Duale, Ahmed Badei; Ayele, Nebiyu Negussu; Macleod, Colin K; Kello, Amir Bedri; Gezachew, Ze-lalem Eshetu; Binegdie, Amsalu; Dejene, Michael; Alemayehu, Wondu; Flueckiger, Rebecca M; Massae, Patrick A; +50 more... Willis, Rebecca; Negash, Biruck Kebede; Solomon, Anthony W; Aboe, Agatha; Adamu, Liknaw; Alemayehu, Wondu; Alemu, Menbere; Alexander, Neal DE; Bero, Berhanu; Brooker, Simon J; Bush, Simon; Chu, Brian K; Courtright, Paul; Dejene, Michael; Emerson, Paul M; Flueckiger, Rebecca M; Foster, Allen; Gadisa, Solomon; Gass, Katherine; Gebre, Teshome; Hab-tamu, Zelalem; Kalua, Danny Haddad; Kello, Amir B; King, Jonathan D; Le Mesurier, Richard; Lewallen, Susan; Lietman, Thomas M; MacArthur, Chad; Macleod, Colin; Mariotti, Silvio P; Massey, Anna; Mathieu, Els; McCullagh, Siobhain; Mekasha, Addis; Millar, Tom; Mpyet, Caleb; Munoz, Beatriz; Ogondi, Jeremiah; Ogden, Stephanie; Pavluck, Alex; Pearce, Joseph; Resnikoff, Serge; Sarah, Virginia; Sarr, Boubacar; Sisay, Alemayehu; Smith, Jennifer L; Solomon, Anthony W; Thomson, Jo; West, Sheila K; Willis, Rebecca; (2018) Epidemiology of trachoma and its implications for im-plementing the "SAFE" strategy in Somali Region, Ethiopia: results of 14 population-based prevalence surveys. OPHTHALMIC EPIDEMIOLOGY, 25 (sup1). pp. 25-32. ISSN 0928-6586 DOI: https://doi.org/10.1080/09286586.2017.1409358

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Epidemiology of trachoma and its implications for implementing the “SAFE” strategy in Somali Region, Ethiopia: results of 14 population-based prevalence surveys

Ahmed Badei Duale, Nebiyu Negussu Ayele, Colin K Macleod, Amir Bedri Kello, Zelalem Eshetu Gezachew, Amsalu Binegdie, Michael Dejene, Wondu Alemayehu, Rebecca M Flueckiger, Patrick A Massae, Rebecca Willis, Biruck Kebede Negash, and Anthony W Solomon*

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ABSTRACT

Purpose: Ethiopia is highly trachoma endemic. Baseline mapping was needed in Ethiopia’s Somali Region to guide elimination efforts.

Methods: Cross-sectional community-based surveys were conducted in 34 suspected trachoma-endemic woredas, grouped as 14 evaluation units (EUs), using a standardised mapping methodology developed for the Global Trachoma Mapping Project.

Results: In total, 53,467 individuals were enumerated. A total of 48,058 (89.9%) were present at the time of survey teams’ visits and consented to examination. The prevalence of trachomatous inflammation--follicular (TF) among children aged 1--9 years ranged from 4.1% in the EU covering Danot, Boh, and Geladin woredas in Doolo Subzone to 38.1% in the EU covering Kebribeyah and Hareshen woredas in Fafan Subzone (East). The trichiasis prevalence among adults aged over 15 years varied from 0.1% in the EU covering Afder, Bare, and Dolobay woredas in Afdar Subzone (West) to 1.2% in the EU covering Awbere in Fafan Subzone (West).

Conclusion: Mass drug administration (MDA) with azithromycin is needed in 13 EUs (population 2,845,818). Two EUs (population 667,599) had TF prevalences of 1--9-year-olds of ≥30% and will require at least 5 years of MDA; 5 EUs (population 1,119,032) had TF prevalences of 10--29.9% and need at least three years of MDA; 6 EUs (population 985,187) had TF prevalences of 5--9.9% and need at least one round of azithromycin distribution before re-survey. In all 13 of these EUs, implementation of facial cleanliness and environmental improvement measures is also needed. Surveys are still needed in the remaining 34 unmapped woredas of Somali Region.

INTRODUCTION

According to a published estimate, there were 32 million blind individuals and 191 million people with moderate-to-severe visual impairment worldwide in 2010. Trachoma is the leading infectious cause of blindness, especially in populations that have poor environmental sanitation, inadequate water supply, and poor socio-economic status. More than 80% of the global burden of active trachoma is concentrated in 14 countries, all of which are in Africa. Ethiopia is the second most populous country in Africa and has a very high burden of trachoma.

Worldwide, considerable progress has been made in trachoma elimination. The Ethiopian government has endorsed the World Health Assembly-supported goal of global elimination of trachoma as a public health problem by the year 2020 (GET2020), yet planning for and progress in elimination has been hampered by the low coverage of existing surveys.

The 2005–2006 Ethiopian National Survey on Blindness, Low Vision and Trachoma estimated region-level trachoma prevalences for Ethiopian Somali Region of 16.7% trachomatous inflammation--follicular (TF) in children aged 1--9 years, and 4.2% trachomatous trichiasis (TT) in adults aged 15 years
and above. However, according to WHO recommendations, district-level prevalence data are generally necessary for determining the need for implementation of the SAFE (surgery, antibiotics, facial cleanliness, environmental improvement) strategy for trachoma elimination. “Districts” in this recommendation are defined as “the administrative unit for health care management” which “for purposes of clarification consists of a population unit between 100,000 and 250,000 persons”. However, where trachoma is expected to be highly and widely endemic, baseline surveys can frame larger populations, so that interventions can be provided to those most in need in a timely manner.

A true picture of trachoma prevalence will direct regional priorities for Somali Region’s blindness control programme, provide baseline data for monitoring and evaluation, and help guide those fighting trachoma to move swiftly towards meeting the GET2020 goal. In collaboration with the Global Trachoma Mapping Project (GTMP), the Ethiopian Somali Regional Health Bureau conducted population-based trachoma prevalence surveys throughout the region, using the standardised GTMP protocol.

Methods
Setting
Ethiopian Somali Region is one of nine regional states that make up the Federal Democratic Republic of Ethiopia. It occupies an area of about 350,000 km$^2$ and is divided into nine zones (Figure 1). These zones are further divided into 68 woredas (districts) and 4 city councils. According to the Central Statistical Authority’s 2007 Population and Housing Census, the total population of the region was 4.40 million in 2007.

Thirty four of the region’s 68 woredas were identified as suspected-trachoma-endemic, secure and accessible to survey teams. Trachoma was expected to be highly and widely endemic, so the 34 woredas were grouped to form 14 evaluation units (EUs) of up to 500,000 inhabitants each, respecting existing administrative boundaries insofar as was possible (Figure 1).

Survey design
Each survey followed a two-stage cluster-random sampling methodology designed to generate EU-level prevalence estimates for TF in children aged 1–9 years, and trichiasis in persons aged 15 years and above. In each EU, clusters were defined as villages, and a sampling frame of all villages in the EU was obtained from district head offices. In the first sampling stage, 26 villages were selected using probability proportional to size sampling. In the second stage, on the day of survey at each cluster, 30 households were selected using compact segment sampling. All residents of selected households aged 1 year or above were invited to participate. Full details of the sample size and the specifics of the survey design are outlined elsewhere.

Figure 1. Evaluation units for trachoma surveys, Global Trachoma Mapping Project, Somali Region, Ethiopia, 2013. Woredas and administrative zones are labelled.
Fieldwork

Prior to fieldwork, all 10 trachoma graders and all 10 data recorders completed the GTMP version 1 training course and passed their respective GTMP examinations. Full details of training and testing are outlined elsewhere.\textsuperscript{10} Community sensitisation was carried out a few days in advance of the survey. Each selected cluster was visited by a survey coordinator, who briefed the village chief and community members and prepared the sampling frame for random segment selection by the survey team. On the day of the survey, at each selected household, consent to survey was obtained from the household head. All household members were enumerated, and present and consenting individuals were examined using sunlight and 2.5x magnifying loupes (Binomag Plastic, USA), for the presence or absence of TF, trachomatous inflammation–intense (TI) and trichiasis using the WHO simplified trachoma grading system.\textsuperscript{12,13} Global Positioning System (GPS) coordinates were recorded at each household for quality control purposes.

