# Derivation and Internal Validation of a Score to Predict Dehydration Severity in Patients over 5 Years with Acute Diarrhea

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Abstract. Diarrheal disease accounts for more than one million deaths annually in patients over 5 years of age. Although most patients can be managed with oral rehydration solution, patients with severe dehydration require resuscitation with intravenous fluids. Scoring systems to assess dehydration have been empirically derived and validated in children under 5 years, but none have been validated for patients over 5 years. In this study, a prospective cohort of 2,172 patients over 5 years presenting with acute diarrhea to International Centre for Diarrhoeal Disease Research, Dhaka Hospital, Bangladesh, were assessed for clinical signs of dehydration. The percent difference between presentation and posthydration stable weight determined severe (≥ 9%), some (3–9%), or no (< 3%) dehydration. An ordinal regression model was derived using clinical signs and demographics and was then converted to a 13-point score to predict none (score of 0–3), some (4–6), or severe (7–13) dehydration. The Novel, Innovative Research for Understanding Dehydration in Adults and Kids (NIRUDAK) Score developed by our team included age, sex, sunken eyes, radial pulse, respiration depth, skin turgor, and vomiting episodes in 24 hours. Accuracy of the NIRUDAK Score for predicting severe dehydration, as measured by the area under the receiver operating characteristic curve, was 0.76 (95% confidence interval = 0.73–0.78), with a sensitivity of 0.78 and a specificity of 0.61. Reliability was also robust, with an Inter-Class Correlation Coefficient of 0.88 (95% confidence interval = 0.84–0.91). This study represents the first empirically derived and internally validated scoring system for assessing dehydration in children ≥ 5 years and adults with acute diarrhea in a resource-limited setting.

#### INTRODUCTION

Diarrheal diseases remain one of the most common acute conditions globally, with 6.29 billion cases in 2017. Though most cases follow a benign course and resolve without significant morbidity, up to 5% of cases in adults and older children lead to moderate or severe disease requiring medical intervention. Despite downward trending mortality over the past few decades, diarrheal illness remains the fifth leading cause of years of life lost globally, with more than one million deaths in adults and children over 5 years in 2017. 3.4

Severity of illness can vary greatly between patients and appropriate treatment requires an accurate assessment of dehydration level. <sup>5–7</sup> Patients with mild to moderate dehydration can be safely treated with oral rehydration solution (ORS) in the outpatient or clinic setting, whereas patients with severe dehydration require resuscitation with intravenous (IV) fluids in a hospital setting. <sup>8</sup> Unrecognized severe dehydration can result in hemodynamic instability, hypoperfusion with endorgan ischemia, and death. Conversely, aggressive treatment of mild to moderate dehydration can lead to adverse events in patients and depletes health care resources, especially if IV fluids are inappropriately used. <sup>9,10</sup>

Several studies have found the diagnostic accuracy of individual clinical signs, symptoms, and tests for dehydration to be limited. Systematic reviews have suggested combining several signs and symptoms together to improve diagnostic accuracy. Although several scoring systems have been empirically derived and validated to assess dehydration in children under 5 years of age with diarrhea, 18-22 none have

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been validated in patients over age 5 years, including the widely used algorithm from the WHO Integrated Management of Adolescent and Adult Illness (IMAI) guidelines.<sup>23</sup> The 4-symptom WHO IMAI algorithm, adapted from the WHO Integrated Management of Childhood Illness guidelines, has never been validated in older children and adults, whose physiology and diarrhea etiology are very different from younger children.<sup>24–30</sup>

In this study, we sought to determine which individual clinical signs and symptoms are significantly associated with dehydration severity in patients over 5 years of age with acute diarrhea and to use these individual predictors to develop a score to assess dehydration severity, with the goal of providing health care workers with a simple yet accurate tool for managing dehydration in this patient population.

