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Health care seeking for Childhood Diarrhea in Developing Countries: Evidence from Seven Sites in Africa and Asia

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Abstract. We performed serial Health Care Utilization and Attitudes Surveys (HUASs) among caretakers of children ages 0–59 months randomly selected from demographically defined populations participating in the Global Enteric Multicenter Study (GEMS), a case-control study of moderate-to-severe diarrhea (MSD) in seven developing countries. The surveys aimed to estimate the proportion of children with MSD who would present to sentinel health centers (SHCs) where GEMS case recruitment would occur and provide a basis for adjusting disease incidence rates to include cases not seen at the SHCs. The proportion of children at each site reported to have had an incident episode of MSD during the 7 days preceding the survey ranged from 0.7% to 4.4% for infants (0–11 months of age), from 0.4% to 4.7% for toddlers (12–23 months of age), and from 0.3% to 2.4% for preschoolers (24–59 months of age). The proportion of MSD episodes at each site taken to an SHC within 7 days of diarrhea onset was 15–56%, 17–64%, and 7–33% in the three age strata, respectively. High cost of care and insufficient knowledge about danger signs were associated with lack of any care-seeking outside the home. Most children were not offered recommended fluids and continuing feeds at home. We have shown the utility of serial HUASs as a tool for optimizing operational and methodological issues related to the performance of a large case-control study and deriving population-based incidence rates of MSD. Moreover, the surveys suggest key targets for educational interventions that might improve the outcome of diarrheal diseases in low-resource settings.

INTRODUCTION

Despite the many studies undertaken during the past three decades to elucidate the epidemiology of childhood diarrhea in developing countries, the overall disease burden remains imprecise, largely because few estimates are available based on prospectively collected population-based data from well-designed studies conducted in the poorest regions of the world, where the incidence and mortality are highest.[1] Studies using health facility-based surveillance may underestimate disease burden when the proportion of cases not seeking care cannot be enumerated, such as in resource-poor settings where access to healthcare is impeded, or in communities where highly frequented healthcare providers are outside of the surveillance system. Moreover, the results can be distorted by confounding or interaction because of factors that can influence care-seeking behavior such as age, sex, socioeconomic status (SES), disease severity, and proximity of the household to the health center.[2–4] Community surveys of healthcare utilization practices have been performed as a means of adjusting facility-based estimates of disease burden for the proportion of episodes not captured at the health facility where surveillance is being conducted. However, many such surveys have had limitations. In most instances, a single survey was performed that did not account for seasonal differences in either disease incidence or factors that might affect access to health facilities, such as planting and harvest times and rainfall with flooding, which impedes local transport.[4] Additionally, the validity of the results generally depends on the ability of the caretaker to correctly ascertain the illness of interest and recall events that may have occurred many weeks earlier.[3,5] Attempts were rarely made to validate the parental perception of case-defining signs and symptoms against observations by trained health workers.

The Global Enteric Multicenter Study (GEMS) was implemented to characterize the burden and etiology of diarrheal disease among children 0–59 months of age living in developing countries. The central component of GEMS is a case-control study at four sites in sub-Saharan Africa (The Gambia, Kenya, Mali, and Mozambique) and three sites in South Asia (Bangladesh, India, and Pakistan) to assess the etiology of moderate-to-severe diarrhea (MSD) among children in three age strata (0–11, 12–23, and 24–59 months of age) as described in detail elsewhere.[6] The sampling frame at each site comprised a population participating in a Demographic Surveillance System (DSS), a longitudinal vital events registration program in which each household in a defined geographic area is visited two to three times per year to record births, deaths, pregnancies, and migrations. Cases were enrolled at health facilities termed sentinel health centers (SHCs) that served the DSS population at each site; matched control children without diarrhea were randomly selected from the DSS population and enrolled at home. Here, we describe Health Care Utilization and Attitudes Surveys (HUASs) among the DSS populations at each site as a platform for the conduct of the case-control study; these surveys provided a mechanism for collecting population-based data to inform operational aspects needed to establish and optimize performance of GEMS, characterizing the study population,

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assessing factors that might influence care-seeking behavior, and performing adjustments to incidence rates to account for the proportion of children with MSD who do not seek care at the SHC to derive population-based incidence rates based on results from the case-control study. To overcome limitations of previous surveys, the GEMS HUASs were repeated on several subsequent occasions to allow for seasonal and secular trends in healthcare use, required a limited recall period, and incorporated efforts to validate parental recall of diarrheal events.

METHODS

Study population. A baseline comprehensive HUAS was conducted at each site in 2007 before initiating the case-control study followed by a series of abbreviated surveys (designated HUAS-lite) that accompanied each DSS round during the second and third years of the case-control study from January 2009 to March 2011. For each survey, a sample of children, stratified by age (0–11, 12–23, and 24–59 months), was randomly selected from the most updated DSS database at each site, with the exception of Kenya, where all children 0–59 months of age belonging to the DSS were included in each HUAS-lite round. If the caretaker was not available, three attempts were made on different days to complete the interview. Children ages > 59 months as well as those children who could not be identified or were no longer living in the DSS area were considered ineligible to participate. If the interviewer found that a child fell outside of his/her expected age stratum but nonetheless remained ≤ 59 months of age, the survey was completed, and the child was assigned to the correct age stratum. The final age determination was calculated at analysis using interview date and birth date. Birth date was determined by examination of the child's birth certificate or vaccination card. If these documents were not available, then the caretaker was queried using a calendar of important community events that was designed for each site.

Interview. The HUAS clinical protocol, consent forms, case report forms, and other supporting documents were approved before initiation of the study by The Institutional Review Board (IRB) of the University of Maryland, Baltimore, MD, and the committees overseeing each site and their collaborating partners from other institutions. The HUAS-lite was performed as part of the DSS at each site and did not undergo separate ethical review.

