Title: Cost-effectiveness analysis of the DHAKA and NIRUDAK clinical diagnostic models for volume deficit in patients with acute diarrhea

Location and name of foreign collaborating institution: International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) located in Dhaka, Bangladesh

Objective/specific aims: The first aim of this project is to compare treatment costs of acute diarrhea management using either the World Health Organization (WHO) guidelines or the Dehydration: Assessing Kids Accurately (DHAKA) model and the Novel, Innovative Research for Understanding Dehydration in Adults and Kids (NIRUDAK) model, previously developed by this team. The second aim of this project is to compare cost-effectiveness of the DHAKA and NIRUDAK models to current standards of care.

Background and significance:

Accounting for over 6.5 billion cases and 1.4 million deaths in 2019, diarrheal diseases are a major cause of morbidity and mortality and exert a heavy burden on health care systems worldwide.[1] As the severity of diarrheal disease can vary widely, accurately assessing dehydration status remains the most critical step in acute diarrhea management. Episodes of acute diarrhea led to dehydration, and existing care algorithms, namely from the WHO, base treatment around categorical estimates for fluid resuscitation. The DHAKA model and the NIRUDAK model, built on machine learning algorithms, predict percentage dehydration (fluid deficit) in individuals with acute diarrhea, to better target treatment and avoid the potential sequelae of over or under resuscitation. Previous analysis has demonstrated that the DHAKA and NIRUDAK models both outperform the WHO algorithm in terms of accuracy and reliability.[2, 3]

Methods:

Data collection procedures:

Data were collected as part of the NIRUDAK study, a prospective cohort study of patients over five years, and the DHAKA study, a prospective cohort study of patients under five years, presenting with diarrhea to the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) Dhaka Hospital in Bangladesh between March 2019 and March 2020 for the NIRUDAK study and in 2015 for the DHAKA study. Local nurses assessed patients and independently assessed patients for symptoms/signs of dehydration on arrival. They then classified patient dehydration status using both the DHAKA score and the WHO algorithm, can continued to collect and record patient weight and amount of fluid administered until the patients were discharged.[1, 4]

IRB review for the collection of this data has already been completed by the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b)'s Ethical Review Committee and the Rhode Island Hospital Institutional Review Board.[1, 4]

Plan for data analysis — cost analysis:

My initial cost analysis for both the DHAKA and NIRUDAK models comprised of generating descriptive statistics (mean, median, interquartile range, summation of costs) using Stata 17. I am continuing to work with this data to ascertain whether differences in costs between actual care, the DHAKA/NIRUDAK models, and the WHO models are primarily driven by differentially allocating patients to the lowest cost tier (i.e., No Dehydration) or by reducing the prescribed amount of fluid administered to each patient. Moreover, while the simple bar graphs I've created using Microsoft Excel are serviceable, I plan to re-do them using ggplot2 in R for creation of posters and the final manuscript. Below is my initial write-up for this first leg of the project:

Costs predicted by the NIRUDAK and DHAKA models were compared to costs predicted by the WHO algorithm. Actual costs from the NIRUDAK and DHAKA prospective cohort studies are presented for reference.

Using the NIRUDAK model, patients had a median projected total cost of $5.18 (IQR: 0 - 25.56), while median projected total costs using the WHO guidelines were $5.23 (IQR: 5.09 - 22.17). Actual total cost of care was $37.75 (IQR: 15.69 - 45.00) (Figure 1 & Table 1). When isolating costs for initial fluid resuscitation, the median projected cost per patient was $3.27 (IQR: 0 - 4.27) using the NIRUDAK model and $4.55 (IQR: 0 - 5.76) using the WHO guidelines, while actual costs of care were $5.43 (IQR: 4.16 - 5.43) (Figure 1 & Table 2).

Due to limitations in available data, the only comparison that could be done in the pediatric population was of total fluid costs. These costs were markedly lower than in the older population: the DHAKA model predicted a median cost of fluid per patient of $0.02 (IQR: 0 - 0.97) as compared to the $0.04 (IQR: 0.03 - 1.24) predicted by the WHO algorithm (Figure 2 & Table 3).

Measuring the societal cost savings (e.g., of hospital beds, physician and nurse labor, transportation to healthcare facilities, etc.) is beyond the scope of this analysis. However, by more accurately diagnosing patient dehydration levels — thus freeing up hospital beds and resources for the most severely ill patients and saving moderately ill patients the costs of in-patient care — the NIRUDAK and DHAKA models also provide positive externalities that are unable to be captured here.