### MATERIALS AND METHODS

Study setting and participants. This study is a secondary analysis of data collected from Novel, Innovative Research for Understanding Dehydration in Adults and Kids (NIRUDAK, which also means "dehydration" in Bangla), a study that created a model to be used in an mHealth tool.31 This article presents an independent score that can be used without any need for technology, such as a computer or cell phone. NIRU-DAK was a prospective cohort study of patients over 5 years presenting with acute diarrhea to the rehydration unit at the International Center for Diarrheal Disease Research, Bangladesh's (icddr,b) Dhaka Hospital between March 2019 and March 2020. All patients over 5 years of age presenting with acute diarrhea were eligible for enrollment. Research staff randomly selected patients for screening on arrival 24 hours per day by drawing colored marbles from a bag with one color indicating the patient was to be screened for inclusion and

exclusion criteria and potentially enrolled in the study, and the other colored marble indicating no enrollment. The proportion of colored marbles was set to allow for the enrollment of a reasonable number of subjects each day and maintain both the quality of data collection and integrity of all study protocols. Selected patients were excluded if they had < 3 loose stools in the previous 24 hours, diarrhea lasting longer than 7 days, a diagnosis other than gastroenteritis as determined by the triage physician, or had been previously enrolled in the study. Patients were enrolled from three age groups based on WHO classification: children/adolescents (age 5-19), adults (age 20–59), and elderly (age  $\geq$  60). <sup>27,32,33</sup> Research staff provided eligible patients or their guardian information about the goals, risks, and benefits of the study, and obtained written or verbal consent in Bangla. All patients were managed according to standard icddr,b protocols, and study procedures were not allowed to delay any emergent care. Ethical approval was obtained from the icddr,b Ethical Review Committee and Rhode Island Hospital Institutional Review Board.

Staff training and oversight. Local general practice nurses with 2 or more years of clinical experience were hired to collect data for this study. These nurses were hired separately from the icddr,b clinical nursing pool to better represent the skills of general practice nurses worldwide. Research nurses received 1 week of practical training on all study procedures, including observed assessment of clinical signs of dehydration as described by study protocols (Supplemental Appendix).

Assessment of dehydration status. Percent weight change with rehydration was used to assess percent dehydration, as has been widely used in prior studies. 17,34-36 As patients are treated for their dehydration, their weight increases until they become euvolemic and they diuresis excess fluid, achieving a stable weight. Immediately upon enrollment in the study, patients were weighed to the nearest 100 g using an electronic Seca 952 chair or Seca 984 bed scale. If a patient received IV fluid before obtaining a baseline weight, study staff recorded the amount of fluid received. Patients were then weighed on the same scale every 4 hours throughout their stay to determine their posthydration stable weight. Stable weight was calculated as the average of the two highest consecutive weights that differed by less than 2%. Those who did not achieve a stable weight before discharge were called daily for up to 10 days, and when their diarrhea had resolved were asked to return for a final weight. Percent dehydration was calculated by the following formula<sup>37</sup>:

Percent Dehydration=100%

\* [(Stable Weight-Admission Weight)/Stable Weight]

Patients were categorized as having severe (> 9%) dehydration, some (3–9%) dehydration, or no (< 3%) dehydration, as has been previously described in the literature. <sup>18,19,38</sup>

**Assessment of clinical signs of dehydration.** After obtaining the initial weight, 2 study nurses then performed independent and blinded assessments of various clinical signs of dehydration, which had been chosen a priori based on a literature review and in consultation with expert clinicians at icddr,b. <sup>11–16</sup> The clinical signs included mental status, thirst, skin pinch, eye level, mucous membranes, respiration

depth, radial pulse, capillary refill, urine output, number of vomiting episodes in the previous 24 hours, number of diarrheal episodes in the previous 24 hours, and diarrhea duration.

Individual clinical signs associated with severe dehydration. For each of the candidate clinical variables, bivariate analysis was performed to assess association with severe dehydration and reported as a  $\chi^2$  statistic. Sensitivities, specificities, negative predictive value, and positive predictive value of predicting severe dehydration were also assessed. For clinical signs with more than two levels, each level was compared only with the reference level. Finally, reliability was assessed by comparing two nurses' assessments for each variable using Cohen's weighted Kappa. Age-specific associations with ordinal dehydration levels were assessed by fitting a proportional odds logistic regression model with each predictor, with odds ratios and significance reported.

