Lepr Rev (2018) **89,** 178–196

Routine Surveillance Data as a Resource for Planning Integration of NTD Case Management

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Accepted for publication 30 August 2018

Summary

Background: There is a high burden of morbidity due to neglected tropical diseases. To help address this, the World Health Organization recommends integration of case management (CM). Here, we present a practical framework designed to identify areas that could benefit from an integrated CM strategy in Ghana. We also investigated the accessibility of primary health care (PHC) to CM cases, and the impact of this on morbidity at diagnosis.

Methods: Routinely detected cases of Buruli ulcer (BU) and leprosy, and suspected lymphedema identified through morbidity surveys during mass drug administration campaigns in Ghana in 2014 were remotely georeferenced. We estimated distances from cases' home communities to the nearest primary healthcare facility (PHC), and compared rates of reported disease, completeness of clinical information, and risk of more severe morbidity, relative to PHC accessibility.

Results: We georeferenced communities of 295/350 reported leprosy cases, 240/333 BU cases, and 1,557/2383 instances of lymphedema. Overlap of these diseases was predominantly around Accra and in the Upper East Region. Rates of

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 0305-7518/18/064053+19 $1.00

reported disease appeared higher in populations with higher accessibility to PHC, and leprosy cases living further from PHC had a higher risk of disability at diagnosis.
Conclusions: This investigation demonstrates the feasibility and value of using routinely collected data to map CM-NTDs at low cost. The maps presented are intended to provide a resource for planning the implementation of integrated CM for NTDs in Ghana. This approach could be easily implemented by national health services in other endemic countries in the future.

Introduction

Several neglected tropical diseases (NTDs) are characterised by chronic infections associated with long-term morbidity.[1] These diseases have a considerable impact on public health as a result of their debilitating and stigmatising symptoms and sequelae, which can lead to permanent disfigurement and disability.[2] The burden of disease due to NTDs falls almost exclusively on poor communities in Africa, Asia and South America.[3]

The NTDs are often categorised by their main control strategy: the preventive chemotherapy (PC) NTDs are amenable to control through mass drug administration (MDA), whereas the intensified case management (ICM) NTDs require an individual-level approach involving early diagnosis and treatment of the infection to reduce morbidity, and the management of complications.[4] While MDA has reduced transmission of the PC-NTDs, the burden of morbidity due to NTDs remains high. Infections including Buruli ulcer (BU), leprosy, lymphatic filariasis (LF), onchocerciasis, trachoma and yaws can result in permanent disfigurement and disability, with patients requiring ongoing treatment for prevention or alleviation of morbidity (hereafter referred to as case management, CM). There is substantial overlap in the strategies for CM for different NTDs. For example, trachoma and leprosy can cause damage to the eye, resulting in vision impairment which can progress to blindness without appropriate clinical management.[5,6] Surgery is required to repair hydrocele resulting from LF and to treat severe cases of BU[7] and complications due to leprosy.[8,9] Physiotherapy can improve cases where mobility is compromised due to lymphedema, BU or leprosy.[10–12] Other common components of CM for these diseases include hygiene, skin care and wound care, which can be delivered by the patient themselves or by a care-giver, following appropriate health education.[12]

Due to the overlap in several aspects of CM, the World Health Organisation (WHO) has recommended the integration of CM interventions, to achieve a more cost-effective use of resources.[12–15] Integration of CM interventions could be implemented through integrated pre- and in-service training of health workers, the delivery of supplies such as footwear, hygiene products and medicines, integrated monitoring and integrated self-care groups in communities that are co-endemic for these diseases.[12] An additional and related aspect of integration is the inclusion of NTD services with general health services, necessary to accompany a move away from vertical programme structures as programmes integrate their activities.

Planning the integration of CM activities requires information on the distribution and burden of NTD-related morbidity, so that resources and activities can be targeted to where disease burdens are highest, and integrated where they overlap. The availability of precise and accurate data on NTD-related morbidity is extremely limited, but prevalence surveys to generate this information are often prohibitively expensive. Existing data sources include health facility case registers and morbidity surveys carried out in the context of MDA for

diseases such as LF and onchocerciasis. While it is recognised that these routine data sources do not provide a complete representation of the burden and distribution of disease, they do indicate the burden of cases already visible to the health system, which may provide a useful resource for the initial phase of integration of CM activities.

As a process within the health system, the integration of CM within NTD programmes would be informed by overlap of disease at the level at which CM activities are managed and coordinated, namely the district level in Ghana. Meanwhile, integration of CM at the point of delivery would be based upon overlap of disease at the level of local health facilities, where patients access basic care. Healthcare delivery structures play a key role in passive surveillance, representing the entry point of patients into the surveillance system as well as the health system. In the context of routine surveillance, the accessibility of services for diagnosis and treatment of NTDs is an essential consideration in planning the integration of CM, and in evaluating the quality of passive surveillance data for this purpose. Previous work has demonstrated that rates of health facility attendance are strongly influenced by the distance patients have to travel to access these facilities.[16] The accessibility of health facilities to populations at risk for NTDs may therefore be expected to impact reporting rates and diagnostic delay, and consequently influence key epidemiological indicators such as rates of reported disease and of more severe morbidity at diagnosis.

In this investigation, we mapped the distributions of routinely reported cases of leprosy, BU, and lymphedema presumably related to LF detected in Ghana in 2014, alongside the locations of health facilities expected to diagnose and treat these conditions. We aimed to investigate rates of reported disease, the completeness of key clinical data, and the risk of more severe morbidity at diagnosis, relative to the accessibility of PHC health facilities. In addition, we integrated data sources to identify co-occurrence of CM-NTD cases at district level, and co-occurrence of morbidity resulting from these diseases at health facility level. The broader goal of this analysis was to assess the potential for integration of CM activities, particularly wound management and prevention of disability for patients with leprosy, BU, and lymphedema.

Methods

STUDY DESIGN, SETTING AND DATA SOURCES

This study was a retrospective cross-sectional study of the distributions of BU, leprosy and LF-related lymphedema in the Republic of Ghana: a country with a population of approximately 28 million and a total land area of 238,537 km^2.[17] It lies on the southern coast of West Africa, bordered by Côte d'Ivoire to the west, Burkina Faso to the north and Togo to the east. The country is divided into 10 administrative regions, which are further divided into 216 districts (Figure 1).

The average population of a district is just over 100,000 people.

Primary health care (PHC) facilities in Ghana include Community-Based Health Planning and Services (CHPS), providing basic essential health services at community level, and health centres at sub-district level.[18] CHPS compounds are intended to service a maximum of 5,000 people, or 1–3 communities.[19,20] Health centres are intended to serve up to 25,000 people.[19]

The disease data mapped in this investigation was collected by the Leprosy Elimination Programme (LEP), the National Buruli Ulcer Control Programme (NBUCP) and the NTD

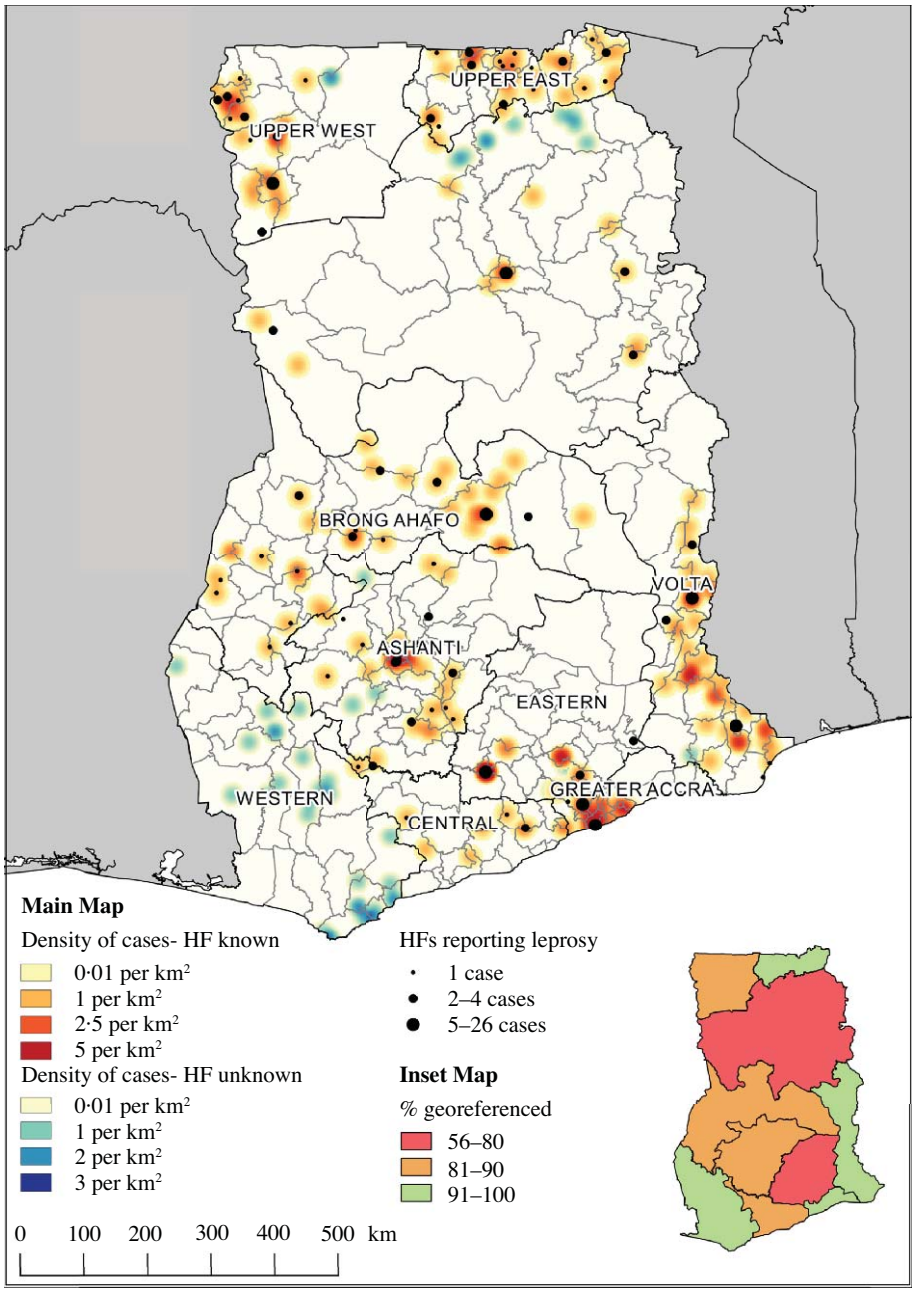

Figure 1. Density distribution of reported leprosy cases in Ghana in 2014 and the locations of the recorded reporting health facilities (HF).

programme in Ghana, as part of their routine surveillance and control activities in 2014. Reflecting the structural organisation of NTD control in Ghana, which consists of separate control programmes for each disease, the methods of primary and secondary data collection varied between datasets for the different diseases.

The Ghana LEP does not undertake active case searches, but implements community health education activities to train volunteers to suspect and refer cases. These activities were implemented in all regions in 2014. Patients who present passively or who are referred by a community volunteer (CV) or health worker (HW) are sent to a health centre or district hospital for diagnosis. Clinicians grade patients according to the WHO leprosy disability grading system[21] and record this information in hospital records. The home address of patients is recorded for case-holding purposes. Data is aggregated to regional level by district programme officers, and reported monthly to the national level. To obtain information on the home residence of cases diagnosed in 2014, all regional officers from the LEP were contacted by telephone, and provided with a standardised electronic form (Microsoft Excel 2010: Microsoft Corporation, Redmond, WA) in which to record the cases from their respective regions. The electronic forms included the district and community of each case, the health facility where treatment was given and the disability grade at diagnosis. All leprosy cases were considered to require CM and so were shown on the integrated morbidity map. The data was validated by comparison of district totals to a district level-aggregated dataset compiled separately by the LEP from routine reports from the regions.

A line-list of all BU cases reported nationally in 2014 was provided by the NBUCP. The NBUCP collects data through passive surveillance from health facilities, and conducts active case searches in known disease foci. In 2014, active case searches were implemented in Ashanti and Brong Ahafo Regions. Cases detected through active case search were not distinguished from those passively reported in the surveillance line-list, although the referral source (self/community volunteer (CV)/health worker (HW)/former patient/other) was recorded. Cases referred by CVs or HWs would include all cases detected through active surveillance, so the proportion diagnosed through these routes may indicate the relative contribution of active case searches. For each case reported, we extracted data on the place of residence (community, district and region name); clinical information including limitation of movement (LOM) at diagnosis, the category and type of lesion;[22] laboratory confirmation by Ziehl Neelsen (ZN) staining and/or polymerase chain reaction (PCR); the referral source; and if available, the health facility where treatment started. We did not restrict the investigation to confirmed cases because a substantial proportion had no laboratory test result recorded. Cases were excluded if they were negative by PCR or negative by ZN if PCR diagnosis was not available. To investigate the possible impact of active surveillance activities on case detection rates, we compared the performance of Ashanti and Brong Ahafo Regions to the country overall in terms of WHO targets for early case detection.[23] Cases with either LOM at diagnosis or category II or III lesions were considered most likely to require ongoing CM and mapped on the integrated morbidity map.

Regarding LF-related lymphedema, the NTD programme provided reporting sheets from the MDA campaigns for LF and onchocerciasis, conducted between June and August 2014. These datasets include morbidity registration data collected by community drug distributors (CDDs) during drug administration. The MDAs were conducted in a total of 141 endemic districts in all regions apart from the Volta Region, which is non-endemic for LF and onchocerciasis, and does not implement morbidity registration for hydrocele and lymphedema. From these reports, we extracted information on the number of suspected cases of lymphedema recorded in each community that had received MDA. The cases recorded are not clinically confirmed, and are only identified based on questioning and visual evidence of lower limb swelling. All suspected lymphedema cases were displayed on the

integrated map; hydrocele cases were not mapped because the main intervention for this condition is surgery, rather than ongoing management and disability prevention.

GEO-REFERENCING CASE REPORT DATA

For community-level disease mapping, we aimed to georeference all communities that reported cases of leprosy, BU, or suspected lymphedema. A range of tools was used to find coordinates, including Bing Maps,[24] Google Maps,[25] the Fuzzy Gazetteer[26] and the OpenStreetMap Project.[27] Other sources were used to estimate the geographical positions of communities that were not found using online search tools. These sources included the Geographic Names Database of the National Geospatial-Intelligence Agency,[28] maps published by the Ghana Statistical Service,[29] the Ghana National Development and Poverty Commission,[30] the Local Governance and Decentralization Program,[31] and the Millennium Development Authority.[32] Paper maps were obtained from the Headquarters of the Survey Department of the Lands Commission in Accra, Ghana. A list of settlements that could not be georeferenced was recorded.

The geo-referenced data was assembled within a geographic information system in QGIS,[33] along with the georeferenced health facilities, and other datasets including national boundary, inland water[34] and population density data.[35] We obtained a list of georeferenced health facilities in Ghana.[36] We used the QGIS Heatmap plugin[37] to map density distributions for leprosy, BU and suspected lymphedema via non-parametric Kernel Density Estimation (KDE), using a Gaussian function and a search radius of 10 km.

