"Cross-Country Analysis of the Effects of Urbanization, Improved Drinking-Water and Improved Sanitation on Cholera"

Authors: Andrew J. Leidner and Naveen C. Adusumilli
Affiliation: Texas A&M University
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Abstract: Demand for adequate provision of drinking-water and sanitation facilities to promote public health and economic growth is increasing in the rapidly urbanizing countries of the developing world. Using panel data and probit estimation, this paper investigates the inter-relationships between the occurrence of cholera outbreaks, urbanization, drinking-water and sanitation facilities, and other economic and environmental-geographic variables. The imputation of missing data is found to be an important consideration. Significant effects are found for environmental-geographic variables and varied effects for sanitation, drinking-water, and urbanization. On balance, the evidence suggests drinking-water levels and urbanization are stronger predictors of cholera outbreaks than sanitation levels.

Introduction

In recent years, public health and economic development research have given a lot of attention to the high correlation between regions with sub-standard health and poverty. Researchers have focused on understanding the health side as it affects economic development (Sachs and Malaney 2002, Bloom et al 2004), the poverty side as it affects health (Tol and Dowlatabadi 2001), and the two sides together as they simultaneously affect each other (Bonds et al. 2009; Tol 2007). Among the illnesses that seem to pervade impoverished regions, the persistence of diarrheal disease poses a particularly tragic problem. Tragic, because well-known and well-executed methods exist in the developed world by which diarrheal disease can largely be prevented and by which many of those that become infected can be medically treated to achieve a full and relatively fast recovery. Simple water treatment methods, whether they be piped water service or simple point-of-use systems, are effective at reducing infections of diarrheal disease (Fewtrell et al. 2005; Zwane and Kremer 2007). Several personal health-based interventions can also be used to prevent diarrheal infection, such as breast feeding and vaccination of children. Equally important, medical interventions, such as nutrient supplementation and oral-rehydration therapy (ORT), can be used to recover from an infection, *ex post* (Zwane and Kremer 2007). In spite of these simple preventative and remedial measures, diarrheal disease persists in many parts of the world. It kills more than 2 million children annually, mostly in developing countries (Kosek et al. 2003).

One of the objectives of the Millennium Development Goals is to half the proportion of people without access to improved sanitation and drinking water (WHO and UNICEF 2010). This goal is in part motivated by the recognition that water and sanitation infrastructure plays a role in preventing disease, encouraging economic growth, and ultimately reducing poverty

(Pruss-Ustun and Corvalan 2006). Furthermore, drinking water and sanitation improvements become more important public health considerations when viewed in the context of rapidly urbanizing human populations across the globe. Greater population densities suggest greater potential for disease transmission and greater susceptibility to disease epidemics. With these dynamics in mind, this paper seeks to better understand the relationships between the development of drinking water facilities, sanitation facilities, urbanization, and the water-borne diarrheal disease, cholera. A cross-country and time-series dataset (i.e., a panel dataset) has been assembled from several sources, integrating disease infection levels, water and sanitation infrastructure levels, economic wealth indicators, and environmental variables. The remainder of the paper will proceed with the following sections: cholera background, conceptual framework, empirical strategy, data description, results, and conclusion.

Cholera Background

Diarrheal disease can originate from a variety of microbiological agents (Jose and Bobadilla 1994), but this paper focuses on just one specific pathogen *Vibrio cholera*. Cholera cases number between 100,000 and 300,000 recorded cases per year worldwide (WHO 2009a). Cholera is a water-borne illness where transmissions occur primarily as a consequence of a contaminated common pool, shared resource, such as lakes (Bompangue et al. 2008) or coastal estuary (Jutla et al. 2010). Since water bodies are the most common environmental reservoirs for cholera, other environmental and water-related factors like climatic and weather events also influence cholera incidences (Akanda et al. 2009; de Magny et al. 2008; Lama et al. 2004; Sack et al. 2003). Greater understanding of the interdependency between water-related diseases and climate, i.e. rainfall and temperature, and understanding the role of climate change on health

(Koelle et al. 2005; Singh et al. 2001; WHO 2002), may yield profound, and potentially dire, implications for developing countries in anticipation of climate change. This makes the task of understanding the most effective disease mitigation strategies, whether they are drinking water facilities, sanitation or medical care, increasingly important.

Disease mitigation strategies have demonstrated effectiveness when it comes to cholera. The most common therapy for acute diarrhea is ORT, the consumption of large amounts of water to replenish the liquids lost due to diarrhea. From Jose and Bobadilla (1994), ORT reduces the length of diarrhea symptoms (morbidity) as well as the death rate of the disease (mortality). The primary management strategy for all types of diarrheal diseases is to prevent and treat dehydration while maintaining nutrient intake levels throughout the course of the disease (Alam and Ashraf 2003). The deployment of ORT has reduced mortalities associated with cholera outbreaks from greater than 40% of reported cases, with tens of thousands of deaths, to less than 4% of reported cases (WHO 2009a).

