Geospatial Modeled Analysis and Laboratory Based Technology for Determination of Malaria Risk and Burden in a Rural Community

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Authors’ contributions
This work was carried out in collaboration among all authors. Author OAO designed the study. Authors GS and OTA performed geospatial model and statistical analyses. Author HOS wrote the protocol. Author MA wrote the first draft of the manuscript. Authors OAO and OTA managed the review process of the draft to final manuscript. Author ET managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Geographical Information System (GIS) has proven to be very useful for large scale mapping of ecosystems, land use and cover, disease prevalence, risk mapping and forecasting. GIS establish relationship or link between vector borne diseases and associated environmental factors thereby providing explanation for spatial distribution pattern, possible causes of diseases outbreak and implications on the community.

Aims and Objectives: Our approach in this study was to define and identify areas and places that are exposed to Malaria risk through proximity analysis and to compare geospatial risk with laboratory diagnosed malaria epidemiology.

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**Methodology:** Garmin GPS was used to capture the geographic coordinates of six (6) selected settlements and overlaid with georeferenced and processed satellite images in the study area. GIS modeling was performed on risk factors using weighted overlay technique to produce malaria risk map. A total of One hundred and thirty-five (135) vulnerable individuals were diagnosed for Malaria with light Olympus microscope and rapid diagnostic kit (RDT). Data were entered and analyzed using R-Package for Statistical Computing and Graphics.

**Results:** Proximity to malaria risk follows relatively the order Apodu > Central Malete > Elemere > KWASU Campus > Gbugudu. Apodu being the largest place with proximity to malaria risk, within 500 m radius. The risk index increases as one move away from the center of the settlement. The possible explanation for this high risk could be the presence of pond / lake in Apodu. This is a good breeding site for mosquito couple with dense vegetation as one move away from the centre of the settlements. Unlike Apodu, Gbugudu was at medium risk at 100 m buffer (60%) but the risk index decreases as one move away from the settlement centre. The absence of thick vegetation and presence of numerous open farms and partly cultivated farmlands on the eastern part could have been responsible for reduction in risk index. Dense vegetation and ponds were observed within Apodu, while Central Malete was built up with dense vegetation are possible reasons for the high-risk index, while settlements within 1 km radius around KWASU campus recorded lower risk index possibly due to low vegetation. The geospatial malaria risk analysis correlates with the laboratory-based test results. RDT kits and light microscopy results showed Apodu having the highest malaria prevalence with 46% and 58.7% followed by Elemere 41% and 30.3% respectively. When calculating prevalence by aggregating results across all communities, Apodu still had the highest malaria prevalence for the whole region. RDT and light microscopy results combined for all communities had Apodu with malaria prevalence of 21.48% and 27.4% followed by Elemere with 11.85% and 12.5% respectively. Gbugudu had the least malaria prevalence within the region with 3.7% and 7.4% respectively.

**Discussion and Conclusion:** Findings of this study showed dense vegetation and ponds within Apodu, Elemere and Central Malete served as good breeding site for mosquitoes and were responsible for the high-risk index at these areas. Settlements within 1 km radius around KWASU campus recorded lower index possibly due to low vegetation. Results from this study indicate that the degree of malaria parasitaemia in the three major settlements correlates directly with the remote sensing data.

**Keywords:** GIS; RDTs; risk mapping; giemsa light microscopy; malaria parasitaemia.

1. **INTRODUCTION**

Infection with single-celled parasites of the genus *Plasmodium* is responsible for malaria in humans, which is transmitted by the bite of female Anopheles mosquitoes. All Nigerians are at risk of malaria and the problem is compounded by the increasing resistance of malaria to hitherto cost-effective drugs and insecticides [1]. Nigeria has the highest cases of malaria worldwide accounting for twenty three percent (23%) of observed malaria cases globally [2]. Over the years, one of the challenges in malaria management, particularly among children, is inaccurate diagnosis of the condition [3]. Clinical diagnosis of malaria without laboratory support may lead to malaria misdiagnosis and wrong treatment [4]. These models incorporate by varying degrees, epidemiological, entomological, climate and environmental information. Decades of experience confirm that successful malaria control depends on accurate identification, diagnosis and geographical reconnaissance of high-risk areas [5].