ESTIMATING THE ACCESSIBILITY OF PRIMARY HEALTH SERVICES

PHC facilities (including CHPS compounds, clinics and health centres in the health facility dataset) were assumed to be the first point of contact with the health system for leprosy and BU cases, which were largely recorded through passive case detection. We used Euclidean (straight-line) distance as indicator of the accessibility of these health facilities. The estimate of Euclidean distance was considered more appropriate than Manhattan distance (through a road network) for measuring distance in this context because it was assumed that journeys to local health facilities were most likely to be made on foot, so may not be well-represented by the mapped road network. This assumption is supported by evidence from household surveys and focus group discussions conducted as part of a study in a rural district of the Upper West Region of Ghana, which revealed walking to be the most common means of transport to CHPS compounds and HCs.[18]

We measured the distance of each mapped case of leprosy, BU and suspected lymphedema to the nearest PHC facility. We defined zones of good accessibility to PHC facilities across the whole country using buffers of radius 5 km around PHC facilities. This follows the approach of Agbenyo *et al.*[18] in categorising the accessibility of CHPS compounds. In each region, the population within 5 km of a PHC facility was estimated by summing pixel values of population per grid square (from a raster dataset obtained from the WorldPop project[35]) within dissolved buffer zones. These values were subtracted from regional population totals to estimate the population beyond 5 km of a PHC in each region.

ESTIMATING THE RATE OF REPORTED CASES AND THE RISK OF MORBIDITY BY DISTANCE TO PHC FACILITY

We estimated reported rates and proportions of leprosy, BU and suspected lymphedema in population zones within and beyond 5 km of a PHC facility at national and regional levels, and calculated rate ratios (RR) of cases in populations within and beyond 5 km of a PHC facility, using the calculated population estimates as denominators. We conducted a sensitivity analysis on the estimated rate ratios by calculating maximum possible rates within and beyond 5 km of a PHC facility assuming all non-georeferenced cases were more than 5 km from a health facility (to calculate the lower boundary for RR) or within 5 km (to calculate the upper boundary). As indicators of more severe morbidity at diagnosis, we calculated the proportion of leprosy cases with G1/2D at diagnosis, and the proportion of BU cases with category II or III lesions or LOM at diagnosis.

IDENTIFYING OVERLAP OF NTD MORBIDITY IN LOCAL HEALTH FACILITIES

Potential treatment facilities were those considered likely to be able to deliver basic case management for patients with leprosy, BU or lymphedema. We included facilities categorised as clinic; health centre; district hospital; hospital; metropolitan hospital; municipal hospital; polyclinic; regional hospital or training institution in this group. We linked all mapped cases of leprosy and lymphedema, and mapped cases of BU with Category II-III lesions or LOM at diagnosis to their nearest health facility, measured by Euclidean distance. We identified health facilities that were linked to at least two cases of morbidity attributable to different diseases (BU, LF or leprosy). This co-distribution was represented using proportional pie chart maps showing the total number of morbidity cases linked to each facility, and the proportion of cases caused by each of the three diseases.

ETHICS STATEMENT

Permission to conduct this work was granted by the Ghana Health Service Ethical Review Committee and the London School of Hygiene and Tropical Medicine MSc Research Ethics Committee (reference number 9798). Patient informed consent was not required because no patient-identifiable information was stored. Data were aggregated to community-level for analysis and presentation, so there was no possibility of identification of individuals.

Results

DISTRIBUTION OF REPORTED LEPROSY, BU, AND SUSPECTED FILARIAL LYMPHEDEMA

In total, 351 new cases of leprosy were reported from 306 communities in 94 districts, with cases recorded from all regions. One case reported from the Upper East Region was excluded as the case was not a resident of Ghana. The separate dataset compiled by the LEP included 317 cases in 84 districts. Precise data on new cases detected from 24 districts in 2014 was not available to the LEP; of these, four were reported by the regional programme officers to have recorded cases in 2014, with a combined total of 29 cases. Of the 192 districts with reporting data verified by the LEP, the number of cases reported was the same as the number extracted

from the district and hospital records in 123 districts (64·1%). In 43 districts, there was a discrepancy of one to two cases, while three districts showed a discrepancy of more than five cases between the datasets (Figure 1S in supplementary file).

Overall, 195 leprosy cases (55·7%) had no disability, 34 (9·7%) had G1D and 35 (10·0%) had G2D at diagnosis. Data on disability grade was missing for 86 cases (24·4%). Fifty-five of the cases (15·7%) were not georeferenced. The clinic was recorded for 310 cases, but was missing from all cases in the Western Region (Figure 1). The distribution of georeferenced leprosy cases, including those whose clinic was recorded and georeferenced ($n = 216$) and those whose clinic was not known or not georeferenced ($n = 79$), is shown on the density map in Figure 1, along with the locations of the reporting facilities. Mapped cases were sparse in the Northern and Eastern Regions, but these regions had high proportions of cases that were not georeferenced.

A total of 409 new clinical diagnoses of BU were reported from 254 communities in six regions (Ashanti, Brong Ahafo, Central, Eastern, Greater Accra and Western). A high proportion of the cases in Ashanti were referred by CVs and HWs, suggesting that active case searches made a greater contribution to case detection in this region than in Brong Ahafo Region, where a lower proportion was referred by health professionals. Table 1S (in supplementary file) shows referral routes and performance against WHO indicators for early diagnosis by region.

Samples from 321 patients (78·5%) had been tested for *M. ulcerans* using PCR, of these 250 (77·9%) had tested positive and 71 (22·1%) were negative. Of the 88 patients not analysed by PCR, 7 had been tested for the presence of mycobacteria using ZN staining; two were positive and five were negative. In total, 333 patients were positive or untested for

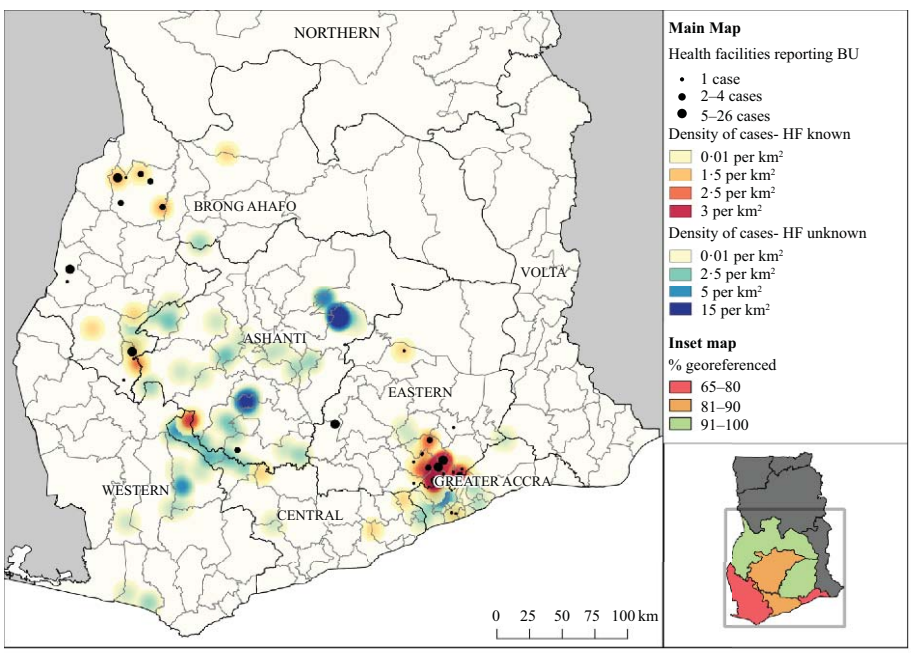

Figure 2. Density distribution of BU cases reported in Ghana in 2014 and the locations of the recorded reporting health facilities (HF).

