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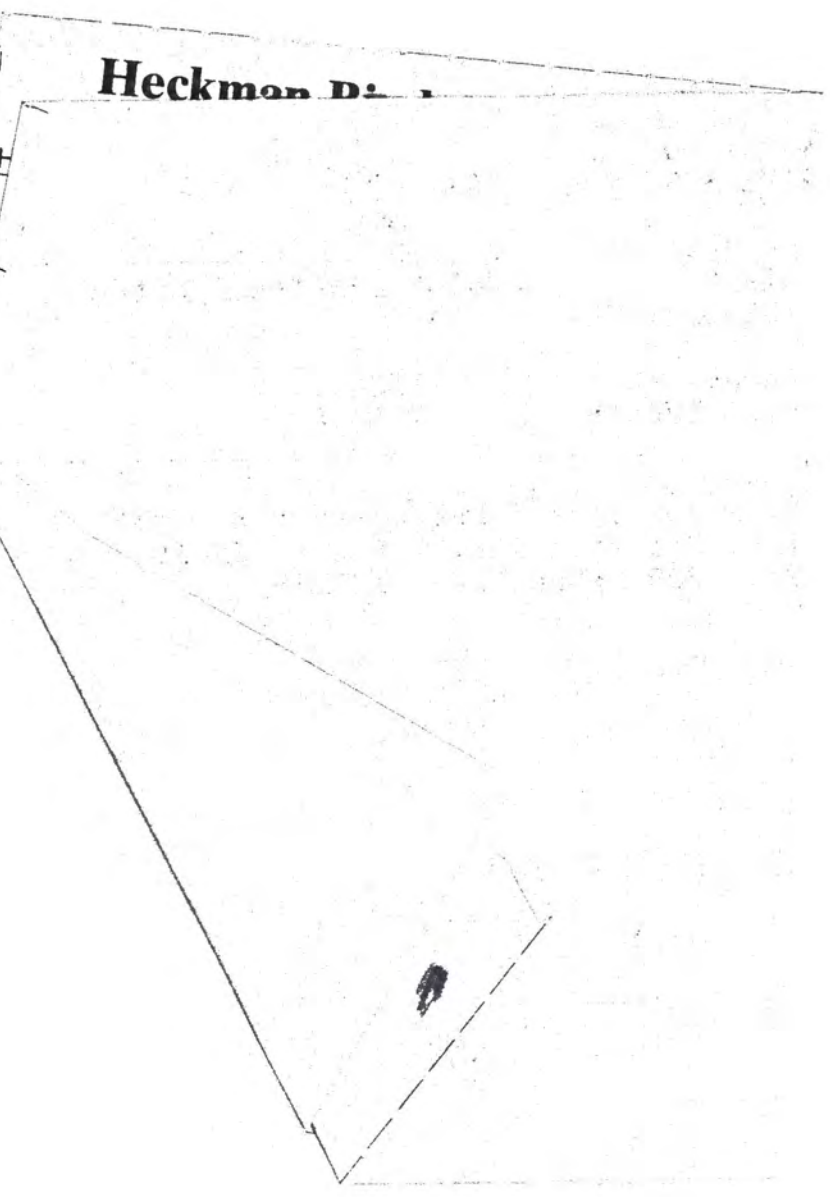
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The objective of the present study was to characterize epidemic cholera in Malawi from 2002 – 2003. National and district-level surveillance records were used for the analyses in this study. The study employed Poisson regression, log-linear analysis, epidemic curve analysis, curve-fitting procedures and epidemic model simulations. District-level determinants of cholera mortality included various sociodemographic indicators. Significant two-way interactions were observed for age and district, with the oldest age group (65+) experiencing the highest risk of symptomatic cholera and residents of Nkhatabay districts also experiencing the most increased risk. Temporal analysis revealed the existence of secondary outbreaks and demonstrated the contribution of preexisting immunity to epidemic dynamics.

EPIDEMIOLOGY OF CHOLERA IN MALAWI, 2002 – 2003

Ella Nkhoma, B.A.

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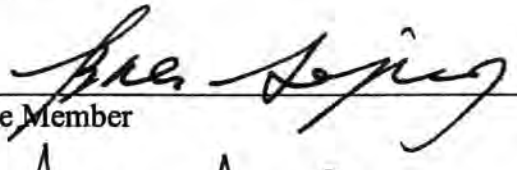
Major Professor



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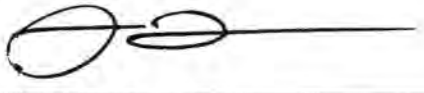

Dean, School of Public Health

EPIDEMIOLOGY OF CHOLERA IN MALAWI, 2003-2003

THESIS

Presented to the School of Public Health

University of North Texas
Health Science Center at Fort Worth

in Partial Fulfillment of the Requirements

for the Degree of

Master of Public Health

By

Ella Thokozane Nkhoma, B.A.

Fort Worth, Texas

August 2004

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This project would not have been feasible without the support of a few key people, namely, my parents, Christopher and Winnie Nkhoma for their constant support and encouragement. I also extend my gratitude to Ed Hsu, Ph.D. and Amanda Medina for their assistance and encouragement.

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July 16, 2004

Dr. Ryan Mowat
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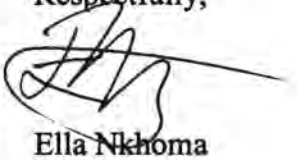
Dear Dr. Mowat,

Please consider the enclosed manuscript, "Epidemiology of Cholera in Malawi, 2002-2003," for publication in *Social Science & Medicine*. This paper employs Poisson regression and mathematical modeling techniques to explore epidemic cholera dynamics in Malawi, Africa. Malawi has experienced a cholera outbreak in the study years and the results of the analyses might contribute to the literature in terms of population-level preventive measures, and be of interest to your readers, specifically those in the fields of cholera and other diarrheal illnesses.