Risk encompasses exposure to harmful environmental, economic or social stresses, susceptibility to these stresses [6] and the capacity to cope or adapt, often within the context of a particular hazard [7,8,9]. Risk assessment is an approach used to describe the potential for harm from a diverse range of hazards at local, regional, national or global scales [10,11]. A range of biophysical, social, economic, or cultural factors may be used as indicators of risk. Natural disasters and climate change hazards have been a particular focus of risk assessment [6,12,13]. Risk assessments often employ risk indicators to simplify and distil complex, real-world information into a format that is relevant and useful for decision-making [7,14,15]. Geographical Information System (GIS) has proven to be a very useful for large
scale mapping of ecosystem and land cover [16,17], disease prevalence, risk mapping and forecasting [10,11,15]. The concept of risk is concerned with identifying those groups and places that experience and are exposed to danger or risk [6,7]. Risk mapping has become a veritable tool to spatially evaluate risk and identify areas that are vulnerable to malaria [14]. Our approach to risk assessment in this study was to define and identify area and places that are exposed to the Malaria risk through proximity analysis [18].

GIS can be used to map the incidence / prevalence of malaria over a geographic area [19]. Mapping with GIS incorporated physical environmental risk variables such as vegetation cover, rivers, ponds and streams, housing and artificial drains, ecological and topographical layout, built up status of the settlements and pathogen-vectorial interphase and interactions with potential host communities. These were fed into an environmental model to predict Malaria risk [20,21].

The world health organization recommends that all malaria case management be based on parasitological diagnosis [22], a policy that was adopted by the Nigerian National Malaria Programme in 2011 [23]. The recommended parasitological tests are light microscopy and immunochromatographic rapid diagnostic tests (RDTs). Microscopy of Giemsa-stained blood smears remains the gold standard for confirmation of malaria diagnosis. Microscopy has numerous advantages. It allows identification and quantification of the causative organism. It is also cheap and excellent in competent hands. However, light microscopy is not a feasible option in most parts of sub-Saharan Africa most especially Nigeria, because of irregular electricity to power microscopes that are in short supply. In addition, suitably trained laboratory technicians are not generally available. Malaria RDTs are more practical at the point of care in communities where community health extension workers (CHEWs) can be trained in their use, as they do not require electricity or special equipment. RDTs may also detect Plasmodium infection even

![Fig. 1. Map of Kwara State showing the study area in Moro LGA](image)
when the parasites are sequestered in the deep vascular compartments and thus undetectable by microscopic examination of a peripheral blood smear. High-quality RDTs have become available [24] and are now the preferred option for programmatic deployment malaria control programs, including Nigeria [24], because of their simplicity and speed in yielding reliable results. Histidine-rich protein II (HRP2)-based RDTs are the preferred options for tropical areas where *Plasmodium falciparum* is responsible for more than 95% of malaria infections. In addition, HRP2-based RDTs can better withstand the heat and temperature fluctuations of tropical Africa than the enzyme-based RDTs where refrigeration and air conditioning is not always feasible. Many have demonstrated their sensitivity, specificity, ease of performance, and reading. This study thus aims to compare geospatial risk for malaria with laboratory-based diagnosed malaria epidemiology in the study.

### 1.1 Study Area

The study area is located in three major wards of Elemere, Kwasu-Malete, Gbugudu-Apodu wards of Moro Local Government Area (LGA) of Kwara State and lies within latitudes 8.6563°N to 8.8136°N of the Equator and Longitudes 4.2359°E to 4.5410°E of the Greenwich Meridian. Settlements comprise of Elemere, Kwasu-Malete, and the adjoining communities of Malete (Gbugudu-Apodu) among others (Fig. 1) covering an area of about (157,701 Hectares) of land.

The study area falls under broad tropical savanna climate with seasonal rainfall mostly in the months of June to September. With total annual rainfall of 1200 mm and mean annual temperature of 26°C the vegetation is characterized by deciduous trees and long grass under story. Farming and marketing of agricultural products are the major economic activities however, the town is fast becoming a trading centre due to establishment of Kwara State University and its closeness to Ilorin metropolis, the Kwara state capital.

