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Cost estimates of diarrhea hospitalizations among children <5 years old in Zimbabwe

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Abstract

Introduction: Diarrhoea is a leading killer of children <5 years old, accounting for 480,000 deaths in 2017. Zimbabwe introduced Rotarix into its vaccination program in 2014. In this evaluation, we estimate direct medical, direct non-medical, and indirect costs attributable to a diarrhea hospitalization in Zimbabwe after rotavirus vaccine introduction.

Methods: Children <5 years old admitted to Harare Central Hospital from June 2018 to April 2019 with acute watery diarrhea were eligible for this evaluation. A 3-part structured questionnaire was used to collect data by interview from the child's family and by review of the medical record. A stool specimen was also collected and tested for rotavirus. Direct medical costs were the sum of medications, consumables, diagnostic tests, and service delivery costs. Direct non-medical costs were the sum of transportation, meals and lodging for caregivers. Indirect costs are the lost income for household members.

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Results: A total of 202 children were enrolled with a median age of 12 months (IQR: 7–21) and 48 (24%) had malnutrition. Children were sick for a median of 2 days and most had received outpatient medical care prior to admission. The median monthly household income was higher for well-nourished children compared to malnourished children (p<0.001). The median total cost of a diarrhea illness resulting in hospitalization was $293.74 (IQR: 188.42, 427.89). Direct medical costs, with a median of $218.81 $251.74 (IQR: 155.42, 390.96), comprised the majority of the total cost. Among children who tested positive for rotavirus, the median total illness cost was $243.78 (IQR: 160.92, 323.84). The median direct medical costs were higher for malnourished than well-nourished children (p<0.001)

Conclusion: Direct medical costs are the primary determinant of diarrhea illness costs in Zimbabwe. The descriptive findings from this evaluation are an important first step in calculating the cost effectiveness of rotavirus vaccine.

Keywords

Rotavirus; diarrhea; economic burden; cost; Zimbabwe

Introduction

Diarrhea caused an estimated 480,000 deaths among children <5 years old worldwide in 2017 [1] and rotavirus remains the leading cause of diarrhea deaths, attributed to 39% in Sub-Saharan Africa [2]. In response to this disease burden, the World Health Organization (WHO) recommended that all countries introduce rotavirus vaccine [3]. Zimbabwe introduced Rotarix, a monovalent human strain rotavirus vaccine, into its routine vaccination program in 2014 with financial support from Gavi, the Vaccine Alliance, and recommended vaccination for all infants at 6 and 10 weeks of age [4]. In the first 2 years after rotavirus vaccine introduction in Zimbabwe, there was a 41% decline in rotavirus-positive specimens among hospitalized children <1 year old [4]. Overall, Rotarix was found to be 71% effective against rotavirus hospitalizations in well-nourished infants, but only 45% effective in infants with stunting [5].

Several sub-Saharan African countries have calculated the direct medical costs of diarrhea hospitalizations to assess the cost-effectiveness of rotavirus vaccines. Published estimates range from just over USD$40 in Rwanda and Uganda to >USD$500 in South Africa [6–8]. Medical systems vary between countries, and therefore the overall costs and financial burden on governments and families vary. Additionally, few of the earlier studies on the costs of diarrhea illnesses captured non-medical and indirect costs. However, rotavirus vaccines are projected to be very cost-effective in countries eligible for Gavi support [9, 10].

Harare Central Hospital is a large, public hospital in the capital city of Zimbabwe with 246 pediatric beds. The government of Zimbabwe subsidizes treatment for children <5 years old, however the children's families are responsible for the costs of some diagnostic tests and medications unavailable through the public system.

In this evaluation, we estimate economic burden attributable to diarrhea hospitalizations among children <5 years old in Zimbabwe admitted to Harare Central Hospital by calculating the direct medical and non-medical costs as well as lost household income. These data are intended to inform decision makers and can be used in modelling of cost-effectiveness of the national rotavirus vaccine program with the available impact and vaccine effectiveness data from Zimbabwe.

