**Title: Cost-effectiveness analysis of the NIRUDAK clinical diagnostic model for dehydration severity in patients over five years**

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**Key words:** cost-effectiveness, fluid resuscitation

**Meetings:** Preliminary results from this work were presented at the 21st International Conference on Emergency Medicine and the American Society for Tropical Medicine and Health 2022 Annual Meeting scientific conferences.

**DECLARATIONS**

**Funding:** Funding for data collection was provided through grants from the \*\*\*. The funders had no role in the study design, data collection or reporting processes.

**Conflict of Interest:** The authors have no conflicts of interest. The content of this manuscript is solely the responsibility of the authors and does not necessarily represent the views of \*\*\* or any governmental bodies or academic organizations.

**Abstract**

**Objective:** To compare the cost-effectiveness of the World Health Organization algorithm and the NIRUDAK model for treatment of severe dehydration due to diarrhea in patient over five years of age.

**Methods:**

**Results:**

**Conclusions:**

**Introduction**

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 lead to dehydration, and existing care guidelines, namely from the World Health Organization (WHO), base treatment on categorical estimates for fluid resuscitation.

The Novel, Innovative Research for Understanding Dehydration in Adults and Kids (NIRUDAK, meaning dehydrated in Bangla) model predicts percentage dehydration (fluid deficit) in individuals with acute diarrhea to better target treatment and avoid the potential sequelae of over or under resuscitation. Unlike the WHO Integrated Management of Adolescent and Adult Illness (IMAAI) algorithm, which is based on the number of symptoms of dehydration exhibited by the patient, the NIRUDAK model employs clinical measurements as inputs into a machine learning model (2). Previous analysis has demonstrated that the NIRUDAK outperforms the WHO algorithm in terms of accuracy and reliability (3).

The aim of this study was to compare the cost-effectiveness of the NIRUDAK model to WHO algorithm in treating patients over five years of age experiencing acute dehydration due to diarrhea. Patients classified has having severe dehydration require treatment with intravenous (IV) fluids, while patients categorized as having some dehydration can be treated with less expensive oral resuscitation fluid, and patients triaged to the no dehydration category need no treatment (1). Thus, the increased accuracy of the NIRUDAK model, as compared to the WHO algorithm, may confer significant cost-saving benefits, as IV fluid and associated supplies are much more expensive than oral resuscitation fluid, which may be particularly significant in low-resource settings (4). This study represents the first comparison of the cost effectiveness of the NIRUDAK model and the WHO algorithm.

**Materials and Methods**

*Study Procedures*

Data were collected as part of the NIRUDAK study, a prospective cohort study of patients over 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 (1). Patients were randomly screened for participation in the study upon arrival to the hospital. Local nurses independently assessed patients for symptoms of dehydration on arrival and continued to collect and record patient weight and amount of fluid administered until the patients were discharged. Patient were treated using local protocols and clinical gestalt (not the WHO algorithm or NIRUDAK model) (1). The true dehydration status (percent dehydration) was determined based on the patient’s weight at the time of admission to the hospital and their “post-illness” weight at the time of discharge from the hospital. Calculated percent dehydration was stratified into three categories of dehydration severity — no, some, and severe — based on current standards in the literature (5–7). The WHO algorithm and NIRUDAK model both attempt to predict patients’ true dehydration status by classifying patients into one of three predicted categories of dehydration severity — no, some, or severe — analogous to the true dehydration categories of dehydration severity.

*Data Analysis*

A decision tree (Figure 1) was constructed to demonstrate expected DALYs and expected costs for each possible combination of true dehydration status and model-assigned dehydration status. Expected cost was calculated for each branch of the decision tree by taking the mean cost of all patients in that branch and multiplying by branch probability. Costs for treatment were calculated using data from icddr,b. Total costs for each individual patient in the study were calculated based on the type and total amount of fluid each patient received, associated equipment costs, length of stay at the hospital, and wages lost while in the hospital. All costs were received directly from icddr,b. All exchange rate conversions from Bangladeshi taka (BDT) to United States dollar (USD) were conducted using data from the World Bank (8,9). Costs are summarized in Table 1.

DALYs were calculated as a sum of years of life lost due to illness and years lived with disability. Per convention, years of life lost for each patient were based on Japanese life tables which outline life expectancies at specified ages (10,11). Years lived with disability were calculated based on estimates from the Global Burden of Disease study and prior literature on the effects of over- and undertreatment of severe dehydration (12–14). Expected DALYs for each branch of the decision tree were calculated by taking the mean number of DALYs for all patients in that branch and multiplying by the branch probability.

**[QUESTION FOR JP — INCLUDE TABLE DEMONSTRATING DALY CALCULATION?]**

For the base case analysis, the probability of death from serious cases of undertreatment (i.e., if a patient had severe dehydration but was predicted to have some or no dehydration) and probability of death from serious cases of overtreatment (e.g., if the patient has some or no dehydration but was predicted to have severe dehydration) were estimated based on clinical input from physicians who have practiced at icddr,b and on prior studies of undertreatment in the context of dehydration due to diarrheal illness (14). An initial incremental cost-effectiveness ratio (ICER) was calculated using these data.

Two-way sensitivity analyses were then conducted; here, the probability of death from under- and overtreatment were both taken as variable. Per WHO recommendations, two willingness-to-pay thresholds were used in analysis: two- and three-times the 2019 Bangladeshi gross domestic product (GDP) per capita in USD (15).

**[JP: METHODS — PSA & COST-EFFECTIVENESS ACCEPTABILITY CURVE/FRONTIER METHODS]**

This study has been approved by the Ethical Review Committee of icddr,b and the Rhode Island Hospital Institutional Review Board.

**Results**

Median age for enrolled patients was 35. Median household income was $447. Children, adults, and elderly patients each account for about one-third of our study population; age categories were based on WHO classification (16,17). Demographic information is summarized in Table 2.

**[JP: RESULTS — PSA & COST-EFFECTIVENESS ACCEPTABILITY CURVE/FRONTIER]**

**Discussion**

*Limitations*

*Future Directions*

**Conclusion**

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