Derivation of the NIRUDAK dehydration score. Standard methods consistent with the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis guidelines, were used to develop the clinical diagnostic model.<sup>39–42</sup> Forward stepwise regression techniques were used to fit the candidate clinical variables into a final ordinal regression model to predict dehydration severity (none, some, or severe). Clinical variables were modeled comparing indicator variables relative to a chosen normal reference level. Vomiting episodes, diarrheal episodes, and duration of diarrhea were converted to categorical variables to account for uneven frequencies and improve score ease of use. Tenfold cross-validation was used to select the number of forward steps in model training, and the model was finalized by fitting to the full data set with the corresponding optimal value of the tuning parameter. Regression coefficients were divided by a common divisor and rounded to the nearest integer, to produce a simple integer score. The reference levels for each clinical variable were assigned a value of 0.

Model assessment and validation. The NIRUDAK Score was assessed for discrimination (accuracy) and reliability in predicting severe dehydration. Discrimination was measured using the area under the receiver operating characteristic (ROC) curve (AUC) for the prediction of both severe dehydration and any dehydration. Levels of sensitivity and specificity were identified at integer score points along the ROC curve. Additionally, the ordinal c-index (ORC) was computed using the average of 3 pairwise c-indices for none versus some, some versus severe, and none versus severe dehydration to create a single measure of discrimination. 43,44 The ORC is interpreted similarly to the better-known binary c-index, and is the probability of correctly separating a pair of randomly chosen cases from two categories: 0.5 is no better than chance, whereas 1 represents a perfect model. Reliability was assessed by comparing the dehydration score predicted by the model with data from each nurse's independent assessment, using the intraclass correlation coefficient. Bootstrapping (random selection with replacement) with 1,000 samples was used to correct for over-optimism in estimating the ORC of the score. 40,45 A new model was trained on each iteration by applying the forward stepwise regression algorithm and a new scoring system was derived based on selected variables and coefficients. Optimism was calculated as the difference between model performance using the data included in the part of the bootstrap sample where the model was derived and that on the data excluded from the bootstrap 1370 BARRY AND OTHERS

sample. The overall optimism was calculated by averaging the optimism from the bootstrap samples. Corrected performance was computed by subtracting the overall optimism from the ORC on the full data. All statistical analyses were performed using R Version 3.6.2.

#### **RESULTS**

**Enrollment and study population characteristics.** Of 4,440 patients randomly selected for screening at icddr,b, 2,293 patients were found to be eligible, and 2,172 patients over 5 years of age with acute diarrhea were enrolled in the study (Figure 1). Before model development, 26 (1.2%) subjects were excluded due to missing data on dehydration predictors or outcome. Overall, 631 children, 752 adults, and 763 elderly patients were included in the final analysis, with a median age of 35 years (interquartile range 18–60 years). Females comprised 49.6% of study participants. On the basis of percent weight change with rehydration, our criterion standard for dehydration category, 100 (15.8%) children, 91 (12.1%) adults, and 87 (11.4%) elderly were classified as having severe dehydration (> 9% total body water loss).

Clinical signs associated with severe dehydration. Clinical signs were assessed to determine which variables were significantly associated with severe dehydration, as well as the degree of association. Of the clinical signs associated with severe dehydration, most were associated consistently across all age groups (Supplemental Table). Because of this, each clinical sign was then further explored as a predictor of severe dehydration across all patients older than 5 years (Table 1). Clinical signs with a high degree of association with severe dehydration included slow or very slow skin pinch, decreased or absent radial pulse, deep respiration, and

sunken eyes. Many clinical signs were highly sensitive for predicting severe dehydration including thirst, sunken eyes, urine output, and vomiting episodes, although none of these had a high degree of specificity for severe dehydration. A few clinical signs showed high specificity for severe dehydration, including confused mental status and absent radial pulse, although they lacked adequate sensitivity. The individual sign with the best combination of sensitivity and specificity for severe dehydration was skin pinch. Clinical signs not statistically associated with severe dehydration included dry mucous membranes, prolonged capillary refill, and duration of diarrhea. No single clinical sign in isolation showed robust accuracy in predicting severe dehydration.