Methods

Data collection

Children <5 years old admitted to Harare Central Hospital from June 2018 to April 2019 with acute watery diarrhea and enrolled in routine diarrhea surveillance were eligible to be included in this evaluation. Acute watery diarrhea was defined as 3 or more loose, non-bloody stools in a 24-hour period lasting less than 7 days [4]. As these children were also eligible for enrollment in routine rotavirus surveillance, a stool specimen was collected within 48 hours of admission and tested at the Zimbabwe National Virology Laboratory for group A rotavirus by enzyme immunosorbent assay (EIA) (ProSpecT, Oxoid, UK).

Caregivers were given detailed information about the project objectives by project staff and written informed consent was obtained prior to enrollment. Data collection included a 3-part structured questionnaire. Part 1 was an interview with the caregiver during the child’s hospitalization and included child and household demographics, type and cost of care received for this illness prior to hospitalization, and type and cost of transportation to the hospital. Part 2 was information abstracted from the child’s medical record at discharge and included comorbidities, duration of the hospital stay, medications received, diagnostic tests conducted, and outcome. Part 3 was an interview conducted with the caregiver over the phone about 2 weeks after discharge. This interview included information recalled by the parent about costs paid by the family for the treatment and medical care, missed work during the child’s illness, and any follow up care costs. Costs of medicines, diagnostic tests, and other consumables during the hospitalizations were abstracted from itemized receipts in each child’s medical records.

Inpatient service delivery estimates, including staff time, capital, and food costs, were calculated by WHO-CHOICE [11, 12]. In the base case analysis, we used the median tertiary care service delivery cost from Zimbabwe from 2005 ($30.77; $39.64 in 2019); confidence limits were not available for that estimate. For the sensitivity analysis, we used the modelled tertiary care service delivery confidence limits from the African Region E countries in 2010 (estimate: $28.38; 95%CI: 11.75, 64.06; $32.77, 95%CI: 13.57, 73.96 in 2019) as Zimbabwe-specific estimates were not available for 2010 [11, 12]. In the WHO sub-regional country groupings, African Region E includes Zimbabwe and 19 other sub-Saharan African countries with high child and very high adult mortality [13]. We adjusted the 2005 and 2010 service delivery estimates to 2019 dollars. Since 2009, Zimbabwe had a multicurrency system that included US dollars and in 2016 local bond notes and coins were introduced to alleviate hard currency shortages. In October 2018, a 2% tax on bank transactions was implemented, further straining the transacting public. In February 2019, the bond notes and coins were absorbed into Zimbabwe’s new currency, the RTGS dollar, and in June 2019 it became the only legal currency in Zimbabwe. During June 2018 to April 2019, we collected all economic data in US dollars and did not attempt to adjust them for changing economic conditions.

Analysis

We estimated that we would need to enroll 218 children to have 10% precision and a coefficient of variation of 1 and 500 total diarrhea cases, according to the WHO guidelines for estimate the economic burden of diarrheal disease [14].

Direct medical costs are the sum of costs associated with the bed, medications, diagnostic tests, and outpatient visits collected by the survey and inpatient service delivery from WHO-CHOICE [14]. Direct non-medical costs are the sum of transportation to and from the hospital and meals and lodging for caregivers while the child was hospitalized [14]. Finally, indirect costs are productivity and time of work missed in the form of the income lost by caregivers due to the hospitalization of a sick child [14]. Selected unit prices for medications and tests are presented in supplementary table 1.

In this descriptive analysis, we estimated the medians and interquartile ranges (IQR) for the absolute total, direct medical, direct non-medical, and indirect costs of the illness as well as the number of days the child was ill prior to being hospitalized, days hospitalized, diagnostic tests and medications ordered during the hospitalization. We also estimated the medians and IQR of the percentage of the direct medical costs due to medications, diagnostic tests, and service delivery costs and the percentage of the total costs paid by the child’s family. Some analyses were stratified by the nutritional status of the child and rotavirus EIA test results. Children were considered malnourished if there was a documented diagnosis of malnutrition, using any definition of malnutrition, in the medical record for this hospitalization. Statistical significance of proportions between malnourished and well-nourished children was tested with chi-square tests and medians were tested using Wilcoxon scores.