The baseline HUAS was conducted after confirming the child's eligibility and obtaining informed written consent from the child's parent or primary caretaker. The caretaker (usually the mother) was interviewed at the child's home in the local language using a standardized questionnaire adapted from the World Health Organization (WHO) generic protocol for community-based survey on use of healthcare services for gastroenteritis in children.[7] The survey contained approximately 60 multiple choice questions that required about 30 minutes to complete (Supplemental Appendix 1). Caretakers were asked whether their child had diarrhea during the previous 2 weeks. If so, details about the illness were solicited, including clinical features (e.g., duration, blood in stool, vomiting, and signs and symptoms of dehydration), household management, care-seeking behaviors, and medical interventions. Caretakers were queried about the time and resources required to seek care and the nature of impediments that they might have faced in receiving care outside the home. Information about parental education, household size and structure, wealth status, and caretaker's knowledge, attitudes, and practices related to diarrheal disease were collected.

The abbreviated HUAS-lite interview determined whether the child had experienced diarrhea during the previous 2 weeks; if so, 21 questions were asked, with an estimated completion time of 5–10 minutes (Supplemental Appendix 2). Questions addressed the onset and nature of the diarrheal illness, home management with fluids and continued feeding, care-seeking behavior, hospitalization, and receipt of intravenous fluids.

Training and quality control. Before the baseline HUAS, interviewers and supervisors underwent onsite training for 4 days. An interviewer manual and a supervisor manual, translated as needed for each site, formed the basis of the training sessions. Ongoing quality control and retraining were performed by field supervisors and coordinating center investigators (D.N., T.H.F., and K.L.K.) using direct observation of interviewer competency and performing abbreviated reinterviews of caretakers to evaluate data quality and accuracy. A supervisor checked each questionnaire for completeness and consistency before submission to the database.

Definition of terms. We defined a household as a group of people who share a kitchen or cooking fire. Diarrhea was defined as three or more abnormally loose stools in a 24-hour period according to the caretaker. Diarrhea was considered acute if it lasted less than 8 days and persistent if it lasted at least 14 days. A new episode began after at least 7 diarrhea-free days. MSD was defined as acute diarrhea associated with at least one of the following observations by the caretaker: sunken eyes (more than usual), wrinkled skin (an indicator of decreased skin turgor recommended for maternal assessments),[8] visible blood in stool, hospital admission, or receipt of intravenous rehydration therapy. Care sought outside the home included a visit to any of the following providers: an unlicensed provider (traditional healer, unlicensed practitioner, or bought remedy from a shop), pharmacy, or a licensed provider working alone or at a health center.

Study objectives. The primary objectives of the baseline HUAS were to (1) estimate the proportion of children with acute diarrhea who sought care according to the type of provider and (2) compare the clinical and demographic characteristics of children who sought care from various types of providers and those children who did not. The primary objectives of the HUAS-lite were to (1) estimate the 1-week incidence of MSD and (2) estimate the proportion of children with MSD who were taken to an SHC within 7 days of diarrhea onset (to derive the MSD incidence rate in the entire DSS population). The HUAS-lite interviews were intentionally spread out over a DSS round to avoid capturing temporal anomalies and repeatedly conducted over a 2-year period to permit collection of more precise data on care-seeking behavior by averaging any seasonal and secular trends that occurred.

Data management and analysis. The completed case report forms were transmitted electronically to a Data Coordinating Center. The DataFax software system (Clinical DataFax Systems, Inc., Hamilton, Ontario, Canada) was used to build and manage the master database and aided in the electronic validation process as described elsewhere.[6,9] Statistical analyses were performed using SAS software (version 9.2).

The proportion of children from the HUAS-lite with MSD who were taken to an SHC within 7 days of diarrhea onset and thus, would be eligible for the case-control study was designated as r. Because a preliminary analysis did not find systematic variation of the r value over the course of 2 years at the sites, the data from all serial HUAS-lite rounds at each site were pooled to estimate r by a time-to-event analysis using the Kaplan–Meier method. Children with MSD who were not yet taken to an SHC within 7 days of diarrhea onset by the time of the interview were censored. At six sites, we calculated r for each age stratum using the site-specific HUAS-lite sampling weights for each enrolled child based on the number of children in each age–sex stratum in the DSS population; in Kenya, weights were unnecessary because all DSS children were included in each HUAS-lite round.[8] We compared the r values over time within each site and age stratum using a χ^2 test.[10]

The 1-week incidence risk of MSD was also estimated using the Kaplan–Meier method, with data from all HUAS-lite rounds pooled and sampling weights applied except for Kenya. To minimize recall bias, only children with MSD whose illness began on the day of the interview or on 1 of the 6 preceding days were counted as having an MSD event. Children with diarrhea that had not progressed to MSD and whose diarrhea began less than 1 week before the HUAS-lite interview were censored after the number of days that they had had diarrhea.

