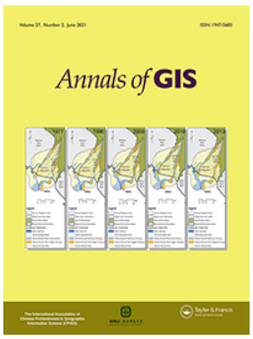

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ARTICLE

Geospatial analysis of malaria mortality in the kintampo health and demographic surveillance area of central Ghana

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ABSTRACT

Malaria remains a menace to the existence of humanity in most contexts. Geospatial analysis of malaria mortality is crucial to identifying clusters of high disease burden and areas with limited access to malaria care for targeted control and remedial interventions. This study identified spatial and space-time clusters of malaria mortality in the Kintampo area of central Ghana. We used 1301 malaria deaths archived from 2005 to 2017 and Global Positioning System (GPS) point locations of the sub-districts in which these deaths occurred for our analysis. Mortality risks were smoothed and mapped using the Spatial Empirical Bayesian smoothing technique in Geoda (version 1.12.1.161) whereas spatial and spatio-temporal clustering analysis was done using SaTScan (version 9.6). Malaria mortality risks ranged between 1.2 and 2.4 deaths per 1000 population for persons of all ages and between 3.3 and 6.0 deaths per 1000 population for children under five years of age by sub-district. Two spatial clusters were detected for all-age malaria mortality with only the primary cluster (RR = 1.42, p = 0.001) being statistically significant. Also, two statistically significant space-time clusters were detected for all-age malaria mortality in the study area. The most likely cluster occurred between 2006 and 2011 in five sub-districts with a relative risk of 2.12 ($p < 0.001$) whilst the secondary cluster which had a relative risk of 2.47 ($p < 0.001$) occurred between 2005 and 2010 in four sub-districts. Similarly, only the most likely spatial cluster of under-five malaria mortality was statistically significant (RR = 1.36, p = 0.024). Furthermore, three spatio-temporal clusters of under-five malaria mortality were detected in the study area. The primary and second secondary clusters were statistically significant whilst the first secondary cluster had borderline significance. The primary cluster (RR = 4.49, p = 0.002) occurred in two sub-districts between 2006 and 2007. The first secondary cluster (RR = 2.21, P = 0.005) covered four sub-districts and was detected between 2006 and 2011 whereas the second secondary cluster (RR = 2.51, p = 0.003) covered two sub-districts between 2008 and 2013. Ultimately, our analysis identified a number of substantial spatial and apace-time clusters of malaria mortality in the study context, which could aid in the strategic planning, implementation and monitoring of targeted malaria control interventions.

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Geospatial analysis; malaria mortality risks; spatial and space-time clustering; Ghana; Kintampo

Introduction

Malaria remains a relevant infectious parasitic cause of morbidity and mortality, particularly in sub-Saharan Africa (World Health Organization 2018; Agyingi, Ngwa, and Wiandt 2016). It is mainly caused by the transmission of plasmodium parasites to humans through infective bites of female anopheles mosquitoes (Pimenta et al. 2015) which are ubiquitous in the tropical world. The disease continues to ravage human populations in Africa south of the Sahara and south-east Asia where it is endemic with variations in transmission intensity and mortality risks. To date, the World Health Organization (WHO) has been the vanguard in mobilizing resources, developing programmes and coordinating efforts by governmental and non-governmental bodies to curb malaria transmission and its concomitant mortality in worst afflicted countries. Prominent among recent WHO-led control and eradication efforts is the commencement of two strategies in 2015 – the Global Technical Strategy for Malaria (GTS) 2016–2030 and Action and Investment to defeat Malaria (AIM) 2016–2030. The former spells out a vision for malaria eradication whereas the latter makes a strong argument for continuous investment in the fight against malaria (World Health Organization 2018).

Though geospatial variations in malaria endemicity, incidence and mortality occur worldwide, the brunt of the disease is invariably borne by populations in the global south particularly South Asia, Southeast Asia, South America and sub-Saharan Africa. However,

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there is evidence of a global slump in the proportion of people living in areas at risk of malaria infection from 48.5% in 2005 to 40.9% in 2017 (Weiss et al. 2019). Even so, sub-Saharan Africa remains the global hotspot of malaria morbidity and mortality as the increase in malaria-free areas did not reflect the gains achieved in other malarious regions (Weiss et al. 2019). Globally, 228 million cases of malaria occurred in 2018 with the greatest proportion (93%) coming from the WHO African region (World Health Organization 2018). Children under five years of age and pregnant women are especially hardest hit largely due to weak immunity in young children and physiological conditions associated with pregnancy that predispose expectant mothers to the disease. An estimated 67% (272,000) of global malaria deaths occurred among children under five years old in 2018 (World Health Organization 2018). The greatest proportion of these fatalities occurred in sub-Saharan Africa (World Health Organization 2018). Moreover, the WHO African Region alone accounted for 94% of the estimated 405,000 global malaria deaths in 2018 with 20 countries in the region and India contributing about 85% of all malaria deaths (World Health Organization 2018).