### 2. MATERIALS AND METHODS

#### 2.1 Sampling Techniques and Malaria Diagnosis

Three of the major settlements around the Kwara state university, Malete campus were randomly selected. A prospective, randomized and non-consecutive method was then used to enrol patients. The sampling formula as found in [25] with an error margin of 5%, Z statistics for confidence level of 95%, prevalence of 35% (national malaria incidence rate) was used to get a minimum of 82 individuals. However, a total of one hundred and thirty-five (135) individuals were screened and diagnosed for Malaria with TM light microscope and rapid diagnostic kits (Care Start, Malaria HRP-2 Pf) from October 2015 till December 2016. The inhabitants were mostly peasant Yoruba farmers, Fulani herdsmen, students and few civil servants and traders. A few significant proportions of the inhabitants had at least primary school education. Malaria transmission occurs year-round, with a peak during the rainy-season months and a nadir during the dry-season months. Children between the ages of 3 and 60 months who presented to community health extension workers (CHEWs) usually with fever or a recent history of fever suggesting malaria, irrespective of the degree of severity of the illness, were enrolled. 5mls of venous blood was collected from all subjects for thin and thick blood film preparation for Giemsa microscopy and Rapid Diagnostics test (RDT) kits.

#### 2.2 Sample Collection and Analysis

All enrollees in the study had thick and thin blood smears prepared on microscope slides from both the same finger prick used for RDTs and 5 ml venous blood collected in EDTA bottles. Dried blood smears were stained with fresh Giemsa stain at pH 7.2 using standard procedures [26]. Stained blood smears were screened in the Microbiology laboratory, College of Pure and Applied Sciences, Kwara State University, Malete for the presence and quantification of malaria parasites using bifocal Olympus light microscopy at a magnification of ×1000. All blood smears were double read by 2 experienced malaria laboratory technologists blind to the result of RDTs. Diagnosis of malaria was based on identification of asexual stages (ring and trophozoite) of *Plasmodium* on thick blood smears. Parasite density was determined by counting the number of asexual parasites against approximately 200 leukocytes on the thick blood film and converted to parasites per microliter using an assumed total white blood cell count of 8000 cells/μl [24]. Blood films were declared negative if no parasite was seen after viewing with a 200 high power held microscope.
2.3 Geospatial Methods

2.3.1 GIS data for risk modeling

A Multi Criteria Assessment (MCA) approach was adopted for the risk modeling in this study [10,27] which includes (1) the identification of risk factors; (2) the processing of the factors into GIS layers; (3) the assigning of weight to layers based on principal components analysis (PCA); (4) spatial data integration using weighted overlay in ArcMap 10.4 and; (5) the display of final map.

Summary of analysis can be explained as shown in Table 1. The steps of analyses across both GIS and Laboratory testing are explained up to the risk map and prevalence end points respectively. The observed prevalence via laboratory testing was then compared with the risk map developed through GIS for convergence of results.

Five risk factors were identified which are considered important in breeding and maintenance of malaria vectors: They are vegetation, elevation, slope, distance from rivers / water bodies and land use. Although we collected rainfall and temperature data to describe the climate of the study area, we did not use it in preparing the risk map for two reasons: first with an average of 26.5°C and total annual rainfall of 1,900 mm recorded across the sampled settlements, there was no visible variation on these climatic factors.

2.4 Vegetation Factor

Vegetation or plant cover is one of the environmental critical factors in assessing malaria risk or risk mapping. Dense vegetation cover has been associated and described as providing suitable habitat for mosquito breeding (Fig. 2).

Normalized Difference Vegetation Index (NDVI) is a GIS technique used over the years by scientists to quantitatively and qualitatively evaluate the vegetation covers of an area [28]. NDVI is mathematically defined as:

\[ \text{NDVI} = \frac{NIR - R}{NIR + R} \]

Where, NIR and R are the reflectance in the near infrared and red regions respectively. It is the algebraic combination of red and near infrared bands to represent the amount of green vegetation in the image. In the NDVI, the values for a given pixel value is always in a number that ranges from -1 to +1. A zero means no vegetation and close to 1 indicates the highest possibility of green leaves [29]. NDVI results were obtained from the analysis of Landsat 7 Enhanced Thematic Mapper (ETM) satellite images captured in 2014. The NDVI was initially classified into seven (0-6). This was further aggregated and reclassified into 3 classes based on risk index: High (5 and 6) medium (3 and 4) and low (0-2) risks (Table 1).