The protocol of this study was approved by the University of North Texas Health Science Center's Institutional Review Board in January 2004. The findings reported in this manuscript are original. They have not been previously published, and the manuscript is not under consideration for publication elsewhere.

Thank you for your consideration, and I look forward to the decision from you and the editorial board.

Respectfully,



Ella Nkhoma

Enclosures (3)

TITLE PAGE

Epidemiology of Cholera in Malawi, 2002 – 2003

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Journal Article Abstract

Epidemic cholera has been recurrent in Malawi starting from 1997 until the present. The objective of the present study was to characterize epidemic cholera in Malawi from 2002–2003. National and district-level surveillance records were used for the analyses in this study. The study employed Poisson regression to determine the district-level determinants of cholera incidence and mortality. Log-linear analysis and Poisson regression for rates was used to examine interactions between sex, age, district and symptomatic cholera infection. Temporal analysis involved epidemic curve analysis, curve-fitting procedures and epidemic model simulations. District-level determinants of cholera mortality included adult literacy rate, female literacy rate, infant mortality ratio, population density, and region; while, adult literacy rate was the only significant predictor of cholera incidence. Significant two-way interactions were observed for age and district, with the oldest age group (65+) experiencing the highest risk of symptomatic cholera (RR = 7.71, 95% CI: 5.23 – 11.35) and residents of Nkhatabay districts also experiencing the most increased risk (RR = 3.56, 95% CI: 2.45 – 5.20). Temporal analysis revealed the existence of secondary outbreaks and demonstrated the contribution of preexisting immunity to epidemic dynamics. A multifaceted approach towards the examination of epidemic cholera is useful in identifying high-risk areas and populations and temporal disease processes. (Word count: 206)

Keywords: *cholera, Malawi, epidemics, temporal analysis*

(Full word count: 6,051)

Introduction

Cholera is an important contributor to morbidity and mortality in Malawi and many other tropical countries. After years of relatively low endemicity, epidemic cholera re-emerged in Malawi in 1997 and has persisted until the present (Zachariah et al., 2002). In 2002, Malawi reported the most number of cases of cholera (33, 966 cases, 950 deaths) to the World Health Organization (WHO, 2003). Although previous cholera epidemics in Malawi occurred in refugee camps, the current resurgence of epidemic cholera seems to be characterized by non-refugee community outbreaks (Hatch, Waldman, Lungu & Piri, 1994; Swerdlow et al., 1997).

Cholera outbreaks tend to occur in areas with poor water treatment and sanitation systems; hence, less developed areas are more affected by the disease. Although the existence of a relationship between development and cholera is generally accepted, very few studies have been conducted to quantify this relationship and to determine the specific components of development that contribute to epidemic cholera. A correlational study by Ackers et al. (1998) examining possible national risk factors for epidemic cholera in the Americas found that infant mortality and female literacy might be related to cholera incidence. In the past ten years, this remains the only study to have examined such factors; thus, there is a remarkable gap in the current knowledge on area-level determinants of epidemic cholera.

Many studies have been conducted, however, that have examined person-level determinants of cholera infection. Studying the age and sex distribution of cholera cases provides important clues about the dynamics of cholera in any given region. The age and

sex distribution of cholera cases tend to vary depending on whether cholera is epidemic or endemic. During an epidemic, all age groups are at risk. In developing countries where cholera is endemic, the age group at the greatest risk of contracting cholera is children ages 2 – 15 (Glass and Black, 1992). Various studies have reported similar observations, with younger age groups experiencing higher levels of symptomatic cholera infection than older age groups. (Swerdlow et al., 1994; Bradley et al., 1996; Chhina, 2000, Hatch et al., 1994) During epidemics, the sex distribution of symptomatic cholera is usually equal. (Motha et al, 2000); Swerdlow et al., 1994; Mujica et al, 1994, Acosta et al., 2001). However, sometimes a secondary peak has been observed in women of childbearing age. (Glass & Black, 1992; Bradley et al., 1996) In endemic areas, however, males have been observed to exhibit symptomatic infection more frequently than women (Gerolomo and Penna, 1999; Hoge et al., 1996; Steinberg et al., 2001). Hence, examining interactions between sex, age and cholera infection would aid in determining the disease dynamic in a given area.

Another method of exploring disease dynamics is by examining the temporal patterns of cholera cases. This can be facilitated through curve-fitting techniques and epidemic modeling. Few studies have utilized temporal analysis beyond epidemic curves for studying cholera. A study conducted by Bradley et al. (1996) in Zimbabwe examined two cholera epidemics using some temporal analysis techniques. Through the examination of epidemic curves, cumulative case frequency curves and computer-simulated epidemic curves, the authors were able to identify different disease processes

operating in different areas. Understanding the role of different disease processes in any given area can provide important information for public health planning.

Many epidemiological studies conducted on cholera have usually involved investigation of isolated outbreaks. Such studies, however, often do not address some of the broader patterns of cholera infection that would aid in identifying high risk areas and populations. The objective of the present study is to examine epidemiological features of cholera in Malawi from October 2002 to June 2003. In keeping with the basic epidemiological parameters, the study aims to characterize the disease in Malawi by place, person and time. Consequently, the specific aims of the study are threefold: one, to identify district-level determinants of cholera incidence; two, to determine if there are interactions between sex, age, district and symptomatic cholera infection using information from outbreaks in the Northern Region of Malawi; and three, to define the temporal spread of the disease.

The epidemiological evidence in the literature suggests the following hypotheses: one, district-level determinants of cholera will consist of indicators that signal less development e.g. higher infant mortality rate, less access to safe water sources, etc.; two, symptomatic cholera infection will be associated with very young and very old age groups and district of residence, but not sex. While temporal analyses will provide descriptive instead of inferential information, the results of the temporal analyses when combined with the results from the person-level and district level analyses should aid in understanding general cholera disease dynamics in Southern Africa and other similar regions around the world.

