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Supplementary appendix 2

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Levine AC, Gainey M, Qu K, et al. A comparison of the NIRUDAK models and WHO algorithm for dehydration assessment in older children and adults with acute diarrhoea: a prospective, observational study. *Lancet Glob Health* 2023; published online Sept 27. https://doi.org/10.1016/S2214-109X(23)00403-5.

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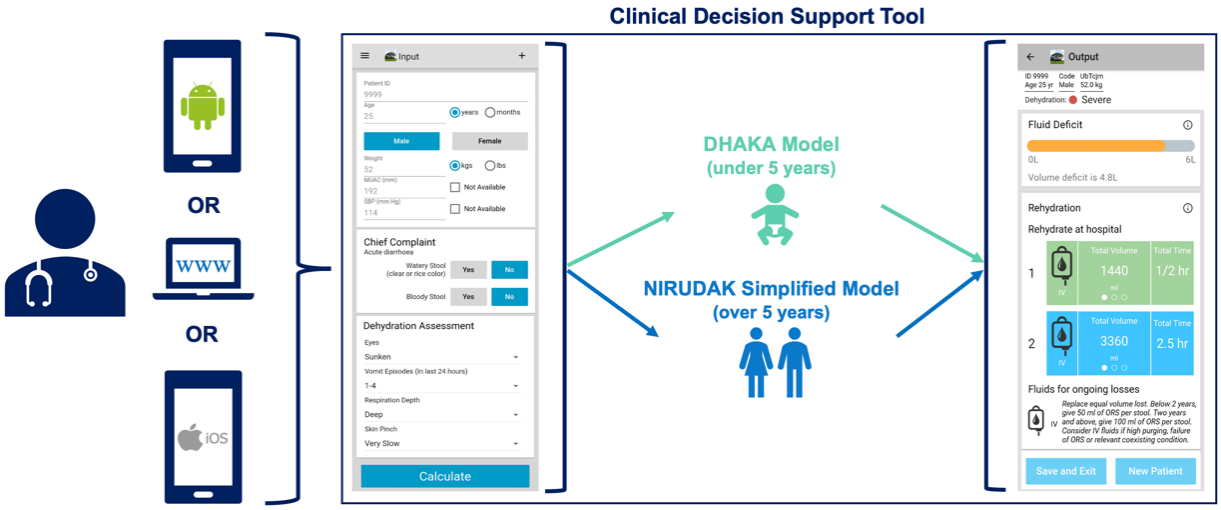
Relationship between the digital platform (Android, iOS, web-based), the clinical diagnostic models (DHAKA, NIRUDAK), and the novel mobile health "app" clinical decision support tool



Description of Models for Patients over Five Years

The Full NIRUDAK model is intended for assessing dehydration in patients over five years of age presenting with acute diarrhea and includes the following clinical signs: eye level, skin pinch, respiration depth, vomiting episodes, sex, age, mid-upper arm circumference (MUAC), blood pressure (see the detailed instructions on the following page for assessing each of these signs and symptoms). To use this model, the *FluidCalc: Rehydration Calculator* Clinical Decision Support Tool (CDST or "app") must be downloaded on a smartphone, tablet, or computer. In addition, an age-appropriate blood pressure cuff and MUAC measuring tape are also required.

The Simplified NIRUDAK model is intended for assessing dehydration in patients over five years of age presenting with acute diarrhea and includes the following clinical signs: eye level, skin pinch, respiration depth, radial pulse, and urine output. It can be applied using the *FluidCalc: Rehydration Calculator* CDST, though does not require any additional equipment. In addition, if a smartphone, tablet, or computer is not available, clinicians can still apply the Simplified NIRUDAK model using a fourteen-point score (see Table 1 in the manuscript). To use this model, the patient should be assessed for each of the above clinical signs and assigned points based on the level of each clinical sign. A total score greater than 6 would be categorized as having severe dehydration based on our predetermined cut-points, which were developed during focus groups with clinicians in Bangladesh to balance the sensitivity and specificity of the model. A total score of 4-6 would categorize the patient as having some dehydration. Finally, a total score less than 4 would categorize the patient as having no dehydration.

