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Best Evidence Topics

BEST EVIDENCE TOPICS

Can a Respiratory Severity Score Accurately Assess Respiratory Distress in Children with Bronchiolitis in a Resource-Limited Setting?

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SCENARIO

You are the resident on call for the acute pediatric ward in a district hospital in a resource-limited setting. A 9-month-old male infant presents with a 3-day history of coryza and cough followed by difficulty in breathing. The infant is admitted to the acute ward for observation but does not need supplementary oxygen or fluid support. During the ward-round it was felt that his condition at presentation did not warrant admission. You are concerned that by being admitted unnecessarily this infant was put at an unnecessary risk of nosocomial infection. Furthermore, the care is paid for by the family and bed spaces are lacking. You wonder if there is a valid and reliable respiratory distress severity score that may help to accurately assess respiratory distress as a useful adjunct for clinical decision making, to help reduce unnecessary admissions in children with bronchiolitis.

WHAT IS ALREADY KNOWN?

The disease burden from respiratory infection is higher than that of any other cause of disease [1]. In 2016, respiratory illness caused 13% of mortality for children younger than 5 years-of-age [2]. According to the WHO, lower respiratory tract infections are by far the most frequent cause of death in the resource-limited setting [2]. A large part of this burden of mortality being related to severe bacterial pneumonia. This BET focuses on bronchiolitis; however, it is important to highlight that there are some challenges found in differentiating between bacterial pneumonia and viral bronchiolitis.

Viral bronchiolitis is a major cause of respiratory tract infection in infants. Supportive care is the mainstay of treatment and children are frequently admitted to hospital for supportive care if they have met particular clinical criteria, for example; apnoea, taking less than 75% of normal feed volume, and/or having severe

respiratory distress and/or hypoxia [3, 4]. The decision to admit a child with a diagnosis of bronchiolitis is based on a combination of history and clinical examination with particular attention on observed or reported apnoea, persistent oxygen saturation <92%, inadequate oral fluid intake and severe respiratory distress [3]. Risks for severe disease, such as prematurity, should also be considered. The degree of respiratory distress on examination is subjective and based on clinical experience. Also, it is often difficult to predict the disease trajectory; whether the child is likely to deteriorate or has reached the peak of illness. Bed pressures globally necessitate that not all child warrant or can be admitted purely for observation, although we acknowledge from our experience that this might be needed in some particular clinical situations, such as the distance between home and the care facility. Several respiratory distress and bronchiolitis severity scores have been developed to assist in clinical decision making and/or for use in research in children with bronchiolitis.

It is important to note that no respiratory severity score is suitable as a standalone measurement instrument and should be used in conjunction with the healthcare professional's (HCPs) assessment on history and examination. Severity scores need to be robust and should undergo a rigorous process of development, validity, and reliability testing in order to assess their measurement properties and to determine that they reliably measure what they intend to measure [5].

The ideal respiratory severity score for young children should be quick and straightforward to undertake and interpret. It should not involve complex measurements, complex descriptions, any equipment and should only include non-invasive parameters [6]. It should be applicable to children from birth to 2 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 HCPs. However, the pathophysiology, co-morbidities, and age-of-child can make these ideals difficult to achieve.

Aims: In this Journal Club we aim to investigate which scores have a potential to be employed or adapted for use in young children (<24 months) with bronchiolitis in a resource-limited setting, such as Rwanda [7].

STRUCTURED CLINICAL QUESTION (PICO)

In young children (<24 months), with a diagnosis of bronchiolitis in the resource-limited setting [patient] could a respiratory distress severity score [intervention] compared to clinical assessment alone [comparison] be used to stratify disease severity [primary outcome] and/or determine the need for hospital admission [secondary outcome].

FULL SEARCH DESCRIPTION AND SEARCH RESULTS

A literature search was performed on PubMed using the search terms described in Table 1. This revealed 338 papers, and among them, 15 papers were relevant to our topic [8–22]. We undertook a manual search of the reference lists of the relevant papers and a Google Scholar search and identified a further

Table 1. Search terms

	(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)
PubMed LIMITS	English language; Human subjects; Infant
Search date:	28th November 2017, repeated 21st September 2018

five relevant papers [4, 23–26]. Studies were included if they described a scoring system allowing objective severity scoring of children (<24 months) with acute respiratory illness using clinical parameters. Exclusion criteria were studies with participants >24 months of age [14], scores designed and described for clinical trials rather than validation studies [20, 25], studies using biomarkers and/or surrogate marker in comparison to a clinical score [17, 23], scores using items frequently not available in the resource-limited setting (e.g., blood gas results), retrospective studies [8, 18, 24, 26], studies which only looked at clinical features likely to predict hospitalization and did not validate these as a scoring system [10–13]. Thirteen papers were excluded as they did not meet the inclusion criteria (Table 1).