On the prevention side, cholera is controllable by improving drinking water and sanitation systems, as evidenced by more developed countries, which have nearly universal coverage of both drinking water and sanitation services and essentially no domestically derived cases of cholera. In developing regions, cholera prevention can be obtained by augmenting water supply systems with simple filters to remove the copepods to which cholera bacterium are known to attach (Huo et al. 1996). This can result in 48% reduction in cholera cases (Colwell et al. 2003).

Other factors that influence disease levels include a society's economic and institutional characteristics. Gerelomo and Penna (2000) show the incidence of cholera are linked to lower household income levels. In Latin America, higher levels of gross national product per capita, above US $2000, was negatively correlated with cholera incidence rates (Ackers et al. 1998). Talavera and Perez (2009) found that the number of cholera cases was highest in countries with low gross national income, strengthening the case that cholera, and poor health in general, are strongly linked to poverty. For greater context, Figure 1 displays scatter plots of several variables used in this study. Notice the apparent negative correlation between GDP and cholera

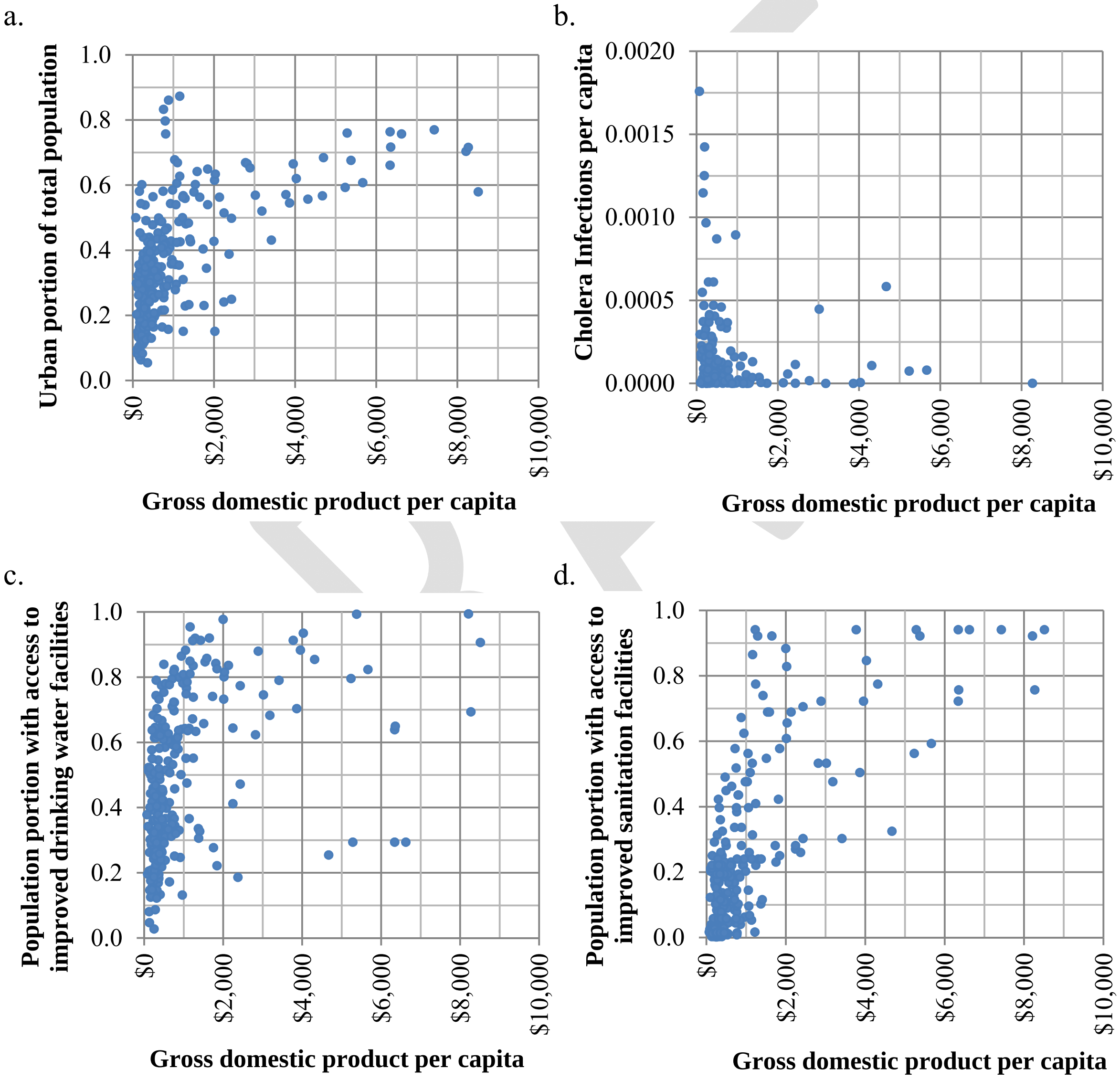

Figure 1. Selected observations in scatter plots of demographic, public health variables, and gross domestic product (GDP) from a panel of African and Asian countries from 1990, 1995, 2000, 2005, and 2008; (a) Urban portion of total population and GDP, (b) Cholera infections per capita and GDP; (c) Drinking water access and GDP; and (d) Sanitation access and GDP. Sources: WHO (2009b) and World Bank (2011).

infection rates, and the positive correlations between GDP and, respectively, urbanization, drinking water levels, and sanitation levels.