2.5 Elevation and Slope Factor

Elevation greatly affects earth surface temperature which directly determines the condition for mosquito larva breeding. A lower elevation such as valleys supports humid and higher temperature which is conducive for mosquito breeding [30,31].

To develop an elevation factor (Fig. 3) for risk assessment, a 90 m Digital Elevation Model (DEM) data from Shuttle Radar Topographic Mission- SRTM for the Africa-West Africa sub-continent was obtained from http://srtm.csi.cgiar.org, with the data sets for the Malete-Elemere subset, masked and imported into GIS environment. This layer was resampled to 30 m resolution before being combined with other raster risk factors data. The DEM data was

<table>
<thead>
<tr>
<th>S/N</th>
<th>GIS analysis</th>
<th>Laboratory testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Elevation, slope, NDVI, proximity to water bodies, land use/land cover</td>
<td>RDT kit</td>
</tr>
<tr>
<td>2</td>
<td>Weighting (PCA)</td>
<td>Light microscopy</td>
</tr>
<tr>
<td>3</td>
<td>Overlay</td>
<td>Percentage statistics</td>
</tr>
<tr>
<td>4</td>
<td>Risk analysis</td>
<td>Prevalence</td>
</tr>
<tr>
<td>5</td>
<td>Risk map</td>
<td>Prevalence</td>
</tr>
</tbody>
</table>

Table 1. GIS and laboratory analysis flow processes
Fig. 2. Reclass NDVI for vegetation factor

processed by using the reclass menu in spatial analyst tool in ArcGIS 10.1 at class interval of 150 metres to produce three classes 0-150 (high) 151-300 (medium) and 301-450 (low). Populations of mosquitoes have been seen to decrease with elevation [31]. Several studies have shown a range of 17°C to 33°C as temperature conducive for mosquitoes from breeding to adulthood however 20°C to 33°C increases the probability for morbidity and mortality in adulthood [30,31,32,33].

2.6 Land Use / Land Cover (LULC)

Georeferenced satellite image of bands 1, 2, 3, 4 and 5 of Landsat 7 Enhanced Thematic Mapper Plus (ETM+), 2016 at 30 m medium resolution of the study area were obtained from Global Land Cover Facility’s Earth Spatial Data Interface (ESDI) for vegetation analysis and land use classification. Bands 1, 2 and 3 are visible bands (0.4 μm – 0.7 μm) Bands 4 and 5 are infrared bands (0.7 μm – 1.1 μm). An image bands combination was performed- Bands 321 has been used in several literatures for identifying urban features [34] and was used for our land use classification. Band 4 (near infrared) was combined with Band 3 and Band 2 to produce image band composite RGB from which Band 3 and Band 4 were used in estimating vegetation index-Normalized Difference Vegetation Index (NDVI). High Resolution (HR) historical satellite image at 10 m from Worldview viewable in Google earth 2017 was used for residential/house counting and used as ancillary data for identify dwelling units and other buildings to determine population density for land use classification. GPS (eTrex Garmin) was used to capture the coordinates (Latitude and Longitude) of selected settlements. The composite images were subset to study area district boundary layers using clip tool of raster processing in ArcMap 10.2. Shape file of the settlement coordinates were prepared and added to the composite images to show the respective location of the sampled settlements.
The LULC was reclassified into three classes based on house counts that were conducted on the images from Google Earth: cluster settlements and heavily built up area, non-settled area and forested and cultivated area (Fig. 4).