COMMENTARY

In our appraisal, we reviewed seven papers (Table 2), which incorporated nine respiratory severity scores. Seven of these are bronchiolitis specific, one modified asthma score (M-WCAS [19]) and one generic respiratory score (CHWRS, [22]) which were used to assess children with bronchiolitis. There are several notable models that have been developed in LICs. The Respiratory Index of Severity in Children (RISC) Score from South Africa [35], RISC-Malawi [36, 37] mRISC from Kenya [38] and the Mamtani score from India [39]. RISC, mRISC, and RISC-Malawi include parameters such as HIV and nutrition status which are important potential risks in this setting. However, these models assessed for primary outcomes of mortality or antibiotic-treatment failure in children with severe bacterial pneumonia rather than bronchiolitis. These LIC models were developed using logistical regression, often being developed during vaccine trials, on large cohorts of patients to identify risk parameters. One further score should be mentioned, the ReSVinet score [26]. ReSVinet is bronchiolitis specific and includes seven parameters all of which are suitable for the resource-limited setting. The seven parameters in ReSVinet were identified from existing respiratory distress scores. Ninety pediatricians assessed the face validity of ReSVinet. However, 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 for this BET.

Parameters

The majority of care facilities in the resource-limited setting do not have access to investigations such as chest radiograph and/or blood gas analysis. Of note, the majority of guidelines for bronchiolitis treatment, even in the developed setting discourage routine use of these investigations [3]. We only included studies utilizing clinical parameters. Parameters employed were (n = number of scores using the clinical measure): Accessory muscle use ($n=2$); Air-entry ($n=1$); Apnea ($n=1$); Breath sounds ($n=4$); 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($n=1$); Mental status ($n=1$); Oxygen need ($n=1$); Poor air movement ($n=1$); Retractions ($n=4$); RR ($n=7$); $Sa0_2$ ($n=5$); Surgical status ($n=1$); Urine output ($n=1$); Wheezing ($n=6$). These parameters would all be feasible in the resource-limited setting. Oxygen saturations (SaO_2) is one potentially notable exception as it requires equipment which has variable availability in this setting. One study (CHWRS) gave a combined parameter of CXR or lung sounds. Therefore, in the resource-limited setting the assessor would be able to assess lung sounds when CXR was not available. Therefore this article was not excluded during the search [22].

Validity

Validity is a question of whether a scale measures what it is intended to measure. Regarding hospital admission, two scores [4, 22] 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 construct [29]. The main form of construct validity employed in our studies was 'convergent' validity, with four studies assessing scores

Table 2. 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
ESBA [27], 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; Accesssory muscle use; expiratory wheezing; cerebral function	Construct (convergent) validity Criterion validity Criterion (predictive) validity Score not assessed for	Correlation of ESBA with WD score. Weighted kappa: −0.17 (poor) Estimation of the Youden index (J) and optimum cut-off points performed. $J = 0.63$ (moderate) 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%. Scale development, content and cross-cultural validity; usability	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 ($n = 75$) [28] Bad Premature infants (<35 weeks of gestation) were excluded
BROSJOD score [9], 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: Criterion validity Criterion (predictive) validity Internal consistency: Inter-rater reliability	Correlation of BROSJOD score and WD score: KTC at admission = 0.66, KTC 24 h = 0.62 48 h = 0.63 ($p < 0.01$) Correlation with expert: Kappa at admission = 0.84 (almost perfect), 24 h = 0.80 (substantial), 48 h = 0.84 (almost perfect) aROC with expert opinion: At admission = 0.80 (moderate), at 24 h = 0.92 (high), at 48 h = 0.93 (high) Cronbach's alpha at admission = 0.77 (good), at 24 h = 0.65 (questionable), at 48 h = 0.68 (questionable) ICC at admission = 0.96 (excellent), 24 h = 0.77 (good), 48 h = 0.94 (excellent),	Good: Data was collected in ED and at 24hrs & 48hrs after admission Comprehensive assessment of validity and reliability Bad: Subjectivity in assessment score variables.

(Continued)

Table 2. (Continued)

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
				Score not assessed for	Scale-development, content validity, responsiveness; cross-cultural validity; usability	
GRSS score [4] 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 [15, 16], Van Miert *et al.*, UK, 2015	Prospective study PhD thesis. Chapter 9 of PhD thesis reviewed	Construct validating ($n = 128$) <3 months ($n = 68$) 3–12 months ($n = 60$) SPR = 14.2 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 patients with mild and moderate bronchiolitis Two different scores for different ages to take into account physiological differences Bad: Two different scores for different age groups makes 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 Weighted Kappa 0.61 (substantial)	

(Continued)

Table 2. (Continued)

