

# Excess mortality by diarrhea simultaneous to a cholera epidemic in Northeastern Brazil

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## Keywords

Diarrhea, mortality. Cholera, mortality. Disease outbreaks, underregistration. Diseases registries.

## Abstract

### Objective

To evaluate excess mortality due to infectious diarrhea without etiological diagnosis, occurring simultaneously to *Vibrio cholerae* circulation.

### Methods

Statistical modeling was applied to a time series of deaths ascribed to "poorly defined intestinal infections" (International Classification of Diseases – ICD-9) and "presumably infectious diarrhea and gastroenteritis" (ICD-10), between 1980 and 1998 in the Northeast Region of Brazil. The prediction of expected values was obtained after a discontinuity point. Excess mortality was calculated as the difference between observed figures and those estimated by the model.

### Results

Between 1992 and 1994, only 19.3% of deaths by cholera were actually notified. In 1993, the year in which the epidemic reached its peak in the area, our modeling estimated underregistration at 82.2%.

### Conclusions

Results indicate substantial underregistration of cholera mortality during the epidemic in Northeastern Brazil.

## INTRODUCTION

Current evaluations of the health and living conditions of the Brazilian population suggest an extremely concerning scenario, related to the superposition of distinct patterns of morbidity and mortality, in which the advance of the so called 'modern' patterns – chronic degenerative diseases and violence, among others – is combined with the persistence of patterns associated with underdevelopment, such as infectious and parasitic diseases.<sup>9</sup>

In a short period, there has been a significant reduction in the participation of infectious and parasitic diseases in Brazilian mortality statistics. This type of disease fell from second place in the ranking of the most important causes of death in 1977 to fifth place in

1984, and mortality levels decreased from 9.3% of all deaths in 1980 to 7.6% in 1984.<sup>11</sup> In 1996, 1997, and 1998, infectious and parasitic diseases were the sixth most important cause of death in Brazil, accounting for 5.8%, 5.3%, and 5.2% of all deaths countrywide, respectively. One of the factors contributing to such a reduction was the increasing accessibility of certain essential goods and services, which, however, were still unequally distributed, being concentrated in more developed regions.

Notwithstanding, deaths associated with infectious and parasitic diseases in the Northeast Region of Brazil are still an important component in the structure of infant and childhood mortality, officially accounting for approximately 16.5% of all deaths in these groups. The actual toll of these diseases is likely to be even

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higher, since in this region there is still a high proportion of deaths attributed to poorly defined causes – 22% of all deaths in 1998. This may be masking the actual percentage of deaths by infectious and parasitic diseases, since poorly defined causes are found predominantly among individuals from poorer social groups, to whom medical care is not always available during the entire process of illness and death.<sup>13</sup> According to Werneck & Reichenheim,<sup>16</sup> diseases with greater impact on infant mortality are usually underestimated when only the proportion of deaths is analyzed. This is demonstrated by studies on the loss of potential years of life.

Clinically, cholera is an acute diarrheic disease, which can lead to the loss of several liters of water and electrolytes in a period of a few hours, which may culminate in a clinical scenario of hypovolemic shock and death, in case these losses are not readily restored.<sup>5</sup> In Brazil, 1,918 cases of cholera were reported to the Ministry of Health's National Sanitary Surveillance System (SNVE) between 1991 and 1998. In the same period, the Mortality Information System (SIM), run by the Department of Informatics of the Brazilian Unified Healthcare System (DATASUS), registered 1,295 deaths (66,8%), which leads us to the assumption that there has been substantial underreporting of cholera deaths in the country.

An evaluation of the impact of *V. cholerae* circulation on mortality may be carried out indirectly through statistical modeling. This can be done by estimating the number of excess deaths during the epidemic period, calculated as the difference between the number of deaths observed and the number of deaths expected in a non-epidemic scenario. This approach has been successful in studying the impact of the Influenza virus and the deleterious effects of atmospheric pollution.<sup>6,12</sup>

The present study is aimed at evaluating excess mortality due to infectious diarrhea without etiological diagnosis in the Northeast Region of Brazil, during the period of circulation of *V. cholerae* in this region.

## METHODS

A time series of the deaths ascribed to "poorly defined intestinal infections" (International Classification of Diseases – ICD-9) for the 1980-1995 period, and to "presumably infectious diarrhea and gastroenteritis" (ICD-10) for the 1996-1998 period, was obtained from the Ministry of Health's Mortality Information System (SIM). The complete time series was used for estimating the point of dis-

continuity its structure. To this end, we employed a local stationary autoregressive model and the Akaike information criteria (AIC) minimum value. Once the discontinuity point was estimated, data from the previous time series were modeled through decomposition into three components: local polynomial trend, global stationary autoregression, and random error. The AIC minimum value was used for selecting the best model.<sup>7</sup> Model parameters were estimated using Kyplot software. The adjusted model was used for predicting expected values after the point of discontinuity. Excess mortality was calculated as the difference between the observed figures and those estimated by the model.