Finally, we also included 3 alternative scenarios. We varied the service delivery costs to the lower and upper 95% confidence intervals of the 2010 AFRO E WHO-CHOICE estimates, we present total illness costs for 3 times periods: June- September 2018, October 2018-January 2019, and February- April 2019, corresponding to inflection points in Zimbabwe’s economic policy during data collection, and we assumed income lost due to informal employment was underreported in our data and supplemented with a report from the International Labour Organization (ILO) [15]. Using data on informal employment in Zimbabwe, we assumed all households that reported $0 of lost wages due to the hospitalization participate in informal employment and underreported their lost income due to the case-patient’s hospitalization. We randomly assigned households to monthly income strata based on the distribution in the ILO report and calculated the total illness cost assuming the highest and lowest value in each strata by dividing the monthly income by 30.4 and multiplying the quotient by the number of days the child was hospitalized twice: for the highest and lowest value in the strata [16]. All costs are reported in US dollars (USD or $). Analyses were performed using SAS v9.4 and R v3.5.2.

This project was determined to be public health non-research by the US Centers for Disease Control and Prevention and the Ministry of Health in Zimbabwe and granted exception by WHO Ethical Review committee (ERC).

Results

A total of 202 children were enrolled and included in this analysis. The median age was 12 months (IQR: 7–21) and 45% (n=91) were female (Table 1). Overall, the median monthly household income was $350 (IQR: 200, 600). There was a median of 5 people (IQR: 4, 5) per household with a median of 1 child <5 years old (IQR: 1, 2). The majority used a borehole (59%, n=119) as their household water source and most had a flush toilet (82%, n=161) as their household toilet. Only 5% (n=8) had health insurance. Of the 202 children, 48 (24%) were diagnosed with malnutrition in addition to acute watery diarrhea during this hospitalization. Among malnourished children, 58% (n=28) were female and the median age was 20 months (IQR: 12, 25); among well-nourished children, 41% (n=63) were female (p=0.041) and the median age was 10 months (IQR: 5, 16) (p<0.001). The median monthly household income for children who were malnourished was $250 (IQR: 200, 300) and was $415 (IQR: 250, 750) among children who were well-nourished (p<0.001).

Prior to the hospital admission, the children had been sick for a median of 2 days (IQR: 2, 3) and most (82%, n=166) had received outpatient medical care (Table 2). Of those, health facility (87%, n=145) and pharmacy (26%, n=43) were the most common places for pre-hospital care. Aside from malnutrition, 30% (n=60) were diagnosed with a comorbidity during this hospitalization, the majority with pneumonia (63%, n=38). We found that well-nourished and malnourished had similar rates of other comorbidities (p=0.631). Overall, 50% (n=101) of the children received oral rehydration solution (ORS) alone and an additional 48% (n=97) received IV rehydration in addition to ORS during the hospitalization. Twenty-three percent (n=46) of the children were positive for rotavirus; 30% (n=45) of the well-nourished children and 2% (n=1) of the malnourished children tested positive (p<0.001). Of the malnourished children, 8% (n=4) died; of the well-nourished children, 1% (n=2) died (p=0.013). After discharge, 14% (n=29) of children received additional medical care for their illness.

The median total cost of a diarrhea illness resulting in hospitalization was $293.74 (IQR: 188.42, 427.89) (Figure 1). Direct medical costs, with a median of $251.74 (IQR: 155.42, 390.96), made up the majority of total cost; the median percent of total costs due to direct medical costs was 90% (IQR: 84, 94). The median direct non-medical were $22.50 (IQR: 15.00, 32.00). Caregivers of 23% (n=45) of the children reported lost income due to the illness. Of those who reported no lost income, 80% (n=119) stated they would have been doing housework, 62% (n=93) would have been caring for children, and 20% (n=30) would have been working while the child was hospitalized. We did not assign an opportunity cost to these activities in the main analysis and do not have further information about their work. The cost of the illness paid by the families represented a median of 12% (IQR: 7, 21) of the total calculated illness costs. Among children who tested positive for rotavirus, the median total illness costs were $243.78 (IQR: 160.92, 323.84) and direct medical costs were $203.56 (IQR: 135.92, 275.56).

