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1. Introduction

On 20 August 2008 an outbreak of 118 cholera cases was declared in St. Mary’s and Zengeza wards of Chitungwiza, a large urban centre on the outskirts of Harare. Vibrio cholerae El Tor 01 was isolated from 18 (30%) of the 59 specimens collected, thus supporting the clinical evidence for an outbreak. Two months after this initial outbreak, a second wave of cases was reported with numerous suburbs being affected within the city of Harare and within every province of the country. This was the largest and most extensive outbreak of cholera recorded in Zimbabwe and indeed in Africa, affecting rural and urban areas with more than 100 000 cases and 4000 deaths, about half of which occurred in the urban centres of Harare and Chitungwiza.

During the 2008–2009 Zimbabwe cholera epidemic the country was in economic crisis and the health care system had become dysfunctional, with most government hospitals unable to provide services or closed due to a lack of essential medical supplies. Many staff in health structures had not been paid, and many were unable to report for duty. Water supplies were irregular and sanitation systems had collapsed. The reason for this was a lack of maintenance of the system, with frequent power interruptions affecting pumping stations.

By 2008, Chitungwiza had been without adequate water supply water for more than two years. People had become dependent on shallow wells that were at risk of contamination because of the lack of sewage disposal. On 1 December 2008, problems with the main pumping station meant that, without prior warning, the water supply was shut off for Harare, leaving large populations without
agents to clean water, may facilitate the spread of diarrheal disease. Food items, particularly those that lack sanitation or access in overcrowded areas, including markets. Markets selling food items, particularly those that lack sanitation or access in markets were closed. Ten ORPs were functioning in Harare city and one in Chitungwiza. In disadvantaged settings Vibrio cholerae is predominantly transmitted by contaminated water and through person to person contact, and the risk of transmission is greatest in overcrowded areas, including markets. Markets selling food items, particularly those that lack sanitation or access to clean water, may facilitate the spread of diarrheal disease agents. In line with the above it can be hypothesised that the distribution of cholera cases by suburb in Harare during the epidemic of 2008-2009 followed an identifiable spatial pattern related to the active population movements and high density population areas.

There are currently no published data showing the spatial distribution and spread of cholera cases in Harare. In this paper we describe the spatial distribution of the cholera epidemic in Harare and Chitungwiza and identify factors that influenced the spatial pattern of the outbreak spread that may explain mechanism of transmission, in order to guide future preparedness and control measures.

### 2. Methods

We developed a population-based ecological study using a secondary data analysis. The study protocol was approved by the Ethical Review Board of Médecins Sans Frontières (MSF).

Data were drawn from the register of cholera treatment centres (CTCs) and oral rehydration points (ORPs) functioning during the cholera epidemic in Harare and Chitungwiza. MSF, in collaboration with the Department of City Health of the Ministry of Health and Child Welfare, implemented and managed three CTCs, in Budiriro Polyclinic, the Beatrice Road Infectious Diseases Hospital and in Chitungwiza. Ten ORPs were functioning in Harare city and one in Chitungwiza.

Population figures by suburb were calculated from the official census of Harare and Chitungwiza, completed in 2002. To estimate the populations’ figures at the time of the epidemic we employed an average constant annual growth rate of 3%, as estimated by the Population Division of the Department of Economic and Social Affairs of the United Nations Secretariat.

For the case definition of cholera, we used the definition as listed in the MSF cholera guidelines: in an area where there is a cholera epidemic a cholera case is defined as any patient presenting three or more liquid stools and/or vomiting for the last 24 hours.

In the statistical analysis we describe the outbreak in the classical way, in terms of person, place and time. We calculated descriptive statistics for the variables related to person (age, sex). To describe the outbreak by place we calculated the attack rates for each suburb, including 95% exact confidence intervals (Cl) under the assumption that the attack rates follow a Poisson distribution. Then, to describe epidemic time evolution, we presented epidemic curves for suburbs with more than fifty cholera cases.