Conceptual Framework

Beginning to address the more specific question about the relative significance of drinking water, sanitation, and urbanization, a broad conceptual model is developed for the behavior of the system (Figure 2). This framework will remain highly generalized to support the dataset which contains macro (i.e., country-level) data. In a nutshell, the conceptual framework argues environmental and anthropogenic conditions contribute to cholera infections. A country's health care institutional capacity to monitor and record those cases determines the number of actual cholera cases that make it into the world's record of cholera infections.

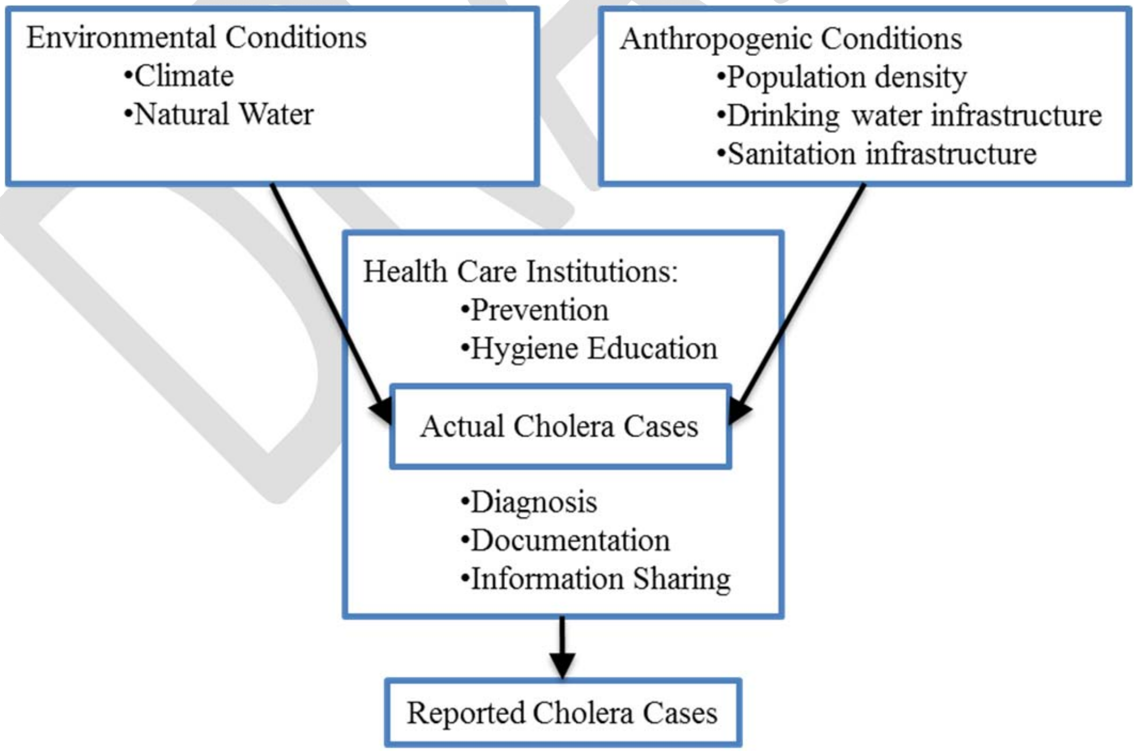

Figure 2: Conceptual framework for the occurrence and recording of cholera cases.

Recent studies have effectively demonstrated climatic variables, such as rainfall and temperature, have influence on the prevalence of cholera (Koelle et al. 2005; Pascual et al. 2002) as well as other diarrheal diseases (Singh et al. 2001). Proximity to coastal waters has also been demonstrated to influence cholera transmissions (Borroto and Martinez-Piedra 2000). These studies underscore the importance of considering the effect of climate and geography when studying diseases in countries over vast spatial scales, which may inherit different levels of fitness for *Vibrio cholera* from their natural environments.

In addition to factors deriving from the natural environment, anthropogenic forces may also influence the spread of cholera. Interestingly, Borroto and Martinez-Piedra (2000) found that areas of low urbanization can predict cholera infections, whereas Osei and Duker (2008) find that higher levels of urbanization and overcrowding are associated with higher incidences of cholera. Theoretically, the effect of urbanization on cholera could be interpreted a number of ways. On the one hand, urban areas are more densely populated, giving rise to greater opportunity for disease transmission between humans to occur. Moreover, urban population, particularly in developing nations, tends to suffer more intense levels of poverty, which can translate into malnutrition and by extension greater vulnerability to infection. But on the other hand, urban populations may have greater opportunities for health education and preventative health care.