Ghana is one of the countries with the highest malaria burden in sub-Saharan Africa. However, some gains have been made in control efforts including the country's achievement of the highest rate (78%) of intermittent preventive treatment for pregnant women in the subregion (USAID President's Malaria Initiative: Ghana Malaria Operational Plan For Year 2016, 2016). Aggressive execution of mass media antimalarial campaigns, community-level distribution of long-lasting insecticide treated nets, indoor residual spraying (IRS) and early diagnosis and treatment of infections with approved artemisinin-based combination therapies (ACTs) are among the strategies deployed to control transmission (Ghana National Malaria Control Programme periodic bulletin 2016). These control efforts have resulted in a significant drop in malaria mortality in the WHO African region from 533,000 in 2010 to 380,000 in 2018 (World Health Organization 2018) though they are yet to be tailored to local control requirements of communities with particular attention to known hotspots of the disease (USAID President's Malaria Initiative: Ghana Malaria Operational Plan For Year 2016, 2016).

Cluster detection is the statistical analysis of spatial or spatio-temporal distribution of diseases or other occurrences of interest in order to identify specific areas and/or periods of their concentration. Clustering is crucial to the control of infectious diseases (Lessler et al. 2017) as it informs implementation of interventions (Musa et al. 2013; Bousema et al. 2016). Consequently, community scale clustering of malaria mortality can aid control interventions through targeting resources at hotspots, identification of ecologically suited areas for malaria for possible modification of the drivers of transmission in high mortality clusters (Cohen et al. 2017) and improved health service delivery. The significance of hotspot detection in malaria control has been described in a scientific analysis using data from Northern Tanzania (Bousema et al. 2012). In this study, the authors showed that targeting malaria hotspots with tools such as long-lasting insecticide-treated nets (LLINs) and indoor residual spraying (IRS) could eliminate the disease whilst untargeted interventions with similar tools would merely result in moderate decreases in parasite prevalence (Bousema et al. 2012). Targeted control interventions therefore allow for cost-efficient use of resources as they are deployed in specific local clusters of high disease burden. The utility of spatial clustering and mapping techniques in studying mosquito-borne infections has also been exemplified in spatial and spatio-temporal analysis of malaria in Brazil (Melchior and Neto 2016), spatial and space-time clustering of malaria mortality in rural Tanzania (Selemani et al. 2015), space-time clustering of chikungunya and dengue fever in Colombia (Desjardins et al. 2018), spatio-temporal clustering of childhood malaria in Mali (Gaudart et al. 2006) and the detection of local clusters of malaria in South Africa (Coleman et al. 2009). Cluster detection methods have also been applied in analysing other public health issues such as childhood asthma in Canada (Torabi 2012), cholera and childhood mortality in Ghana (Osei, Duker, and Stein 2012; Nettey et al. 2010).

Furthermore, spatio-temporal clustering and mapping of malaria mortality could provide relevant information to effectively guide, monitor and evaluate progress of control initiatives and their eventual impact on its burden in the affected areas (Musa et al. 2013; Bousema et al. 2016; Hay et al. 2009). Space-time cluster analysis could also reveal areas with lack of access to malaria care as people do not usually die if they are adequately treated.

The objective of this analysis was to identify significant spatial and space-time clusters of malaria mortality in the Kintampo area of the middle belt of Ghana. To achieve this, we used verbal autopsy-determined cause of death data and background population statistics obtained from

the archives of the Kintampo Health Research Centre's (KHRC's) Health and Demographic Surveillance System (HDSS) spanning the period 2005 to 2017.

Materials and methods

Study area

The Kintampo Health and Demographic Surveillance area encompasses the Kintampo North Municipality and Kintampo South District in the Northern part of the Bono East Region of central Ghana. Its geographic location is between latitudes 8°10′ and 8°65′ north of the equator and Longitudes 1°35′ and 2°00′ west of the Greenwich meridian. It covers an area of about 6,621 square kilometres. Northwards, it is bounded by the Black Volta River and westwards by the Banda and Bole districts. It is bounded by the East Gonja and Pru districts eastwards whilst it shares borders with the Wenchi Municipality, Techiman North and Nkoranza North districts southwards. The area covers 161 mainly rural communities with a resident population of 159,701 (Kintampo Health Research Centre GHS, Kintampo, Ghana 2017), which is tracked by trained fieldworkers in three-monthly cycles for updates on health and demographic events. It has a forest-savannah vegetation as it lies between the southern forest region and the northern savannah belt of the country. It experiences a continental tropical type of climate with a double maxima rainfall regime, which makes it conducive for agricultural productivity. The prevailing environmental conditions also drive malaria transmission by creating favourable grounds for vector breeding (Kelly-Hope, Hemingway, and McKenzie 2009).

Subsistence farming is the mainstay of most of the residents; though petty retail trading and commercial farming of maize, mango and cashew provides a source of livelihood for both urban and rural folks in the study area. Though Mo and Bono are the indigenous tribal groups, the area is ethnologically diverse as it hosts a large immigrant population from other parts of the country, particularly the northern territories. There are two hospitals (The Kintampo North Municipal Hospital and Kintampo South District Hospital), four private clinics, two public rural clinics, six health centres, two maternity homes and twenty-nine functional community-based health planning and services (CHPS) compounds in the area from which people access health services. The area is divided into 12 administrative sub-districts to facilitate health service planning and delivery (Figure 1).

