly (p<0.05) higher than the incidence outside. For a given transmission period, we defined that a village was hotspot if it belonged in a significant cluster detected by SaTScan.

Third, we used a generalized additive mixed model (GAMM) [32] to assess the spatio-temporal variation of hotspot status for each village according to successive transmission periods. We examined the relationship between hotspot status and the 2 environmental factors: vegetation and rainfall. Thus, a spline smoothing function of time by vegetation type, $f_1(Time, \ by=Vegetation)$ (eq.1), was used to estimate the temporal variation of the association between vegetation type and hotspot status. As the impact of rainfall on malaria can be modified by vegetation, a spline smoothing function of rainfall by vegetation type, $f_2(Rain, \ by=Vegetation)$ (eq.1), was used to estimate the variation of the association between rainfall and hotspot status according to vegetation type.

We also included in the model a village-level binary variable, SMC, to estimate the effect of SMC interventions [16] on hotspot status.

A bivariate spline function of the geographical coordinates of villages [32], $f_3(Longitude, Latitude)$ (eq.1) was used to estimate the spatial variation of hotspot status, and to thereby obtain spatial interpolations for the entire study area.
The link between each village and its corresponding health post was expressed as a random effect of the “HealthPost” variable.

A first-order autoregressive correlation was integrated into the variance-covariance matrix to account for the temporal autocorrelation. The final model was selected by minimizing the Akaike criterion.

\[
\text{logit}(P(\text{Hotspot}=1)) = \beta_0 + \beta \cdot \text{SMC} + f_1(\text{Time, by=Vegetation}) + f_2(\text{Rain, by=Vegetation}) + f_3(\text{Longitude, Latitude}) + u \cdot \text{HealthPost} + \epsilon
\]  

(eq.1)

where \(\beta_0\) was the intercept, \(\beta\) was the associated fixed parameter estimating the SMC effect, \(f_1, f_2\), and \(f_3\) the spline functions, \(u\) the random parameter associated with the \(\text{HealthPost}\), and \(\epsilon\) the residuals whose covariance matrix had a first-order autoregressive structure.

Statistical analyses were done with R 3.4.2 (The R Foundation for Statistical Computing, Vienna, Austria) (packages\{changepoint\}\{mgcv\}). Hotspot detection was performed with SaTScan 9.4 (Information Management Services Inc, Silver Spring, Maryland, USA). Maps were produced using QGIS 2.14.2 (Open Source Geospatial Foundation, Boston, USA).

Results

**Temporal evolution of malaria incidence rate**

During 2008-2012, the malaria incidence rate for the entire area showed an annual resurgence dependent on rainfall (Figure 1). The incidence rate peaks of epidemic periods ranged from 26.4 cases/100,000 person-weeks in 2009 (October) to 115.34 cases/100,000 person-weeks in 2012 (October). Low to very low incidences of malaria were recorded even during the driest and hottest seasons.

**Identification of malaria transmission periods**

The change-point analysis helped to detect 5 LTPs and 5 HTPs (Figure 1).
The HTPs (except for the last one) overlapped 2 consecutive years. Annual epidemics began in July or August and ended in January or February of the following year. The median HTP duration was 28 weeks. The 2012 HTP had the highest cumulative malaria incidence rate (38.1 cases/100,000 person-weeks). The 2009-2010 HTP had the lowest cumulative malaria incidence rate (7.53 cases/100,000 person-weeks) (Table 1).

LTPs began in January or February and ended between June and August. The median LTP duration was 27.5 weeks. The 2011 LTP had the highest cumulative malaria incidence rate (2.73 cases/100,000 person-weeks), and the 2010 LTP had the lowest (0.83 cases/100,000 person-weeks) (Table 1).

Evolution of weekly malaria incidence rate (continuous red curve); High Transmission Period (HTP, in grey) and Low Transmission Period (LTP, in white) with duration (weeks, in black) and their cumulative incidence rates (in red numbers); total weekly rainfall (in blue).

Table 1.