In most of Europe and North America, cholera is not a great public health concern, though it once was (Pyle 1969). Much of the reduction in the prevalence of cholera in more developed countries is likely due to advancements in water treatment and sanitation. Therefore, it stands to reason, and research has demonstrated, that in developing economies access to clean water and water-treatment systems can be effective at reducing infections of diarrheal disease

(Fewtrell et al. 2005; Zwane and Kremer 2007). Increasing access to clean and reliable drinking water as well as increasing urbanization are all related phenomena in developing regions, which contribute to different ways to cholera infections, and public health in general.

While improving and expanding health care institutions can undoubtedly improve the public health and the social welfare of a developing country, the effect of a health care institution on the records used in public health analysis, such as this paper, is slightly more ambiguous. Suppose a cholera infection has occurred, then the accurate documentation of that infection is determined by how effectively the region's health care institutions can recognize and record the infection. This process—health care institutions' monitoring and maintaining of cholera data—most likely varies greatly across the globe. Particularly so in developing nations where health issues are most critical, medical professionals are, on the margin, more likely to expend their resources treating patients rather than collecting and maintaining vast amounts of data on cholera, or for that matter any of the many other diseases. Zuckerman et al. (2007) identified the importance of health expenditures towards more accurate reporting of disease outbreak data. Understanding health care institutions and data collection becomes quite important for this study, in particular when considering different procedures for the imputation of missing data.

Empirical Strategy

To empirically estimate the effects of the different components in the conceptual framework, a linear, reduced-form regression model is used. This model imposes minimal structure on the data, as opposed to a stricter structure that might come from a formal theoretical model of disease transmissions. Therefore, no specific disease transmission parameters or other specific economic parameters will be estimated. This study only aims to capture the broad relationships that may exist between the independent and dependent variables. Explicitly, the model is as follows:

$$y_{i,t} = \alpha_0 + \alpha_{DW} DW_{i,t} + \alpha_{San} San_{i,t} + \alpha_{urb} Urban_{i,t} + \alpha_{gdp} GDP_{i,t}$$

$$+\alpha_{ca} CoastToArea_i + \alpha_{wa} WaterToArea_i + \alpha_{ca} Latitude_i + \alpha_{time} Time_t + \varepsilon,$$

where $y_{i,t}$ represents the occurrence of one or more cholera infections reported in country i at time t; $DW_{i,t}$ and $San_{i,t}$ is each country's portion of population with access to "improved" drinking water and sanitation facilities through time, with the definition of "improved" taken from WHO (2010). $Urban_{i,t}$ is each country's portion of urban population through time. $GDP_{i,t}$ refers to each country's annual gross domestic product. Finally, three environmental or geographic variables are included: $CoastToArea_i$, $WaterToArea_i$, and $Latitude_i$. These variables are, respectively, the ratio of a country's coastline (km) to its land area (km^2); the ratio of the country's water area (km^2) (water surfaces within domestic borders) to its land area (km^2); and the country's latitude. All remaining unobserved variables are assumed to be included in the error term ε. The α's are the coefficients to be estimated.

Heterogeneity among countries, including environmental, climatic, cultural, and political—any of which may affect cholera occurrences—is difficult to control for in such a model. Using a fixed-effect term for each country would be ideal, or at least more desirable. Unfortunately the available data does not support such a model. The time-series dimension is small relative to the cross-sectional dimension and there is insufficient variation in the dependent variable to identify fixed effects for all countries. The intended purpose of $CoastToArea_i$, $WaterToArea_i$, and $Latitude_i$ is to approximate each nation's spatial-environmental-heterogeneity with continuous variables. From the review of literature, these variables seem to be the most appropriate as well as being more readily available, i.e., annual rainfall and temperature could not be found for several countries in the data set, for which $Latitude_i$ serves as a proxy. Any remaining heterogeneity, cultural, political or environmental, is assumed to be included in the error term.

The role of most of the other independent variables in the conceptual model is fairly straightforward. One remaining exception may be $GDP_{i,t}$. As described by the conceptual model, health care institutions can play a role in prevention, diagnosing, treating, and reporting cholera cases. Defined broadly enough, health care institutions can potentially include any number of educational programs, extension programs, or public awareness campaigns, any of which could be designed to mitigate the harmful impacts of diseases like cholera. Erdil and Yetkiner (2009) found a one-way causal relationship that runs from income to health expenditure in low and middle income countries. Hence, a reasonable assumption is made that all such health related activities are correlated with a country's $GDP_{i,t}$, and therefore $GDP_{i,t}$ is used as a proxy for intensity of health care institutions.

While not directly used in this analysis, data for another variable, $Cholera_{i,t}$ (Table 1), is the annual number of cholera cases, as reported in the *Weekly Epidemiological Record* (WHO 2009b), divided by the country's total population at time t. Since many years occur with no cholera cases reported for a given country, $Cholera_{i,t}$ contains many missing values that can be interpreted as years when no cholera cases occurred, or years when no records of cholera were reported to the WHO. Therefore, the missing values must either be imputed as zeros, or left as missing and thereby omitted from any regression analysis. Once the missing values have been imputed, the empirical estimation procedure selected is a probit regression on the binary variable representing occurrence and non-occurrence of cholera cases.