The median direct medical costs were higher among malnourished children ($401.48, IQR: 304.27, 461.53) than well-nourished children ($207.92, IQR: 137.92, 313.92) (p<0.001) (Figure 2). Though the median number of medications ordered during the hospitalization was 3 (IQR: 3, 5) for both groups, malnourished children were hospitalized for a median 6 days (IQR: 5, 8) and had 10 diagnostic tests ordered (IQR: 9, 15). Well-nourished children were hospitalized for a median 2 days (IQR: 1–4) and had 6 diagnostic tests ordered (IQR: 0, 9). Among well-nourished children, there was no statistically significant difference in direct medical costs between rotavirus positive and negative children (p=0.338). Only one malnourished child was positive for rotavirus.

We considered 3 alternative scenarios. In looking at variation by time period, 9% (n=7) of children admitted June-September 2018, 24% (n=21) of children admitted October 2018-January 2019, and 49% (n=20) of children admitted February- April 2019 were diagnosed with malnutrition. The median direct medical costs for malnourished children were $408.76 (IQR: 355.48, 419.12), $394.12 (IQR: 296.56, 498.40), and $402.44 (IQR: 320.34, 476.08) during the three time periods, respectively. The median direct medical costs for well-nourished children were $156.92 (IQR: 123.28, 237.56), $264.56 (IQR: 177.28, 381.48), and $203.56 (IQR: 129.92, 378.48), respectively. Among well-nourished children, the median number of inpatient days was 2 (IQR: 1, 3), 3 (IQR: 2–6), and 3 (IQR: 1–7) during the 3 time periods, respectively. We also varied the bed costs to the 95% confidence limits of $13.57 and $73.96. Under the lowest scenario, the overall median direct medical costs would be $144.00 (IQR: 81.71, 210.56); under the highest scenario, the overall median direct medical costs would be $376.34 (IQR: 253.88, 629.68). Finally, we varied the amount of lost informal income for those reporting no lost income. Assuming the lowest monthly earnings in each strata, indirect costs for all study participants were a median of $6.64 (IQR: 0.16, 25.00) and total hospitalization costs were a median of $299.84 (IQR: 191.49, 440.85). Assuming the highest monthly earning in each strata, indirect costs for all study participants were a median of $19.73 (IQR: 9.87, 39.47) and total hospitalization costs were a median of $306.21 (IQR: 192.78, 457.63).

Discussion

In this description of the cost of acute watery diarrhea requiring hospitalization among children <5 years of age in Zimbabwe, we found that the median total cost of the illness was nearly $300. In most cases, almost all of the cost was attributable to direct medical costs from outpatient visits and the inpatient stay. This proportion is much higher than findings from Rwanda, where less than half of total costs were attributed to direct medical costs [6]. Overall, caregivers reported the children's households were responsible for a relatively low proportion of the total cost of the illness, including direct medical costs. The high proportion due to direct medical costs in our study may be specific to the data collection period because unemployment was estimated to be ~65% in 2019 by the Zimbabwe National Statistics Agency [17] and, in our population, more than 75% of the children's households reported no lost income due to the illness; in a sensitivity analysis assuming underreporting, we found minimal impact on the overall illness costs, though lost income likely is significant to individual families. We found that the government of Zimbabwe is financially responsible for a large proportion of the hospitalization, which is an important consideration for decision makers evaluating the rotavirus vaccination program.

There were important differences in the demographics, care, and direct medical costs by nutrition status in our evaluation population. In general, malnourished children were older, had lower socio-economic status, had longer inpatient stays, and had a higher median number of diagnostic tests as compared to well-nourished children. Correspondingly, the median direct medical costs for malnourished children were nearly double those of well-nourished children. Vaccine effectiveness findings from Zimbabwe and other countries in the region suggest that rotavirus vaccine may not perform as well in malnourished children as well-nourished children [5, 18, 19]. In this evaluation, we found that nearly all of the rotavirus positive children were well-nourished. Therefore, while rotavirus vaccine has had a substantial impact on rotavirus hospitalizations in Zimbabwe, rotavirus vaccination may not be preventing many of the more expensive hospitalizations among children with malnutrition admitted with acute watery diarrhea.