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
				Inter-rater reliability ($n = 128$)	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 [21], 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: 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	
M-WCAS [19] Duarte-Dorado *et al.*, Columbia, 2013	Prospective cohort and a validation study	Hospitalised children <24 months ($n = 54$) Median age 5 months (IQR 2–9) Single centre SPR=	M-WCAS: 5 parameters: Sa02; Inspiratory breath sounds; Expiratory wheezing; Accessory muscle use; Mental status	Criterion (predictive) validity	M_WCAS compared for PICU (4.5/10, $n = 6$) and ward 2.5/10, $n = 48$) admissions using MWU p, 0.001	Good: Well described methodology Bad: Small sample size. Raters were pulmonologists or residents in pulmonology, therefore external validity of results may be compromised aROC not undertaken for predictive validity of PICU admission
				Construct (convergent) validity	Comparison of M-WCAS with Tal as "gold standard". SRC at admission 0.761 (strong), SRC at discharge 0.712 (strong)	
				Responsiveness	M-WCAS at admission (2.5/10) and immediately before hospital discharge 1.0/10), WSR $p < 0.001$	
				Inter-rater reliability	Kappa 0.897 (almost perfect) Bland and Altman plo	
				Feasibility (ease of use)	Time to complete M-WCAS = 1 to 3 min	

(Continued)

Table 2. (Continued)

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
				Score not assessed for	Scale development, content and cross-cultural validity	
RDAI and CHWRS scores [22], Destino *et al.*, USA, 2012	Prospective cohort study	Infants <1 year ($n = 195$) SPR = 19.5	CHWRS: 10 parameters: Breath 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	Construct (convergent) validity	Correlation of each score versus LoS, SRC for RDAI $r = 0.04$ (very weak, $p = 0.71$) or CHWRS $r = 0.05$ (very weak, $p = 0.61$).	Good: Clear consort figure 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 min). 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	

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; MLR, Multivariate logistical regression; MWU, Mann–Whitney U test; M-WCAS, Modified Wood's Clinical Asthma Score; 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; WSR, Wilcoxon signed-rank. *Statistical parameters:* aROC: 0.50 = no different then random (i.e. useless), 0.50–0.70 low; 0.70–0.90 moderate, >0.90 high [29]; Cronbach's: <0.70 poor, >0.70 good (if <7 items), interpretation is dependent on number of parameters [29]; Intra-class correlation (ICC): <0.75 poor to moderate, >0.75 is good, >0.9 is excellent [29, 30]; 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 [31, 32]; Kendall-tau: Between −1 and +1 where positive values represent positive correlation between ranked items; Spearmans' rank correlation (SRC): *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 [33]; Youden: 0.1 (low), 0.5 (medium), and 0.9 (high) [34].

against other established scores [4, 9, 19, 27] and one assessing two scores against length of stay [22]. 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 HCP, which was used in two papers [9, 16]. Even if a well validated scale were identified it would not be possible to say, 'this scale is valid', because the most that we can conclude from any one particular study is that 'we have shown the scale to be valid with this group of children, in this context' [6, 29]. Therefore, validation needs to be undertaken relative to the population that needs to be measured.

Cross-cultural validity:

All of the scores were assessed in High-Income Countries, except the M-WCAS which was assessed in Colombia (Upper-Middle Income Country). The scores were developed and in some cases validated in the following countries: Australia ($n = 2$), Colombia ($n = 1$), Spain ($n = 2$), UK ($n = 1$), and 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.

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 (namely; BROSJOD, [9], LIBBS [15, 16] and Tal, M-WCAS [19], M-Tal scores [21], and RDAI & CHWRS [22]) (Table 2).

Responsiveness

Two studies (RDAI/CHWRS [22] and M-WCAS [19]) assessed for responsiveness to change [22]. Though this is not required for assessing the need for admission it is useful for planning discharge and for monitoring progress in hospital as deterioration is characteristic in the first few days of bronchiolitis.

AT THE BEDSIDE: APPLYING THE EVIDENCE

1. No respiratory severity scores have been prospectively validated in the resource-limited setting, specifically for use in children with bronchiolitis.
2. Several well-designed respiratory severity scores show potential for use in the resource-limited setting (BROSJOD [9], LIBBS [15, 16], and Tal, M-Tal scores [21]), but these will need to be validated in this setting.

What Next

1. The most substantial burden of disease lies in the resource-limited setting, therefore, the validation of a robust respiratory distress severity score for children (<24 months) with bronchiolitis in this setting is needed.
2. Any score that is to be used should also have an assessment for the responsiveness to change in disease over time.

FUNDING

No funding was sought or gained for this BET.

ORIGINALITY

This manuscript is original and has not been published elsewhere.

POTENTIAL CONFLICTS OF INTEREST

C.v.M. undertook a PhD to develop the Liverpool Infant Bronchiolitis Severity Score. The LIBSS is one of the scores that is analyzed in the BET.

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