Mortality and population data

We extracted malaria-specific deaths archived for communities in the Kintampo Health and Demographic Surveillance area for our analysis. These data included personal characteristics of the deceased persons such as age, gender and place of residence. The Kintampo Health and Demographic Surveillance System (KHDSS) has continuously collected, processed and archived mortality statistics in the HDSS catchment area since 2005. This is done through a team of trained field workers and Community Key Informants (CKIs) in well-structured

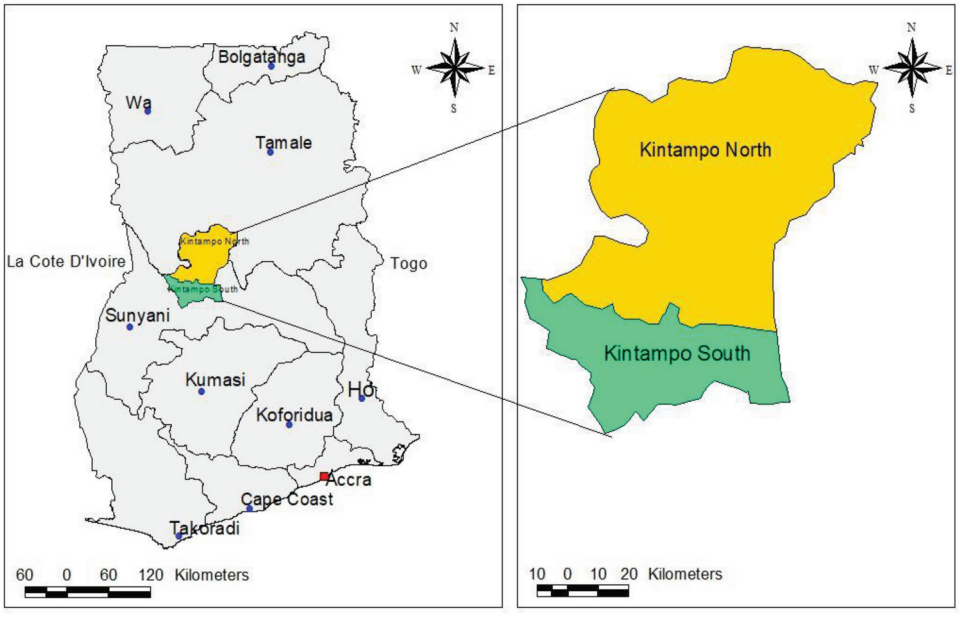

Figure 1. Map of Ghana highlighting the study area.

routine household visits. To ensure data integrity, field supervisors and/or research officers make unannounced spot-checks on field workers during data collection and conduct quality control by revisiting and interviewing a sample (1%) of the respondents interviewed earlier. Specific causes of death are determined through Verbal Postmortems (VPMs) conducted by trained field supervisors; and the forms independently coded by two qualified physicians using the 11th version of the coding manual of the International Classification of Diseases (ICD-11). Where the cause of death is undetermined, the physicians come together for consensus coding to ascertain the most probable cause of death. Additionally, we generated and summed mid-year population statistics for the 13-year period from the KHDSS' database for the respective sub-districts as the background population at risk of malaria mortality.

Geographic data

We recorded centroids of all sub-districts with handheld Global Positioning System (GPS) devices (Garmin etrex 10). These centroids were processed and archived in database file format using FoxPro version 6.0. Malaria mortality statistics for each sub-district were geocoded and visualized using unique sub-district codes embedded in the shapefile of the study area.

Spatial smoothing and mapping of malaria mortality risks

We computed malaria mortality risks for this analysis using all-age and under-five malaria deaths recorded in the study area between 2005 and 2017 for each sub-district as the numerator and a summation of the estimated mid-year all-age and under-five resident populations over the period as the background population at risk (denominator) (Buescher 1998). We did not adjust for age as our focus was on all-age and under-five malaria mortality risks, which we computed separately.

To curb variance instability or reduce the occurrence of spurious values in areas with small populations, we smoothed the crude mortality rates using the Spatial Empirical Bayesian (SEB) smoothing method in GeoDa version 1.12.1.161 (Anselin, 2004). We achieved this by first creating a contiguity-based second order rook spatial weights file (lower orders inclusive) covering all sub-districts in the study area with the weights manager in GeoDa (Anselin, Syabri, and Kho 2006). The SEB smoothing technique has an additional advantage of capturing the effect of spatial autocorrelation in the distribution of malaria mortality risks in the study area. With the weights file active in GeoDa, we calculated the smoothed risks as the weighted sum of the observed rate in each sub-district and the local or global mean rate. The weights were proportional to the neighbouring background population at risk. Hence, the risks in low population sub-districts with well-defined neighbours shrunk to the local mean whereas they adjusted towards the global mean in sub-districts without a clear spatial pattern. We subsequently created graduated-colour choropleth maps showing malaria mortality risks in the study area using ArcView GIS software (version 3.1) (Environmental Systms Research Institute (ESRI): ArcView GIS Version 3.1 2002). The risks were ranked in order of the relative burden of malaria mortality for persons of all ages and children under five years of age. Hence, mortality risks are low in sub-districts with lower rates of malaria deaths per 1000 population whereas they are high in areas with higher rates of malaria deaths.

Statistical analyses

We conducted spatial and spatio-temporal clustering analyses of malaria deaths using SaTScan version 9.6 (Kulldorff 2018). With this software, retrospective spatial and space-time scan statistics were employed to detect areas and periods with more than expected malaria mortality rates (clusters/hotspots). We used a Poisson probability model to scan for high rates, which is appropriate for dealing with count data particularly when there is a background population at risk of the event of interest (Talbot, Kumar, and Kulldorff 2014). As SaTScan usually detects the most likely clusters and secondary clusters of similar significance, the criteria for reporting hierarchical clusters was set to exclude geographical overlap in order to avoid possible overlapping of the most likely clusters by secondary clusters. We set the maximum cluster size to default (that is 50% of the background population at risk) as the study area is not large enough to warrant the choice of a smaller cluster size. Furthermore, we set the number of Monte Carlo replications to 999 so as to increase the statistical power of our analysis and ensure that the p-values produced have a finite number of decimals (Talbot, Kumar, and Kulldorff 2014). Finally, clusters with p-values <0.05 were considered statistically significant.