The cost of treating a child with both malnutrition and acute watery diarrhea was consistent across the enrollment period, though the proportion of children diagnosed with malnutrition doubled from June- September 2018 to October 2018- January 2019, and in February- April 2019. However, we found some variation in the direct medical costs for well-nourished children with acute watery diarrhea. The direct medical costs for well-nourished children were 71% higher in October 2018- January 2019 compared to June- September 2018; length of stay was also higher during the second time period. In addition to the economic policy changes during the enrollment period, there was a cholera outbreak that impacted Harare from September to December 2018. We did not find a statistically significant difference between rotavirus positive and rotavirus negative well-nourished children. As this is a cross sectional evaluation and we did not specifically include questions related to non-rotavirus diarrhea outbreaks, we are unable to determine what impact the cholera outbreak may have had on our findings. These differences may also represent normal seasonal variation, as higher incidence of rotavirus has been reported in Zimbabwe during the winter months before and after rotavirus vaccine introduction [4].

This evaluation has several important limitations. Data were collected from one tertiary care hospital located in Harare and may not be representative of other hospitals in Zimbabwe. Additionally, these data do not allow us to estimate to costs for outpatient care of children with acute watery diarrhea who are not admitted to hospital for their illness. Second, we relied on caregiver recall for information about the child’s illness and care prior to and after hospitalization as well as non-medical costs, which may have introduced bias. Third, we were limited by the availability of modeled service delivery estimates specific to Zimbabwe. Though the Zimbabwe-specific estimate was from 2005, it was comparable to the regional estimate from 2010. Better understanding of the contemporary service delivery estimate at Harare Central would improve the specificity of our findings. Finally, the economic instability, hyperinflation, and changes in currency in Zimbabwe during the enrollment period may have impacted caregiver responses and perceptions. While we tried to account for bias in reporting, especially in indirect costs, we are unable to fully account for possible underreporting of informal income and did not assign opportunity costs to other activities such as housework.

The descriptive findings from this evaluation are an important first step in calculating the cost effectiveness of rotavirus vaccine in Zimbabwe for local decision makers. Our findings show that direct medical costs, and especially length of stay, are the primary determinant of acute watery diarrhea illness costs in Zimbabwe. Further research is needed to understand the implications of differences in costs between malnourished and well-nourished children on the cost-effectiveness of rotavirus vaccine.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements:

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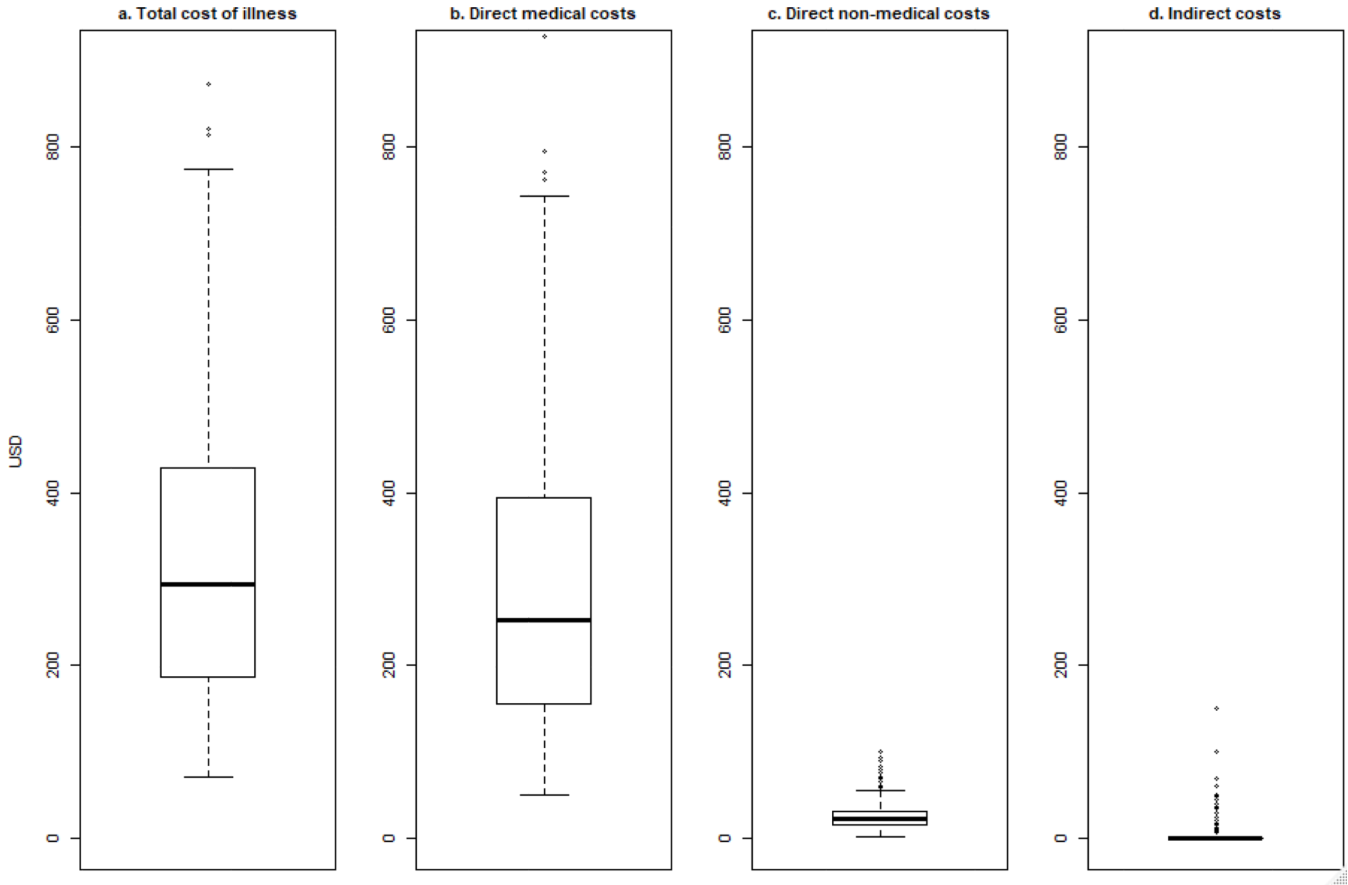

