VALIDATION STUDY OF TWO STANDARDISED RESPIRATORY SEVERITY SCORES (LIBSS and ReSVinet) IN INFANTS PRESENTING TO TERTIARY HOSPITALS IN RWANDA.

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VALIDATION STUDY OF TWO STANDARDISED RESPIRATORY SEVERITY SCORES (LIBSS and ReSVinet) IN INFANTS PRESENTING TO TERTIARY HOSPITALS IN RWANDA.

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MASTERS of Pediatric and Child health

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DECLARATION

I declare that this Dissertation contains my own work except where specifically acknowledged.

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10103318

Signature…….

Date: March 22nd, 2019

DEDICATION

To The Almighty God who made me, saved me and protect me.

To my beloved mother, Bernadette MUKAKIMENYI.

To My Brothers and Sisters

To Penny and Mike Herlihy family and Brother Malisaba straton

To My teachers and Mentors

I humbly dedicate this work.

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My thanks go first to God Almighty for having given me the courage and perseverance to pursue my dream.

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Finally, I would like to thank the residents in Pediatrics especially the promotion 2015 for their support during the past 4 years.

May God bless all the above and anyone who contributed to my training in a way or another. It would not have been possible without you.

ABSTRACT

Background: There is a large burden of respiratory disease in infants in the sub-Saharan Africa region. The aim of this study was to assess the validity of two standardized respiratory distress severity scores (LIBSS and ResVinet) in the Rwandan population.

Methods: A cross-sectional validation study was conducted in four tertiary hospitals in Rwanda. Infants presenting with difficulty in breathing were included. The LIBSS and ResVinet scores were independently employed by nurses and residents to assess severity of disease in each infant.

Results: 100 infants were recruited with a mean age of 201 days. Infants presented with pneumonia (n=51), bronchiolitis (n=36) and other respiratory infections (n=13). Thirty-three infants had severe disease and survival was 94%. Regarding inter-rater reliability, the intra-class correlation coefficient (ICC) for LIBSS between nurses and residents was 0.985 (CI: 0.978- 0.990, SD±16.7, $p<0.001$). For ResVinet ICC was 0.980 (0.971 - 0.987, SD±6.9, $p<0.001$). Regarding validity, the convergent validity (Pearson's correlation) between LIBSS and ReSVinet for residents was R=0.815, ($p<0.001$) and R= 0.836 for nurses ($p<0.001$). Regarding criterion validity the area under the receiver operator curve (aROC) for admission to PICU or HDU was 0.956 (CI: 0.918-0.995, $p<0.001$) and 0.880 (CI: 0.798-0.962, $p<0.001$) for nurse completed LIBSS and ReSVinet respectively. The aROC for hospital admission was 0.976 (CI: 0.947-1.0, $p<0.001$) and 0.974 (CI: 0.944-1.0, $p<0.001$) respectively.

Conclusion: Both LIBSS and ResVinet demonstrated good reliability and validity results and they are therefore suitable for use in this population. Severity scores can be used as an adjunct to clinical assessment to identify infants with severe respiratory disease.

KEY WORDS

Respiratory tract infection, Severity of illness index, Validity, Reliability, Respiratory distress**.**

LIST OF SYMBOLS AND ACRONYMS

BUTH: Butare university teaching Hospital
CPAP: Continuous Positive Airway Pressure
IMCI: Integrated Management of Childhood Illness
KFH: King Faisal Hospital
KUTH: Kigali University Teaching Hospital
LIBSS: Liverpool Bronchiolitis severity score
ORS: Oral rehydration salt
ReSVinet: Respiratory Syncytial Virus Network Scale
RMH: Rwanda Military Hospital
AROC: Area under receiver operating curve
OPD: Outpatient Department
WHO: World Health Organization
HCPs: Health Care Providers

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CHAPTER 1: INTRODUCTION

1.1.Pediatric respiratory distress

Acute pediatric respiratory distress is one of the most common causes of pediatric emergency department admissions. Common etiologies include conditions such as bronchiolitis and pneumonia which remain major causes of pediatric respiratory distress in infants (Øymar et al. 2014; Rudan et al. 2008).

Bronchiolitis is an acute lower respiratory tract infection (LRTI) in early childhood caused by different viruses including respiratory syncytial virus (RSV) (Øymar et al. 2014). Bronchiolitis presents with cough, wheezing, breathing difficulty, poor feeding as main symptoms (Øymar et al. 2014). It is the most common cause of hospitalization in infants consulting in developed countries but data are lacking in resource-limited countries (Caffarelli et al. 2015).

Pneumonia is defined as a pulmonary parenchyma infection that cause alveolar air spaces inflammation, mucous secretion that appear as consolidation on chest radiography secondary to various infectious agents (Scott et al. 2008) while WHO defines clinical pneumonia simply as an acute episode of cough or difficulty breathing associated with an increased respiratory rate (Scott et al. 2008) . In addition pneumonia remains a major cause of death in under 5 years old children with 19% of all death in this age group worldwide where 70 % of those death are taking place in Sub-Saharan African and South- East Asia (Rudan et al. 2008; Øymar et al. 2014).

1.2.Pediatric Respiratory Disease in the Resource-Limited Setting

Respiratory distress due to LRTI is associated with higher morbidity and mortality in children worldwide (Brown et al. 2013; Gowraiah et al. 2014). This is especially in the resource-limited setting where mechanical ventilation facilities are limited or unavailable (Brown et al. 2013). Left untreated pediatric respiratory distress will lead to respiratory failure which has been identified as the main cause of cardiac arrest in children (Donoghue et al. 2005).

The management of bronchiolitis remain challenging as commonly used treatments including bronchodilators, steroids, chest physiotherapy, nebulising with 3% hypertonic saline antiviral and antibiotics are not recommended with the exception of supportive care with nasal suctioning, hydration and provision of oxygen (Baraldi et al. 2014).

In the resource-limited setting the availability of bubble CPAP which is cost effective can help maintain the alveoli open in infants with acute LRTI struggling with respiratory distress to help to prevent progression to respiratory failure, complications and/or death (Brown et al. 2013).

For pneumonia, limited laboratory capacities in identifying causative bacteria on timely basis to guide the treatment and getting samples from the respiratory tract to identify the causative bacteria remain challenging due to a lack of skills or trained personnel that can help in particularly retrieving lower respiratory tract samples by bronco-alveolar lavage (Scott & Hall 1999).

In addition, many of primary health care providers that initially receive infants with respiratory distress are not skilled enough to differentiate bacterial pneumonia and viral induced infection (for example the expertise of recognising expiratory wheezing that are typical for bronchiolitis by a stethoscope) might lead to poor management and outcome (Gowraiah et al. 2014).
In order, to reduce under 5 year mortality where a big part is due to acute respiratory infection particularly pneumonia in resource limited countries, WHO not only promoted vaccination against streptococcus pneumonia, haemophilus influenza type b, measles and pertussis to reduce pneumonia related death but also implemented IMCI where community health workers are trained and provide antibiotics to every child suspected to have pneumonia but death due to respiratory infection remain high compared to diarrheal associated deaths that decline with introduction of ORS and Zinc supplement (World Federation of Hemophilia 2012; WHO 2013). we are still lacking the best approach of differentiating viral induced and bacterial pneumonia or mixed disease as the treatment will be individualize together with a tool that helps early identification of children at high risk of death (Mackenzie 2016; Levine et al. 2012).

1.3. Incidence and risk factors of respiratory diseases (limited setting)

Respiratory diseases constitute a major public health problem worldwide where more than one billion people globally are affected each year and remain among the predominant causes of mortality and morbidity in children (Smith et al. 2000). The most common respiratory illnesses contributing to the global burden are acute respiratory infections, chronic obstructive pulmonary disease, asthma, tuberculosis, and lung cancer where acute respiratory infections causes more than 4 million death annually (Zar & Ferkol 2014). Indoor Air pollution by biomass fuel has been contributing to respiratory morbidity and mortality in infants and children residing in resource-limited settings where indoor cooking smoke induces airway irritation, inflammation and increase the risk of developing bronchiolitis and bronchopneumonia (Smith et al. 2000; Janjua et al. 2012; Sofoluwe 1968).

Angela et al , report that the prevalence of acute respiratory tract infection in under five years children in resource-limited settings is 13 % and socio economic inequalities and living in high risk indoor environment was highly associated with developing Acute Respiratory Infections (Pinzón-Rondón et al. 2016). In resource-limited settings, around 150 million episodes of pneumonia occur every year and 2 million of them resulting in death (WHO 2013). Deaths from pneumonia have been linked to low health coverage, lack of exclusive breastfeeding, incomplete immunization and lack of access to an appropriate health care services (UNICEF 2006). Maternal exposure to tobacco smoking during pregnancy and the mother being not the primary caregiver was associated with the likelihood of coughing symptoms indicating respiratory infection (Shibata et al. 2014).

In addition, malnutrition contribute to more than a half of all death in resource-limited settings and Undernutrition expose children to increased risk of developing pneumonia in two possibilities. Initially, undernutrition weakens child's immune system due to inadequate amount of protein and energy required for proper immune system functions Secondary, malnourished children have weakened respiratory muscle that struggle in clearing respiratory tract secretions exposing them to respiratory infection (UNICEF 2006; Singh 2005).

Moreover, the management of infants and children who present with respiratory distress is challenging as the commonly used method in adults of measuring pulmonary function to determine the severity of airways obstruction using spirometry is not feasible due to their under developed airways (Abbasi et al. 2012). Therefore, to reduce childhood mortality, the severity of illness in infants with respiratory distress need to be identified and select children who have an increased risk of death to provide appropriate care and improve their outcome (Diana M. Duarte-Dorado et al. 2013).

1.4. Clinical measurement instruments

The validation of clinical measurement instrument is an essential process for their measurement properties to ensure that they measure what it is intended to be measured. A clinical measurement instruments is defined as a clinical assessment tool made by clinical signs and symptoms that are validly grouped together to measure the construct they intend to measure.
This validation process should include assessment of reliability (internal consistency, test–retest reliability, and inter-rater agreement), validity (face validity, construct validity, content validity and criterion validity), responsiveness, and usability or interpretability (Diana M Duarte-Dorado et al. 2013; Downing 2003; Sullivan 2011). However validity has been split into distinct types content, criterion and construct validity traditionally but contemporary thinking suggest that all validity should be conceptualized under one framework of construct Validity (Cook & Beckman 2006).

Reliability of a clinical score is defined as the extent to which a test will produce consistent results on similar subjects under similar condition with precision of certain measurement (Cook & Beckman 2006). While validity is defined as the accuracy of measurement of a clinical assessment tool (Cook & Beckman 2006). However, reliability is one of essential component of validity of a clinical assessment tool (Ursachi et al. 2015; Beckman et al. 2008; Downing 2004).

CHAPTER 2: LITERATURE REVIEW

2.1 Literature search

The aim of this literature search and review was to identify published scoring instruments for use in pediatric respiratory distress and to assess their measurement properties.

A literature search was performed using Pubmed and Google Scholar using the search terms in Appendix 1. The Pubmed search revealed 316 papers and among them 14 papers were relevant to our topic (Mussman et al. 2017; Balaguer et al. 2016; van Miert et al. 2014; Miert 2015a; Bobek et al. 2010; Mosalli et al. 2015; Diana M Duarte-Dorado et al. 2013; Fernandes et al. 2015; McCallum et al. 2013a; Destino et al. 2012; Marlais et al. 2011; Gajdos et al. 2009; Walsh et al. 2006; Walsh et al. 2004; Liu et al. 2004). We undertook a manual search of the reference lists of the relevant papers and identified a further five relevant papers (Chin & Seng 2004; Pavón et al. 1999; Alario et al. 1995; Caserta et al. 2017; Justicia-Grande et al. 2016). Twelve papers were excluded as they did not meet the inclusion criteria (Appendix 1). We therefore critically reviewed seven articles (Appendix 2) which described potential respiratory distress scores which could be used in this study.

2.2. Respiratory distress scores

The ideal respiratory severity score for young children should be quick and straightforward to undertake and interpret. It should not involve complex measurements, descriptions or equipment. It should be applicable to children from birth to two years of age, adequately validated and responsive to clinical change. Though scores should measure what they intend to measure, in this case an ideal respiratory distress score would be able to assess severity in all respiratory conditions, including bronchiolitis, to ensure a simple approach for healthcare professionals (HCPs). However, the pathophysiology, age of child makes these ideals difficult to achieve.

To overcome the issue of challenge in the management of children presenting with respiratory distress validated respiratory severity score combining clinical symptoms and physical signs can contributes in the assessment of severity of respiratory distress in an infant presenting with acute respiratory illness (Diana M Duarte-Dorado et al. 2013). Different researchers have developed and validated different severity scores for respiratory distress assessment that were used mainly in developed countries and some Asian countries.

However, many of these have been published and validated for assessment of infant or children with acute respiratory infection none of them have been sufficiently validated to allow meaningful use in children (Justicia-Grande et al. 2016). they have important limitations where they showed a limited validity when systematically evaluated and for that reason many clinical scale have been undergoing modification to meet individual outcome (Gajdos et al. 2009).

I would mention the Respiratory index of Severity in Children (RISC) Scoring and the Modified Respiratory index of Severity in Children (mRISC) scoring, Scores validated Kenya and Malawi to assess respiratory distress. However, they limit themselves on prediction of mortality among hospitalized patients for pneumonia(Hooli, Colbourn, Lufesi, Costello, Nambiar, Thammasitboon, Makwenda, Mwansambo, McCollum, et al. 2016; Hooli, Colbourn, Lufesi, Costello, Nambiar, Thammasitboon, Makwenda, Mwansambo, Mccollum, et al. 2016; Emukule et al. 2014)

Among those severity scores some was developed for assessment of distress in specific respiratory illness like asthmas and bronchiolitis as causes of respiratory distress, however few were designed to assess respiratory distress severity in all acute respiratory illness regardless of the cause (Smith et al. 2002; Balaguer et al. 2016; Walsh 2006; Ho Jen Chin & Quah Ban Seng 2004; Bekhof et al. 2014).

In addition, none of them was developed and validated to be used in African sub-Saharan setting to stratify patients severity of distress before admission and take a wise decision about medical treatment and needed respiratory support to improve the management of children with respiratory illness in low setting area.

Some of those respiratory severity score are the ReSVinet and LBSS score that appear to be appropriate score in the assessment distress of respiratory infection particularly bronchiolitis (Justicia-Grande et al. 2016; Miert 2015b). Therefore, the use of single tool that have a good validity in evaluation of respiratory status of an infant in a resource limited setting by different healthcare providers is important in improving patient care and reducing morbidity in children presenting with acute respiratory distress (Gajdos et al. 2009).