Two experienced ophthalmologists were employed as supervisors throughout the mapping, with field visits to each team at least once every 5 days. All field data were recorded in Android devices running the LINKS application (Task Force for Global Health, Decatur GA, USA).\textsuperscript{10,14} Upon completion of fieldwork each day, the recorder uploaded data from the phone over an encrypted connection to the GTMP secure server. Subsequent data processing and approval was undertaken as described elsewhere.\textsuperscript{10}

Data processing and analysis

All data analysis, which included replication of automated analyses undertaken centrally within the GTMP, was carried out using SPSS Version 20.0 statistical software (IBM Corp, Armonk, NY, USA, 2011). TF prevalences were adjusted for age in 1 year age groups, and trichiasis prevalences were adjusted for sex and age in 5 year age groups,\textsuperscript{11} using the latest available census data.\textsuperscript{4} EU-level prevalence estimates were calculated as the means of all cluster-level estimates of the same outcome. This accounted for unanticipated variability in the numbers examined at each cluster, but equally weighting all clusters. Prevalence estimates for all EUs combined (project-level estimates) were calculated as means of all EU-level outcome estimates.

To account for the clustered design of the survey, confidence intervals for EU-level estimates were calculated by bootstrapping adjusted cluster-level estimates. Confidence intervals for project-level estimates were calculated by bootstrapping adjusted cluster-level estimates with the inclusion of stratification of clusters by EU. Both EU- and project-level confidence intervals were estimated over 10,000 bootstrapping iterations, by taking the 2.5th and 97.5th centiles of these results. Logistic regression was used to investigate age and sex associations with trichiasis.

Ethical considerations

Ethical approval was obtained from the ethics committee of the London School of Hygiene & Tropical Medicine (Protocol no. 6319), and the Somali Regional State Health Bureau Ethics Committee (Protocol no. KS/we/01892/06). Informed verbal consent was obtained from all adult participants. For participants under 15 years of age, informed verbal consent was obtained from a parent or guardian. Individuals found to have active trachoma (TF ± TI) were offered treatment with 1% tetracycline eye ointment and individuals with trichiasis were referred for management.

Results

Training and fieldwork were conducted between February and July 2013. A total of 364 clusters were visited. From 10,955 selected households, 53,467 individuals were enumerated; 48,058 (89.9%) people were present and examined by the survey team, 5365 (10%) individuals were absent, and 42 (0.1%) refused to participate. 23,620 (44.2%) of those enumerated were children aged 1–9 years (Table 1). The median age of those enumerated was 12 years (25th centile: 5, 75th centile: 31). The sex distribution of those examined was 46.2% male and 53.8% female.

In 1–9-year-olds, the highest age-specific proportion of TF cases (21.4%) was noted in children aged 2 years, with the burden of TF decreasing with increasing age thereafter ($\chi^2$ for trend = 799.0, $P < 0.0001$). Similarly, the prevalence of TI decreased with increasing age, although this trend was not statistically significant ($\chi^2$ for trend = 3.6, $P = 0.055$) (Figure 2).

Table 2 shows the prevalence of TF and TI in children aged 1–9 years in each EU. The TF prevalence in children aged 1–9 years by EU is shown in Figure 3. The overall age-adjusted TF prevalence in children aged 1–9 years for all project EUs combined was 13.7% (95% confidence interval 11.9–15.7%).

Table 1. Age and sex distribution of enumerated individuals, Global Trachoma Mapping Project, Somali Region, Ethiopia, 2013.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Female</th>
<th>Male</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–9</td>
<td>12158</td>
<td>11462</td>
<td>23620</td>
</tr>
<tr>
<td>10–14</td>
<td>2833</td>
<td>2380</td>
<td>5213</td>
</tr>
<tr>
<td>15+</td>
<td>11291</td>
<td>13343</td>
<td>24634</td>
</tr>
<tr>
<td>Total</td>
<td>27,185</td>
<td>26,282</td>
<td>53467</td>
</tr>
</tbody>
</table>