Characteristics of transmission periods and hotspots: High Transmission Periods (HTP) and Low Transmission Periods (LTP) with cumulative incidence rate, start and end dates, and duration (in weeks); hotspot status of villages (hotspot or non-hotspot); number of hotspot and non-hotspot villages; cumulative incidence rate in hotspot and non-hotspot villages; number and percentage of hotspot and non-hotspot villages that received seasonal malaria chemoprevention (SMC); weekly average rainfall and standard deviation in hotspot and non-hotspot villages; dominant vegetation type (open shrublands, grasslands, croplands, mixed vegetation) for each period in hotspot and non-hotspot villages.

| Period: (cumulative inc*, dates, duration) | Hotspot status | Number of villages | Cumulative incidence rate * | SMC** (%) | Weekly average rainfall (mm/week) (SD***%) | Mod veg type (%) |
|-------------------------------------------|----------------|-------------------|----------------------------|-----------|--------------------------------------------|-----------------|
| 2008 LTP (0.93) 01/01/2008 - 30/06/2008 - 26 weeks | Hotspot | 19 | 9.82 | 0 (0.00%) | 1.9 (0.99) | Mixe |
|                                           | Non-Hotspot | 556 | 0.44 | 0 (0.00%) | 1.6 (0.77) | Mixe |
| Year         | Type  | Start Date       | End Date       | Duration | Hotspot Count | % of Hotspot | Non-Hotspot Count | % of Non-Hotspot | Mixed Count | % of Mixed |
|-------------|-------|------------------|---------------|----------|---------------|---------------|-------------------|------------------|-------------|-----------|
| 2008-2009   | HTP   | 01/07/2008       | 12/01/2009    | 28 weeks | 128           | 33.53         | 447               | 5.46             | 28          | 21.87     |
|             |       |                  |               |          |               |               |                   |                  |             |           |
| 2009 LTP    | (0.88)| 13/01/2009       | 03/08/2009    | 29 weeks | 27            | 10.66         | 548               | 0.5              | 0           | 0.00      |
| 2009-2010   | HTP   | 04/08/2009       | 15/02/2010    | 28 weeks | 62            | 27.04         | 513               | 5.17             | 23          | 37.1%     |
| 2010 LTP    | (0.83)| 16/02/2010       | 12/07/2010    | 21 weeks | 22            | 12.61         | 553               | 0.41             | 0           | 0.00      |
| 2010-2011   | HTP   | 13/07/2010       | 24/01/2011    | 28 weeks | 142           | 80.26         | 433               | 19.61            | 77          | 54.22     |
| 2011 LTP    | (2.73)| 25/01/2011       | 22/08/2011    | 30 weeks | 43            | 12.69         | 532               | 1.57             | 0           | 0.00      |
| 2011-2012   | HTP   | 23/08/2011       | 09/01/2012    | 20 weeks | 105           | 34.35         | 470               | 9.59             | 0           | 0.00      |
| 2012 LTP    | (1.66)| 10/01/2012       | 09/07/2012    | 26 weeks | 10            | 19.16         | 565               | 1.24             | 0           | 0.00      |
|             |       |                  |               |          | 147           | 119.24        |                   |                  | 0           | 0.00      |

Grasslands: 40.79%
| 2012 HTP (38.1)          | 10/07/2012 - 31/12/2012 - 24 weeks |
|-------------------------|------------------------------------|
| Non-Hotspot             | 428                                |
| 25.74                   | 0 (0.00%)                          |
| 30.49 (1.93)            | Mix                                |

* Cumulative incidence rate (cases/100,000 person-weeks)

** Number and percentage of villages that received SMC (seasonal malaria chemoprevention)

*** Standard deviation

**** Dominant vegetation type for each period

**Hotspot characterization during HTPs**

The cluster analysis helped to detect 356 villages (out of 575) that were malaria hotspots at least once during HTPs (Table 2).

During HTPs, the median malaria incidence in hotspot and non-hotspot villages was 33.94 and 7.53 cases/100,000 person-weeks, respectively (Table 1).

The 2012 HTP had the largest number of hotspot villages (147). These villages were mostly located in the northeast of the study area (Figure 2), and were dominated by grasslands (representing 59.9% of villages). By contrast, the 428 non-hotspot villages were dominated by mixed vegetation (representing 51.2% of villages). This HTP showed the highest cumulative malaria incidence rate in both hotspot and non-hotspot villages (119.24 and 25.74 cases/100,000 person-weeks, respectively) (Table 1). It also showed the highest weekly average rainfall in both hotspot and non-hotspot villages (31.71 and 30.49 mm/week, respectively).