Derivation of the NIRUDAK score. Stepwise forward selection was performed on the clinical signs, to derive an ordinal regression model to predict dehydration severity. The clinical signs included in the final model were age category, sex, eye level, radial pulse, respiration depth, skin pinch, and number of vomiting episodes in the past 24 hours. The regression coefficients for each clinical sign were converted into integer scores, producing a 13-point scoring system (Table 2). The sensitivity and specificity of the various score cut points for determining some and severe dehydration were calculated, with lower score cut points more sensitive but less specific (Table 3). Score ranges were then chosen to predict none (score of 0-3), some (score of 4-6), or severe (score of 7-13) dehydration, attempting to optimize the sensitivity and specificity of the scoring system.

**Model performance and validation.** Discrimination, measured using the AUC, was 0.76 (95% confidence interval [CI] = 0.73–0.78) for severe dehydration and 0.75 (95% CI = 0.72–0.78) for some (any) dehydration (Figure 2). For predicting severe dehydration, the NIRUDAK Score had a sensitivity

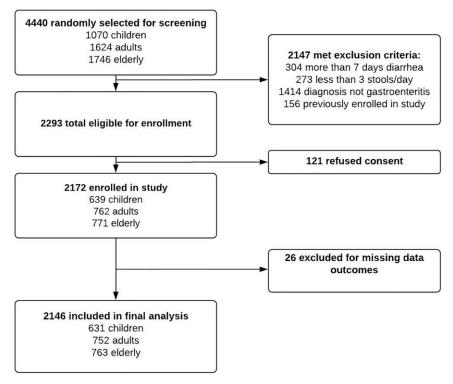


FIGURE 1. Novel, Innovative Research for Understanding Dehydration in Adults and Kids (NIRUDAK) study enrollment.

Table 1
Association of clinical signs with severe dehydration in bivariate analysis

	Sensitivity	Specificity	PPV	NPV	$\chi^2$	P value	Reliability
Mental status*					10.51	0.001	0.65
Confused/lethargic	0.08	0.96	0.25	0.88			
Thirst*					9.60	0.008	0.62
Drinks eagerly	0.92	0.13	0.12	0.92			
Refuses/unable to drink	0.89	0.21	0.16	0.92			
Skin pinch†					150.41	< 0.001	0.82
Slow	0.84	0.47	0.16	0.96			
Very slow	0.73	0.82	0.32	0.96			
Eye level*					35.26	< 0.001	0.82
Sunken eyes	0.89	0.28	0.16	0.95	00.20		0.02
Mucous membranes‡	0.00	0.20	0.10	0.00	0.63	0.43	0.27
Dry	0.99	0.02	0.13	0.92	0.00	0.10	0.27
Respiration depth*	0.00	0.02	0.10	0.02	60.33	< 0.001	0.63
Deep	0.81	0.44	0.18	0.94	00.00	< 0.001	0.00
Radial pulse§	0.01	0.44	0.10	0.54	42.19	< 0.001	0.61
Decreased	0.84	0.33	0.15	0.93	42.15	< 0.001	0.01
Absent	0.26	0.94	0.19	0.93			
Capillary refill*	0.20	0.34	0.23	0.33	0.91	0.34	0.51
Prolonged	0.03	0.98	0.19	0.87	0.31	0.04	0.51
Urine output*	0.03	0.90	0.19	0.07	13.77	0.001	0.73
Decreased/dark	0.93	0.11	0.13	0.92	13.77	0.001	0.73
Minimal/none	0.74	0.49	0.13	0.92			
	0.74	0.49	0.20	0.92	8.34	0.004	
Sex∥ Male	0.50	0.51	0.15	0.89	0.34	0.004	
	0.59	0.51	0.15	0.69	00.00	< 0.001	
Vomiting episodes in 24 hours¶	0.07	0.00	0.10	0.05	26.00	< 0.001	
1–5	0.87 0.92	0.23	0.10	0.95			
6–10		0.23	0.15	0.95			
> 10	0.87	0.36	0.17	0.95	4.07	0.00	
Diarrhea episodes in 24 hours#	0.04	0.00	0.44	0.00	4.97	0.08	
10–19	0.64	0.30	0.11	0.86			
> 19	0.63	0.38	0.15	0.86			
Duration of diarrhea (hours)**					2.61	0.27	
13–23	0.25	0.69	0.11	0.86			
> 23	0.55	0.41	0.12	0.86			
Age††					6.80	0.03	
Children	0.54	0.56	0.16	0.89			
Adults	0.51	0.51	0.12	0.89			