Table 1. Summary statistics used in the analysis of cholera in Asian and African countries.

Variable	Obs.	Mean	Std. Dev.	Min.	Max.
Cholera					
cholera[a]	179	0.0006	0.0020	9.86E-08	0.0171
cc1	305	0.5869	0.4932	0	1
cc2	255	0.7020	0.4583	0	1
cc3	228	0.7851	0.4117	0	1
Water and sanitation access					
DW[b]	285	0.66364	0.19216	0.0318	1
San[b]	287	0.42631	0.27900	0.04	1
Economics and demographics					
Urban[b]	305	0.3759	0.1963	0.054	1
Population[b]	305	6.57E+07	2.02E+08	116117	1.33E+09
GDP[b]	286	2,352.79	6,286.46	69.31	41,967.65
Environmental					
coastToLand[c]	305	0.0164	0.0481	0	0.2769
waterToLand[c]	305	1	5	0	40
coastline[c]	305	3,099	9,053	0	54,716
waterArea[c]	305	24,768	51,740	0	314,070
landArea[c]	305	779,382	1,356,396	697	9,596,961
latitude[c]	305	15.4959	10.7641	0	48
Time					
time[b]	305	1999.6	6.5407	1990	2008

[a]. Source: Cholera case numbers come from WHO (2009b) and converted to per capita levels using population from [b].

[b]. Source: World Bank (2011).

[b]. Source: The World Fact Book (2009).

Data Description

The dataset used for this study comes from several sources. The countries included in this data set include most of Asia and Africa, with no data from Europe, North America, South America, or Australia. Data cover the following years: 1990, 1995, 2000, 2005, and 2008. The data and their sources are itemized in Table 1. The variables $cholera_{i,t}$, $DW_{i,t}$, $San_{i,t}$, and

$Urban_{i,t}$ are the per capita rates for each country. In the case of $DW_{i,t}$, it was necessary to do some minor algebraic manipulation to the World Bank data on urban and rural drinking water access, the urbanization rate, and total population to calculate the variable used in this study. The environmental and geographic variables are all found in The World Factbook (2009).

Another noteworthy dataset characteristic is the nature of $cholera_{i,t}$ and its derivatives $c1_{i,t}$, $c2_{i,t}$, and $c3_{i,t}$, which are the indicator variables used in the probit estimation. If $cholera_{i,t}$ was not reported for a country, we must assume either (1) cholera infections were zero for that year, or (2) the country did not or could not report the cholera cases that did occur. Hence, indicator variables $c1_{i,t}$, $c2_{i,t}$, and $c3_{i,t}$ are developed that represent three different ways to impute the missing values. All three variants are equal to one if a cholera case was reported in the given country and time. Variants are equal to zero depending on the imputation method.

The indicator variants are organized in increasing levels of sophistication, with $c1_{i,t}$ being a simple zero-imputation of all missing values. The next level of indicator variant considers that some nations do not participate in WHO initiatives, such as the reporting of epidemiological data. These countries' non-participation could be for political reasons as well as for practical reasons. For example, some nations may not have the health infrastructure and resources to readily diagnose, monitor, and transmit medical case records. With these circumstances in mind, $c2_{i,t}$, zero-imputes all missing values except for those countries that have never reported a value. Countries that never reported a cholera case are assumed to have been either unwilling or unable to report it to WHO. Values $c2_{i,t}$ for these countries were left as missing and those observations were omitted from the regression.

The final indicator variant $c3_{i,t}$ takes the idea of non-reporting one step further. Suppose that a nation, during the 28-year timeframe captured by the dataset, obtained either the willingness or the ability to start reporting cholera cases for the first time, and then did so from that time forward. This suggests that any reporting of cholera cases by country i in year t reveals country i's ability and willingness to report additional cases in year $t + 1$, and so on. In this way, for $c3_{i,t}$ any missing data point that is prior to a reported cholera case is left as missing. Any missing data point that follows a reported level of cholera cases is interpreted to be zero cholera cases for that year. Table 2 contains an illustrative example of the imputation procedure for a few selected countries.

Table 2. Examples of cholera cases per capita and the three variants of imputed indicator variables for selected countries in Africa and Asia (1990, 1995, 2000, 2005, 2008).

Country	time	cholera	c1	c2	c3
Afghanistan	1990		0	0	
Afghanistan	1995	9.57E-04	1	1	1
Afghanistan	2000	1.84E-04	1	1	1
Afghanistan	2005	1.23E-06	1	1	1
Afghanistan	2008		0	0	0
Central African Republic	1990		0		
Central African Republic	1995		0		
Central African Republic	2000		0		
Central African Republic	2005		0		
Central African Republic	2008		0		
Ghana	1990	1.96E-04	1	1	1
Ghana	1995	2.72E-04	1	1	1
Ghana	2000	1.71E-04	1	1	1
Ghana	2005	1.45E-04	1	1	1
Ghana	2008	5.24E-05	1	1	1
Japan	1990	5.89E-07	1	1	1
Japan	1995	2.57E-06	1	1	1
Japan	2000	2.68E-07	1	1	1
Japan	2005	3.36E-07	1	1	1
Japan	2008		0	0	0