2.7 Distance to Rivers / Water Bodies’ Factor

Shape file of the major rivers that run through the area were obtained from the Google satellite images 2017 of the area through digitization. Buffering at 500 m, 1000 m and 1500 m were performed (Fig. 5) and was overlay on the raster images of other risk factors layers. It has been observed that rivers, pools of water or water bodies that are dammed could serve as conducive sites for mosquitoes to lay their eggs [35]. Water is crucial for oviposition and larval stage of mosquito development hence higher density of mosquitoes during rainy season than dry season and resultant seasonal malaria epidemiology [31]. Table 2 shows the classification across five different risk factors for GIS analysis.

To determine Weight to be allocated to each risk factors; Principal Component Analysis (PCA) was performed in Microsoft Excel using the XLSTAT extension on all the variable factors in each selected settlements; the Eigen values and % variance of each factor were used to allocate weight for modeling in Arc GIS thus the PCA results shows that vegetation factor was allocated 60% as contribution to total influence 25% for distance to water bodies, 10% for elevation, 3% for land use and 2% for slope (Table 3) Weighted overlay was run on the factors to produce Malaria risk map (Fig. 5).

Multiple buffering at 500 m, 1000 m and 1500 m in selected settlements with focus on the three experimental settlements – Apodu, Gbugudu and Elemere. Simple percentage in R Statistics package was used to determine the proportion (%) of area on the risk map that falls within three buffer zones.
Table 2. Classification of factors by weights

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Values</th>
<th>Rank</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevation</td>
<td>0-100 m</td>
<td>3</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>201-300 m</td>
<td>2</td>
<td>Medium</td>
</tr>
<tr>
<td></td>
<td>&gt;300 m</td>
<td>1</td>
<td>Low</td>
</tr>
<tr>
<td>Slope</td>
<td>0 – 10</td>
<td>3</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>10 – 20</td>
<td>2</td>
<td>Medium</td>
</tr>
<tr>
<td></td>
<td>20 – 30</td>
<td>1</td>
<td>Low</td>
</tr>
<tr>
<td>Vegetation cover / NDVI</td>
<td>&gt;0.6</td>
<td>3</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>0.3 – 0.6</td>
<td>2</td>
<td>Medium</td>
</tr>
<tr>
<td></td>
<td>0.0 – 0.3</td>
<td>1</td>
<td>Low</td>
</tr>
<tr>
<td>Distance to rivers / Ponds</td>
<td>0-100 m</td>
<td>3</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>500 m</td>
<td>2</td>
<td>Medium</td>
</tr>
<tr>
<td></td>
<td>1000 m</td>
<td>1</td>
<td>Low</td>
</tr>
<tr>
<td>Land use / House count</td>
<td>&gt;400</td>
<td>4</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>200 – 399</td>
<td>3</td>
<td>Medium</td>
</tr>
<tr>
<td></td>
<td>&lt;100</td>
<td>2</td>
<td>Low</td>
</tr>
</tbody>
</table>

Author (2020)

Table 3. Factors weight for weighed overlay

<table>
<thead>
<tr>
<th>S/No</th>
<th>Risk factors</th>
<th>Eigen value</th>
<th>% variance</th>
<th>Assigned weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Vegetation</td>
<td>6.201</td>
<td>60.123</td>
<td>60</td>
</tr>
<tr>
<td>2</td>
<td>Distance to water</td>
<td>2.011</td>
<td>25.321</td>
<td>25</td>
</tr>
<tr>
<td>3</td>
<td>Elevation</td>
<td>1.702</td>
<td>10.024</td>
<td>10</td>
</tr>
<tr>
<td>4</td>
<td>Land use</td>
<td>0.008</td>
<td>2.712</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>Slope</td>
<td>0.002</td>
<td>1.532</td>
<td>2</td>
</tr>
</tbody>
</table>

Author (2020)
3. RESULTS

3.1 Malaria Risk Map and Laboratory Assessment

Vegetation cover, and distance to water bodies greatly defined the Malaria risk level in the study area as shown by Eigen values and % variance (Table 3), vegetation account for over 60% variance. Dense vegetation and ponds within Apodu, Central Malete showed high risk index. High risk was observed along river course throughout the study area especially in the adjoining high forest in the North east and south eastern sectors (Fig. 5) of settlements within 1 km radius around KWASU campus recorded lower index possibly due to low vegetation, This supported [36] reports that high vegetation and water bodies provide a suitable places for mosquito breeding and resting. Although where elevation was not high enough to significantly affect the risk level; the presence of other factors such as dense vegetation, ponds and proximity to water body, the risk level changes, Elemere was on relatively higher elevation (Fig. 3) but due to the presence of high forest (Fig. 2), the malaria risk level was raised to medium.