2.3. Commentary of articles from our literature search

In our appraisal, we reviewed six papers (Appendix 2) which incorporated eight respiratory severity scores. Seven of these are bronchiolitis specific, and one generic respiratory score (CHWRS**,** (Destino et al. 2012)) used to assess children with bronchiolitis. One further score should be mentioned, the ReSVinet score (Justicia-Grande et al. 2016). ReSVinet is bronchiolitis specific and includes seven parameters suitable for the resource-limited setting. Items for inclusion in ReSVinet were identified from existing scores. Ninety pediatricians assessed face validity. Validity (construct), reliability (inter-rater) and internal consistency were undertaken retrospectively using information obtained from patient records. Because of the retrospective methodology, it did not meet the inclusion criteria.

Parameters: The majority of care facilities in the resource-limited setting do not have access to investigations such as chest radiograph and blood gas analysis. Of note, the majority of guidelines for bronchiolitis treatment, even in the developed setting discourage routine use of these investigations (NICE 2015). We only included studies utilizing clinical parameters. Parameters employed were (n=number of scores using the clinical measure): Accessory muscle use (n=1); Air-entry (n=1); Apnea (n=1); Breath sounds (n=3); Capillary refill time (n=1); Chest x-ray (CXR)/lung sound (n=1); Cough ability/secretion(n=1); Cyanosis (n=2); Dyspnea (n=3); Feeding(n=1); General appearance (n=3); HR (n=4); Lethargy(n=1); Oxygen Need (n=1); Poor air

movement (n=1); Retractions (n=4); RR (n=7); $Sa0_2$ (n=4); Surgical status (n=1); Urine output (n=1); Wheezing (n=5). These parameters would all be feasible in the resource-limited setting except for SaO_2, which requires equipment which has variable availability. One study (CHWRS**)** gave a combined parameter of CXR or lung sounds. Therefore, in the resource-limited setting the assessor could use lung sounds when CXR was not available. Therefore this article was not excluded during the search (Destino et al. 2012).

2.3.1. Validity

Regarding hospital admission, two scores (Caserta et al. 2017; Destino et al. 2012) assessed for discriminative validity. This is important in terms of our PICO question which aims to clarify if the clinical score can be used to assist decision making to discriminate between children who need admission to hospital or not. The purpose of construct validity is to establish an association between a score and how it measures a hypothetical construct (Streiner, FDA guidance). Criterion validity is the level of agreement between a new score and the reference standard. There is no pre-defined reference standard other than clinical assessment by an expert healthcare professional, which was used in one paper (Balaguer et al. 2016).

2.3.2. Cross-cultural validity

All of the scores were assessed in High-Income Countries (HICs) The scores were developed and, in some cases, validated in the following countries: Australia (n=2); Spain (n=2); UK (n=1); USA (n=3). None of the scores have been assessed for cross-cultural validity. This is a potential limitation to use in the resource-limited setting, due to language considerations, and the clinical skills and educational level of the HCPs undertaking the scoring.

2.3.3. Reliability

Inter-rater reliability is important as any tool should reliably give the same score irrespective of the professional using it. This is vital for both clinical use and research. Five of the scores had inter-rater reliability performed with varying levels of reliability (BROSJOD, LIBSS, Tal and M-Tal scores, RDAI & CHWRS), (Table 2).

2.3.4. Responsiveness

Only one study assessed responsiveness to change (Destino et al. 2012). Though this is not required for assessing the need for admission, it is useful for monitoring progress in hospital as deterioration is characteristic in the first few days of illness.

2.4. PROBLEM STATEMENT

Respiratory diseases are common in Rwanda and throughout sub-Saharan Africa. Many respiratory severity scores have been developed and validated but none were developed and/or validated for use in Sub-Saharan Africa to stratify children severity of distress before admission (Justicia-Grande et al. 2016). Respiratory distress scores are useful for both clinical practice and to ensure robust findings from future research.

2.5. RESEARCH AIMS AND OBJECTIVES

2.5.1 Research aims:

To translate and evaluate the measurement properties (validity and reliability) of two previously validated scoring instruments (LIBSS and ReSVinet) in a population of Rwandan children and to assess the severity of respiratory distress in infants (1-12 months) consulting tertiary pediatric hospitals.

2.5.2 The specific research questions are:

1. What are the inter-rater reliability and internal consistency of LIBSS severity score and ResVinet score?
2. What is the association/correlation between the severity scores and important outcomes, namely; admission to admission to hospital care and admission to high dependent care unit (HDU) or pediatric intensive care unit (PICU)?
3. What is the severity of respiratory distress of children consulting tertiary hospitals with respiratory illness?

CHAPTER 3.METHODOLOGY

3.1.1 Study design and description

We conducted a cross-sectional, validation study from September 2018 till February 2019. Reporting of this study has been verified in accordance with the STARD and TRIPOD checklists for diagnostic studies (Collins et al. 2015; Bossuyt et al. 2015).

3.1.2 Study sites

This was a multi-centre study, conducted at five Rwandan Hospitals namely; Kigali University Teaching hospital (CHUK), King Faisal Hospital (KFH), Rwanda Military Hospital (RMH), Butare University Teaching hospital (CHUB) and Ruhengeri Referral Hospital (RRH). CHUK, KFH and RMH are all located in Kigali, the capital city of Rwanda. CHUB and RRH are in provincial towns. All hospitals are tertiary referral centres. These sites are all located in urban settings but receive patient from both rural and urban settings.

3.1.2 Selection of study population

3.1.2.1 Inclusion criteria

We included infants aged between 1-12 months of age presenting with respiratory distress (Monto & Sullivant 1993; Hazinski MF 2010) due to respiratory illnesses (e.g. pneumonia, bronchiolitis etc).

3.1.2.2. Exclusion criteria

This study not only excluded infants with known chronic lung disease (CLD), ones that parents didn't sign the patient consent form as well as Infants that presented with non-respiratory cause of respiratory distress (e.g. established cardiac disease). In addition, children from parents who are under 18-years-of-age and therefore unable to legally sign a consent form were not able to participate.

3.1.3. Sampling

Prospective convenience sampling was employed at the study sites from both the outpatient departments and the pediatric emergency room (ER). We enrolled infants with mild, moderate and severe respiratory distress.

3.1.4. Case definition

Our case definition of symptoms and signs indicative of respiratory distress were (Miert 2015b; Justicia-Grande et al. 2016) apnoea, recessions, tracheal tug, nasal flaring, head bobbing, grunting, cyanosis, oxygen desaturation, tachypnea, wheezing, stridor, oxygen requirement, reduced air-entry.

3.1.5 Data collection tools

Five sections were present in the data collection tools,

1. Unique Patient Identifier Sheet (Appendix 4)
2. Patient demographics information, we used the Demographics and Health Survey (DHS) parameters to design the *Study specific questionnaire* (Monto & Sullivant 1993)
3. *LIBSS,* A validated score for use in children with bronchiolitis between the ages of 0-12 months (Appendix 5&5a). LIBSS has two scoring systems 0-3

months score and 3-12 months to take into account for age dependent vital signs (Miert 2015b). The LIBSS score has 10 parameters (Table 1)

4. *ReSVinet,* is a validated clinical severity scale that was developed to assess severity of illness in infants with bronchiolitis (Justicia-Grande et al. 2016). ResVinet Score has 7 parameters.
5. Follow-up questionnaire for final outcomes, admission pediatric ward; admission to HDU or PICU and outpatient treatment (Appendix 3). This section was specifically designed for the purposes of this study

Both LIBSS and ResVinet employ clinical parameters assessed by healthcare professionals. The parameters of both scores that we used are applicable to all respiratory diseases that can cause respiratory distress in infants.

Translation: to overcome language related barriers, LIBSS and ReSVinet were translated into Kinyarwanda by the principal investigator (PI) and then back-translated for accuracy by a native-Kinyarwanda speaking pediatric resident (Appendix 5, 5a and 5b). Discrepancies were reviewed with a third native-Kinyarwanda speaking pediatric resident for consensus.

Table 1: Parameters assessed in ReSVinet and LIBBS

LIBBS (10 parameters)	**ReSVinet (7 parameters)**
1. General condition; 2. Apnea; 3. Increased work of breathing; 4. Sa02; 5. Respiratory Rate; 6. Appearance 7. Heart Rate; 8. Feeding; 9. Urine output; 10. Capillary refill time	1. Feeding intolerance; 2. Medical intervention; 3. Respiratory difficulty; 4. Respiratory rate; 5. Apnea; 6. General condition; 7. Fever

3.2. Study procedures

3.2.1. Procedures at enrolment

After gaining a signed informed consent form from the parent or caretaker allowing the infant to participate in the study. The data collectors recorded each participants name and file identification number on the unique patient identifier sheet, thus creating a code for each to appear on his/her data collection papers. Then a background data collection sheet was completed by one data-collector (Appendix 4).

Thereafter one pediatric resident and one nurse independently assessed the infant using LIBSS and ReSVinet. The order of assessment was not fixed. Each data collector used both the LIBSS and the ReSVinet severity scores and they didn't share their findings in order to remain blind to each other's assessment. The pediatric residents and nurses undertaking the assessments had been trained in how to use the scores. They were healthcare professionals involved in the care of the child and were therefore not blind to the previous condition and treatment of the child.

3.2.2. Outcomes

The main outcomes were the validity and reliability of the two standardised severity scores in a Rwandan population of infants.

The secondary outcome was the description of severity of respiratory distress in infants aged between 1-12 months enrolled in the study.

3.2.3. Sample size calculation

The 'rule of thumb' to determine sample size for a clinical field-test is 10 and 15 participants for each included parameter/item where the sample size will be 10K or 15 k (K being the number of parameter in a test) (David L. Streiner, Geofrrey R.Norman n.d.). This would give sample sizes of 100-150 for LIBSS (10 parameters) and 70-105 for ReSVinet (7 parameters).

Cicchetti and Fleiss (1977) state that with two raters:

$$\text{Sample size} = 2k^2$$

Where k is the number of parameters on the scale

For **LIBSS** there are 10 parameters (k) on the score.

$$\text{Therefore sample size} = 2 \times 10^2 = 2 \times 100 = 200 \text{ subjects}$$

For ReSVinet there are 7 parameters (k) on the score.

$$\text{Therefore sample size} = 2 \times 7^2 = 2 \times 49 = 98 \text{ subjects}$$

For Streiner, the sample size is 10 K= for LIBSS= 100 and for ReSVinet= 70

Therefore we are aimed for a sample size between100 to 200.

3.2.4. Data Management and statistical analysis

Data will be entered into Microsoft Excel and analyzed using SPSS version 24. The following statistical analysis is planned

Even though the validation of clinical measurement instrument requires different aspect as described in the literature review; in our study we only evaluated inter-rater reliability and internal consistence for reliability and for validity we evaluated the convergent validity and criterion validity.

3.2.4.1. Reliability

Reliability, was evaluated by

1. Inter-rater reliability (agreement) between nurse and pediatric resident using LIBSS and the ReSVinet severity scores. To address reliability during data correction, two raters (one nurse and one pediatric resident/specialist) worked independently for both scores. Inter-rater reliability (agreement) between nurse and pediatric resident using LIBSS and the ReSVinet severity scores will be assessed using Cohen's Kappa and Intraclass correlation coefficiency (ICC). The agreement will be good for a kappa above 0.8 and moderate for a weighted kappa ranging between 0.61 to 0.80.

2. Internal consistency of the parameters within each score using Cronbach alpha. Cronbach alpha >0.7 was pre-defined as being good.

3.2.4.2. Validity

Validity was assessed in two categories

1. Correlation of LIBSS and ResVinet scores whereby, a Pearson's r correlation coefficient was calculated between the score of LIBSS and the score ResVinet to evaluate how both scores provide the same information of severity of respiratory distress when applied to the same patient in a similar condition.
2. Criterion validity that is also known as a predictive validity relative to admission to hospital care and admission to high dependent care unit (HDU) or pediatric intensive care unit (PICU) based on the severity score of the patient was calculated using an area under the receiver operating curve (aROC).

3.2.4.3. Severity of disease

Severity of disease will be compared with risk factors using bivariate analysis and description of Odds Ratios using Chi-square. Multivariate logistical analysis with Adjusted Odds Ratios was performed to minimise for confounding.

3.3. ETHICAL CONSIDERATIONS

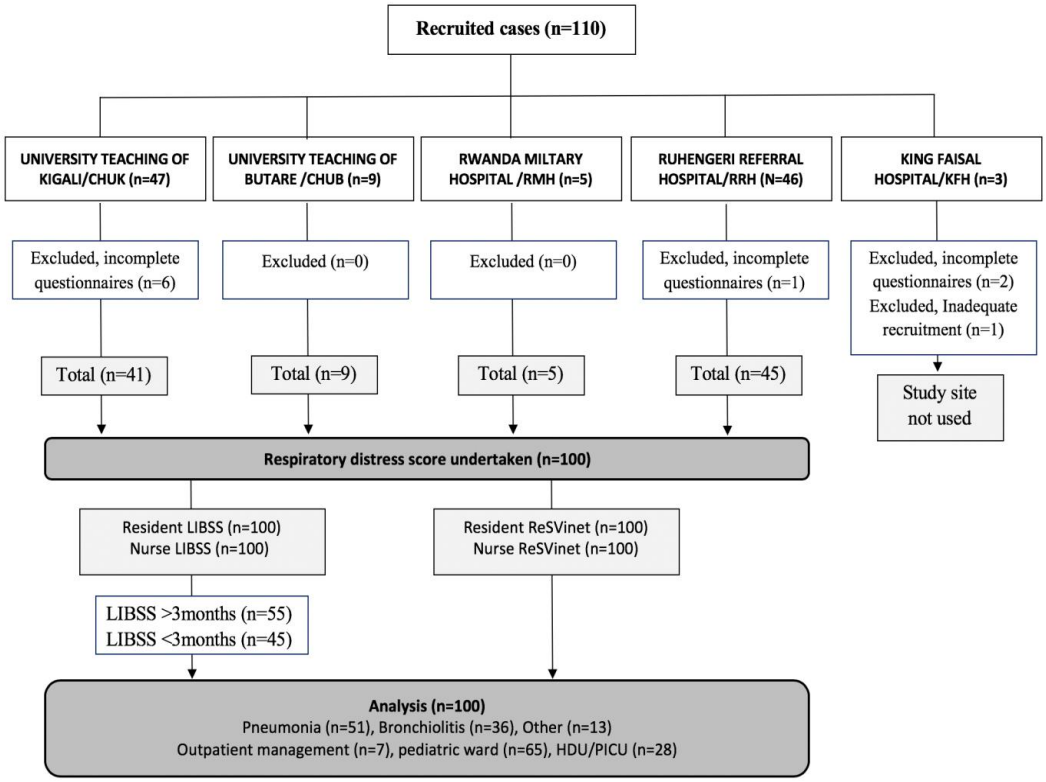
The research proposal was submitted and approved by the Research and Ethics Committees of the School of Medicine at the University of Rwanda, the local ethics and research committee of the University Teaching Hospital of Kigali, University Teaching Hospital of Butare, Rwanda Military Hospital, Ruhengeri referral Hospital and King Faisal Hospital (Appendix 12&12a).