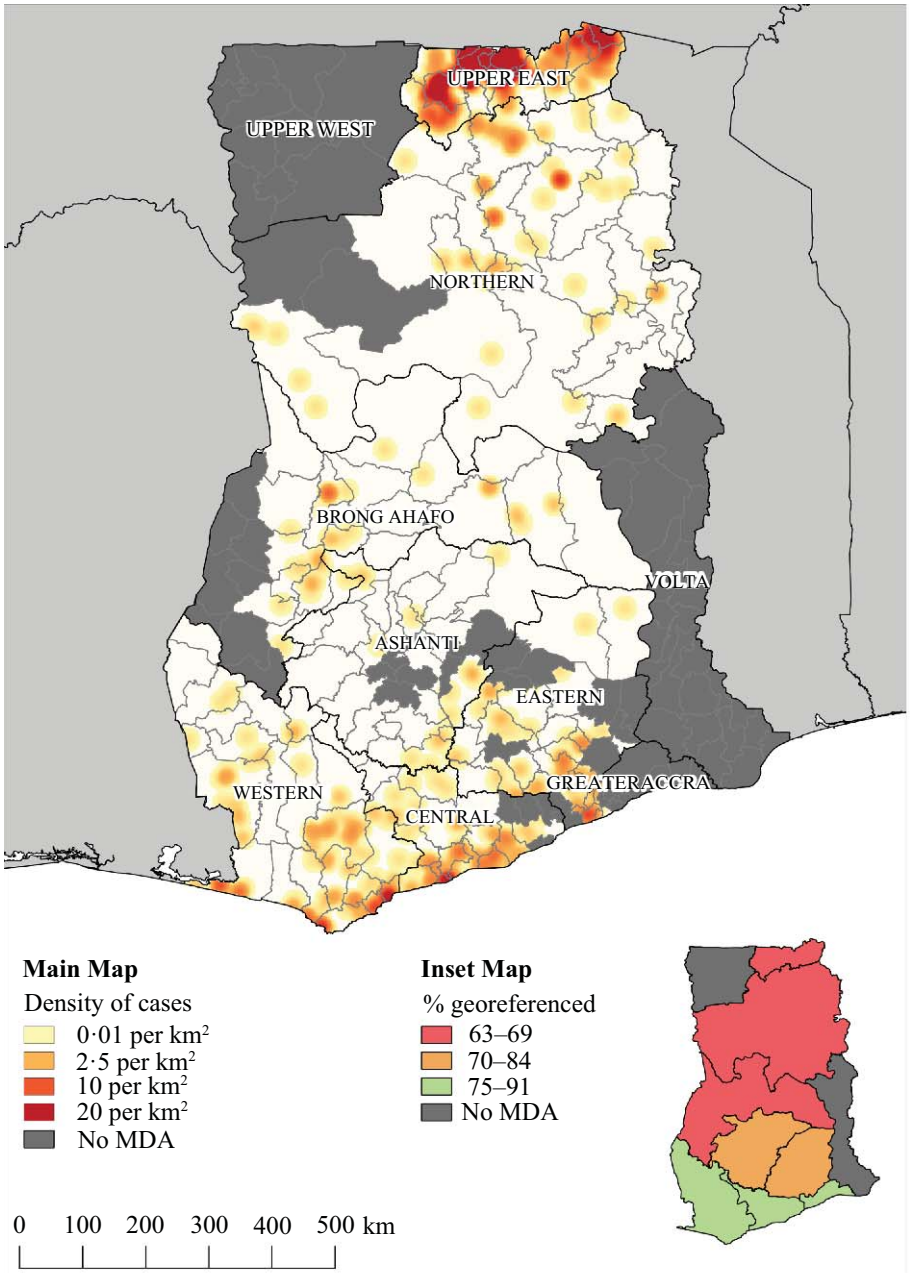

Figure 3. Density distribution of suspect cases of filarial lymphedema detected in morbidity surveys for mass drug administration campaigns (MDA) in Ghana in 2014.

M. ulcerans but considered suspicious of BU; these are hereafter referred to as 'cases'. Two hundred and fourteen cases (64·3%) had either category II or III lesions or LOM at diagnosis.

Fifty-three cases (15·6%) were not georeferenced. Health facility was recorded for 137/333 BU cases (41·1%). Thirty-three out of 43 recorded health facilities (76·7%) were

georeferenced. The distribution of georeferenced BU cases, including those whose clinic was recorded and georeferenced ($n = 82$), and those for which reporting clinic was unknown or not georeferenced (198), is shown on the density map in Figure 2, along with the reporting facilities.

Morbidity registration conducted through LF and onchocerciasis community-based MDA identified 2,383 suspect cases of lymphedema in 1,043 communities. The communities of 826 individuals (34·7%) could not be georeferenced. Cases were heavily concentrated in the Upper East Region, and the distribution was scattered throughout the rest of the country (Figure 3).

The density of mapped cases was low in the Northern and Brong Ahafo regions, and increased towards the south of the country. There were some pockets of high concentration along the coast. The proportion of communities that were georeferenced was lowest in the Upper East, Northern and Brong Ahafo Regions, and highest in the southern regions.

ACCESSIBILITY OF PHC FACILITIES

Seventy-five percent of the overall population was within 5 km of a PHC facility. This proportion varied between regions (Table 1).

At national level, rates of reported and georeferenced leprosy, BU and suspect filarial lymphedema were higher in the population within 5 km of a PHC facility. All regions had higher rates of reported and georeferenced leprosy and most had higher rates of reported and georeferenced BU in the population within 5 km of a PHC facility. This pattern was not observed for filarial lymphedema: four out of eight regions that reported data- including the two regions with the lowest access to PHC facilities- had lower rates of recorded cases in the population within 5 km of a PHC facility (Table 1). The relationship between the rate of reported cases and the accessibility of PHC was sensitive to the location of the non-georeferenced cases: when these were assumed to occur beyond 5 km of a PHC facility (rather than excluded), rates of leprosy and BU at national level and in most regions were higher in populations beyond 5 km of PHC (Table 2S, supplementary file).

Regardless of the assumed location of non-georeferenced cases, the rate of reported leprosy was higher in the population within 5 km of a PHCF in the Volta and Upper West Regions, and the rate of reported BU was higher within 5 km of a PHCF in the Eastern and Brong Ahafo Regions (Table 2S, supplementary file).

Georeferenced leprosy cases occurring more than 5 km from a PHC facility were less likely to have been graded at diagnosis than those living within 5 km of a PHC facility (Table 3S, supplementary file).

Among graded cases, the proportion with G1/2D was higher in those living further away from a PHC facility (Table 2).

The completeness of clinical indicators for BU cases was high, both in cases located within and beyond 5 km of a PHC facility (Table 3S, supplementary file). The proportion of BU cases with LOM or category II-III lesions was similar in populations within and beyond 5 km of a PHC facility, but was higher in non-georeferenced cases (Table 2).

OPPORTUNITIES FOR INTEGRATED CM

Overlap of morbidity due to leprosy and lymphedema occurred in all regions apart from the Volta Region, where LF-related morbidity was not recorded, and the Upper West, from which reporting sheets were not available. In the Upper East Region, there were high case numbers

Table 1. Regional rates of reported leprosy, Buruli ulcer (BU) and suspected filarial lymphedema, within and beyond 5 km of a primary healthcare (PHC) facility in Ghana in 2014

