STUDY PROTOCOL
Médecins sans Frontières and University of Cape Town, South Africa

COUNTRY: **Zimbabwe**

SITE: **Harare and Chitungwiza**

STUDY TITLE:

Altitude and cholera risk: A spatial analysis of the Cholera epidemic in Zimbabwe 2008-09.

INVESTIGATORS /AFFILIATIONS

South Africa: Dr. Miguel Ángel Luque Fernández, PhD, Epidemiologist[1]
Miguel.luquefernandez@uct.ac.za
Dr. Michael Schomaker, Statistician[1]
Michael.Schomaker@uct.ac.za
Dr. Andrew Boulle, PhD, Epidemiologist[1]
Andrew.boulle@uct.ac.za

Zimbabwe: Dr.Peter R. Mason, PhD, Microbiology, Professor[2]
pmason@vet.uz.ac.zw, pmason@brti.co.zw

MSF Head-quarters and Belgium:

Dr. Yves Baudot, PhD, Geographer[3]
nadir@skynet.be
Jean François Fesselet, Msc[4]
Jean.francois.fesselet@amsterdam.msf.org
Peter Maes, Msc[6*]
Peter.Maes@brussels.msf.org

1) Centre for Infectious Disease, Epidemiology and Research, UCT University, Cape Town, South Africa.
2) Biomedical Research and Training Institute, University of Zimbabwe College of Health Sciences, Harare, Zimbabwe.
3) Manager of N.A.D.A.R sprl
4) Médecins Sans Frontières, Public health department, Water, Hygiene and Sanitation Unit, Amsterdam Operational Centre, Holland.
5) Médecins sans Frontières, Medical department: Water, hygiene and sanitation, Brussels Operational Center, Belgium.
**** Peter Maes is the promoter and mentorship of this study.***

BACKGROUND

In recent years Zimbabwe has faced increased problems of water supply, and more frequent reports of diarrhoeal disease outbreaks.[1-4] The cholera season in Zimbabwe is usually from January-February until April-May. On 20th August 2008 an outbreak of 118 cases was declared in St. Mary's and Zenenga wards of Chitungwiza, a large urban centre on the outskirts of Harare.[2, 5-7] *Vibrio Cholerae* El Tor 01 was isolated from 18 (30%) of the 59 specimens submitted for examination, thus supporting the clinical evidence for an outbreak of cholera.[2]

Following this initial outbreak, a second wave of infections was reported a few months later with numerous wards being affected and rapidly transmitted to the whole Harare city. This is by far the largest and most extensive outbreak of cholera yet recorded in Zimbabwe and indeed in Africa affecting rural and urban areas.[2, 3, 6]

Cholera is closely related to poor environmental status and lack of basic infrastructure in developing countries. In this manner, high population densities, poor access to safe water and proper sanitation along with other environmental conditions contribute to the spread of cholera in Africa.[8, 9] They have been described several environmental factor risks related with the start of a cholera epidemic such as sea surface temperature and height, and more recently with ambiance temperature and rainfall.[10, 11, 12] However there is slight evidence about the risk of cholera and topographical altitude.

Since the times of Farr, who hypothesizes the causal relation between the cholera cases and the altitude, indicating that there was an underlying "natural law" linking infection with cholera inversely to elevation above high water, there is no much more published.[13, 14] New findings about possible factors risk of cholera in a specific context are highly valuables being as it could be use as a toll to prevent and plan future cholera epidemic responses.

STUDY OBJECTIVE

This study aims to analyze the association between topographic altitude and the distribution of cholera cases by suburbs, in Harare 2008-09.

METHODS:

Type of study:

The study will be conceptualized as an ecological study.

Study data:

This study is a secondary (retrospective) data analysis.

Information about the number of cholera cases by suburbs were drawn from the register books of Cholera Treatment Centers (CTCs) and Oral Rehydration Points (ORP) which were functioning during the cholera epidemic in Harare city and Chitungwiza near Harare. CTCs were located in Buidiro Policlinic and Beatrice Road Infections Diseases Hospital and the third one in Chitungwiza. Ten ORPs were functioning in Harare city and one in Chitungwiza. Data collection was put in place in the CTCs and ORP.

Study period:

Two months.