Results

Malaria deaths

The total number of malaria deaths recorded in the study area from 2005 to 2017 is presented in Table 1.

Table 1. Summary statistics of malaria mortality in the Kintampo HDSS area from 2005-2017.

Variable	Total mortality	Percentage
Malaria deaths	1,301	100
Sex		
Male	668	51.3
Female	633	48.7
Age group		
<5 years	539	41.4
5-19 years	158	12.1
20-59 years	291	22.4
60+	313	24.1
Place of residence		
Urban	334	25.7
Rural	967	74.3

Malaria deaths constitute about 12% of all-cause mortality. Males contributed a higher proportion of malaria deaths compared with females. Children aged less than five years recorded the highest proportion of deaths followed by persons aged 60 years and older. Likewise, majority of the deaths occurred among rural inhabitants (Table 1). The population for 2017 and malaria mortality rates per 1,000 population for the twelve sub-districts from 2005 to 2017 are shown in Table 2.

Spatial distribution of all-age and under-five malaria mortality risks

Overall, all-age malaria mortality risks for the thirteen-year period ranged between 1.2 and 2.4 deaths per 1000 population in the respective sub-districts. The Kintampo sub-district in the central part of the study area had the lowest risk of malaria mortality (range: 1.2 to 1.3 deaths per 1000 population). Moderately high risks of malaria mortality were observed in four sub-districts (Busuama, Kunsu, Amoma and Jema) with mortality risks ranging between 1.3 and 1.5 deaths per 1000 population. However, the risks of malaria mortality were higher in the Dawadawa, New Longoro, Anyima and Apesika sub-districts as the mortality rates in these areas ranged between 1.5 and 1.8 deaths per 1000 population. The highest malaria mortality risks (range: 1.8 to 2.4 deaths per 1000 population) were recorded in the two northernmost sub-districts (Kadelso and Gulumpe) and the Mansie sub-district in the southwestern part of the study area (Figure 2).

The distribution of malaria mortality risks for children under five years of age also highlights spatial variations in the study area. The risks map showed low mortality rates in two sub-districts located in the central and western parts of the study area with 3.3 to 3.5 deaths per 1000 population. Likewise, moderate mortality risks were observed in three areas to the north, west and south-west of the Kintampo sub-district (Dawadawa, New Longoro and Anyima). Though five of the sub-districts had relatively high under-five malaria mortality risks (4.8 to 5.2 deaths per 1000 population), the highest risks were observed in the two northernmost sub-districts (Kadelso and Gulumpe). Each of these three sub-districts had mortality risks between 5.2 and 6.0 deaths per 1000 population (Figure 2).

Spatial and space-time clusters of malaria mortality

The purely spatial and space-time scan statistical analyses respectively detected two spatial and spatio-temporal clusters of malaria mortality for all ages in the study area. Temporal variations in all-age malaria mortality clustering were also observed between 2005 and 2017 with both the primary and secondary temporal clusters showing high rates in 2010 (Figure 3). For the purely spatial analysis, only the most likely cluster of all-age malaria mortality was statistically significant (RR = 1.42, p = 0.001) (Table 3). This cluster comprised of the Kadelso and Gulumpe sub-districts in the northernmost part of the study area. The secondary spatial cluster of all-age malaria mortality covered the Mansie and Anyima sub-districts in the south-west of the study area though it was not statistically significant (RR = 1.26, p = 0.103) (Figure 4).

Table 2. Population and malaria mortality rates by sub-district and year (2005 - 2017).

Sub-district	Population (2017)	Yearly malaria mortality rates (per 1,000 population)*											
		2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Busuama	4,958	1.6	0.7	0	3.1	0.5	3.7	4.3	1.3	1.9	0.7	0.6	0.3
Dawadawa	6,444	6.2	1.0	1.8	0.8	2.4	3.3	3.0	1.8	1.3	0.7	0.6	0
Gulumpe	12,365	3.2	3.4	6.2	0.7	1.7	4.1	3.8	1.8	1.7	1.3	0.5	0.1
Kadelso	6,463	8.8	6.5	4.5	4.4	4.5	4.1	4.3	1.8	0.9	1.9	1.0	0
Kunsu	6,511	1.6	0.7	0	3.2	3.4	4.6	0.7	2.6	1.7	1.8	0	0
New Longoro	4,528	2.3	0	2.0	4.0	0	4.6	4.5	2.5	3.1	0.8	0.7	0
Kintampo	52,924	2.9	3.2	1.3	1.1	1.5	2.8	2.3	1.0	1.1	0.8	0.9	0.2
Amoma	14,169	1.7	2.3	2.4	2.2	1.4	2.5	3.5	1.5	1.0	0.9	0.5	0.1
Apesika	12,124	2.1	2.5	3.5	2.0	2.5	3.9	2.1	2.6	1.4	0.9	0.7	0
Jema	24,111	2.9	3.5	2.6	1.5	2.0	3.5	2.4	1.6	1.4	1.0	0.7	0.3
Mansie	6,634	1.5	1.4	1.9	3.9	4.5	4.6	2.0	2.8	2.8	1.9	0.7	0
Anyima	8,470	2.5	3.2	4.2	2.2	2.6	4.0	3.0	1.7	1.7	1.1	1.2	0
Total	159,701	2.9	2.8	2.5	1.8	2.0	3.4	2.8	1.6	1.4	1.1	0.7	0.1

*The yearly malaria mortality rates were calculated using the sub-district mid-year populations of the respective years (2005 - 2017) as the denominators.