Area	%[1]	Reported leprosy cases				
		<5 km from PHC		>5 km from PHC		
		N	Rate (95% CIs)	N	Rate (95% CIs)	Rate Ratio[4]
All Regions	**75·4**	**251**	**1·3 (1·1–1·4)**	**44**	**0·7 (0·5–0·9)**	**1·86**
Greater Accra	**95·5**	28	0·7 (0·5–1)	0	0 (0–1·9)	–
Upper East	**93·0**	31	3 (2–4·2)	2	2·6 (0·3–9·3)	1·17
Ashanti	**83·7**	34	0·8 (0·5–1·1)	3	0·4 (0·1–1)	2·20
Central	**74·5**	6	0·3 (0·1–0·7)	2	0·3 (0–1·2)	1·03
Volta	**74·5**	46	2·7 (2–3·6)	3	0·5 (0·1–1·5)	5·24
Western	**70·0**	22	1·2 (0·8–1·9)	7	0·9 (0·4–1·9)	1·35
Eastern	**68·7**	24	1·2 (0·8–1·8)	0	0 (0–0·4)	–
Brong Ahafo	**61·6**	25	1·6 (1·1–2·4)	10	1 (0·5–1·9)	1·56
Upper West	**58·3**	23	5·3 (3·3–7·9)	7	2·3 (0·9–4·6)	2·35
Northern	**51·1**	12	0·9 (0·5–1·5)	10	0·8 (0·4–1·4)	1·15
Area	**%[1]**	**Reported BU cases**				
		< 5 km from PHC		**> 5 km from PHC**		
		N	**Rate (95% CIs)**	**N**	**Rate (95% CIs)**	**Rate Ratio[4]**
All Regions	**75·4**	**246**	**1·2 (1·1–1·4)**	**34**	**0·5 (0·4–0·7)**	**2·36**
Greater Accra	**95·5**	30	0·7 (0·5–1)	1	0·5 (0–2·9)	1·42
Ashanti	**83·7**	94	2·2 (1·8–2·7)	17	2 (1·2–3·3)	1·07
Central	**74·5**	25	1·4 (0·9–2·1)	9	1·5 (0·7–2·8)	0·95
Western	**70·0**	12	0·7 (0·3–1·2)	3	0·4 (0·1–1·1)	1·71
Eastern	**68·7**	56	2·9 (2·2–3·7)	1	0·1 (0–0·6)	25·53
Brong Ahafo	**61·6**	29	1·9 (1·3–2·7)	3	0·3 (0·1–0·9)	6·03
Area	**%[2]**	**Reported cases of suspected filarial lymphedema**				
		< 5 km from PHC		**> 5 km from PHC**		
		N	**Rate[3] (95% CIs)**	**N**	**Rate[3] (95% CIs)**	**Rate Ratio[4]**
All Regions	**72·8**	**1296**	**10·2 (9·7–10·8)**	**261**	**4·9 (4·3–5·5)**	**2·09**
Greater Accra	**99·2**	25	0·9 (0·6–1·3)	0	0 (0–2·5)	–
Upper East	**93·0**	948	91·4 (85·7–97·4)	62	80·2 (61·5–102·9)	1·14
Ashanti	**71·8**	8	0·4 (0·2–0·8)	7	0·9 (0·3–1·8)	0·49
Central	**71·2**	103	7·6 (6·2–9·2)	20	3·2 (2–5)	2·34
Western	**70·0**	117	6·5 (5·4–7·8)	61	7·9 (6–10·1)	0·83
Eastern	**67·8**	43	3·1 (2·2–4·1)	19	2·3 (1·4–3·6)	1·33
Brong Ahafo	**56·8**	12	1·2 (0·6–2·2)	27	3·1 (2–4·5)	0·40
Northern	**52·5**	40	3·1 (2·2–4·2)	65	5·4 (4·2–6·9)	0·57

[1]Proportion of population living within 5 km of a primary health facility (PHF).

[2]Proportion of population within 5 km of a PHF, in districts where LF morbidity registration was implemented in 2014.

[3]Rates of leprosy and BU were calculated from the number of newly reported cases in 2014 per 100,000 population; rates of suspected lymphedema were calculated from the number of suspect cases recorded during morbidity registration, per 100,000 population.

[4]Ratio of the rate within 5 km of PHC to that beyond 5 km of PHC.

Regional populations, populations in districts where morbidity registration was implemented, and populations within 5 km of a PHC facility were estimated using data from the WorldPop project (1).

CIs = confidence intervals, calculated using Byar's method.

Table 2. Numbers and proportions of leprosy cases with grade 1/2 disability at diagnosis, and Buruli Ulcer (BU) cases with category II/III lesions or limitation of movement (LOM) at diagnosis, by distance to nearest primary health care facility in georeferenced cases, and in non-georeferenced cases. Data are from Ghana in 2014 and are shown by region

	Reported leprosy cases											
	<5 km			**>5 km**			**Total Mapped**			**Total not georeferenced**		
	N. graded	**With G1/2D**		**N. graded**	**With G1/2D**		**N. graded**	**With G1/2D**		**N. graded**	**With G1/2D**	
		N	**% (95% CIs)**		**N**	**% (95% CIs)**		**N**	**% (95% CIs)**		**N**	**% (95% CIs)**
All Regions	**208**	**53**	**25·5 (20–31·8)**	**27**	**9**	**33·3 (18·6–52·2)**	**235**	**62**	**26·4 (21·2–32·4)**	**29**	**7**	**24·1 (12·2–42·1)**
Ashanti	34	14	41·2 (26·4–57·8)	3	3	100 (43·9–100)	37	17	45·9 (31–61·6)	9	3	33·3 (12·1–64·6)
Brong Ahafo	25	9	36 (20·2–55·5)	10	3	30 (10·8–60·3)	35	12	34·3 (20·8–50·8)	7	3	42·9 (15·8–75)
Central	6	1	16·7 (3–56·4)	2	0	0 (0–65·8)	8	1	12·5 (2·2–47·1)	1	1	100 (20·7–100)
Eastern	13	7	53·8 (29·1–76·8)	0	0	0	13	7	53·8 (29·1–76·8)	1	0	0 (0–79·3)
Greater Accra	28	11	39·3 (23·6–57·6)	0	0	0	28	11	39·3 (23·6–57·6)	0	0	0
Northern	2	2	100 (34·2–100)	0	0	0	2	2	100 (34·2–100)	0	0	0
Upper East	31	2	6·5 (1·8–20·7)	2	0	0 (0–65·8)	33	2	6·1 (1·7–19·6)	2	0	0 (0–65·8)
Upper West	23	6	26·1 (12·5–46·5)	7	3	42·9 (15·8–75)	30	9	30 (16·7–47·9)	7	0	0 (0–35·4)
Volta	46	1	2·2 (0·4–11·3)	3	0	0 (0–56·1)	49	1	2 (0·4–10·7)	2	0	0 (0–65·8)
Western	0	0	0	0	0	0	0	0	0	0	0	0
	Reported BU cases											
	< 5 km			**> 5 km**			**Total Mapped**			**Total not georeferenced**		
	N. graded	**With cat II-III or LOM**		**N. graded**	**With cat II-III or LOM**		**N. graded**	**With cat II-III or LOM**		**N. graded**	**With cat II-III or LOM**	
		N	**% (95% CIs)**		**N**	**% (95% CIs)**		**N**	**% (95% CIs)**		**N**	**% (95% CIs)**
All Regions	**216**	**156**	**72·2 (65·9–77·8)**	**29**	**20**	**69 (50·8–82·7)**	**245**	**55**	**67·9 (57·1–77·1)**	**53**	**42**	**84 (71·5–91·7)**
Ashanti	69	47	68·1 (56·4–77·9)	12	8	66·7 (39·1–86·2)	81	22	81·5 (63·3–91·8)	25	16	72·7 (51·8–86·8)
Brong Ahafo	24	20	83·3 (64·1–93·3)	3	2	66·7 (20·8–93·9)	27	26	76·5 (60–87·6)	0	0	0
Central	25	19	76 (56·6–88·5)	9	7	77·8 (45·3–93·7)	34	36	63·2 (50·2–74·5)	5	4	80 (37·6–96·4)
Eastern	56	36	64·3 (51·2–75·5)	1	0	0 (0–79·3)	57	22	71 (53·4–83·9)	5	5	100 (56·6–100)
Greater Accra	30	22	73·3 (55·6–85·8)	1	0	0 (0–79·3)	31	15	100 (79·6–100)	10	10	100 (72·2–100)
Western	12	12	100 (75·8–100)	3	3	100 (43·9–100)	15	0	0 (0–0)	8	7	87·5 (52·9–97·8)

[1]out of those with DG recorded. [2]out of cases with at least one of these indicators available.
CIs = confidence intervals, calculated using the Wilson Score method.