The 2009-2010 HTP was the least affected HTP by malaria, with only 62 hotspot villages (37.1% of which received SMC intervention) compared to 513 non-hotspot villages (39.18% of which received SMC intervention). Hotspot villages were mainly located in the southeast.
of the study area (Figure 2). The cumulative malaria incidence rate in hotspot and non-hotspot villages was 27.0 and 5.17 cases/100,000 person-weeks, respectively. The weekly average rainfall was low (but not the lowest) at 20.61 and 18.21 mm/week, respectively. Both hotspot and non-hotspot villages were dominated by mixed vegetation (representing 93.55% and 83.04% of villages, respectively).

**Hotspot characterization during LTPs**

The cluster analysis helped to detect 82 villages (out of 575) that were malaria hotspots at least once during LTPs (Table 2).

During LTPs, the median malaria incidence in hotspot and non-hotspot villages was 12.65 and 0.87 cases/100,000 person-weeks, respectively (Table 1).

The 2011 LTP had the longest duration (30 weeks) and showed the highest number of hotspot villages (43). These villages were located mainly in the south of the study area (Figure 2). This LTP showed a high cumulative malaria incidence rate in hotspot villages and the highest cumulative malaria incidence rate in non-hotspot villages (12.69 and 1.57 cases/100,000 person-weeks, respectively). The weekly average rainfall was fairly high at around 9 mm/week in both hotspot and non-hotspot villages. Hotspot villages were dominated by mixed vegetation (representing 72.09% of villages), whereas non-hotspot villages were dominated by grasslands (representing 40.79% of villages).

The 2010 LTP had the shortest duration (21 weeks) and 22 hotspot villages located in the northwest and west-central parts of the study area (Figure 2). The cumulative malaria incidence rate in hotspot villages was 12.61 cases/100,000 person-weeks, compared to a very low cumulative malaria incidence rate of 0.41 cases/100,000 person-weeks in the 553 non-hotspot villages. The weekly average rainfall was low at around 3 mm/week in both hotspot and non-hotspot villages.

The description of the others periods transmission is available in additional file 2.
Spatio-temporal distribution of hotspot villages (red dots) and non-hotspot villages (black dots) along with vegetation type (Landcover: open shrublands in beige, grasslands in orange, croplands in yellow, and mixed vegetation in green) over transmission periods (LTP, HTP) from 2008 to 2012 in Bambey and Fatick districts, Senegal.

Factors associated with the spatio-temporal variation of malaria hotspots

According to the multivariate analysis (GAMM, 38% deviance explained), villages receiving SMC intervention were protected from the risk of being a hotspot (OR=0.48, 95%CI: (0.33, 0.68). The random effect of health posts was significant (τ=0.53, 95%CI: (0.31, 0.88).

To make easy the interpretation, the value of smooth (spline) functions of covariates on different values of the covariates were called SRE as “smooth relationship estimation”.

For villages dominated by open shrublands, the risk of being a hotspot did not vary over time (Figure 3, panel A). A non-linear association was found between rainfall and the risk of being a hotspot (p=0.0002; Figure 4, panel A). When rainfall was not very abundant, these villages were relatively protected from the risk of being a hotspot. However, this risk became significant from 15 mm/week rainfall (SRE=1.26, 95%CI: (0.09, 2.43)); it continued to increase before stabilizing at a maximum rainfall of around 22 mm/week (SRE=2.47, 95%CI: (1.24, 3.7)).

For villages dominated by grasslands, the risk of being a hotspot varied significantly over time (p<0.0001; Figure 3, panel B). This risk became significant and increased from late December 2009 (SRE=0.76, 95%CI: (0.12, 1.40)), peaked in early November 2010 (SRE=2.13, 95%CI: (1.45, 2.82)), and then decreased until late September 2011 (SRE=0.46, 95%CI: (0.03, 0.9)). These villages were protected from the risk of being a hotspot from early January 2012 (SRE= -0.65, 95%CI: (-1.2, -0.1)) to late December 2012 (SRE= -2.04, 95%CI: (-3.22, -0.84)). Moreover, a non-linear association was found between
rainfall and the risk of being a hotspot (p<0.0001; Figure 4, panel B). When rainfall was not very abundant, these villages were relatively protected from the risk of being a hotspot. However, this risk became significant from 19 mm/week rainfall (SRE=0.52, 95%CI: (0.01, 1.04)) and increased with rainfall.