Figure 1. Summary of cost comparisons — NIRUDAK model

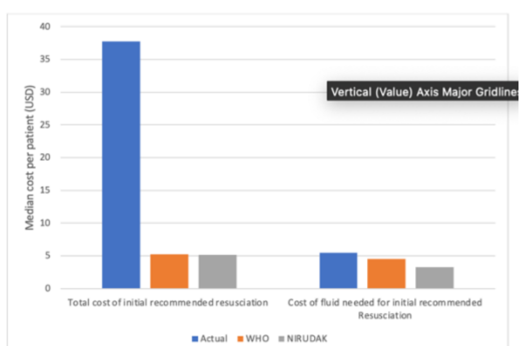

Table 1. Total cost of initial recommended resuscitation — NIRUDAK model

	ACTUAL MEDIAN	WHO MEDIAN	NIRUDAK MEDIAN	ACTUAL IQR	WHO IQR	NIRUDAK IQR	ACTUAL TOTAL	WHO TOTAL	NIRUDAK TOTAL	ACTUAL OBSER-VATIONS	WHO OBSER-VATIONS	NIRUDAK OBSER-VATIONS
ALL PATIENTS	37.75 (3222)	5.23 (449)	5.18 (445)	15.69 - 45.00 (1332 - 3841)	5.09 - 22.17 (437 - 1883)	0 - 25.46 (0 - 2166)	68684 (5854650)	28458 (2425359)	30515 (2602843)	2168	2168	2136
NO DEHYD-RATION	37.39 (3200)	0 (0)	0 (0)	12.26 - 44.99 (1052 - 3842)	0 - 0 (0 - 0)	0 - 0 (0 - 0)	13122 (1120904)	0 (0)	0 (0)	430	491	606
SOME DEHYD-RATION	37.77 (3231)	5.21 (448)	5.16 (443)	16.17 - 44.93 (1369 - 3836)	5.18 - 5.24 (445 - 451)	5.14 - 5.18 (441 - 446)	45746 (3897372)	4861 (417865)	3208 (275687)	1435	933	622
SEVERE DEHYD-RATION	39.14 (3331)	30.31 (2579)	28.22 (2405)	18.99 - 45.48 (1611 - 3860)	21.45 - 38.27 (1820 - 3259)	20.01 - 36.50 (1704 - 3109)	9298 (791346)	23598 (2007496)	27306 (2327156)	278	744	908

Actual costs are the sum of the costs of the actual amount of fluid administered plus the actual cost of hospital stay in the NIRUDAK study. Costs are set to zero for patients classified as having No Dehydration by the WHO or models, as both models recommend that these patients be managed expectantly. For patients classified as experiencing Some Dehydration by either model, costs equal four hours of hospital stay (for observation) plus the amount of fluid needed for resuscitation as predicted by the model. For patients a with Severe Dehydration classification, costs equal the actual length of hospital stay in the NIRUDAK prospective cohort study, plus the amount of fluid needed for resuscitation as predicted by either model, plus the actual amount of fluid in the given in the NIRUDAK prospective cohort study after 6 hours of admission to the hospital. Observations missing diagnostic labels for a particular model were omitted in analysis for that model. Costs outside parentheses are in USD; costs within parentheses are in BDT.

Table 2. Cost of fluid needed for initial recommended resuscitation — NIRUDAK model

	ACTUAL MEDIAN	WHO MEDIAN	NIRUDAK MEDIAN	ACTUAL IQR	WHO IQR	NIRUDAK IQR	ACTUAL TOTAL	WHO TOTAL	NIRUDAK TOTAL	ACTUAL OBSER-VATIONS	WHO OBSER-VATIONS	NIRUDAK OBSER-VATIONS
ALL PATIENTS	5.43 (449)	4.55 (375)	3.27 (3217)	4.16 - 5.43 (345 - 553)	0 - 5.76 (0 - 476)	0 - 4.27 (0 - 354)	10625 (880330)	8574 (708647)	5850 (483949)	2173	2172	2139
NO DEHYD-RATION	2.96 (245)	0 (0)	0 (0)	1.06 -4.80 (89 - 398)	0 - 0 (0 - 0)	0 - 0 (0 - 0)	1397 (115975)	0 (0)	0 (0)	431	491	607
SOME DEHYD-RATION	5.44 (451)	4.45 (367)	3.34 (276)	4.18 - 6.68 (347 - 553)	3.81 - 5.12 (314 - 423)	2.84 - 3.85 (235 - 318)	7492 (620577)	4125 (340489)	2072 (171002)	1437	937	624
SEVERE DEHYD-RATION	5.64 (468)	6.04 (500)	4.30 (356)	5.42 -6.75 (449 - 559)	5.16 - 6.81 (427 - 563)	3.54 - 4.92 (293 - 407)	1668 (138098)	4449 (368158)	3778 (312946)	278	744	908