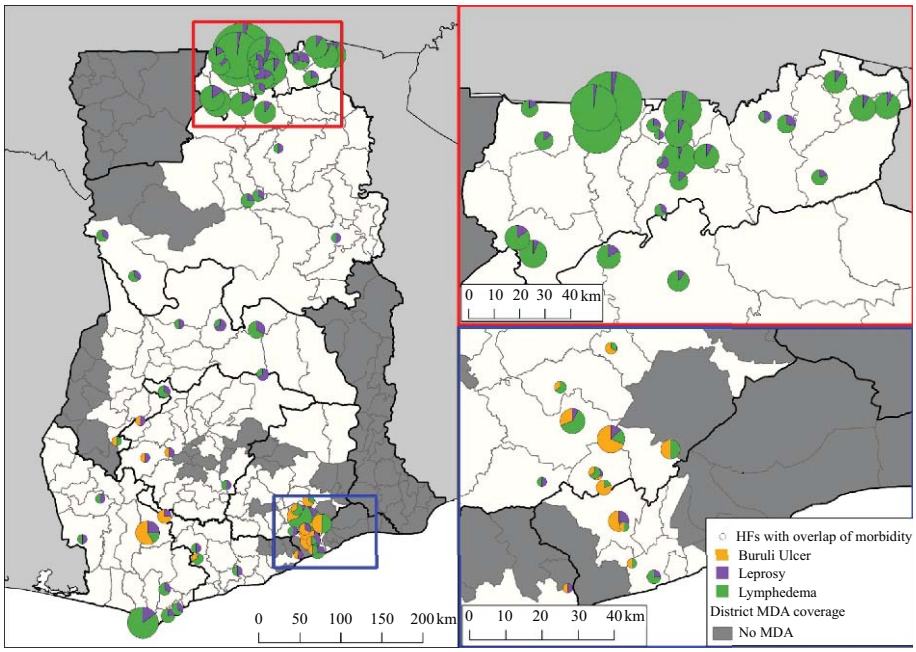

Figure 4. Overlapping morbidity caused by leprosy, BU and lymphedema in health facilities Ghana, in the Upper East Region, and in and around Accra.

of lymphedema and leprosy, and extensive overlap between these two causes of morbidity. In parts of Greater Accra and across the northern border into the Eastern Region, there was overlap of morbidity due to BU, leprosy, and lymphedema (Figure 4).

At district-level, overlap of these conditions was relatively common: 42 of 216 districts reported at least two of BU, leprosy and lymphedema (Table 3).

Discussion

The maps presented in this work show the burden of BU, leprosy and filarial lymphedema that is already visible to the health system in Ghana. We have used the mapped data to identify

Table 3. The number of districts in Ghana reporting routinely detected cases of lymphedema, leprosy and Buruli ulcer (BU) in 2014

Number of conditions recorded (BU, leprosy, lymphedema)	Number of districts	%
0	52	*24·1*
1	122	*56·5*
2	39	*18·1*
3	3	*1·4*
Total	**216**	

overlap of CM-disease within existing health care facilities that would deliver care for patients. NTD-related morbidity was primarily identified in areas where the population had a greater level of geographical access to primary healthcare. The accessibility of PHC facilities may impact the rate of recorded cases, although specific reasons for this are not clear and multiple factors are likely to be involved. Lower accessibility of PHC facilities was related to a higher risk of more advanced morbidity for leprosy, but not for BU. These results could help to inform the implementation of integrated morbidity management, in line with WHO recommendations for NTD control.

The use of routine data was a key aspect of this investigation, and we recognise that these data sources entail certain limitations, especially around under-detection and under-reporting of cases. There were some discrepancies between the numbers of leprosy cases collated by the regional programme officers from hospital and district registers, and the numbers reported by the regional programme officers to the LEP. The main cause of the discrepancy in the national totals is likely to be that four districts in which cases had been recorded did not report data to the NLP. The main cause of discrepancies in the totals at district-level is different allocation of cases to districts within this exercise and by the LEP. Within this exercise, cases were allocated to district of residence, while the LEP allocates cases to the district of the facility in which they were diagnosed.

Leprosy and BU are recognised to be under-reported globally,[38,39] with evidence of under-diagnosis and under-reporting in passive case detection systems in a range of settings.[40–42] It is also important to note that the data on LF was collected by volunteers, and is not clinically verified; a proportion of the recorded lymphedema cases included here may not be caused by LF. Validation studies would be required to assess the impact of this on our results. Meanwhile, we expect that the data used in this investigation gives an underestimate of the burden of filarial lymphedema: morbidity surveys conducted in the context of MDA campaigns are demonstrated to detect fewer cases than dedicated surveys,[43] and furthermore, cases in districts that did not implement MDA for LF in 2014 would not be detected in this system.

The impact of under-detection by passive surveillance is potentially more extreme in communities with a lower level of access to PHC, which could introduce bias due to spatial differences in availability and accessibility of health facilities to the population. We sought to assess this by mapping the distribution of reported cases alongside that of reporting health facilities, and by comparing the rates of reported disease in populations with higher and lower estimated access to health facilities. The disease distribution maps show that cases whose reporting health facility was recorded were generally close to those facilities. We also found that rates of recorded and mapped leprosy and BU were higher in the population within 5 km of a PHC facility, which may reflect higher rates of case ascertainment in populations with better access to PHC facilities. Another possibility is that cases may travel for diagnosis and treatment, and the community recorded in the clinic is not the case's permanent place of residence, but a temporary address where they are staying while under treatment. An increased rate in populations closer to PHC facilities was also observed for suspected cases of filarial lymphedema. The detection of this condition was not expected to be affected by the accessibility of health services, as the MDA campaigns through which the cases were recorded are supposed to be implemented homogeneously and massively across endemic areas. An alternative explanation is that the apparent concentration of lymphedema cases closer to PHC facilities is due to spatial differences in the availability of coordinates for remote georeferencing: cases in larger towns are presumably more likely to be georeferenced,

and more likely to be near a health facility, compared to those in smaller communities. This would apply to the other morbidity conditions as well.

We undertook a sensitivity analysis to further explore the association between the rates of detected NTD cases and the proximity of PHC facilities (results in Table 2S in supplementary file).

In most regions, the calculated rate ratios of BU and leprosy cases within and beyond 5 km of the nearest health facility were sensitive to assumptions about the distribution of non-georeferenced cases. Of the estimated upper and lower limits for the rate ratios, we expect the latter (in which all non-georeferenced cases were assumed to occur >5 km from the nearest PHC facility) to be more realistic, since non-georeferenced communities are probably small and remote, and therefore less likely to be well served by PHC. Regardless of where non-georeferenced cases were assumed to occur, calculated rates of reported leprosy were higher in populations within 5 km of PHC in the Upper West and Volta Regions. Rates of reported BU were higher in populations within 5 km of PHC in the Eastern and Brong Ahafo Regions, regardless of the assumed location of non-georeferenced BU cases. These four regions all had low or moderate levels of accessibility of PHC, implying more robust evidence for an effect of PHC accessibility on the rate of reported disease in regions lacking good access to PHC. When it was assumed that all cases of suspect filarial lymphedema occurred >5 km from the nearest PHC facility, all regions had a higher rate in this population. This implies that the entire effect of accessibility of PHC facilities on the rate of this condition may be explained by varying availability of geo-data.

Leprosy cases that occurred more than 5 km from PHC facilities or were not georeferenced were less likely to have been graded at diagnosis than cases located within 5 km of PHC facilities. This may be due to variation in data completeness between regions: most regions had no missing clinical data whereas three regions had significant numbers whose disability grading was unknown. This suggests a potentially high burden of undiagnosed or unreported morbidity among cases in these regions, which is an important consideration in terms of targeting resources for case management. Missing clinical data on BU cases occurred in only two regions, but with little variation between mapped and unmapped cases, or between cases within and beyond 5 km of primary healthcare facilities.

Six regions reported leprosy cases who were living further than 5 km from PHC facilities. Overall, cases living further from PHC showed an increased risk of more advanced morbidity at diagnosis (Table 2). This may reflect the impact of diagnostic delay on patients who have to travel further to obtain health care.