## RESULTS

The time series of deaths by infectious diarrhea without etiological diagnosis in the Northeast Region of Brazil between 1980 and 1993 (Figure 1), shows that the number of deaths declined continuously until 1992 – the first year of the cholera epidemic in the region – when this trend was reversed. From then on the variation in the number of such deaths follows the incidence of cholera.

The point of discontinuity in the behavior of the time series identified by the model was 1991, as shown in Table 1. The work of Kitagawa & Gersch<sup>7</sup> may be referred to for a better understanding of the modeling techniques employed.

The model selected for adjusting the data from the 1980-1990 period is presented in Table 2. These results are presented again in Figure 2, which also includes expected and observed mortality for the period starting in 1992.

A Table 3 shows observed and estimated mortality, the upper and lower limits of the confidence interval, and estimated, observed, in the 1992-1995 period and in 1998, minimal, and maximal excess mortality, the

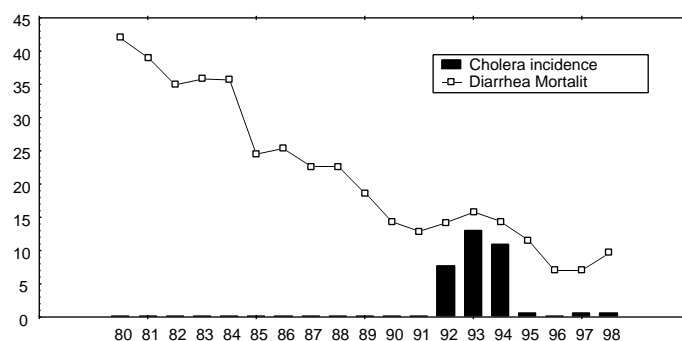


Figure 1 - Mortality rate by intestinal infectious diseases, per 100,000 population and cholera incidence per 10,000 population. Northeast Region, Brazil, 1980-1998.

latter two of which were based on the limits of the confidence interval and on the number of cholera deaths registered by SIM.

## DISCUSSION

The choice of statistical method was due to the greater appropriateness of this model for use in time series with important trends, in comparison with the Arima method proposed by Box & Jenkins,<sup>2</sup> which is more appropriate for stationary series. Another advantage of the present method is the semi-automatic character of the choice between the different possible models based on the minimum AIC. This is strengthened by the model's good prediction of the last years of the time series, despite it being a seven-year prediction based on an eleven-year period. The appropriateness of this model, even when dealing with short series, is one of its advantages.<sup>7</sup>

Our results indicate substantial underregistration of cholera mortality during the epidemic in the Northeast Region. Assuming that the excess mortality be-

**Table 1** - Estimation of the point of discontinuity of the statistical structure of the series.

Year	AIC
1989	248.4012
1990	247.9795
1991	244.7536
1992	244.8000
1993	246.2553
1994	246.3117

AIC: Akaike information criteria<sup>7</sup>

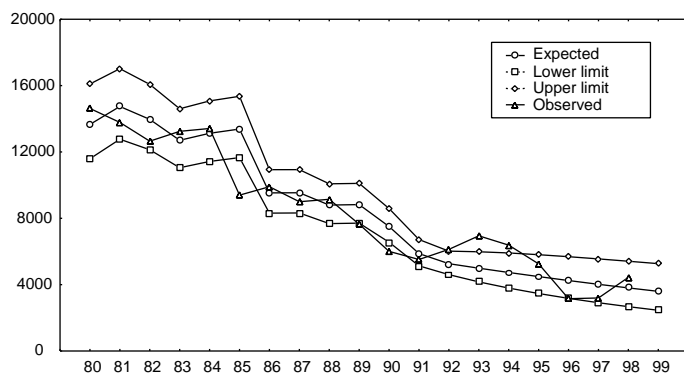
**Table 2** - Model selected for data adjustment from 1980 to 1990.

Number of interactions	26
Log (L)	6.595886
AIC	2.808227
Observed noise	2.20E-07
Trend component	
Order	2
Observed noise	4.12E-08
Autoregressive component	
Order	2
Observed noise	0.015941

**Table 3** - Deaths by diarrhea, without specification, observed and expected, with upper and lower confidence interval limits (95%), and deaths by cholera registered in the Mortality Information System. Northeast Region, Brazil, 1991-1998.

