

Setting the malaria epidemic threshold in the Central Health Region of Burkina Faso using historical data

Running Title: Setting malaria epidemic threshold

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Abstract

Introduction: Malaria has been endemic in Burkina Faso. Setting epidemic thresholds is then crucial for early detection and responses. We compared three methods for epidemic detection in the Central Health Region of Burkina Faso using historical data between 2013-2016.

Methodology: Monthly malaria data from 2013 to 2015 were used as the baseline to set the thresholds. Three methods were applied: quartiles, mean + 2 Standard Deviation (SD), and cumulative sum (C-sum). The median and third quartile, as well as the mean and the mean + 2 SD were calculated per month, for the baseline period, and plotted in a graph with the monthly malaria cases of 2016. For each month, the number of cases of the previous and following months between 2013-2015 was summed up and divided by 9. These monthly average numbers were refined with the 1.96 SD and plotted with the 2016 monthly malaria cases. Any time that the 2016 line crossed the quartiles, the mean and the C-sum thresholds, an unexpected increase in malaria cases was caught.

Results: Cases were higher every month of 2016 compared to the corresponding months of the previous three years. The Quartiles method detected the whole 2016 year as unusual. Using the mean + 2SD method, malaria cases raised unusually in 2016, except for August, whereas the C-sum + 1.96 SD method did not detect outbreaks in July.

Conclusions: Not dependent on extreme values, the quartiles method seems more reliable to capture an abnormal rise in malaria cases. This increase in cases would be due to the free healthcare policy for children and pregnant women launched in 2016. Abnormal rise should always be investigated before confirming an epidemic.

Keywords: malaria, threshold, epidemic, mean, median, cumulative sum

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Fixer le seuil épidémique du paludisme dans la Région Sanitaire du Centre du Burkina Faso en utilisant des données historiques.

Titre courant : Fixer le seuil épidémique du paludisme

Résumé

Introduction: Le paludisme est endémique au Burkina Faso. La définition de seuils épidémiques est essentielle pour la détection précoce et la réponse du système de santé. Nous avons comparé trois méthodes de détection du seuil épidémique de paludisme en utilisant des données retrospectives dans la Région Sanitaire du Centre du Burkina Faso en 2016.

Méthodologie: Les données mensuelles sur le paludisme de 2013 à 2015 ont été utilisées comme base de référence pour définir les seuils épidémiques. Trois méthodes ont été appliquées : quartiles, moyenne + 2 écarts types (ET) et somme cumulée (C-sum). La médiane et le troisième quartile, ainsi que la moyenne et la moyenne + 2 ET ont été calculés par mois, pour la période de référence, et représentés sur un graphique avec les cas de paludisme mensuels de 2016. Pour chaque mois, le nombre de cas dudit mois, le nombre de cas du mois précédent et du mois suivant de 2013 à 2015 ont été additionnés et divisés par 9. Ce nombre moyen de cas par mois a été affiné avec l'écart-type de 1,96 et représenté sur un graphique avec les cas de paludisme mensuels de 2016. Chaque fois que la courbe de 2016 franchit les seuils des quartiles, de la moyenne et de la somme cumulée, une augmentation inattendue des cas de paludisme est ainsi edétectée.

Résultats: Les cas de paludisme ont été plus nombreux chaque mois de 2016 par rapport aux mois correspondants des trois années précédentes. La méthode des quartiles a détecté l'ensemble de l'année 2016 comme inhabituelle. En utilisant la méthode de la moyenne + 2 ET, 2016 a été épidémique à l'exception du mois d'août, tandis que la méthode de la somme cumulée + 1,96 ET n'a pas détecté d'épidémie de paludisme en juillet.

Conclusion: Ne dépendant pas des valeurs extrêmes, la méthode des quartiles semble plus fiable pour saisir une augmentation anormale des cas de paludisme. Cette augmentation des cas serait due à la gratuité des soins pour les enfants et les femmes enceintes commencée en 2016. Une hausse anormale doit toujours être investiguée avant de confirmer une épidémie.

Mots-clés: paludisme, seuil, épidémie, moyenne, médiane, somme cumulée

Introduction

Malaria is a mosquito-borne disease caused by a parasite of the genus *Plasmodium*. Worldwide, malaria cases decreased from 227 million in 2000 to 198 million in 2013 (1). In 2015, 212 million new cases and

429 000 deaths were reported, representing about a 50% decrease compared to 2000 and a 22% decrease regarding 2010 (2). Key actions including preventive measures, early detection and prompt management contributed to the reduction in the number of cases. The preventive measures included insecticide-treated nets (LLINs), indoor residual spraying (IRS), seasonal malaria chemoprevention (SMC) in young children and intermittent preventive treatment of malaria in pregnancy (IPTp) (3). In particular, the SMC has proven to be 88% effective against clinical malaria at 28 days and 61% effective at 29-42 days in Mali, The Gambia, Chad, Nigeria and Burkina Faso for children 3-59 months old (4).

Although a reduction in death rates has been observed between 2010 and 2018 worldwide, ninety percent (90%) of the cases and 90% of deaths occur in the African Region (5). Malaria is endemic in Burkina Faso and is the leading cause of morbidity and mortality in health facilities in the Central Health Region (6-8). The endemicity and magnitude of malaria mean that the notion of an epidemic is not usually evoked with malaria in Burkina faso. However, it must be recognised that there may be an usual baseline level of malaria, with the possibility of sporadic increases above this baseline, due to various reasons. The reference to an epidemic gives an opportunity to respond effectively. The challenge is to detect the epidemic as early as possible to put in place the necessary responses.

According to the World Health Organization (WHO), malaria is a priority for integrated disease surveillance and response in the African Region (9). Such monitoring aims to detect early an abnormal rise in the cases and to provide appropriate responses (9,10). Hence, in endemic areas like Burkina Faso, there is a need to set epidemic thresholds. For this purpose, several methods like quartiles, mean and cumulative sum are available (11-13). WHO recommends the quartiles method, using the median and the third quartile, to set the epidemic threshold (9,12). Cullen *et al.* suggested an approach using the Mean + 2 standard deviation (SD) of previous monthly malaria cases (10). The Centers for Disease Control and Prevention (CDC) developed the cumulative sum (C-sum) method that takes into account aberrant months in the threshold calculation (12,14). Mean +2SD, quartiles, and cumulative sum using daily, weekly, monthly or simulation data have shown excellent performance in detecting malaria epidemics in Ethiopia, Kenya, Thailand or Iran (10,15-18). These methods used

historical data to calculate the expected malaria cases, allowing to set a threshold for epidemic detection.

In this study, we report the use of the mean + 2SD, quartiles, and cumulative sum methods to detect malaria epidemics in 2016 in the Central Health Region of Burkina Faso.

I. Methodology

1.1. Study setting

Burkina Faso comprises 13 health regions. In each Region, disease surveillance and control are carried out by a regional health directorate. The estimated population of the Central Health Region increased from 2,329,499 inhabitants in 2013 to 2,637,303 in 2016 (6,19). It covers 2869 km² and consists of 5 health districts and many private health facilities (19). The Central Region has two seasons, which are: a dry season from October to April, and a rainy season from May to September.

The Central Health Region is endemic for malaria with a prevalence varying significantly between rainy and dry seasons, and a global sporozoite rate of 6.31% (20). According to the Rapid Urban Malaria Appraisal (RUMA) in Sub-Saharan Africa, malaria represents 29.3% to 41.4% of all admissions in Ouagadougou (21). Although malaria case fatality rates in the Central Health Region were not the highest of the country, its incidence remains high, lying above 13.7 per 10,000 person-weeks (22,23). The Entomological Inoculation Rates (EIR) of malaria were estimated at 7 infected bites/person/year in 1986 for the urban areas of Ouagadougou, but recent data lack (24,25).

Malaria case definition

Malaria cases were defined based on clinical diagnosis (fever or recent history of fever over 72 hours) and a positive rapid diagnostic test or microscopic evidence of *Plasmodium* by thick drop/blood smear (9).

1.2. Data source

Monthly reports on malaria in the Central Health Region were collected from the National Health Information System (NHIS) of Burkina Faso. Malaria data covering 2013 to 2016 were obtained following a request to the Regional Health Directorate of the Centre.

Data in the NHIS goes through several stages of check and validation at all health system levels. Monthly reports from public and private health facilities are centralized at the district level by the Health Information and Epidemiological Surveillance Centres (CISSE). Hospital Information and Planning Services (SPIH) or Medical Information Services (SIM) are responsible for data management at the hospital level. Then, CISSE and SPIH or SIM enter the data into the Health Data Warehouse (Endos-BF) by the 20th of the month for M-1 data. The Central regional health directorate has until the 25th of the month to validate the Endos-BF M-1 data online. Finally, 15 more days are needed for final validation at the central level.

Data analysis

Quartiles, mean + 2SD, and cumulative sum were performed with historical malaria data, and the statistics were plotted using Microsoft Excel 2016.

Median and third quartile method

This method is recommended by the World Health Organization for malaria early warning system (9). To set the threshold for epidemic detection in 2016, we calculated the median and third quartile for monthly cases of malaria from 2013 to 2015. Then, we plotted the results on a graph. The area between the two curves was defined as the “normal channel.” Finally, the monthly malaria data for 2016 were plotted on the same graph. Whenever malaria cases were within the “normal channel”, an endemic situation was assumed. An epidemic was warned when the 2016 malaria cases were above the third quartile.

Mean and mean + 2 SD method

This method was developed by Cullen *et al.* (10). To apply this method, we calculated the mean and standard deviation of monthly malaria cases from 2013 to 2015. Then, we plotted the results of the mean values and the mean +2SD for each month on the same graph to obtain the boundaries of the epidemic detection, respectively, the lower and the upper limits. Lastly, the monthly malaria data for 2016 were plotted on the graph. Each time that the number of cases exceeded the upper limit, an epidemic was suspected.

Cumulative sum method at the 3-months moving average

The cumulative sum has been developed by the Centers for Disease Control and Prevention (CDC) to set epidemic thresholds. We used a 3-years baseline data of malaria from 2013 to 2015 to calculate the C-sum. For each month, we calculated the average cases of the previous and following months from 2013 to 2015. For instance, the cumulative sum for February was calculated by summing the number of cases of January, February, and March 2013 to 2015 and dividing by 9.

The method was refined by adding 1.96 times standard deviations (SD) for each month to capture 95% of malaria cases. The C-sums and C-sums +1.96 SD were finally plotted on the same graph with the monthly malaria cases of 2016.

1.3. Ethics

The study used epidemiological data from the Regional Health Directorate that was secondary and already aggregated. They did not contain individual patients' identities and data. Thus, the study did not require an ethical approval.

II. Results

2.1. Trends in malaria cases between 2013 and 2016

From 2013 to 2016 (Jan 2013 to Dec 2016), 3,621,668 malaria cases were reported in total in the Central Health Region. Malaria was endemic, as cases were reported over the study period and every month within the year (Figure 1). Malaria cases were stable in the first half of the year and rose during the rainy season and after the rainy season, from July to December each year, with a peak in October. This situation defines two transmission levels: low from January to June; high from July to December. Further, cases were irregularly high in every month of 2016 compared to those from 2013 to 2015.

