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Preface

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Diarrheal disease constitutes one of the top two causes of mortality among young children in developing countries, accounting for more than 1 in 10 deaths among children 1–59 months of age.[1] Despite many studies that have attempted to address the overall burden, etiology, and consequences of diarrheal disease in infants and young children, at the turn of the millennium, many knowledge gaps remained, making it difficult to set priorities for implementing existing interventions and investing in new ones.[2] To address these gaps, the Bill and Melinda Gates Foundation sponsored the Global Enteric Multicenter Study (GEMS), a project designed to quantify the population-based incidence, mortality, and sequelae of moderate-to-severe diarrheal illness (MSD) attributable to different etiologies in children < 60 months of age in sub-Saharan Africa and South Asia.[2] The GEMS research agenda was pursued in seven representative field sites (four sites in sub-Saharan Africa and three sites in South Asia), with each site linked to a defined population (of ~200,000 subjects) under continuous demographic surveillance, where all births, deaths, and migrations were recorded during three to four annual visits to each household.[3]

The keystone component of GEMS is completion of a meticulously designed case control study undertaken to investigate the etiology of MSD; it is linked to a demographically monitored and defined population at each site, with surveillance activities and case enrollment proceeding at selected healthcare facilities (i.e., sentinel health centers). Of note, GEMS also happens to be one of the largest case control studies ever undertaken of an infectious disease syndrome. Over 3 years, GEMS accumulated ~467,000 child-years of observation of children in three age strata (0–11, 12–23, and 24–59 months of age) and enrolled ~9,500 cases of MSD and > 13,100 age- and sex-matched controls. Biostatistical methods used by GEMS biostatisticians and investigators allowed adjusted attributable fractions for the various pathogens associated with MSD to be calculated.[4]

As described in this supplement, before the initiation of the 3-year GEMS case control study, a baseline Healthcare Utilization and Attitudes Survey (HUAS) was performed at each of the seven GEMS sites. Caretakers of ~1,000 children < 60 months of age were queried with a detailed questionnaire to determine knowledge and attitudes about clinical signs of diarrheal illness and its treatment, occurrence of diarrhea among children within the 2 weeks preceding the HUAS household visit, and healthcare-seeking behavior. After the initial baseline HUAS, several additional abbreviated surveys (called HUAS-lite surveys) were conducted at the GEMS sites to detect variations in healthcare-seeking behavior over time.

To be able to extrapolate findings from surveillance and case enrollment at the sentinel health centers to the entire demographic surveillance population to estimate MSD incidence in a particular child age group, it was necessary to calculate an adjustment factor designated *r*. The HUAS-lite data from each site provide the basis for calculating the *r* value. By use of *r*, data from the sentinel health centers can be generalized to estimate the numbers of overall MSD cases and cases attributable to specific pathogens that occur among all children in each age group residing within the entire demographic surveillance population. The factor *r* also allows the calculation of overall MSD incidence and pathogen-specific incidences for the entire demographic surveillance population of children in each of the three age strata.

Although there have been multiple previous reports of the use of HUAS to ascertain care-seeking preferences in diverse geographic venues and socioeconomic levels and estimate the occurrence of diarrheal illness within 1–4 weeks before the survey visit,[5–11] several features make the GEMS HUAS and HUAS-lite strategies unique. First, a standardized common HUAS protocol was systematically followed at all seven sites, thereby allowing comparisons among sites. Second, GEMS investigators recognized that climatic variations (e.g., monsoons, other severe rainy seasons, and extreme heat), circumscribed seasonality in the circulation of certain pathogens (e.g., cholera season), temporary disruptions of civil society (general strikes, manifestations surrounding elections, and coup d'états), and force majeure (floods and earthquakes) can markedly modify healthcare-seeking behavior or alter the incidence of MSD and the transmission of specific pathogens. Accordingly, after the initial baseline HUAS, multiple additional sequential HUAS-lite surveys were systematically implemented at the GEMS sites to detect and quantify differences in healthcare-seeking behavior that might accrue from the above-mentioned events or influences. These repetitive HUAS surveys have added substantial precision to the critical *r* adjustment factors at each site, because they address the issue of potential variability of healthcare-seeking practices by season and from year to year.

In this supplement to *The American Journal of Tropical Medicine and Hygiene*, Nasrin and others[12] provide a composite overview of the HUAS and HUAS-lite data from all seven GEMS sites, drawing attention to both global similarities and heterogeneity. In addition, each of the seven GEMS field sites provides an individual detailed report of their HUAS data from Basse, Gambia[13]; Nyanza Province, Kenya[14]; Bamako, Mali[15]; Manhiça, Mozambique[16]; Mirzapur, Bangladesh[17]; Kolkata, India[18]; and Karachi, Pakistan.[19] Collectively, these HUAS data provide important context for understanding the GEMS project and offer insights on how mothers and caretakers of infants and young children in areas with high or

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moderate < 5-year-old child mortality perceive diarrheal illness in their child and what steps they take to deal with the illness.

When the comprehensive data from GEMS are fully analyzed, the public health community will have at their disposal detailed assessments of the burden and etiology of diarrheal disease in young children in sub-Saharan Africa and South Asia, the two global regions contributing ~80% of all diarrheal disease mortality. In turn, this information will help guide the implementation of existing interventions and the selection of targets for enhanced investment. The HUAS surveys described in this supplement remind readers that these field exercises comprised a critical initial step that helped guide the design and implementation of the GEMS case control study at each site, and they provided indispensable data to allow population-based incidence rates to be calculated.

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