Results

Estimation results from the probit regressions are reported in Table 3. The models only differ in their use of one of the imputed variants as the dependent variable. By looking at model fitness results, the model using dependent variable $c3_{i,t}$ is superior to the other two in terms of explanatory power (Psuedo-R^2). These statistical results coupled with the intuitive appeal of $c3_{i,t}$'s imputation method, make this seem to be the preferred imputation and model from which to draw conclusions. Across all three models, $Latitude_i$, which is the proxy for climate and temperature, is highly significant and associated with reduced probabilities of cholera outbreaks. This indicates that as one moves from country-to-country away from the equator, towards the poles, the country's natural environment becomes less conducive to cholera outbreaks. This effect is likely due to the correlation between latitude and climate.

The significance of sanitation and drinking water facilities is interesting. $San_{i,t}$ is significant in the first two models, but $DW_{i,t}$ is significant in the last model. When they are significant, they both have the expected sign and the calculation of marginal effects confirms their relationship is with decreasing probabilities of cholera occurrence. Due to the non-robust impact (i.e., loss of significance across models) of $San_{i,t}$ and $DW_{i,t}$, the debate over which of the two mitigation strategies is the better investment for reducing water-borne disease is not settled by these results. That said, on the balance, due to the greater explanatory power and the intuitive appeal of the $c3_{i,t}$ model, the evidence here suggests that drinking water improvements may have a stronger relationship to the probability of non-occurrence of cholera outbreaks than sanitation improvements. In all likelihood, both mitigation activities are correlated with each other, both contribute to reduced levels of disease, and their effects are likely coupled in a much more complex human-environmental-ecological system than could be modeled here.

Table 3. Probit regressions on presence of cholera, urbanization, drinking water and sanitation levels, and environmental-geographic variables for nations of Africa and Asia (1990, 1995, 2000, 2005, 2008).

Dependent Variable:	c1		c2		c3	
	Coefficients	Marginal Effects	Coefficients	Marginal Effects	Coefficients	Marginal Effects
Independent Variables	α	dy/dx	α	dy/dx	α	dy/dx
constant	30.669		52.272		210.735 ***	
	0.249		*0.110*		*0.000*	
DW	0.229	0.087	0.107	0.032	-2.455 **	-0.452 **
	0.732	*0.732*	*0.901*	*0.900*	*0.032*	*0.032*
San	-1.057 **	-0.400 **	-1.567 ***	-0.467 ***	-0.903	-0.166
	0.029	*0.029*	*0.008*	*0.007*	*0.215*	*0.221*
Urban	0.021	0.008	1.220	0.364	1.797 *	0.331 *
	0.971	*0.971*	*0.108*	*0.107*	*0.050*	*0.055*
GDP	0.000 **	0.000 **	0.000 *	0.000 *	0.000 *	0.000 *
	0.010	*0.010*	*0.068*	*0.068*	*0.091*	*0.095*
time	-0.015	-0.006	-0.025	-0.008	-0.104 ***	-0.019 ***
	0.267	*0.267*	*0.120*	*0.120*	*0.000*	*0.000*
coastToArea	-4.558	-1.725	-7.338 **	-2.189 **	-5.996	-1.104
	0.174	*0.174*	*0.039*	*0.038*	*0.133*	*0.139*
waterToArea	-0.020	-0.007	-0.022	-0.006	-0.045 *	-0.008 *
	0.315	*0.315*	*0.286*	*0.289*	*0.062*	*0.070*
latitude	-0.031 ***	-0.012 ***	-0.024 **	-0.007 **	-0.029 **	-0.005 **
	0.001	*0.001*	*0.022*	*0.021*	*0.020*	*0.024*
sample size	265		218		203	
LnLikelihood	-159.25		-106.15		-68.14	
P>chi2	0.000		0.000		0.000	
Psuedo R^2	0.096		0.130		0.314	

Values in italics immediately below estimates are p-values.
*, **, *** indicate significance level less than or equal to 10, 5, and 1%.

Considering just the third model (i.e., $c3_{i,t}$), both sanitation and drinking water access have downward associations with the probability of cholera outbreaks. Urbanization is positively, and significantly, related to cholera outbreaks, suggesting that urbanization and a more compact living environment is conducive to cholera, a similar finding to Osei and Duker (2008).

The coefficient on the proxy for health care institutions, $GDP_{i,t}$, is very small but positive, and significant across all models. One's first thought might expect $GDP_{i,t}$ to be negatively related to the occurrence of a disease like cholera. However, as explained in the conceptual model, health care institutions hold an ambiguous position with reference to recorded disease levels. Given that the sample of countries includes much of the developing world, many of these countries may be transitioning into a health care environment that has only recently began recording data and/or is becoming more accurate and more exhaustive in their surveillance systems. The increasing sophistication of the imputation methods tries to address this issue and to their credit, the significance on $GDP_{i,t}$ is less strong in the final two more sophisticated variants. Analysis of the relationship between $GDP_{i,t}$ and health care institutions remains an avenue for future research.

