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

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**DECLARATIONS**

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**Abstract** (draft from preliminary results)

**Objective:**

**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. 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 algorithms, namely from the WHO, base treatment around categorical estimates for fluid resuscitation.

The NIRUDAK model, built on machine learning algorithms, predicts 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 NIRUDAK outperforms the WHO algorithm in terms of accuracy and reliability.

The aim of this study was to compare the cost-effectiveness of the NIRUDAK model to WHO guidelines in treating patients over five years of age experiencing acute dehydration due to diarrhea. This study represents the first comparison of the cost effectiveness of the NIRUDAK model and the WHO algorithm.

**Materials and Methods**

*Study Design and Setting*

*Study Participants*

*Staff Training and Oversight (if relevant)*

*Study Procedures*

*Data Analysis*

STATA Version 15.0 (Stata Corp; College Station, USA) was used for initial analysis of intervention costs. The study population was stratified based on the exposure of interest as \*\*\*. R was used for the cost effectiveness-analysis.

Variables were described using frequencies with percentages or medians with associated interquartile ranges (IQR). Characteristics based on the exposure categories were compared using Pearson *X2* tests for categorical variables and by Mann-Whitney or t-tests for non-normally and normally distributed continuous variables, respectively.

Multiple imputation was used for missing data. A total of \*\*% of eligible variables had at least 1 missing data, and \*\*\*% of patients had at least 1 missing variable. The percentage of missing data per variable ranged from \*\*\* to \*\*\*%, with a missing completely at random pattern (test of Little, P=\*\*\*). \*\*\* cases in which information about \*\*\* was missing were used for the imputations, but not in the final analysis.

For the purposes of this analysis, culture sensitivities with the result of intermediate were grouped with those with result of resistant. We grouped antimicrobials according to class because pathogens generally exhibit the same resistance profile for all antimicrobials in a given class (i.e., a pathogen will either be resistant or sensitive to all first generation cephalosporins tested). If a pathogen was resistant to any member of a class, it was classified as resistant. First-generation cephalosporins included cefadroxil, cefazolin and cephalexin; second-generation cephalosporins included cefotetan, cefoxitin, cefuroxime; third-generation cephalosporins included cefotaxime, cefixime, ceftazidime and ceftriaxone; and quinolones included ciprofloxacin, gemifloxacin, levofloxacin and norfloxacin. We did not include cephalothin in the first-generation cephalosporin group because, in our data and in other studies, resistance to cephalothin is inconsistent with resistance to other first-generation cephalosporins.(2) We grouped amoxicillin and ampicillin together (from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4808618/pdf/nihms746647.pdf>

Logistic regression models were used test the independent association between demographic and clinical characteristics and resistance to narrow-spectrum antimicrobials.

Univariate regression was performed for patient characteristics to evaluate for differences between those who received \*\*\* who did not for the primary outcome. Magnitudes of effects were quantified using regression models to yield unadjusted and adjusted odds ratios (aOR) with 95% confidence intervals (CI). For the final model gender, \*\*\* were included *a priori* based on prior literature. \*\*\* were included given their effect on the outcome of \*\* document in acute care settings. A sensitivity analysis was run evaluating the association between \*\*\* and \*\*\* primary outcome.

**Results**

* Need clinical intuition on the range of values that is clinically reasonable (death from overtreatment vs. undertreatment) — Dr Levine
* Table 1: population characteristics (if need to cut, refer to prior NIRUDAK papers)
* Figure 1: decision tree
* Figure 2: 2 way sensitivity analysis — Jonah will take care of
* Table 2: results for base case & PSA — Jonah will take care of
  + Total DALYs
  + Incremental DALYs
  + Total Costs
  + Incremental Costs
  + ICER

Anagha holds off on writing (not before Step 1)

**Enrollment and Baseline Characteristics**

**Table 1.**

|  |  |  |  |
| --- | --- | --- | --- |
| Variable | n (%) | *P* value |  |
| Sex |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
| Age |  |  |  |
| Stool Culture |  |  |  |
| E. coli PCR |  |  |  |
| Resistance by Drug Class |  |  |  |
| Multiple Drug Resistance (MDR) |  |  |  |

* **A.** An introduction to the analysis you carried out (e.g., state that you ran a binomial logistic regression).
* **B.** Information about your sample, including any missing values (e.g., sample size).
* **C.** An examination of all the assumptions of the binomial logistic regression, including any remedies that were taken for violations of any of these assumptions.
* **D.** The use of measures, such as the Hosmer-Lemeshow test, to assess how well the model fits the data.
* **E.** The regression coefficients and/or odds ratios for your binomial logistic regression model, including which are statistically significant, and 95% confidence intervals.

(from: <https://statistics.laerd.com/stata-tutorials/binomial-logistic-regression-using-stata.php>)

You could write up the results as follows: A binomial logistic regression was conducted to determine the effects of variables\*\*\* on the presence of multi-drug resistance. \*\*\*Variable 1\*\*\*\* statistically significantly predicted MDR (*p* = \*\*\*), but \*\*\*variable 2\*\*\* did not (*p* = \*\*\*).

|  |  |  |  |
| --- | --- | --- | --- |
| Characteristic | Odds Ratio | 95% CI | P value |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
| *Abbreviations: CI, confidence interval* | | | |

**Discussion**

* Can list out key takeaways

Paragraph 1: The NIRUDAK model is more cost-effective than WHO guidelines in this study population. The results of the current study suggest an association between \*\*\* in this population.

This association may be due to unmeasured confounding factors or properties of the therapies involved. Given the retrospective design of this research it is hypothesis generating and further study regarding in these and similar limited resource settings is needed.

*Limitations*

*Future Directions*

**Conclusion**

Restate main findings again and also next step for research and implications for world at large.

**REFERENCES**