Demographic and clinical characteristics associated with care-seeking behavior for diarrhea were evaluated using logistic regression, applying the sampling weights to obtain results that relate to the DSS population. Variables with $P < 0.1$ in bivariate analysis were included in the multivariable models. Adjusted odds ratios (aORs) and the corresponding 95% confidence intervals (95% CIs) were calculated for variables found to be significantly ($P < 0.05$) associated with care-seeking behavior in these models. Each household's wealth status was determined by calculating a wealth index based on asset ownership (e.g., electricity, television, radio, phone, bike, car, boat, or refrigerator) and home construction (e.g., quality of flooring and number of sleeping rooms) using the methods of Filmer and Pritchett.[11] To assess the perceived importance to the caretakers of preventive measures, such as vaccines for diarrhea, we constructed a series of questions in the context of the Health Belief Model, which postulates that health-seeking behavior is influenced by a person's perception of a threat posed by a health problem and the value associated with actions aimed at reducing the threat.[12]

Sample size calculations. The sample size for each site's HUAS was based on the width of a two-sided 95% CI around r for observed $r = 0.5$ or 0.8 and total proportion of children with MSD of 0.03–0.4. The variance of r was approximated using a Taylor series expansion. Assuming a constant r for children 0–59 months of age, a total sample size of 999 would be sufficient for a 95% CI to have a total width, at most, of 0.20 if the total proportion of children with MSD were between 0.1 and 0.4. To allow for children on the randomization list who were not eligible for the HUAS because of migration or other factors, we oversampled (400 children aged 0–11 months and 370 children each aged 12–23 and 24–59 months), with the intent of enrolling 1,000 children at each site (333 per age stratum).

RESULTS

Description of the study sites. The study sites are diverse with respect to demographic and health indicators (Table 1). Two sites are located in urban centers (Mali and India), and four sites are in rural settings (The Gambia, Mozambique, Kenya, and Bangladesh), whereas the study villages in Pakistan, located on the coast approximately 20 km outside Karachi, are considered periurban. Human immunodeficiency virus (HIV) prevalence rates among young adults range from 6.3% to 11.5% in Kenya and Mozambique, respectively, and from 1% to 2% in Mali and The Gambia, respectively, to < 0.4% in the three Asian sites.[13] Under 5 years mortality ranks range from 2 in Mali to 61 in Bangladesh. All but India are ranked in the lowest stratum of the United Nations Human Development Index.[13,14] Mozambique and Mali are among the six countries in the world with the highest number of reported malaria-related deaths.[15]

Baseline HUAS: A platform for optimizing the performance of a case-control study of MSD among children 0–59 months. *Enrollment and demographic characteristics.* A total of 8,567 children were randomly selected from the DSS database at the seven sites combined; 837 children were deemed ineligible (57 had died, 744 could not be identified, 32 were aged > 59 months, and 4 were duplicates). Among the 7,734 eligible children, 161 caretakers refused to participate (2.1%), 174 caretakers could not be contacted (2.3%), and 144 caretakers completed interviews but were excluded from analysis, because either data were insufficient to calculate the child's age or the calculated age was > 59 months, leaving 7,259 analyzable interviews. Demographic features of the participants are shown in Table 1.

Diarrheal illnesses and care-seeking behavior. Overall, 15.4% of children (ranging from 4.3% in Mozambique to 31.1% in Pakistan) had at least 1 day with diarrhea during the 2 weeks that preceded the interview, 74.2% of which met the criteria for MSD (range from 24.6% in Mozambique to 87.0% in Pakistan). Criteria used to fulfill the definition of MSD are shown in Table 2. Among the children with MSD, 43.2% (range from 29.9% in Pakistan to 78.7% in India) fulfilled a single criterion, whereas 42.5% (range from 14.1% in Mozambique to 55.4% in Pakistan) fulfilled two criteria, and 14.3% (range from 1.2% in India to 33.3% in Mozambique) met three to five criteria. Most caretakers (81.3%) sought some care outside the home for the diarrheal illness (range from 67.0% in Mozambique to 87.9% in Bangladesh), but only 49.6% (range from 24.3% in Bangladesh to 75.9% in Pakistan) sought care from a licensed provider. As shown in Table 3, the first point of contact was most commonly the traditional healer in Mali (52.3%), the pharmacy in Bangladesh (44.3%) and Kenya (36.3%), health centers in Mozambique (84.3%) and The Gambia (49.6%), and licensed private practitioners in Pakistan (55.5%) and India (45.0%). The proportion who sought care at a GEMS SHC within 7 days of diarrhea onset was 24.3% for all children with diarrhea (range from 6.7% in India to 65.1% in Mozambique) and 30.5% for children with MSD (range from 6.7% in India to 86.1% in Mozambique).

Information useful for conduct of the case-control study. The HUASs provided data that informed the design and conduct of the case-control study, such as whether each site's DSS population was likely to support the sample size requirements for the case-control study. For example, the baseline survey in Mozambique was performed among a DSS population of 48,200 individuals, 17% of whom were 0–59 months of age. Only 16 children with MSD during the previous fortnight sought care during the first 7 days of illness at the GEMS SHC. To be better positioned to meet our target of enrolling