The World Health Organization (WHO) Integrated Management of Adult and Adolescent Illness (IMAI) guidelines algorithm is intended for assessing dehydration in patients over five years presenting with acute diarrhea and includes the following clinical signs: eye level, skin pinch, mental status, and thirst level. The WHO IMAI algorithm does not require a smartphone, but does require a cup of water that can be offered to the patient at triage to assess their thirst. To be categorized as having severe dehydration, a patient must present with at least two of the following signs: lethargy/unconscious mental status, sunken eye level, drinks poorly/not able to drink, skin pinch goes back very slowly ($\geq$ 3 seconds). To be categorized as having some dehydration, a patient must present with at least two of the following signs: sunken eye level, drinks eagerly/thirsty, skin pinch goes back slowly (2 – 3 seconds). If none of the above criteria are met, the patient is categorized as having no dehydration.

Pre-Defined Protocols for Measurement of Clinical Signs and Symptoms

Mental Status

Mental status was assessed by observing and interacting with the patient. If the patient was awake and able to respond appropriately to questions and commands, the mental status was classified as "Normal." If the patient's eyes were closed, or the patient was staring into space, or the patient was slow to respond to questions or commands, the patient's mental status was classified as "Confused/Lethargic".

Eye Level

The patient's eye level was evaluated by viewing the patient's face from the side of the stretcher at the level of the patient and identifying whether the patient's eyelid was below their orbital rim with their eyes closed. If so, their eye level was classified as "Sunken", otherwise it was classified as "Normal." If it was unclear based on visualization, nurses were instructed to place the lateral aspect of one finger across the patient's orbital rim, with their finger touching both the superior and inferior portions of their orbital rim while the patient's eyes were closed. The eye level was classified as "Normal" when the nurse could feel the eyelid touching their finger and "Sunken" when the eyelid was below the level of the orbital rim and not touching their finger.

Thirst

Thirst was evaluated by pouring a small amount of water into a cup and offering it to the patient. The patient's thirst was classified as "Normal" if the patient sipped the water slowly or "Drinks Eagerly" if they drank it quickly. The patient's thirst was classified as "Refuses/Unable to Drink" if they refused or were unable to drink water.

Skin Pinch

A skin pinch test was performed on the patient by grasping a fold of skin on the side of their abdomen between the thumb and index finger and rapidly releasing the skin while counting how many seconds it took for the skin to flatten again. "Rapid" was defined by the skin flattening immediately (in the blink of an eye). "Slow" was defined by the skin flattening in about one second. "Very Slow" was defined by the skin flattening in two or more seconds.

Respiration Depth

Respiration depth was evaluated by observing the patient's abdomen while lying flat. If their skin did not sink below the level of their lower ribs at any point during the respiratory cycle, their respiration depth was classified as "Normal." If their skin did sink below the level of the lower ribs at any point during the respiratory cycle, their respiration depth was classified as "Deep."

Radial Pulse

Radial pulse was evaluated by placing two fingers just proximal to the patient's wrist crease on the radial side of the forearm and comparing the patient's radial pulse to one's own. If they were similar, the patient's radial pulse was classified as "Strong." If the patient's radial pulse felt weaker, it was classified as "Decreased." When the patient's radial pulse could not be felt at all, it was classified as "Absent."

Urine Output

Urine output was evaluated by asking the patient or their family about their urination in the last 8 hours. If the patient felt their urine output was normal for them over this time period, it was classified as "Normal." If the patient felt their urination was less frequent or darker (more concentrated) than normal over this time period, their urine output was classified as "Decreased/Dark." If the patient had not urinated at all in the past 8 hours or only a few drops, their urine output was classified as "Minimal/None."

Vomiting Episodes in 24 hours

Vomiting episodes in 24 hours were assessed by asking the patient or their family member how many discrete episodes of vomiting the patient had within the past 24 hours of presentation.