Table 2 shows the prevalence of TF and TI in children aged 1–9 years in each EU. The TF prevalence in children aged 1–9 years by EU is shown in Figure 3. The overall age-adjusted TF prevalence in children aged 1–9 years for all project EUs combined was 13.7% (95% confidence interval 11.9–15.7%).
TF prevalence was particularly high in the EU covering Awbere woreda in Fafan Subzone (East) (38.1%) and in the EU covering Awbere woreda in Fafan Subzone (West) (33.1%). The overall project-level age-adjusted prevalence of TI in children aged 1–9 years was 1.7% (95% CI; 1.2–2.4). There was marked variation in the TI prevalence in this agegroup between EUs. The highest prevalences were in the EU covering Awbere woreda in Fafan Subzone (West) (7.0%), and the EU covering Kebribeyah and Hareshen woredas in Fafan Subzone (East) (6.8%). The project-level age- and sex-adjusted prevalence of trichiasis among those aged 15+ years was 0.5% (95% CI; 0.4–0.7). The estimated trichiasis prevalence was

Table 2. Prevalence of trachomatous inflammation–follicular (TF) and trachomatous inflammation–intense (TI) among children aged 1–9 years, Global Trachoma Mapping Project, Somali Region, Ethiopia, 2013.

<table>
<thead>
<tr>
<th>Evaluation unit</th>
<th>Zone</th>
<th>TF+ (1–9) number of cases, (unadjusted %)</th>
<th>TF+ (1–9) adjusted a (%)</th>
<th>TF+ (1–9) number of cases, (unadjusted %)</th>
<th>TI+ (1–9) number of cases, (unadjusted %)</th>
<th>TI+ (1–9) adjusted a (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afder, Bare, Dolobay</td>
<td>Afder Subzone (West)</td>
<td>213 (11.4%)</td>
<td>10.7</td>
<td>[6.3–17.7]</td>
<td>6 (0.3%)</td>
<td>0.35</td>
<td>[0.0–0.7]</td>
</tr>
<tr>
<td>Guradamole, Goro Baqaqsa, Chereti/Weyib</td>
<td>Afder Subzone (Central)</td>
<td>224 (12.7%)</td>
<td>11.3</td>
<td>[6.2–14.2]</td>
<td>3 (0.2%)</td>
<td>0.14</td>
<td>[0.0–0.5]</td>
</tr>
<tr>
<td>Jijiga Rural, Gursum, Babile</td>
<td>Fafan Subzone (Central)</td>
<td>273 (21.1%)</td>
<td>18.5</td>
<td>[12.7–25.3]</td>
<td>21 (1.6%)</td>
<td>1.31</td>
<td>[0.3–2.7]</td>
</tr>
<tr>
<td>Kebribeyah, Hareshen</td>
<td>Fafan Subzone (East)</td>
<td>578 (42.1%)</td>
<td>38.1</td>
<td>[30.4–45.1]</td>
<td>93 (6.8%)</td>
<td>6.77</td>
<td>[2.7–12.6]</td>
</tr>
<tr>
<td>Maeso, Erer, Shinile</td>
<td>Sity Subzone (Central)</td>
<td>150 (10.2%)</td>
<td>8.8</td>
<td>[4.8–13.6]</td>
<td>11 (0.7%)</td>
<td>0.71</td>
<td>[1.4–9.6]</td>
</tr>
<tr>
<td>Afdem, Ayisha, Dembel</td>
<td>Sity Subzone (West)</td>
<td>125 (8.6%)</td>
<td>8</td>
<td>[4.9–13.3]</td>
<td>76 (5.2%)</td>
<td>5.45</td>
<td>[1.4–9.6]</td>
</tr>
<tr>
<td>Gashamo, Aware</td>
<td>Korah and Jere Subzone</td>
<td>111 (5.7%)</td>
<td>5.6</td>
<td>[2.7–9.1]</td>
<td>0 (0.0%)</td>
<td>0</td>
<td>[0.0–0.0]</td>
</tr>
<tr>
<td>Danot, Boh, Geladin</td>
<td>Dooalo Subzone</td>
<td>94 (4.7%)</td>
<td>4.1</td>
<td>[1.9–8.7]</td>
<td>4 (0.2%)</td>
<td>0.16</td>
<td>[0.0–0.4]</td>
</tr>
<tr>
<td>Godre, Adalie</td>
<td>Shebelle zone</td>
<td>151 (7.5%)</td>
<td>7.2</td>
<td>[3.9–10.4]</td>
<td>2 (0.1%)</td>
<td>0.08</td>
<td>[0.0–0.3]</td>
</tr>
<tr>
<td>Elkere, West Imj</td>
<td>Afder Subzone (East)</td>
<td>154 (8.3%)</td>
<td>7.5</td>
<td>[3.9–11.9]</td>
<td>5 (0.3%)</td>
<td>0.35</td>
<td>[0.6–3.9]</td>
</tr>
<tr>
<td>Moyale</td>
<td>Liben Subzone (West)</td>
<td>214 (13.9%)</td>
<td>12.6</td>
<td>[7.5–16.3]</td>
<td>37 (2.4%)</td>
<td>2.17</td>
<td>[0.4–2.0]</td>
</tr>
<tr>
<td>Hudet, Dolo Odo</td>
<td>Liben &amp; Afder (Central)</td>
<td>306 (19.1%)</td>
<td>16.9</td>
<td>[12.1–20.5]</td>
<td>20 (1.2%)</td>
<td>1.07</td>
<td>[0.4–2.0]</td>
</tr>
<tr>
<td>Filtu</td>
<td>Liben &amp; Afder (West)</td>
<td>152 (10%)</td>
<td>8.9</td>
<td>[5.6–12.5]</td>
<td>8 (0.5%)</td>
<td>0.44</td>
<td>[0.1–0.8]</td>
</tr>
<tr>
<td>Awbere</td>
<td>Fafan Subzone (West)</td>
<td>426 (35.9%)</td>
<td>33.1</td>
<td>[22.0–40.2]</td>
<td>87 (7.3%)</td>
<td>6.95</td>
<td>[1.4–12.0]</td>
</tr>
</tbody>
</table>