Ethical approval references: Ref: NO237/CMHSIRB/2018, Ref: NO375/CMHSIRB/2018, Ref: EC/CHUK/620/2018, Ref: 1409/HDR/HRR/2018(RRH), Ref: RMH/IRB/008/2018, REF: CHUB/DG/SA/07/1399/2018

For each eligible infant, the parents or authorized legal person were fully cognizant about the study and signed the informed consent written in Kinyarwanda, before being included in the study. Enrollment in the study was based on the consent given and patient confidentiality was observed.

CHAPTER 4: RESULTS

Figure 1: Patient Recruitment in Our Study



4.1. Recruitment

A total of 110 eligible infants were recruited (Figure 1). Forty-seven infants were recruited at CHUK; however, for six of these the data collection by the nurse data-collector was incomplete and inadequate despite training. This was one data-collector out of five data-collectors; the data most commonly omitted were the heart rate and respiratory rate. Therefore, these cases were removed and the data-collector ceased being a member of the data-collection team. At KFH, the only private facility recruitment site, only three patients were recruited. Two of these were excluded with incomplete data. Therefore, only one patient remained. This patient was therefore removed as it was deemed that recruitment was insufficient enough to give the nurse data-collectors adequate experience to become skilled at using the two respiratory distress scores.

Data quality:

The questionnaires contained a total of 82 measurable variables. No variables contained any missing data points.

4.2. Demographic characteristics of the participants

Table 2: Demographic characteristics of the participants

		Frequency (n= 100)	Mean
Gender			
	Male	63(63%)	
	Female	37(37%)	
Mean age (days)			201. (SD ±114.73)
Mean weight			6.6 (SD ± 2.43)
Social Group (Ubedehe)			
	High (3 & 4)	47 (47%)	
	Low (1 & 2)	53(53%)	
Residence			
	Urban	32 (32%)	
	Rural	68(68%)	
Living sibling			
	No	20 (20%)	
	Yes	80(80%)	
Vaccination			
	No	0 (0%)	
	Yes	100 (100%)	
Maternal marital status			
	Married	84(84%)	
	Single, divorced, Widowed	16(16%)	
Maternal age			
	Young (<25 years)	32 (32%)	
	Old (≥25years)	68(68%)	
Maternal occupation			
	Unemployed	19(19%)	
	Manual labourer	64(64%)	
	Professional	17(17%)	
Maternal educational level			
	High	49(49%)	
	Low	51(51%)	
Diagnosis			
	Pneumonia	51(51%)	
	Bronchiolitis	36(36%)	
	Other	13(13%)	
Co-morbidities			
	Malnutrition	12(12%)	
	Prematurity	5(5%)	
	HIV positive	2(2%)	
Management			
	Outpatient	7(7%)	
	Pediatric ward	65(65%)	
	HDU/PICU	28(28%)	
Median length of stay (days)			6.5 (SD ±7.14)
Mortality rate/ Died			
	Yes	6 (6%)	
	No	94(94%)	

We retained in total 100 participants (Figure 1), 63% were male. Their mean age was 201days (SD ± 114.73). Mean weight and length of hospital stay were6.6kg (SD ± 2.43) and 6.5days (SD ±7.14) respectively (Table1). Our participants were diagnosed with pneumonia (51%), bronchiolitis (36%) and other infections (13 %). Survival rate was 94%.

Management: Twenty-eight patients required HDU or PICU management, with only 7% requiring outpatient management alone and were seen once (Table 2).

4.3. Severity of respiratory disease

Nurses undertook severity assessment with LIBSS and ReSVinet and found 33% and 16% with severe disease respectively (Table 3).

Table 3: Severity of Distress LIBSS and ReSVinet

		Mild	Moderate	Severe	Inter-rater reliability (Kappa)
LIBSS	**Residents**	14	48	38	
	Nurses	13	54	33	0.900 (p<0.001)
ReSVinet	**Residents**	16	67	17	
	Nurses	16	68	16	0.899 (p<0.001)

4.4. Treatment

The majority of participants were treated with antibiotics (82%) and oxygen therapy (93%) (Table3). In infants with bronchiolitis, non-standard therapy such as adrenaline (47%) and salbutamol nebulisation (58%) and steroid (14%) were given. In patients with severe disease 5% required intubation and mechanical ventilation while 8% required CPAP (Table 4).

Table 4: Treatment

	Pneumonia (n=51)	Bronchiolitis and others (n=36)	Other (n=13)
Antibiotic	51 (100%)	26 (72.2%)	5 (38,5%)
Oxygen therapy	50 (98%)	35 (97.2%)	8 (61.5%)
Salbutamol nebulisation	13 (25.5%)	21 (58.3%)	8 (61.5%)
CPAP	5 (9.8%)	3 (8.3%)	0 (0.0%)
Adrenaline nebulization	4 (7.8%)	17 (47%)	4 (30.8%)
Steroid administration	3 (5.9%)	5 (13.9%)	4 (30.8%)
Intubation and ventilation	1 (2%)	3 (8.3%)	1 (7.7%)

Co-morbidities:

Regarding co-morbidities, malnutrition (12%), and prematurity (5%) and HIV (2%) were identified (Table 2).

Table 5: Validity Results

		LIBSS	ReSVinet
Validity statistics			
Convergent validity (LIBSS versus ReSVinet)	Pearson's correlation (resident)	R=0.81 (p<0.001)	
	Pearson's correlation (nurse)	R=0.836 (p<0.001)	
Convergent validity (Score versus length of stay	Pearson's correlation (nurse)	R= 0.461(p<0.001)	R= 0.361(p<0.001)
	Pearson's correlation (resident)	R= 0.484 (p<0.001)	R= 0.374(p<0.001)
Criterion Validity for Hospital admission	aROC (nurse)	0.956 (CI: 0.876-1.0)	0.973 (CI: 0.943-1.0)
	aROC (resident)	0.955 (CI : 0.873-1.00)	0.956 (CI: 0.916-0.997)
Criterion Validity for HDU/PICU	aROC (nurse)	0.956 (CI: 0.918 – 0.995) (p<0.001)	0.880 (CI: 0.798 – 0.962) (p<0.001)
	aROC (resident)	0.951 (CI: 0.911- 0.990) (p<0.001)	0.872 (CI: 0.787- 0.957) (p<0.001)
Criterion Validity for mortality	aROC (nurse)	0.976 (CI: 0.947 – 1.0) (p<0.001)	0.974 (CI: 0.944 -1.0) (p<0.001)
	aROC (resident)	0.974 (CI: 0.944 – 1.0) (p<0.001)	0.980 (CI: 0.954 – 1.0) (p<0.001)
Length of hospital stay	aROC (nurse)	0.718 (CI: 0.619– 0.818) (p<0.001)	0.637 (CI: 0.531 – 0.747) (p<0.001)
	aROC (resident)	0.722 (CI: 0.623 -0. 821) (p<0.001)	0.639 (CI: 0.531 – 0.747) (p<0.001)
Reliability statistics			
Internal reliability	Cronbach's alpha (Nurse)	0.831	0.850
	Resident	0.823	0.848
Inter-rater reliability	Intra-class correlation (Nurse to resident)	0.985 (0.978- 0.990) (SD±16.741) (p<0.001)	0.980 (0.971 - 0.987) (SD±6.899) (p<0.001)
Inter-rater reliability	Kappa (Nurse to resident)	0.900 (p<0.001)	0.899 (p<0.001)

Interpreting Validity and Reliability statistics

aROC: 0.50=no different than random (i.e. useless), 0.50-0.70 low; 0.70-0.90 moderate, >0.90 high (David L. Streiner, Geofrrey R.Norman n.d.)

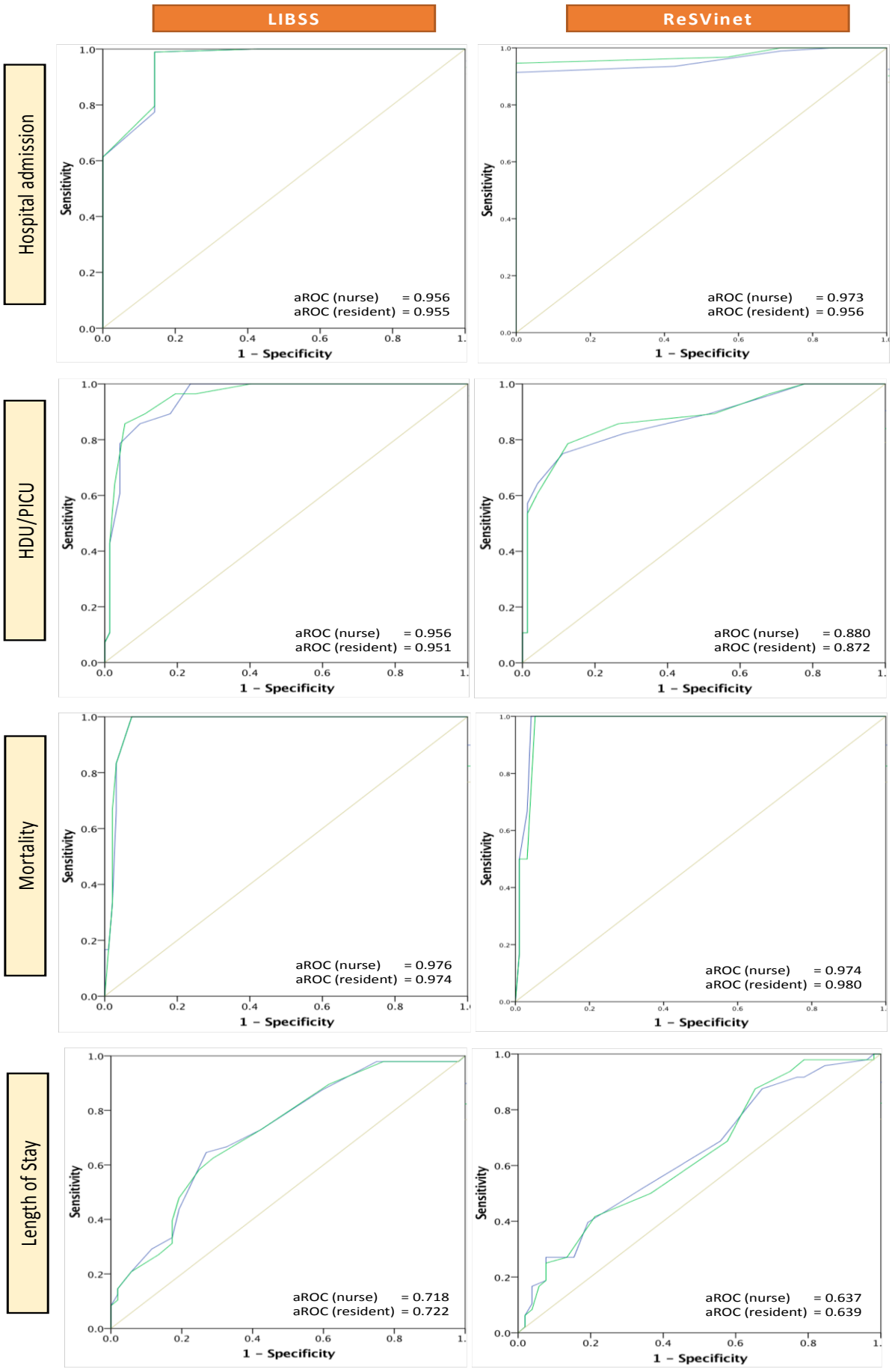
Cronbach's: <0.70 poor, >0.70 good (if <7 items), interpretation is dependent on number of parameters (David L. Streiner, Geofrrey R.Norman n.d.)

Intra-class correlation (ICC): <0.75 poor to moderate, >0.75 is good, >0.9 is excellent (Portney & Watkins 2000; David L. Streiner, Geofrrey R.Norman n.d.).

Kappa for reliability: <0 poor, 0–0.20 slight, 0.21–0.40 fair, 0.41–0.60 moderate, 0.61–0.80 substantial, and 0.81–1 almost perfect (Landis & Koch 2019; Cicchetti 1994).

Pearson and SPR correlation: r, 0-0.19 very weak, 0.2-0.39 weak, 0.40-0.59 moderate, 0.6-0.79 strong and 0.8-1 very strong correlation (Swinscow 2019).

Figure 2: aROC for criterion validity



4.5. Convergent validity

The Pearson's correlation between ResVinet and LIBSS for residents (R=0.815) and nurses (R=0.836) were both very strong (Swinscow 2019) (Table 5 and Figure 3). The p-value of <0.001 for both these results confirmed that it was unlikely that these results occurred by chance.

4.6. Criterion Validity

Both LIBSS and ReSVinet performed highly for predicting mortality, hospital admission, and HDU/PICU admission (Table 5). The most important findings for criterion validity being that prediction of hospital admission by nurse undertaken LIBSS (aROC=0.956, CI: 0.918 – 0.995) and ReSVinet (0.973, CI: 0.943-1.0) that were both high (Figure 2). Both LIBSS and ReSVinet performed only moderately for predicting prolonged length of stay.

4.6. RELIABILITY RESULTS

4.6.1. Internal Reliability

Internal consistency for both scores was good with marginally higher reliability amongst the data of the ReSVinet items (Table 6). The scores share five items. All items revealed consistent reliability with no individual items leading to a large increase in the internal reliability (Cronbach's) of either score (Table 6).

Table 6: Internal Reliability (Internal consistency) of LIBSS & ReSVinet

		LIBSS		**ReSVinet**	
		NURSE	**RESIDENTS**	**NURSE**	**RESIDENTS**
LIBSS only	Appearance	0.804	0.799	-	-
	Central capillary refill time	0.820	0.810	-	-
	Heart rate	0.826	0.822		
	Oxygen requirement	0.809	0.796	-	-
	Urine output	0.804	0.801	-	-
Shared parameters	Apnea	0.833	0.824	0.870	0.864
	Feeding	0.804	0.789	0.810	0.817
	General condition	0.810	0.808	0.823	0.812
	Increased work of breathing (Respiratory difficulty in)	0.809	0.801	0.811	0.808
	Respiratory rate	0.831	0.821	0.812	0.810
ReSVinet only	Fever	-	-	0.844	0.843
	Medical intervention	-	-	0.829	0.825
	Overall Scale Cronbach	**0.831**	**0.823**	**0.850**	**0.848**

4.6.2. Interrater Reliability

The inter-rater agreement (inter-rater reliability) between residents and nurses was excellent for both LIBSS (ICC=0.985) and ReSVinet (ICC=0.980) (Table 5). ICC and Kappa both measure inter-rater reliability but with continuous and categorical data respectively. It is therefore not surprising that the Cohen's kappa, for LIBSS (Kappa=0.900) and ReSVinet (Kappa=0.899) were almost perfect.

4.7. Risk factors

On reviewing the results of the validity and reliability testing LIBSS appeared to be performing better therefore the Nurse-LIBSS score was used to determine the severity of disease when assessing for risk factors. On univariate analysis we found three risk factors that were significantly associated with severe respiratory disease namely; maternal occupation (OR=4.47, CI: 1.0 to 20.9, p=0.049*)*, malnutrition (OR= 3.34, CI: 1.0 to 11.5, p=0.047), and exclusive breastfeeding (OR= 0.21, CI: 0.049 to 0.90, p=0.024) (Table 7).

On multivariate logistical exclusive breastfeeding remained significantly associated with lower odds of severe disease (AOR=0.068, CI: 0.006 to 0.726, p=0.026),
(Table 7).

Table 7: Risks factors for severe disease or death

Risks Factors		n=100	[Δ]Unadjusted Odds ratio (df=1)	[Δ]Adjusted Odds Ratio (AOR)* (df=1)
Social Group	Low	21/53 (39.6%)	OR=1.914 (CI: 0.813 to 4.505) p=0.135[Δ]	AOR=1.097 (CI: 0.401 to 3.003) p=0.857[Δ]
	High	12/47 (25.5%)		
Marital status	Married	28/84 (33.3%)	OR=0.909 (CI:.0.288 to2.872) p=0.871[F]	**NA**
	Divorced, single, Widow	5/16 (31.3%)		
Living children	Yes	23/80 (28.8%)	OR= 2.478 (CI: 0.910 to 6.746) p=0.071[Δ]	AOR=1.782 (CI:0.601 to 5.28) p=0.298[Δ]
	No	10/20 (50%)		
Maternal Education	Low	19/51 (37.3%)	OR= 1.484 (CI: 0.641 to 3.440) p=0.356[Δ]	**NA**
	High	14/49 (28.6%)		
Maternal occupation	Manual labour or unemployed	31/83	OR=4,47 (0.958 to 20.877) **p=0.049** [F]	AOR=7.950 (CI: 0.782 to 80.78) p=0.080[Δ]
	Professional	2/17		
Malnutrition	Yes	7/12 (58.3%)	OR= 3.338 (CI: 0.970 to 11.486) **p=0.047**[Δ]	AOR=2.181 (CI:0.524 to 9.07) p=0.080[Δ]
	No	26/88 (29.5%)		
History of Prematurity	Yes	1/5 (20%)	OR=0.492 (CI: 0.053 to 4.587) p=0.526[F]	**NA**
	No	32/95 (33.7%)		
Parental Smoking	Yes	3/11 (27.3%)	OR=0.738 (CI: 0.182 to 2.984) p=0.668[F]	**NA**
	No	30/89 (33.7%)		
Use of biomass fuel	Yes	30/82 (36.6%)	OR= 2.885 (CI: 0.772 to 10.782) p=0.104[F]	AOR=2.827 (CI: 0.564 to 14.1) p=0.206[Δ]
	No	3/18 (16.2 %)		
Exclusive breastfeeding	Yes	27/91 (29.7%)	OR= 0.211 (CI: 0.0490 to 0.906) **p=0.024**[Δ]	AOR=0.068 (CI: 0.006 to 0.726) **p=0.026**[Δ]
	No	6/9 (66.7%)		

[Δ]CHI-squared' [F]Fisher's Exact test; Multivariate analysis was undertaken on all variables with significance, of p<0.20

CHAPTER 5: DISCUSSION

Study objective and key result related to this**:** This project aimed to assess the validity and reliability of two standardized respiratory severity distress scores (LIBSS and ResVinet) for infants (under 1-year-of-age) with respiratory illness. We found results with good validity and reliability in the selected population of Rwandan infants with acute respiratory illness presenting to tertiary level hospitals.

5.1. Why use LIBSS and/or ReSVinet

In our evidence appraisal, we identified two scores LIBSS and ReSVinet which are both bronchiolitis specific. However, they were chosen over other scores as they do not include symptomology that would be limited to bronchiolitis (e.g. wheeze). LIBSS has ten parameters and ResVinet has seven parameters. Apart from the five shared parameters (Table 6), LIBSS also includes; general appearance, central capillary refill time (CRT), heart rate, oxygen saturation and urinary output. ResVinet includes fever and medical intervention that are not included in LIBSS (Table 6 and Appendix 5,5a&5b).

We identified also two scores used for respiratory illness in the resource-limited setting. Respiratory index of Severity in Children (RISC-Malawi) score developed in Malawi (Hooli, Colbourn, Lufesi, Costello, Nambiar, Thammasitboon, Makwenda, Mwansambo, Mccollum, et al. 2016) and the Modified-RISC score developed in Kenya(Emukule et al. 2014). RISC score includes both "risk" items (e.g. poor nutrition) and "protective factors" (e.g. history of night sweats) which are more likely to be found in chronic illness rather than acute illness. RISC and M-RISC includes items such as Malaria, HIV and nutrition status which are not included in LIBSS or ReSVinet. Both scores were developed to predict mortality of hospitalized under five children with pneumonia and had a good C-statistics values of 0.852 and 0.79 respectively(Emukule et al. 2014; Hooli, Colbourn, Lufesi, Costello, Nambiar, Thammasitboon, Makwenda, Mwansambo, Mccollum, et al. 2016).

These scores were validated in older children RISC (0-24 months) and M-RISC (0 -64 months) of age. Burden of disease and outcomes are worse the younger a child as their immunity is weaker and they have narrowed airways(Simon et al. 2015). However, they didn't evaluate reliability and they deviate from our main research question which aims to categorize severity of distress and thereafter in combination with clinical assessment help in making decision of patient admission and identification of patient requiring HDU or PICU admission. Therefore, they were not chosen for our study.

5.2. SEVERITY OF DISEASE

ReSVinet identified fewer infants as having severe disease compared to LIBSS, while both scores had almost similar patients categorized to have mild disease. However, one patient classified as having moderate disease by ResVinet required intubation, mechanical ventilation and was admitted to PICU, showing a possible limited capacity of ResVinet to identify severe disease. The majority of our patients presented in moderate and severe respiratory distress which is probably related to our choice of

study sites which were referral hospitals and commonly receive patients with severe disease transferred from other healthcare facilities.

5.3. Treatments

Many children with bronchiolitis received non-evidence-based treatments, namely adrenaline (47%), salbutamol (58%), steroids (14%), and antibiotics (72%) which are not only costly for families but are clinically ineffective. Infants who had pneumonia, the most common cause of death related to respiratory infection in sub-Saharan Africa, received antibiotics and oxygen therapy which are the recommended treatments.

5.4. VALIDITY:

5.4.1. Face and content validity

Face and content validity were not assessed in this study as it had already been undertaken in other studies during the development process. During the development process LIBSS was evaluated for content validity by HCPs who rated each domain/item on a 1-4 Likert scale for clinical relevance(Miert 2015a). ReSVinet face validity was assessed by 90 pediatricians, where the proposed score was submitted to those pediatricians for evaluation from outpatient, hospital care, and pediatric critical setting from the Galician Pediatric Research Network (REGALIP) and From the Five Research group; they agreed on the easy of recording and value of the parameter (Justicia-Grande et al. 2016).

Construct validity

Validity is a question of whether a scale measures what it is intended to measure (David L. Streiner, Geofrrey R.Norman n.d.). This was measured using criterion and convergent validity.

5.4.2. Criterion validity

Criterion validity can be measured using an area under the receiver operator curve (aROC, Figure 2) where an aROC: 0.50=no different than random (i.e. useless), 0.50-0.70 low; 0.70-0.90 moderate, >0.90 is deemed as high (David L. Streiner, Geofrrey R.Norman n.d.).

5.4.2.1. Admission Prediction

By comparing patients' severity scores and decision to admit or not, we found high aROC for both scores demonstrating how good these scores were at identifying need for hospital admission. Therefore they are likely to be highly useful when used in conjunction with HCP clinical assessment. This is important as it responds to our research question which aims to clarify if the clinical score can be used to assist decision making between children who need admission to hospital or not. Caserta *et al* reported a high aROC 0.96 ($P<0.001$) regarding prediction of hospitalization aROC (Caserta et al. 2017) while Destino *et al* reported lower and poor aROC for admission prediction using CHWRS 0.68($P<0.001$) and RDAI scores 0,51($P<0.001$) (Destino et al. 2012).

However, it is important to note that our population of outpatient managed cases was only small (n=7), probably reflecting the hospitals where assessment was undertaken. Therefore, further assessment at a district hospital and health centre level would be beneficial.

5.4.2.2. HDU/PICU Admission prediction

Once the decision to admit an infant is made, it is also clinically helpful to identify infants who are at an increased risk of needing high dependency unit (HDU) or intensive care unit (ICU) care. HDU and PICU are often needed in severe disease to optimize respiratory and medical support hence reduce the morbidity and mortality associated with respiratory infections especially in sub-Saharan Africa(Rudan et al. 2008), however HDU/PICU care is expensive and labor intensive therefore identifying the right patients for this level of care is important. Both LIBSS and ReSVinet had high aROC as predictive capacity for admission in HDU/PICU that involves mainly infant with severe disease(Justicia-Grande et al. 2016; Miert 2015b).
Rivas-Juesas *et al*, using ESBA and WD scores to predict severe disease in infant with bronchiolitis in 2018 reported a moderate aROC 0.82(P<0.001) and 0.79 (P<0.001) for prediction of severe disease (Appendix 2) (Rivas-Juesas et al. 2018).

5.4.2.3. Mortality prediction

In terms of prediction of mortality, we found high aROC curve to predict mortality. Those results were stronger to the both RISC and M-RISC that showed a C-Statistic of (aROC) values of 0.852 and 0.79 respectively(Hooli, Colbourn, Lufesi, Costello, Nambiar, Thammasitboon, Makwenda, Mwansambo, McCollum, et al. 2016; Emukule et al. 2014). However, our sample size was small and few children dies therefore, further study are needed to confirm this superiority.

5.4.2.4. Length of stay prediction

We used LIBSS and ReSVinet scores to see if they were able to assess short (below median) or long (above median) length of stay (LOS). The aROC for LOS was moderate and low, therefore both scores have limited capability to estimate or predict the LOS in these hospitalized infants (Figure 6.).

5.5. Convergent validity

As part of construct validity, we aimed to evaluate the convergent validity of both scores, to assess whether the severity scores are convergent. We found that the correlation of both nurses and residents using LIBSS and ResVinet had very strong correlation with high Pearson correlation coefficients, which reflect the scores' ability

to give similar results. However, the results' correlation of the scores with length of hospital stay was weaker than the convergent validity of GRSS and length of hospital stay that had a moderate Pearson correlation coefficient r=0.586 (P<0.001) reported by Caserta et al(Caserta et al. 2017). Balaguer et al compared the BROSJOD score with Woods down score and found a positive and moderate Kendall's Tau coefficient of 0.66.

In respect to the differences in "severity of disease" noted by each score, the observation that the scores were well convergent suggests that the cut-off value for "severe" for either, or both, of LIBSS and ReSVinet are incorrect and further research may be required to better identify cut-off values for this setting.

5.6. Cross cultural validity

With reference to our literature search (Appendix 2) and exception of RISC and M-RISC, all of the scores were assessed, developed and validated in High-Income Countries (HICs). None of the scores have been assessed for cross-cultural validity which is a potential limitation to use in the resource-limited setting, due to language considerations, and the clinical skills and educational level of the HCPs undertaking the scoring. To overcome such challenge, we undertook translation in Kinyarwanda and nurses and resident who assessed patients and collected data were trained before participating in the study. (More details on RISC and M-RISC)

5.7. Translation

LIBSS and ReSVinet were translated into the local language, Kinyarwanda. Translating those scores in Kinyarwanda was an obligatory and a preliminary step in this project so that nurses who had a limited knowledge in English were able to understand each item of the score and categorize each patient correctly according to their findings. It is obvious that this was the cornerstone of getting good reliability and validity between nurses and pediatric residents who were expected to have advanced knowledge in interpretation of the respiratory terminology used in these scores and had better clinical assessment skills. Therefore, we hope that those translated scores will continue to be helpful in further implementation of these scores in the Rwandan Population. LIBSS and ResVinet were translated into Kinyarwanda by the principal investigator (PI) and then back-translated for accuracy by a native-Kinyarwanda speaking pediatric resident (Appendix 5,5a&5b) and discrepancies were reviewed with a third native-Kinyarwanda speaking pediatric resident for consensus.

5.7. Reliability

5.7.1. Inter-rater reliability

Inter-rater reliability is important as any tool should reliably give the same score irrespective of the professional using it. This is vital for both clinical use and research. In our study, we aimed to determine the inter-rater reliability of LIBSS and ResVinet when used by nurses and residents. We found almost perfect weighted kappa values and excellent intra-class correlation coefficiency for both scores which implies that our scores produce the same information when applies by both nurses and Pediatric residents on the same patient. Comparing to previous literature, five of the scores in our review table (Appendix 2) had inter-rater reliability performed with fluctuant levels of reliability whereby CHWRS, Tal and modified Tal scores had substantial weighted kappa of 0.73, 0.72 and 0.70 respectively (Diana M Duarte-Dorado et al. 2013; McCallum et al. 2013b). However, Balaguer et al using BRASJOD had excellent an ICC of 0.96 at admission which was similar to our findings(Balaguer et al. 2016).

In addition, our findings regarding LIBSS were in contrast to LIBSS initial UK validation population which provided a moderate kappa of 0.62. Looking at the Intra-class correlation coefficiency findings, our results had narrowed confidence intervals and were superior to the Initial LIBSS validation ICC that was good at 0.83 and 0.84 respectively (Miert 2015a). Our findings suggest that nurses involved in our study performed well, producing almost the same results as pediatric residents. The use of qualified nurses working in tertiary hospitals could also be a secondary explanation. However, we don't have a real explanation of this superiority to the initial validation results. This implies that with training and familiarization with those scores, nurse working in health centers and district hospital can perform better in the assessment infant with respiratory distress, which warrants further validation at those levels.

5.7.2. Internal Reliability

For internal reliability, we aimed to determine the internal consistency of the data for both scores when used by nurses or residents. We found a good overall Cronbach for both scores when employed by nurses or residents. Those findings are superior to the initial internal reliability of ResVinet that had acceptable Cronbach alpha of 0.7 obtained in Spain(Justicia-Grande et al. 2016). However, the initial validation of LIBSS in England didn't evaluate internal validity (Miert 2015a).

Comparing our findings with articles included in our appraisal table (Appendix 2), Balaguer et al employing BRASJOD score had also an acceptable Cronbach of 0.77 and MCallum et al assessed Tal and Modified Tal had questionable Cronbach of 0.6 for Tal and 0.66 for M-Tal (Diana M. Duarte-Dorado et al. 2013). However, Rivas-Juesas et al reported a good Cronbach's alpha of 0.83 that was similar to our findings by assessing ESBA score validity(Rivas-Juesas et al. 2018).

5.8. General Comparison of ReSVinet versus LIBSS

Both scores performed well in our study with good validity and inter-rater reliability. Therefore there is little to differentiate between the scores. Our study found that LIBSS identified more cases of severe disease than ResVinet which can help to optimize medical care to those specific patients and therefore improve their outcome. In addition LIBSS demonstrated higher predictive capability regarding prediction of admission to HDU and PICU and also to the prediction of length of hospital stay with higher area under receiver operating curve compared to ResVinet. Hence, LIBSS might be the preferred score for use in the Rwandan population with acute respiratory infections.

Scores not only give a quantitative assessment of disease but they may also act as an "aide-memoire" for better clinical care. For example LIBSS including urine output may not only quantify disease but guide the HCP to act on the problem at hand.

5.9. Responsiveness

In this study it was not feasible to undertake repeated assessments using the LIBSS or ReSVinet scores. Therefore, responsiveness is not assessed. Testing responsiveness could have allowed us to monitor progress in hospital as deterioration or improvement. However, in most cases responsiveness is tested to assess the response to a medical intervention which was not our study design.

5.10. Ease of Use

No formal assessment of ease of use was undertaken. The general perception from the investigators and data-collectors was that LIBSS was simpler to use. Despite having more parameters (ten versus seven), the parameters are more straightforward whereas ResVinet that had longer questions and parameter descriptions (Appendix.5, 5a&5b). However, it is important to note that one data-collector did not complete the HR and RR in the LIBSS tool and this resulted in cases being excluded. Therefore the length/complexity of the parameter is not necessarily a good indicator of ease of use. Training is an important part of using a clinical assessment tool and these needs to be considered by any department wanting to use these resources.

5.11. Who can use these scores?

The finding of the study showed that nurses are able to use the two scores and get reliable and valid results; however, the nurses involved our study were experienced and qualified working in referral center which put them in position of having advanced knowledge to those one in district hospitals. In addition, they were trained for 2 days prior data collection to all study sites. Therefore, we assume that those scores can be used by experienced health care providers such as nurses and medical doctors working in health centers and hospitals. However, most of Nurse and doctors who are not familiar with treating children will require training before employing these scores. In addition, LIBSS has more parameters containing age dependant vital sign which are straightforward to collect, compared to ReSVinet that has some longer more complicated items.

5.12. Importance of the Findings

The findings of this study are important to the Rwandan health system where our health care facilities have limited resources and HCPs have to take wise decisions of patient who need admission or not based on the severity of disease. The ability of these scores to identify infants at increased risk for clinical deterioration when used in conjunction with health care provider clinical assessment will allow timely medical care and optimized respiratory support to infants and therefore improve their survival and well being. In addition, these severity scores can help to match the challenge of respiratory infections associated mortality in under-five that remain high despite implementation of IMCI and Other WHO healthy Polices and Interventions (WHO 2013).

It also matches well with the third sustainable development goal that aims to ensure healthy lives and promote well-being for all, at all ages (World Health Statistics 2017 2017). Respiratory infections are the leading cause of under-five years' mortality specifically in sub-Saharan Africa and Asia where Rwanda is located (Rudan et al. 2008)

5.12. Strengths and Limitations

5.12.1. Strengths of this study

This study was conducted in a referral hospital by qualified nurses and pediatric residents and we met the minimum sample size. Our participants were randomly selected in a consecutive fashion and all patients were assessed by nurses and Resident using both scores (LIBSS and ReSVinet). Moreover, the methodology of our study is straightforward to allow replication in the further validation.

5.12.2. Limitations

This study had various limitations; the first challenge was the recruitment of participants to meet the minimum sample size. Considering the four initial study sites, only one site CHUK was having a dynamic recruitment in the first 3 months of data collection where we had only 40% participants to meet the required number. There were two issues: one was few infants that were presenting with breathing difficulties and respiratory infection and the second was the high workload of nurses that made them busy and therefore missing potential participants. We requested an amendment to include the fifth study sites which is located in the north Province near the Volcanoes National parks that has many infants who present with acute respiratory infections that helped us to complete the sample size. We also had a small number of patients who required intubation and mechanical ventilation; we suspect that a limited number of PICU beds in respective study sites could have affected clinician decisions about intubation and PICU admission. On the other hand, we realized that the lack of fund to hire full time nurses to collect data impacted negatively the participants' recruitment especially at the three study sites namely, KFH, RMH and CHUB. Lastly, the deadline of the MMed thesis submission to the University of Rwanda limited us to keep collecting data to increase our participants and increase the power of the study.

OPD patients; We don't have any mechanism to know if they were re-admitted or admitted elsewhere because we only saw once our patients at outpatient care or pediatric emergency unit.

CHAPTER6: CONCLUSION AND RECOMMENDATIONS

6.1. Conclusion

Both LIBSS and ResVinet demonstrate good validity and reliability results; however LIBSS proved to identify more severe disease that needed timely and advanced medical care.

6.2. Clinical relevance of the findings (impact)

Respiratory infections are the leading cause of under five years' mortality and mortality. Despite efforts of WHO via immunization and IMCI Integrated management of childhood illness there have been suboptimal results on respiratory diseases(WHO 2013). We found that in Rwanda, the provision of national health insurance has facilitated the population to consult health care facilities. Once presented to health care institution, identification of infant with severe disease that are at increased risk for deterioration can be accurately identified using these scores and

clinical assessment to allow a early and adequate medical treatment and respiratory support, therefore, tackle under five mortality associated with respiratory diseases. In addition, these scores will help decide who needs admission or not to use appropriately the national limited resources.

6.3. Recommendations

6.3.1. Recommendations for Tertiary Hospitals in Rwanda

- Regular training on Nurses and Doctors treating Children on Pediatric advanced Life Support (PALS).
- Use LIBSS and/or ReSVinet Scores in conjunction with clinical assessment to categorize children severity of distress and take timely and appropriate medical decisions.
- Ensure sufficient and proper functioning CPAP and ventilator Machine for Every child Transferred for Specialized Respiratory Support.
- Have appropriate numbers of trained HCPs to take care of Children. (Nurses and Pediatrician)

6.3.2. Recommendations for the Ministry of health

- Regular training of community health workers and health care providers on early Recognition of sign of respiratory distress and acute Respiratory infection for timely transfer and treatment.
- Avail Infrastructures and Train required medical staffs for Pediatric Intensive Care Units in All Tertiary Hospitals in Rwanda.

- Fund future research "VALIDATION STUDY OF TWO STANDARDISED RESPIRATORY SEVERITY SCORES (LIBSS AND RESVINET) IN INFANTS PRESENTING TO HEALTH CENTERS AND DISTRICT HOSPITALS".
- Strengthen the community health coverage for All Rwandan

- Strengthens the culture of Breastfeeding among Childbearing age.

6.4. Future research

These scores have to undergo another validation at the level of district hospital level and be conducted on larger participants' number before we start using them with general practitioner clinical assessment and to decide which patients are increased risk of morbidity and mortality for earlier transfer for respiratory support optimization at the level of tertiary hospitals.

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APPENDICES

Appendix 1: Literature search strategy

Table 1: Search terms (MeSH terms in italics)

	(*Bronchiolitis, viral OR bronchiolitis*)
AND	(*Severity of illness index* OR severity score OR score OR *Decision Support Techniques* OR clinical score OR scale OR tool OR screen OR assessment)
AND	(Validation OR validity OR reliability OR responsiveness OR kappa OR Cronbach OR receiver operator characteristic curve OR prognosis OR diagnosis OR hospitalization)
NOT	(Interleukin OR genetic* OR surfactant OR croup OR physiotherapy OR physical therapy OR Lactate dehydrogenase OR caspase OR neutrophil OR hypertonic OR saline OR glucocorticoids OR steroids OR tobacco OR viral load OR ultrasound OR ultrasonography)
LIMITS	English language Human subjects Infant (birth to 23 months)
Inclusion Criteria	Scoring system allowing objective categorization of infants with acute respiratory infection Studies with a sample size >100 Studies assessing a scoring system need for hospitalization (all study sizes)
Exclusion criteria	Scores designed and described for clinical trials (i.e. not validated and rather used to measure effectiveness of clinical interventions) Scores validated in assessing respiratory disease in the intensive-care unit. Studies using biomarkers and/or surrogate marker in comparison to a clinical score. Retrospective only studies (mixed retrospective/prospective included) Studies which only looked at clinical features likely to predict hospitalization and didn't validate these as a scoring system
Search date:	28th November 2017

Appendix2: Evidence Summary Table

Author, date, citation, country (Economy)	Study type	Study group (Population and comparison) Inclusion/exclusion criteria	Parameters used in the score	Outcome measure	Key Results	Appraisal comments
BROSJOD score (Balaguer et al. 2016), Balaguer et al Spain, 2017	Prospective, observational study. Two-independent physicians at admission, 24 and 48 hours.	Children <2 years (n=112). Mean age = 52.5 days SPR=18.7	Bronchiolitis specific **6 parameters:** Wheezes; Indrawing; Air-entry; Sa02; RR; HR	Construct (convergent) validity:	Correlation of BROSJOD score and WD score: KTC at admission=0.66, KTC 24hrs=0.62 48hrs=0.63 (p<0.01)	**Good:** Data was collected at ED And 24hrs & 48hrs after admission Comprehensive assessment of validity and reliability **Bad:** Subjectivity in assessment score variables.
				Criterion validity	Correlation with expert: Kappa at admission=0.84 (almost perfect), 24hrs=0.80 (substantial), 48hrs=0.84 (almost perfect)	
				Criterion (predictive) validity	*aROC* with expert opinion: At admission=0.80 (moderate), at 24hrs=0.92 (high) , at 48hrs=0.93 (high)	
				Internal consistency:	Cronbach's alpha at admission=0.77 (good), at 24h=0.65 (questionable), at 48hrs=0.68 (questionable)	
				Inter-rater reliability	ICC at admission=0.96 (excellent), 24hrs=0.77 (good),, 48 hr=0.94 (excellent),	
				Score not assessed for	Scale-development, content validity, responsiveness; cross-cultural validity; usability	
GRSS score (Caserta et al. 2017) Caserta et al USA, 2017	Prospective cohort study	Infants under <10 months (n=139) Mix of inpatient and outpatient SPR=15.4	Bronchiolitis specific **9 parameters:** General appearance; Wheezing; Rales/Rhonchi; Retractions; Cyanosis; Lethargy, Poor air movement; RR; Sa02	Construct (convergent) validity	Pearson correlation coefficient between the GRSS and LOS was 0.586 (moderate) (p<0.001)	**Good:** In and outpatient case Factor analysis to calculate scores **Bad:** Severity score not predicting outcome Only developed for RSV infection
				Construct validity	Factor analysis – factors compared to hospitalization	
				Criterion (predictive) validity	aROC 0.961 (high) for hospitalization	
				Score not assessed for	Scale-development, cross-cultural validity; reliability; responsiveness; usability	
LIBBS score (van Miert et al. 2014; Miert 2015a), Van Miert et a UK, 2015	Prospective study PhD thesis. Chapter 9 of PhD thesis reviewed	Construct validating (n=128) SPR=14.2 <3 months (n=68) 3-12 months (n=60) Total study included >1100 participants for full development and validation	Bronchiolitis specific **9 parameters:** General condition; Apnea; Increased work of breathing; Sa02; RR; HR; Feeding; Urine output; CRT	Scale development	Items identified from systematic review and stakeholder consultation. Focus group of parents (n=9) HCPs (n=18). Parent Interviews (n=16). Delphi Survey of HCPs (n=195). Cognitive Interviews HCPs (n=16)	**Good:** This tool showed a good validity and reliability especially for patient with mild and moderate bronchiolitis Two different scores for different ages to take into account for physiological differences **Bad:** Two different scores for different age groups making implementation more challenging. Only assessed for children up to 12 months.
				Content validity	HCPs rated each domain/item on a 1-4 Likert scale for clinical relevance and to identify redundant domains/items.	
				Construct validity (n=128)	Exact weighted agreement Kappa=0.89 (substantial)	
				Criterion validity: (n=123)	Comparison with expert opinion: exact weighted agreement Kappa=0.78 (substantial)	
				Face validity	Assessed by steering group and HCPs groups	
				Inter-rater reliability (n=128)	Weighted Kappa 0.61 (substantial) ICC: 0.83 (good) and 0.84 (good) at repeated time-points Test re-test reliability 0.92 (excellent) and 0.93 (excellent) for separate raters	
				Usability	HCPS rated items on ease of administration, interpretation, layout and timeliness,	
				Score not assessed for	Responsiveness, cross-cultural validity (research ongoing)	
Tal and M-Tal scores (McCallum et al. 2013a), MCallum et al Australia, 2013	Prospective cohort study	Median age 5.4 months (IQR: 2.9–10.4) (n=115) SPR = 28.8	Bronchiolitis specific **4 parameters:** RR; Accessory muscle use; Wheezing; Cyanosis; **M-Tal** replaces cyanosis with Sa02	Criterion (predictive) validity	Prediction of O_2 requirement, aROC: Tal=0.69 (low); M-Tal=0.75 (moderate)	**Good:** Those scores showed a good reliability. **Bad:** Limited prediction of oxygen requirement
				Inter-rater reliability	Weighted kappa: Tal=0.72 (substantial); M-Tal=0.70 (substantial)	
				Internal consistency	Cronbach alpha: Tal=0.66 (moderate); M-Tal= 0.70 (good)	
				Score not assessed for	Scale development, responsiveness; construct, content and cross-cultural validity, usability	
RDAI & CHWRS	Prospective cohort study	Infants < 1 year (n=195)	**CHWRS: 10 parameters:** Breath	Construct (convergent)	Correlation of each score versus LOS, SRC for RDAI r=0.04 (very weak,	**Good:** Clear consort figure

scores (Destino et al. 2012), Destino et al USA, 2012		SPR=19.5	sounds; Dyspnea; Retraction; RR; HR Oxygen Need; Activity appearance; Cough ability/secretion; Chest x-ray/lung sound Surgical status **RDAI 7 parameters:** Wheezing; expiration, inspiration, location. Retractions; suprasternal, intercostals, subcostal & RR	validity	p=0.71) or CHWRS r=0.05 (very weak, p=0.61).	describing patient flow **Bad:** Poor construct validity Poor RDAI reliability CHWRS requires CXR which is normally not required with bronchiolitis and frequently not available in LICs. Used non-therapeutic interventions to assess responsiveness (e.g. bronchodilators)
				Criterion (predictive) validity	aROC for hospital admission: CHWRS=0.68 (low) & RDAI=0.51 (useless) (no cutoff agreed as no prediction of admission)	
				Item analysis	MLR of individual parameters versus hospital admission using. CHWRS: No score had significant association with admission (except oxygen requirement which is obvious) RDAI: Subcostal retractions significantly associated with admission (OR 2.67, CI:1.41-5.05).	
				Inter-rater reliability	ICC for CHWRS=0.73 (moderate) and RDAI=0.39 (poor).	
				Responsiveness	Short term (15 minutes). mild correlation between the change in the CHWRS and RACS after an intervention (r = 0.39, weak, p=0.04).	
				Score not assessed for	Scale development, content and cross-cultural validity; usability	
ESBA (Rivas-Juesas et al. 2018), Rivas-Juesa et al, Spain, 2018	Multi-center (n=5) prospective cohort study	Infants < 1 year (n=201) Median age 2.3 months SPR=33.5	**ESBA 6 parameters** Wheezing; Crackles; Exertion; Inspiratory/expiration ratio; RR; HR **WD 5 parameters** Sa02 (or cyanosis); Inspiratory breath sounds; Accessory muscle use; expiratory wheezing; cerebral function	Construct validity	Correlation of ESBA with WD score. Weighted kappa: −0.17 (poor)	**Good** Used McConnochie criteria modified by age for diagnosis Comparison with WD score "severe disease" was well described Internal consistency (Cronbach's=0.83), Inter-rater (Kappa=0.682) and test-retest (Kappa 0.93) reliability assessed in a separate paper with <100 subjects (n=75) (Ramos Fernández et al. 2014) **Bad** Premature infants (<35 weeks of gestation) were excluded
				Criterion validity	Estimation of the Youden index (*J*) and optimum cut-off points performed. J= 0.63 (moderate)	
				Criterion (predictive) validity	aROC for "severe disease": ESBA=0.82 (moderate), WD=0.79 (moderate). Severe disease SEBA: PPV=21.6%, NPV=98.7%. WD: PPV=12.4%, NPV=45.2%.	
				Score not assessed for	Scale development, content and cross-cultural validity; usability	

aROC: area under receiver operating curve; BROSJOD: Bronchiolitis Score of Sant Joan de Deu; CCC: concordance correlation coefficient; CHWRS: Children's Hospital of Wisconsin Respiratory Score; CRT: Capillary Refil Time; CXR: Chest radiograph; ESBA: Acute Bronchiolitis Severity Scale (Escala de Severidad de la Bronquiolitis Aguda); GRSS: Global Respiratory Severity Score for Respiratory Syncytial Virus Infection in Infants; HCPs: Healthcare professionals; ICC: Intraclass correlation coefficient; KTC=Kendall's tau coefiicient; LIBSS: Liverpool Bronchiolitis Severity Score; LoS: Length of Stay; M-WCAS: modified wood clinical asthma score; MLR: Multivariate logistical regression; NPV: Negative predictive value; PPV: Postive predictive value; RACS: Respiratory Assessment Change Score; RDAI: Respiratory Distress Assessment Instrument; RST: Risk score tool in comparison; SRC: Spearmans' rank correlation; SPR: Subject to Domain Ratio; WD: Wood Downes Score;

Appendix 3: Study specific Data collection tool

Data collection tool of the study on "**"

Contact person: Boniface……

Date/time of data collection:.../……/201… …….h……min

Patient Identification	
Unique Patient Identifier Gender: Current Weight: Height Age	…… M ☐ F ☐ unknown☐ Kg Cm --/---/----
Arrival	
Hospital Date of arrival at Hospital Time of arrival: Daytime/Nighttime Day of arrival:	CHUK ☐ CHUB☐ KFH☐ RMH☐ …../……./201.. ……h…… Daytime ☐ Night ☐ M ☐ T☐ W☐ Th ☐ F ☐ S ☐ Su ☐
Background details	
Ubudehe category	1 ☐ 2 ☐ 3 ☐ 4 ☐ unknown ☐
Marital status of mother	Single ☐ Married ☐ Divorced ☐ widowed ☐
Number of living children	0 ☐1-2☐ 3-4 ☐5+ ☐
Residence	Urban ☐Rural ☐
Maternal age	15-19 ☐ 20-24 ☐ 25-29 ☐ 30-34 ☐ 35-39 ☐ 40-44 ☐ 45-49 ☐
Paternal age	15-19 ☐ 20-24 ☐ 25-29 ☐ 30-34 ☐ 35-39 ☐ 40-44 ☐ 45-49 ☐
Maternal education	No education ☐ Primary ☐ Secondary ☐ Higher ☐
Paternal education	No education ☐ Primary ☐ Secondary ☐ Higher ☐
Maternal occupation status	Unemployed ☐ manual labourer ☐ professional ☐
Paternal occupation status	Unemployed ☐ manual labourer ☐ professional ☐
Parental Smoking	Yes ☐ No ☐
Use of biomass fuel	Yes ☐ No ☐
Vaccination	Yes ☐ No☐, which ones received: …… ….

	…… ……..
Exclusively breastfeed	YES☐ NO ☐ if yes till 6 months or age less than 6 months.
Treatment provided	
Adrenaline nebulisation	Yes ☐ No ☐ DNA ☐
Salbutamol nebulisation	Yes ☐ No ☐ DNA ☐
Steroid administration	Yes ☐ No ☐ DNA ☐
Antibiotic	Yes ☐ No ☐ DNA ☐
Oxygen therapy	Yes ☐ No ☐ DNA ☐
CPAP	Yes ☐ No ☐ DNA ☐
Intubation and ventilation	Yes ☐ No ☐ DNA ☐
Other	
Data collector personnel	
Nurse	Yes ☐ No ☐
Pediatric resident	Yes ☐ No ☐
Possible comorbidities	
Malnutrition	
Known asthmatic	
History of prematurity	
HIV status	

Patient ReSVinet score:	**Nurse Total:** **Resident/doctor Total:**
Patient LBSS score	**Nurse Total:** **Resident/doctor Total:**
Outcomes	
Admission to pediatric ward	Yes ☐ No ☐ DNA ☐
Admission to HDU	Yes ☐ No ☐ DNA ☐
Admission to PICU	Yes ☐ No ☐ DNA ☐
Outpatient management	Yes ☐ No ☐ DNA ☐
Date of discharge	--/--/--

Survival/death	
Died	Yes ☐ No ☐ DNA ☐
Discharged	Yes ☐ No ☐ DNA ☐
Diagnosis (Final main):	Bacterial pneumonia ☐ Bronchiolitis ☐ Viral induced wheezing/ Reactive Upp Air way disease ☐ Acute Asthma ☐ URTI ☐ Other ☐……..

Appendix4: Unique Patient Identifier Code Sheet

Unique Code	Name:	Hospital ID:

Appendix 5: LIBSS Score including translation

Liverpool Infant Bronchiolitis Severity Score: **children aged three months and over**/ *Abana bafite amezi atatu gusubiza hejuru*			
Day of illness: *Iminsi y'ubarwayi*			
1. Do you have any concerns relating to the infant's overall condition? *Hari ikibazo ufite kijyanye nuko umwana ameze?*			
No concerns *ntakibazo* **(condition is stable or improving/** *ameze neza cg arikoroherwa***)**	**0**		**Comments:** *ibisobanuro*
Some concerns (may become unstable/requires close observation) *Dufite impungenge (ashobora kuremba/akeneye gukurikiranirwa hafi)*	**4**		
Extremely concerned (unstable requires immediate medical review) *Turahangayitse cyane (Ararembye akeneye guhita avurwa)*	**8**		
2. Apnoea *guhagarika guhumeka*			
None *Ntanarimwe*	**0**		**Comments:** *ibisobanuro*
Occasional self-correcting apnoea / short pauses *Ahagarara guhumeka byikosora /guhagarika guhumeka akanya gato*	**2**		
Apnoea's increasing frequency & duration *guhagarika guhumeka byiyongera mu nshuro n'igihe bimara*	**4**		
Apnoea's requiring stimulation *Guhagarara guhumeka biri gusaba kumukoraho ngo yongere ahumeke*	**6**		
Apnoea's requiring bag & mask ventilation *Guhagara guhumeka bikeneye kumuhumekesha hakoreshejwe Ambubag.*	**8**		
3. Increased work of breathing **(Absent or mild =0) Please complete all boxes in this section** *kongera imbaraga ahumekesha (ntazo cg nkeya =0) uzuza udusanduku twose kuri iki gice*			
Moderate/severe recession *Biringaniye/ bikabije mugukoresha imbaraga zo guhumeka*	**0**	**2**	**Comments:** *ibusobanuro*
Moderate/severe tracheal tug *iringaniye/ ikabije tracheal tug*	**0**	**2**	
Moderate/severe nasal flare *Biringaniye/ bikabije muguhumekesha amazuru*	**0**	**2**	
Moderate/severe head bobbing *Kuzunguza umutwe*	**0**	**4**	
Grunting *Kuniha*	**0**	**4**	
Central cyanosis (blue lips / tongue) *Guhinduka ubururu (iminwa/ ururimi bisa n'ubururu)*	**0**	**6**	
4. % oxygen to maintain saturations ≥92% (or usual saturation level if infant has congenital heart defect) *Umwuka wa ogisijene ukenewe ngo saturation igume heuru ya 92%(cg saturasiyo fatizo mubana bafite uburwayi bw'umutima)*			
21% **(room air ,** *umwuka usanwe dumeka***)**	**0**		**Comments:** *ibusobanuro*
22 - 40% **(0.02 - 6L/min)**	**2**		
41 - 50% **(7 - 10L/min)**	**4**		
>50% **(>10L/min)**	**6**		
Actual amount of oxygen administered *Igipimo cya ogisijene yatanzwe*			
Mode of oxygen delivery/ *uburyo ogisijene itangwa* **:** Nasal specs (NS); Face Mask (FM); Head box (HB); HiFlow (HF); nCPAP (CP)			
5. Respiratory rate (breaths per minute) *Inshuro ahumeka mu munota*			
20 – 55	**0**		**Comments:** *ibusobanuro*
56 – 65	**2**		
<20 or >65	**4**		
6. Heart rate (beats per minute) *Inshuro umutima utera mu munota*			
95 – 145	**0**		**Comments:** *ibusobanuro*
146 – 160	**2**		
<95 or >160	**4**		

7. Appearance *Uko agaragara*			
Alert & active / normal sleep *Arakangutse & arakina / arasinziriye bisanzwe*	**0**		**Comments:** *ibisobanuro*
Irritable / fractious / restless *Afite amahane/ arikurira cyane / ntagobwo atuje*	**2**		
Floppy / lethargic / poor interaction *Yacitse intege cyane/ararembye / ntabasha gukina*	**4**		
Only responds to pain/unresponsive *Asubiza kububabare bwonyine/ ntasubiza*	**6**		
AVPU Score			
8. Feeding **Kugaburira**			
>75% of feeds or normal amount of feeds via usual route *Afata ibyokurya byuzuye cyangwa hejuru ya 75% byibyo akwiye gufata.*	**0**		**Comments:** *Ibisobanuro*
50 - 75% of feeds via usual route *Arya 50-75% by'ibyo kurya akwiye gufata*	**2**		
<50% of feeds or needing NG feeds / IV fluids Abona munsi ya 50% byibyokurya bisanzwe cyangwa akeneye kugaburirwa binyuze muri sonde cyangwa mu mutsi	**4**		
9. Urine output *Inkali yihagarika*			
Usual number of wet nappies (> 2 mLs /kg/hr) *Umubare usanzwe wa pamperisi*	**0**		**Comments:** *ibisobanuro*
Reduction in number of wet nappies (1 - 2 mLs /kg/hr) *Umubare wa pampegisi wagabanutse*	**2**		
Small volumes of concentrated urine / no urine (< 1mL/kg/hr) *Afite inkari nke ziri consantere/ nta nkari afite*	**4**		
10.Central capillary refill time (preferably press on the sternum for 5 seconds)			
≤ 2 seconds	0		**Comments:** *Ibisobanuro*
> 2 seconds	2		
Actual capillary refill time in seconds			
LIBSS Score Total **Mild (0-10); Moderate (11-20); Severe (≥21)** *Guhumeka nabi byoroshe (0-10), guhumeka nabi biringaniye (11-20), guhumeka nabi bikabije (>21)*			**Comments:** *Ibisobanuro*

Appendix 5a: LIBSS Score including translation

Liverpool Infant Bronchiolitis Severity Score: Infant aged under three months *Abana bafite munsi y' amezi atatu*			
Day of illness: *Iminsi y'ubarwayi*			
1. Do you have any concerns relating to the infant's overall condition? *Hari ikibazo ufite kijyanye nuko mwana ameze?*			
No concerns *ntakibazo* **(condition is stable or improving/** *ameze neza cg arikoroherwa***)**	**0**		**Comments:** *ibisobanuro*
Some concerns *Dufite impungenge* **(may become unstable/requires close observation/** *ashobora kuremba/akeneye gukurikiranirwa hafi* **)**	**4**		
Extremely concerned (unstable requires immediate medical review) *Turahangayitse cyane (Ararembye akeneye guhita avurwa)*	**8**		
2. Apnoea *guhagarika guhumeka*			
None *Ntanarimwe*	**0**		**Comments:** *ibisobanuro*
Occasional self-correcting apnoea / short pauses *Ahagarara guhumeka bikosora /guhagarika guhumeka akanya gato*	**2**		
Apnoea's increasing frequency & duration *guhagarika guhumeka byiyongera mu nshuro n'igihe bimara*	**4**		
Apnoea's requiring stimulation *Guhagarara guhumeka biri gusaba kumukoraho ngo yongere ahumeke*	**6**		
Apnoea's requiring bag & mask ventilation *Guhagara guhumeka bikeneye kumubaginga ngo yongere ahumeke*	**8**		
3. Increased work of breathing/ *kongera imbaraga ahumekesha* **(Absent or Mild =0)** **Please complete all boxes /** *uzuza udusanduku twose kuri iki gice*			
Moderate/severe recession *Biringaniye/ bikabije mugukoresha imbaraga zo guhumeka*	**0**	**2**	**Comments:** *Ibisobanuro*
Moderate/severe tracheal tug *iringaniye/ ikabije tracheal tug*	**0**	**2**	
Moderate/severe nasal flare *Biringaniye/ bikabije muguhumekesha amazuru*	**0**	**2**	
Moderate/severe head bobbing *Kuzunguza umutwe*	**0**	**4**	
Grunting *Kuniha*	**0**	**4**	
Central cyanosis (blue lips / tongue) *Guhinduka ubururu (iminwa/ ururimi bisa n'ubururu)*	**0**	**6**	
4. % oxygen to maintain saturations ≥92% (or usual saturation level if infant has congenital heart defect) *Umwuka wa ogisijene ukenewe ngo saturation igume heuru ya 92%(cg saturasiyo fatizo mubana bafite uburwayi bw'umutima*			
21% **(room air** *umwuka usanwe dumeka)*		**0**	**Comments:** *Ibisobanuro*
22 - 40% (0.02 - 6L/min)		**2**	
41 - 50% (7 - 10L/min)		**4**	
>50% **(>10L/min)**		**6**	
Actual amount of oxygen administered *Igipimo cya oxygen yatanzwe*			
Mode of oxygen delivery/*uburyo uxygen itangwa:* Nasal specs (NS); Face Mask (FM); Head box (HB); HiFlow (HF); nCPAP (CP)			
5. Respiratory rate (breaths per minute) *Inshuro ahumeka mu munota*			
25 - 59		**0**	**Comments:** *Ibisobanuro*
60 - 70		**2**	
<25 or >70		**4**	
6. Heart rate (beats per minute) *Inshuro umutima utera mu munota*			
105 - 165		**0**	**Comments:** *Ibisobanuro*
166 - 180		**2**	
<105 or >180		**4**	

7. Appearance *Uko agaragara*			
Alert & active / normal sleep *Arakangutse & afite imbaraga / arasinziriye bisanzwe*	**0**		**Comments:** *Ibisobanuro*
Irritable / fractious / restless *Afite amahane/ arikurira cyane/ intege nke*	**2**		
Floppy / lethargic / poor interaction *Yacitse intege cyane/ararembye*	**4**		
Only responds to pain / unresponsive *Asubiza kububabare bwonyine/ cyangwa ntasubiza*	**6**		
AVPU SCORE			
8. Feeding *Kugaburira*			
>75% or normal amount of feeds via usual route *Afata ibyokurya byuzuye cyangwa hejuru ya 75% byiko akwiye gufata.*	**0**		**Comments:** *Ibisobanuro*
50 - 75% of feeds of normal feeds via usual route *Arya 50-75% by'ibyo kurya akwiye gufata*	**2**		
<50% of feeds or needing NG feeds / IV fluids *Abona munsi ya 50% byibyokurya bisanzwe cyangwa akeneye kugaburirwa binyuze muri sonde cyangwa mu mutsi*	**4**		
9. Urine output			
Usual number of wet nappies (> 2 mLs /kg/hr) *Umubare usanzwe wa Diapers*	**0**		**Comments:** *Ibisobanuro*
Reduction in number of wet nappies (1 - 2 mLs /kg/hr) *Umubare wa Diapers wagabanutse*	**2**		
Small volumes of concentrated urine / no urine (< 1mL/kg/hr) *Afite inkari nke ziri concentre/ nta nkari afite*	**4**		
10. Central capillary refill time (preferably press on the sternum for 5 seconds)			
≤ 2 seconds	**0**		**Comments:** *Ibisobanuro*
> 2 seconds	**2**		
Actual capillary refill time in seconds			

LIBSS Score Total: **Mild (0-10); Moderate (11-20); Severe (≥ 21)** *Guhumeka nabi byoroshe (0-10), guhumeka nabi biringaniye (11-20), guhumeka nabi bikabije (>21)*		**Comments:** *Ibisobanuro*

Appendix 5b: ReSVinet Score (including translation)

ReSVinet scale. This table presents the original scale, and was the one used by the three investigators.

	Item Uduce	0 points 0 amanota	1 points inota rimwe	2 points amanota 2	3 points amanota 3
1	Feeding intolerance Ikibazo mwigogora ry'ibiryo	No oya	Mild Decreased appetite and/or isolated vomits with cough. Kugira apeti nke cyangwa kuruka birikumwe nogukorora	Partial Frequent vomits with cough, rejected feed but able to tolerate fluids sufficiently to ensure hydration. Kuruka burikanya bivanze ninkorora , kwanga ibiryo ariko akanywa bihagije kuburyo ntamwuma afite	Total Oral intolerance or absolute rejection of oral feed, not able to guarantee adequate hydration orally. Required nasogastric and/or intravenous fluids Kwanga ibyokurya byose, kuburyo yagira umwuma. Yakeneye sonde yo mugifu cyangwa serumu yo mumutsi
2	Medical intervention Ubutabazi bwakigang a bwakozwe	No Oya	Basic Nasal secretions aspiration, physical examination, trial of nebulized bronchodilators, antipyretics. Gusukura amazuru, gusuzuzuma, nebulization n'imiti ifungura ibihaha, imiti igabanya umulilo.	Intermediate Oxygen therapy required. Complementary exams were needed (chest X-rays, blood gases, hematimetry.. .). Maintained nebulized therapy with bronchodilators. Oxygen iringaniye, ibizami byuzuza nk'amafoto yagatuza, imyuka y'amaraso, nebilization ihoraho y'imiti ifungura agatuza	High Required respiratory support with positive pressure (either non-invasive in CPAP, BiPAP or high-flow O2; or invasive through endotracheal tube). Gukenera ibyuma bifasha guhumeka nka CPAP, BiPAP, ogisigene nyishi, cg imashini imuhumekera.
3	Respiratory difficulty Ibibazo muguhu meka	No Oya	Mild Not in basal situation but does not appear severe. Wheezing only audible with stethoscope, good air entrance. If modified Wood Downes, Wang score or any other respiratory distress score is applied, it indicates mild severity. Guhumeka nabi byoroheje ariko wheezing zumvikana kuri stethoscope. Niba indi score yakoresheje nayo yerekanye guhumeka nabi byoroheje.	Moderate Makes some extra respiratory effort (intercostal and/or tracheosternal retraction). Presented expiratory wheezing audible even without stethoscope, and air entrance may be decreased in localized areas. If modified Wood Downes, Wang score or any other respiratory distress score is applied, it indicates moderate severity. Guhumeka nabi biringaniye ariko akoresha inyama zo mugatuza. Wheezing zumivikana na stetoscope mugihe cyo gusohora umwuka. Cyangwa indi score yakoreshejwe yerekanye guhumeka nabi biri murugero.	Severe Respiratory effort is obvious. Inspiratory and expiratory wheezing and/or clearly decreased air entry. If modified Wood Downes, Wang score or any other respiratory distress score is applied, it indicates high severity. gukoresha imbaraga nyinshi ngo ahumeke bigaragarira buri wese. Wheezing mukwinjira no gusohoka ku mwuka Umwuka muke winjira mubihaha. Indi score yerekanye guhumeka nabi bikabije.

4	Respiratory frequency Inshuro zo guhumeka	Normal < 2 m: 40–50 bpm 2–6 m: 35–45 bpm 6-12m: 30–40 bpm 12-24m:25–35 bpm 24-36m: 20–30 bpm bizima <2 m : 40-50 bpm Hagati ya m 2-6:35-45 bpm Hagati ya m 6-12:30-40 bpm Hagati ya m 12-24:25-35 bpm Hagati ya m 24-36 : 20-30	Mild or occasional tachypnea Presented episodes of tachypnea, well tolerated, limited in time by self-resolution or response to secretion aspiration or nebulization. Byoroheje cyangwa guhumeka vuba rimwe narimwe. Byoroheje,byo byikijije cyangwa byakize nyuma yo gusukura amazuru cyangwa nebilizasiyo.	Prolonged or recurrent tachypnea Tachypnea persisted or recurred despite secretion aspiration and/or nebulization with bronchodilators. Imara igihe kirekire cyangwa guhumeka nabi burikanya cyangwa bihoraho nyuma yo gusukura amazuru cyangwa nebilization n'imiti ifungura ibihaha.	Severe alteration Severe and sustained tachypnea. Very superficial and quick breath rate. Normal/low breath rate with obvious increased respiratory effort and/or mental status affected. Orientative rates of severe tachypnea: < 2 m: > 70 bpm 2–6 m: > 60 bpm 6-12m: >55 bpm 12-24m: >50 bpm 24-36m: >40 bpm Guhumeka nabi bikabije kandi bihoraho. Guhumeka atitsa kandi vuba cyane. Guhumeka bisanzwe cyangwa gake hamwe n'ibimenyetso byerekanako ari gukoresha imbaraga nyinshi ngo ahumeke cyangwa gutakaza ubwenge. Ibipimo byoguhumeka nabi bikabije Munsi ya m 2 >70 bpm Hagati ya m 2-6 >60 bpm Hagati ya m 6-12 >55 bpm Hagati ya m 12-14 >50bpm Hagati ya m 24-36 >40bpm
5	Apnea Guhagarika guhumeka	No Oya			Yes At least one episode of respiratory pause medically documented or strongly suggested through anamnesis. Nibura inshuro imwe yoguhagarika guhumeka yanditswe.
6	General Condition Uko agaragara muri rusange	Normal Ni bizima	Mild Not in basal situation, child was mildly uncomfortable but does not appear to be in a severe condition, not impress of severity. Parents are not alarmed. Could wait in the waiting room or even stay at home. Ntabwo ameze neza buhoro ntanubwo agaragara nkurembye. Ababyeyi ntakibazo bafitye barategerejye bashoraga no kwigumira murugo.	Moderate Patient looks ill, and will need medical exam and eventually further complementary exams and/ or therapy. Parents are concerned. Cannot wait in the waiting room. Ameze nkurwaye murugero kandi akeneye gusuzumwa nibindi bizamini cyangwa kuvurwa. Ababyeyi barahangayitse. Ntibashobora gutegereza mu cyumba cyogutereza.	Severe Agitated, apathetic, lethargic. No need of medical training to realize severity. Parents are very concerned. Immediate medical evaluation and/or intervention were required. Afite amahane, yacitse integer, ari gutakaza ubwenge. Ntabumenyi bukenewe ngo umenyeko arembye. Ababyeyi barahangayitse cyane. Yahawe ubutabazi bwakiganga n'ubuvuzi bwihuse.
7	Fever Umulilo	No Oya	Yes, mild Central T < 38.5°C Yego, umulilo muke < 38.5°C	Yes, moderate Central T > 38.5°C Yego , umulilo uringaniye > 38.5°C	

Appendix 6: Consent

We are performing this project to better understand how we identify children with breathing problems. There are international "scores" available that may be able to tell us if children have severe breathing problems. This project is aimed to validate two of these standardized respiratory severity score (LIBSS and ReSVinet). We will be doing this project in the biggest teaching hospitals in Rwanda.

You are invited to participate in this study. Doing so will be voluntary. Your will receive no incentive or payment fee for participating in this study. We are asking you do take part in the knowledge that it will help sick children in the future. We will collect some information about you and your child and then a nurse and a doctor will assess your child using the scores. The provided information will used for research purpose only. During the time of data collection you will be asked some questions and examined for the required data. The scoring of your child should not cause her/him any discomfort and are normal examinations that we perform regularly. The questions you need to fill in may take up to approximately 30 minutes.

Your child's identity will be protected. We will not keep your child's name, date-of-birth with any data about your child. The principal investigator will keep records for participant in a secure database and we will use unique code identifiers to protect the identity of your child. Only Professional investigators will have access to participant data so that all participant data will be kept confidential. We aim to publish the results of the research project, but this will not include any personal details from any patient.

If you have any question related with this study or you have found any aspects distressing, please contact Dr HAKIZIMANA Boniface on this phone number +250783545161 who will arrange to speak with you. You will not benefit directly from this research but your contribution will be used by researcher and medical doctors so that in the future children with respiratory distress will have better care. Your signature on this form means that you understand the information presented and you participate in this study. You understand that participate in this study is voluntary and you may withdraw from the study at any time without penalty. Your contribution is gratefully received.

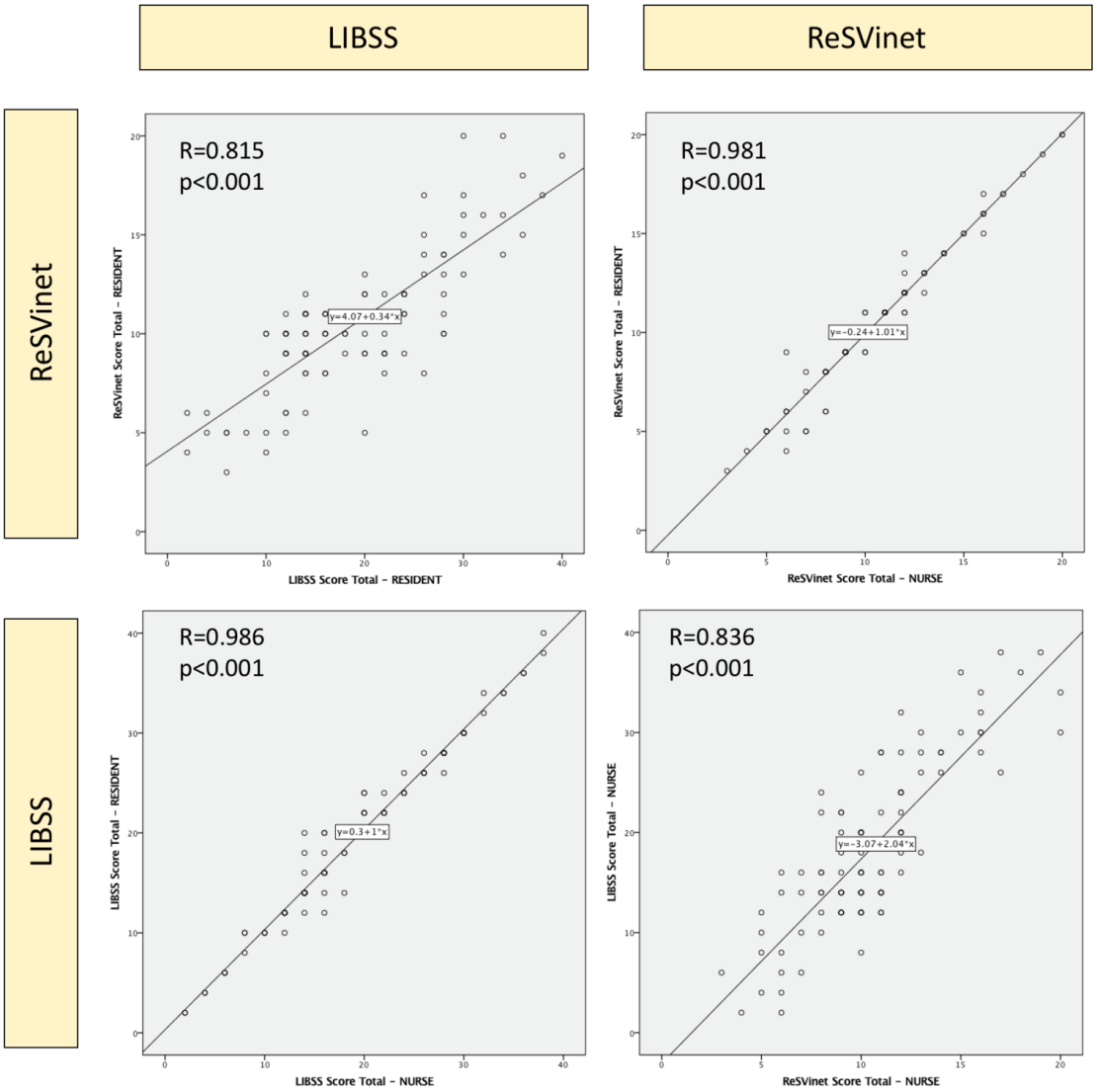
Parent informed consent

Name of the parent or guardian of the child: ……

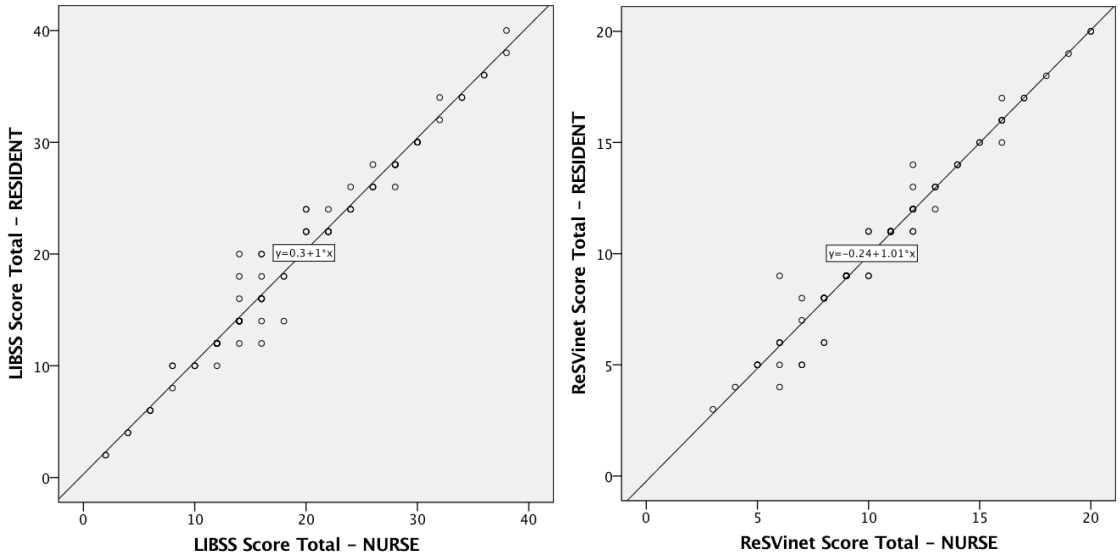
Signature of Parent or guardian of the child: ……

Contact information /Contact for Dr Hakizimana Boniface/Email: Bonifaceh69@gmail.com /Phone: + 250783545161

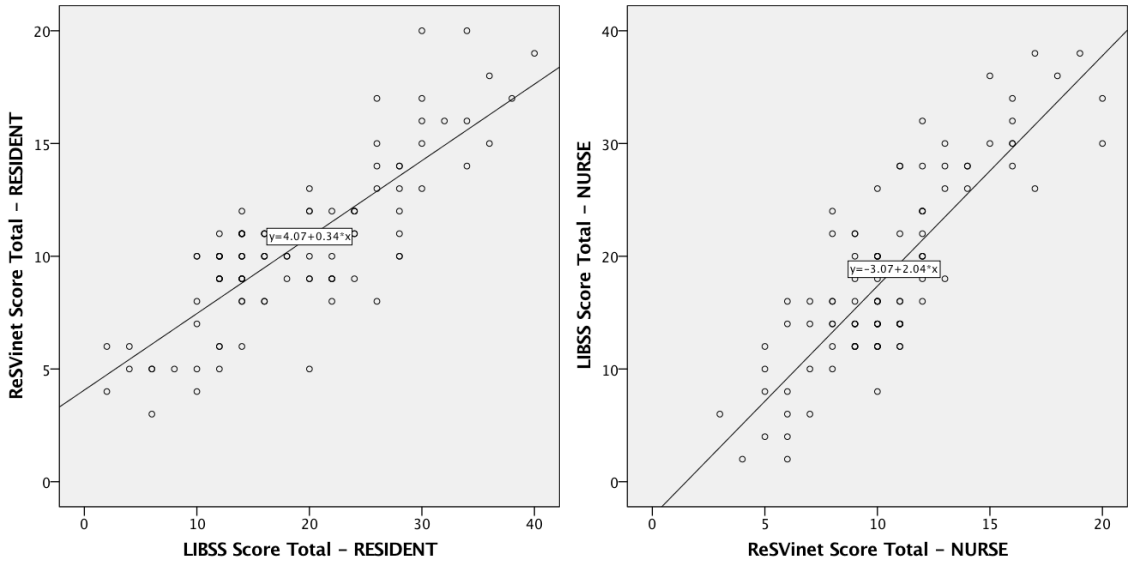
Appendix 7: Figure 3.Convergent validity



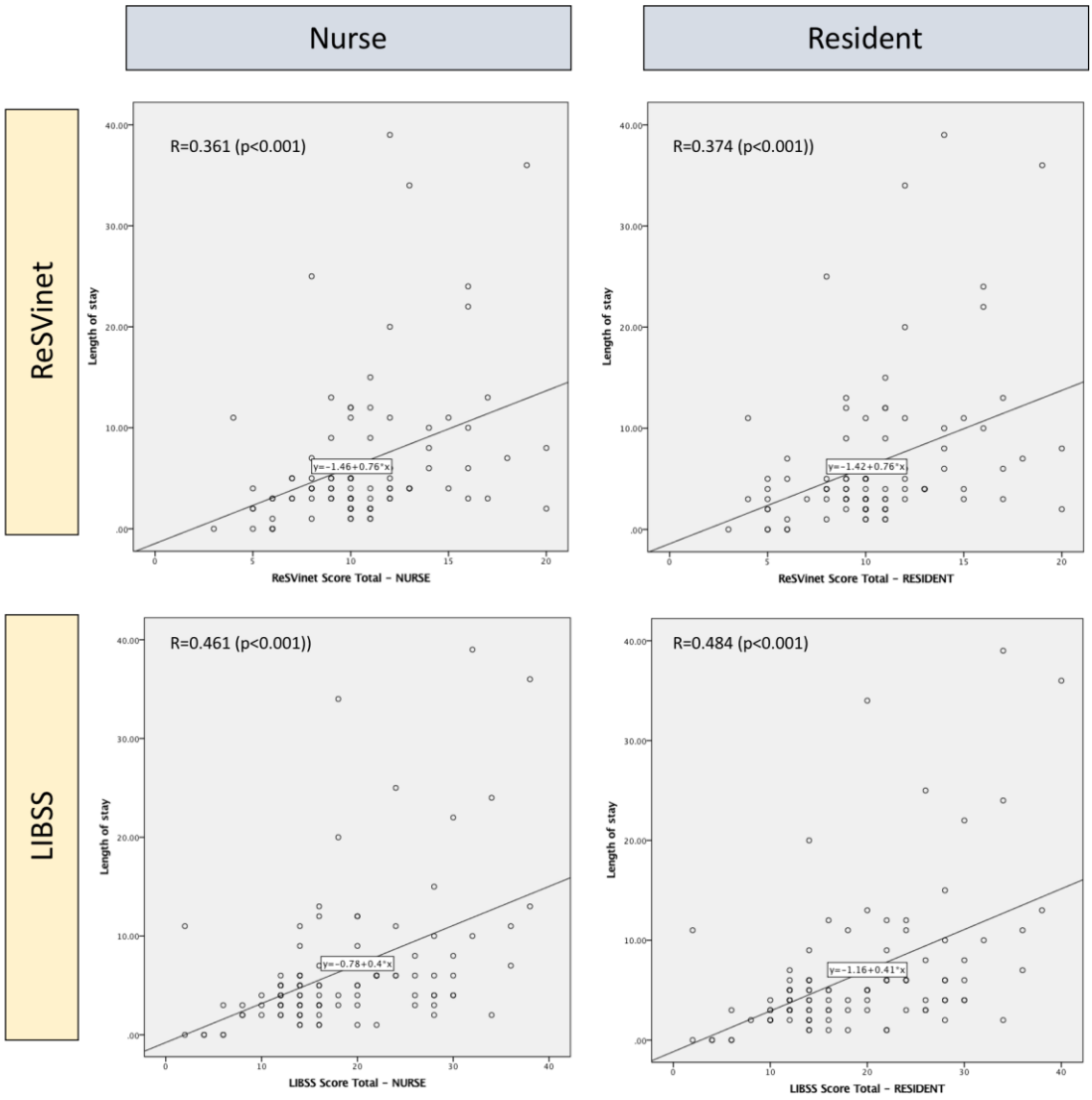
Appendix 8: Figure4. Intra-class correlation between nurse and resident raters



Appendix 9: Figure 5. Intra-class correlation between distress scores for HCP



Appendix 10: Figure 6. Length of stay correlation to scores



Appendix 11: Ethical Clearance

UNIVERSITY OF RWANDA — COLLEGE OF MEDICINE AND HEALTH SCIENCES

CMHS INSTITUTIONAL REVIEW BOARD (IRB)

Kigali, 12 /June /2018

Boniface Hakizimana
School of Medicine and Pharmacy
MMED IN PEDIATRIC AND CHILD HEALTH,

Approval Notice: No 237 /CMHS IRB/2018

Your Project Title ***"Validation of two standardised respiratory severity scores in infants presenting to tertiary hospitals in Rwanda"*** has been evaluated by CMHS Institutional Review Board.

Name of Members	Institute	Involved in the decision		
		Yes	No (Reason) Absent	Withdrawn from the proceeding
Prof Kato J. Njunwa	UR-CMHS		X	
Prof Jean Bosco Gahutu	UR-CMHS	X		
Dr Brenda Asiimwe-Kateera	UR-CMHS	X		
Prof Ntaganira Joseph	UR-CMHS	X		
Dr Tumusiime K. David	UR-CMHS	X		
Dr Kayonga N. Egide	UR-CMHS	X		
Mr Kanyoni Maurice	UR-CMHS	X		
Prof Munyanshongore Cyprien	UR-CMHS		X	
Mrs Ruzindana Landrine	Kicukiro district		X	
Dr Gishoma Darius	UR-CMHS	X		
Dr Donatilla Mukamana	UR-CMHS	X		
Prof Kyamanywa Patrick	UR-CMHS		X	
Prof Condo Umutesi Jeannine	UR-CMHS		X	
Dr Nyirazinyoye Laetitia	UR-CMHS	X		
Dr Nkeramihigo Emmanuel	UR-CMHS		X	
Sr Maliboli Marie Josee	CHUK	X		
Dr Mudenge Charles	Centre Psycho-Social	X		

After reviewing your protocol during the IRB meeting of where quorum was met and revisions made on the advice of the CMHS IRB submitted on 12 June 2018, **Approval has been granted to your study.**

EMAIL: researchcenter@ur.ac.rwP.O. Box: 3286 Kigali, Rwanda WEBSITE:

Please note that approval of the protocol and consent form is valid for **12 months**.

You are responsible for fulfilling the following requirements:

25. Changes, amendments, and addenda to the protocol or consent form must be submitted to the committee for review and approval, prior to activation of the changes.
26. Only approved consent forms are to be used in the enrolment of participants.
27. All consent forms signed by subjects should be retained on file. The IRB may conduct audits of all study records, and consent documentation may be part of such audits.
28. A continuing review application must be submitted to the IRB in a timely fashion and before expiry of this approval
29. Failure to submit a continuing review application will result in termination of the study
30. Notify the IRB committee once the study is finished

Sincerely,

Date of Approval: The 12th June 2018

Expiration date: The 12th June 2019

For Professor Kato J. NJUNWA
Chairperson Institutional Review Board,
College of Medicine and Health Sciences, UR

Cc:
- Principal College of Medicine and Health Sciences, UR
- University Director of Research and Postgraduate Studies, UR

Appendix 11a: Ethical Clearance/ Amendment

UNIVERSITY OF RWANDA

COLLEGE OF MEDICINE AND HEALTH SCIENCES

CMHS INSTITUTIONAL REVIEW BOARD (IRB)

Kigali, 29th November, 2018
No 375 /CMHS IRB/2018

Dr HAKIZIMANA Boniface

School of Medicine and Pharmacy, CMHS, UR

Re: Amendment Request for Research Protocol

Dear Dr HAKIZIMANA Boniface

We thank you for submitting your request for research project amendments in the project titled "***Validation of Two Standardised Respiratory Severity Scores in Infants Presenting to Tertiary Hospitals in Rwanda***".

After reviewing your protocol, the amendments have been approved with a change in the following areas:

1. Ruhengeri Referral Hospital is accepted to host your study as an additional study area.

We wish you success in this important study.

Professor Gahutu Jean Bosco,
Chairperson Institutional Review Board,
College of Medicine and Health Sciences, UR

Cc:
- Principal College of Medicine and Health Sciences, UR
- University Director of Research and Postgraduate studies, UR