Conclusion

This paper investigates the relationship between drinking water facilities, sanitation facilities, urbanization, and the public health issue of cholera. By collecting a novel dataset from many sources and handling the missing data through deliberate data imputation methods, relationships were estimated between cholera outbreaks, levels of accessible drinking water and sanitation, economic and demographic variables, and environmental conditions. These relationships reinforce several things that have been studied before, increasing levels of sanitation and drinking water facilities are negatively related to disease outbreaks. Equatorial regions have environments that are more conducive to the outbreaks of certain diseases, in this case cholera.

Beyond the basic findings, the results also contribute to the ongoing discussion as to the nature of the inter-relationships between sanitation and drinking water services. In the model with the most intuitive appeal and statistical explanatory power, on balance, the evidence suggests that increasing drinking water facilities are more strongly related to outbreak non-occurrence than increasing sanitation levels. In the same model, urbanization strongly predicts outbreak occurrence. These results are conditional on data-imputation methods. The difference in estimation results across the models (i.e., across the different data-imputation methods) underscores the importance of addressing missing variables, understanding the nature of the data collection process, and encouraging thorough data collection procedures in developing countries, where resources are limited.

Bibliography

Ackers, Marta-Louise, Robert E. Quick, Christopher J. Drasbek,,Lori Hutwagner, and Robert V. Tauxe.1998. Are there National Risk Factors for Epidemic Cholera? The Correlation between Socio-Economic and Demographic Indices and Cholera Incidence in Latin America. *International Journal of Epidemiology* 27: 330-334.

Alam N.H. and H. Ashraf. 2003. "Treatment of Infectious Diarrhoea in Children." *Pediatric Drugs* 5(3): 151-165.

Akanda, Ali S., Antarpreet S. Jutla, and Shafiqul Islam. 2009. Dual Peak Cholera Transmission in Bengal Delta: A Hydroclimatological Explanation. *Geophysical Research Letters* 36: L19401.

Alam N.H. and H. Ashraf. 2003. "Treatment of Infectious Diarrhoea in Children." *Pediatric Drugs* 5(3): 151-165.

Bloom, David E., David Canning, and Jaypee Sevilla. 2004. The Effect of Health on Economic Growth: A Production Function Approach. *World Development* 32 (1): 1-13. doi:10.1016/j.worlddev.2003.07.002.

Bompangue, Didier, Partick Giraudoux, Pascal Handschumacher, Martine Piarroux, Bertrand Sudre, Mosiana Ekwanzala, Ilunga Kebela, and Renaud Piarroux. 2008. Lakes as Source of Cholera Outbreaks, Democratic Republic of Congo. *Emerging Infectious Diseases* 14(5): 798-800.

Bonds, Matthew H., Donald C. Keenan, Pejman Rohani, and Jeffrey D. Sachs. 2009. Poverty Trap formed by the Ecology of Infectious Diseases. *Proceedings of the Royal Society B: Biological Sciences* 277(1685): 1185-1192. doi:10.1098/rspb.2009.1778.

Borroto, R.J. and R. Martinez-Piedra. 2000. Geographical patterns of cholera in Mexico, 1991-1996. *International Journal of Epidemiology* 29(4): 764-772.

Colwell Rita R., Anwar Huq, M. Sirajul Islam, K.M.A. Aziz, Md. Yunus, N. Huda Khan, A. Mahmud, R. Bradley Sack, G.B. Nair, J. Chakraborty, D. A. Sack, and E. Russek-Cohen. 2003. Reduction of Cholera in Bangladeshi Villages by Simple Filtration. *Proceedings of the National Academy of Sciences* 100(3): 1051-1055.

de Magny, Guillaume C., Raghu Murtugudde, Mathew R. P. Sapiano, Azhar Nizam, Christopher W. Brown, Antonio J. Busalacchi, Mohammad Yunus, G.B. Nair, Ana I. Gil, Claudio F. Lanata, John Calkins, Byomkesh Manna, Krishnan Rajendran, Mihir K. Bhattacharya, Anwar Huq, and R.B. Sack and Rita R. Colwell. 2008. Environmental Signatures Associated with Cholera Epidemics. *Proceedings of the National Academy of Sciences* 105(46):17676-17681.

Erdil, Erkan and Ibrahim H. Yetkiner. 2009. The Granger-Causality between Health Care Expenditure and Output: A Panel Data Appraoch. *Applied Economics* 41: 511-518.

Fewtrell, Lorna, Rachel B. Kaufmann, David Kay, Wayne Enanoria, Laurence Haller, and John M. Colford, Jr. 2005. Water, Sanitation, and Hygiene Interventions to Reduce Diarrhoea in Less Developed Countries: A Systematic Review and Meta-Analysis. *Lancet Infectious Diseases* 5(1): 42-52.

Gerolomo, Moacir and Maria L.F. Penna. 2000. Cholera and Living Conditions. *Revista de saúde pública* 34(4): 342-347.