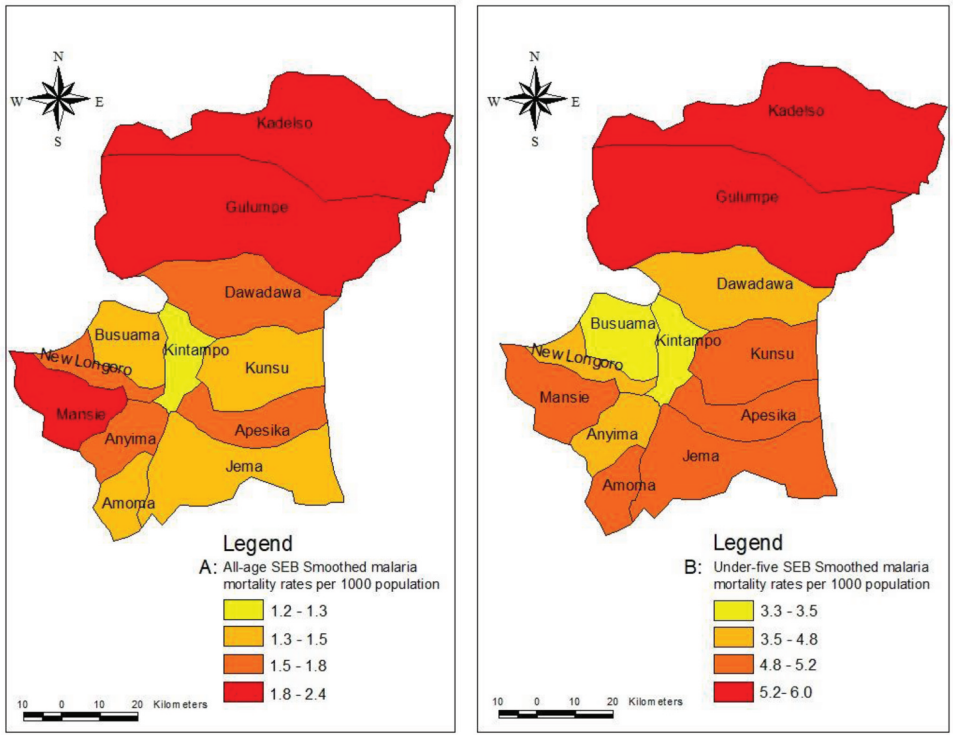

Figure 2. Spatial Empirical Bayesian smoothed all-age and under-five malaria mortality risks per 1000 population by sub-district.

The two all-age malaria mortality clusters detected using the space-time scan statistic were both statistically significant. The most likely cluster occurred between 2006 and 2011 in five sub-districts (Mansie, Anyima, Jema, New Longoro and Amoma) with a relative risk of 2.12 ($p < 0.001$) (Table 4). The secondary space-time cluster (RR = 2.47, $P < 0.001$) for all-age malaria mortality occurred between 2005 and 2010 in four (4) sub-districts (Dawadawa, Gulumpe, Kunsu and Kadelso) (Figure 4).

Furthermore, the purely spatial analysis for under-five malaria mortality detected two (2) clusters across the study area (Table 5); though only the most likely cluster had a statistically significant mortality risk (RR = 1.36, $p = 0.024$). This cluster comprised of the Dawadawa, Gulumpe, Kunsu and Kadelso sub-districts in the northern and eastern parts of the study area. The secondary cluster (RR = 1.18, $p = 0.608$) for under-five malaria mortality covered the Mansie, Anyima and Jema sub-districts (Figure 5).

For children under five years, the spatio-temporal analysis revealed three statistically significant space-time clusters over the study period (Table 6). The primary cluster, detected between 2006 and 2007 comprised of the Gulumpe and Kadelso sub-districts in the north with a relative risk of 4.49 ($p = 0.002$). The first secondary cluster encompassed four sub-districts (Amoma, Anyima, Jema and Mansie) between 2006 and 2011 with a relative risk of 2.21 and a borderline p-value of 0.005. The second secondary cluster (RR = 2.51, $p = 0.003$) was detected between 2008 and 2013 in the Apesika and Kunsu sub-districts (Figure 5).

Discussion

Overall, there has been a steady reduction in the number of malaria deaths nationwide due to improved diagnosis and treatment (Ghana National Malaria Control Programme periodic bulletin 2016). However, there remain areas of high malaria mortality risk in the country, which require the use of exploratory spatial data analysis (ESDA) and cluster detection methods (Anselin, Syabri, and Kho 2006) to identify as demonstrated in this study. The analysis has revealed a number of spatial and spatio-temporal clusters of significantly high malaria mortality risks for persons of all ages and children under five years within the study context. In general, we have observed a strong similarity between the sub-districts encompassed in both the purely spatial and space-time malaria mortality clusters detected by the respective scan statistics. Moreover, the observed space-time clustering of malaria deaths mostly occurred between 2005 and 2013 with the most likely all-age mortality cluster