The geospatial malaria risk analysis agrees with the laboratory-based test results of Apodu being with the highest malaria risk across the three settlements. However, the risk map saw a reversal of prevalence with Gbugudu having a higher malaria risk than Elemere. R Statistical package was used to analyze malaria prevalence based on RDT kits and light microscopy within each settlement. Table 4 showed malaria prevalence within each settlement. RDT and light microscopy results across all communities showed that Apodu had the highest malaria prevalence of 21.48% and 27.4% respectively followed by Elemere with 11.85% and 12.5% respectively. Gbugudu had the least malaria prevalence within the region with 3.7% and 7.4% respectively.

Fig. 6a shows the malaria risk for the broader study area while Fig. 6b zoomed into the sampled settlements to determine their individual malaria risk indices at 500 m, 1000 m and 1500 m buffers.
Fig. 6a. Malaria risk map

Fig. 6b. Cross section of malaria risk buffer within the selected rural communities

Table 4. Malaria prevalence aggregated across whole study area

<table>
<thead>
<tr>
<th>Settlements</th>
<th>RDT Kits</th>
<th>Light microscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Malaria burden (%)</td>
<td>Malaria burden (%)</td>
</tr>
<tr>
<td>Apodu</td>
<td>(29/135) 21.48</td>
<td>(37/135) 27.4</td>
</tr>
<tr>
<td>Gbugudu</td>
<td>(5/135) 3.7</td>
<td>(10/135) 7.4</td>
</tr>
<tr>
<td>Elemere</td>
<td>(16/135) 11.85</td>
<td>(17/135) 12.59</td>
</tr>
</tbody>
</table>

Source: Author (2020)
3.2 Proximity Analysis in Risk Assessments

GIS proximity analysis has been used in recent time as a tool to show and explain interrelationship among hazardous substances facilities and various land uses and their health implication and environmental injustice as reflected in the disproportionate exposure and risk among different classes of people [37]. Apodu and Central Malete settlements had their communities prone to malaria risk within 1000 m to 1500 m radius buffer as the risk index increases as one moves away from the center of the settlement (Fig 6 a and b). Dense vegetation and ponds within Apodu, and Central Malete accounted for high risk index, while settlements within 1 km radius around KWASU campus with low vegetation cover recorded lower index. Areas around Apodu from 1000 m and above buffer particularly had high risk index when compared to other settlements, the possible explanation for this high risk could be the presence of pond / lake in Apodu which hitherto was planned to serve as dam to the community but abandoned and left to be overgrown with aquatic plants, thus providing a good breeding site for mosquito. This supports the findings of [31] who reported that areas closer to the mosquito marshland breeding sites and bushes where adult mosquitoes rest in are more vulnerable to malaria. Gbugudu about 1 km away from KWASU campus was moderately at risk but the risk index decreases as one move away from the settlement centre in the North East direction. The absence of thick vegetation and presence of numerous open farms and partly cultivated farmlands on the eastern part could have been possible explanation for this reduction in risk index.

4. CONCLUSION

It could be seen that the geospatial modeled analysis was able to further explain the dynamics of malaria prevalence established through the laboratory-based diagnostics to determine malaria epidemiology in the region studied. Thus, suggesting that geospatial analysis of environmental variables could be used to model malaria epidemiology. This could really become imperative if incorporated into the “one health” approach of WHO in eliminating malaria in Tropical Africa.

ETHICAL APPROVAL

All aspects of the study were approved by Kwara State University Research Committee and Ethical Review Board. Verbal and written Informed consent were obtained from all the community leaders and respondents in the three major settlements screened. They were assured of voluntary participation, confidentiality of their test results and responses and the opportunity to withdraw at any time without prejudice in line with the Helsinki Declaration [38]. The history, demographic data of presenting clients or respondents were obtained and entered into the case report form (CRF) and study register.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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