Systolic/Diastolic Blood Pressure

The patient's blood pressure was obtained while the patient was lying flat using an automated blood pressure cuff. If the patient was receiving IV fluids, the arm opposite of the IV line was used so as to not interfere with treatment. If the automatic blood pressure cuff was not able to obtain a measurement on the first try, a manual cuff was used instead. For children, a manual, child-sized blood pressure cuff was used to measure blood pressure. A second blood pressure measurement was taken while the patient was sitting up by elevating the head of the stretcher to 90 degrees (with a 30 second delay between obtaining the flat and seated measurements to allow time for the heart rate to adjust). The blood pressure difference was calculated as the seated blood pressure minus the flat blood pressure. Standing blood pressure was not assessed as many patients were unable to stand due to the severity of illness.

MUAC

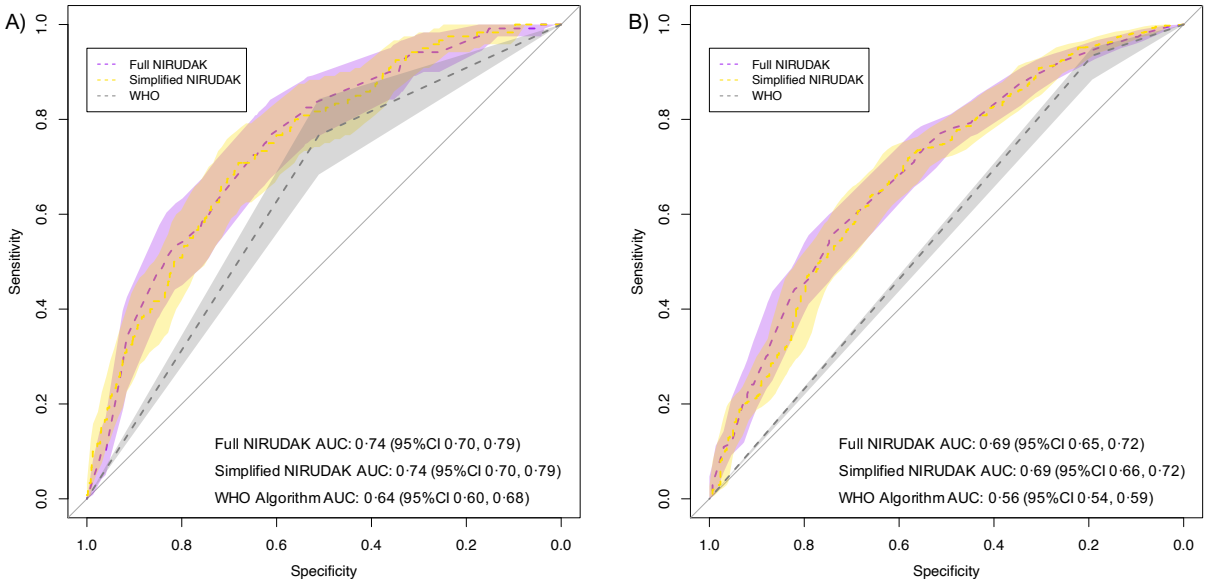
The mid-upper arm circumference (MUAC) was assessed by bending the patient's left elbow to 90 degrees while their left arm was hanging loosely at their side (not stretched out) and measuring the midpoint between the tip of the shoulder and the tip of the elbow. A standard MUAC tape was wrapped around the arm at the measured midpoint, and the observed number was recorded in millimeters.