Huo, A., B. Xu, M.A. Chowdhury, M.Sirajul Islam, R. Montilla, and Rita R. Colwell. 1996. A Simple Filtration Method to remove Plankton-Associated *Vibrio Cholerae* in Raw Water

Supplies in Developing Countries. *Applied and Environmental Microbiology*, 62(7): 2508-2512.

Jose Marco V. and J. Roman Bobadilla. 1994. Epidemiological model of diarrhoeal diseases and its application in prevention and control. *Vaccine* 12(2): 109-116.

Jutla, Antarpreet S., Ali S. Akanda, and Shafiqul Islam. 2010. Tracking Cholera in Coastal Regions using Satellite Observations. *Journal of the American Water Resources Association* 46(4): 651-662.

Koelle, Katia, Xavier Rodo, Mercedes Pascual, Mohammad Yunus, and Golan Mostafa. 2005. Refractory Periods and Climate Forcing in Cholera Dynamics. *Nature* 436(7051): 696 – 700.

Kosek, Margaret, Caryn Bern, and Richard L. Guerrant. 2003. The Global Burden of Diarrhoeal Disease, as estimated from Studies Published between 1992 and 2000. *Bulletin of the World Health Organization* 81(3): 197-204.

Lama, Javier R., Carlos R. Seas, Raul Leon-Barua, Eduardo Gotuzzo, and R. Bradley Sack. 2004. Environmental Temperature, Cholera, and Acute Diarrhoea in Adults in Lima, Peru. *Journal of Health Population and Nutrition* 22(4): 399-403.

Osei, F.B., and A.A. Duker. 2008. Spatial and demographic patterns of Cholera in Ashanti region – Ghana. *International Journal of Health Geographics* 7:44. doi:10.1186/1476-072X-7-44

Pascual, Mercedes, Menno J. Bouma, Andrew P. Dobson. 2002. *Microbes and Infection* 4: 237-245.

Prüss-Üstün, Annette and Carlos F. Corvalán. 2006. *Preventing Disease through Healthy Environments: Towards an Estimate of the Environmental Burden of Disease.* World Health Organization. Geneva, Switzerland.

Sachs, Jeffrey and Pia Malaney. 2002. The Economic and Social Burden of Malaria. *Nature* 415 (6872): 680-685. doi:10.1038/415680a.

Sack, R.B., A.Kasem Siddique, Ira M. Longini, Jr., Azhar Nizam, Mohammad Yunus, M. Sirajul Islam, J.Glenn Morris, Jr., Afsar Ali, Anwar Huq, G. Balakrish Nair, Firduasi Qadri, Shah M. Faruque, David A. Sack, and Rita R. Colwell. 2003. A 4-Year Study of the Epidemiology of *Vibrio Cholerae* in Four Rural Areas of Bangladesh. *The Journal of Infectious Diseases* 187(1): 96-101.

Singh, Reena B. K., Simon Hales, Neil de Wet, Rishi Raj, Mark Hearnden and Phil Weinstein. 2001. The Influence of Climate Variation and Change on Diarrhoeal Disease in the Pacific Islands. *Environmental Health Perspectives* 109(2): 155–159.

Talavera, Arturo and Ela M. Perez. 2009. Is Cholera Disease Associated with Poverty? *The Journal of Infection in Developing Countries* 3(6): 408-411.

The World Factbook. 2009. Washington, DC: Central Intelligence Agency, 2009. https://www.cia.gov/library/publications/the-world-factbook/index.html

Tol, Richard S. J. 2007. Climate, Development and Malaria: An Application of FUND. *Climatic Change* 88(1): 21-34. doi:10.1007/s10584-007-9253-4.

Tol, Richard S.J., and Hadi Dowlatabadi. 2001. Vector-Borne Diseases, Development & Climate Change. *Integrated Assessment* 2(4): 173-181.

World Bank, Development Data Group, World Development Indicators. 2011. Datasets published online. Available at: http://data.worldbank.org/indicator (accessed June 10, 2011).

World Health Organization. 2002. *The World Health Report 2002*. World Health Organization, Geneva, Switzerland.

World Health Organization. 2009a. Diarrhoeal Diseases : Cholera. Initiative for Vaccine Research. Available at http://www.who.int/vaccine_research/diseases/diarrhoeal/en/ index3.html (accessed August 10, 2010).

World Health Organization. 2009b. *Weekly Epidemiological Record: Cholera Articles*. Available at http://www.who.int/topics/cholera/wer/en/index.html (accessed June 12, 2010.

World Health Organization and UNICEF. 2010. *Progress on Sanitation and Drinking-Water: 2010 Update.* WHO Press: Geneva, Switzerland.

Zuckerman, Jane N., Lars Rombo, and Alian Fisch. 2007. The True Burden and Risk of Cholera: Implications for Prevention and Control. *The Lancet Infectious Diseases* 7(8): 521-530.

Zwane, Alix Peterson, and Michael Kremer. 2007. What Works in Fighting Diarrhoeal Diseases in Developing Countries? A Critical Review. *World Bank Research Observer* 22(1): 1-24.