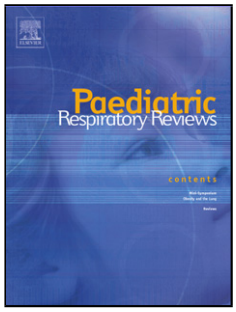

Title: Systematic review of instruments aimed at evaluating the severity of bronchiolitis

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Systematic review of instruments aimed at evaluating the severity of bronchiolitis

Running title: Instruments to assess bronchiolitis severity

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Summary

Objective: No recent studies have performed a systematic review of all available instruments aimed at evaluating the severity of bronchiolitis. The objective of the present study was to perform a systematic review of instruments aimed at evaluating the severity of bronchiolitis and to evaluate their measurement properties.

Methods: A systematic search of the literature was performed in order to identify studies in which an instrument for evaluating the severity of bronchiolitis was described. Instruments were evaluated based on their reliability, validity, utility, endorsement frequency, restrictions in range, comprehension, and lack of ambiguity.

Results: A total of 77 articles, describing a total of 32 different instruments were included in the review. The number of items included in the instruments ranged from 2 to 26. Upon analyzing their content, respiratory rate turned out to be the most frequently used item (in 26/32, 81.3% of the instruments), followed by wheezing (in 25/32, 78.1% of the instruments). In 18 (56.3%) instruments, there was a report of at least one of their measurement properties, mainly reliability and utility. Taking into consideration the information contained in the instruments, as well as their measurement properties, one was considered to be the best one available..

Conclusions: Among the 32 instruments aimed at evaluating the severity of bronchiolitis that were identified and systematically examined, one was considered to be the best one available. However, there is an urgent need to develop better instruments and to validate them in a more comprehensive and proper way.

Abbreviations:

COSMIN - COnsensus based Standards for the selection of health Measurement Instruments

ED - Emergency department

ICC - Intraclass correlation coefficient

Kw - Weighted κ-statistics

LOS - Length of stay

LTRI - Lower tract respiratory infection

NPV - Negative predictive value

PICU - Pediatric Critical Care Unit

PMF - Pediatric medical floor

PPV - Positive predictive value

RDAI - Respiratory Distress Assessment Instrument

ROC - Receiver operating characteristic

RSV - Respiratory syncytial virus

SpO2 - Oxygen saturation level

Keywords: bronchiolitis; bronchiolitis severity scoring; psychometric testing; reliability; validation.

Introduction

Acute bronchiolitis represents the most important cause of lower respiratory tract infection during the first year of life and the leading reason for hospitalization for infants beyond the neonatal period [1]. The disease is usually associated with substantial direct and indirect costs, not only for healthcare systems, but also for families and society as a whole [2]. The assessment of the severity of bronchiolitis is important not only for the clinical management of patients (clinical-decision making and evaluation of response to

therapeutic interventions), but also for clinical research (as an outcome measure to evaluate the efficacy of treatment interventions in randomized controlled trials). A variety of respiratory scores and other instruments, generally consisting of a combination of clinical symptoms and physical signs, have been used to assess the severity of bronchiolitis. However, despite the importance of the assessment of bronchiolitis severity, to date only a few instruments for measuring bronchiolitis severity have been correctly validated [3, 4]. The validation of severity scoring instruments, as well as other outcome measures, is an essential process for assessing their measurement properties in order to guarantee that they measure exactly what they intend to measure [5]. This assessment of measurement properties typically includes appraisal of validity (face validity, construct validity, and criterion validity), reliability (internal consistency, test-retest reliability, and inter-rater agreement), responsiveness, and usability [5]. However, despite their widespread use, many of the available severity scoring instruments for bronchiolitis have never been validated or have been only incompletely validated, and for the majority of those that have been validated, the process has often been restricted to only assessing the inter-rater agreement [6, 7]. A systematic review of all available instruments could be of help in choosing the best instruments for evaluating the severity of bronchiolitis, not only for research but also for clinical purposes. Identifying the correct and optimal measurement instrument for evaluating the severity of bronchiolitis probably will ultimately contribute to good clinical management and to the recognition of optimal outcomes in clinical trials. However, although there are previous reports of such reviews, the most recent search for these reviews was conducted almost five years ago [3], and new instruments with a more rigorous evaluation of their measurement properties have been reported after their publication [8-10]. Additionally, although these reviews have provided valuable data on the available instruments for assessing the severity of bronchiolitis as well as their measurement properties, they haven't provided specific recommendations for the busy

clinician or for researchers on which could be the best instruments for use in clinical practice or which are those that make it worthwhile to perform additional validation studies. The aim of the present study was to perform a systematic review of instruments aimed at evaluating the severity of bronchiolitis and to evaluate the measurement properties of the identified instruments.

Methods

Search strategy

A systematic search of the literature was performed by two independent reviewers (CERM and MPS) in the electronic databases PubMed and Embase from the inception of the database to February 2016 in order to identify studies in which an instrument for evaluating the severity of bronchiolitis was described. The following search strategy, mesh terms, and free text words were used to search in the PubMed database: (severity scoring OR respiratory scores OR severity assessment tool) AND (psychometric testing OR reliability OR validity) AND bronchiolitis. For the purpose of gathering additional studies, we examined the references of the identified articles and we contacted experts in the field. Any disagreements were resolved through discussion, and if necessary a third reviewer was involved. We considered studies in any language.

Inclusion and exclusion criteria

Studies that included scales or other instruments were included if they evaluated the severity of bronchiolitis or Respiratory syncytial virus (RSV) infection/disease in infants, whether or not they assessed the measurement properties of the instruments. Articles that reported on instruments that evaluated the severity of asthma or of acute respiratory infections other than bronchiolitis were not considered for inclusion in the review. Likewise,

studies that described the use of a single clinical symptom or clinical sign instead of their combination into a score were not eligible for inclusion in the review.

Data extraction

Two reviewers (CERM and MPS) independently performed the data extraction by using a data extraction sheet specifically designed for the study. From the included studies, we extracted descriptive data (author, year, respondents, and disease characteristics) and the key characteristics and measurement properties of selected instruments (source of instrument, number of items, response options, scoring, interpretation, validity, reliability, usability, responsiveness). In addition, we recorded the references that each of the instruments used and whether evaluation of any measurement property was presented as the main study objective.

Assessment of measurement properties of selected instruments

For the purpose of evaluating the measurement properties of identified and selected instruments, we used the checklist for evaluating the usefulness of rating scales proposed by Streiner [5]. This checklist consists of 5 domains, each dealing with one of the following measurement properties: where the instrument's items originated (previous scales, clinical observation, expert opinion, patients' reports, research findings, theory); assessment by the instrument's items of endorsement frequency, restrictions in range, comprehensiveness, and lack of ambiguity; reliability (internal consistency, test-retest reliability, inter-rater agreement); validity (face validity, content validity, criterion validity, construct validity); and utility or usability (completion time, training time, scoring). Each domain of this checklist contains 3 to 6 items on relevant aspects of domain appraisals (Table 1). Responsiveness was added to the checklist in order to get a complete evaluation of the measurement properties of the instruments.

Studies were not rejected on the basis of these measurement properties; rather, the results were synthesized in order to assist in selecting the best available instrument. All measurement properties were scored independently by two researchers (CERM, GN) before reaching a consensus.

Selection of the best available instruments

When deciding on the best available instruments we considered the following criteria: First, we took into account the inclusion of simple and well-categorized items that measure respiratory status in an objective manner with no involvement of complicated measurements or calculations, and that in turn are useful, relevant, practical for use in daily clinical practice, and readily available even in resource-limited settings. Second, the instrument should contain items appropriate for use for all infants with bronchiolitis under 24 months of age, including very young children, and items suitable to be used by all healthcare providers, including non-physician providers. Third, items contained in the instrument should be generated from various sources, including an evidence-based review of the literature and stakeholder consultation (ensuring adequate representation of parents/caregivers of infants with bronchiolitis), using formal consensus techniques, and should use a formal procedure for their selection and reduction. Fourth, in order to ensure that the instrument measures what it is intended, besides the face and content validity measures, instruments should demonstrate adequate reliability, validity, and responsiveness. Finally, the instrument should be easy to score and should lend itself to prompt completion [5].

Results

Results of the search

The study selection process is shown in Figure 1. The systematic search of databases retrieved 11 studies. Among those, 3 were excluded. Sixty-nine additional studies that met the inclusion criteria were identified from reference lists. Finally, a total of 77 articles, describing a total of 32 different instruments aimed at evaluating the severity of bronchiolitis, were included in the review.

Content and properties of the instruments

In the majority of included studies (60 out of 77, 77.9%), evaluation of a measurement property of a bronchiolitis severity instrument was not presented as the main study objective, but instead these studies used a bronchiolitis severity instrument for evaluating the efficacy of specific therapeutic interventions.

Table 1 summarizes the characteristics of the 32 retrieved bronchiolitis severity instruments and the references of the studies that each of the instruments used. The Respiratory Distress Assessment Instrument (RDAI) proposed by Lowell et al. [11] is by far the most used instrument for assessing the severity of bronchiolitis in the literature, followed by those proposed by Tal et al. [12] and by Wang et al. [13].

The number of items included in the instruments ranged from 2 to 26. All but one (3.1%) of the instruments summed up individual item scores in order to generate a combined unweighted bronchiolitis severity score. All but 5 (15.6%) instruments specified the scoring range for items, ranging from 0 to 60, with 6 (18.8%) instruments scoring items from 0 to 12. Upon analyzing the content of the instruments, respiratory rate turned out to be the most frequently used item (in 26/32, 81.3% of the instruments), followed by wheezing (in 25/32, 78.1% of the instruments), retractions (in 20/32, 62.5% of the instruments), accessory respiratory muscle utilization (in 10/32, 31.2% of the instruments), and oxygen saturation (in 8/32, 25.0% of the instruments) (Figure 2). All other items were used infrequently.

Measurement properties of the instruments

In 18 (56.3%) instruments, there was a report of at least one of their measurement properties. The measurement properties most frequently assessed and reported were reliability (in 15/32, 46.9% of the instruments) and validity (in 14/32, 43.8% of the instruments), and the least frequently assessed was usability (in 2/32, 6.3% of the instruments).

Table 1 and Table 2 give the frequency and content of reporting of the six checklist criteria by the 32 bronchiolitis severity instruments. Detailed findings for each of the criteria are described below.

1. *Where the instrument's items originated*: in 17 (53.1%) instruments, items were derived or adapted from previous instruments; in 5 (15.6%) instruments, clinicians' opinions were used as the basis for item generation; in 2 (6.3%) instruments, items were derived using a formal procedure for their selection (ordinal regression or logistic regression model); and in 8 (25.0%) instruments, where the items originated was not stated.
2. *Assessment of the instrument's items for endorsement frequency, restrictions in range, comprehensiveness, and lack of ambiguity*: items were assessed for endorsement frequency by two instruments [11, 14], and for comprehensiveness by one instrument [14]. No instrument assessed item homogeneity, restrictions in range, or lack of ambiguity.
3. *Reliability*: Fifteen instruments (46.9%) reported on reliability measures. Inter-rater agreement was described for 15 instruments, ten of them using weighted κ-statistics (Kw) with reported values ranging from 0.25 to 0.94. Four of the 15 instruments used the intraclass correlation coefficient (ICC), with reported values ranging from 0.39 to 0.99. Four of the 15 instruments reported perfect agreement or scores not differing by more than one point between observers in the majority of observations. Three scores

measured internal consistency, with Cronbach alpha values ranging from 0.66 to 0.83. Only one instrument measured test-retest reliability, reporting a Kw of 0.93.

4. *Validity*: Fourteen instruments (43.8%) measured construct validity. In order to assess the construct validity, instrument scores were correlated with other variables and measures related to the construct of bronchiolitis severity, such as oxygen requirements, oximetry, hospital admission, length of stay (LOS), hospital costs, resource utilization, other markers of breathing work not contained in the instruments, and disposition type (outpatient, stay in the emergency department, hospitalized in the pediatric medical floor - PMF, or hospitalized in the Pediatric Critical Care Unit - PICU). Multiple diverse analyses were used to test for these correlations, such as the area under a receiver operating characteristic (ROC) curve, sensitivity, specificity, predictive values, the Pearson correlation coefficient, and an adequate statistical test for comparing scores in patients with different disposition types. Construct validity ranged from inadequate (when instrument scores were correlated with LOS) to adequate (when instrument scores were correlated with disposition type). Face validity was formally assessed by three instruments, by having a multidisciplinary group of professionals review the instrument. With regard to content validity, in only 2 instruments were items derived using a formal procedure for their selection (ordinal regression or logistic regression model). Only one instrument measured criterion validity, using the Tal scoring system as the gold standard measure, reporting a positive and significant correlation between the two scores ($r= 0.761$, $p< 0.001$).
5. *Usability*: Only two instruments (6.3%) measured usability, one of them formally assessing the speed, understandability, and subjective experience when completing the instrument. All raters qualified this instrument as easy to score, and reported that the time required to complete the instrument ranged from 1 to 3 min. Ease of scoring was qualitatively reported as "easy" in the other instrument.

6. *Responsiveness*: Four instruments (12.5%) measured responsiveness. The responsiveness of the instruments was determined by measuring the change in severity scores following a treatment of known efficacy (and comparing with the change in the score of other instruments), and by comparing the severity scores obtained at admission to the PMF with those obtained immediately before discharge from the hospital. The responsiveness of the instruments ranged from moderate to adequate.

Results of the selection of the best available instruments

When considering what the instruments measures and how well they have been validated, we determined that the best available instruments are those used by Marlais et al. [15], Rodriguez et al. [16], Liu et al. [7], Gadjos et al.[6], Wood DW al.[17], and Flores-Gonzalez et al. (Table 2). Among these, the instrument proposed by Marlais et al. was considered to be the best available instrument, because it met a greater number of the above-mentioned criteria.

Discussion

The present study shows that at least 32 instruments devoted to evaluating the severity of bronchiolitis have been reported in the literature. The majority of these instruments were reported in studies primarily aimed at assessing the efficacy of specific therapeutic interventions, not to evaluating any of their measurement properties. The instruments vary greatly in composition, from 2 to 26 items, most of which were derived or adapted from previous instruments, and they added up individual item scores to generate a combined unweighted bronchiolitis severity score. Respiratory rate, wheezing, and retractions were the most frequently used items. In a little more than half of the instruments, there was a report of at least one of their measurement properties, mainly reliability and validity.

The findings of the present study are important because they could help clinicians to choose the best instrument for clinical decision-making and to evaluate the response to therapeutic interventions, and furthermore could help researchers to decide the most suitable instruments for performing additional validation studies. Due to the fact that the most recent systematic review of clinical scores for the assessment of acute dyspnea in children that present with wheezing concluded that instead of developing new scores, it would more useful to validate existing dyspnea scores in a more comprehensive and proper way[3], and that new studies with a more rigorous evaluation of the instrument's measurement properties have been reported since then [8-10], the present review will allow busy clinicians and researchers to make a well-balanced and up-to-date decision with respect to which bronchiolitis severity scoring instrument will be most suitable for their specific purposes. This decision is particularly important when treating a patient with bronchiolitis, because it is a very common disease with few proven effective therapeutic options.

As mentioned above, we determined that the best available instruments are those used by Marlais et al. [15], Rodriguez et al. [16], Liu et al. [7], Gadjos et al. [6], Wood et al. [17], and Flores-Gonzalez et al [9]. However, none of these instruments is perfect. For example, the instrument proposed by Marlais et al. [15] contains items that were derived from an evidence-based literature review and used a formal procedure for their selection, but it fails to meet one of the above-mentioned criteria, because it includes oxygen saturation, whereas pulse oximeters are not always easily accessible. Additionally, the instrument demonstrated adequate construct validity but failed to assess other aspects of validity, as well as reliability, responsiveness, and usability. Likewise, the instrument proposed by Rodriguez et al. [16] fails to meet only one of the above-mentioned item criteria (wheezing, which requires auscultation skills, which not all non-physician providers may have) and demonstrated adequate inter-rater agreement and construct validity, but failed to assess

other aspects of validity, other aspects of reliability, responsiveness, and usability. Similarly the instruments proposed by Liu et al. and Gadjos et al. [6, 7] also fail to meet only one of the above-mentioned item criteria (wheezing, which requires auscultation skills, which not all non-physician providers may have), and both instruments demonstrated adequate inter-rater agreement, but failed to assess other measurement properties.

On the other hand, the instrument proposed by Wood et al. [17] demonstrated adequate construct validity, criterion validity, inter-rater agreement, responsiveness, and usability, and the instrument proposed by Flores-Gonzalez et al. [9] demonstrated adequate construct validity and responsiveness. However, both instruments contain items that fail to meet more than one of the above-mentioned item criteria (oxygen saturation, inspiratory breath sounds, and expiratory wheezing for the former, and wheezing, crackles, and inspiratory/expiratory ratio for the latter). However, as mentioned above, we consider that the instrument proposed by Marlais et al. is the best available instrument, because it met a greater number of the criteria mentioned for selecting the optimum instrument.

Our results are in overall agreement with previous studies that have performed systematic reviews of clinical scores for the assessment of acute dyspnea in children that present with wheezing [3] and asthma severity scores for preschoolers [4], which have concluded that most clinical scores for the assessment of acute dyspnea in children that present wheezing and most asthma severity scales for use in preschool children have been informally developed and insufficiently validated. We agree with Bekhof et al. [3] that the limited methodological quality of the available instruments does not necessarily mean that these existing instruments are not suitable for use in clinical practice and research. Although none of the many available instruments is perfect, in any case providers must use the best available instruments to make clinical decisions such as evaluation of

response to therapeutic interventions. However we disagree with Bekhof et al. [3] in that instead of developing new scores, it would be more useful that existing dyspnea scores be validated in a more comprehensive and proper way. The main reason for this disagreement is that none of the many available instruments generated items that incorporate all the recommended scale development and psychometric methods [5]. Specifically, none of the available instruments generated items and domains using all recommended sources and methods (evidence-based literature review, stakeholder consultation including parents/caregivers of infants with bronchiolitis, formal consensus techniques such as the Delphi technique, and a formal procedure for selection and reduction of items), so it is highly probable that none of the available instruments contain all the items required for the appropriate assessment of bronchiolitis severity. If this is the case, it would be inappropriate to validate some of the existing instruments in a more comprehensive and proper way, as proposed by Bekhof et al. [3], and it would be more appropriate to develop a new instrument by means of a conceptual framework and using qualitative methods to identify important items and domains associated with bronchiolitis severity. With respect to this, there is a promising instrument aimed at evaluating the severity of bronchiolitis (the Liverpool infant bronchiolitis severity score) [18] that is being planned to incorporate all recommended scale development and psychometric methods and is to be developed and validated in the next few years.

The most important limitation of the present paper has to do with the fact that the COnsensus based Standards for the selection of health Measurement INstruments (COSMIN) initiative developed a checklist aimed at evaluating the methodological quality of studies on measurement properties, and it has been widely used for this purpose [19]. However, our main objective was to identify all available instruments aimed at evaluating the severity of bronchiolitis, instead of performing a systematic review of the measurement

properties of these instruments. For this reason, and because we anticipated a significant number of studies not primarily aimed at examining the measurement properties of the instruments and because we lacked information on the majority of these measurement properties, we decided not to use the COSMIN checklist in our study.

The main strength of our study is that the search for instruments aimed at evaluating the severity of bronchiolitis was comprehensive and active, not limited only to the title, subject heading, and abstract, thus yielding more than double the instruments identified by previous reviews. Additionally, we provide specific recommendations for the busy clinician or for researchers about which the most suitable instrument for their specific purposes could be.

In conclusion, at least 32 instruments devoted to evaluating the severity of bronchiolitis have been reported in the literature. Due to the fact that none of the many available instruments incorporate all recommended scale development and psychometric methods, there is an urgent need to develop better instruments and to validate them in a more comprehensive and proper way. With respect to this, there is a promising instrument that is planned to be developed and validated in the next few years. In the meanwhile, due to the urgent necessity of having an adequate instrument intended to facilitate the clinical decision-making processes in bronchiolitis, we found one instrument to be the best one available, and therefore we consider it to be the one most suitable for use in clinical practice and research.

Educational aims

- To discuss the importance of the assessment of bronchiolitis severity not only for the clinical management of patients, but also for clinical research

- To highlight the importance of the validation of severity scoring instruments, in order to guarantee that they measure exactly what they intended to measure
- To identify all available instruments for measuring the severity of bronchiolitis and to evaluate the measurement properties of the identified instruments.
- To try to choose one instrument as the best one available, to facilitate the clinical decision-making processes in bronchiolitis

Future research directions

Due to the fact that none of the many available instruments incorporate all recommended scale development and psychometric methods, there is an urgent need to develop better instruments and to validate them in a more comprehensive and proper way.

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FIGURE LEGENDS

Figure 1. Study flow diagram for studies reporting instruments aimed at evaluating the severity of bronchiolitis

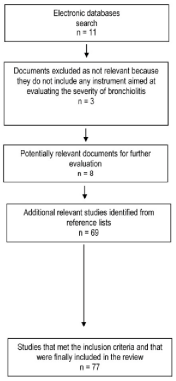

Figure 2. Items more frequently used by instruments aimed at evaluating the severity of bronchiolitis

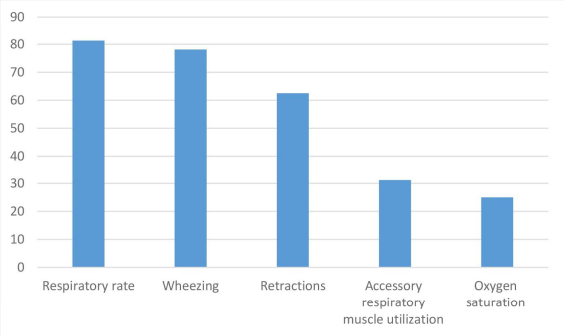

Table 1. Principal findings of instruments aimed at evaluating the severity of bronchiolitis

Instrument	References of studies that used the instrument	Measured characteristics	Scoring	Where the instrument's items originated	Assessment of the items for	Reliability	Validity	Usability
Respiratory distress index score (RDI). (Alario, A.J. et al.) [20].	[20]	- Color - Wheezing - Accessory muscle use - Flaring - Grunting - Distressfulness	Clinical impressions with regard to each of the six variables were coded on separate, continuous 12-cm lines that were calibrated to represent increasing degrees of severity. The distance along the line to the marked point was measured, and the total for all six variables was summed.	Findings of respiratory distress previously shown to be important in the evaluation of children with LTRI [a]	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	*Inter-rater agreement*: For any variable on the RDI, there was no greater than 3 cm of discordance on the12-cm line between investigators. The weighted percentage agreement ranged from 90% to 98%, and Kw [b] ranged from 0.60 to 0.72.[20]	Not assessed	Not assessed
A modified score of Wang et al. (Beck R. et al) [21].	[21]	- Wheezing (0-3) - Retractions (0-3) - Oxygen saturation (0-3) - Respiratory rate (0-3) - Heart rate (0-3)	Score (0-15) with higher scores indicating more severe disease	Adapted from a previous score	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	Not assessed	Not assessed	Not assessed
Scoring system. (Bentur, L. et al.) [22].	[22]	- Respiratory rate (0-2) - Wheezing (0-2) - Retraction (0-2) - General condition (0-2) - Oxygen saturation (0-2)	Score (0-10) with increasing severity receiving a higher score.	The scoring system is based on those used in past studies.	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	Not assessed	Not assessed	Not assessed
Clinical score (Bentur, L. et al.) [14].	[14]	- Heart rate (0-1) - Respiratory rate (0-1) - Dyspnea (0-1) - Accessory muscle use (0-1) - Wheezing (0-1)	Score (0-5) with increasing severity receiving a higher score	Not stated	- Endorsement frequency: yes - Restrictions in range: no - Comprehensiveness: yes Lack of ambiguity: no	Not assessed	Not assessed	Not assessed
Clinical scoring system. (Berger I. et al) [23].	[23]	- Accessory muscle use (0-3) - Wheezing (0-3) - Respiratory rate (0-3)	Score (0-9) with higher scores indicating greater severity of bronchiolitis	Previous scale	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	Not assessed	Not assessed	Not assessed
Pulmonary index (Bierman CW. et al) [24].	[24]	- Respiratory rate (0-3) - Wheezing score (0-3) - Inspiratory/Expiratory ratio (0-3) - Accessory respiratory muscle utilization (0-3)	Score (0-12) where higher scores indicate more severe disease	Adapted from a previous instrument	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	Not assessed	Not assessed	Not assessed

Severity of illness scoring system. (Conrad DA. et al) [25].	[25]	Nose - Discharge (0-3) Throat - Dysphagia (0-3) - Dysphonia (0-3) - Exudate (0-3) Chest - Retractions (0-3) - Stridor (0-3) - Rales (0-3) - Tubular breath sounds (0-3) - Cough (0-3) - Ronchi (0-3) Gastrointestinal tract - Anorexia (0-3) - Vomiting (0-3) - Nausea (0-3) - Diarrhea (0-3) - Abdominal pain (0-3) Other - Headache (0-3) - Myalgias (0-3) - Arthralgias (0-3) - Rash (0-3)	Score (0-60) with higher scores indicating greater severity of bronchiolitis	Not stated	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	Not assessed	Not assessed	Not assessed
The bronchiolitis score (Dabbous IA. et al) [26].	[26]	- Cyanosis (0-3) - Activity (0-3) - Cough (0-3) - Respiratory rate (0-3) - Retraction score (0-3) - Resonance (0-3) - Wheezing (0-3) - Expiration/ inspiration (0-3) - Liver spleen (0-3)	Score (0-27) with higher scores indicating greater severity of bronchiolitis	Not stated	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	*Inter-rater agreement*: overall scores on duplicate comparisons were within 1 point of each other in greater than 95% of observations.[26]	Not assessed	Ease of scoring was qualitatively reported as “easy to score”.
A simplified bronchiolitis score. (Dabbous, I.A. et al.) [26].	[26]	- Respiratory rate (0-3) - Retraction score (0-3) - Wheezing (0-3) - Expiration/ inspiration ratio (0-3) - Liver and spleen (0-3)	Score (0–15), with higher scores indicating more severe disease.	Previous score	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	Not assessed	Not assessed	Not assessed
Modified-Tal scoring system. (De Boeck K. et al) [27].	[27-31]	- Respiratory rate (0-3) - Wheezing (0-3) - Oxygen saturation (0-3) - Accessory respiratory muscle utilization (0-3)	Score (0–12), with higher scores indicating greater severity of bronchiolitis	Adapted from a previous instrument	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	*Internal consistency*: Cronbach alpha value: 0.70. *Inter-rater agreement:* Kw: 0.70 (95% CI: 0.63, 0.76).[29]	*Construct validity*: For predicting requirement for oxygen at 12 and 24 aROC [c]: 0.75 (95% CI: 0.34, 1.0).[29]	Not assessed

A modified Respiratory Distress Assessment Instrument (RDAI). (De Brasi, D. et al) [32].	[32]	- Wheezing (0-8) - Retractions (0-9) Modification concerns lung fields location of wheezing	Score (0–17), with higher scores indicating more severe disease	Previous scale	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	Not assessed	Not assessed.	Not assessed
Children's Hospital of Wisconsin Respiratory Score (CHWRS). (Destino L. et al) [33].	[33]	- Breath sounds (0-3) - Dyspnea (0-3) - Retractions (0-3) - Respiratory rate (0-3) - Heart rate (0-3) - Oxygen need (0-3) - Activity appearance (0-3) - Cough ability/ secretions (0-3) - Chest x-ray/ lung sounds (0-3) - Surgical status (0-3)	Score (0–30), with higher scores indicating greater severity of bronchiolitis	The score was created by a panel of local clinicians and respiratory therapists after reviewing scores in existence	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no - *Responsiveness:* there was a mild correlation between the change in the CHWRS and RACS after an intervention (r= 0.39, p= 0.04).[33]	Inter-rater agreement: ICC [d]: 0.73 (95% CI: 0.60–0.82).[33]	*Construct validity*: aROC: 0.68 with a cutoff point of 7.5 (scores >7.5 predicting admission), giving a sensitivity of 0.65 and a specificity of 0.65.[33] There was no statistically significant correlation between RDAI and LOS [e] (r= 0.05, p=0.61).[33]	Not assessed
Clinical scoring. (Gadomski, A.M. et al.) [35].	[35, 36]	- Grunting (0-3) - Nasal flaring (0-3) - Supraclavicular retractions (0-3) - Intercostal retraction (0-3) - Chest indrawing (0-3) - Air entry (0-3) - Air hunger (0-3) - Wheezing (0-3) - General appearance (0-3)	Not specified. Scores are missing in intermediate grades, such as 1 and 2, because these categories were omitted from the scoring instrument due to high inter-rater variability during reliability testing.	Compilation of other scoring systems used in past studies	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	*Inter-rater agreement*: the mean two-rater agreement on all items were 77% for grading of the clinical signs.[36]	*Construct validity*: the correlation coefficients for total score versus SpO2 [f] ranged from r= -0.31 to -0.46, p<0.001.[36]	Not assessed
Severity Score. (Goh A. et al) [37].	[37]	- Respiratory rate (0-4) - Subcostal retractions (0-3) - Presence of crepitations (0-1) - Presence of wheeze (0-4) - Oxygen requirement (0-1) - Nebulization (0-1) - Intravenous infusion (0-1)	Score (0–15), with higher scores indicating more severe disease.	Not stated	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	Not assessed	Not assessed	Not assessed
Respiratory Score. (Groothuis JR. et al) [38].	[38, 39]	- Oxygen saturation (0-5) - Respiratory rate (0-5) - Retractions, wheezing, crackles (0-5)	The score (0-5) is the mode of the three component scores, or the mean if there is no mode.	Not stated	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	Not assessed	Not assessed	Not assessed
The Kristjansson Respiratory Score. (Kristjansson S. et al) [40].	[40]	- Respiratory rate (0-2) - Chest recession (0-2) - Breath sound	Score (0–10), with higher scores indicating more severe disease	Not stated	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	*Inter-rater agreement*: ICC: 0.89.[41]	*Construct validity*: There was a significant negative correlation	Not assessed

		(0-2) - Skin color (0-2) - General condition (0-2)					between the Kristjansson Respiratory Score and SO2 for two observers (r = –0.75, p <0.001) and (r= –0.73, p <0.001).[41]	
The Respiratory Distress Assessment Instrument (RDAI). When used as a marker of change with respiratory rate, it is called the Respiratory Assessment Change Score (RACS). (Lowell DI. et al) [11].	[11, 33, 42-64]	- Wheezing (0-8) - Retractions (0-9) - Respiratory rate (included when measuring change)	Score (0–17), with higher scores indicating more severe disease	Derived from underlying pathophysiology and variables frequently used by clinicians in assessing improvement in wheezing children	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no - *Responsiveness:* there was a mild correlation between the change in the CHWRS and RACS after an intervention (r= 0.39, p= 0.04).[33] aROC: RDAI: 0.64 to 0.70; RACS: 0.72.[64]	*Inter-rater agreement*: Kw: 0.90 for wheezing and 0.64 for retractions.[11] ICC: 0.39 (95% CI: 0.17–0.58).[33] Kw: 0.93 (95% CI: 0.89, 0.97).[45] ICC: 0.65.[48] Kw: 0.94.[52] ICC: 0.91.[60] ICC: 0.93.[64]	*Construct validity*: The aROC for the RDAI was 0.51 being not predictive of disposition.[33] There was no statistically significant correlation between RDAI and LOS (r= 0.04,p=0.71).[33] The changes in work of breathing markers such as inspiratory to expiratory ratio, breath sounds, grunting, nasal flaring, and global clinical response to treatment, was consistent with the three respiratory variables used in the RAID.[11] Baseline RDAI were positively correlated with respiratory rate (r=0.38, p<0.01), and scores increased in lower oxygen saturation categories (p<0.01). Scores differed between participants who were discharged, admitted, or stayed in the ED [g] (p<0.001).[64]	Not assessed
Clinical score. (Maayan C. et al) [65].	[65]	- Retractions (0-3) - Expiratory Wheezing (0-3)	Score (0-6) with increasing severity receiving a higher score	Not stated	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	Not assessed	Not assessed	Not assessed

The W.A.R.M. Respiratory Scoring Tool. (Marks M PR. et al) [66].	[66]	- Wheezing (0-2) - Air exchange (0-2) - Respiratory rate (0-1) - Muscle use/retractions (0-2)	Score (0-7) with higher scores indicating greater severity of bronchiolitis	Not stated	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	Not assessed	Not assessed	Not assessed
Acute Bronchiolitis Severity Scale (ABSS). (Ramos Fernandez JM. et al) [10].	[10]	- Wheezing (0-4) - Crackles (0-4) - Respiratory effort (0-3) - Inspiration/ expiration ratio (0-2) - Heart rate (0-2) - Respiratory rate (0-2)	Score (0-17) with higher scores indicating more severe disease	Items were derived from underlying pathophysiology, previous scales, and discussion with local clinicians who attend patients suffering from bronchiolitis.	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	*Internal consistency*: Cronbach alfa value: 0.83. *Test-retest reliability*: Kw: 0.93 Inter-rater agreement: Kw: 0.682.[10]	*Construct validity*: The scores of the ABSS were different between patients who required ambulatory treatment, admission to the PMF, and those who required admission to the PICU.[10]	Not assessed
A clinical scoring system. (Richter H. et al) [67].	[67]	- Respiratory rate - Retractions - Wheezing - Oxygen saturation - Need for IV fluids or nasogastric tube feeding	Score not described	Scoring system adapted from a previous score	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	Not assessed	Not assessed	Not assessed
Tal scoring system. (Tal A. et al) [12].	[12, 29, 69-73]	- Respiratory rate (0-3) - Wheezing (0-3) - Cyanosis (0-3) - Accessory respiratory muscle utilization (0-3)	Score (0–12), with higher scores indicating greater severity of bronchiolitis	Previous instrument	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	*Inter-rater agreement*: the instrument showed no differences greater than one point,[12] and scores did not differ by more than 1 unit for scores less than 5.[71] Kw: 0.72 (95% CI: 0.63–0.83).[29] *Internal consistency:* (Cronbach alpha value): 0.66.[29]	*Construct validity*: For predicting requirement for oxygen at 12 and 24 hrs aROC: 0.69 (95% CI: 0.13, 1.0).[29]	Not assessed
Severity score. (Wainwright C. et al) [74].	[74]	- Respiratory-effort score (1-3) - Oxygen saturation (0-2) - Respiratory rate (0-2)	Score (1-7) where higher scores indicate more severe disease	Not stated	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	Not assessed	Not assessed	Not assessed
A bronchiolitis severity assessment tool. (Walsh P. et al) [75].	[75, 76]	- Retractions - Heart rate - Age - Dehydration	Score not described. The assessment tool is an ordinal regression model	Derived from a ordinal regression model	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	*Inter-rater agreement*: Kw: 0.676, $p < 0.0001$.[76]	*Construct validity*: The model predicted admission with 91% sensitivity and 83% specificity in a validation cohort.[75]	Not assessed

The Wang Respiratory Score. (Wang EE. et al) [13].	[13, 41, 77-80]	- Respiratory rate (0-3) - Wheezing (0-3) - Retraction (0-3) - General condition (0-3)	Score (0–12), with higher scores indicating greater severity of bronchiolitis	Adapted from a previous instrument	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	*Inter-rater agreement*: ICC: 099.[41] The rater agreement for the four clinical signs of the score ranged from Kw 0.25-0.48.[13]	*Construct validity*: There was a significant negative correlation between the Wang Respiratory Score and SpO2 for two observers (r = –0.41, p=0.04) and (r= –0.43, p =0.03).[41] There was a poor correlation between total score and oximetry (r= -0.04).[13]	Not assessed
The pediatric component of the Comprehensive Severity Index (CSI). (Willson, D.F. et al.) [81].	[81]	Digestive - Difficult feeding (0-3) - Vomiting (0-3) Lab-ABG´s - PO2/FiO2 ratio (0-4) - O2 sat/FiO2 ratio (0-4) - Highest PH (0-4) - Lowest PO2 (1-2) - Lowest pH (0-4) - Highest PCO2 (0-4) Lab-Heme - Highest WBC (0-4) - Highest Bands (0-3) - Lowest WBC (0-4) Neurology - Mental Status (0-4) Radiology - Hyperexpansion of Lungs (0-1) Respiratory - Cyanosis (0-1) - Sputum/secretions (0-3) - Apnea/Dyspnea (0-1) - Rales (0-3) - Breath Sounds (0-4) - Nasal Flaring (0-3) - Retractions (0-4) - Expiratory grunt (0-3) - Wheezing (1-2) - O2 saturation (0-4) Vital signs - Highest RR (1-4) - Lowest Temp (oral) (0-4)	Not specified	CSI is a severity scoring system based on physiologic and laboratory measures of the patient's clinical status and is age and disease specific. The pediatric CSI is a modification of the adult CSI. Expert physician panels from the participating institutions developed explicit pediatric severity criteria to rate severity for each ICD-9-Clinical Modification (CM) diagnosis code or groups of similar codes. These criteria are based on objective clinical or historical findings (ie, physiologic signs and symptoms of a disease and not on treatment).	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	Not assessed	*Construct validity*: Maximum CSI had the highest correlation coefficient with hospital costs (r2= 0.42) and lengths of stay (r2= 0.41). CSI scores also correlated well with measures of resource utilization in subgroups of bronchiolitis patients with comorbidities or other risk factors for severe disease.[81]	Not assessed

		- Highest Temp (oral) (0-3)							

a. LTRI: lower tract respiratory infection

b. Kw: weighted kappa

c. aROC: area under the ROC curve

d. ICC: intraclass correlation coefficient

e. LOS: length of stay

f. SpO2: oxygen saturation level

g. ED: emergency department

Table 2. Principal findings of instruments selected as the best available ones, based on what the instruments measures and how well they have been validated

Instrument	References of studies that used the instrument	Measured characteristics	Scoring	Where the instrument's items originated	Assessment of the items for	Reliability	Validity	Usability	Key points that make the instrument outstanding
Wood Downes's modified by Ferres score (WDF). (Flores-Gonzalez JC) [9].	[9, 34]	- Cyanosis (0-1) - Ventilation (0-3) - Wheezing (0-3) - Retractions (0-3) - Respiratory rate (0-3) - Heart rate (0-1)	Score (0–14), with higher scores indicating more severe disease.	Previous score	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no - *Responsiveness*: The WDF scale decreased an average of 3.87 points (95% CI, 2.5–6.5) from admission to the time of discharge.[9]	Not assessed	*Construct validity*: The WDF scores in patients who required subsequent admission to the PICU [a] were significantly higher than those inpatients who required admission only to the PMF [b] (6 (4–8) vs 5 (4–8), p = 0.026).[9] Patients with scores of the WDF between 4 and 7 had a significant lower LOS compared to patients with scores >7 (4.8 vs. 13.44 days, p<0.0001).[34]	Not assessed	Adequate construct validity and responsiveness
The respiratory score. (Gajdos V. et al) [6].	[6]	- Age-based respiratory rate (1-3) - Retraction signs (0-3) - Wheezing (0-3)	Score (1-9) where higher scores indicate more severe disease	The score included parameters of respiratory status easily assessable in children of all ages, particularly in young	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	*Inter-rater agreement*: For all provider pairs: 93.1%, with a Kw: 0.72 (95% CI, 0.66–0.78). For the various age groups ranged	Not assessed	Not assessed	Inclusion of simple and well-categorized items readily

				children, at discretion of authors.		from 87% to 93%, with Kw[c] ranging from 0.62 to 0.78.[6]			available even in resource-limited settings), and suitable by all healthcare providers (except wheezing). Adequate inter-rater agreement
A respiratory clinical score. (Liu LL. et al) [7].	[7]	- Respiratory rate (0-3) - Retractions (0-3) - Dyspnea (0-3) - Auscultation (0-3)	Score (0-12) with higher scores indicating greater severity of bronchiolitis	Items selected for use in the score were derived from a literature review of clinical scores, and were common signs of respiratory status that were easily measured in children of all ages, particularly young children.	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	*Inter-rater agreement*: rater pairs had high observed agreement on total score of 82–88% and Kw ranging from 0.52 (95% CI: 0.19 - 0.79) to 0.65 (95% CI: 0.46 - 0.87).[7]	Not assessed	Not assessed	Inclusion of simple and well-categorized items readily available even in resource-limited settings), and suitable by all healthcare providers (except wheezing). Adequate inter-rater agreement
Bronchiolitis risk of admission score. (Marlais, M. et al.) [15].	[15]	- Duration of symptoms (0-1) - Respiratory rate (0-1) - Heart rate (0-1) - Oxygen saturation (0-1) - Age at presentation (0-1)	Score (0-5) with higher scores indicating greater severity of bronchiolitis	Clinical predictors of admission were determined through case note review and logistic regression analysis. The strongest predictors of admission were assimilated into a simple clinical risk scoring system using widely accepted statistical methods.			*Construct validity*: The aROC[d] for the final clinical risk score was 0.81 (95% CI 0.77 to 0.85). The optimal cut-off using this score was found to be a score of ≥3 requiring admission. At this cut-off the sensitivity was 74% and specificity was 77%. The PPV [e] was 67% and the NPV [f] 83%.[15]		Inclusion of simple and well-categorized items readily available even in resource-limited settings (except oxygen saturation), and suitable by all healthcare providers, including nonphysician providers. Items were derived from an evidence-based literature review and used a formal procedure for their selection.

									Adequate construct validity
Respiratory severity scoring (RSS-HR). (Rodriguez H. et al) [16].	[16, 68]	- Respiratory rate (0-3) - Wheezing (0-3) - Heart rate (0-3) - Accessory muscle use (0-3)	Score (0–12), with higher scores indicating more severe disease.	Previous score	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no	*Inter-rater agreement*: a perfect agreement was found between observers in the wheezing and accessory muscle scores in six of eight patients. In two patients these scores differed by one point between observers.[68]	*Construct validity*: The RSS-HR median score was higher in infants that were hospitalized vs. outpatient (8.0 vs. 4.0, p < 0.001).[16]	Not assessed	Inclusion of simple and well-categorized items readily available even in resource-limited settings), and suitable by all healthcare providers (except wheezing). Adequate construct validity and inter-rater agreement.
The modified Wood's Clinical Asthma Score (M-WCAS). (Wood DW. et al) [17].	[8, 82]	- Oxygen saturation (0-2) - Inspiratory breath sounds (0-2) - Expiratory wheezing (0-2) - Use of accessory muscles (0-2) - Mental status (0-2)	Score (0–10), with higher scores indicating greater severity of bronchiolitis. The M-WCAS includes ''mild'' categories of 0.5 points to better define the clinical response to therapy	Previous instrument	- Endorsement frequency: no - Restrictions in range: no - Comprehensiveness: no - Lack of ambiguity: no - Responsiveness: The scores of the M-WCAS in patients at admission to the PMF were significantly higher than those obtained immediately before discharge from the hospital [2.5 (1.9–3.0) vs. 1.0 (0.5–1.6), p< 0.001].[8]	*Inter-rater agreement*: Kw: 0.897 (p<0.001), 95% CI (0.699–1.000).[8] Kw: 0.831.[82]	*Criterion validity*: The scores of the M-WCAS correlated positively with the scores of the Tal score (r=. 0.761, p< 0.001).[8] *Construct validity*: The scores of the M-WCAS in patients who required subsequent admission to the PICU were significantly higher than those inpatients who required admission only to the PMF [4.5 (3.6–5.2) vs. 2.5(1.5–2.5), p<0.001].[8]	All raters qualified the M-WCAS as easy to score, and they reported that the time required to complete the score ranged from 1 to 3 min.[8]	Adequate construct validity, criterion validity, inter-rater agreement, responsiveness, and usability

a. PICU: pediatric intensive care unit

b. PMF: pediatric medical floor

c. Kw: weighted kappa

d. aROC: area under the ROC curve

e. PPV: positive predictive value

f. NPV: negative predictive value