Table 1
Overview of sites

Variables	The Gambia	Mali	Mozambique	Kenya	India	Bangladesh	Pakistan
National health and demographic indicators							
Under 5 years mortality rate 2010	98	178	135	85	63	48	87
Adult HIV prevalence 2009 (%)[13]	2.0	1.0	11.5	6.3	0.3	< 0.1	0.1
HDI rank 2011[14]	168	175	184	143	134	146	145
Geography and climate at study site							
Setting	Rural	Urban	Rural	Rural	Urban	Rural	Periurban
DSS area (km^2)	1,084	16.0	500	500	10.5	374	10.1
Main seasons	Dry: November to April; wet: May to October	Cold dry: November to February; hot dry: March to May; wet: June to October	Cold dry: May to October; warm wet: November to April	Dry: June to September; December to February; wet: March to May and October to November	Cold dry: November to February; hot dry: March to May; wet: June to October	Cold dry: November to February; hot dry: March to May; wet: June to October	Dry: October to May; wet: June to September
Population of study site							
Total DSS population	136,793	204,664	90,000	135,000	195,313	238,463	78,858
No. (%) of children 0–59 months	21,445 (15.7)	31,903 (15.6)	17,100 (19.0)	20,853 (15.4)	12,054 (6.2)	24,874 (10.4)	11,894 (15.1)
Population per square kilometer	126	12,832	180	270	18,601	638	7,808
Main ethnicities	Mandinka, Fula, Sarahulleh	Bambara, Peulh, Malinké, Senoufo	Xangana	Luo	Bengali	Bangladeshi	Sindhi, Urdu, Bengali
Major occupation	Agriculture	In kind, small business	Agriculture	Small business, agriculture, fishing	Daily labor	Agriculture	Fishing
Healthcare facilities at study site							
Distance from an SHC (km)	< 1–15	3–5	1–5	< 1–2.2	4–10	< 1–24	< 1–5
Transport to an SHC	Donkey cart, bicycle	Motorbike, public transport, bush taxi	Private, walking	Walking, bicycle, public transport	Cycle rickshaw, auto rickshaw, taxi	Rickshaw, bus, walking	Walking, public transport
Payment for outpatient consultations at SHC	Free	$1–2	Free	Free	Free	Study children free	Free
Barriers to access SHC during study	Floods	Healthcare worker strikes	Healthcare worker strikes, floods	Riots	–	Floods	Floods
Characteristics of HUAS participants*							
Total no. analyzable interviews	1,012	1,000	1,059	1,043	1,058	1,128	959
No. (%) girls	468 (48.8)	508 (50.7)	512 (49.4)	501 (49.4)	511 (48.6)	567 (51.0)	485 (50.0)
Mean no. (%) caretakers completed primary school	53 (5.3)	169 (17.1)	343 (31.1)	549 (52.4)	685 (63.5)	708 (61.6)	129 (11.3)
No. (%) with household assets							
Electricity	321 (32.5)	740 (73.8)	210 (19.6)	16 (1.7)	1004 (95.3)	692 (61.5)	920 (95.8)
Television	253 (24.7)	682 (67.5)	194 (18.1)	64 (6.6)	745 (72.4)	452 (38.7)	511 (51.8)
Telephone	761 (74.2)	870 (86.4)	625 (59.6)	290 (28.5)	521 (49.7)	531 (46.1)	331 (33.0)
Refrigerator	110 (11.0)	224 (22.4)	104 (9.7)	1 (0.2)	178 (17.2)	62 (5.5)	134 (13.0)
Household mean (SD)							
Inhabitants	25.1 (19.1)	16.9 (13.4)	6.7 (3.3)	5.8 (2.0)	5.9 (2.7)	5.7 (2.8)	9.2 (5.4)
Sleeping rooms	9.0 (6.6)	5.2 (4.9)	2.3 (1.1)	1.7 (0.7)	1.5 (0.9)	2.3 (1.5)	2.2 (1.4)
Children ages < 5 years	5.0 (3.5)	3.3 (2.3)	1.9 (1.0)	2.0 (0.9)	1.4 (0.6)	1.4 (0.6)	2.2 (1.4)

HDI = Human Development Index.
*All percentages, means, and SDs are weighted according to age and sex distribution in the demographic surveillance system population at each site.

Table 2
Prevalence of any diarrhea and MSD during the 14 days preceding the baseline HUAS

	The Gambia	Mali	Mozambique	Kenya	India	Bangladesh	Pakistan
Number interviewed	1,012	1,000	1,059	1,043	1,058	1,128	959
N (%) any diarrhea	258 (23.2)	126 (11.8)	67 (4.3)	275 (22.3)	92 (7.9)	95 (7.4)	349 (31.1)
N (%) MSD	211 (19.1)	79 (7.3)	21 (1.1)	182 (15.2)	66 (6.1)	73 (5.5)	294 (27.1)
N (%) of any diarrhea with the following criteria for MSD							
Sunken eyes (more than normal)	191 (75.9)	68 (52.2)	16 (19.3)	162 (60.6)	64 (74.7)	63 (67.3)	263 (77.6)
Wrinkled skin	117 (45.7)	33 (23.5)	7 (7.2)	92 (36.2)	3 (3.6)	14 (13.0)	200 (59.1)
Dysentery	62 (26.0)	16 (12.1)	4 (5.3)	34 (16.3)	10 (13.0)	26 (24.2)	25 (9.1)
Received intravenous rehydration	3 (1.4)	5 (3.5)	8 (9.0)	18 (9.0)	1 (0.4)	0	37 (9.2)
Hospitalized	8 (3.0)	5 (3.5)	7 (8.1)	15 (6.6)	5 (3.1)	2 (1.3)	35 (9.0)

Any diarrhea was defined as the passage of three or more abnormally loose stools in a 24-hour period (according to the primary caretaker) that began within the previous 14 days. MSD was defined as an episode of any diarrhea associated with at least one of the following criteria: sunken eyes, wrinkled skin, visible blood in stool, hospital admission, or receipt of intravenous rehydration therapy. Proportion of children meeting each criterion for MSD may exceed 100%, because most children met more than one criterion. All percentages are weighted according to age and sex distribution in the demographic surveillance system population at each site.

24 episodes of MSD per fortnight into the case-control study, we increased the size of the DSS area and population (N = 90,000). The HUAS data on the specific health centers where care was sought allowed us to select additional SHCs that would maximize our ability to capture episodes of MSD (in turn, increasing the r used in our calculations of diarrheal incidence) and remove underused sites in Mozambique, The Gambia, India, and Kenya.