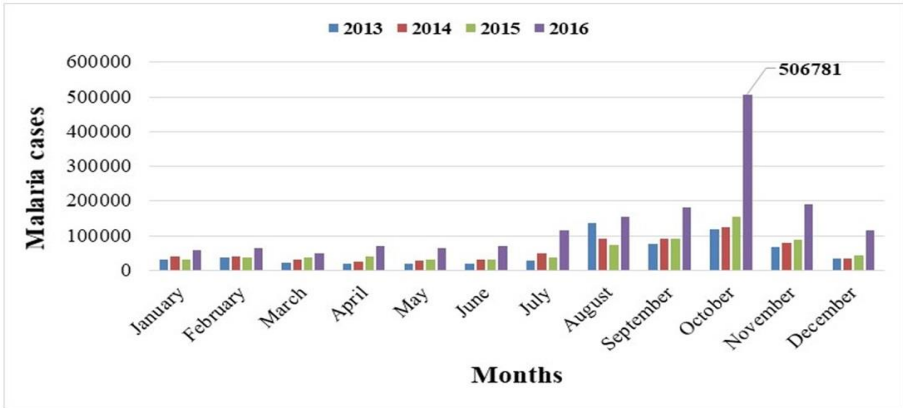


Figure 1. Monthly malaria cases in the Central Health Region, from 2013 to 2016, Burkina Faso

2.2. Malaria epidemic detection using quartiles and mean + 2SD methods

The malaria epidemic threshold is higher from July to December than from January to June. For the whole of 2016, malaria cases lay above the third quartile graph for each month, signalling an abnormal rise in cases (Figure 2). The Mean + 2SD method confirmed the unexpected increase in malaria cases in 2016, except in August, where the curve fell below the threshold. Indeed, the cut-off was set at 163,578 cases in August, while 153,310 malaria cases were reported in August 2016 (Table 1). Thus, 2016 showed an unusual increase in malaria cases in the Region, regardless of the method used, with a few exceptions.

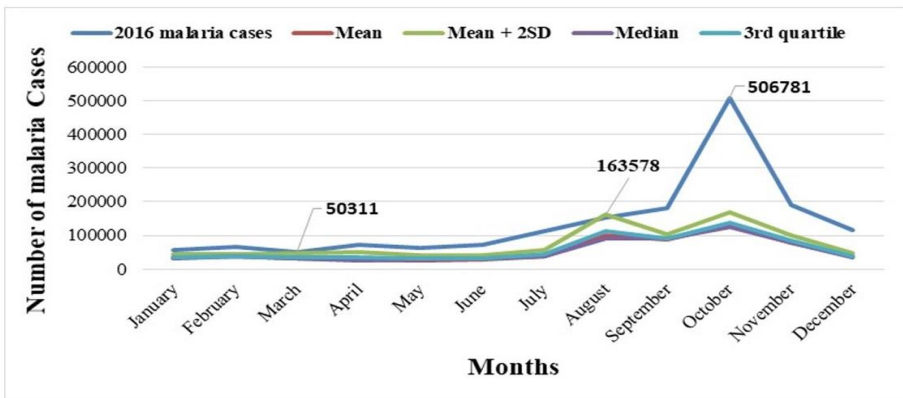


Figure 2. Malaria epidemic detection in 2016 in the Central Health Region of Burkina Faso using quartiles and mean + 2SD

Table I: Malaria epidemic cut-offs according to mean and quartiles methods in the Central Health Region of Burkina Faso

	Jan.*	Feb.	Mar.	Apr.	May	Jun.	Jul.	Aug.	Sep.	Oct.	Nov.	Dec.
Total number of cases in 2016	57934	64732	50311	71268	64359	70811	114071	153310	181113	506781	190176	114883
Median	31367	37379	32593	26662	28729	30861	38363	90914	92035	124012	80053	35444
3rd quartile	36082	39160	35427	33675	30475	31349	43464	113316	92333	138641	84787	38747
Mean	34189	38378	30706	28696	26867	27355	38770	100498	87390	131463	79344	36985
Mean + 2 SD	45675	42851	48014	50926	39842	41225	57965	163578	104524	169860	100441	45978

* *Jan.: January; Feb.: February; Apr.: April; Jun.: June; Aug.: August; Sept.: September; Oct.: October; Nov.: November; Dec.: December*

2.3. Malaria epidemic detection using cumulative sum

The cumulative sum method identified the whole 2016 year as unusual since malaria cases exceeded this lower limit (C-sum) throughout the year (Figure 3). After refining the technique with C-sum + 1.96 SD, only July 2016 was below this upper limit. The refined C-sum set the July cut-off at 130,048 cases; nonetheless, reported cases in the same month were lower at 114,071 cases (Table 2).