a Adjusted for age based on 2007 Central Statistical Authority (CSA) census data.
highest in the EU covering Awbere in Fafan Subzone (West) (1.2%) and the EU covering Jijiga Rural, Gursum, and Bable woredas in Fafan Subzone (Central) (1.1%) (Table 3, Figure 4).

Overall, after adjusting for age, females had 3.4 times higher odds of having trichiasis than males (Likelihood ratio test; OR = 3.43, 95%CI [2.6–4.5], p-value<0.0001).

Discussion

Our data have important implications for implementation of the SAFE strategy in the Ethiopian Somali Region. There was significant variation in the prevalence of TF, TI, and trichiasis across the 14 EUs studied. Among adults aged over 15 years, the Fafan Zone overall had the EUs with the highest trichiasis prevalences, and delivery of community-based trichiasis surgery services in these areas is a public health emergency. In other EUs, the overall need is less pressing, but every individual with trichiasis should be offered an operation to correct it as soon as possible, in order to limit the risk of irreversible visual impairment. In our surveys, trichiasis was far more likely to be found in women. This excess risk of trichiasis in women compared to men has been found in other

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Table 3. Prevalence of trichiasis among adults aged over 15 years, Global Trachoma Mapping Project, Somali Region, Ethiopia, 2013.

<table>
<thead>
<tr>
<th>Evaluation unit</th>
<th>Zone</th>
<th>Trichiasis (15+), number of cases (unadjusted %)</th>
<th>Trichiasis (15+) Adjusted</th>
<th>95% Confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afder, Bare, Dolobay</td>
<td>Afder Subzone (West)</td>
<td>7 (0.5%)</td>
<td>0.1</td>
<td>[0.0–0.2]</td>
</tr>
<tr>
<td>Guradamole, Goro Baqua, Chereti/Weyib</td>
<td>Afder Subzone (Central)</td>
<td>18 (1.3%)</td>
<td>0.7</td>
<td>[0.3–1.4]</td>
</tr>
<tr>
<td>Jijiga Rural, Gursum, Bable</td>
<td>Fafan Subzone (Central)</td>
<td>39 (2.7%)</td>
<td>1.1</td>
<td>[0.5–1.9]</td>
</tr>
<tr>
<td>Kebribeyah, Hareshen</td>
<td>Fafan Subzone (East)</td>
<td>19 (1.3%)</td>
<td>0.3</td>
<td>[0.2–0.6]</td>
</tr>
<tr>
<td>Maeso, Erer, Shinile</td>
<td>Sity Subzone (Central)</td>
<td>22 (1.4%)</td>
<td>1.0</td>
<td>[0.4–1.8]</td>
</tr>
<tr>
<td>Afdem, Ayisha, Dembel</td>
<td>Sity Subzone (West)</td>
<td>7 (0.5%)</td>
<td>0.2a</td>
<td>[0.1–0.3]</td>
</tr>
<tr>
<td>Gashamo, Aware</td>
<td>Koraha and Jerer</td>
<td>2 (0.1%)</td>
<td>0.0</td>
<td>[0.0–0.1]</td>
</tr>
<tr>
<td>Subzone</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Danot, Boh, Geladin</td>
<td>Doolo Subzone</td>
<td>6 (0.4%)</td>
<td>0.2c</td>
<td>[0.0–0.5]</td>
</tr>
<tr>
<td>Gode, Adadie</td>
<td>Shebelle zone</td>
<td>7 (0.5%)</td>
<td>0.2a</td>
<td>[0.0–0.4]</td>
</tr>
<tr>
<td>Elkere, West Imi</td>
<td>Afder Subzone (East)</td>
<td>9 (0.6%)</td>
<td>0.2c</td>
<td>[0.1–0.4]</td>
</tr>
<tr>
<td>Moyale</td>
<td>Liben Subzone (West)</td>
<td>30 (2.1%)</td>
<td>0.8</td>