Validating the caretaker's assessment of MSD. Determination of the presence of MSD in the HUAS required the caretaker to report whether the child had signs of dehydration, including sunken eyes (more than usual) and wrinkled skin. We attempted to validate caretakers' perceptions of these case-defining signs during the case-control study by comparing each caretaker's determination with those determinations of the SHC clinicians.[6] Overall, there was high agreement for sunken eyes (κ statistic for interobserver agreement = 0.82, 95% CI = 0.80–0.83) and substantial agreement for wrinkled skin (κ = 0.64, 95% CI = 0.62–0.66); however, there was considerable variation in agreement across sites. Nonetheless, all values fell into the moderate agreement category or higher with the exception of sunken eyes in Kenya (κ = 0.19, 95% CI = 0.16–0.21) and wrinkled skin in Kenya (κ = 0.37, 95% CI = 0.34–0.39) and Bangladesh (κ = 0.25, 95% CI = 0.23–0.28).[16]

Features associated with seeking care at an SHC for MSD. To estimate the extent to which children with MSD who seek care at an SHC are representative of children with MSD in the DSS population, we compared characteristics of children reported to have MSD in the baseline HUAS according to whether they visited the SHC. We compared the following demographic factors: child's age, sex, education of caretaker, wealth index, household size and composition, mode of transport, and time to reach the health center; only two of these factors were different in a multivariate model. In India, older children were less often taken for care (aOR = 0.9, 95% CI = 0.84–0.94, $P < 0.0001$), and in Bangladesh, girls were taken to the SHC more often than boys (aOR = 5.7, 95% CI = 1.27–25.90, $P = 0.02$). When clinical presentations were compared, we found that children with MSD who had the following associated clinical signs were more likely to visit an SHC: lethargy in The Gambia (aOR = 2.7, 95% CI = 1.23–5.92, P = 0.01), longer duration of diarrhea in Mali (aOR = 1.28, 95% CI = 1.04–1.57, $P = 0.02$), vomiting in India (aOR = 6.4, 95% CI = 1.09–38.21), and rice water stools in Bangladesh (aOR = 8.0, 95% CI = 1.31–48.74, $P = 0.02$).

Management and care-seeking behavior for diarrheal episodes of any severity. The baseline HUAS also provided an opportunity to examine the management of diarrheal diseases in the community, regardless of severity. Overall, 20.3% of caretakers (range from 10.0% in Mali to 32.5% in Pakistan) gave their child oral rehydration solution (ORS), 31.8% (range from 8.5% in Mozambique to 63.7% in India) provided homemade fluids, 50.1% (range from 15.8% in Mozambique to 71.4% in Mali) offered more fluids than usual, and 41.2% (range from 15.7% in Kenya to 71.4% in Bangladesh) continued to offer the child food (Table 4). In contrast, many children were offered unproven therapies, including herbal medication (20.2%; range from 3.7% in Pakistan to 41.3% in Kenya) and leftover antibiotics (9.5%; range from 2.4% in Bangladesh to 16.0% in Kenya).

Children with any diarrhea taken to a licensed provider (including an SHC) were more likely to have fever (The Gambia: aOR = 3.0, 95% CI = 1.37–6.40; Mozambique: aOR = 5.5, 95% CI = 1.28–23.89; India: aOR = 3.9, 95% CI = 1.19–12.85; Pakistan: aOR = 2.5, 95% CI =1.27–4.76), lethargy (The Gambia: aOR = 2.3, 95% CI = 1.13–4.58; Pakistan: aOR = 2.7, 95% CI = 1.09–6.76), or sunken eyes (Mali: aOR = 4.6, 95% CI = 1.57–13.40; Kenya: aOR = 3.2, 95% CI = 1.74–5.83).

Table 3
First point of care sought for diarrhea by site

Type of provider (number with diarrhea)	The Gambia (N = 258)	Mali (N = 126)	Mozambique (N = 67)	Kenya (N = 275)	India (N = 92)	Bangladesh (N = 95)	Pakistan (N = 349)
No care	15.0	23.2	33.0	18.5	27.2	12.2	19.1
Pharmacy	8.3	8.7	11.7	36.3	2.4	44.3	1.2
Traditional healer	4.8	52.3	1.4	14.9	3.5	4.1	0.7
Unlicensed practitioner	13.9	3.4	0	3.0	32.3	11.0	7.6
Licensed practitioner	14.0	1.7	0	1.7	45.0	1.8	55.5
Bought remedy from market	9.1	8.7	2.5	7.2	1.1	25.6	4.7
Health center	49.6	25.1	84.3	35.1	15.8	13.2	29.8

All percentages are weighted according to age and sex distribution in the demographic surveillance system population at each site.

Table 4
Home and hospital management of childrens' diarrhea by site

Intervention	The Gambia	Mali	Mozambique	Kenya	India	Bangladesh	Pakistan
Management of diarrhea at home							
Number with diarrhea	N = 258	N = 126	N = 67	N = 275	N = 92	N = 95	N = 349
ORS	17.0	10.0	26.6	24.5	26.7	12.2	32.5
Homemade fluids	19.1	18.2	8.5	58.1	63.7	27.6	26.7
Herbal remedy	19.1	20.7	30.3	41.3	12.3	4.3	3.7
Zinc	0.4	0	5.9	0.7	0	0	0.2
Leftover antibiotics	9.8	11.1	3.6	16.0	3.8	2.4	5.0
Offered more than usual to drink	64.0	71.4	15.8	16.1	45.9	27.9	66.1
Offered usual/more than usual to eat	27.7	49.8	61.7	15.7	31.3	71.4	66.4
Management of diarrhea at the hospital or health center Number with diarrhea	N = 125	N = 33	N = 41	N = 123	N = 23	N = 21	N = 117
Intravenous fluids	2.8	13.8	13.9	17.7	2.7	0	18.8
ORS	54.9	46.9	74.0	72.6	63.2	75.8	46.2
Zinc	2.2	0	0	1.9	2.7	45.9	3.9
Antibiotics for dysentery	10.4	100.0	17.9	34.4	0	83.1	12.9

All percentages are weighted according to age and sex distribution in the demographic surveillance system population at each site.