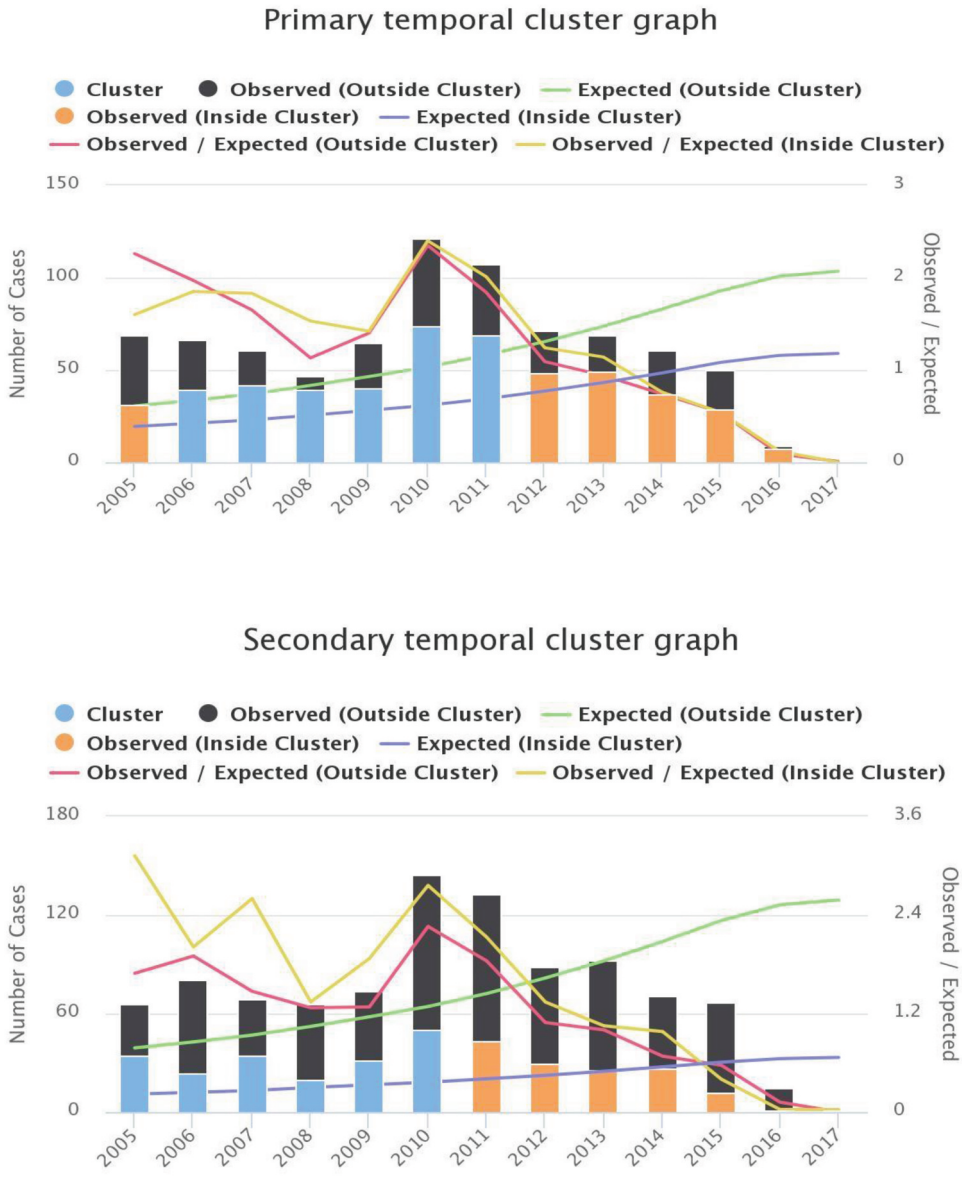

Figure 3. Primary and secondary temporal cluster graphs showing yearly variations in all-age malaria mortality clustering in the study area from 2005–2017.

Table 3. Spatial scan statistics of all-age malaria mortality clusters in the Kintampo area using purely spatial analysis, scanning for high rates (2005 - 2017).

Cluster	Location (sub-districts)	Observed	Expected	Relative risk	P-value
Primary	Kadelso and Gulumpe	219	161.93	1.42	p=0.001
Secondary	Mansie and Anyima	153	124.74	1.26	P=0.103

occurring between 2006 and 2011 in five sub-districts in the southern part of the study area.

Undoubtedly, the statistically significant primary and secondary clusters identified by the spatial and space-time scan statistics correspond with the areas of high malaria mortality risk identified by the SEB smoothed risks distribution maps. For instance, the smoothed all-age risks distribution map identified a higher concentration of malaria deaths in two sub-districts of the study area (Kadelso and Gulumpe) that overlap with the statistically significant spatial and space-time mortality clusters detected by the scan statistics. These same sub-districts were identified among others (Dawadawa, Kunsu and Apesika) as areas of significant under-five spatial and