Integration of the morbidity maps for leprosy, BU and lymphedema revealed co-distribution of disease in all regions where at least two of the diseases had been reported. The extent of overlap was most common in the Upper East and the Greater Accra Regions. These regions had relatively high concentrations of both leprosy and lymphedema, and also had the highest levels of access to primary healthcare facilities. The detected disease overlap may be a result of higher rates of case detection in these areas. Forty-two instances of disease overlap were identified at district level. These districts would be considered target areas for trialling integration of NTD programme activities, including health worker training and coordination of programme management.

Although routine surveillance data entails limitations, and is recognised to underestimate true numbers of cases, the approach piloted here has many advantages that support its use in mapping NTDs and their associated morbidity in the future. For autonomy and sustainability, NTD programmes require access to internally and routinely generated data sources over

which they have full ownership. This investigation demonstrates how such datasets can be integrated and used to create a resource for the planning of interventions against NTD morbidity. The datasets were readily available, and remote geo-referencing meant there was no need for travel within country, implying a significant saving in monetary and time costs. The process could be implemented by technical staff in NTD-endemic countries with some support during the orientation of the protocol, and following basic GIS training. Overall, these advantages mean that this approach to mapping could be developed into a sustainable and routine component of NTD surveillance, implemented as part of national disease control programmes.

Management of the mapping process by national programme officers would overcome some of the limitations encountered in this pilot, in particular by reducing the impact of missing data. Firstly, local knowledge would be used as a tool to locate communities that could not be georeferenced using online or paper maps. Secondly, the use and feedback of surveillance data in the form of morbidity and disease occurrence maps to the officers responsible for reporting the data would likely lead to improvements in data collection, management and reporting. Finally, updating the maps annually with newly reported morbidity cases would provide a more complete representation of existing morbidity. The accuracy and completeness of surveillance data could be further improved through the use of modern electronic platforms such as smart phones for data collection and reporting (i.e. via SMS and electronic forms).[43] Overall, the method is likely to become more sensitive to detect community-level overlap of morbidity over time.

In Ghana, the District Health Information Management System software DHIMS II, developed and used by the GHS for reporting and analysing health data, would be an appropriate platform for integrating datasets for mapping. Investment in improving the data collection and reporting functions of this system would complement integrated data collection activities, and avoid duplication in software development and maintenance, and in training for data managers.

Achieving full population coverage of integrated CM services will require broader development of NTD surveillance, strengthening of national control programmes, and of the primary health care system.[13,44] Integrated mapping of NTD morbidity, alongside the primary healthcare system, is an essential first step in identifying population health needs, to ensure that investment in these areas is appropriately directed. We recommend the use of routine data sets in this undertaking, in order to promote in-country ownership and management of all aspects of NTD control.

Conclusions

This study has identified substantial overlap of NTD-related morbidity in Ghana. There was an apparent concentration of cases and morbidity overlap in areas which have higher levels of access to primary health facilities, although it is not clear whether this is due to differences in surveillance coverage, the availability of geo-data, or differences in disease distribution. Validation surveys would clarify this issue. In Ghana, the maps presented here are already supporting the development of a strategic plan for integrated case management of morbidity associated with NTDs. As this plan is implemented, it will be critical to update these maps with current data.

The exercise piloted here is intended to represent the start of an iterative process to provide detailed and up-to-date information to target integrated interventions against CM-NTDs. As the approach develops, parallel improvements to data collection systems will be vital to provide a more accurate and reliable representation of disease burden, in order to inform targeting of resources and activities on a national scale. It is hoped that the integration of data collection tools will lead to an overall improvement in surveillance systems for NTDs.

NTD-related morbidity affects the lives and livelihoods of millions of people worldwide, and cannot be tackled simply by interrupting transmission of NTDs. Addressing the burden of NTD-morbidity requires detailed information on the location of individuals requiring CM, which is often lacking in maps of NTD distribution. It is intended that the approach piloted here will be implemented in other countries where CM NTDs are endemic, supporting the improvement of data on the distribution of NTD-related morbidity. This would help inform investment in integrated CM and the integration of case detection activities in Africa, promoting earlier, wider, and more equitable access to care for all those affected by NTDs.

Acknowledgements

We would like to express our thanks to individuals who have lent their expertise at various stages of the work. We would like to acknowledge the work of community health workers, district programme officers and regional programme officers of the disease control programmes in Ghana, who have worked together to collect the data used in this investigation.

Contributors

The idea for the work was conceived through discussion between Professor Simon Brooker, Dr. Emmy van der Grinten, Dr. Paul Saunderson and Dr. Nana-Kwadwo Biritwum. Dr Jorge Cano and Hope Simpson developed the methodological approach. The data were collected through routine surveillance via the Neglected Tropical Diseases Programme, managed by Dr Nana-Kwadwo Biritwum with Mr. Samuel Odoom as data manager; the Leprosy Elimination Programme, managed by Dr Ekow Amankrah-Otabir with Dr Benedict Quao in a deputizing role; the National Buruli Ulcer Control Programme, managed by Dr. Edwin Ampadu and the National Yaws Eradication Programme, managed by Dr. Cynthia Kwakye MacLean. Ms. Hope Simpson wrote the manuscript with input from all listed authors.

Data availability

The data mapped in this investigation are confidential and are under ownership of the Ghana Health Service in Ghana. Access to the data is at the discretion of the Director for Public Health within the Ghana Health Service, with ethical approval from the Ghana Health Service Ethical Review Committee.

Funding source

The AIM Initiative was the sole funder of this work.

Conflict of interest

This paper was edited by Prof. W.C.S. Smith to avoid conflict of interest.

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Supplementary

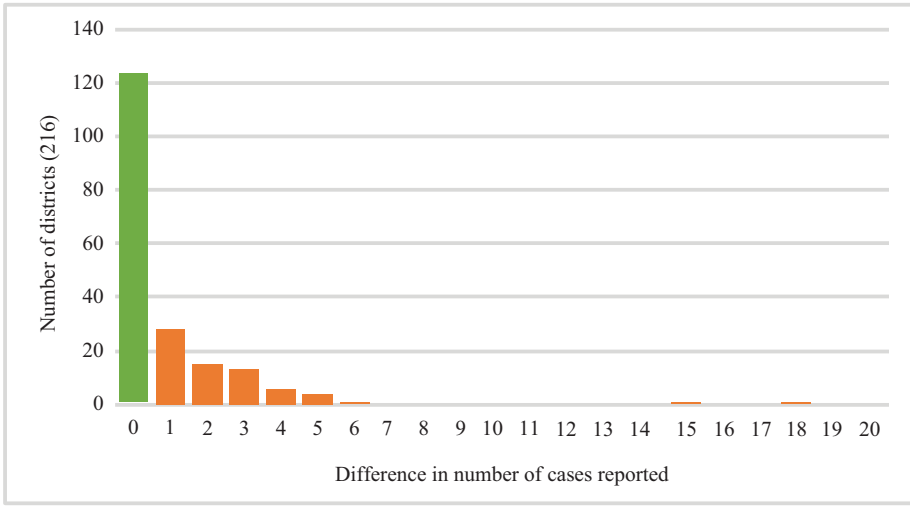

Figure 1S. Frequency distribution of differences in case numbers recorded in leprosy district registers and district totals reported to the Leprosy Elimination Program.