However, other signs of more severe illness, such as indicators of dehydration (decreased urination, excessive thirst, dry mouth, and wrinkled skin), bloody stool, rice water stool, frequent (more than six) loose stools per day, and vomiting more than three times per day, were not associated with seeking licensed care.

In a multivariate modified Health Belief Model, caretakers who believed that there are effective ways to prevent diarrhea were more likely to seek licensed care. The preventive measures in which mothers expressed confidence included breastfeeding in Mali (aOR = 7.2, 95% CI = 1.5–34.0) and Kenya (aOR = 6.2, 95% CI = 1.2–32.1) and maintaining a good nutritional state in Bangladesh (aOR = 5.1, 95% CI = 1.1–22.7). In this same multivariate model, Kenyan caretakers who believed that ORS effectively treats diarrhea (aOR = 2.6, 95% CI = 1.2–5.7) were also more likely to seek licensed care. A higher wealth index in The Gambia (aOR = 1.5, 95% CI = 1.1–2.1) and higher educational attainment of the primary caretaker in India (aOR = 3.8, 95% CI = 1.2–12.0) were also associated with seeking care from licensed providers. Among children taken to a health center, 59.1% were given ORS (range from 46.2% in Pakistan to 75.8% in Bangladesh), and 4.1% were given zinc (range from 0% in Mali and Mozambique to 45.9% in Bangladesh) (Table 4).

Among caretakers who did not seek care from any provider outside the home, 52.0% said that they considered the illness to be mild and not warranting a visit to a care provider (range from 35.2% in Pakistan to 91.2% in India). The remaining 48.0% of caretakers (range from 8.7% in India to 64.8% in Pakistan) believed that care from outside was needed, although they did not seek it; these caretakers cited the high cost of treatment (46.4%; range from 0% in Mozambique to 100% in India) and travel (6.3%; range from 0% in India and Bangladesh to 13.1% in The Gambia) as the main reasons followed by the inability to take time off from work (9.2%) and local impediments (e.g., floods and social unrest; 8.7%). The main mode of transport to the health facility of choice was walking in the rural and periurban sites and commercial transport in urban sites. In the rural sites, 27.2% of caretakers needed more than 30 minutes to reach the health facility of choice (range from 20.1% in The Gambia to 34.8% in Bangladesh) compared with 15.6% of caretakers in urban sites (range from 1.8% in India to 20.7% in Mali) and 4.5% of caretakers in the periurban site.

A case for introducing vaccines or other measures to prevent the major causes of MSD. We assessed the likelihood that caretakers would accept new measures such as vaccines for prevention of diarrhea, in the context of the health belief model. Most caretakers (80%) said that they worried about their child contracting a diarrheal illness. Many said that they knew a child who had died from diarrhea, including an illness with rice water diarrhea (29.8%; range from 5% in Mozambique to 77.3% in Mali), simple watery diarrhea (21.8%; range from 0.7% in Bangladesh to 42.8% in Mali), and bloody diarrhea (22.9%; range from 1.6% in Mozambique to 63.4% in Mali). In general, caretakers considered bloody diarrhea as the most dangerous type (50.0%; range from 35.2% in Pakistan to 67.6% in The Gambia) and simple watery diarrhea as the least dangerous type (76.9%; range from 42.4% in Pakistan to 100% in India). Approximately one-half of the caretakers (52.7%) believed that the treatment of bloody diarrhea was the most costly (range from 28.0% in Pakistan to 73.2% in The Gambia), and 74.9% believed that treatment of simple watery diarrhea was the least costly (range from 35.3% in Pakistan to 97.8% in Bangladesh). When asked about the best way to prevent diarrheal diseases, the most common responses were clean food and water (51.1%; range from 33.1% in Mozambique to 92.6% in Bangladesh), hand washing (29.7%; range from 22.3% in Mali to 38.1% in India), and good nutrition (19.7%; range from 10.6% in Kenya to 34.6% in Mali). In general, caretakers had a positive attitude toward vaccines; 98.8% (range from 90.1% in Pakistan to 100% in Mali and Bangladesh) considered vaccines to be an effective strategy for protecting a child's health. Nearly all (98%) caretakers said they would like to use vaccines to prevent their children from contracting all types of diarrhea.

HUAS-lite as a platform for deriving population-based incidence rate of MSD by extrapolating data from the case-control study. *Study enrollment and demographic characteristics of participants in the HUAS-lite.* Each site conducted three to six HUAS-lite rounds over a 2-year period, with each round lasting approximately 3–6 months. Among the six sites that used random sampling, 33,697 children aged 0–59 months were randomly selected from the DSS database; 1,654 children

(20.4%) were considered ineligible (157 had died, 1,496 could not be located, and 1 was > 59 months of age). Among 32,043 eligible children, primary caretakers for 2,085 children could not be contacted after three attempts (6.5%), and 63 caretakers refused to participate (0.2%), resulting in a total of 29,895 analyzable interviews (range from 2,854 in Mozambique to 6,567 in Bangladesh). In Kenya, caretakers of all children 0–59 months in the DSS were targeted for interviews in each HUAS-lite round. Among 101,317 interviews attempted in Kenya during the 2-year period, 96,492 (95.2%) interviews were conducted. Thus, a total of 126,386 interviews was conducted at the seven sites over 2 years.

One-week incidence of diarrhea detected in the HUAS-lite rounds. We compared the number of episodes of all diarrhea and MSD that occurred during 1–7 days (week 1) versus 8–14 days (week 2) before the interview. Fewer diarrheal episodes were reported in week 2 compared with week 1, but the proportion of episodes considered to be MSD was higher in week 2. This result suggests that caretakers may have been selectively recalling the more severe episodes with increasing time and that episodes reported during week 1 provide a better estimate of episode occurrence. Consequently, we restricted our 1-week incidence calculation to those episodes that occurred during week 1.