NPV = negative predictive value; PPV = positive predictive value. Calculations performed by comparing to reference level for each category. Reference Levels: \*normal, †rapid, ‡moist, §strong, ||female, ¶none, #< 10, \*\*< 13, ††elderly.

TABLE 2
Thirteen-point Novel, Innovative Research for Understanding Dehydration in Adults and Kids (NIRUDAK) Score with assigned dehydration categories

Predictor/clinical sign	Level	Points		
Age (years)	> 59	0		
	20-59	1		
	< 20	2		
Sex	Female	0		
	Male	1		
Eye level	Normal	0		
	Sunken	1		
Radial pulse	Strong	0		
	Decreased	1		
	Absent	2		
Respiration depth	Normal	0		
	Deep	1		
Skin pinch	Rapid	0		
	Slow	2		
	Very slow	4		
Vomiting episodes in 24 hours	< 1	0		
	1–10	1		
	> 10	2		
Dehydration score categories	Points			
No dehydration	0–3			
Some dehydration	4–6			
Severe dehydration	7–13			
-				

of 0.78 and a specificity of 0.61, as well as a positive predictive value of 0.23 and a negative predictive value 0.95 at the cut points chosen. For predicting some (any) dehydration, the score has a sensitivity of 0.92 and a specificity of 0.38, as

Table 3
Test characteristics of various cut points for dehydration score category

	Dehydration category							
Score Cut Point	Some dehydration				Severe dehydration			
	Sensitivity	Specificity	PPV	NPV	Sensitivity	Specificity	PPV	NPV
1	1.00	0.01	0.80	0.83	-	-	-	
2	0.99	0.06	0.81	0.74	-	-	_	_
3	0.97	0.20	0.83	0.61	1.00	0.08	0.14	1.00
4	0.92	0.38	0.85	0.53	0.99	0.16	0.15	0.99
5	0.81	0.56	0.88	0.42	0.97	0.30	0.17	0.98
6	0.67	0.70	0.90	0.35	0.91	0.45	0.20	0.97
7	0.51	0.82	0.92	0.30	0.78	0.61	0.23	0.95
8	0.36	0.91	0.94	0.26	0.63	0.75	0.27	0.93
9	0.19	0.96	0.95	0.23	0.38	0.87	0.30	0.90
10	0.06	0.98	0.92	0.21	0.13	0.96	0.32	0.88
11	0.02	1.00	0.97	0.20	0.04	0.99	0.37	0.88
12	_	_	_	_	0.01	1.00	0.50	0.87
13	-		_	_	< 0.01	1.00	1.00	0.87

NPV = negative predictive value; PPV = positive predictive value.

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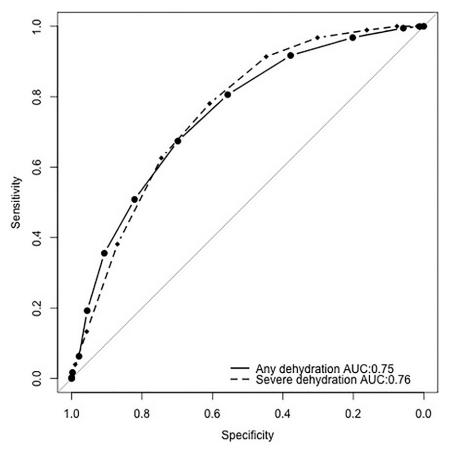


FIGURE 2. Receiver operating characteristic (ROC) curves of the Novel, Innovative Research for Understanding Dehydration in Adults and Kids (NIR-UDAK) Score for Some (Any) and Severe Dehydration. AUC = area under the ROC curve.

well as a positive predictive value of 0.85 and a negative predictive value 0.53 at the chosen cut points. Reliability of the score, as measured by the intraclass correlation coefficient between the scores calculated from the blinded admission exams by two nurses, was 0.88 (95%  $\rm CI=0.84-0.91$ ), with an average of 6 minutes between nursing assessments.