Actual costs are the sum of the costs of ORS administered in the first six hours after admission (if applicable), plus IVF administered in the first six hours after admission and associated intravenous (IV) equipment (if applicable). For patients classified as having No Dehydration by the WHO or NIRUDAK model, costs were set to zero as both models recommend that these patients be managed expectantly. For patients with a classification of Some Dehydration, costs equal the cost of ORS needed for initial resuscitation as predicted by either model. Patients classified as having Severe Dehydration were assigned costs equal to the amount of IVF needed for resuscitation (as predicted by the model), plus associated IV equipment. Observations missing diagnostic labels for a particular model were omitted in analysis for that model. Costs outside parentheses are in USD; costs within parentheses are in BDT.

Figure 2. Total cost of fluid — DHAKA model

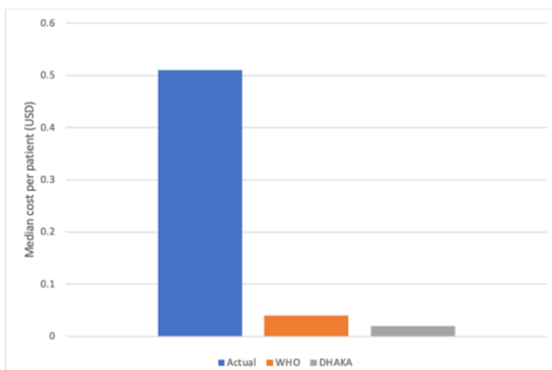

Table 3. Total cost of fluid — DHAKA model

	ACTUAL MEDIAN	WHO MEDIAN	DHAKA MEDIAN	ACTUAL IQR	WHO IQR	DHAKA IQR	ACTUAL TOTAL	WHO TOTAL	DHAKA TOTAL	ACTUAL OBSER-VATIONS	WHO OBSER-VATIONS	DHAKA OBSER-VATIONS
ALL PATIENTS	0.51 (44)	0.04 (4)	0.02 (2)	0.45 - 1.71 (39 - 146)	0.03 - 1.24 (3 - 105)	0 - 0.97 (0 - 83)	885 (74499)	421 (35669)	432 (36912)	820	849	847
NO DEHYD-RATION	0.46 (39)	0 (0)	0 (0)	0.45 - 0.50 (39 - 43)	0 - 0 (0 - 0)	0 - 0 (0 - 0)	226 (19339)	0 (0)	0 (0)	349	91	267
SOME DEHYD-RATION	1.10 (93)	0.03 (3)	0.01 (1)	0.47 - 1.73 (41 - 145)	0.03 - 0.04 (3 - 4)	0.01 - 0.02 (1 - 2)	447 (37551)	18.08 (1627)	2.67 (240)	341	496	176
SEVERE DEHYD-RATION	1.73 (145)	1.55 (131)	0.98 (84)	1.10 - 2.37 (93 - 198)	1.30 - 1.73 (110 - 146)	0.80 - 1.24 (69 - 106)	162 (13536)	403 (34042)	429 (36672)	83	262	404

Actual costs are the sum of the costs of all ORS administered during the hospital stay (if applicable), plus all IVF administered during the hospital stay and associated IV equipment (if applicable). For patients classified as having No Dehydration by the WHO or DHAKA model, costs were set to zero as both models recommend that these patients be managed expectantly. For patients with a classification of Some Dehydration, costs equal the cost of ORS needed for initial resuscitation as predicted by either model. Patients classified as having Severe Dehydration were assigned costs equal to the amount of IVF needed for resuscitation (as predicted by the model), plus associated IV equipment. Observations missing diagnostic labels for a particular model were omitted in analysis for that model. Costs outside parentheses are in USD; costs within parentheses are in BDT.

Plan for data analysis — cost-effectiveness analysis:

I am using a Markov cohort model, implemented in the R package Health Economic Simulation Modeling and Decision Analysis (hsim), in order to conduct the cost-effectiveness analysis. For my own learning, I plan to explore implementation of this analysis in Excel, Julia, and Python (languages with which I am already familiar) after the analysis is finalized.