The proportion of children 0–59 months who experienced a new episode of diarrhea during the 7 days before the interview (1-week incidence of diarrhea) ranged from 0.9% in Bangladesh to 10.2% in The Gambia, less than one-half of which met criteria for MSD (1-week incidence of MSD; range from 0.4% in Bangladesh to 3.2% in The Gambia). The 1-week incidence of MSD generally decreased with age and ranged from 0.7% in Bangladesh to 4.4% in Mali for infants (0–11 months), range from 0.4% in Bangladesh to 4.7% in The Gambia for toddlers (12–23 months), and range from 0.3% in Bangladesh to 2.4% in The Gambia for preschoolers (24–59 months) (Table 5).

Use of SHCs for MSD: Calculation of the r value. Caretakers of 75.1% of children with MSD sought care from outside home (range from 65.8% in Mozambique to 96.9% in Bangladesh), caretaker of 30.3% of children sought care from a hospital/health center (range from 19.3% in India to 58.6% in Mozambique), and caretaker of 24.8% of children (range from 13.4% in India to 58.6% in Mozambique) sought care from a GEMS SHC. The proportion of MSD cases taken to one of our designated SHCs within 7 days of onset of diarrhea (r) varied with age: range from 0.15 in India to 0.56 in Mozambique in infants, range from 0.17 in Mali to 0.64 in Mozambique in toddlers, and range from 0.07 in India to 0.33 in Mozambique in preschool children (Table 6). When r values were compared over time within each site and age stratum using applied χ^2 tests for homogeneity,[10] only 1 of these 21 tests (The Gambia, age 0–11 months) showed significant differences among the r values at the 5% significance level. This finding supports the calculation of one r value for the study period.

DISCUSSION

We have shown the use of a single, detailed, baseline HUAS followed by repeated abbreviated HUAS-lite interviews at seven sites in sub-Saharan Africa and South Asia as a means for optimizing operational and methodological issues related to the performance of a large case-control study. We attempted to overcome the limitations of previous surveys by conducting serial interviews over a 2-year period to account for seasonal and secular influences, limiting the recall period to 1 week for data used to calculate the r value, and trying to validate the diagnostic criteria reported by caretakers against the clinician's diagnosis. Our findings allowed us to implement targeted strategies at selected sites to increase case enrollment. Most importantly, by providing population-based data on use of the SHC for MSD, the HUAS-lite provided a means for deriving incidence rates of MSD based on cases seen at the SHC during the GEMS case-control study that are applicable to the entire cohort of children 0–59 months of age belonging to the DSS population.

There are simple, inexpensive interventions that can be lifesaving if used appropriately in children with diarrheal illness. These interventions include oral rehydration (or intravenous rehydration if dehydration is severe), continued feeding, zinc, selective use of antibiotics, and appropriate case management of children with nutritional issues, suspected HIV infection, or danger signs as defined by the WHO. We found pervasive, systemic weaknesses in implementing these interventions at our sites, beginning with management at home. Despite longstanding WHO recommendations, only 20.3% of children from the seven sites were given ORS at home, and only one-half were offered increased fluids, whereas 58.8% of caretakers offered less than usual to eat and 23.6% offered less than usual to drink. Moreover, the use of ineffective and potentially deleterious remedies, such as herbal medicines and

TABLE 5

One-week incidence of any diarrhea and MSD as determined by serial HUAS-lite interviews over a 2-year period

Age stratum (no. enrolled)	The Gambia (N = 6,304)	Mali (N = 3,016)	Mozambique (N = 2,854)	Kenya (N = 96,492)	India (N = 6,077)	Bangladesh (N = 6,567)	Pakistan (N = 5,076)
One-week incidence of diarrhea by age stratum in months							
0–11	14.1	12.7	5.0	3.3	5.5	1.2	11.0
12–23	14.8	8.9	4.9	3.9	3.1	1.3	11.3
24–59	7.4	4.2	1.6	1.5	1.9	0.6	6.2
0–59	10.2	6.8	3.0	2.3	2.8	0.9	8.0
One-week incidence of MSD diarrhea by age stratum in months							
0–11	4.1	4.4	1.4	1.4	4.0	0.7	2.0
12–23	4.7	3.3	2.3	2.0	2.5	0.4	2.6
24–59	2.4	1.7	0.7	0.7	1.2	0.3	1.8
0–59	3.2	2.4	1.2	1.1	2.0	0.4	1.9

All percentages are weighted according to age and sex distribution in the demographic surveillance system population at each site, except in Kenya.

Table 6
SHC visit within 7 days of onset of MSD (r value): results from serial HUAS-lite interviews over 2 years

	Mean proportion with MSD who sought care at an SHC within 1 week of illness onset, r value (95% CI)						
Age stratum in months	The Gambia (N = 612)	Mali (N = 240)	Mozambique (N = 103)	Kenya (N = 3,262)	India (N = 340)	Bangladesh (N = 92)	Pakistan (N = 199)
0–11	0.35 (0.28, 0.42)	0.22 (0.16, 0.30)	0.56 (0.39, 0.76)	0.20 (0.18, 0.23)	0.15 (0.10, 0.21)	0.39 (0.24, 0.58)	0.25 (0.16, 0.37)
12–23	0.26 (0.21, 0.32)	0.17 (0.10, 0.28)	0.64 (0.45, 0.81)	0.19 (0.17, 0.21)	0.22 (0.15, 0.31)	0.23 (0.13, 0.39)	0.21 (0.13, 0.33)
24–59	0.22 (0.16, 0.30)	0.09 (0.03, 0.28)	0.33 (0.11, 0.75)	0.16 (0.14, 0.18)	0.07 (0.03, 0.19)	0.21 (0.06, 0.57)	0.30 (0.17, 0.50)