Methods

Data

The surveillance records and enumerations of cholera cases and deaths were obtained from the Disease Surveillance Department of the Community Health Science Unit (CHSU) of the Malawi Ministry of Health (MOH). The surveillance records were available for five northern districts of Malawi: Mzimba, Nkhatabay, Nkhotakota, Rumphi and Karonga. The records consisted of district-level line-listings of cholera cases including the variables age, sex, date of onset of disease, date seen at health facility, treatment, lab tests (whether taken and results), outcome (alive or dead), and major risk factor for each case. The latter five variables were excluded from analysis. The case definition for symptomatic cholera was according to WHO criteria (WHO, 1992).

In addition to the line-listings, the Disease Surveillance Department also supplied the author with weekly enumerations of cholera cases and deaths for each district from October 2002 – May 2003. Data concerning sociodemographic variables e.g. female literacy rate, infant mortality rate and so on were obtained from the 1998 Malawi Census results available online from the National Statistics Office (NSO) (NSO, 2004).

Analytical Procedures

To determine the district-level determinants of cholera incidence rates, Poisson regression modeling was used. The two response variables were cholera cases and cholera deaths per district from October 2002 to May 2003, where the number of trials was the total population and the total cases, respectively. Successive Poisson regression

models were constructed using as predictors region, population density, adult literacy rate, female literacy rate, infant mortality rate, and percent without access to safe water (piped).

To examine interactions between sex, age, district and infection, log-linear analysis was utilized. Ancillary analyses included analysis of variance (ANOVA) for mean ages of cases, Kolmogorov-Smirnov (K-S) test for the age distributions of the five districts, and Poisson regression on cases using sex, age group, and district as predictor variables and date of onset of illness as an offset variable. Temporal analysis was performed using three methods. One, epidemic curves for the five districts were made. Two, successive linear regression was performed on the ascending portion of the cumulative case frequency curve for each district using the following equation:

$$\ln N(t) = \ln N(0) + \lambda t \qquad (1)$$

where $N(t)$ is the number of cases at time t, $N(0)$ is the initial number of cases and λ is the slope. Doubling time, d, was calculated using the following formula (Bradley et al., 1996):

$$d = \ln 2/\lambda \qquad (2)$$

Three, disease processes were explored using the following basic SIR (Susceptible-Infected-Recovered) model (Anderson and May, 1982):

$$dX/dt = -\beta XY \qquad (3)$$

$$dY/dt = \beta XY - vY \qquad (4)$$

$$dZ/dt = vY \qquad (5)$$

where X is the number of susceptibles, Y is the number infected (i.e. with symptomatic infection), Z is the number of recovered and immune individuals, β is the transmission coefficient, and ν is the rate at which infected cases recover or become immune.

Using the above SIR model (Equation 3-5), three simulations were performed for Mzimba district to explore the disease processes that contributed to the observed patterns of temporal spread of cases. Since cholera outbreaks are normally point source or continuous point source outbreaks, the background population was estimated as the average population of an enumeration area for the Malawi Census (NSO, 2004). The simulations were conducted for a period of 40 days using Euler's method of integration. Three runs were conducted with the values of $X(0)$ decreasing incrementally from 7,000 to 5,000, and the values of $Z(0)$ increasing incrementally from 0 to 2,000. For all simulations, the infection rate constant, β, was kept constant at 8.23×10^{-4}. The recovery rate constant, ν, was kept at 0.2, and $Y(0)$ was equal to six.

Log-linear analyses and Poisson regression were conducted using the SAS system for Windows version 8.2 (Cary, North Carolina: SAS Institute, Inc.1999-2001) ANOVA was conducted using SPSS 11.5.0 (Chicago, Illinois: SPSS, Inc. 1989-2002). Computations for the K-S test statistic, linear regression, doubling times and the construction of epidemic curves were performed using Microsoft Excel 2000 (Redmond, Washington: Microsoft Corporation, 1985-1999). All epidemic model simulations were conducted using STELLA 8.0 (Lebanon, New Hampshire: Isee systems, Inc. 1985 – 2003).

Results

District- Level

From October 2002 to May 2003, there were 2,784 cases of cholera reported by public health facilities in Malawi, resulting in a cumulative incidence of 28.3 per 100,000. Most of the cases were reported from the Central Region, with 1,407 total cases resulting in a cumulative incidence of 34.8 cases per 100,000. While the Southern Region had more cases reported than the Northern Region (1029 and 354, respectively), the Northern Region had a higher cumulative incidence of cases than the Southern Region (28.8 and 22.5 per 100,000, respectively). In the Northern Region, 3.39% of cases progressed to death, compared with a case fatality ratio (CFR) of 2.42% for the Southern Region and 1.28% for the Central Region.

Cholera cumulative incidence and mortality for each district and region were explored using Poisson regression. Two separate models were constructed for cases and deaths, using district population and cases, respectively, as the offset variables. The results of the analysis are summarized in Table 1. Adult literacy rate was found to be a significant positive predictor of cholera incidence ($p = 0.05$), while female literacy rate was a marginally significant negative predictor of cholera incidence ($p = 0.06$). Adult literacy rate was also found to be a significant positive predictor of cholera mortality, while female literacy rate was found to be significant negative predictor of cholera mortality ($p = 0.005$). Additionally, infant mortality ratio, population density and the Northern Region were found to be negatively associated with cholera mortality.

Person-Level

Most of the cases in the five districts studied were from Mzimba district, and Nkhotakota contained the fewest number of reported cases (see Table 2). The number and proportion of cases by sex and age groups are presented in Table 2. Log-linear analysis was used to examine interactions between sex, age, district and infection. The results of the three separate two-way analyses and the three separate three-way analyses that were performed are presented in Table 3. The results show significant age and district effects, and a non-significant sex effect. However, there are no significant interactions among different combinations of age, sex and district with infection.

Ancillary analyses were conducted to further understand the relationships between age, sex, district and infection. It was found that while there were no differences in the sex distribution of the background population of the five districts ($\chi^2 = 0.08$, degrees of freedom (df) = 4, $p > 0.05$), there were some differences observed in the age distributions. The Kolmogorov-Smirnov (KS) test revealed significant differences in the age distributions between Mzimba and Karonga ($D = 0.6$, $p<0.01$), Nkhatabay ($D = 0.6$, $p<0.01$), Rumphi ($D = 0.73$, $p<0.01$), and Nkhotakota ($D = 0.53$, $p<0.05$). The KS test also revealed a significant difference in the age distributions of Rumphi and Nkhotakota ($D = 0.4$, $p<0.05$).

One way ANOVA was conducted to examine differences between the five districts in the age of cases. ANOVA revealed significant differences in the mean age of cases among the different districts ($F(4, 307) = 3.485$, $p < 0.01$). Post hoc comparisons using Tukey Highly Significant Difference (HSD) revealed that the mean age of cases

from Rumphi was significantly higher than cases from Karonga ($p<0.05$), and Mzimba ($p<0.05$). The mean age of cases from Rumphi was 36 (N = 54, standard deviation (s.d.) = 20.2) with cases from Karonga and Mzimba having a mean age of 24 (N = 45, s.d. = 15.6) and 27 (N = 157, s.d. = 17.9), respectively. The mean age of cases from Nkhatabay was 32 (N = 47, s.d. = 18.0); and Nkhotakota, 26 (N = 9, s.d. = 13.2).

Poisson regression was performed using the log of time (days) as the offset variable to examine rate ratios for infection using age and district as indicator variables. Due to the sparse nature of the cases in Nkhotakota, the district was excluded from analysis. The results of the Poisson regression are summarized in Table 4. When the age group 15 – 44 was used as a reference category, the other age groups, excluding children between 5 and 14, were found to be at greater risk of cholera infection than the reference category ($p < 0.0001$). Residents of Mzimba were found to be at the lowest risk of cholera infection, while residents of Nkhatabay had more than three times greater risk than the reference category (see Table 4).

Temporal Analysis

The epidemic curves for four districts are presented in Figure 1. Due to sparse data, the cases from Nkhotakota were excluded from analysis. The most striking feature of the epidemic curves is the presence of a smaller epidemic following the first epidemic. This is observed for Mzimba and Nkhatabay districts. Another distinguishing feature is the initial rise in cases which seems to be similar for all districts except Rumphi. To compare initial rates of increase in cases in the four districts, linear regression models

were fitted to the ascending phase of each epidemic, averaging 13 days. Results from the linear regression revealed a doubling time of 3.02 days for the outbreak in Rumphi (λ = 0.23, R^2 = 0.97, $p<0.01$) and 2.69 days for the initial outbreak in Mzimba (λ = 0.26, R^2 = 0.98, $p<0.01$). The initial outbreaks in Nkhatabay and Karonga exhibited the same doubling time of 2.65 days (λ = 0.26, R^2 = 0.96, $p<0.01$; λ = 0.26, R^2 = 0.97, $p<0.01$, respectively).

To examine disease processes, three simulations of the SIR model were performed. The results are presented in Figure 2 with the accompanying specifications for each simulation. The third simulation with a smaller ratio of susceptible to immune individuals resulted in a lower initial rate of infection than when the ratio of susceptible to immune individuals was greater, even though the force of morbidity was kept constant for all simulations. The first and second simulation generated a log-normal case frequency curve, while the third curve was near normal from the first to the twenty-fifth day i.e. the last day of the actual epidemic occurring in Mzimba.

Discussion

District-Level Analysis

One of the stated purposes of this study was to elucidate some of the district-level determinants of cholera incidence and mortality and we found that region, population density, adult literacy rate, female literacy rate and infant mortality ratio are associated with cholera mortality, while cholera incidence is positively associated with adult literacy rate and marginally associated with female literacy rate. These findings are consistent with the Ackers et al. (1998) study, which reported a marginally significant correlation between female literacy rate and cholera incidence. However, the results of the present study depart from the Ackers et al study in that a significant association was not found for infant mortality rate and cholera incidence, but for cholera mortality. The present study also differs in that the relationship between cholera incidence and mortality was explored using additional indicator variables.

An interesting finding was that while districts did not differ in cholera incidence by region, there were variations in the risk ratios for cholera mortality by region, with the Northern Region exhibiting lower risk of cholera mortality among the three regions. The risk ratios of the other variables provide important clues about this relationship. It was observed that for every one unit increase in population density, there was a decreased probability of cholera mortality in a given district (see Table 1). This result seems unusual because in populous districts, there is less access to health facilities. Access to health care facilities has been found to be associated with an increased case fatality ratio for cholera (NSO, 2001a; Gunnlaugsson, 2001). Although, the risk ratios are adjusted for

region, the result may be a result of interaction between the population density variable and the Northern Region variable, because the Northern Region is the least populated and least developed area of Malawi, but at the same time, it also has the most educated residents among all Malawians (NSO, 2001b). The finding that less access to unsafe water sources in not associated with cholera incidence or mortality is also not surprising given than there was little variation in this indicator among the districts (NSO, 2001b).

The finding that higher adult literacy rates increase the risk of cholera incidence and mortality for a given district seems anomalous and is inconsistent with the characteristics of the regions in Malawi. Although the Northern Region is the least developed, its residents are the most educated with significantly higher overall and female literacy rates than the other regions. The result that higher female literacy rates are associated with a decreased probability of cholera incidence and mortality for districts is not unexpected, since women, as the primary household laborers, are generally responsible for domestic hygienic practices (Curtis, Cairncross & Yonli, 2000). Education, from primary onwards, increases feelings of self-efficacy, which in turn increase the likelihood of adopting behaviors that decrease opportunity for cholera infection (Quick et al., 1996). This finding is also consistent with decreased risk of mortality for the Northern Region which exhibits the highest female literacy rates in Malawi (NSO, 2001b).

The finding that higher infant mortality rate was associated with reduced risk of cholera incidence for a given district appears aberrant. The study by Ackers et al. (1998) found infant mortality rate to be positively correlated with cholera incidence in the

Americas. However, the authors asserted that the finding may have been confounded by poor sanitation and general poverty which correlate with both infant mortality rate and cholera incidence and mortality. Additionally, although the leading cause of death for children is diarrheal illness, *V. cholerae* is not among the main etiological agents. (Ackers et al., 1998)

These findings are the result of an ecological analysis of cholera incidence and mortality in Malawi and are thus subject to certain limitations and considerations. One, it should be noted that reporting practices vary by district and by region. This may result in some information bias. However, generally, underreporting would have been observed in the lesser populated areas and would have resulted in bias towards the null for those areas. Secondly, these results are not generalizable to individual-level risk factors. However, being cognizant of the factors that may be responsible for broader patterns of disease is invaluable in health planning.

Person-Level

The results of the person-level analyses revealed significant effects for district and age, but did not show a significant effect for sex. Residents of Mzimba, the most populated district, were found to have three times less risk of symptomatic cholera than residents of the other districts (excluding Nkhotakota). Furthermore, adults 65 and older were found to have the greatest risk of symptomatic cholera infection. The finding that older age groups experienced higher risk of cholera infection than younger age groups is unusual. What is most unusual is that the age group of 5 -14 years old was not associated

with a higher risk of cholera, since this is normally the age group that is most affected by cholera (Glass & Black, 1992; Swerdlow et al., 1994; Mujica et al, 1994; Acosta et al., 2001). The observed risk in the youngest age group, however, is consistent with a previous studies conducted in Malawi and Zimbabwe which document younger childres, especially below five year old as being at increased risk of cholera. (Hatch et al., 1994; Bradley et al., 1996)

Since Malawi has been experiencing regular cholera epidemics since 1997, it could be assumed that many of the adults should have preexisting immunity and should thus have a lower risk of symptomatic cholera infection than younger age groups. However, it was observed that the age distribution of cases was generally similar to the age distribution of the background population of each given district. This result indicates that the areas in which these outbreaks took place may not previously have experienced epidemic cholera.

When ancillary analyses were performed, we found that the age distributions of the districts were not the same. However, even though the age distributions of the cases seem to follow the age distributions of the districts, no significant interaction was found between age, district and infection. The age distribution of Mzimba was significantly different from that of the other districts, but at the same time, Mzimba had a much larger population than the other districts. Hence, this result may have occurred because the difference in the age distributions may have been one of location, as opposed to shape. The finding of no interaction was also unexpected because the mean age of cases was

significantly different. However, the mean ages of cases were all within the 15-44 age group, the largest age group.

The findings concerning the interactions between age, sex, district and infection should be interpreted in light of some limitations and considerations. One, the analyses relied on secondary data which was originally collected for the purposes of outbreak investigation and surveillance. Not all cases were laboratory confirmed cases, so there is some potential for misclassification. However, since the background population also included asymptomatic cases of cholera, the misclassification was non-differential and would have resulted in bias towards the null. Thus, the observed effects may underestimate and not overestimate the actual risk. Another limitation is the presence of missing values for gender and age for some of the cases. However, the occurrence of this was minimal, and the cases for which there was incomplete data were excluded from the analyses.

Temporal Analysis

The results of the temporal analysis indicate that different disease processes may have been operating in different districts. When the epidemic curves were examined, it was found that the outbreaks in Karonga, Mzimba, and Nkhatabay exhibited log-linear growth patterns, while Rumphi exhibited an erratic temporal spread pattern. Furthermore, when the cumulative case frequencies were examined, the outbreak in Rumphi was observed to have a higher doubling time than the other districts, whose doubling times were similar to one another. From the person-level analysis, it was

observed that Rumphi had a significantly older mean age of cases than two of the other districts, with over 91% of cases aged over 15 years. Given the age distribution of cases, it is unlikely that the observed pattern of temporal spread is explained by endemicity (Glass & Black, 1992).

The existence of two separate outbreaks was shown for Mzimba and Nkhatabay. It was unclear whether the two outbreaks originated from the same source population, from two interacting populations or from two separately mixing populations. In the study conducted by Bradley et al. (1996) examining disease processes in Zimbabwe using epidemic modeling, a similar temporal spread pattern was proposed to be the result of two separate sub-epidemics with independent (non-mixing) populations. There are several factors that may explain these secondary outbreaks. One, the behavioral risk factor profiles for some of the patients revealed a history of travel, so the second wave might be due to the introduction of infected individuals into a susceptible population i.e. two interacting populations. Two, cross-contamination of water sources with *V. cholerae* may have occurred between neighboring areas perhaps through rainfall. The time period in which the Mzimba outbreaks occurred was concurrent with a heavy rain season. The two outbreaks in Nkhatabay, however, were a sufficient period of time apart to preclude the effects of travel and cross-contamination.

The primary epidemic in Mzimba was further explored using the basic SIR model. The findings from the epidemic model simulations contrast with the findings from the person-level analyses in that they do not suggest the existence of epidemic cholera. When the simulations were conducted using different ratios of initial susceptible

to immune (recovered) individuals, the simulation with the lowest susceptible-to-immune ratio produced the results most consistent with the actual progression of the epidemic in Mzimba. This finding suggests that the progression of the epidemic observed in Mzimba may have been affected by a large number of individuals with preexisting immunity.