To internally validate the NIRUDAK Score, the ORC (a measure of discrimination for ordinal models similar to the AUC) was calculated in the original population and then across 1,000 bootstrap iterations to determine the optimism corrected performance of the model. The predictive accuracy of a model typically has overestimation bias, known as optimism, relative to the actual performance in an external population. The ORC was 0.78 in the original population and the optimism corrected performance was 0.76 (95% CI = 0.73–0.79) across 1,000 bootstrap iterations of score derivation, indicating that our score will likely only be slightly less accurate in an external population.

## DISCUSSION

This study presents the first empirically derived and internally validated scoring system for assessing dehydration in patients over 5 years of age with acute diarrhea in a resource-limited setting. The diagnostic accuracy of individual clinical parameters for diagnosing severe dehydration was first investigated. Although skin pinch was found to have the best test characteristics, no single clinical predictor in isolation

showed high accuracy, findings consistent with prior literature in the field. 11-16

To overcome the limitations of individual clinical signs, forward stepwise regression was used to identify a subset of clinical predictors that in combination best discriminated between patients with no, some, and severe dehydration. <sup>42</sup> The ordinal regression coefficients for this model were then converted into a simplified score that could be easily used in resource-limited clinical settings. The NIRUDAK Score was found to have good discrimination in predicting some and severe dehydration, and high reliability of the assessments between two nurses blinded to each other's assessments. Additionally, the score showed only modest optimism, a measure of overestimation bias compared with when the score is used in an external population, suggesting it will continue to perform well in new populations of patients.

Although this score can be used in a variety of clinical settings, it was created to be fully functional in a resource-limited setting where medical equipment may not be readily available. The target audience of this score is not highly trained specialists but rather front-line providers such as nurses at primary health centers, who serve as the first point of contact between patients and the healthcare system in resource-limited settings. With this score, front-line providers could more effectively triage which patients are exhibiting some dehydration and can be safely managed at the primary health centers with ORS and then sent home and which patients are suffering from severe dehydration and require referral to the

district or tertiary care hospital, involving possibly lengthy transports and investment of resources including IV fluids, personnel, and an inpatient bed. For this reason, we chose to use local nurses to collect our study data, to best represent the end-user of the score. On the basis of the local resources available, this score could possibly even be used by community health workers. When creating the ordinal regression model, only clinical variables that could be easily assessed without medical equipment were included, omitting variables such as blood pressure, laboratory values such as lactate, or evaluation of inferior vena cava by ultrasound because these measurements require access to sophisticated equipment that is often not available to front-line providers in resourcelimited setting. Even without these more sophisticated variables, the score showed good discrimination. Additionally, although some variables (such as sunken eye level) are more subjective, the score reassuringly showed good reliability based on literature standards.46

In choosing the score ranges for none (score of 0-3), some (score of 4-6), and severe (score of 7-13) dehydration, we attempted to optimize the sensitivity and specificity of the score. This specific score range prioritizes recognition of a patient with some (any) dehydration, with a cut point for any dehydration that has high sensitivity but lower specificity, to ensure initiation of rehydration with ORS in a dehydrated patient. However, a more stringent cut point for severe dehydration was chosen, resulting in higher specificity but somewhat lower sensitivity, with the recognition that overly aggressive fluid resuscitation can result in harm such as arrhythmias, pulmonary edema, and increased mortality.9 This strategy also conserves medical resources for resuscitation with IV fluids for patients who benefit most. However, if a different degree of sensitivity/specificity of detection of either some or severe dehydration is desired in a particular setting, different score ranges may be chosen. For example, if a more sensitive (although less specific) recognition of severe dehydration is desired to miss fewer patients with severe dehydration, a lower score cut point may be selected. Conversely, if a more specific but less sensitive score is desired, a higher cut point may be chosen, such as during a cholera outbreak in a remote location where conservation of scarce medical resources is a priority.