Figure 1.
Median total, direct medical, direct non-medical, and indirect costs of illness due to acute watery diarrhea among children <5 hospitalized at Harare Central Hospital, Zimbabwe. The dark central bar in each figure represents the median, the box represents the interquartile range, and the dotted lines represent the range. Outliers are shown by the small circles.

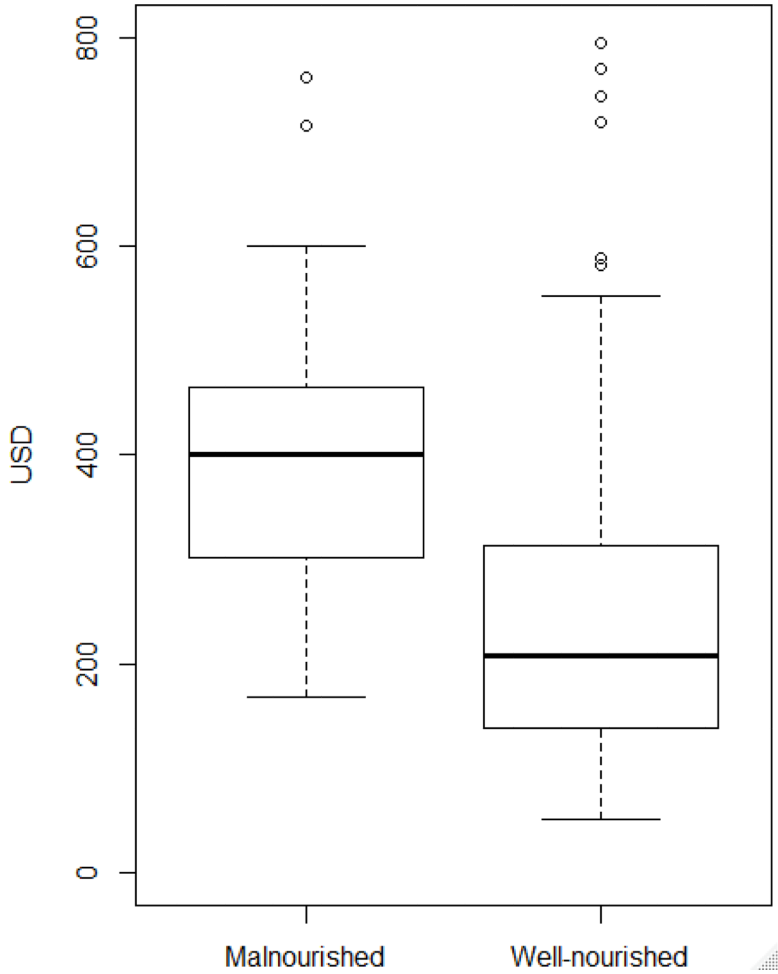

Figure 2.