In order to describe the relation between the cholera cases and high density population areas, we computed the Pearson’s correlation coefficient (R) between the number of cholera cases and the number of bus stops plus markets by suburbs. Then, we represented a scatter plot, taking out extreme values, to show the relation between cholera cases and the number of bus stops plus markets by suburbs. Both variables were drawn from the Department of the Surveyor-General of the government of Zimbabwe, and have been used as proxies of overcrowded and high mobility areas, where the probability of person to person contact is high.

### Table 1

<table>
<thead>
<tr>
<th>Variables</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>10 071 (51.9)</td>
</tr>
<tr>
<td>Females</td>
<td>9272 (47.7)</td>
</tr>
<tr>
<td>Data missing</td>
<td>79 (0.4)</td>
</tr>
<tr>
<td>Age in years</td>
<td></td>
</tr>
<tr>
<td>≤5</td>
<td>3542 (18.2)</td>
</tr>
<tr>
<td>6-14</td>
<td>1932 (9.9)</td>
</tr>
<tr>
<td>15-24</td>
<td>3811 (19.6)</td>
</tr>
<tr>
<td>25-34</td>
<td>4828 (24.9)</td>
</tr>
<tr>
<td>35-44</td>
<td>2682 (13.8)</td>
</tr>
<tr>
<td>≥45</td>
<td>2627 (13.5)</td>
</tr>
<tr>
<td>Children ≤5 years</td>
<td></td>
</tr>
<tr>
<td>0-2</td>
<td>2356 (66.5)</td>
</tr>
<tr>
<td>3-5</td>
<td>1186 (33.5)</td>
</tr>
</tbody>
</table>

Access to potable water. With no water supply, the limited health structures that continued to operate could not maintain an acceptable level of infection control and many hospitals were closed.

The city of Harare is characterised by lower density affluent suburbs in the north and high density poorer areas in the south. Chitungwiza is a high density dormitory city in the south of Harare, which was established mainly to house workers commuting daily to Harare. The main form of transport in Harare and Chitungwiza is the minibus, a privately-owned small bus that collects passengers from designated bus stops.

Also in Harare and Chitungwiza a large proportion of economic activity is concentrated at informal markets. Markets are particularly common in high density suburbs where they serve the needs of commuters. In the past, city regulations restricted market trading, particularly of food products, to sites with appropriate water and sanitation facilities. At the time of the cholera outbreak, however, implementation of this regulatory framework had already broken down, and most trading was at informal sites with limited or no access to clean water.

In disadvantaged settings Vibrio cholerae is predominantly transmitted by contaminated water and through person to person contact, and the risk of transmission is greatest in overcrowded areas, including markets. Markets selling food items, particularly those that lack sanitation or access to clean water, may facilitate the spread of diarrheal disease agents.

### Table 2

<table>
<thead>
<tr>
<th>Age by sex</th>
<th>Male, n (%)</th>
<th>Female, n (%)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤5</td>
<td>1955 (19.4)</td>
<td>1566 (16.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>5-14</td>
<td>1041 (10.3)</td>
<td>879 (9.5)</td>
<td></td>
</tr>
<tr>
<td>15-24</td>
<td>1672 (16.6)</td>
<td>2126 (22.9)</td>
<td></td>
</tr>
<tr>
<td>25-34</td>
<td>2486 (24.7)</td>
<td>2328 (25.1)</td>
<td></td>
</tr>
<tr>
<td>35-44</td>
<td>1587 (15.8)</td>
<td>1088 (11.7)</td>
<td></td>
</tr>
<tr>
<td>≥45</td>
<td>1330 (13.2)</td>
<td>1285 (13.9)</td>
<td></td>
</tr>
</tbody>
</table>

*Pearson $\chi^2$-stat = 177.3

transmission is higher. After that, we added a linear interpolation computing the linear coefficient of determination (R²).23

In order to control for variance instability resulting from heterogeneity in cholera cases and population data (overdispersion), we estimated smoothed rate ratios (SRR) of cholera by suburb using an Empirical Bayesian Smoothing (EBS) model. The EBS consists of computing a weighted average between the raw rate for each suburb and the regional average, with weights proportional to the underlying population at risk.24,25 In effect, districts with relatively small populations tend to have their raw rates adjusted considerably, whereas for districts with relatively large populations the raw rates show little change.