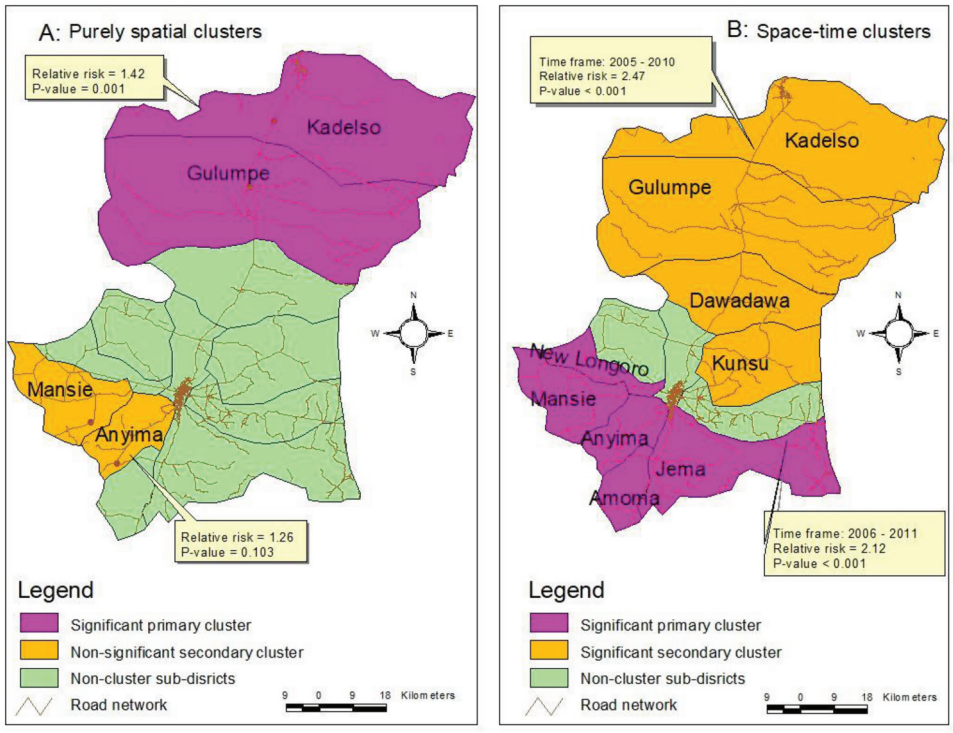

Figure 4. Spatial and space-time malaria mortality clusters for persons of all ages in the Kintampo area (2005–2017).

Table 4. Space-time scan statistics of all-age malaria mortality clusters in the Kintampo area using spatio-temporal analysis, scanning for high rates (2005 - 2017).

Cluster	Location (sub-districts)	Time frame	Observed	Expected	Relative risk	P-value
Primary	Mansie, Anyima, Jema, New Longoro and Amoma	2006-2011	303	162.83	2.12	P<0.001
Secondary	Dawadawa, Gulumpe, Kunsu and Kadelso	2005-2010	193	85.54	2.47	P<0.001

Table 5. Spatial scan statistics of malaria mortality clusters for children under five years in the Kintampo area using purely spatial analysis, scanning for high rates (2005 - 2017).

Cluster	Location (sub-districts)	Observed	Expected	Relative risk	P-value
Primary	Dawadawa, Gulumpe, Kunsu and Kadelso	153	121.69	1.36	p=0.024
Secondary	Masie, Anyima and Jema	153	135.79	1.18	p=0.608

space-time malaria mortality concentration using both the smoothed mortality risk maps and spatial and spatio-temporal scan statistical analysis methods. Besides, they were identified as areas of significant clustering of all-cause mortality for under-fives in a previous analysis (Nettey et al. 2010). The congruence of the results of the SEB smoothed mortality risks analysis with those of the scan statistical analysis suggests a high malaria burden in the cluster sub-districts. This requires the urgent attention of local health managers to turn the tide of malaria deaths in the affected sub-districts.

Though the reasons for the observed spatial and spatio-temporal patterns are unclear, the situation could be due to a combination of factors. First, the health seeking behaviour of residents in the cluster sub-districts could be poor given that people with malaria infections either do not seek prompt professional help or only seek care when their conditions deteriorate. A case in point is the study by Romay-Barja et al. (Romay-Barja et al. 2016) in which poor health seeking behaviour was reported as a major factor contributing to malaria mortality in the Bata district of Equatorial Guinea. The authors found that malaria deaths mainly occurred among children whose caregivers did not seek early treatment compared with those who did (Romay-Barja et al. 2016). It is also conceivable that most residents in these communities do not use insecticide treated nets for protection against malaria. All-cause mortality is

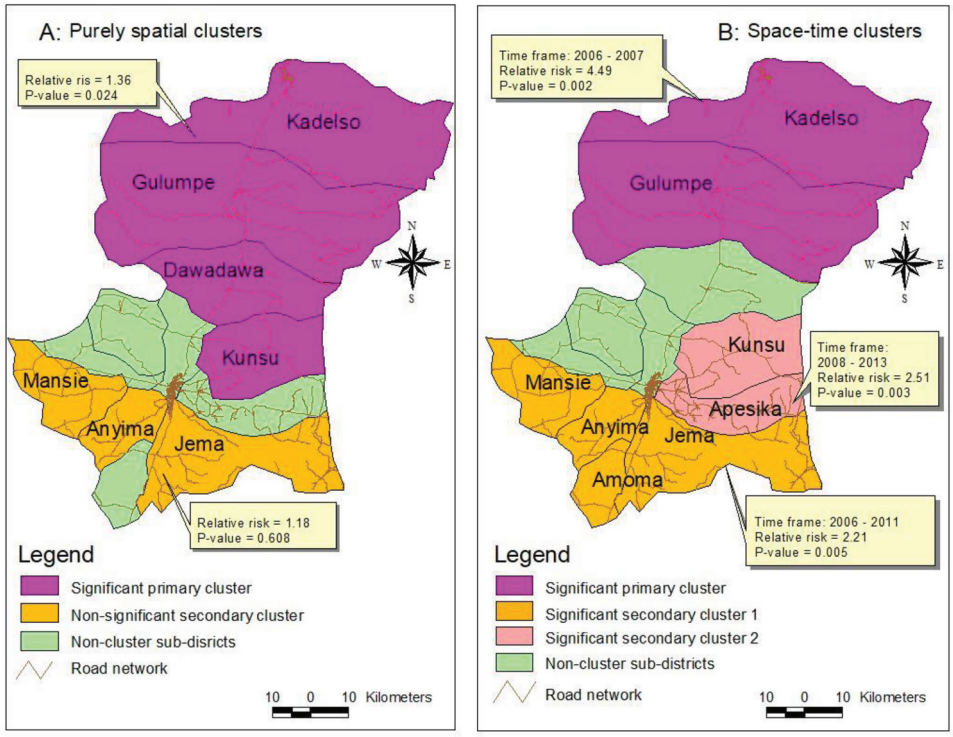

Figure 5. Spatial and space-time malaria mortality clusters for children under five years in the Kintampo area (2005–2017).