Year	Expected deaths			N	Observed deaths			SIM
	N	Lower limit	Upper limit		Estimated excess	Maximum excess	Minimum excess	
1991	5.874	5.134	6.719	5.518	-	-	-	1
1992	5.265	4.604	6.021	6.129	864	1.525	108	281
1993	4.993	4.166	5.984	6.945	1.952	2.779	961	423
1994	4.735	3.793	5.911	6.382	1.647	2.589	471	360
1995	4.487	3.467	5.808	5.251	764	1.784	-	30
1996	4.249	3.176	5.686	3.154	-	-	-	17
1997	4.022	2.913	5.554	3.198	-	-	-	29
1998	3.804	2.674	5.413	4.440	636	1.766	-	-

SIM: Mortality Information System, Ministry of Health



**Figure 2** - ARMA model (2,2,0) for deaths by diarrhea. Estimated based on data from 1980 to 1991. Prediction for 1992 to 1998.

tween 1992 and 1994 was indeed caused by cholera, this would mean that only 19.3% of cholera cases in the period were actually reported. For 1993, the year in which the epidemic reached its peak in the Northeast, the present modeling estimated underregistration at 82.2% (69.4-86.8%).

Mortality attributable to influenza, heat, and atmospheric pollution is traditionally calculated by statistical models based on the estimation of excess mortality.<sup>14,15</sup> As in the present case, there is no definitive proof in these studies that such deaths were indeed due to influenza, or to the other events mentioned. Nevertheless, the biological logic which supports these studies, along with the disappearance of excess mortality upon termination of the event at hand, support the hypotheses proposed.

The number and percentage of deaths ascribed to poorly defined causes decreased throughout the entire study period, from 48.6% in 1980 and 42.1% in 1990 to 34.4% in 1995 and finally to 28.8% in 1998.

It is estimated that roughly 20% of all deaths in Brazil are not registered, and that this proportion exceeds 50% in certain areas of the Northeast Region. This region also shows the highest levels of deaths attributed to poorly defined causes.<sup>10</sup> Considering that the present study was based on registered deaths with well defined

underlying causes, the numbers here presented, although quite high, probably still do not reflect the actual excess mortality brought about by cholera in this region.

Until 1991, the Ministry of Health lacked a structure responsible for developing activities related to the epidemiological surveillance of diarrhea. As states and municipalities tend to reproduce the model developed at the Federal level, there were, apart from rare exceptions, no activities in Brazil aimed at studying and understanding diarrheas, despite the awareness of the impact of these diseases on the population. With the emergence of cholera, such a structure was implemented as an emergency measure; however, due to operational issues, this structure still works precariously and with extreme difficulty in detecting and reporting cases of cholera, especially those from remote regions. With respect to assistance, despite the large investments made in the management of diarrheas and dehydration, a study conducted in nine Brazilian capitals showed that a large proportion of the care provided is inadequate.<sup>3</sup>

According to World Health Organization (WHO) recommendations, all suspect cases reported were confirmed based on laboratory (positive stool test for *V. cholerae*) or clinical-epidemiological criteria (with or without negative stool tests, but with clinical aspects and epidemiological antecedents compatible with the disease). These criteria are described in detail elsewhere.<sup>8</sup> Due to a political decision, in 1991 and early 1992, the National Committee for the Prevention and Control of Cholera (CNPC) – responsible, at the time, for all activities related to controlling the epidemic in the country – only counted cases which had been confirmed by laboratory exams (namely, positive stool culture for *V. cholerae*), even in areas in which the circulation of this agent had already been established. In

the subsequent period, in spite of changes in orientation promoted by the Ministry of Health, still very few cases were confirmed based on the clinical-epidemiological criterion, in all Brazilian states. The states in the Northeast Region, with the exception of Pernambuco and Bahia, confirmed more than 50% of their cholera cases by laboratory testing. This proportion was as high as 85%, or even higher, in the states of Maranhão, Paraíba, Piauí, and Sergipe.<sup>4</sup>

The inconvenience of chemoprophylaxis for contacts of cholera patients is widely described in the international literature. In addition to its failure to restrict the dissemination of the disease in the population, chemoprophylaxis may easily lead to the emergence of strains resistant to the antibiotics used, rendering inefficient a weapon designed to be used in severe cases, mainly for reducing disease lethality. Its widespread use in Brazil has also led to the failure to diagnose a large number of cases, since the use of antibiotics before the collection of rectal swab samples leads to negative test results.

Mortality statistics are an important element in diagnosis and healthcare policy making, and the death certificate is the main source of data for these statistics.<sup>1</sup> Using SIM data for planning measures in the field of epidemiological surveillance is a limited approach, mainly because of the two to three-year lag between death notification and the availability of data at federal level. This does not prevent the use of this information at municipal level, in real time, as an important monitoring instrument for the early identification of alterations in the health conditions of the population. In the specific case of cholera, an increase in the number of deaths due to diarrhea is an important alert for the early detection of outbreaks of the disease.

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