In order to explain the relation between the cholera cases and overcrowded and high mobility areas, we introduced the number of bus stops plus markets in the glimm model used as a fixed effect. Then, we derived the risk ratio and its 95% CI which represented the risk of cholera per one unit increase in the number of bus stops plus markets for each suburb.

Finally, we represented graphically the epidemiological information generated in our analysis in two maps. The absolute number of cholera cases by suburbs and the SRR of cholera by suburb. We used Harare’s digital base map, which was developed by the Department of the Surveyor-General of the government of Zimbabwe. The map was digitized based on satellite imagery with Arcview software (Esri, Redlands, CA, USA), including streets, railroads, bus stops, markets and administrative boundaries of suburbs.

We used Stata (StataCorp LP, College Station, TX, USA) for statistical analysis and Arcview to present spatial geographical information.

3. Results

3.1. Epidemic description by person, place and time

During this cholera outbreak, CTCs and ORPs managed by MSF in Harare and Chitungwiza registered and cared for 19,422 persons meeting the case definition. The description of the epidemic by person shows that the population of working age and thus mobile (15 to 44 years old) represented 58.4% of cholera cases during the outbreak in Harare. Children <2 years of age represented 67% of the total cholera cases amongst children <5 years of age (Table 1).

As shown in Table 2, there were gender differences in the proportion of cholera cases by categories of age. There was a higher proportion of men >35 years than women of the same age, although this was not the case with younger men (15–24 years).

The description of the number of cases and attack rates by place (suburb) is presented in Table 3. The suburb with highest attack rate was Hopley with 90.3 cholera cases per 1000 people, 95% CI: 82.8–98.2, followed by Waterfalls, Mbare, Budiriro, Glen View and Glen Norah.

The epidemic curves by suburbs starting from epidemiological week 31 in 2008 (27 July - 2 August) to week 29 in 2009 (19–25 July) showed that the first cholera cases were registered during epidemiological week 34 in 2008.
in Chitungwiza (17–23 August). The epidemic then rapidly spread to the whole of Harare city starting with Epworth, Waterfalls, Mbare and Glen View. The total duration of the outbreak was 46 weeks. The epidemic presented two peaks; the first one took place in week 50 of 2008 (7-13 December) and the second in week 11 of 2009 (15-21 March) (Figure 1).

3.2. Spatial distribution of cholera cases and smoothed rate ratios

The distribution of cholera cases by suburb showed that the south west of Harare and Mbare suburbs were the most affected while industrial areas and north suburbs the least. In Hopley and Waterfalls more than 5% of the population were affected by cholera, and over 2% of the population in Mbare, Budiriro, Glen View and Glen Norah (Figure 2).

The number of cholera cases correlated positively with the number of markets and bus stops by suburb, with an R of 0.52 ($P=0.01$). The scatter plot of the rates ratios showed that the increase in number of bus stops plus markets by suburbs augmented the risk of cholera, with an $R^2$ of 0.31 ($P=0.01$) (Figure 3). The increase of one unit in the number of bus stops plus markets by suburbs increased the risk of cholera by 11% ($\text{Risk Ratio} = 1.11; 95\% \text{ CI} = 0.99–1.23$).

The spatial representation of smoothed rate ratios by suburb compared to the whole rate ratio of Harare and Chitungwiza showed a high risk of cholera in Mbare and south west suburbs of Harare (Figure 4).

4. Discussion

This study shows a spatial pattern of the distribution of cholera cases during the epidemic in Harare. This pattern is characterised by a low risk of cholera in the north of Harare, in low density residential areas, and a higher risk in low lying high density south west areas.