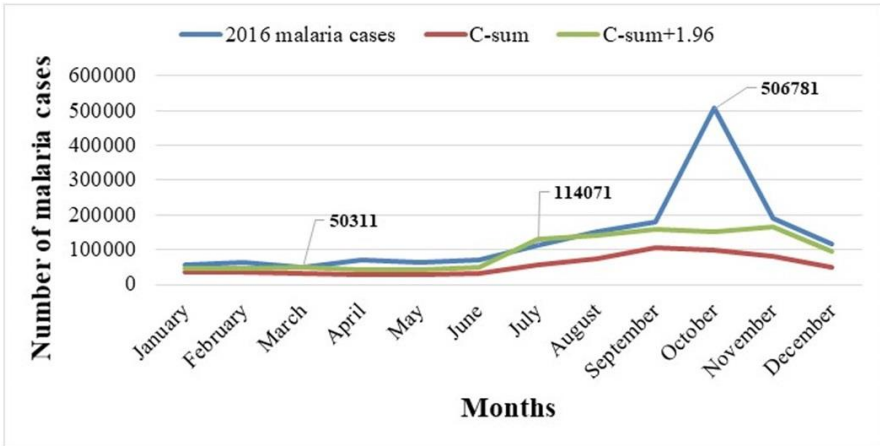


Figure 3. Malaria epidemic detection in 2016 in the Central Health Region of Burkina Faso, using the C-sum method

Table II. Malaria epidemic cut-offs using the C-sum method in the Central Health Region of Burkina Faso

	Jan.	Feb.	Mar.	Apr.	May	Jun.	Jul.	Aug.	Sep.	Oct.	Nov.	Dec.
Year 2016	57934	64732	50311	71268	64359	70811	114071	153310	181113	506781	190176	114883
C-sum	36517	34424	32593	28756	27639	30997	55541	75553	106450	99399	82597	50172
C-sum + 1.96	44824	46709	49043	44300	42056	48485	130048	140063	159888	152310	165859	94921

III. Discussion

In this paper, we reported the use of three simple tools to set thresholds and detect malaria epidemics in the Central Health Region of Burkina Faso.

In the Central Region, malaria cases followed a “seasonal peak” from July to December, probably due to optimal climatic conditions during the rainy season (26). Particularly, malaria cases peaked in October, beyond the rainy season. It is crucial for policymakers and implementers to know that malaria cases remain high at the end of the rainy season, allowing for better planification of the responses. Although rainfall, humidity and temperature are the most critical climatic factors that drew malaria transmission, its natural transmission simultaneously requires a certain range of rainfall, temperature, and relative humidity, with the former influencing the latter (27,28). High rainfall floods breeding sites while high temperatures would be harmful to mosquito larvae. Adequate rainfall during the rainy season will create mosquito breeding sites, while heat is known to influence egg-laying by female *Anopheles* mosquitoes and the hatching interval of eggs (27). Besides, relative humidity determines the survival and activity of female mosquitoes and affects the development and multiplication of Plasmodium, depending on temperature (27,29). However, the mechanisms leading to malaria transmission are complex, implying host immunity, environmental, and socio-economic factors.