As described above, the cost-analysis for this project is essentially a series of descriptive statistics comparing cost of actual care to the costs of the NIRUDAK/DHAKA and WHO models, whereas cost-effectiveness analyses compare an intervention to another intervention (or the status quo) by estimating how much it costs to gain a unit of a health outcome, like a life year gained or a death prevented.(5) This project has potential to make a methodological contribution to the field, as the typical health outcomes used in this type of analysis are QALYs (Quality-Adjusted Life Years) and DALYs (Disability-Adjusted Life Years)(5) — neither of which are directly applicable to diarrhea. I will either need to adapt these outcome measures or use different ones, in consultation with my primary mentor for this aspect of my project, Jonah H. Popp, MS, PhD (Investigator in Health Services, Policy and Practice at the Brown School of Public Health). This work may be helpful to researchers looking to model cost-effectiveness for other acute, non-lethal illnesses.

Project timeline and plan for dissemination:

I have already submitted an abstract covering my initial cost analysis for the NIRUDAK model to the 21st International Conference on Emergency Medicine (ICEM). I will submit a covering the DHAKA model portion of this work to the American Society of Tropical Medicine and Hygiene Annual Meeting. I will further submit a complete manuscript of this work which will include both the DHAKA and NIRUDAK cost analyses.

I have recently begun the cost-effectiveness analysis for both the DHAKA and NIRUDAK models and will submit this work to the American Public Health Association Annual Meeting (which carries out global health projects through its International Health Section). I will then submit a manuscript of the cost-effectiveness analysis over the summer.

ITEM	TYPE	TARGET	COMPLETION
Initial NIRUDAK cost analysis	Abstract	21st International Conference on Emergency Medicine (ICEM)	*done*
Initial DHAKA cost analysis	Abstract	American Society of Tropical Medicine and Hygiene Annual Meeting (ASTMH)	April 6, 2022
Complete NIRUDAK & DHAKA cost analysis	Manuscript	*Will consult with Dr. Levine*	June 2022

Initial NIRUDAK & DHAKA cost-effectiveness analysis	Abstract	American Public Health Association (APHA) Annual Meeting	April 30, 2022
Complete NIRUDAK & DHAKA cost-effectiveness analysis	Manuscript	*Will consult with Dr. Levine & Dr. Popp*	July 2022
Literature review, copyediting, drafting for Dr. Levine's R01 Grant Renewal	Grant	*n/a*	July 2022

Budget:

ITEM	EXPLANATION	COST
Conference fees (ICEM, ASTMH, APHA)	Not all registration rates are yet available, so this estimate is based on fees in previous years. If the abstracts are rejected from these conferences, they will be submitted elsewhere, so total costs will remain similar. Alpert Medical School only funds students for two conferences per fiscal year; I have already previously reached my limit for this year.	$600
Research stipend	I'm a first-year medical student on financial aid; this support would be instrumental to my ability to carry out this work.	$2900

Total: $3500

I am happy to accept any amount of support available/deemed appropriate.

References:

1. Levine AC, Barry MA, Gainey M, Nasrin S, Qu K, Schmid CH, et al. Derivation of the first clinical diagnostic models for dehydration severity in patients over five years with acute diarrhea. PLOS Neglected Tropical Diseases. 2021;15(3).
2. Levine AC, Glavis-Bloom J, Modi P, Nasrin S, Atika B, Rege S, et al. External validation of the DHAKA score and comparison with the current IMCI algorithm for the assessment of dehydration in children with diarrhoea: a prospective cohort stud. The Lancet Global Health. 2016;4(10).
3. Monique Gainey, Kexin Qu, C. Garbern S, A. Barry M, John Austin Lee, Sabiha Nasrin, et al. Assessing the performance of clinical diagnostic models for dehydration among patients with cholera and undernutrition in Bangladesh. Tropical Medicine & International Health. 2021;1(14).
4. Levine AC, Glavis-Bloom J, Modi P, Nasrin S, Rege S, Chu C, et al. Empirically Derived Dehydration Scoring and Decision Tree Models for Children With Diarrhea: Assessment and Internal Validation in a Prospective Cohort Study in Dhaka, Bangladesh. Global Health: Science and Practice. 2015;3(3).
5. Cost-Effectiveness Analysis Centers for Disease Control and Prevention: U.S. Department of Health & Human Services; 2021.