For villages dominated by croplands, the risk of being a hotspot varied little over time (p=0.0013; Figure 3, panel C). This risk became significant from late April 2010 (SRE=0.58, 95%CI: (0.07, 1.08); it peaked in mid-November 2010 (SRE=1.08, 95%CI: (0.48, 1.68)), and then decreased until mid-May 2011 (SRE=0.7, 95%CI: (0.01, 1.42)). These villages were relatively protected from the risk of being a hotspot from late January 2012 to late December 2012 (SRE= -0.63, 95%CI: (-1.2, 0.05) to SRE= -1.17, 95%CI: (-2.12, -0.25)). Moreover, a non-linear association was found between rainfall and the risk of being a hotspot (p<0.0001; Figure 4, panel C). When rainfall was not very abundant, these villages were relatively protected from the risk of being a hotspot. However, this risk became significant from 18 mm/week rainfall (SRE=0.72, 95%CI: (0.09, 1.36); it continued to increase roughly with rainfall.

For villages dominated by mixed vegetation, the risk of being a hotspot varied over time (p<0.0001; Figure 3, panel D). This risk increased from mid-June 2008 (SRE=0.42, 95%CI: (0.14, 0.7)), peaked in early April 2011 (SRE=2.16, 95%CI: (1.61, 2.71)), and then decreased until mid-October 2011 (SRE=0.48, 95%CI: (0.09, 0.87)). These villages were protected from the risk of being a hotspot from late November 2011 (SRE= -0.4, 95%CI: (-0.76, -0.03)) to late December 2012 (SRE= -2.65, 95%CI: (-3.22, -1.97)). Moreover, a non-linear association was found between rainfall and the risk of being a hotspot (p<0.0001; Figure 4, panel D). Once again, when rainfall was not very abundant, the villages were relatively protected from the risk of being a hotspot. This risk became significant from 21 mm/week rainfall (SRE=0.29, 95%CI: (0.02, 0.56); it continued to
increase linearly with rainfall.

Temporal evolution of the risk of being a hotspot (continuous black curve) with 95% confidence interval (discontinuous black curves) according to each vegetation type: open shrublands (panel A), grasslands (panel B), croplands (panel C), and mixed vegetation (panel D). HTPs and LTPs are indicated in grey and white, respectively. The vertical red lines indicate the dates of interest in which villages were at risk to be hotspot. The horizontal red lines indicate the zero reference line.

Evolution of the risk of being a hotspot (continuous black curve) with 95% confidence interval (discontinuous black curves) according to weekly rainfall and to each vegetation type: open shrublands (panel A), grasslands (panel B), croplands (panel C) and mixed vegetation (panel D). Vertical red lines show the amount of rainfall from which the rainfall became a risk factor.

According to the spatial interpolation obtained with the multivariate GAMM for the entire study (Figure 5), 2 zones (red colour) located in the southwest and southeast of the study area had the highest risk of being a hotspot (SREmin=0.64, 95%CI: (0.02, 1.27); SREmax=4.1, 95%CI: (3.29, 4.92)). Moreover, villages located in 2 geographically restricted areas—one in the extreme northwest and the other in the east-central part of the study area (blue colour)—were relatively protected from this risk (SREmin= -8.99, 95%CI: (-12.96, -5.02); SREmax= -0.8, 95%CI: (-1.57, -0.03)).

Spatial distribution of the different hotspot types and the associated non-linear effect of village location from spatial interpolation: smooth relationship estimation (SRE). X is the longitude, Y the latitude, Z is SRE, the black curves are the contour for SRE, the coloured
bar indicated the ascending level risk of SRE from blue to red, Red dots represent the villages that were a hotspot during all 5 LTPs (Hot5LTP), orange dots those that were a hotspot mainly during HTPs (MajoHotHTP), yellow dots those that were a hotspot mainly during LTPs (MajoHotLTP), blue dots those that were a hotspot equally during HTPs and LTPs (EquaHTPLTP), green dots those that were never a hotspot (NeverHot), brown dots those that were a hotspot only during HTPs (OnlyHotHTP), and black dots those that were a hotspot only during LTPs (OnlyHotLTP).