Malaria cases were higher every month in 2016 compared to the years 2013-2015. This abnormal increase in malaria cases could warn an epidemic (18). Indeed, the quartiles method identified an unusual rise in malaria cases the entire year 2016. However, malaria cases did not exceed the mean + 2SD threshold in August 2016. It is so because the median is insensitive to extreme values, contrary to the mean. The quartiles method should be more reliable with the expected variability in malaria cases count within the year and from year to year. Large year-to-year variability would increase the threshold level of the Mean + 2 SD method and decrease the model sensitivity (12). But, this has been minimized here, as malaria cases reported during baseline years (2013-2015) had a similar level. These two methods were used successfully to set malaria epidemic thresholds in Ethiopia, Thailand, and Sudan (10,15,30).

The CDC cumulative sum method adjusts for seasonality, i.e., considers the within-year variability of malaria cases. From the C-sum results, the year 2016 showed an increase of malaria cases except in July. The C-sum +1.96 SD technique covers 95% of the malaria cases and raises the

threshold, leading to failure to alert an abnormal increase in cases for these months. This refinement aimed to improve the specificity in detecting outbreaks. But when there is significant variability in year-to-year cases, it would extend the 95% confidence interval, increase the threshold level, and influence the sensitivity (12). The C-sum technique and its refined version are considered more accurate than mean + 2 SD and quartiles. In Sudan, the latter caught more alerts than the mean + 2 SD and quartiles (30).

The increase in malaria cases captured by the epidemic thresholds tools must be confirmed or infirmed. Indeed, any unexpected increase in cases requires eliminating changes related to case definition, availability of diagnostic kits, or better reporting of cases. The introduction of free healthcare for pregnant women and children under five years in 2016 has probably increased the use of health services and improved the testing capacities, which increased reported cases. Therefore, malaria data before 2016 would reflect an underestimation of the situation, with data from 2016 closer to the actual figure. However, further research is needed to conclude on sources of the unexpected increase in malaria cases in 2016 in the Central Health Region of Burkina Faso. Given the lack of data before 2013, as ENDOS-BF has operated since 2013, further studies should also consider setting thresholds under the free healthcare regimen.

The ultimate goal of an early warning system is to respond early enough to influence the course of the epidemics. For vector-borne diseases like malaria, the primary intervention is to reduce the exposure to *Anopheles* mosquitoes, in addition to strengthening the case management (9). Hay *et al.* emphasized the necessity of an intersectoral response to handle malaria epidemics, as some causes may be out of the health system and require collaboration and engagement with other sectors to control the ongoing outbreak (31).

The main limitation of our study is the use of a 3-year baseline when the methods require a 5-year baseline (9,10,12). Despite this sprain, all three techniques detected the unexpected increase in malaria cases in 2016, except for some months. Then, these methods are reliable in detecting malaria epidemics in the Central Health Region of Burkina Faso, but the quartiles method turned to be more effective compared to the methods based on the mean (Mean, C-sum and refined), subject to outliers.

Conclusion

Winning the fight against malaria requires a responsive surveillance system. We reported in this study the use of routine data to set thresholds for detecting malaria epidemic in the Central Health Region of Burkina Faso. The quartiles method alerted an abnormal rise in malaria cases in the whole of 2016, seeming more reliable in setting epidemic thresholds in the region. Further exercise would question whether it is a true increase - epidemic - or a mechanical one due to case definition or policy change. In Burkina Faso, the free healthcare policy for vulnerable populations - pregnant women, children under five- ongoing since 2016 resulted in more reported malaria cases. A study using the data after 2016 will be considered, as they could reflect the actual level of malaria in the country.

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Conflict of interest

The authors declared no conflicts of interest regarding this article research, authorship, and/or publication.

Author contributions statement

JCRPO obtained the data following a request to the Regional Health Directorate of the Central Health Region. JCRPO and EMB analysed and interpreted the data, then wrote the manuscript with IY. DT, TAL, YD, JWJ, NT and DNN reviewed the manuscript and made substantial contributions. All the authors read and approved the final version.

Data availability

The dataset analysed during this study is available from the corresponding author or the Regional Health Directorate of the Centre on reasonable request.

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