Dehydration Categories

	Method of Classification[a]			
	Criterion Standard[b]	**NIRUDAK Full Model**	**NIRUDAK Simplified Model**	**WHO IMAI Algorithm**
Dehydration category				
Severe	120 (7·5)	838 (53·1)	1043 (66·0)	338 (21·4)
Some	1159 (72·5)	450 (28·5)	278 (17·6)	1112 (70·4)
None	301 (18·8)	290 (18·4)	259 (16·4)	130 (8·2)

[a]Categorical variables are presented as number (%)
[b]Percent weight change with rehydration was used as the criterion standard for assessing dehydration severity

ROC curves for discrimination between severe dehydration and the absence of severe dehydration (A) and for the discrimination between any dehydration (some/severe) and no dehydration (B) for each model



Test characteristics, including sensitivity (sens), specificity (spec), positive likelihood ration (LR), negative likelihood ratio, chi square (X^2), and weighted Cohen's kappa (K), of the individual clinical signs used in the three clinical diagnostic tools for any dehydration (AD) or for severe dehydration (SD)

	Sens	Spec	LR Positive	LR Negative	X^2	p-value	K
Skin pinch*†‡							0·98
Slow (AD)	0·68	0·49	1·34	0·65	69·40	<0·001	
Very Slow (SD)	0·55	0·79	2·67	0·57	81·23	<0·001	
Eye level*†‡							0·94
Sunken (AD)	0·93	0·19	1·14	0·40	35·76	<0·001	
Sunken (SD)	0·98	0·10	1·09	0·24	6·98	0·008	
Vomiting episodes*							0·97
> 0 episodes (AD)	0·88	0·17	1·06	0·70	17·92	<0·001	
> 9 episodes (SD)	0·63	0·45	1·15	0·82	3·79	0·29	
Respiration Depth*†							0·98
Deep (AD)	0·39	0·84	2·41	0·73	56·86	<0·001	
Deep (SD)	0·62	0·68	1·93	0·56	42·31	<0·001	
Radial Pulse†							0·74
Decreased (AD)	0·85	0·35	1·31	0·42	63·82	<0·001	
Absent (SD)	0·23	0·88	1·94	0·87	21·10	<0·001	
Urine Output†							0·91
Decreased/Dark (AD)	0·83	0·25	1·12	0·66	24·19	<0·001	
Minimal/None (SD)	0·41	0·74	1·54	0·81	11·40	0·003	
Mental Status‡							0·96
Lethargic/Unconscious (AD)	0·20	0·88	1·65	0·91	9·96	0·002	
Lethargic/Unconscious (SD)	0·44	0·84	2·68	0·67	54·20	<0·001	
Thirst‡							0·38
Drinks Eagerly (AD)	0·97	0·09	1·07	0·36	13·30	0·001	
Refuses/Unable to Drink (SD)	0·56	0·60	1·38	0·74	11·52	0·003	

*Clinical sign included in the Full NIRUDAK model
†Clinical sign included in Simplified NIRUDAK model
‡Clinical sign included in WHO IMAI algorithm

Test Characteristic Definitions

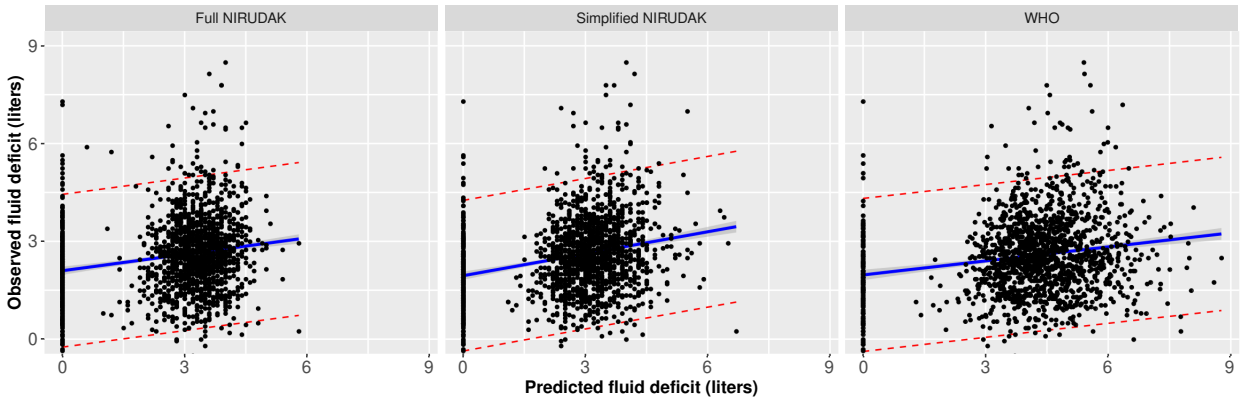
Sensitivity = Number of True Positives / (Number of True Positives + Number of False Negatives)