Table 1S. Number of Buruli ulcer cases recorded in Ghana in 2014, by region, referral source, category of lesion and limitation of movement. WHO programmatic targets are shown in brackets in column headings

		Detected by CV or HW		Category of lesion					Limitation of movement (LOM ≤15%)				Ulcerative	
	Total	n	%	I	II	III	Unknown[1]	% Cat III[2] (≤25%)	No	Yes	Unknown[1]	% with LOM[2] (≤15%)	n	% (≤60%)
Ashanti	136	114	*83·8*	66	39	24	7	*30·2*	96	11	29	*10·3*	82	*60·3*
Brong Ahafo	32	11	*34·4*	10	9	8	5	*33·3*	28	4	0	*12·5*	30	*93·8*
Central	39	14	*35·9*	8	20	11	0	*51·3*	30	9	0	*23·1*	29	*74·4*
Eastern	62	36	*58·1*	27	12	23	0	*19·4*	44	18	0	*29·0*	57	*91·9*
Greater Accra	41	26	*63·4*	16	5	20	0	*12·2*	29	12	0	*29·3*	37	*90·2*
Western	23	2	*8·7*	0	7	16	0	*30·4*	20	3	0	*13·0*	16	*69·6*
Total	333	203	*61·0*	127	92	102	12	*28·7*	247	57	29	*18·8*	251	*75·4*

[1]Data not recorded. [2]% of cases for whom this information was recorded.
CV = community volunteer, HW = health worker.

Table 2S. Sensitivity analysis of the distribution of non-georeferenced cases on rates of disease by distance to health facility

	Reported leprosy							
	<5 km from PHC		>5 km from PHC					
Area	N	Rate[1]	N	Rate	N. not geo referenced	RR Estimate[2]	RR Lower[3]	RR Upper[4]
All Regions	**251**	**1·26**	**44**	**0·68**	**55**	**1·86**	**0·83**	**2·27**
Greater Accra	28	0·68	0	0·00	**0**	–	–	–
Upper East	31	2·99	2	2·56	**2**	1·17	0·58	1·24
Ashanti	34	0·79	3	0·36	**9**	2·20	0·55	2·79
Central	6	0·34	2	0·33	**1**	1·03	0·68	1·20
Volta	46	2·73	3	0·52	**2**	5·24	3·15	5·47
Western	22	1·23	7	0·91	**3**	1·35	0·94	1·53
Eastern	24	1·23	0	0·00	**7**	–	1·56	–
Brong Ahafo	25	1·63	10	1·04	**7**	1·56	0·92	2·00
Upper West	23	5·28	7	2·25	**7**	2·35	1·17	3·06
Northern	12	0·89	10	0·77	**17**	1·15	0·43	2·77
	Reported Buruli ulcer							
	< 5 km from PHC		> 5 km from PHC					
Area	N	Rate	N	Rate	N. not geo referenced	RR Estimate	RR Lower	RR Upper
All Regions	**246**	**1·23**	**34**	**0·52**	**53**	**2·36**	**0·92**	**2·87**
Greater Accra	30	0·73	1	0·52	**10**	1·42	0·13	1·89
Ashanti	94	2·19	17	2·03	**25**	1·07	0·44	1·36
Central	25	1·41	9	1·49	**5**	0·95	0·61	1·14
Western	12	0·67	3	0·39	**8**	1·71	0·47	2·86
Eastern	56	2·86	1	0·11	**5**	25·53	4·26	27·81
Brong Ahafo	29	1·89	3	0·31	**0**	6·03	6·03	6·03
	Suspected filarial lymphedema							
	< 5 km from PHC		> 5 km from PHC					
Area	N	Rate	N	Rate	N. not geo referenced	RR Estimate	RR Lower	RR Upper
All Regions	**1296**	**10·23**	**261**	**4·90**	**826**	**2·09**	**0·50**	**3·42**
Greater Accra	25	0·86	0	0·00	**8**	–	0·16	–
Upper East	948	91·42	62	80·23	**632**	1·14	0·10	1·90
Ashanti	8	0·42	7	0·86	**8**	0·49	0·23	0·98
Central	103	7·61	20	3·25	**31**	2·34	0·92	3·05
Western	117	6·53	61	7·90	**48**	0·83	0·46	1·17
Eastern	43	3·06	19	2·30	**25**	1·33	0·57	2·10
Brong Ahafo	12	1·24	27	3·10	**20**	0·40	0·23	1·06
Northern	40	3·05	65	5·39	**54**	0·57	0·31	1·33

Rates of leprosy and BU were calculated from the number of newly reported cases in 2014 per 100,000 population; rates of suspected lymphedema were calculated from the number of suspect cases recorded during morbidity registration, per 100,000 population.

[1]RR = Ratio of the rate within 5 km of PHC to that beyond 5 km of PHC.

[2]All non-georeferenced cases were assumed to occur < 5 km from the nearest PHC facility.

[3]All non-georeferenced cases were assumed to occur > 5 km from the nearest PHC facility.

Table 3S. Completeness of morbidity grading data among leprosy and Buruli ulcer (BU) cases by region

	Reported leprosy cases											
	<5 km			>5 km			Total Mapped			Total not georeferenced		
		Graded			Graded			Graded			Graded	
	Total	N	% (95% CIs)	Total	N	% (95% CIs)	Total	N	% (95% CIs)	Total	N	% (95% CIs)
All Regions	**251**	**208**	**82·9 (77·7–87)**	**44**	**27**	**61·4 (46·6–74·3)**	**295**	**235**	**79·7 (74·7–83·9)**	**55**	**29**	**52·7 (39·8–65·3)**
Ashanti	34	34	100 (89·8–100)	3	3	100 (43·9–100)	37	37	100 (90·6–100)	9	9	100 (70·1–100)
Brong Ahafo	25	25	100 (86·7–100)	10	10	100 (72·2–100)	35	35	100 (90·1–100)	7	7	100 (64·6–100)
Central	6	6	100 (61–100)	2	2	100 (34·2–100)	8	8	100 (67·6–100)	1	1	100 (20·7–100)
Eastern	24	13	54·2 (35·1–72·1)	0	0	0	24	13	54·2 (35·1–72·1)	7	1	14·3 (2·6–51·3)
Greater Accra	28	28	100 (87·9–100)	0	0	0	28	28	100 (87·9–100)	0	0	0
Northern	12	2	16·7 (4·7–44·8)	10	0	0 (0–27·8)	22	2	9·1 (2·5–27·8)	17	0	0 (0–18·4)
Upper East	31	31	100 (89–100)	2	2	100 (34·2–100)	33	33	100 (89·6–100)	2	2	100 (34·2–100)
Upper West	23	23	100 (85·7–100)	7	7	100 (64·6–100)	30	30	100 (88·6–100)	7	7	100 (64·6–100)
Volta	46	46	100 (92·3–100)	3	3	100 (43·9–100)	49	49	100 (92·7–100)	2	2	100 (34·2–100)
Western	22	0	0 (0–14·9)	7	0	0 (0–35·4)	29	0	0 (0–11·7)	3	0	0 (0–56·1)

	Reported BU cases											
	< 5 km			> 5 km			Total Mapped			Total not georeferenced		
		Graded[1]			Graded[1]			Graded[1]			Graded[1]	
	Total	N	% (95% CIs)	Total	N	% (95% CIs)	Total	N	% (95% CIs)	Total	N	% (95% CIs)
All Regions	**246**	**216**	**87·8 (83·1–91·3)**	**34**	**29**	**85·3 (69·9–93·6)**	**280**	**245**	**87·5 (83·1–90·9)**	**53**	**50**	**94·3 (84·6–98·1)**
Ashanti	94	69	73·4 (63·7–81·3)	17	12	70·6 (46·9–86·7)	111	81	73 (64–80·4)	25	22	88 (70–95·8)
Brong Ahafo	29	24	82·8 (65·5–92·4)	3	3	100 (43·9–100)	32	27	84·4 (68·2–93·1)	0	0	0
Central	25	25	100 (86·7–100)	9	9	100 (70·1–100)	34	34	100 (89·8–100)	5	5	100 (56·6–100)
Eastern	56	56	100 (93·6–100)	1	1	100 (20·7–100)	57	57	100 (93·7–100)	5	5	100 (56·6–100)
Greater Accra	30	30	100 (88·6–100)	1	1	100 (20·7–100)	31	31	100 (89–100)	10	10	100 (72·2–100)
Western	12	12	100 (75·8–100)	3	3	100 (43·9–100)	15	15	100 (79·6–100)	8	8	100 (67·6–100)

[1]Presence/absence of LOM and category of lesion recorded.