Table 2.
Distribution of hotspot and non-hotspot villages: number and percentage of villages that were a hotspot during all 5 LTPs ; a hotspot mainly during HTPs ; a hotspot mainly during LTPs ; a hotspot equally during LTPs and HTPs ; never a hotspot ; a hotspot only during HTPs ; and a hotspot only during LTPs .

| Hotspot type                  | Hotspot during all 5 LTPs | Hotspot mainly during HTPs | Hotspot mainly during LTPs | Hotspot equally during LTPs and HTPs | Never a hotspot | Hotspot only during HTPs | Hotspot only during LTPs | Hot dur |
|------------------------------|----------------------------|----------------------------|----------------------------|-------------------------------------|----------------|--------------------------|--------------------------|---------|
| Number of villages (%)       | 3 (0.52%)                  | 47 (8.17%)                 | 5 (0.87%)                  | 13 (2.26%)                         | 205 (35.65%) | 288 (50.1%)              | 14 (2.4)                 |         |

Discussion

In our study, the risk of a village being a malaria hotspot varied over time and space, depending on meteorological, environmental, and preventive factors. Two malaria transmission periods types were identified, with HTPs extending from July-August to January-February of the next year, well after the end of the rainy season. Similar transmission dynamics have been reported in Mali (Bamako and Bandiagara) [15, 33] and Burkina Faso (Ouagadougou) [34].

During LTPs, malaria remained present at low to very low incidence in the study area, only 5 weeks showed no recorded cases (3 non-consecutive weeks in 2009, 1 week in 2010 and 2012) this confirmed malaria was endemic in the study area.

Our findings indicate that the temporal dynamics of malaria incidence should be taken into account in studies of malaria in the Sahel. Moreover, they highlight the importance of
collecting data beyond the end of the rainy season, as opposed to aggregating them by calendar year. The latter approach fails to accurately represent HTPs and may therefore hinder the effectiveness of control strategies. In our study, the last HTP was slightly incomplete due to the fact that data were collected from January 1st, 2008 to December 31st, 2012.

While hotspots have enjoyed renewed interest since the 2000s [35], there is no consensus on their definition or on the method to be adopted for their detection [8, 21, 36, 37]. Our study used the statistical definition given by the Kulldorff cluster detection method [31]. Because its performances are known to be sensitive to edge effects and non-circular clusters [38, 39], an elliptical window was used to minimize this impact and the Oliveira measure to assess the clusters edge [40]. However, 14 villages located in the southwest of the study area were never identified as hotspot villages in our cluster analysis, even though spatial interpolation obtained with the multivariate GAMM found that the risk of being a hotspot was high in this zone (Figure 5). Knowing that SaTScan performance improves with incidence level, size of at-risk population, and relative risk [41, 42], we divided the malaria incidence rate time series into HTPs and LTPs with the change point analysis method before assessing spatial clusters to facilitate the detection of hotspot villages during low transmission period. In addition, in a highly seasonal transmission setting, the dynamics can greatly vary between the seasonal peak (where incidence is expected to increase) and the low-transmission season (where incidence might persist at low intensity). The spatial location of cases in the high incidence season, due to favourable conditions for transmission is expected to be more spread out compared to the low-transmission season. While analysis of high transmission periods allows the identification of zones that have contain the highest burden in terms of cases, a separate
analysis of low transmission could lead to the identification of persisting transmission foci, which could play a significant role in the restauration of yearly epidemics. These elements can help the Senegal malaria program to refine their targeted control strategies. Moreover, the study area is one of global low transmission (incidence <5%), there, the Senegal malaria program is already focused on hotspots: focal test and treat, focal screen and test, focal drug administration, epidemic response indoor residual spraying, primaquine single low-dose [43]. Our approach was similar to other studies in Mali and Burkina Faso [33, 34, 44].