The use of an epidemic model is valuable in elucidating disease dynamics that may be operating during a given epidemic. However, the findings from simulations must be interpreted with caution. The accuracy of the results of the model simulations is dependent upon the assumptions upon which the model is built. The model utilized in the present study makes the assumptions that the study population is stable, there is no latent period for infectiousness, and the duration of infectiousness is equal to the duration of symptomatic disease (Bradley et al., 1996; Giesecke, 2002; Daley & Gani, 1999). Since the birth rate in Malawi is much higher than the death rate, it may appear that the first assumption is violated, but the epidemic takes place over a sufficiently short period of time that the effects of births and deaths on the progression of the epidemic is minimal (NSO, 2004). The incubation period of cholera varies from 2 – 5 days, hence there is a short latent period between infection and infectiousness, since the infectious period coincides with the onset of diarrheal illness. The last assumption is problematic for the study of cholera since cholera presents with a large volume of asymptomatic cases that are infectious despite the absence of clinical disease. However, asymptomatic cases of cholera shed a much smaller volume of vibrios into the environment than symptomatic cases. Hence, the contribution to infectivity by asymptomatic cases is minimal relative to that of symptomatic cases. Also, because of the large number of asymptomatic cases, the

number of infected individuals projected by the model will clearly be much greater than the observed (symptomatic) cases and may be closer to the actual total number of infected cases. Therefore, notwithstanding these limitations, the model remains useful in predicting the effects of various disease dynamics on the progression of epidemics.

A number of studies have been conducted in Malawi describing cholera epidemics in refugee populations. The current cholera epidemic in Malawi, however, also has had a tremendous effect on non-refugee populations. The findings from the present study illustrate some of the salient features of epidemic cholera in Malawi. The results of this study have many implications for health planning and appropriate allocation of health resources in the prevention and control of cholera outbreaks. One, examination of socio-demographic indicators may be very useful in determining risk of cholera mortality by district and region. Health planners and decision-makers can examine sociodemographic indicators such as female literacy rate to identify high-risk districts. An awareness of high-risk areas would aid in determining appropriate measures to reduce the case-fatality ratio, perhaps by increasing access to health facilities or even creating temporary treatment centers during peak cholera season.

An examination of demographic characteristics and cholera infection aids in determining target populations for preventive health education efforts and outbreak control measures. For example, since the risk of cholera is higher in older age groups, social marketing techniques against diarrheal illness should be tailored towards this particular age group. Furthermore, the results of the present study indicate that very young children and older adults are at highest risk of symptomatic cholera infection.

Since these age groups usually experience severe as opposed to moderate disease, treatment resources should be allocated appropriately. Public health facilities serving these regions should ensure that adequate stocks of intravenous solution and adjunct antibiotic treatment are available for administration during outbreaks.

Models also serve as an important tool for health planning. Epidemic modeling can act as a form of surveillance for disease processes and dynamics in different populations. Knowledge of changing disease dynamics can help health planners to adjust preventive and control measures to optimize their impact in targeted populations. The current study demonstrates that the observed patterns of disease in northern Malawi may be affected by large numbers of people with previous immunity. As the number of immune individuals grows relative to susceptible populations, the demographic characteristics of cases during outbreaks will change. Additionally, awareness of secondary epidemics will aid health planners in determining the most effective allocation of resources. The examination of initial rates of cholera incidence and doubling times can aid in not only forecasting the size of outbreaks, but also in allowing for the optimization of epidemic models to increase their practical utility in the design of effective strategies for cholera prevention and control.

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Tables

Table 1.

Adjusted Risk Ratios (RR) for Cholera Incidence and Mortality Related to Selected Sociodemographic Variables Using Poisson Regression

	Cholera Incidence			Cholera Mortality		
Variable	RR	95% Confidence Interval	*p*	RR	95% Confidence Interval	*p*
Southern Region	1.00 (ref.)	-	-	1.00 (ref.)	-	-
Central Region	2.403	0.539 - 10.725	0.2505	1.777	0.460 - 6.857	0.4041
Northern Region	0.385	0.015 - 9.994	0.5654	0.049	0.003 - 0.719	0.0277
Population Density	0.993	0.983 - 1.004	0.2201	0.982	0.974 - 0.991	0.0001
Adult Literacy Rate	1.471	1.002 - 2.159	0.0486	1.835	1.278 - 2.634	0.0010
Female Literacy Rate	0.763	0.575 - 1.011	0.0599	0.669	0.506 - 0.884	0.0048
Infant Mortality Ratio	0.941	0.863 - 1.028	0.1770	0.901	0.829 - 0.980	0.0145
Percent without access to safe water sources	1.037	0.968 - 1.111	0.3052	1.002	0.931 - 1.078	0.9655

Table 2.

Demographic Characteristics of Study Population.

District	Age group	Total Population (%)	Cases		
			Male	Female	Total (%)
Rumphi	<1 - 4	22188 (17)	0	0	0 (0)
	5 - 14	35001 (27)	1	4	5 (9)
	15 - 44	56153 (44)	17	17	34 (63)
	45 - 64	10658 (8)	5	3	8 (15)
	65+	4360 (3)	4	3	7 (13)
	All	128360 (100)	27	27	54 (100)
Karonga	<1 - 4	32707 (17)	0	0	0 (0)
	5 - 14	55220 (28)	5	9	14 (32)
	15 - 44	82639 (42)	10	14	24 (55)
	45 - 64	17489 (9)	0	6	6 (14)
	65+	6517 (3)	0	0	0 (0)
	All	194572 (100)	15	29	44 (100)
Nkhatabay	<1 - 4	26919 (16)	1	1	2 (4)
	5 - 14	45122 (27)	5	1	6 (13)
	15 - 44	70320 (43)	11	12	23 (49)
	45 - 64	15359 (9)	7	8	15 (32)
	65+	7041 (4)	0	1	1 (2)
	All	164761 (100)	24	23	47 (100)
Nkhotakota	<1 - 4	41410 (18)	0	0	0 (0)
	5 - 14	62909 (27)	1	1	2 (22)
	15 - 44	98838 (43)	2	4	6 (67)
	45 - 64	18707 (8)	0	1	1 (11)
	65+	7596 (3)	0	0	0 (0)
	All	229460 (100)	3	6	9 (100)
Mzimba	<1 - 4	104497 (17)	13	9	22 (14)
	5 - 14	167418 (27)	12	12	24 (15)
	15 - 44	262467 (43)	49	36	85 (53)
	45 - 64	53551 (9)	13	12	25 (16)
	65+	23061 (4)	3	2	5 (3)
	All	610994 (100)	90	71	161 (100)

Note. There were twelve additional cases in Mzimba and one in Karonga for which age and gender data were not available.

