While diarrhea is often considered more of an inconvenience than a threatening medical condition in industrialized countries like the United States, it poses a grave threat to the health of residents of impoverished areas, especially children under the age of five. A combination of environmental conditions in impoverished areas—poor sanitation, crowding, and the lack of clean water—foster the spread of diarrhea-causing parasites. Although many children still die of diarrheal diseases—an estimated 4.9 million between 1992 and 2000—mortality from diarrhea has declined drastically since oral rehydration therapy (ORT) revolutionized the care of diarrhea patients in the developing world. This treatment reduced deaths from diarrhea from 13.6 million between 1955 and 1979 to 5.6 million between 1980 and 1989. This promising improvement leads many to believe that the need for public health attention to diarrheal disease is diminishing. However, in the time that mortality has drastically declined, morbidity, or general incidence of diarrheal disease, has not; in fact, it is on the rise.

Mortality rates have traditionally been used to estimate the global burden of diarrheal disease. With morbidity increasing and mortality in decline, however, a critical need arises to further understand the impact of non-fatal diarrheal diseases on residents of impoverished areas. Researchers have begun reassessing the impact of diarrhea by measuring its influence on outcomes such as nutrition, fitness, and intelligence. More specifically, within the past five years important research has linked early childhood diarrhea (ECD), diarrhea during the first two years of life, with deficits in cognitive abilities several years later. This association is attributed to the concept that the first two years of life represent a “critical period” in brain development, and that if severe diarrhea causes its characteristic dehydration and nutrient loss during this time, permanent or semi-permanent effects on cognitive function may result. While these studies associate illness in the first two years to cognitive function later in life, they fail to take into account the disease, malnutrition, and social environment in the years after infancy and before the cognitive assessment. Consequently, it is not known whether diarrhea in the first two years of life exclusively causes the cognitive effects seen years later, or if higher levels of diarrhea during early childhood foreshadow the effects of illness and a poor environment throughout all of childhood.

In addition to the timing of diarrheal illness, different etiologies of diarrhea may result in unique physical effects according to their distinct pathogeneses. Entamoeba histolytica is one of the many intestinal parasites that causes diarrhea in impoverished areas. In places like Dhaka, Bangladesh, where the current study was carried out, E. histolytica is associated with 8% of diarrheal episodes and 8.7% of dysenteric episodes. However, an estimated 90% of all patients colonized with E. histolytica never manifest clinical symptoms. This distinctive pattern of illness calls for a more complete understanding of the consequences of E. histolytica infection.
The current study seeks to address these gaps in knowledge by assessing the cognitive impact of diarrheal disease and *Entamoeba histolytica* infection during the ages of 2-9. Towards these ends, the current study undertook cognitive testing of a cohort of 191 children, ages 6-9, living in an urban slum of Dhaka, the capital of Bangladesh. Each child took a nonverbal test of general intelligence, the Raven’s Coloured Matrices, and a verbal subtest of general intelligence, an adapted form of the definitions section of the Wechsler Abbreviated Scale of Intelligence. Comprehensive health surveillance of these children had taken place in the four years prior to the cognitive testing, beginning in these children’s 2\textsuperscript{nd} to 5\textsuperscript{th} years, carried out by a team of researchers at the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B). Cognitive scores were compared to illness data from the preceding four years, including the frequency, duration, and etiology of all diarrheal episodes; the amount of time colonized with *Entamoeba histolytica* and its associated diarrheal and dysenteric episodes; as well as anthropometric data such as height and weight in order to evaluate nutritional status. Additionally, socioeconomic and educational history surveys for each child were completed to estimate the effects of the social environment on cognitive scores.

The data collected can be classified into four main categories: demographic or socioeconomic variables; disease-related variables; malnutrition and anthropometric variables; and cognitive test scores. Each of first three categories could lead to deficits in cognitive test scores, the fourth category. Most likely, all of these factors are intertwined; e.g., parents with lower levels of education will also earn less for the household and their children will perform worse on cognitive tests; or families with lower household income will also have poorer sanitation and will find themselves at higher risk for contracting diarrheal illnesses. Bivariate analysis examines the direct associations between one variable and one outcome, without considering the influence of other variables on the association. For example, bivariate analysis demonstrates the negative association between the number of episodes of diarrhea and test scores, without controlling for other factors that might contribute to this association. Ordinary logistic regression and ordinal logistic regression were used for bivariate analysis. Multivariate analysis attempts to control for the effect of outside influencing factors by statistically removing the influence of these variables from consideration. For instance, the association between episodes of diarrhea and test scores were controlled for the influence of the family's income, which could also contribute to a child's low test scores. Those environmental or sociological variables that were found to explain variations in cognitive scores to a statistically significant degree (association of p<0.05 with cognitive scores) were controlled for in multivariate analysis.

The current study draws three main conclusions. First, malnutrition is significantly associated with cognitive scores when malnutrition is measured both at the starting point of the study (termed “baseline malnutrition”) and also in terms of duration throughout the 4-year surveillance period. The association of baseline malnutrition with cognitive scores supports earlier studies that found that early childhood malnutrition is a strong predictor of later cognitive function.\textsuperscript{3} In addition to what is already known about the effects of early malnutrition on
cognitive function, the current study highlights the ongoing importance of nutrition throughout childhood. Second, indicators of individual incidence diarrhea are significantly associated with cognitive test scores in bivariate analysis, but the statistical significance of these associations are lost after controlling for environmental variables. The dependence of these associations on environmental variables indicates the interconnected, harmful nature of diarrheal diseases and the setting that fosters them. Finally, while statistically significant associations were not found between any other measures of *E. histolytica* infection and cognitive scores, an association was seen between *E. histolytica*-associated dysentery and verbal test scores both before and after controlling for environmental variables. This finding could point out the negative cognitive effect of dysentery caused by *E. histolytica*. Also, because children with *E. histolytica*-associated dysentery tend to experience lower levels of nutrition and higher levels of diarrhea, it could simply serve as a marker for children who have poorer health in general. It is important to note that no data was gathered from the subject children before enrollment at 2-5. Controlling cognitive outcomes for baseline stunting attempts to take into account in some way those events that occurred before enrollment, but it cannot fully estimate early childhood conditions. Although the current study cannot establish causation of any one of these nutritional, diarrheal, or social factors on cognitive abilities, the associations presented do stress that later childhood cannot be ignored in future research and public health interventions, and that the same types effects of diarrhea and malnutrition on cognitive outcomes are seen during school age as they are during early childhood.

These results clearly show that diarrhea in the years following infancy are connected with cognitive childhood function and therefore should not be neglected either in future research or in public health responses to diarrheal disease. They support the findings of earlier research that childhood diarrhea and malnutrition manifest themselves in a child’s cognitive abilities. These conclusions imply that effective medical and public health responses should take into account the full span of childhood, even if whether through improved ORT, vaccinations for childhood diarrheal diseases, or other improved treatments. Furthermore, they highlight the strong influence of a child’s family life and social environment on his or her cognitive development, as shown in the links between environmental variables, especially the level of parental education, and diarrhea and cognitive scores. Finally, while improved disease therapies and increased awareness of social factors in cognitive development will assist in lessening the detrimental effects of poor health on cognitive abilities, the influence of lack of access to resources—education, sanitation, and health care—on children’s health and cognitive outcomes, underscores that poverty is at the root of the observed illness, malnutrition, and cognitive deficits. An effective solution to alleviating the effects of diseases of poverty will not be found until the multitude of social, economic, and health-related factors are considered as a whole.
References:


