Check for updates

RESEARCH ARTICLE

REVISED **Derivation and internal validation of a data-driven prediction model to guide frontline health workers in triaging children under-five in Nairobi, Kenya** [version 3; peer review: 2 approved]

Alishah Mawji [1,2], Samuel Akech [3], Paul Mwaniki [3], Dustin Dunsmuir[4], Jeffrey Bone [5], Matthew O. Wiens [2], Matthias Görges [1], David Kimutai[6], Niranjan Kissoon [2,7], Mike English [3,8], Mark J. Ansermino [1,2]

[1]Department of Anesthesiology, Pharmacology & Therapeutics, University of British Columbia, Vancouver, British Columbia, V6T1Z3, Canada
[2]Centre for International Child Health, BC Children's Hospital Research Institute, Vancouver, British Columbia, V5Z4H4, Canada
[3]Kenya Medical Research Institute/Wellcome Trust Research Programme, Nairobi, Kenya
[4]Digital Health Innovation Lab, BC Children's Hospital Research Institute, Vancouver, British Columbia, V5Z4H4, Canada
[5]Department of Obstetrics and Gynaecology, University of British Columbia, Vancouver, British Columbia, V6T1Z4, Canada
[6]Mbagathi County Referral Hospital, Nairobi, Kenya
[7]Department of Pediatrics, University of British Columbia, Vancouver, British Columbia, V6H3V4, Canada
[8]Centre for Tropical Medicine and Global Health, Nuffield Department of Clinical Medicine, University of Oxford, Oxford, UK

**Open Peer Review**

**Reviewer Status** ✓✓

|  | Invited Reviewers | |
|---|---|---|
|  | **1** | **2** |
| **version 3** (revision) 19 Apr 2021 | ✓ report | ✓ report |
| **version 2** (revision) 15 Dec 2020 | ✓ report | ? report |
| **version 1** 14 Aug 2019 | ✗ report | |

1. **Andrew Argent** [iD], University of Cape Town, Cape Town, South Africa

**Abstract**

**Background:** Many hospitalized children in developing countries die from infectious diseases. Early recognition of those who are critically ill coupled with timely treatment can prevent many deaths. A data-driven, electronic triage system to assist frontline health workers in categorizing illness severity is lacking. This study aimed to develop a data-driven parsimonious triage algorithm for children under five years of age.

**Methods:** This was a prospective observational study of children under-five years of age presenting to the outpatient department of Mbagathi Hospital in Nairobi, Kenya between January and June 2018. A study nurse examined participants and recorded history and clinical signs and symptoms using a mobile device with an attached low-cost pulse oximeter sensor. The need for hospital admission was determined independently by the facility clinician and used as the primary outcome in a logistic predictive model. We focused on the selection of variables that could be quickly and easily assessed by low skilled health workers.

**Results:** The admission rate (for more than 24 hours) was 12% (N=138/1,132). We identified an eight-predictor logistic regression model including continuous variables of weight, mid-upper arm circumference, temperature, pulse rate, and transformed oxygen saturation, combined with dichotomous signs of difficulty breathing, lethargy, and inability to drink or breastfeed. This model predicts overnight hospital admission with an area under the receiver operating characteristic curve of 0.88 (95% CI 0.82 to 0.94). Low- and high-risk thresholds of 5% and 25%, respectively were selected to categorize participants into three triage groups for implementation.
**Conclusion:** A logistic regression model comprised of eight easily understood variables may be useful for triage of children under the age of five based on the probability of need for admission. This model could be used by frontline workers with limited skills in assessing children. External validation is needed before adoption in clinical practice.

**Keywords**

sepsis, prediction, risk, model, triage, children, developing countries

2. **Babar Hasan** (iD), Aga Khan University, Karachi, Pakistan

Any reports and responses or comments on the article can be found at the end of the article.

**KEMRI wellcome** This article is included in the KEMRI | Wellcome Trust gateway.

REVISED **Amendments from Version 2**

This revised paper differs from the previous version as it clarifies that we do not claim superiority of the developed model over ETAT, or suggest it should replace existing triage systems. The model has the potential of impact due to data-driven risk prediction, device based acquisition and simplicity of predictor variables with high accuracy. External validation is necessary prior to drawing conclusions regarding the clinical utility of the model.

**Any further responses from the reviewers can be found at the end of the article**

## Introduction

Infectious diseases contribute to most deaths of children under five worldwide[1]. Sub-Saharan Africa has the highest under-five mortality rate in the world, with one child in 13 dying before his or her fifth birthday[1]. Death from infectious diseases is commonly due to a shared final pathway: sepsis, a dysregulated immune response leading to multi-organ dysfunction[2]. Sepsis mortality rates in Africa are eight times higher than North America[3].

More than half the cases of infectious disease-related child mortality are preventable through prompt diagnosis and early initiation of emergency treatment[1]. Triage, the practice of prioritizing patients for treatment based on the severity of illness, is critical to ensuring timely treatment[4]. Triage systems in low-income settings continue to face challenges including limited numbers of expert clinicians and lack of adequately trained health workers[4,5].

The World Health Organization (WHO) advocates the use of the Emergency Triage Assessment and Treatment (ETAT) guidelines to triage sick children in resource limited settings. The ETAT system is widely adopted in low- and middle-income countries (LMICs), where effective implementation has seen reductions in inpatient child mortality rates in Malawi and Sierra Leone[6,7]. However, ETAT relies on training, memorization, and clinical competence of the triage examiner rendering implementation difficult, and uptake uneven in many LMICs[5,8,9]. ETAT is based on clinical decision rules which may limit generalizability, while the manual mechanisms of implementation provide little opportunity for monitoring and feedback, and there is limited ability to update it [10]. Additionally, at hospitals affected by staff shortages, wait times to a formal ETAT triage are lengthy (can take multiple hours).

One solution to these shortcomings is the use of a digital, data-driven approach to strengthen triage systems at first contact. Digital health platforms can facilitate quality improvement, while data-driven algorithms are easily updateable with emergence of new information and can be optimized to meet the specific needs of each setting. The purpose of this study was to develop a flexible, logistic triage model for children under five years of age that can be easily integrated into a digital platform and is operable with minimal clinical training. The digital triage tool can be used alongside ETAT to rapidly identify children at risk of developing severe infections, including sepsis upon arrival to the hospital.

## Methods

This report was written in accordance with STROBE guidelines[11]. A completed STROBE checklist is available[12].

### Ethics statement

This study was conducted at the Kenya Medical Research Institute (KEMRI)-Wellcome Trust Research Programme (KWTRP), and ethics approval was obtained by the KEMRI's scientific and ethics review committee (certificate number, SERU/3407). The initial approval date was May 16th, 2017. Parents or caregivers of eligible children provided written informed consent prior to enrollment by the study nurse. Consent was deferred in emergency cases and taken after the child was stable to avoid introducing any delays.

### Population

This prospective observational study was conducted between January and June 2018 at the pediatric outpatient department of Mbagathi County Referral hospital in Nairobi, Kenya. Mbagathi County Hospital is a first-referral level (district) hospital located in Nairobi in the neighbourhood of a high-density urban informal settlement. During a typical working shift, the outpatient area has nutritionists who take anthropometric measurements, a single nurse who conducts triage, plus providing treatments such as oral rehydration, and another nurse in the emergency area who administers emergency treatment, and one or two non-degree trained clinicians (clinical officers) who provide consultation, prescribe treatments, and make decisions on admissions. The outpatient department (OPD) serves over 20,000 children per year and admits approximately 2,500 pediatric patients per year.

### Eligibility

Children aged 2–60 months seeking treatment for an acute illness at Mbagathi hospital on weekdays between 8:00 am and 5:00 pm were eligible for enrollment. Patients coming for elective procedures, such as elective surgery or for cardiac follow up, were excluded from the study. Patients presenting for elective care or treatment for chronic illnesses were excluded from the study.

### Study procedures

A study nurse competent to provide care and attend to emergencies was recruited and trained on study specific procedures and research ethics. The study nurse was expected to assist with emergency resuscitation if required but not expected to perform routine duties. Following introduction and orientation to hospital staff, the study nurse was stationed at the OPD, alongside hospital staff (nurses and clinicians). Children who presented to the OPD during study hours that did not require emergency treatment were screened for eligibility by the study nurse. For emergency cases (determined by hospital staff), treatment was started immediately, and data collection by the study nurse began only after emergency treatment initiation.

After consent and enrollment, the study nurse obtained patient history of presenting illness and performed clinical examination using a standardised checklist. The study nurse then entered all observations into a mobile data collection app on a tablet. This app recorded automated measurement of oxygen saturation and heart rate data using a pulse oximeter (LionsGate Technologies, Inc.) attached to the tablet and respiratory rate via the embedded RRate application[13]. A total of 17 continuous variables and 37 categorical variables were selected for capture (54 in total), including patient demographics, anthropometric measurements, vitals, and clinical signs and symptoms (Table 1). The patient was then reviewed by the hospital clinician on duty at the OPD who, without access to the study data, assessed the child, allocated treatment, and independently decided on whether or not to admit the patient or continue outpatient management. The study nurse recorded the clinician's decision on the tablet. Study procedures did not delay care.

**Table 1. Candidate predictor variables (N=54).** Transformed oxygen saturation = $4.314 \times \log_{10}(103.711 - SpO_2) - 37.315$
Abbreviation: AVPU: Alert, Voice, Pain, Unresponsive.

| Patient Characteristics |
| --- |
| Age in months |
| Male sex |
| Urgent referral status |
| Data collected after emergency treatment |
| Length of illness in days prior to admission |
| **Anthropometrics** |
| Weight in kg |
| Height in cm |
| Weight-for-height z-score |
| Weight-for-age z-score |
| Left mid-upper arm circumference in centimeters |
| **Vitals** |
| Axillary temperature in degrees Celsius |
| Pulse rate |
| Respiratory rate |
| Oxygen saturation (raw) |
| Oxygen saturation (transformed based on saturation gap*) |
| **Respiratory distress** |
| Chest indrawing |
| Apnoea |
| Central cyanosis |
| Difficulty breathing (parent reported) |
| Obstructed breathing |
| Nasal flaring |

| Patient Characteristics |
| --- |
| Grunting |
| Wheezing |
| Stridor |
| Acidotic breathing |
| Head nodding/bobbing |
| Cough |
| Cough duration in days prior to admission (parent reported) |
| **Circulation** |
| Capillary refill time ≥ 2 seconds |
| Weak, rapid pulse |
| Pallor (palmar, oral or conjunctival) |
| Skin warm at elbow or shoulder |
| **Neurological** |
| AVPU (patient does not respond to voice, pain or is unresponsive) |
| Difficulty feeding (parent reported) |
| Cannot drink or breastfeed |
| Irritability/restlessness |
| Convulsing now, actively |
| Convulsions (parent reported, history of convulsions) |
| Convulsion frequency in the past 24 hours (parent reported) |
| Newly onset hemiparesis |
| **Gastrointestinal/Genitourinary** |
| Diarrhoea (parent reported) |
| Diarrhoea duration in days prior to arrival (parent reported) |
| Vomiting (parent reported) |
| Vomiting frequency in the past 24 hours (parent reported) |
| Jaundice |
| **Malnutrition** |
| Visible severe wasting |
| Oedema of Kwashiorkor on feet, knees or face |
| **Dehydration** |
| Lateral abdominal skin pinch (delayed elasticity observed) |
| Sunken eyes |
| **Infection** |
| Fever (Axillary temperature > 38°C) |
| Fever duration in days prior to admission (parent reported) |
| **Trauma** |
| Uncontrolled bleeding |
| **Other** |
| Lethargy/reduced activity level (parent reported) |
| Appears in severe pain |

For those children who were sent home, a telephone interview was conducted 14 days post-discharge to determine to determine 1) mortality status, 2) whether the child completely recovered from the illness, 3) if the child returned to a hospital or health center seeking help for the same illness, 4) if the child was admitted to a hospital or health center for the same illness.

## Outcome

The primary outcome was admission to hospital for greater than or equal to 24 hours. After assessing the child, the attending clinician independently decided on whether to admit the patient for further care in the hospital.

## Data management

Each participant was assigned a unique study identification number upon registration. Clinical observations and vital sign measurements were collected with a custom, password protected application, on a Dell Venue 7® tablet and uploaded every day to a secure REDCap database[14], hosted on a KWTRP server.

## Statistical analysis

All statistical analyses were performed using R (3.5.1)[15].

## Candidate predictor variables

Candidate predictor variables were selected based on a combination of a literature review, availability, and ease of measurement in resource-limited facilities[16]. A physiological transformation of the oxygen saturation (using a virtual shunt concept) was used to address the non-linear relation between oxygen saturation and impairment of gas exchange. Transformation was based on the saturation gap [$49.314\times \log_{10}(103.711 - SpO2) - 37.315$], which has been demonstrated to improve the fit of logistic regression models[17]. This transformed $SpO_2$ was not available to the clinician but only calculated during analysis. Anthropometric z-scores were also calculated during analysis (computed via the zscorer package in R; v6.0-79, https://cran.r-project.org/web/packages/zscorer/zscorer.pdf). All variables were assessed using univariate logistic regression to estimate their level of association with the outcome.

## Missing data

Participants missing greater than 50% of predictors or missing the outcome variable were excluded from multivariate analysis. The remainder of missing data were assumed to be missing at random and imputed using multiple imputations by chained equations (MICE)[18]. Ten imputed data sets were created and checked visually for similarity. Model development procedures were performed separately on each imputed data set and the results were pooled using Rubin's Rules[19]. If missingness was minimal, measures to evaluate model performance would be performed on one randomly selected imputed data set.

## Model development

Candidate predictors with less than 10 events per variable were not selected for inclusion in the final model to reduce the potential of overfitting[20]. When similar information was collected both continuously and categorically, continuous variables were preferred[20]. Continuous variables were assessed graphically for linear associations with the outcome and transformed where appropriate. Predictors to be included in the final model were selected using recursive feature elimination (RFE)[21] with repeated 10-fold cross validation (computed via the caret package in R; v6.0-79)[22]. RFE eliminates features by fitting the model multiple times and at each step, removing the weakest predictors, determined by the coefficient attribute of the fitted model. The best subset of predictors is based on the model with the lowest cross validation error. Further inclusion into the list of variables was made based on clinical knowledge. The list of predictors included in the final model was checked for collinearity indicated as variance inflation factor > 5 or absolute correlation coefficient > 0.9.

## Model discrimination

Model performance was primarily estimated as the area under the receiver operating curve (AUC). Low- and high-risk thresholds were selected to stratify participants into three triage groups (non-urgent, priority, emergency). The low-risk threshold was selected with the goal to maximize sensitivity in order to limit misclassification of emergency and priority cases as non-urgent (avoiding false-negatives). Specificity was used for selection of the high-risk threshold to maximize correct classification of emergency cases (avoiding false positives) in order to optimize resource utilization such that children in need of immediate treatment do not experience delays. A risk stratification table was used to evaluate model classification accuracy, defined as the ability of the model to separate the population into risk strata, such that cases with and without outcomes are more likely to be in the higher and lower risk strata, respectively. Performance characteristics (sensitivity, specificity, positive and negative predictive values, and positive and negative likelihood ratios) were calculated for each triage group. A five-time repeated 10-fold cross validation procedure was applied to all performance evaluation measures and results were pooled to provide a single estimate[20].

## Model calibration

Calibration was assessed with the GiViTI calibration belt and the associated likelihood based test[23–25]. The calibration belt is a graphical representation of the relationship between the estimated probabilities and observed outcome rates of a fitted polynomial logistic regression model.

# Results

## Participants

Over the 6-month recruitment period, 10,621 children were seen at the OPD and a sample of 1,132 participants were enrolled in the study (Figure 1). Of these, 23 were excluded from multivariable analysis as they were older than five years (N=5), missing more than half of the predictor variables (N=5) or missing the outcome (N=13). Demographic data, alongside all other variables measured, are available as *Underlying data*[26].

The median age of admitted participants (N=138) was 13 months (IQR 8 to 23), compared to a median age of 16 months (IQR 10 to 30) for discharged participants (N=971) (Table 2). The proportion of males in the admitted and discharged groups
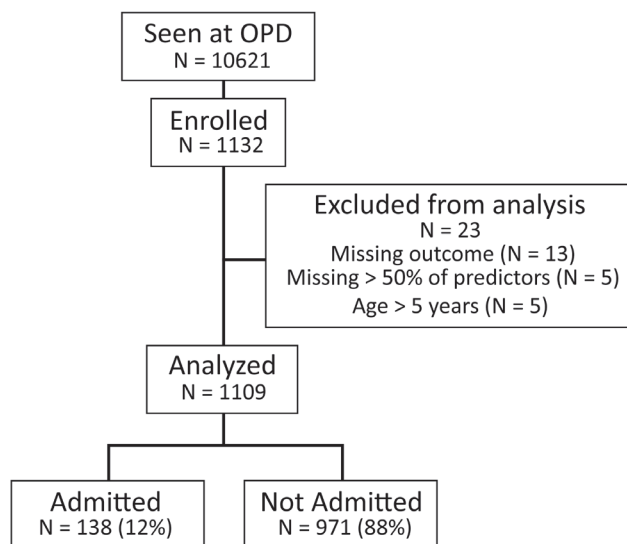
**Figure 1. Flowchart of study population and distribution of outcomes.** OPD, outpatient department.

was 62% and 45%, respectively. Rate of overnight hospital admission was 12% (N=138), and the most common reason for admission was pneumonia (N=84) (Table 3). Of the admitted participants, 37% were urgent referral cases and 86% were consented after emergency treatment (Table 2). Results from the 14 day follow up call revealed that 837 (86%) of discharged participants completely recovered from the illness and 89 (9%) returned to a hospital or health center for reassessment, of which 24 were admitted (Table 4). Mortality outcomes for both the admitted participants (N=4) and discharged participants (N=2) were minimal (Table 4).

Three categorical variables, apnoea, bleeding, and newly onset hemiparesis, had events per variable below 10 and were not included in multivariable analysis (Table 2). Missing observations were minimal (≤ 3% missing per predictor) and results were near identical across each of the 10 imputed data sets (Table 2). Univariate analysis revealed that many variables had a significant association with the outcome (Table 2). Of these variables, data collected after emergency treatment had the highest AUC: 0.80 (95% CI 0.74 to 0.85).

**Table 2. Predictor variable distribution for admitted and non-admitted children.** *Values include medians (quartiles) for continuous predictors and number of children (percentage) for dichotomous predictors. OR, odds ratio; AUC, area under the curve.

| Predictor Variables | Missing | Admission Required* | Admission not required* | OR (95% CI) | AUC (95% CI) | p Value |
|---|---|---|---|---|---|---|
| **Continuous (N = 17)** | | | | | | |
| Age (months) | 0 | 13 (8-23) | 17 (2-30) | 0.97 (0.96 to 0.99) | 0.61 (0.56 to 0.66) | <0.001 |
| Length of illness (days) | 4 | 3 (2-7) | 4 (2-7) | 1.00 (0.96 to 1.03) | 0.52 (0.47 to 0.57) | 0.827 |
| Weight (kg) | 6 | 8 (6-10) | 10 (8-12) | 0.21 (0.03 to. 6.00) | 0.69 (0.62 to 0.73) | <0.001 |
| Height (cm) | 14 | 71 (65-80) | 77 (70-88) | 0.04 (0.01 to 4.92) | 0.64 (0.59 to 0.69) | <0.001 |
| Left mid-upper arm circumference (cm) | 17 | 12 (12-14) | 14 (13-15) | 0.64 (0.57 to 0.71) | 0.68 (0.64 to 0.73) | <0.001 |
| Axillary temperature (°C) | 8 | 37 (36-38) | 36 (36-37) | 2.24 (1.87 to 2.69) | 0.71 (0.65 to 0.76) | <0.001 |
| Oxygen saturation (raw) | 35 | 93 (87-97) | 95 (92-97) | 0.95 (0.92 to 0.97) | 0.58 (0.52 to 0.64) | <0.001 |
| Oxygen saturation (transformed) | 35 | 13 (3-23) | 9 (3-15) | 1.03 (1.01 to 1.05) | 0.58 (0.52 to 0.64) | <0.001 |
| Respiratory rate (breaths per minute) | 6 | 54 (40-67) | 43 (36-54) | 1.04 (1.03 to 1.05) | 0.65 (0.60 to 0.70) | <0.001 |
| Pulse rate (beats per minute) | 35 | 155 (136-175) | 140 (125-156) | 1.02 (1.02 to 1.03) | 0.64 (0.59 to 0.70) | <0.001 |
| Weight-for-age z-score | 11 | -1 (-2-0) | -1 (-2-0) | 0.93 (0.84 to 1.04) | 0.46 (0.41 to 0.51) | 0.200 |
| Weight-for-height z-score | 18 | 0 (-2-0) | 0 (-1-0) | 0.67 (0.58 to 0.77) | 0.41 (0.36 to 0.47) | <0.001 |
| Fever duration (days) | 1 | 3 (2-5) | 3 (1-5) | 1.13 (1.08 to 1.18) | 0.69(0.65 to 0.73) | <0.001 |
| Vomiting frequency (per 24 hours) | 1 | 3 (2-4) | 3 (2-3) | 1.09 (1.00 to 1.20) | 0.52 (0.48 to 0.58) | 0.053 |
| Diarrhoea duration (days) | 0 | 2 (2-5) | 3 (2-5) | 1.05 (0.99 to 1.20) | 0.55 (0.51 to 0.60) | 0.078 |
| Convulsion frequency (per 24 hours) | 4 | 2 (2-3) | 1 (1-3) | 1.83 (1.64 to 2.08) | 0.57 (0.54 to 0.60) | <0.001 |
| Cough duration (days) | 1 | 3 (2-5) | 4 (2-7) | 0.97 (0.99 to 1.12) | 0.48 (0.43 to 0.53) | 0.191 |

| Predictor Variables | Missing | Admission Required* | Admission not required* | OR (95% CI) | AUC (95% CI) | p Value |
|---|---|---|---|---|---|---|
| **Dichotomous (N = 37)** | | | | | | |
| Urgent referral | 3 | 51 (37) | 23 (2) | 5.30 (3.58 to 7.81) | 0.65 (0.56 to 0.74) | <0.001 |
| Data collected after emergency treatment | 7 | 120 (86) | 265 (23) | 17.06 (10.55 to 29.09) | 0.80 (0.74 to 0.85) | <0.001 |
| Fever | 2 | 99 (71) | 344 (35) | 4.53 (3.09 to 6.76) | 0.67 (0.60 to 0.75) | <0.001 |
| Vomiting | 3 | 52 (37) | 338 (34) | 1.14 (0.79 to 1.65) | 0.51 (0.44 to 0.59) | 0.473 |
| Diarrhoea | 2 | 52 (37) | 261 (27) | 1.67 (1.15 to 2.42) | 0.56 (0.48 to 0.63) | <0.01 |
| Convulsions | 6 | 25 (18) | 30 (3) | 6.61 (3.71 to 11.68) | 0.57 (0.48 to 0.67) | <0.001 |
| Convulsing now | 10 | 3 (2) | 8 (1) | 3.60 (0.95 to 11.58) | 0.51 (0.42 to 0.60) | <0.050 |
| Cough | 3 | 92 (66) | 646 (66) | 1.00 (0.69 to 1.47) | 0.44 (0.38 to 0.51) | 0.999 |
| Lethargy | 10 | 121 (87) | 452 (46) | 8.81 (5.31 to 15.62) | 0.70 (0.65 to 0.75) | <0.001 |
| Indrawing | 10 | 54 (39) | 19 (2) | 32.24 (18.58 to 58.21) | 0.69 (0.59 to 0.78) | <0.001 |
| Difficulty breathing | 2 | 82 (59) | 240 (24) | 4.51 (3.13 to 6.56) | 0.67 (0.60 to 0.75) | <0.001 |
| Irritability or restlessness | 12 | 64 (46) | 172 (18) | 4.05 (2.79 to 11.58) | 0.64 (0.56 to 0.73) | <0.001 |
| Cannot drink or breastfeed | 10 | 49 (35) | 81 (8) | 0.15 (0.11 to 0.24) | 0.63 (0.55 to 0.73) | <0.001 |
| Nasal flaring | 9 | 40 (29) | 24 (2.4) | 16.12 (9.40 to 28.21) | 0.63 (0.54 to 0.73) | <0.001 |
| Pallor | 12 | 52 (37) | 133 (14) | 3.85 (2.60 to 5.67) | 0.62 (0.53 to 0.71) | <0.001 |
| Appears in severe pain | 10 | 40 (29) | 58 (6) | 6.43 (4.07 to 10.11) | 0.61 (0.52 to 0.70) | <0.001 |
| Lateral abdominal skin pinch | 10 | 30 (22) | 53 (5) | 4.81 (2.93 to 7.82) | 0.58 (0.49 to 0.67) | <0.001 |
| Weak, rapid pulse | 12 | 27 (19) | 37 (4) | 0.16 (0.10 to 0.27) | 0.58 (0.49 to 0.67) | <0.001 |
| Sunken eyes | 11 | 42 (30) | 163 (17) | 2.17 (1.45 to 3.22) | 0.57 (0.48 to 0.65) | <0.001 |
| Acidotic breathing | 10 | 21 (15) | 24 (2) | 6.80 (3.66 to 12.52) | 0.56 (0.47 to 0.66) | <0.001 |
| Skin warm | 10 | 20 (14) | 25 (3) | 6.17 (3.30 to 11.36) | 0.56 (0.47 to 0.65) | <0.001 |
| Alert, Verbal, Pain, Unresponsive scale | 12 | 16 (12) | 17 (2) | 7.37 (3.60 to 15.02) | 0.55 (0.46 to 0.64) | <0.001 |
| Difficulty feeding | 2 | 78 (56) | 476 (49) | 1.37 (0.96 to 1.96) | 0.54 (0.48 to 0.60) | 0.089 |
| Grunting | 10 | 26 (19) | 106 (11) | 1.90 (1.16 to 3.00) | 0.54 (0.45 to 0.63) | <0.010 |
| Visible severe wasting | 10 | 14 (10) | 23 (2) | 4.66 (2.28 to 9.19) | 0.54 (0.45 to 0.63) | <0.001 |
| Wheezing | 9 | 26 (19) | 249 (25) | 0.68 (9.40 to 28.21) | 0.53 (0.47 to 0.60) | 0.090 |
| Male Sex | 4 | 85 (62) | 440 (45) | 1.27 (0.88 to 1.82) | 0.53 (0.47 to 0.59) | 0.206 |
| Head nodding/bobbing | 10 | 8 (6) | 13 (1) | 4.54 (1.77 to 10.98) | 0.52 (0.43 to 0.61) | <0.001 |
| Oedema | 0 | 7 (5) | 15 (2) | 14.28 (1.47 to 11.97) | 0.52 (0.43 to 0.61) | <0.010 |
| Central cyanosis | 9 | 4 (3) | 13 (1) | 2.20 (0.61 to 6.33) | 0.51 (0.42 to 0.60) | 0.173 |
| Jaundice | 10 | 4 (3) | 15 (2) | 1.90 (0.54 to 5.34) | 0.51 (0.42 to 0.60) | 0.259 |
| Newly onset hemiparesis | 11 | 1 (1) | 6 (1) | 2.37 (0.34 to 10.39) | 0.50 (0.41 to 0.59) | 0.294 |
| Obstructed Breathing | 9 | 6 (4) | 38 (4) | 1.11 (0.41 to 2.51) | 0.48 (0.40 to 0.57) | 0.805 |
| Stridor | 8 | 9 (6) | 59 (6) | 1.08 (0.49 to 2.12) | 0.48 (0.40 to 0.56) | 0.836 |
| Capillary refill time (≥ 2 seconds) | 11 | 27 (19) | 31 (3) | 7.38 (4.23 to 12.83) | 0.58 (0.48 to 0.68) | <0.001 |
| Apnoea | 9 | 0 (0.0) | 3 (0) | low event rate (N=3) | | 0.980 |
| Uncontrolled bleeding | 11 | 0 (0.0) | 3 (0) | low event rate (N=3) | | 0.980 |

**Table 3. Profile of reasons for admission.**

| Admission Reason | Frequency (%) |
|---|---|
| Pneumonia | 84 (61) |
| Malnutrition | 28 (20) |
| Dehydration | 22 (16) |
| Diarrhea | 16 (12) |
| Malaria | 10 (7) |
| Convulsions/convulsive disorder | 10 (7) |
| Anemia | 6 (4) |
| Sickle Cell Disease | 6 (4) |
| Meningitis | 3 (2) |
| Ricketts | 3 (2) |
| Asthma | 2 (1) |
| Trauma | 1 (1) |
| Aspiration | 1 (1) |
| Bronchiolitis | 1 (1) |
| Hypoglycemia | 1 (1) |
| Neonatal Sepsis | 1 (1) |
| Obstructive Jaundice | 1 (1) |
| RTI | 1 (1) |
| Shock | 1 (1) |
| Vaso-occlusive crisis | 1 (1) |
| Vomiting | 1 (1) |

**Table 4. General characteristics of admitted and discharged participants.**

| Admitted Participants (N=138) | Frequency (%) | Discharged Participants (N=971) | Frequency (%) |
|---|---|---|---|
| Age (months) | | Age (months) | |
| <12 | 64 (46.4) | <12 | 306 (31.5) |
| 12–24 | 45 (32.6) | 12–24 | 318 (32.7) |
| 24–36 | 13 (9.4) | 24–36 | 158 (16.3) |
| 36–48 | 5 (3.6) | 36–48 | 109 (11.2) |
| 48–60 | 9 (6.5) | 48–60 | 74 (7.6) |
| 60 | 2 (1.4) | 60 | 6 (0.6) |
| **Male Sex** | 85 (61.6) | **Male Sex** | 440 (45.3) |
| **Mortality** | 4 (2.9) | **Mortality** | 2 (0.2) |
| **Length of hospital stay (days)** | | **Recovered** | 837 (86.2) |
| <3 | 11 (8.0) | **Returned to hospital** | 89 (9.2) |
| 3–5 | 43 (31.2) | **Readmitted** | 24 (2.5) |
| 6–10 | 64 (46.4) | | |
| >10 | 20 (14.5) | | |

**Table 5. Odds ratios of predictors in the final model.**
$*p < 0.05$, $**p < 0.0001$. Transformed oxygen saturation $= 4.314 \times \log_{10} (103.711 - SpO_2) - 37.315$. OR, odds ratio; CI, confidence interval; MUAC, mid-upper arm circumference.

| Predictors | Regression estimate | OR(95% CI) |
|---|---|---|
| (Intercept) | -3.447 | |
| Weight (kg) | -0.006** | 0.994 (0.991 to 0.998) |
| Lethargy | 1.512** | 4.537 (3.784 to 5.470) |
| MUAC (cm) | -0.027** | 0.973 (0.967 to 0.979) |
| Cannot drink or breastfeed | 1.188** | 3.280 (2.807 to 3.833) |
| Transformed oxygen saturation | -0.004* | 0.997 (0.987 to 1.000) |
| Axillary temperature (°C) | 0.046** | 1.047 (1.039 to 1.054) |
| Difficulty breathing | 1.149** | 3.516 (2.755 to 3.62) |
| Pulse rate (bpm) | 0.006** | 1.006 (1.003 to 1.009) |

### Final multivariable model

The final model was reduced to 8 predictor variables (Table 5) and achieved an AUC of 0.88 (95% CI 0.82 to 0.94) (Figure 2). The final model equation was: logit (p)= -3.45 +(-0.006,weight)+ (1.51,lethargy)+(-0.03,MUAC)+(1.19,cannot drink/breastfeed)+ (-0.004,transformed oxygen saturation)+(0.05,temperature)+ (1.15,difficulty breathing)+(0.006,pulse rate).

The model, at a low risk threshold of 5%, had a sensitivity of 97% (95% CI 91% to 99%), and a specificity of 54% (95% CI 45% to 58%) (Table 6) (Figure 2). In the model derivation cohort, the positive predictive value was 22% (95% CI 20% to 26%), and the negative predictive value was 99% (95% CI 98% to 100%). At a high-risk threshold of 25% the model attained a specificity of 91% (95% CI 83% to 95%) and a sensitivity of 62% (95% CI 53% to 79%). The positive and negative predictive values were 50% (95% CI 39% to 64%) and 94% (95% CI 93% to 97%), respectively.
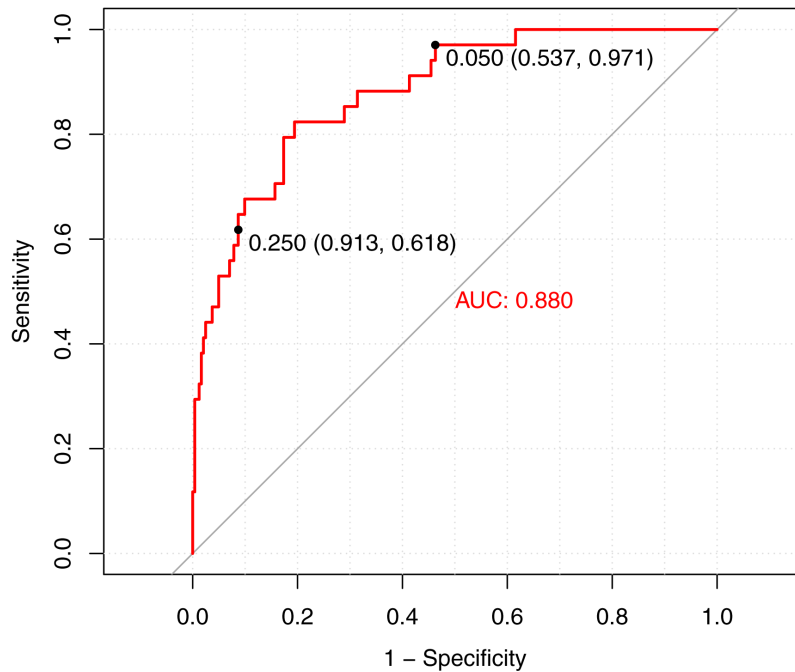
**Figure 2. Cross validated receiver operating characteristic curve of the final model in the study cohort.** Points represent low risk (0.05) and high risk (0.25) thresholds. AUC, area under the curve.

**Table 6. Risk stratification table using three triage groups.** Computed using the upper limit, median and lower limit of the risk threshold range for the non-urgent, priority and emergency categories respectively.

| Triage Category: | Non-Urgent | Priority | Emergency |
|---|---|---|---|
| Risk threshold range | ≤ 5 | 5 < r < 25 | ≥ 25 |
| Participants, n (%) | 519 (47) | 418 (38) | 172 (16) |
| Participants with outcome, n (%) | 11 (8) | 48 (35) | 79 (57) |
| TP:FP | 1:19 | 3:17 | 1:3 |
| Sensitivity (95% CI) | 0.97 (0.91 to 0.99) | 0.76 (0.61 to 0.88) | 0.62 (0.53 to 0.79) |
| Specificity (95% CI) | 0.54 (0.45 to 0.58) | 0.79 (0.74 to 0.84) | 0.91 (0.83 to 0.95) |
| NPV (95% CI) | 0.99 (0.98 to 1.00) | 0.97 (0.94 to 0.99) | 0.94 (0.93 to 0.97) |
| PPV (95% CI) | 0.22 (0.20 to 0.26) | 0.37 (0.30 to 0.45) | 0.50 (0.39 to 0.64) |
| NLR (95% CI) | 0.05 (0.01 to 0.38) | 0.26 (0.13 to 0.50) | 0.42 (0.27 to 0.64) |
| PLR (95% CI) | 2.10 (1.82 to 2.44) | 4.16 (3.04 to 5.68) | 6.88 (4.23 to 11.20) |

The calibration belt and associated likelihood ratio-based test suggest the model is well calibrated (p = 0.715) (Figure 3). The majority of participants identified in the non-urgent category (46.7%, $n$ = 519) had low rates of admission (7.9%, $n$ = 11) (Table 6). Participants in the emergency category (15.5%, $n$ = 172) had high admission rates (57.2%, $n$ = 79). This is much greater than the population prevalence of admission (12.4%), as

reflected by the high positive likelihood ratio (PLR) associated with this category (6.88, 95% CI 4.23 to 11.20).

## Discussion
### Key results
We have developed, and internally validated, a prediction model for triage of children under-five years of age presenting
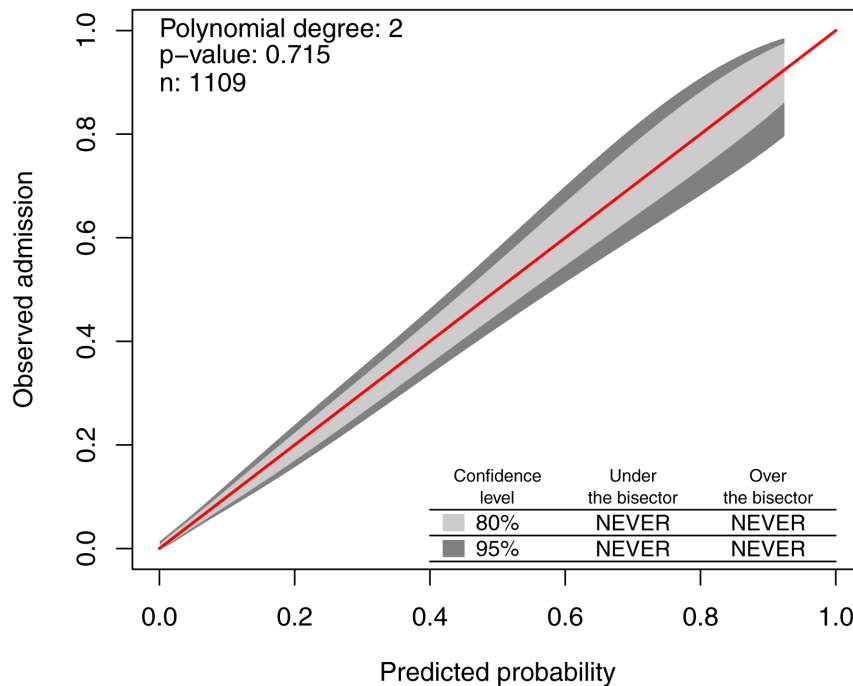
**Figure 3. Calibration belt of the final model.** The 45-degree bisector represents the identity between predicted probabilities and observed responses. The 80% and 95% confidence level calibration belt are plotted, in light and dark grey respectively. The test's p-value, the sample size *n*, and the polynomial order *m* of the calibration curve are reported in the top left corner.

to an outpatient department based on the need for hospital admission. The final model includes eight predictor variables, five of which are objectively measurable (transformed oxygen saturation, pulse rate, temperature, weight, MUAC), and three of which are parent reported (lethargy, inability to drink/breastfeed, difficulty breathing). This simple model is derived from predictors that are readily available globally at relatively low cost and can be easily measured by low skilled frontline health workers. The predictors included in the model reflect what has been observed in previous studies[27–29] and what is often included in international guidelines[30]. After internal validation, the model affords high discrimination, with an AUC of 0.88 (95% CI 0.82 to 0.94) and good calibration (p = 0.715).

Clinical interpretation
Triage of children is typically categorized into three levels of risk (emergency, priority, and non-urgent). If using a risk threshold of 5% to differentiate non-urgent from priority and emergency cases, the model showed 97% sensitivity and 54% specificity (Figure 2). The high sensitivity demonstrates good ability of the model to accurately identify non-urgent cases (rule out). This is not without a cost of specificity, evident in the ratio of one true positive to 19 false positives (Table 6). However, in the case of triage this trade off may be acceptable to ensure that priority and emergency cases are not misclassified and treated as non-urgent. This is reflected by the negative likelihood ratio which suggests that the 47% of participants that were categorized as non-urgent are 20 times less

likely be in need of hospital admission compared to participants categorized as priority or emergency (Table 4).

Using a risk threshold of 25% to identify emergency cases, the model attained 91% specificity and 62% sensitivity (Figure 2). A highly specific model can be useful in correctly ruling in participants categorized as emergency, illustrated by a ratio of one true positive to only three false negatives (Table 6). In the case of identifying emergency cases, high specificity is crucial to optimize time and resource allocation to children, who are truly in need of emergency treatment. The positive likelihood ratio suggests that the 16% of participants in the emergency category are 6.88 times more likely to need hospital admission compared to participants categorized as priority (Table 6). The associated sensitivity cost is less important in this case as correct identification of emergency cases holds precedence and children who are incorrectly classified as priority cases will still receive prompt assessment.

Of children who required hospital admission, 92% were assigned into the priority and emergency triage categories, while the majority of non-outcome cases were assigned into the non-urgent category (Table 6). This suggests good risk stratification capability.

Strengths and limitations
This study represents a step forward in strengthening triage systems in LMICs by presenting a data-driven prediction

model to be integrated into a real time electronic digital platform. There is increasing evidence to suggest that mHealth (use of mobile devices with software applications to provide health services and manage patient information) can be used to strengthen health systems[31]. The computing power and display capability of even the entry level smartphones in low resource settings can be used as platforms to implement clinical prediction models[32]. The digital platform also allows for real time monitoring of user performance and compliance and optimization of work flow. In addition, pulse oximetry can be conducted with mobile device by attaching low-cost sensors to enable objective measurements and alleviate the need to perform manual data entry of values read from a separate monitor[29,32,33]. The inclusion of RRate, an app for measure respiratory rate by tapping on the screen also enables faster collection of respiratory rate with less effort than counting breaths[11]. The data-driven model is comprised of eight objectively measurable or parent reported variables, minimizing need for subjective assessment and clinical expertise. Integration of this eight-predictor model into a mobile device could result in a simple, low cost triage tool that is easily implementable in low resource health facilities.

The objectivity of five of the predictors would significantly support their adoption by lower skilled health workers. Having one study nurse perform data collection prevented introduction of inter-examiner measurement bias. However, due to time constraints, the study nurse did not have time to record information on participants that did not meet the inclusion criteria. The outcome variable (decision to admit) which was based on the opinion of the facility clinician on duty, was subject to inter-examiner variability. Opinions between physicians vary and are impacted by training, resource constraints, exposure and expertise.

A significant limitation of this study was the use of admission as a surrogate for acuity. Need for hospital admission is difficult to assess and may not accurately reflect a state of critical illness in children. We accounted for this by defining a positive outcome as admission for at least 24 hours to filter out those non-critically ill cases. We also conducted a 14-day post-discharge follow up call to identify children inappropriately sent home and found that both mortality and readmission rates were minimal (Table 4).

Furthermore, many predictors used in modelling were likely used by the facility physicians in outcome ascertainment. This inherently biases the model in favour of the chosen variables. Future studies should capture hospital outcomes as well to help inform the triage model.

Some risk factors could not be used in multivariable analysis due to low prevalence in the study population. This may indicate need for a study with a larger sample size. When a single sign or symptom with low population prevalence, such as unconsciousness, is well known to indicate risk this should be used as a danger sign prior to the use of any risk prediction tool. Risk prediction within a mobile app is only necessary when multiple predictors are required to augment the prediction. Alternatively, if these danger signs are easy to assess and strongly correlated

with admission, these predictors may be treated as independent triggers for admission. This cascade of decision rules can be readily implemented in a digital platform with the complexity hidden from the user.

A further limitation was the poor signal quality for oxygen saturation (50% of participants had a signal quality index of less than 80%). Nevertheless, the finding of oxygen saturation as a strong predictor of overnight hospital admission is consistent with existing literature[27,34]. This could be improved with enhanced training and optimized technology.

Finally, the lack of external validity poses a significant limitation to this study. The model is currently being validated in an independent multi-site study that will include clinical implementation to assess performance in varied geographical locations, seasons, and with different disease prevalence and severity[35].

## Conclusion
We developed a logistic triage model for rapid identification of critical illness in children at first contact. The triage model, comprised of five objectively measurable variables (transformed oxygen saturation, pulse rate, temperature, weight, MUAC) and three parent reported variables (lethargy, inability to drink/breastfeed, difficulty breathing) had good discrimination, calibration, and internal validation. The model can be easily integrated into a digital health platform and used with minimal clinical training. External validation is required prior to adoption.

## Data availability
### Underlying data
Figshare: Derivation and internal validation of a data-driven prediction model to guide frontline health workers in triaging children under-five in Nairobi, Kenya. https://doi.org/10.6084/m9.figshare.9104918[26].

### Reporting guidelines
Figshare: STROBE checklist for article 'Derivation and internal validation of a data-driven prediction model to guide frontline health workers in triaging children under-five in Nairobi, Kenya'. 10.6084/m9.figshare.9037406[12].

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

## References

1. World Health Organization: **Children: reducing mortality**. 2019.

2. Kissoon N, Uyeki TM: **Sepsis and the Global Burden of Disease in Children.** *JAMA Pediatr.* 2016; **170**(2): 107–8.
   **PubMed Abstract** | **Publisher Full Text** | **Free Full Text**

3. Tan B, Wong JJ, Sultana R, *et al.*: **Global Case-Fatality Rates in Pediatric Severe Sepsis and Septic Shock: A Systematic Review and Meta-analysis.** *JAMA Pediatrics.* 2019; **173**(4): 352–362.
   **PubMed Abstract** | **Publisher Full Text** | **Free Full Text**

4. Baker T: **Critical care in low-income countries.** *Trop Med Int Health.* 2009; **14**(2): 143–8.
   **PubMed Abstract** | **Publisher Full Text**

5. Hategeka C, Mwai L, Tuyisenge L, *et al.*: **Implementing the Emergency Triage, Assessment and Treatment *plus* admission care (ETAT+) clinical practice guidelines to improve quality of hospital care in Rwandan district hospitals: healthcare workers' perspectives on relevance and challenges.** *BMC Health Serv Res.* 2017; **17**(1): 256.
   **PubMed Abstract** | **Publisher Full Text** | **Free Full Text**

6. Robison JA, Ahmad ZP, Nosek CA, *et al.*: **Decreased pediatric hospital mortality after an intervention to improve emergency care in Lilongwe, Malawi.** *Pediatrics.* 2012; **130**(3): e676–82.
   **PubMed Abstract** | **Publisher Full Text**

7. Clark M, Spry E, Daoh K, *et al.*: **Reductions in inpatient mortality following interventions to improve emergency hospital care in Freetown, Sierra Leone.** *PLoS One.* 2012; **7**(9): e41458.
   **PubMed Abstract** | **Publisher Full Text** | **Free Full Text**

8. Irimu GW, Gathara D, Zurovac D, *et al.*: **Performance of health workers in the management of seriously sick children at a Kenyan tertiary hospital: before and after a training intervention.** *PLoS One.* 2012; **7**(7): e39964.
   **PubMed Abstract** | **Publisher Full Text** | **Free Full Text**

9. Robertson MA, Molyneux EM: **Triage in the developing world--can it be done?** *Arch Dis Child.* 2001; **85**(3): 208–13.
   **PubMed Abstract** | **Publisher Full Text** | **Free Full Text**

10. Taylor RA, Pare JR, Venkatesh AK, *et al.*: **Prediction of In-hospital Mortality in Emergency Department Patients With Sepsis: A Local Big Data-Driven, Machine Learning Approach.** *Acad Emerg Med.* 2016; **23**(3): 269–78.
    **PubMed Abstract** | **Publisher Full Text** | **Free Full Text**

11. von Elm E, Altman DG, Egger M, *et al.*: **The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.** *Int J Surg.* 2014; **12**(12): 1495–9.
    **PubMed Abstract** | **Publisher Full Text**

12. Mawji A: **Reporting guidelines: Derivation and internal validation of a data-driven prediction model to guide frontline health workers in triaging children under-five in Nairobi, Kenya.** *figshare.* Journal contribution. 2019.
    **http://www.doi.org/10.6084/m9.figshare.9037406.v2**

13. Gan H, Karlen W, Dunsmuir D, *et al.*: **The Performance of a Mobile Phone Respiratory Rate Counter Compared to the WHO *ARI Timer.*** *J Healthc Eng.* 2015; **6**(4): 691–703.
    **PubMed Abstract** | **Publisher Full Text**

14. Harris PA, Taylor R, Thielke R, *et al.*: **Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support.** *J Biomed Inform.* 2009; **42**(2): 377–81.
    **PubMed Abstract** | **Publisher Full Text** | **Free Full Text**

15. R Core Development Team: **R: a language and environment for statistical computing, 3.2.1.** Document freely. 2015.
    **Reference Source**

16. Fung JST, Akech S, Kissoon N, *et al.*: **Determining predictors of sepsis at triage among children under 5 years of age in resource-limited settings: A modified Delphi process.** *PLoS One.* 2019; **14**(1): e0211274.
    **PubMed Abstract** | **Publisher Full Text** | **Free Full Text**

17. Zhou A, Karlen G, Brant W, *et al.*: **The saturation gap: A simple transformation of oxygen saturation using virtual shunt.** *bioRxiv.* 2018; 3–10.
    **Publisher Full Text**

18. van Buuren S: **Package 'mice': Multivariate Imputation by Chained Equations.** *CRAN Repos.* 2019.
    **Reference Source**

19. Campion WM, Rubin DB: **Multiple Imputation for Nonresponse in Surveys.** *J Mark Res.* 2006.
    **Publisher Full Text**

20. Steyerberg EW, Vergouwe Y: **Towards better clinical prediction models: seven steps for development and an ABCD for validation.** *Eur Heart J.* 2014; **35**(29): 1925–31.
    **PubMed Abstract** | **Publisher Full Text** | **Free Full Text**

21. Guyon I, Weston J, Barnhill S, *et al.*: **Gene selection for cancer classification using support vector machines.** *Mach Learn.* 2002; **46**(1–3): 389–422.
    **Publisher Full Text**

22. Kuhn M, TH. Contributions from Jed Wing, Weston S, *et al.*: **caret: Classification and Regression Training.** *R Packag. version 6.0-79.* 2018.
    **Reference Source**

23. Nattino G, Finazzi S, Bertolini G: **A new calibration test and a reappraisal of the calibration belt for the assessment of prediction models based on dichotomous outcomes.** *Stat Med.* 2014; **33**(14): 2390–407.
    **PubMed Abstract** | **Publisher Full Text**

24. Nattino G, Lemeshow S, Phillips G, *et al.*: **Assessing the Calibration of Dichotomous Outcome Models with the Calibration Belt.** *Stata J Promot Commun Stat Stata.* 2017; **17**(4): 1003–1014.
    **Publisher Full Text**

25. Nattino G, Finazzi G, Bertolini D, *et al.*: **The GiViTi calibration test and belt. R package version 1.3.** [Online] 2017.
    **Reference Source**

26. Mawji A: **Derivation and internal validation of a data-driven prediction model to guide frontline health workers in triaging children under-five in Nairobi, Kenya.** *figshare.* Dataset. 2019.
    **http://doi.org/10.6084/m9.figshare.9104918.v1**

27. Raihana S, Dunsmuir D, Huda T, *et al.*: **Development and Internal Validation of a Predictive Model Including Pulse Oximetry for Hospitalization of Under-Five Children in Bangladesh.** *PLoS One.* 2015; **10**(11): e0143213.
    **PubMed Abstract** | **Publisher Full Text** | **Free Full Text**

28. George EC, Walker AS, Kiguli S, *et al.*: **Predicting mortality in sick African children: the FEAST Paediatric Emergency Triage (PET) Score.** *BMC Med.* 2015; **13**: 174.
    **PubMed Abstract** | **Publisher Full Text** | **Free Full Text**

29. Garde A, Zhou G, Raihana S, *et al.*: **Respiratory rate and pulse oximetry derived information as predictors of hospital admission in young children in Bangladesh: a prospective observational study.** *BMJ Open.* 2016; **6**(8): e011094.
    **PubMed Abstract** | **Publisher Full Text** | **Free Full Text**

30. Duke T: **New WHO guidelines on emergency triage assessment and treatment.** *Lancet.* 2016; **387**(10020): 721–4.
    **PubMed Abstract** | **Publisher Full Text**

31. Källander K, Tibenderana JK, Akpogheneta OJ, *et al.*: **Mobile health (mHealth) approaches and lessons for increased performance and retention of community health workers in low- and middle-income countries: a review.** *J Med Internet Res.* 2013; **15**(1): e17.
    **PubMed Abstract** | **Publisher Full Text** | **Free Full Text**

32. Ansermino JM: **Universal access to essential vital signs monitoring.** *Anesth Analg.* 2013; **117**(4): 883–90.
    **PubMed Abstract** | **Publisher Full Text**

33. Enoch AJ, English M, Shepperd S: **Does pulse oximeter use impact health outcomes? A systematic review.** *Arch Dis Child.* 2016; **101**(8): 694–700.
    **PubMed Abstract** | **Publisher Full Text** | **Free Full Text**

34. Jensen CS, Aagaard H, Olesen HV, *et al.*: **A multicentre, randomised intervention study of the Paediatric Early Warning Score: study protocol for a randomised controlled trial.** *Trials.* 2017; **18**(1): 267.
    **PubMed Abstract** | **Publisher Full Text** | **Free Full Text**

35. Mawji A, Li E, Komugisha C, *et al.*: **Smart triage: triage and management of sepsis in children using the point-of-care Pediatric Rapid Sepsis Trigger (PRST) tool.** *BMC Health Serv Res.* 2020; **20**(1): 493.
    **PubMed Abstract** | **Publisher Full Text** | **Free Full Text**

# Open Peer Review

## Current Peer Review Status: ✓ ✓

---

**Version 3**

Reviewer Report 04 May 2021

https://doi.org/10.21956/wellcomeopenres.18511.r43523

✓ **Babar Hasan** [iD]

Department of Paediatrics and Child Health, Aga Khan University, Karachi, Pakistan

I am satisfied with the responses by the authors and the changes made. I also want to thank the authors for answering my queries very coherently and scientifically.

*Competing Interests:* No competing interests were disclosed.

*Reviewer Expertise:* Pediatric cardiology, Quality improvement sciences

**I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.**

Reviewer Report 29 April 2021

https://doi.org/10.21956/wellcomeopenres.18511.r43522

✓ **Andrew Argent** [iD]

Department of Paediatrics and Child Health, University of Cape Town, Cape Town, South Africa

Thank you for the changes. I have no further suggestions for this paper.

*Competing Interests:* No competing interests were disclosed.

*Reviewer Expertise:* I have experience in the evaluation of critically ill children for admission, particularly in areas of lower resource availability

**I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.**

- - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - -

Version 2

Reviewer Report 15 March 2021

https://doi.org/10.21956/wellcomeopenres.18080.r42880

? **Babar Hasan** iD

Department of Paediatrics and Child Health, Aga Khan University, Karachi, Pakistan

It is well conducted work and does come up with a tool that has the potential of impact due to the simplicity of its use, device based data acquisition and simplicity of predictor variables with high accuracy.

Following concerns can be addressed mainly by either changing some of the text in intro, discussion and conclusion or adding more details to the limitation section. This work is more at a proof of concept stage and needs larger validation studies and a possible RCT to truly reveal its worth.

General comments:
- Keeping the eventual physician recommendation to admit as a surrogate to the gold standard which is actual mortality and morbidity may lead to several biases.

- A lot of their criticism of WHO-ETAT is that it is expert opinion based and the prediction power of each individual variable is not known. Additionally they mention that it is not real time and thus doesn't have the ability to look at compliance and QC. Also they question generalizability of the tool as it is based on decision rules. Now if one was to look at their tool, it also has the exact same issues as the WHO-ETAT, how are they claiming that it is innovative or different. It was not developed as a real time tool. The tool had questions pretty similar to the WHO-ETAT. They haven't demonstrated a tool which tracks compliance or quality. Additionally have they truly proven it to be better than WHO-ETAT for which an RCT is required?

- A little more description about the Mbaghati hospital where the study was conducted is needed. I want to know what is the spectrum of pediatric patients they deal with as inpatients, do they have ICU facilities, do they has pediatric surgical services etc? I need this information to judge the level of pediatric expertise in this hospital. This may determine the generalizability of their findings. Skills of a triage nurse in a well "oiled" pediatric hospital may be far different than someone in a remote primary health care facility. The tool may

perform very differently in that setting.

○ Were the anthropometric z-score derived using online calculators or was it built into the data capturing software thus automating its calculations.

○ Fever of >38 degree was determined by the study nurse or as per parents report?

○ The RRATE application which ingested data from the pulse oximeter, is it a free application? Does it work with any operating system? Is it compatible with other pulse ox devices?

○ If primary outcome was 24hrs admission, how were patients who were sent home and died accounted for in the analysis. I mean these patients were the false negative of the screening tool.

○ Did they do the 10 fold cross validation at both the feature selection and model prediction stages on the whole dataset or did they do a 70/30 data split to test their final model of an unseen 30% of the data?

○ If the missing data was minimal (<3% missing per predictor), why did the authors do an imputation exercise?

○ "Of these variables, data collected after emergency treatment had the highest AUC: 0.80 (95% CI 0.74 to 0.85)." Isn't this pretty intuitive. I mean whoever received emergent treatment (and thus they got their data collected after those emergent services were given) will get admitted. Thus, in my view, the clinical application of such a predictor variable is meaningless.

○ Table 4, mortality in discharged patients was 2 while the parenthesis says (0%). It is 0.2%. I think one has to be accurate with such percentages especially if it represents a grave, rare event.

○ "to suggest that mHealth (use of mobile devices with software applications to provide health services and manage patient information) can be used to strengthen health systems31. The computing power and display capability of even the entry level smartphones in low resource settings can be used as platforms to implement clinical prediction models32. The digital platform also allows for real time monitoring of user performance and compliance and optimization of work flow." This is something the authors mention in their introduction and even as a conclusion. Their current data is not enough to drive the conclusion around the utility of this model as an mobile app. Additionally they can't claim superiority over WHO- ETAT, for that they have to really do a proper trial.

○ "In addition, pulse oximetry can be conducted with mobile device by attaching low-cost sensors to enable objective measurements and alleviate the need to perform manual data entry of values read from a separate monitor". It is true but sometimes that cross talk between the device output and auto-populating data into another software may not be that easy of device company agnostic. The commercial value of such a software which facilitates this cross talk may not be affordable.

○ "The inclusion of RRate, an app for measure respiratory rate by tapping on the screen also enables faster collection of respiratory rate with less effort than counting breaths". Again company proprietorship and device agnostic cross talk may preclude its generalizability.

○ The greatest flaw in the model is that it excluded a very "serious" sign and symptoms like apnea, bleeding and new onset hemiparesis due to unavailability of data.

**Is the work clearly and accurately presented and does it cite the current literature?**
Yes

**Is the study design appropriate and is the work technically sound?**
Yes

**Are sufficient details of methods and analysis provided to allow replication by others?**
Yes

**If applicable, is the statistical analysis and its interpretation appropriate?**
Yes

**Are all the source data underlying the results available to ensure full reproducibility?**
Yes

**Are the conclusions drawn adequately supported by the results?**
Partly

***Competing Interests:*** No competing interests were disclosed.

***Reviewer Expertise:*** Pediatric cardiology, Quality improvement sciences

**I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.**

Author Response 31 Mar 2021
**Alishah M**, University of British Columbia, Vancouver, Canada

Thank you for your comments!

We have modified the introduction, discussion, and conclusion specifically to convey the message that we are not claiming superiority of this model over ETAT, but instead that we developed a model that has the potential to strengthen (not replace) existing triage systems. We acknowledge that external validation is needed before drawing any conclusions regarding model utility. In a study, currently in progress, we are conducting a clinical evaluation of this model:

Mawji A, Li E, Komugisha C, *et al.*: **Smart triage: triage and management of sepsis in**

**children using the point-of-care Pediatric Rapid Sepsis Trigger (PRST) tool.** *BMC Health Serv Res.* 2020; **20**(1): 493.

**General comments:**

○ **Keeping the eventual physician recommendation to admit as a surrogate to the gold standard which is actual mortality and morbidity may lead to several biases.**

We do agree with you. As the study was only funded for a duration of 6 months, we could not capture enough mortality outcomes (N=6 deaths) to conduct meaningful analysis of mortality as an outcome. In these cases, admission is often used as the surrogate. We have acknowledged the limitations associated with this in the manuscript:

*A significant limitation of this study was the use of admission as a surrogate for acuity. Need for hospital admission is difficult to assess and may not accurately reflect a state of critical illness in children (Strengths and limitations, Paragraph 3).*

○ **A lot of their criticism of WHO-ETAT is that it is expert opinion based and the prediction power of each individual variable is not known. Additionally, they mention that it is not real time and thus doesn't have the ability to look at compliance and QC. Also, they question generalizability of the tool as it is based on decision rules. Now if one was to look at their tool, it also has the exact same issues as the WHO-ETAT, how are they claiming that it is innovative or different. It was not developed as a real time tool. The tool had questions pretty similar to the WHO-ETAT. They haven't demonstrated a tool which tracks compliance or quality. Additionally, have they truly proven it to be better than WHO-ETAT for which an RCT is required?**

We agree with you. We do not wish to claim that the tool is superior to ETAT or should be used as a replacement to ETAT. We are suggesting that digital triage tools can be used in conjunction with existing care pathways to strengthen existing systems. The introduction has been updated to reflect this:

*One solution to these shortcomings is the use of a digital, data-driven approach to strengthen triage systems at first contact. Digital health platforms can facilitate quality improvement, while data-driven algorithms are easily updatable with emergence of new information and can be optimized to meet the specific needs of each setting. The purpose of this study was to develop a flexible, logistic triage model for children under five years of age that can be easily integrated into a digital platform and is operable with minimal clinical training. The digital triage tool can be used alongside ETAT to rapidly identify children at risk of developing severe infections, including sepsis upon arrival to the hospital (Introduction, Paragraph 4).*

○ **A little more description about the Mbaghati hospital where the study was conducted is needed. I want to know what is the spectrum of pediatric patients they deal with as inpatients, do they have ICU facilities, do they has pediatric**

**surgical services etc.? I need this information to judge the level of pediatric expertise in this hospital. This may determine the generalizability of their findings. Skills of a triage nurse in a well "oiled" pediatric hospital may be far different than someone in a remote primary health care facility. The tool may perform very differently in that setting.**

We have updated the manuscript to include more about Mbagathi hospital:

*This prospective observational study was conducted between January and June 2018 at the pediatric outpatient department of Mbagathi County Referral hospital in Nairobi, Kenya. Mbagathi County Hospital is a first-referral level (district) hospital located in Nairobi in the neighbourhood of a high-density urban informal settlement. During a typical working shift, the outpatient area has nutritionists who take anthropometric measurements, a single nurse who conducts triage, plus providing treatments such as oral rehydration, and another nurse in the emergency area who administers emergency treatment, and one or two non-degree trained clinicians (clinical officers) who provide consultation, prescribe treatments, and make decisions on admissions. The outpatient department (OPD) serves over 20,000 children per year and admits approximately 2,500 pediatric patients per year (Methods, Population).*

A more extensive description is below:

Mbagathi County Hospital is a first-referral level (district) hospital located in Nairobi in the neighbourhood of a high-density urban informal settlement. The hospital has outpatient services that attends to patients coming from home seeking medical care or referred from lower-level facilities that provide only outpatient services. Patients arriving at the outpatient department who need emergency care are taken straight to the emergency/resuscitation room for emergency treatment.  The outpatient area also serves patients coming for clinical follow-ups. During a typical working shift, the outpatient area has nutritionists who take anthropometric measurements, a single nurse who conducts triage, plus providing treatments such as oral rehydration, and another nurse in the emergency area who administers emergency treatment, and 1-2 non-degree trained clinicians (clinical officers) who provide consultation, prescribe treatments, and make decisions on admissions.  The hospital has a newborn ward, admitting sick newborns born within the hospital aged less 1 month, and a paediatric ward that admits other children aged up to 12 years.  The paediatric ward is a general ward with one room closest to the nursing station equipped with portable oxygen to attend to acutely ill who may need oxygen or closer observation. Like many hospitals, the hospital has shortage of skilled health workforce and it is usual to have about 2 nurses attending to even up to 40 patients and covering all nursing tasks.  The clinical team in the paediatric ward is led by one paediatrician who works with intern clinicians (doctors and clinical officers). The hospital does not have a high dependency unit (HDI) or intensive care unit (ICU) and patients requiring these levels of care are referred.

- ○ **Were the anthropometric z-score derived using online calculators or was it built into the data capturing software thus automating its calculations.**

Anthropometric z-scores were calculated using the zscorer package in R as it was

unnecessary to calculate them at the time of data collection. When implemented as a digital platform this would be built in and automated. Our team has already included this in other digital tools. The manuscript has been updated to include this information:

*Anthropometric z-scores were also calculated during analysis (computed via the zscorer package in R; v6.0-79, https://cran.r-project.org/web/packages/zscorer/zscorer.pdf) (Methods, Candidate predictor variables)*

- **Fever of >38 degree was determined by the study nurse or as per parent's report?**

This was an observed variable. Axillary temperature was measured by the study nurse.

- **The RRATE application which ingested data from the pulse oximeter, is it a free application? Does it work with any operating system? Is it compatible with other pulse ox devices?**

Pulse oximetry and respiratory rate were measured using two different but integrated applications. A 1-minute pulse oximetry spot check was performed with the LGT pulse oximeter connected directly to the Android tablet – LGT is cited in the text. They also have pulse oximeters that can connect to iOS (Apple devices). The pulse oximeter spot check in our data collection tool can also work with Nonin or Masimo pulse oximeters. The RRate application for measuring respiratory rate by tapping on the screen each time the child breaths. RRate is thoroughly described in the cited paper, citation 13. RRate is also a stand-alone free application available for Android or iOS.

- **If primary outcome was 24hrs admission, how were patients who were sent home and died accounted for in the analysis. I mean these patients were the false negative of the screening tool.**

This is an unfortunate limitation of the study. However, the mortality rate for patients sent home was very low (0.2%, N=2). This is unlikely to have impacted the result. For future studies, mortality, date and cause of death will be recorded so that we can alter the positive admission outcome to include those patients who were sent home and died within a predetermined time period (capture the false negatives). This is described in the manuscript:

*A significant limitation of this study was the use of admission as a surrogate for acuity. Need for hospital admission is difficult to assess and may not accurately reflect a state of critical illness in children. We accounted for this by defining a positive outcome as admission for at least 24 hours to filter out those non-critically ill cases. We also conducted a 14-day post-discharge follow up call to identify children inappropriately sent home and found that both mortality and readmission rates were minimal ( Table 4) (Strengths and limitations, Paragraph 3).*

- **Did they do the 10-fold cross validation at both the feature selection and model prediction stages on the whole dataset or did they do a 70/30 data split to test their final model of an unseen 30% of the data?**

We used recursive feature elimination with 5 time repeated 10-fold cross validation to select features to include in the model. For internal validation, we also used 10-fold cross validation where 9/10 folds comprised the "training set" (used to build the model), and the remaining fold comprised the "validation set" (used to test the model). This process was repeated 10 times, with each of the 10 subsamples used once as the validation data. The 10-fold internal validation procedure was repeated 5 times and the results were pooled to produce a single estimate of model performance.

- **If the missing data was minimal (<3% missing per predictor), why did the authors do an imputation exercise?**

We still wanted to maximize the number of cases included in the analysis. We did not want to discard the valuable information that was collected in the other fields that was not missing.

- **"Of these variables, data collected after emergency treatment had the highest AUC: 0.80 (95% CI 0.74 to 0.85)." Isn't this pretty intuitive. I mean whoever received emergent treatment (and thus they got their data collected after those emergent services were given) will get admitted. Thus, in my view, the clinical application of such a predictor variable is meaningless.**

We agree with you. This variable was not included in the final prediction model. Univariate analysis was conducted on all candidate predictors to assess individual associations with the outcome, but it would not be appropriate to include this variable in a clinical prediction model. For future studies, this should not be considered a candidate predictor variable for the reasons you mentioned above.

- **Table 4, mortality in discharged patients was 2 while the parenthesis says (0%). It is 0.2%. I think one has to be accurate with such percentages especially if it represents a grave, rare event.**

Reporting for values in table 4 have been updated accordingly.

- **"to suggest that mHealth (use of mobile devices with software applications to provide health services and manage patient information) can be used to strengthen health systems31. The computing power and display capability of even the entry level smartphones in low resource settings can be used as platforms to implement clinical prediction models32. The digital platform also allows for real time monitoring of user performance and compliance and optimization of work flow." This is something the authors mention in their introduction and even as a conclusion. Their current data is not enough to drive the conclusion around the utility of this model as an mobile app. Additionally they can't claim superiority over WHO- ETAT, for that they have to really do a proper trial.**

We agree with you. We mention that the study represents a step forward in strengthening

triage systems in LMICs by presenting a data-driven prediction model to be integrated into a real time electronic digital platform. The model needs to be implemented into a mobile app and externally validated in a variety of settings in low-and-middle-income countries to for any conclusions regarding model utility can be drawn, which we acknowledged in the limitations:

*Finally, the lack of external validity poses a significant limitation to this study. The model is currently being validated in an independent multi-site study that will include clinical implementation to assess performance in varied geographical locations, seasons, and with different disease prevalence and severity [35] (Strengths and limitations, Paragraph 7).*

[35] Mawji A, Li E, Komugisha C, *et al.*: **Smart triage: triage and management of sepsis in children using the point-of-care Pediatric Rapid Sepsis Trigger (PRST) tool.** *BMC Health Serv Res.* 2020; **20**(1): 493.

We also modified the conclusion to reflect this:

*We developed a logistic triage model for rapid identification of critical illness in children at first contact. The triage model, comprised of five objectively measurable variables (transformed oxygen saturation, pulse rate, temperature, weight, MUAC) and three parent reported variables (lethargy, inability to drink/breastfeed, difficulty breathing) had good discrimination, calibration, and internal validation. The model can be easily integrated into a digital health platform and used with minimal clinical training. External validation is required prior to adoption (Conclusion).*

1. **"In addition, pulse oximetry can be conducted with mobile device by attaching low-cost sensors to enable objective measurements and alleviate the need to perform manual data entry of values read from a separate monitor". It is true but sometimes that cross talk between the device output and auto-populating data into another software may not be that easy of device company agnostic. The commercial value of such a software which facilitates this cross talk may not be affordable.**

We agree that this can be the case, but for this study it was not, and thus was an advantage of our data collection app. For this study, the pulse oximeter we used from LGT connected directly to the tablet and there was no intermediate software needed – the app itself contained the library to use the incoming values from the pulse oximeter. Stand-alone pulse oximeters that communicate with apps through Bluetooth are becoming more popular, but you are generally restricted to using the manufacturer's app. Since we do not need to do this, it is an advantage and a cost-saving approach. We would also like to provide incentives for device manufacturers to add differentiators to their products. A algorithm could be added to any of the current stand alone devices without significant technical modification.

  ○ **"The inclusion of RRate, an app for measure respiratory rate by tapping on the screen also enables faster collection of respiratory rate with less effort than counting breaths". Again, company proprietorship and device agnostic cross**

> **talk may preclude its generalizability.**
>
> RRate is a free application available for Android or iOS. Both versions are setup to provide their resulting respiratory rate values to other apps on the same device free of charge, in much the same way as many apps switch to the camera app and let you take a photo and then feed that photo back into the requesting app. This then takes some development work for the developer of the app but is done in a standard method and is free. These technical details are beyond the scope of this paper.
>
> - ○ **The greatest flaw in the model is that it excluded a very "serious" sign and symptoms like apnea, bleeding and new onset hemiparesis due to unavailability of data.**
>
> These are rare events that are clear signs of emergency. The model was designed to guide frontline health workers in those identifying critically ill (or high risk) children for which there are no obvious indicators such as those mentioned above. We have addressed this in the manuscript:
>
> *Some risk factors could not be used in multivariable analysis due to low prevalence in the study population. This may indicate need for a study with a larger sample size. When a single sign or symptom with low population prevalence, such as unconsciousness, is well known to indicate risk this should be used as a danger sign prior to the use of any risk prediction tool. Risk prediction within a mobile app is only necessary when multiple predictors are required to augment the prediction. Alternatively, if these danger signs are easy to assess and strongly correlated with admission, these predictors may be treated as independent triggers for admission. This cascade of decision rules can be readily implemented in a digital platform with the complexity hidden from the user (Strengths and limitations, Paragraph 5).*
>
> **Competing Interests:** No competing interests were disclosed.

Reviewer Report 26 January 2021

https://doi.org/10.21956/wellcomeopenres.18080.r41846

✔ **Andrew Argent** iD
Department of Paediatrics and Child Health, University of Cape Town, Cape Town, South Africa

**General Comments**
My thanks to the authors for the positive response to the review, the changes that have been made, and the additional data that has been provided.

**Specific Comments**
*Title*
I wonder if the title is accurate in the use of the term "triage". The study showed that certain features were associated with hospital admission (in children who were reviewed and entered into the study after initial clinical assessment and treatment).

*Introduction*
Thanks for the modifications.

*Methods*
*Ethics*
I accept that the data was not collected regarding the actual numbers of patients who refused consent. Unfortunately it does put a question mark over the extent to which patients and their families gave free consent to participate in this study. I think that this should be highlighted in the shortcomings of the study.

*Population*
I think that the terminology of "outpatient department" is potentially confusing. In many settings the outpatient department will see patients who have booked appointments and re not presenting primarily for emergency treatment. Most "outpatient" departments are open only during normal working hours. What the authors are describing is a clinical area that sees all the patients presenting for assessment and therapy at all hours of the day and night, including weekends and public holidays. That would be described as an emergency service in many settings.

If in fact the elective visits for ongoing care are seen in the same setting and by the same team that provides triage, emergency care and intervention, then that has to be expressed clearly. It also has significant implications for the population that is being screened.

I am still not clear if trauma/burns/acute surgical emergencies were seen in the same area.

*Results*
Thank you for the clarification of the data as requested.

As regards the comment from me that: "It seems strange that the 3 children with "uncontrolled bleeding" and the 3 children with apnoea did not require admission. Both events would seem as if they were good reasons for admission. Similarly, it seems strange that 6 of the children with "newly onset hemiparesis" were not admitted to the hospital." – I accept the authors response, but would be happier if there was some comment on these events in the discussion (not just in the response to me).

*Discussion*
I wonder if it is worth highlighting (possibly also in the title), that this model seems to be accurate to differentiate between those who can be sent home and those who require hospital admission. That is very different to a common discussion of triage, where the process is used to separate patients into groups with different priorities for acute medical attention.

**Is the work clearly and accurately presented and does it cite the current literature?**

Partly

**Is the study design appropriate and is the work technically sound?**
Partly

**Are sufficient details of methods and analysis provided to allow replication by others?**
Partly

**If applicable, is the statistical analysis and its interpretation appropriate?**
Partly

**Are all the source data underlying the results available to ensure full reproducibility?**
Partly

**Are the conclusions drawn adequately supported by the results?**
Partly

*Competing Interests:* No competing interests were disclosed.

*Reviewer Expertise:* I have experience in the evaluation of critically ill children for admission, particularly in areas of lower resource availability

**I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.**

---

Version 1

Reviewer Report 04 September 2019

✗ **Andrew Argent** iD
Department of Paediatrics and Child Health, University of Cape Town, Cape Town, South Africa

General Comments
In this study, data at the time of paediatric outpatient presentation was collected. The data was collected by a research nurse, with some of the information coming from parents, and some from patient records (when patients had been identified as being emergency patients by the clinical staff).

The standard outcome for "triage" was whether the patient was admitted to hospital. There is

unfortunately no information as to the outcomes for those patients including mortality, duration of hospital stay, interventions required etc.

It would also have been useful to have a sense of the fit across a range of different patients in different settings.

Specific Comments
Introduction
Para 1
I do understand that sepsis is a major cause of mortality for children, but this study does not provide information as to the diagnosis in the children who were admitted to hospital. The study is not specific to sepsis, and presumably involves a cohort of children with a wide range of diagnoses. In that context it does not seem entirely appropriate to focus so clearly on sepsis in the introductory material.

I wonder if there are better references to support the statement that "triage systems in low-income settings continue to face challenges including limited numbers of expert clinicians and lack of adequately trained health workers". The references supplied are 10 years or more old.

Methods
Ethics
Was consent actually refused in any case? It would be useful to see this data.

Population
The outpatient department is quoted as serving approximately 20 000 children per annum. During the 6-month period approximately 10 000 children were seen, suggesting that the clinic was open only for the study hours (Monday to Friday, 8am to 5pm).  Firstly, do all emergency patients (children) present to the outpatient department, or are there other routes of presentation? Secondly what happens to children who present as emergencies outside of those hours?

I am not sure of the qualifications and experience of "two or three clinicians".  Are these doctors, nurses, clinical assistants, or any other category of staff?

Eligibility
It is not clear from this statement as to whether children with trauma, burns, or acute surgical conditions would have been seen in the paediatric OPD. It does seem from the table of candidate predictor variables (Table 1) that trauma patients were included, but it would be useful to clarify this, as in many settings trauma patients are not seen by the paediatric teams.

Study procedures
It seems that children who did require emergency treatment would only have been seen by the study nurse after receiving therapy, and so the data collected would not have been the presenting findings. To what extent could the results have been affected by this (particularly as 86% of the admitted participants were seen after emergency treatment)?

The oxygen saturation was presumably measured while in room air (that is not specifically stated in the methods), but that information seems essential to the estimation of the transformed

saturation.

To what extent could the data regarding saturation have been affected by the fact that Nairobi is at nearly 6000ft above sea level?

Outcome
The outcome recorded was admission to hospital for 24 hours or longer. Unfortunately, that means that children who were inappropriately sent home (and perhaps died or sought help elsewhere) were not picked up in the study. It also means that there is no differentiation between an acute illness that needs urgent intervention and a more chronic illness that requires admission and investigation (but possibly not immediate life-saving therapy).

Results
It would have been useful to have a sense of the age-spread of the study population, and the profile of reasons for admission.

It is demonstrated that 35 patients had missing data for oxygen saturation and heart rate. Was the missing data primarily in the group who were admitted, or was it evenly distributed across the groups?  Clearly one is concerned that saturation data may be more difficult to achieve in very sick children.

It seems strange that the 3 children with "uncontrolled bleeding" and the 3 children with apnoea did not require admission. Both events would seem as if they were good reasons for admission. Similarly, it seems strange that 6 of the children with "newly onset hemiparesis" were not admitted to the hospital.

Discussion
As highlighted by the authors a major limitation of the study is that hospital admission was used as a surrogate for acuity of illness. In addition, there was probably overlap between the criteria used by the research team and those used by the clinical team which may have biased the study.

It does seem to make sense to exclude rare events from the triage data collection, but as a category "rare events" may be a strong indication for admission.  As an example it would seem likely that a child with a large tumour would be admitted to hospital regardless of the overall triage score.

Conclusions
The model has been shown to conform with the rate of patient admission. That has potential, but as the authors point out, it will require validation in other settings. It will also need to be applied prospectively to patients coming through the system to see how well it actually predicts in another set of patients in the same setting.

**Is the work clearly and accurately presented and does it cite the current literature?**

Yes

**Is the study design appropriate and is the work technically sound?**

Partly

**Are sufficient details of methods and analysis provided to allow replication by others?**
No

**If applicable, is the statistical analysis and its interpretation appropriate?**
Yes

**Are all the source data underlying the results available to ensure full reproducibility?**
No

**Are the conclusions drawn adequately supported by the results?**
Partly

*Competing Interests:* No competing interests were disclosed.

*Reviewer Expertise:* I have experience in the evaluation of critically ill children for admission, particularly in areas of lower resource availability

**I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.**

Author Response 02 Dec 2020
**Alishah M**, University of British Columbia, Vancouver, Canada

**General Comments**
**In this study, data at the time of paediatric outpatient presentation was collected. The data was collected by a research nurse, with some of the information coming from parents, and some from patient records (when patients had been identified as being emergency patients by the clinical staff).**

**The standard outcome for "triage" was whether the patient was admitted to hospital. There is unfortunately no information as to the outcomes for those patients including mortality, duration of hospital stay, interventions required etc.**

We would agree that information on mortality, duration of hospital stay, and interventions would also be valuable outcome indicators. The resources available for the study did limit our ability to collect a comprehensive set of outcome information. While we did capture mortality, the number of deaths was minimal over the 6-month study duration (N=6) and thus we could not conduct meaningful mortality analysis (insufficient outcomes). We chose admission status, defined as "children admitted >24 hours", as we believe that this should also predict who might need community referral for admission. We have included information on mortality and duration of stay in the updated version of the manuscript.

**It would also have been useful to have a sense of the fit across a range of different patients in different settings.**

We agree with the reviewer. This is mentioned in the strengths and limitations section. Future ongoing research is assessing the implementation and performance assessment of the model in varied geographical locations, seasons, and with different disease prevalence and severity.

**Specific Comments**
**Introduction**
**Para 1**
**I do understand that sepsis is a major cause of mortality for children, but this study does not provide information as to the diagnosis in the children who were admitted to hospital. The study is not specific to sepsis, and presumably involves a cohort of children with a wide range of diagnoses. In that context it does not seem entirely appropriate to focus so clearly on sepsis in the introductory material.**

This study involves a cohort of children with a wide range of infectious diseases. We agree that this study is not specific to sepsis, but rather a wide range of infectious diseases that can lead to sepsis if not diagnosed and treated in a timely manner. We have clarified in the introduction section of the updated manuscript that *"The model can be used to guide frontline health workers in early identification of children at risk of developing severe infections, including sepsis so that lifesaving treatment can be instituted."*

**I wonder if there are better references to support the statement that "triage systems in low-income settings continue to face challenges including limited numbers of expert clinicians and lack of adequately trained health workers". The references supplied are 10 years or more old.**

We have included a newer reference in the updated manuscript.

Hategeka C, Mwai L, Tuyisenge L. Implementing the Emergency Triage, Assessment and Treatment plus admission care (ETAT+) clinical practice guidelines to improve quality of hospital care in Rwandan district hospitals: healthcare workers' perspectives on relevance and challenges. BMC Health Serv Res. 2017;17(1):256–12

**Methods**
**Ethics**
**Was consent actually refused in any case? It would be useful to see this data.**

Unfortunately, we did not collect data on refused cases. We will keep this in mind for future studies.

**Population**
**The outpatient department is quoted as serving approximately 20 000 children per annum. During the 6-month period approximately 10 000 children were seen, suggesting that the clinic was open only for the study hours (Monday to Friday, 8am to**

**5pm).  Firstly, do all emergency patients (children) present to the outpatient department, or are there other routes of presentation? Secondly what happens to children who present as emergencies outside of those hours?**

The manuscript states that the OPD is serves **over** 20,000 children per year. This was an estimate based on the last couple years that was provided to us by the hospital. All children present to the OPD, including those emergency patients seen outside study hours. There are significantly fewer patients presenting to the OPD between 5pm – 6am as well as on weekends.

**I am not sure of the qualifications and experience of "two or three clinicians".  Are these doctors, nurses, clinical assistants, or any other category of staff?**

This refers to physicians. I have clarified this in the updated version of the manuscript.

**Eligibility**
**It is not clear from this statement as to whether children with trauma, burns, or acute surgical conditions would have been seen in the paediatric OPD. It does seem from the table of candidate predictor variables (Table 1) that trauma patients were included, but it would be useful to clarify this, as in many settings' trauma patients are not seen by the paediatric teams.**

At Mbagathi Hospital, all paediatric patients are initially seen at the pediatric OPD. I have clarified the eligibility criteria in the updated version of the manuscript:

*"Children aged 2–60 months seeking treatment for an acute illness at Mbagathi hospital on weekdays between 8:00 am and 5:00 pm were eligible for enrollment. Patients coming for elective procedures, such as elective surgery or for cardiac follow up, were excluded from the study. Patients presenting for elective care or treatment for chronic illnesses were excluded from the study."*

**Study procedures**
**It seems that children who did require emergency treatment would only have been seen by the study nurse after receiving therapy, and so the data collected would not have been the presenting findings. To what extent could the results have been affected by this (particularly as 86% of the admitted participants were seen after emergency treatment)?**

We do appreciate that data collection after initiation of emergency treatment may have affected the results. However, patient safety is the first priority. We did not want study procedures to delay or interfere with clinical care to any patient and so we had to wait until emergency treatment was initiated and the patient was stable before collecting data. We did try to minimize the effect of this by prioritizing collection of variables that are subject to change (vitals, danger signs). The need for emergency treatment is indicative of a serious illness. It would thus make sense that many of the admitted cases were children who were seen after emergency treatment.

**The oxygen saturation was presumably measured while in room air (that is not specifically stated in the methods), but that information seems essential to the estimation of the transformed saturation. To what extent could the data regarding saturation have been affected by the fact that Nairobi is at nearly 6000ft above sea level?**

Data on oxygen saturation could certainly be affected by the altitude of Nairobi. In future studies, we will use an altitude adjusted saturation gap formula to account for this:

Zhou A, Karlen G, Brant W, et al.: The saturation gap: A simple transformation of oxygen saturation using virtual shunt. *bioRxiv.* 2018;3–10. 10.1101/391292

**Outcome**
**The outcome recorded was admission to hospital for 24 hours or longer. Unfortunately, that means that children who were inappropriately sent home (and perhaps died or sought help elsewhere) were not picked up in the study. It also means that there is no differentiation between an acute illness that needs urgent intervention and a more chronic illness that requires admission and investigation (but possibly not immediate life-saving therapy).**

The eligibility criteria actually included only children with acute illnesses who presented to the OPD. Children with chronic illnesses, or patients coming for elective procedures and follow up were not eligible for this study. I have clarified this in the updated version of the manuscript:

*"Children aged 2–60 months seeking treatment for an acute illness at Mbagathi hospital on weekdays between 8:00 am and 5:00 pm were eligible for enrollment. Patients coming for elective procedures, such as elective surgery or for cardiac follow up, were excluded from the study. Patients presenting for elective care or treatment for chronic illnesses were excluded from the study."*

We also conducted a phone interview 14 days post-discharge for those participants who were not initially admitted to the hospital to determine mortality status, children returning to the hospital with the same illness, and children admitted to a hospital (the study hospital or elsewhere) for the same illness. This was to capture those children who were inappropriately sent home. I have included this information in the updated manuscript:

*"A telephone interview was conducted post-discharge to determine 1) mortality status, 2) whether the child completely recovered from the illness, 3) if the child returned to a hospital or health center seeking help for the same illness, 4) if the child was admitted to a hospital or health center for the same illness."*

*"Taking into consideration that children could be inappropriately sent home, we captured mortality and admission to a hospital or other health facility after being sent home using a telephone interview 14 days following discharge. Among discharged participants, mortality (0.2%) and re-admission (2%) rates were minimal (Table 4)."*

**Results**
**It would have been useful to have a sense of the age-spread of the study population, and the profile of reasons for admission.**

I have included this in the updated version of the manuscript (see Tables 3 and 4).

**It is demonstrated that 35 patients had missing data for oxygen saturation and heart rate. Was the missing data primarily in the group who were admitted, or was it evenly distributed across the groups? Clearly one is concerned that saturation data may be more difficult to achieve in very sick children.**

Both the admitted (N = 4 missing) and not admitted (N = 31 missing) groups had an even distribution of missing data for oxygen saturation (~3% missing).

**It seems strange that the 3 children with "uncontrolled bleeding" and the 3 children with apnoea did not require admission. Both events would seem as if they were good reasons for admission. Similarly, it seems strange that 6 of the children with "newly onset hemiparesis" were not admitted to the hospital.**

We would strongly agree with these observations. We are unable to verify this information. It is also possible that some of these may have been data entry errors.

**Discussion**
**As highlighted by the authors a major limitation of the study is that hospital admission was used as a surrogate for acuity of illness. In addition, there was probably overlap between the criteria used by the research team and those used by the clinical team which may have biased the study.**

We have explained above the motivation to use hospital admission as a surrogate for triage category. Due to the nature of this study, the overlap is inevitable and would be present in any study exploring predictors of critical illness in children. This is an ecological study in a clinical setting, so of course there will be bias, we agree and have acknowledged this.

**It does seem to make sense to exclude rare events from the triage data collection, but as a category "rare events" may be a strong indication for admission. As an example, it would seem likely that a child with a large tumour would be admitted to hospital regardless of the overall triage score.**

In the discussion, we do mention how these rare events can be used as individual triggers for admission prior to the use of any risk prediction tool. The prediction tool will be most useful in the cases where the need for admission is not obvious. It is not realist to model these rare outcomes.

**Conclusions**
**The model has been shown to conform with the rate of patient admission. That has potential, but as the authors point out, it will require validation in other settings. It will also need to be applied prospectively to patients coming through the system to**

**see how well it actually predicts in another set of patients in the same setting.**

The model is currently being validated in an independent multi-site study that will include clinical implementation to assess performance in varied geographical locations, seasons, and with different disease prevalence and severity.

*Competing Interests:* No competing interests to disclose.