All proportions are weighted according to age and sex distribution in the demographic surveillance system population at each site, except in Kenya.

administration of antibiotics without a prescription, was prevalent, which is consistent with earlier studies.[17]

The caretakers' ability to identify danger signs that should trigger appropriate care-seeking behavior is an important component of case management of childhood illness in developing countries. In our study, a limited number of signs (fever, lethargy, and sunken eyes) were independently associated with seeking care from a licensed provider at several sites; however, many children with these signs and other danger signs were not taken for licensed care. Our findings are consistent with other published results that show that caregivers often do not seek medical care, even when they recognize that an illness is life-threatening.[18] The propensity to seek care from licensed providers in our study seemed to be more a function of the site than specific features of the illness, with high levels (> 80%) reported in Pakistan and Mozambique and generally low levels (< 50%) reported in Mali and Bangladesh. This observation supports the notion that efforts to enhance appropriate healthcare-seeking behavior must be adapted to the local context and cannot simply focus on improving caretakers' recognition of danger signs in childhood diarrhea. Experience suggests that interventions are likely to be more effective if (1) a limited number of sensitive and specific criteria for triggering care-seeking behavior from a licensed provider can be identified, (2) beliefs about the efficacy of traditional medicines for various conditions are understood, (3) syndromes are described in the context of local terms, (4) health education is integrated with other disease-control strategies, and (5) caretakers are informed that interventions are available that can effectively prevent diarrheal disease.[18–20]

Although most caretakers sought some type of care for their child's diarrheal illness, a substantial number did not choose a licensed health provider as their first point of contact, potentially delaying opportunities for optimal intervention. Care-seeking behavior in resource-poor settings has been described as a hierarchical process, where caretakers first seek less-expensive alternatives before visiting a formal or licensed care provider.[21] As in other studies in low-resource settings, caretakers in our study cited the cost of treatment as the major deterrent to care-seeking behavior outside the home.[22,23] We have previously estimated the direct and indirect costs of a diarrheal episode at our sites and the considerable burden that these costs can place on poorer households.[24,25] Provision of free consultations (clinicians' fees) does not fully address this issue, because more than 75% of direct costs comes from the purchase of medications. Other factors influencing care-seeking that were explored but found to be of lesser importance include distance to the facility, impediments related to weather or social unrest, dissatisfaction with the quality of care, lack of supervision for other children at home, and lack of transport. Mali, the country with the second highest mortality of under 5-year-old children worldwide in 2010,[13] was the only GEMS African site where caretakers paid a fee for accessing services at a government health center (Table 1). As a result, the direct household expenditures for consultation fees and medications for diarrheal episode treated by a licensed provider were five to seven times higher in Mali than in the two other African sites and approximately threefold higher than treatment by a traditional healer.[25] Thus, it is notable that traditional healers were the most common first point of contact, which is consistent with previous observations,[19] whereas the use of licensed care by Malian caretakers was the lowest among the African sites in GEMS.

The caretakers' reports of case management in the health center, if corroborated by prospective observations during the case-control study, suggest a pressing need for continuing education and motivation of practitioners to follow the Integrated Management of Childhood Illness (IMCI) guidelines.[26,27] Disappointingly, among the children who were treated at a health center, only 59% of caretakers reported that their child received ORS. Treatment of diarrheal illnesses with zinc has been estimated to prevent 4% of all under 5 years deaths,[28] but its use was negligible at the GEMS sites, even when a child was treated in a health center. Programmatic introduction of zinc has been slow in many developing countries; however, even in Bangladesh, where zinc was nationally introduced in 2006, only 45.9% of the caretakers reported receiving zinc from a health center. Finally, our findings suggest that if vaccines against the major etiologic agents of diarrhea became available, caretakers, in principle, would be accepting of their use.

The primary limitation of our study is related to its reliance on the ability of caretakers to recall and accurately ascertain whether their child had an episode of MSD during the preceding week as well as the healthcare and other interventions that the child received. We chose a 7-day period for calculating incidence in the HUAS-lite because our data indicated that recall could be maximized by including episodes that began during the preceding week, which is supported by other studies showing that underreporting of up to 45% of diarrheal episodes can be seen when recall extends beyond 7 days.[29,30] In fact, other studies have found that recall beyond 48 hours underestimates diarrheal disease incidence.[31] Even with this 7-day limit, caretakers may selectively recall episodes that are more severe, which could bias estimates of the proportion of MSD among total diarrhea episodes. There is a possibility of ascertainment bias, even though we found that overall agreement was good for certain clinical signs used in the MSD case definition (sunken eyes and wrinkled skin),[6] because there was marked variation among the sites, with both over- and underdiagnosis by caretakers compared with clinicians. For logistical reasons, we linked the HUAS-lite interviews with the DSS rounds, which do not necessarily correspond with seasons, thus limiting our ability to assess seasonal variations in healthcare use. We also recognize limitations in the ability of the HUAS-lite to provide high values of r, which will be desirable for estimating diarrheal incidence.[7] Approximately 25% of children with MSD sought care from one of the GEMS SHCs, and there was a large variation among the sites (from 13.5% in India to 58.6% in Mozambique). We take into account the variability of *r* in our analyses of case-control data.

In sum, the HUAS and HUAS-lite interviews proved to be useful tools that served many purposes in the preparation and conduct of the GEMS population-based case-control study, including characterizing the catchment population's demography as well as healthcare-seeking attitudes and practices, assessing bias, and enhancing the ability to capture cases. In addition, the surveys provided important information that can be harnessed to design targeted interventions aimed at improving the case management of diarrhea in the home and healthcare facilities and building an introduction case for anticipated vaccines. Information from the surveys can be used to strengthen uptake of existing interventions and to guide implementation and facilitate uptake of future interventions.

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