Main outcome measures:

-Number of cholera cases by suburbs

-Suburbs average altitude in meters and distance of the centroide (geometric centre) of each suburb to the epicenter (Chitungwiza centroide).

-Observed and smoothed rate ratios of cholera by suburb adjusted for the topographic altitude and taken into account the spatial correlation of the data.

Study population:

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 & 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.[15]

Cholera case definition:

The case definition as listed in the MSF cholera guidelines. A cholera case is defined in any area where there is a cholera epidemic as: "Any patient presenting 3 or more liquid stools and/or vomiting for the last 24 hours" after a cholera epidemic has been confirmed.[16]

Statistical analysis:

Descriptive analysis:

By suburb:

-Number of cholera cases.

-Average altitude in meters.

-Distance in meters to Chitungwiza categorised in quintiles.

Analytic analysis:

To model the relation between the risk of Cholera by suburbs and the altitude in meters in Harare, taken into account the spatial correlation of the data, we are going to use a ***generalized linear mixed model*** under the assumption of a poisson distribution and a link log. Predictions from the model will be estimated using an Empirical Bayes Estimation.[17]

This approach will allow us to deal with extra variation due to uncorrelated heterogeneity (overdispersion) and correlated heterogeneity (spatial autocorrelation).[18]

To build the model, we are going to use a random intercept model with the number of cholera cases as dependent variable, the log of the population figures by suburb as offset and the suburb's average altitude as independent variable. The quintiles of the distance of each suburb to Chitungwiza, is going to be used as a hierarchical random effect in order to control the spatial correlation of the data. Therefore relying on the distance to Chitungwiza, five groups of suburbs will be built under the assumption of a

clustered variance estimation which specifies that the standard errors allow for intra suburbs correlation within each of the five groups, relaxing the usual requirement that the observations are independent.[17-20]

The model will be the following:

$Ln(cases_j)=ln(population_j)+\beta_0+\beta_1$*Altitude in meters+ U_i(Random effect: five clusters)
$Ln(cases_j)-ln(population_j)=ln(Cases/population)=\beta_0+\beta_1$*Altitude+$U_j$

Smoothed rate ratios (SRR) of cholera by suburb will be predicted from the model using an Empirical Bayesian Smoothing (EBS) approach (posterior probability). 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.[17-20]

Finally, we're going to develop a sensitive analysis in order to confirm the consistence of our findings, consisting in an iterative randomly selection of the cluster aggregation effect. The aiming of this process is to estimate the variability of the coefficient of the altitude taking as reference our first estimation and proof its consistence.

The final interpretation of the measure of association will be the increase or decrease of cholera risk per 100 meters of altitude increase or decrease taking into account correlated and uncorrelated structure of the data.

GIS component:

We are going to represent graphically the risk of cholera by suburb's average altitude controlling for spatial autocorrelation. The elevation information is contained in a raster digital model (each cell has an elevation value). Vector polygons define the extent of each urban district.. With ArcGIS "zonal statistics" module of the "Spatial Analyst" extension we are going to compute the suburbs mean altitude and the distance between each suburb centroide (geometric center of the polygon) to Chitungwiza centroide.

The statistical software programme that we are going to use will be Stata v.11.2, GIlamm module included and the module ArcMAP of ArcGIS (ESRI, v. 9.2) software for spatial and geographical representation.

Confidentiality of data:

No personal or confidential information was collected in the data base. There are no patient identifiers in the data base.

Feedback and dissemination of information:

In order to disseminate the information gained, attempts will be made to publish the study in a regional or international peer reviewed journal.

Benefits to the population (Community benefit)

The results of this study would BENEFIT international community due to the fact of the applicability of the findings. Altitude in meters could be a risk factor to take into account in cholera preparedness and responses.

Ethical approval:

The Protocol of this study has been previously submitted to the "Ethical Committee" of Médecins Sans Frontières OCB. We have written proof of the acceptance of this study.

Address for correspondence:

Peter Maes
Medical department (Operational research)
Medecins sans Frontieres (Brussels Operational Center)
94, rue Dupré
1090 Brussels
Belgium

E.mail : peter.maes@brussels.msf.be or Miguel.luquefernandez@uct.ac.za

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