Median direct medical costs of illness due to acute watery diarrhea among children <5 hospitalized at Harare Central Hospital, Zimbabwe by nutrition status. The dark central bar represents the median, the box represents the interquartile range, and the dotted lines represent the range. Outliers are shown by the small circles.

Table 1.

Characteristics of patients

	Total (n=202)		Malnourished[1] (n=48)		Well-nourished[1] (n=153)		
	n	%	n	%	n	%	p-value
Female[2]	91	45	28	58	63	41	0.041
Age in months (median, IQR)	12	7–21	20	12–25	10	5–16	<0.001
Monthly household income[3] (median, IQR)	350	200–600	250	200–300	415	250–750	<0.001
Number of household members (median, IQR)	5	4–5	4	3–5	5	4–6	0.073
<5 years old (median, IQR)	1	1–2	1	1–2	1	1–2	0.425
Household water source							
Private tap	34	17	9	19	25	16	0.719
Borehold	119	59	26	54	92	60	
Covered well	47	23	13	27	34	22	
Open well	2	1	0	0	2	1	
Household toilet[4]							
Bush/field	1	1	0	0	1	1	<0.001
Pit latrine	4	2	4	9	0	0	
Improved latrine	31	16	15	33	16	11	
Flush toilet	161	82	26	58	134	89	
Health insurance	8	5	0	0	8	5	0.106

[1] Missing for 1 child

[2] Missing for 1 well-nourished child

[3] Missing for 7 well-nourished and 6 malnourished children

[4] Missing for 2 well-nourished and 3 malnourished children

Table 2.

Characteristics of illness and medical care

	Total (n=202)		Malnourished (n=48)		Well-nourished (n=153)		
	n	**%**	**n**	**%**	**n**	**%**	**p-value**
Before hospitalization							
Days sick (median, IQR)	2	2–3	3	2–4	2	2–3	0.002
Received medical care	166	82	42	88	123	80	0.263
Health post	145	87	40	95	105	85	
Traditional healer	2	1	2	5	0	0	
Self	23	14	1	2	21	17	
Pharmacy	43	26	7	17	36	29	
Transportation to hospital							<0.001
Car	56	28	2	4	53	35	
Bus	5	2	4	8	1	1	
Taxi	132	65	39	81	93	61	
Ambulance	9	4	3	6	6	4	
During hospitalization							
Any comorbidity	60	30	13	27	47	31	0.631
Pneumonia	38	63	6	46	32	68	
Other	25	42	7	54	18	38	
Rehydration							0.009
ORS	101	50	33	69	83	54	
IV fluids	4	2	1	2	3	2	
ORS and IV fluids	97	48	14	29	67	44	
Rotavirus positive	46	23	1	2	45	30	<0.001
Outcome							0.013
Survived	196	97	44	92	151	99	
Died	6	3	4	8	2	1	
After discharge							
Received medical care	29	14	5	10	24	16	0.365
Health post	3	10	0	0	3	13	

	Total (n=202)		Malnourished (n=48)		Well-nourished (n=153)		
	n	%	n	%	n	%	p-value
Pharmacy	26	90	5	100	21	88	

Table 3.

Components and percentage contributing to total direct medical costs

	Number per patient							Percentage of direct medical costs						
	Total (n=202)[1]		Malnourished (n=48)		Well-nourished (n=153)			Total (n=202)		Malnourished (n=48)		Well-nourished (n=153)		
	Median	IQR	Median	IQR	Median	IQR	p-value	Median	IQR	Median	IQR	Median	IQR	p-value
Days hospitalized	3	2–6	6	5–8	2	1–4	<0.001	73	64–79	75	69–80	72	63–78	0.083
Medications	3	3–5	3	3–5	3	3–5	0.109	8	5–10	6	4–8	9	6–11	<0.001
Diagnostic tests	8	2–10	10	9–15	6	0–9	<0.001	12	9–16	10	8–13	13	9–17	0.020

[1] Nutrition status is missing for 1 child