This spatial distribution of cases could be linked to the social and historical construction of the city which is characterised by the geographical location of more affluent suburbs, with low densities of population in the north and high density poorer areas in the south. High density population areas and lower socioeconomic status have both been identified as important risk factors in cholera transmission. Despite the changes in social and economic conditions since independence, the differences in density of housing persist. In the 1990s, two articles warned about the deficit of water supplies in the suburbs of the south of Harare and the problems related with the urban drainage system for resource recovery.
Figure 2. Map of greater Harare, including administrative boundaries, industrial areas, railway, bus stops and markets (2A) in relation to the distribution of cholera cases by suburbs (2B), 2008-2009 (n = 19 422 cases).
Figure 3. Scatter plot between cholera cases and the number of bus stops plus markets by suburbs in Harare, with a linear interpolation and 95% confidence interval, 2008–2009 (n = 19,422 cholera cases).

Figure 4. Distribution of smoothed rates ratios by suburbs in Harare 2008–2009 (n = 19,422 cholera cases).
and protection of drinking water supplies in downstream areas that coincided with south west Harare suburbs and Chitungwiza,26,27

Up to now it has been accepted that cholera has become endemic in some rural areas in Zimbabwe but following this outbreak, we can suggest the possibility that there is now a natural reservoir of Vibrio cholerae in Harare. In endemic areas cases have been shifting to younger children, with a peak of severe cases at the age of two.28 By contrast, in epidemic patterns of transmission, such as when Vibrio cholerae is introduced into an immunologically naive population, all age groups seem equally susceptible to symptomatic infection.29 Our study shows that amongst the children five years old or younger, children two years of age or younger were the most affected by the cholera epidemic, suggesting an endemic rather than epidemic epidemiological pattern. Clearly, more in-depth studies of the environment are needed to verify whether an endemic reservoir of Vibrio cholerae exists in Harare city or Chitungwiza.

The first cases reported by the CTCs were in Chitungwiza, probably a natural environmental reservoir of Vibrio cholerae. Southern suburbs of Harare have numerous bus stops, where people from Chitungwiza arrive in the city for work. Often adjacent to these bus stops are crowded informal markets, popular with commuters, with very poor sanitary conditions.14,15 Our results show that the mobile working population (15–44 years of age) represented the greatest proportion of cases, strongly suggesting that the combination of a highly mobile infectious working population coming together in the overcrowded and unsanitary conditions found in markets significantly influenced the spread of cholera into the city through person to person transmission.29,30

Our data are based on an estimated suburb population and we recognize that the estimates may not reflect the real figures during the epidemic. However we tried to take into account the natural average growth of the population in order to work with most realistic population estimates possible. Waterfalls and Hopley, where there are not bus stops and markets, have a high cholera risk, whereas other suburbs where there are many, as in Dzivarasekwa and Kuwadzana, have a low risk. It may be explained by population figures, with high population density in the former and lower in the later case. However more in-depth analyses are needed in order to understand the dynamic of the epidemic in these suburbs. Another limitation is the impossibility to control the effect of age on the comparison of the rates ratios by suburbs. Though an indirect standardisation is introduced into the overcrowded and unsanitary conditions found in markets significantly influenced the spread of cholera into the city through person to person transmission.29,31

In conclusion, it has been shown that the distribution of cholera cases by suburb in Harare during the outbreak of 2008–2009 followed an identifiable spatial pattern related to the active population movements and high density population areas. The identification of this clear spatial pattern could guide public health action in order to advocate for improving water and sanitation conditions and specific cholera preparedness measures in the most affected areas.

Authors’ contributions: MALF and PM developed the concept and design of the study; JF acquired the data; MALF developed analyses; MALF carried out the analyses and all authors interpreted the data; MALF wrote the manuscript. All authors drafted the manuscript, revised critically the content and gave technical support and conceptual advice. Finally, all authors read and approved the final manuscript. MALF is guarantor of the paper.

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Conflicts of interest: None declared.

Ethical approval: The study protocol was approved by the Ethical Review Board of Médecins Sans Frontières.

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