Specificity = Number of True Negatives / (Number of False Positives + Number of True Negatives)

Likelihood Ratio Positive = Sensitivity / (1 – Specificity)

Likelihood Ratio Negative = (1 – Sensitivity) / Specificity

RMSE figures for the fluid deficit of each model.



Legend:

Blue line: line of best fit
Shaded grey line around the blue line is the confidence interval for the fitted line
Red dotted line: 95% prediction interval around the line of best fit

NIRUDAK Study
Validation Study Demographics & Questionnaire Form

The researchers who are running this study collect descriptive information in order to describe the people who are asked to participate in the study. Please place an "X" next to the response that closely matches your opinion.

DEMOGRAPHICS

AGE
___ 18 – 24
___ 25 – 34
___ 35 – 44
___ 45 – 54
___ 55 – 64
___ 65+

GENDER
___ Male
___ Female

MARITAL STATUS
___ Single
___ Married
___ Divorced
___ Widowed

WORKING STATUS
__ Full Time
__ Part Time

EDUCATION
___ Diploma
___ College Degree
___ Master's Degree
___ Doctorate

CURRENT POSITION
___ Physician
___ Nurse
___ Other: _____

NUMBER OF YEARS OF EXPERIENCE AT CURRENT POSITION
___ Years

HOUSEHOLD MONTHLY INCOME
___ 0 – 10,000 taka
___10,001 – 50,000 taka
___ 50,001 – 100,000 taka
___ 100,000 taka +

APP USAGE

1. Have you used a smartphone in the past? ☐Yes ☐No
   If yes, how many years of smartphone experience do you have? _____ years
2. Do you have experience with an Android phone? ☐Yes ☐No
   If yes, experience with a Samsung phone? ☐Yes ☐No
3. Do you have a smartphone now? ☐Yes ☐No
   If yes, what type:
   ☐Android_Samsung ☐Android_Other – please specify_____
   ☐iPhone ☐ Other – please specify_____
4. Do you regularly engage with email on your phone? ☐Yes ☐No
5. Do you regularly engage with social media (e.g. Facebook) on your phone? ☐Yes ☐No
6. Do you regularly engage with clinical decision support (e.g. MDCalc) on your phone? ☐Yes ☐No

Version Date: 2022-01-15

NIRUDAK Surveys for App Evaluation

Protocol Title*:* Formative Research for the Development of mHealth tool using Age-Specific Algorithms for Dehydration Assessment in Patients with Acute Diarrhoeal Disease

Investigator's name*:* Dr. Nur H. Alam (PI, icddrb); Dr. Adam C. Levine and Dr. Rochelle Rosen

Instructions: This is a survey to better understand about your experience and opinions on using the NIRUDAK App. Please fill this out to the best of your ability There is no right or wrong answer. Your feedback will be kept confidential. You will only be identified with your ID number.

ID:_____ Date:_____

How much do you agree with the following statements:	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
I feel comfortable with using the app.	☐	☐	☐	☐	☐
Entering the data takes a long time.	☐	☐	☐	☐	☐
It will be easy to use the app when working with patients in the hospital.	☐	☐	☐	☐	☐
Using the app will allow me to give better care to the patients.	☐	☐	☐	☐	☐
The output page gives me useful information.	☐	☐	☐	☐	☐
I can easily use the recommended treatment for my patients.	☐	☐	☐	☐	☐
Please use the space to the left to write any general feedback about using the app in a clinical setting:					