Table 3.

Results of Log-Linear Analysis (Type 3)

Effect	Degrees of freedom	Partial $\chi 2$	p
Age x Infection	4	39.58	<0.0001
Sex x Infection	1	0.09	0.7685
District x Infection	4	46.07	<0.0001
Sex x Age x Infection	1	0.02	0.8864
District x Sex x Infection	4	4.76	0.3128
District x Age x Infection	4	7.57	0.1089

Table 4.

Adjusted Rate Ratios (RR) for Symptomatic Cholera Using Poisson Regression

Factor	RR	95% Confidence Interval	*p*
Age			
<5	2.68	1.76 - 4.07	<0.0001
5 - 14	1.26	0.90 - 1.76	0.1706
15 - 44	1.00 (ref.)	-	-
45 - 64	3.51	2.31 - 5.32	<0.0001
<64	7.71	5.23 - 11.35	<0.0001
District			
Mzimba	1.00 (ref.)	-	-
Karonga	2.59	1.85 - 3.63	<0.0001
Rumphi	3.09	2.24 - 4.28	<0.0001
Nkhatabay	3.56	2.45 - 5.20	<0.0001

Figures

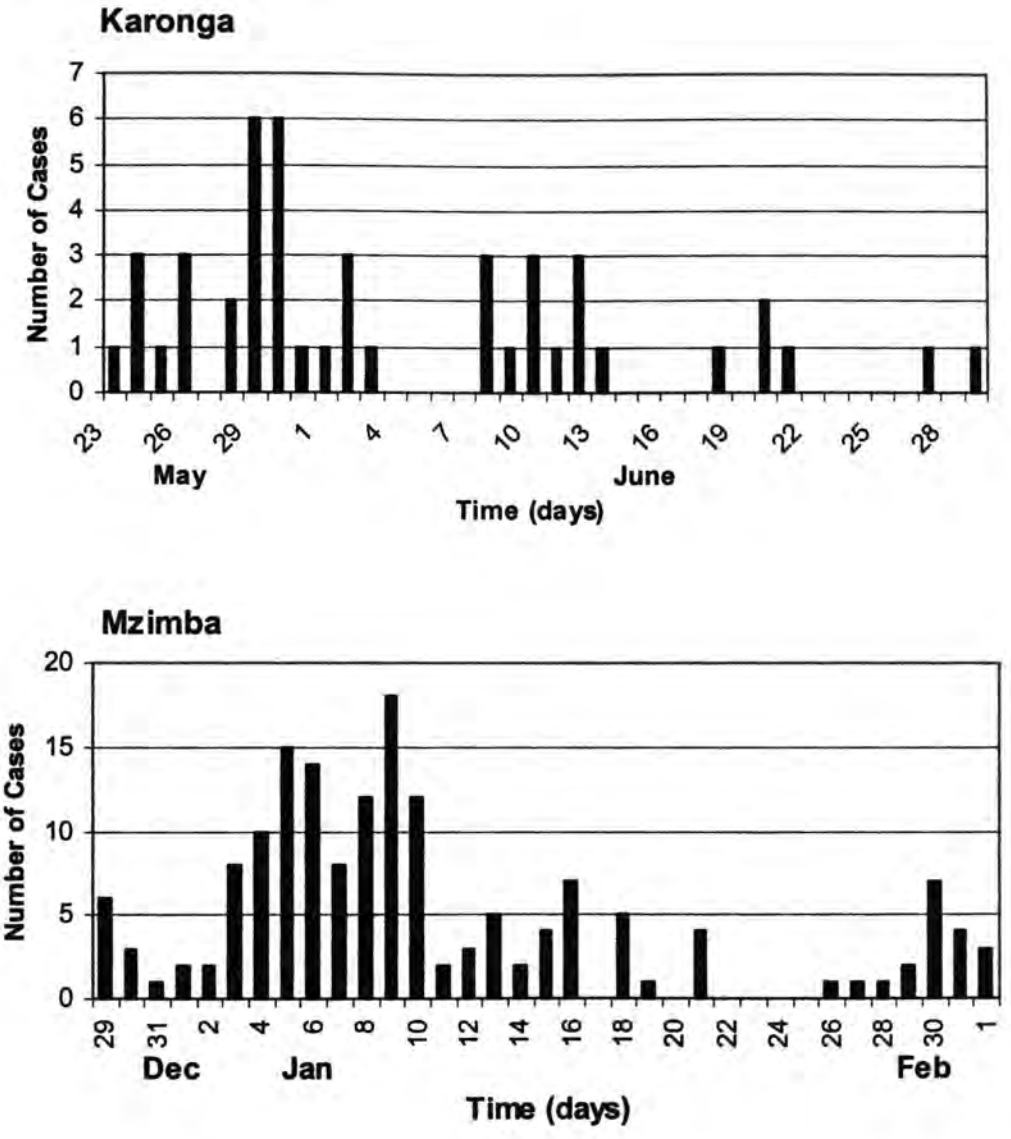

Figure 1. Epidemic Curves for Symptomatic Cholera Reported in Karonga, Mzimba, Nkhatabay and Rumphi Districts. Note that the Mzimba and Karonga curves exhibit a secondary outbreak following the initial.