The hotspot variation is not obvious. In our study, the location of hotspots was unstable over transmission periods (LTPs and HTPs). Seasonal and annual instability of malaria hotspots (household and village scales) was also reported in Kenya and in Sudan (Khartoum) [3, 7, 8, 21, 45]. By contrast, malaria hotspots was relatively stable in Burkina Faso (Ouagadougou and Nanoro) and in Mali [15, 34, 44] and P. falciparum carriers hotspots was stable in Kenya [8]. Moreover the data on parasite carriage were not available for this study. Thus, the relation between hotspot, the force of infection and clinical incidence was not studied as in other study [8].

Our study found non-linear associations between meteorological, environmental, and preventive factors and the risk of being a hotspot that varied over time and space and according to health post (significant random effect).

The aim was here to see more how the variation of factors (as meteorological and environmental factors) could impact on the variation of being hotspot for a village over time and space. Our results showed that rainfall was positively associated with the risk of being a hotspot, and this non-linear association depended on vegetation type. While the relationship between rainfall and malaria occurrence has been widely discussed [15, 33, 34, 46, 47], our study indicates that the impact of rainfall on malaria occurrence depends
on both amount of rainfall and vegetation type, and this interaction in turn modifies hotspot distribution. Thus, for villages dominated by open shrublands, the risk of being a hotspot increases from the first rains and then reaches a plateau from 22mm/week, likely because heavy rains destroy breeding sites [48, 49]. By contrast, for villages dominated by grasslands, croplands, or mixed vegetation, the risk of being a hotspot increases only when rainfall is above 10 or 15mm/week. The low SRE corresponding to the beginning of the curves (Figure 4, panel C) may be explained by soil quality or ploughing practices that increase water infiltration [50] and reduce breeding sites. In view of the spatio-temporal instability of hotspots, we attempted to give similar particularities of hotspots based mainly on environmental and meteorological factors changing. These latter contribute to the heterogeneity of malaria distribution. So, surveillance on these factors [51], knowing the similar environmental and meteorological particularities of hotspots, could lead targeted public health interventions in local context.

Moreover, in our study, the risk of being a hotspot varied according to the geographical location of villages (Figure 5), which confirms results from studies conducted in India [52], Kenya [21], and Ghana [53]. Thus, almost all of the villages that were never a hotspot during the 10 transmission periods were located in the 2 zones with the lowest risk, i.e., in the northwest and east-central part of the study area (Figure 5). While the risk of being a hotspot was highly variable in the south, 3 villages located in the zone with the highest risk were hotspot during all LTPs. Such persisting hotspots during LTPs can be the source of the seasonal increase in malaria transmission [3, 5, 54]. Furthermore, data on mobility and asymptomatic parasite carriers were not available in this study to assess the source of transmission or the reservoir of infections [55], but they are an important and increasingly reported source of malaria in low transmission areas [37, 56]. These data could be one of the factor explaining the instability of the hotspots over space and time.
Lastly, our study found that villages receiving SMC intervention were protected from the risk of being a hotspot, corroborating studies that highlighted the effectiveness of SMC interventions in Senegal [16, 57]. Yet despite the implementation of malaria control strategies combining SMC, mass drug administration, long-lasting insecticide-treated nets, and indoor residual spraying [6, 57–60], malaria incidence remains high in the country [2]. Malaria control strategies are generally implemented at the beginning or in the middle of the rainy season [16, 57–60], which effectively corresponds to HTPs. Yet our findings, suggest that the increase in malaria incidence in hotspot villages and persisting hotspots observed during LTPs can also affect malaria transmission during HTPs. In view of this, we recommend that spatially targeted strategies identifying transmission bottlenecks, be further addressed during LTPs, as this may shrink the parasite reservoir and thereby prevent malaria transmission during subsequent HTPs.

**Strengths**

We worked on quality data from a randomized trial with a very fine and precise temporal and spatial scale. With a set of spatial and temporal analysis methods, our study developed a methodology that explained the variation over time and space of malaria hotspots. This allowed an estimate of the risk of hotspot at any time and in anywhere in the study area. This study also allowed to assess the impact of the interaction between rainfall and vegetation on the risk of hotspots. Therefore we obtained an estimate of the risk of hotspot depending on the amount of rain and the type of vegetation. This can be done for any other factors.

**Limitations**

Data on rainfall and vegetation types were not observed but were obtained from remote sensing data. Thus some villages had the same rainfall as their neighbours because of the pixel resolution. Socio-economic and behaviour data were not available to further explain the variation of hotspots. Parasite reservoirs were not taken account in this study because asymptomatic parasitaemia data were not available.