<td>[0.4–1.4]</td>
</tr>
<tr>
<td>Hudet, Dolo Odo</td>
<td>Liben &amp; Afder (Central)</td>
<td>38 (2.6%)</td>
<td>1.0</td>
<td>[0.6–1.4]</td>
</tr>
<tr>
<td>Filtu</td>
<td>Liben &amp; Afder (West)</td>
<td>12 (0.8%)</td>
<td>0.2c</td>
<td>[0.1–0.5]</td>
</tr>
<tr>
<td>Awbere</td>
<td>Fafan Subzone (West)</td>
<td>45 (3.1%)</td>
<td>1.2</td>
<td>[0.6–2.1]</td>
</tr>
</tbody>
</table>

aAdjusted for sex and age in 5 year bands based on 2007 Central Statistical Authority (CSA) census data.
bRounded up to 0.2%
cRounded down to 0.2%
surveys\textsuperscript{15–23} and is presumed to stem from more frequent infection of women with ocular \textit{C. trachomatis} infection, due to their greater exposure to children, the main infection reservoir.\textsuperscript{24} Specific measures to increase women’s access to trichiasis surgery are needed here.

Based on TF prevalences in 1–9 year-olds, and following WHO recommendations, Kebribeyah and Hareshen woredas in Fafan Subzone (East) and Awbere woreda in Fafan sub zone (West), need five years of A, F, and E implementation prior to an impact survey; 5 EUs require three years of A, F, and E implementation before impact surveys; and 6 EUs warrant a single round of azithromycin in the first instance, together with implementation of the F and E components of SAFE, before re-survey.

It will be noted that there is a large block of central Somali Region, comprising some 21 woredas, for which we currently have no data on trachoma prevalence (Figures 3 and 4). This is an important limitation to our work as a whole. Whether or not the current absence of data from these areas will affect prospects for trachoma elimination from Ethiopia will depend on whether trachoma is present there, on the extent of population movement between that area and other areas of the country, and the length of time that elapses before the necessary data are acquired, and interventions—if needed—can be commenced.

In conclusion, the prevalence of active trachoma in Ethiopian Somali region is high, with 13 of 14 EUs surveyed needing at least one round of MDA with azithromycin, plus implementation F and E. The trichiasis prevalence was high in four EUs and significant scale-up of efforts to train surgeons to address the backlog of trichiasis surgeries is needed urgently. To achieve the goal of GET2020, further baseline mapping will also be needed in the unmapped woredas of Somali Region, once security has improved.

**Declaration of interest**

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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Notes on contributors

ABD oversaw field work, interpreted the data, and drafted the manuscript. NNA and RW analysed the data. BK reviewed the data. RMF provided key geographical information system input. All authors reviewed the draft manuscript critically for intellectual content, and read and approved the final version.

References


Appendix

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