Table 6. Space-time scan statistics of malaria mortality clusters for children under five years in the Kintampo area using spatio-temporal analysis, scanning for high rates (2005 - 2017).

Cluster	Location (sub-districts)	Time frame	Observed	Expected	Relative risk	P-value
Primary	Gulumpe and Kadelso	2006 - 2007	37	8.7	4.49	p=0.002
Secondary 1	Amoma, Anyima, Jema and Mansie	2006 - 2011	121	62.54	2.21	p=0.005
Secondary 2	Kunsu and Apesika	2008 -2013	61	26.04	2.51	p=0.003

higher among children in populations where ITN use is low. For example, in a pooled analysis of data from 29 demographic and health surveys in 22 malaria endemic countries in sub-Saharan Africa, ITN use was found to be associated with 23% reduction in all-cause child mortality (Lim et al. 2011). Other studies have reported a 44% reduction in child mortality in Kenya (Fegan et al. 2007) and a range of 23% to 50% reduction in Malawi (Florey et al. 2017) due to ITN use. Besides, the terrain in the northern cluster communities is generally flat (Ghana Statistical Service 2010) with bogs favourable for breeding malaria vectors.

The economic activities of residents in these communities which include farming, hunting, logging and charcoal burning may expose them to infective mosquito bites and perhaps contribute to their high malaria mortality burden. This is buttressed by the fact that more than 74% of the deaths occurred in rural areas where the aforementioned livelihood activities are predominant. In essence, the observed age disparities in malaria deaths with a concentration on children under five years was anticipated. This is because prior evidence from Navrongo in Northern Ghana shows that the mortality effect of malaria reduces with age as immunity steadily improves (Bawah and Binka 2007). Our finding therefore validates the notion that malaria-specific mortality is concentrated in young children (Carneiro et al. 2010); especially in settings where the disease is endemic.

Additionally, the reasons for the temporal clustering of deaths between 2005 and 2013 are not explicitly known. However, one factor that possibly explains this state of affairs is our observation that most sub-districts, particularly those in the mortality clusters lacked adequate health services during this period as many of the communities in these sub-districts had no well-equipped functional CHPS compounds to provide for the health needs of the populace. Moreover, we have observed that most of the communities in the mortality clusters are far from the main district hospitals and health centres in the sub-districts. This, coupled with the weak public transport system in the study area probably made it difficult for

persons who died of malaria to reach health facilities in the major urban centres and sub-district headquarters for care.

Though we used retrospective mortality data for this study, the identified areas and periods of significant spatial and space-time clustering of malaria deaths are crucial for planning, monitoring and evaluating malaria control initiatives in the study area. Currently, malaria control programmes in sub-Saharan Africa use health facility mortality data in determining areas and periods of high malaria burden. However, the use of health facility data may underestimate the burden of malaria especially in areas where health services are weak (WHO 2018; Whiting et al. 2006). The use of community-based longitudinal mortality data as we have done in this analysis, is likely to produce better estimates of malaria mortality (Rowe et al. 2006). These estimates will complement geographical speciation of malaria based on regional prevalence data.

Our study was limited in some respects. The number of malaria deaths recorded for the study area could be less or more than the actual number since there were difficulties coding the specific causes of death in some cases due to insufficient autopsy information. This could have led to the attribution of malaria deaths to other causes and vice versa. Also, the Spatial Empirical Bayesian smoothing technique employed for mapping the mortality risks is predisposed to boundary effects which limit the number of local neighbours for sub-districts on the fringes of the study area. Hence, the unstable rates for such sub-districts shrink towards the global rather than local mean as the neighbourhood information required for smoothing is insufficient. Environmental determinants of malaria burden were not assessed in this study. Future research could focus on the use of drone aerial imagery to identify physical environmental features such as bogs, refuse pits and stagnant waterbodies that possibly contribute to the predicament of the cluster sub-districts for remedial action.

Despite the foregoing weaknesses, our analysis draws its strengths from the use of community-level mortality and mid-year population statistics extracted from a continuously updated health and demographic surveillance system. Besides, the spatial and space-time scan statistics used for detecting significant mortality clusters also strengthens our analysis as SaTScan is one of the best applications for exploratory spatial data analysis in public health with regard to statistical power (Huang, Pickle, and Das 2008).

Conclusions

This study identified statistically significant spatial and space-time clusters of all-age and under-five malaria mortality in the study area, using a composite of exploratory spatial data analysis techniques. The analysis revealed malaria mortality clusters in predominantly rural sub-districts with communities that are distant from the major urban centres in the study area. This finding calls for the provision of adequate malaria treatment services to the economically disadvantaged and young children in high malaria mortality cluster communities in particular and populations in remote rural settings in general for obvious reasons. Our findings hold potential to aid in the strategic planning, implementation, monitoring and evaluation of targeted malaria control interventions for its eventual elimination in the study area.

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Data availability statement

The data that support the findings of this study are available from enquiries@kintampo-hrc.org upon reasonable request.

Disclosure statement

The authors declare that they have no conflict of interest.

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