**Conclusion**

This study highlights the important variability (even at a very local scale) of malaria transmission in central Senegal over space and time, as well as the impact of meteorological, environmental, and protective factors on malaria risk. Knowing the similar
environmental and meteorological particularities of hotspots, surveillance on these factors could lead targeted public health interventions in local context. Moreover, the issue of spatial hotspots and foci of malaria persistence during LTPs needs to be further addressed.

Declarations

**Ethics approval and consent to participate**

Not applicable in our study.

But the one of the institutions responsible of the SMC trial is « The SMC trial protocol was approved by Senegal’s Conseil National pour la Recherche en Santé and the ethics committee of the London School of Hygiene & Tropical Medicine. The trial is registered at www.clinicaltrials.gov, number NCT 00712374. »

**Consent for publication**

Not applicable.

**Availability of data and materials**

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request. But a request of raw data is possible with this reference:

Milligan, P (2016). Effectiveness of Seasonal Malaria Chemoprevention in children under 10 years of age in Senegal: a stepped-wedge cluster-randomized trial. [Data Collection]. London School of Hygiene & Tropical Medicine, London, United Kingdom.

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**Competing interests**

The authors declare that they have no competing interests.

**Authors’ contributions**

SD and JG designed the study, performed data validation and cleaning, performed the
statistical analysis and interpretation, and wrote the first draft of the article; EB, BC, CS, MP, SR coordinated the data collection and description; KS contributed to the cleaning and validation of the data, KS, BO, MP, JL and RP contributed to the interpretation of the results; AG contributed to the statistical analysis. All authors read and approved the final manuscript.

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Additional Files

Additional file 1.

Additional file 1.tiff

Vegetation type for each village determination: A 0.55 km radius buffer zone is defined around a village (light blue point) in 2012. Each colour represents a vegetation type: open shrublands (beige, 67.2%), grasslands (orange, 26.2%), croplands (yellow, 3.1%), and mixed vegetation (green, 3.5%). Thus, the modal vegetation type for this village in 2012 is open shrublands.

Additional file 2.
The descriptions of the others transmission periods: 2010-2011 HTP, 2011-2012 HTP, 2008-2009 HTP, 2012 LTP, 2009 LTP and 2008 LTP

Figures

Figure 1

Evolution of weekly cumulative malaria incidence rate (continuous red curve); High Transmission Period (HTP, in grey) and Low Transmission Period (LTP, in white) with duration (weeks, in black) and their cumulative incidence rates (in red); weekly cumulative rainfall (in blue).
Spatio-temporal distribution of hotspot villages (red dots) and non-hotspot villages (black dots) along with vegetation type (Landcover: open shrublands in beige, grasslands in orange, croplands in yellow, and mixed vegetation in green) from 2008 to 2012 in Bambey and Fatick districts, Senegal.
Figure 3

Temporal evolution of the risk of being a hotspot (continuous black curve) with 95% confidence interval (discontinuous black curves) according to each vegetation type: open shrublands (panel A), grasslands (panel B), croplands (panel C), and mixed vegetation (panel D). HTPs and LTPs are indicated in grey and white, respectively. The red lines indicate the dates of interest.
Figure 4

Evolution of the risk of being a hotspot (continuous black curve) with 95% confidence interval (discontinuous black curves) according to weekly rainfall and to each vegetation type: open shrublands (panel A), grasslands (panel B), croplands (panel C) and mixed vegetation (panel D).
Spatial distribution of the different hotspot types and the associated log(OR) from spatial interpolation. Red dots represent the villages that were a hotspot during all 5 LTPs (Hot5LTP), orange dots those that were a hotspot mainly during HTPs (MajoHotHTP), yellow dots those that were a hotspot mainly during LTPs (MajoHotLTP), blue dots those that were a hotspot equally during HTPs and LTPs (EquaHTPLTP), green dots those that were never a hotspot (NeverHot), brown dots those that were a hotspot only during HTPs (OnlyHotHTP), and black dots those that were a hotspot only during LTPs (OnlyHotLTP).
Supplementary Files

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Additional File 1.jpg
Addional file 2.pdf