The NIRUDAK Score has been empirically derived and internally validated specifically for patients over 5 years of age with acute diarrhea. Although several scoring systems have been created and validated for children under 5 years of age, 18-22 none have been validated for patients over 5 vears. The NIRUDAK Score shares some clinical predictors with the other scoring systems; for example, the Clinical Dehydration Scale also includes sunken eyes,<sup>20</sup> and the DHAKA Score includes both skin pinch and respiration depth.<sup>19</sup> However, both of these scoring systems also include clinical predictors that may be more applicable to young children, such as decreased or absent tear production. The WHO IMAI algorithm is generally considered the standard of care for managing dehydration related to diarrhea in resource-limited settings. 23,30 However, this algorithm was adapted almost verbatim from the WHO Integrated Management of Childhood Illness algorithm, created for children under age 5 years. Two of the signs in the IMAI algorithm, lethargic mental status and thirst, were not chosen for inclusion in the NIRUDAK Score based on our forward stepwise selection process, suggesting they may not function well as predictors of dehydration in older patients.

In the creation of the NIRUDAK Score, the model selected for two variables with less established relation to dehydration: age and sex. Prior models that did not include these two factors performed slightly less robustly in predicting dehydration severity.31 The relative protection with advancing age may be related to lower rates of cholera, a disease known to be associated with profuse watery stool and severe dehydration.<sup>47</sup> Infection with Vibrio cholerae typically induces long-lasting immunity,48 resulting in an adult population in an endemic area with lower incidence of cholera. V. cholerae is an important cause of diarrhea virtually worldwide, 47 and although V. cholerae is comparatively more prevalent in our study site, overall, the causes of diarrhea in patients over 5 years of age are similar to what is found in other resource-limited settings, including enterotoxigenic Escherichia coli and Shigella spp. 24,27,49,50 Interestingly, there is emerging epidemiologic evidence of sex differences in acute diarrhea, with boys being disproportionally affected compared with girls,51 which can be seen both in resource-limited settings, <sup>52–56</sup> as well as in the United States, 57-59 where it was found that not only are boys disproportionally affected by diarrheal disease, they are also more likely to be hospitalized and die. Whether this sex difference is related to cultural factors, 60-62 such as the belief that boys are of more value than girls and thus will be given increased access to medical care; environmental factors. 53,54,56 such as the increased mobility allowed to boys to play freely or work out of the home, thereby exposing them to more infectious pathogens; or biological differences,53 with boy's pathophysiology making them more susceptible to diarrheal illness, has yet to be elucidated. These studies are reassuring that the correlation of age and sex with severe dehydration will likely be seen in other resourcelimited settings but will need to be validated in new populations to ensure repeatable accuracy of all the clinical predictors of dehydration that comprise the NIRUDAK Score.

Although this study was conducted at a single center, we believe that the NIRUDAK Score will be generalizable to other populations of patients. The icddr,b serves a catchment area of nearly 17 million people, with a diverse mix of urban, suburban, and rural settings. 49 The patients presenting for medical care at icddr,b were likely more dehydrated on average than those who do not seek medical care; nonetheless, our score will presumably be valid in the ambulatory setting because we enrolled sufficient numbers of patients in each dehydration category to develop a stable model. To ensure future reliability of the score, the study nurses were hired from outside icddr,b to better represent the training level of nonspecialized nurses practicing in resource-limited settings. Ultimately, internal validation with bootstrap sampling suggested good generalizability of our score, but external validation in a new study population will be required before widespread implementation can be recommended.

In the creation of our NIRUDAK Score, we hope to provide health care workers who are familiar with the format of the WHO IMAI algorithm, and other commonly used clinical prediction scores, a simple and accurate tool to assist in determining dehydration severity and thus the appropriate rehydration management strategy for patients over 5 years of age with acute diarrhea.

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Received February 5, 2021. Accepted for publication May 6, 2021. Published online August 16, 2021.

Note: Supplemental appendix and table appear at www.ajtmh.org.

Financial support: Funding for data collection was provided through grants from National Institute for Diabetes and Digestive and Kidney Diseases, National Institutes of Health (DK116163). The funders had no role in the study design, data collection or reporting processes.

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