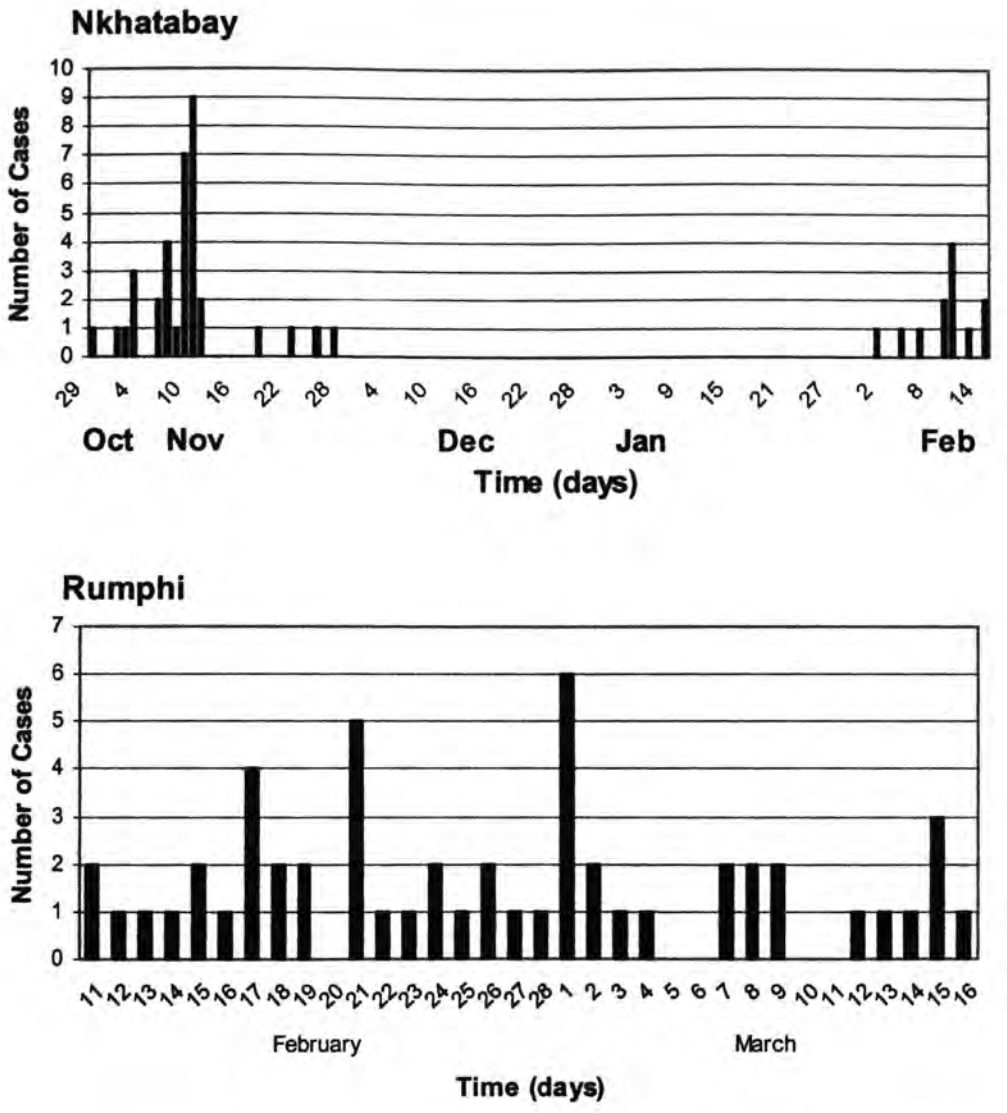

Figure 1. Epidemic Curves for Symptomatic Cholera, continued.

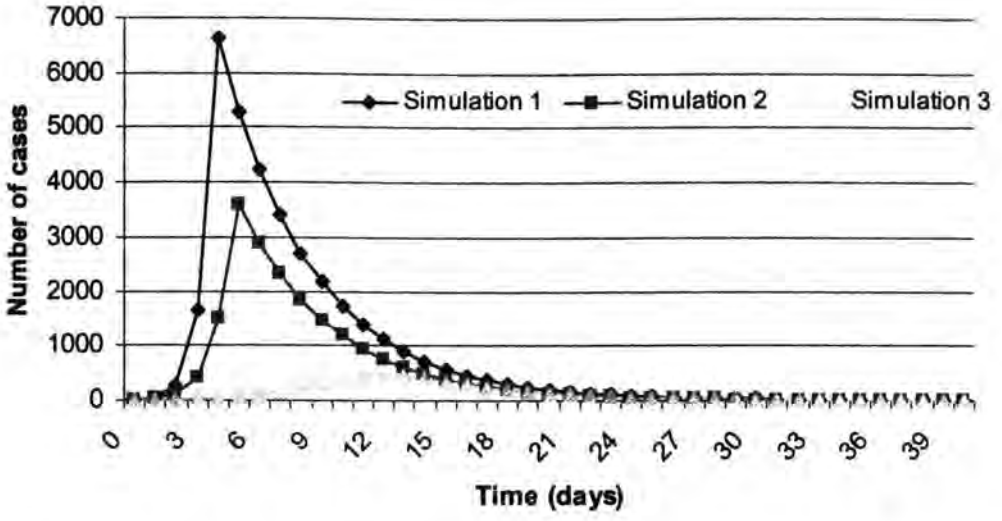

Figure 2. Results of SIR Model Simulations using Mzimba District Specifications. For all simulations, $\beta = 8.23 \times 10^{-4}$, $\nu = 0.2$ and $Y(0) = 6$. For simulation 1, $X(0) = 7{,}000$ and $Z(0) = 0$. For simulation 2, $X(0) = 6000$ and $Z(0) = 1{,}000$. For simulation 3, $X(0) = 5{,}000$ and $Z(0) = 2{,}000$. The y-axis represents the total number of infected individuals (symptomatic and asymptomatic).

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