Measuring Clinical Severity in Infants with Bronchiolitis

A thesis submitted in accordance with the requirements of the University of Liverpool for the Degree of Doctor in Philosophy.

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June 2015

Acknowledgments

I am extremely grateful to a number of people and institutions who have provided continued support and guidance, particularly over the last four years, to enable me to complete this clinical research fellowship. Firstly, I have to thank my supervisory team; Dr Paul McNamara, Dr Steven Lane and Professor Bernie Carter. They have been a constant source of encouragement and inspiration which has enabled me to develop in confidence and grow as an individual. Without their belief in my abilities I would have struggled to surmount the many challenges encountered throughout this research journey. I am grateful to Professor Janice Abbott for the help and advice received regarding psychometric theory and instrument development. I am also grateful for the clinical mentorship provided by Dr Francine Verheoff. I am extremely appreciative of Professor Matthew Peak for providing me with the opportunity to apply for this clinical research fellowship. Furthermore, as my line manager, I wish to acknowledge his endless support, guidance and mentorship over the past decade. I would also like to acknowledge the important contribution of the Children's Nursing Research Unit in promoting nursing research. The help and support provided from this unit has been invaluable. I could not have successfully completed this clinical research fellowship without the help received from the Comprehensive Local Research Network particularly from the following research nurses; Janet Clark, Caroline Burchett, Lucy Lewis, Sharon Hughes, Zena Haslam, Moira Morrision, Jo Shippey Samantha Tapscott, Natalie Rogers, Claire Jonas, Coral Smith, Julie Lynch and Kate Moscovici. I am extremely grateful to the National Institute of Health Research for giving me the opportunity to undertake this clinical research fellowship which I have whole heartedly embraced. I am sincerely grateful to all those health care professionals, parents and/or carers and infants who have participated and engaged with the research across the eleven research sites. Finally, I am overwhelmed by the continued love, support and patience shown to me from all my family and friends.

Abbreviations

AfC – Agenda for Change

ANP – Advanced Nurse Practitioner

APLS – Advance Paediatric Life Support

AVPU – Alert, Verbal, Pain, Unresponsive

BC – Bernie Carter

BPM – Breaths or Beats Per Minute

CARIFS – Canadian Acute Respiratory Infection and Flu Scale

CLD – Chronic Lung Disease

CLRN – Comprehensive Local Research Network

CHD – Congenital Heart Disease

CI – Confidence Intervals

COMET – Core Outcome Measures in Effectiveness Trials

CSI - Comprehensive Severity Index

CvM – Clare van Miert

CVS – Cardiovascular System

nCPAP – Nasal Continuous Positive Airway Pressure

COSMIN – Consensus Based Standards for the Selection of Health Measurement Instruments

CRT – Capillary Refill Time

DGH - District General Hospital

ED – Emergency Department

FDA – Food and Drugs Administration

GCS – Glasgow Coma Scale

GP – General Practitioner

HCA – Health Care Assistant

HCP – Health Care Professional

HFNC – High Flow Nasal Cannula

hMPV- Human Metapneumo Virus

HR – Hazards Ratio

HRR - Hazard Rate Ratio

ICC – Intra-class Correlation Coefficient

IRR – Incidence Rate Ratio

IV – Intravenous

JC – Julie Cummings

JSC – Janet Clark

LIBSS-PRO – Liverpool Infant Bronchiolitis Severity Score –Proxy Reported Outcome

MAU – Medical Assessment Unit

MCRN – Medicines for Children's Research Network

NHS National Health Service

NICE – National Institute for Health and Care Excellence

NIHR – National Institute of Health Research

NIV – Non-Invasive Ventilation

NG – Nasogastric

NGT – Nominal Group Technique

OR – Odds Ratio

PCR - Polymerase Chain Reaction

PBE – Previous Bronchiolitis Episode

PEG – Percutaneous Endoscopic Gastrostomy

PEWS – Paediatric Early Warning Score

PHDU – Paediatric High Dependency Unit

PICU – Paediatric Intensive Care Unit

PMH – Past Medical History

PRISM – Paediatric Risk of Mortality

RCT - Randomised Controlled Trials

RDAI – Respiratory Distress Assessment Instrument

ROC – Receiver Operating Curve

rhDNASE – Recombinant deoxyribonuclease

RV - Rhinovirus

RR – Risk Ratio

RSV - Respiratory Syncitial Virus

SD – Standard Deviation

SIGN – Scottish Intercollegiate Guidelines Network

SHO – Senior House Officer

SO – Sarah Olsen

UIM/F – Unidentified Male/Female

UK- United Kingdom

USA – United States of America

WOB – Work of Breathing

Dedication

I dedicate the work in this thesis to my two children Joseph and Holly and to all those other children who have and will be a part of my life in so many ways. I hope that I can be an inspiration to you as you have been to me. Providing the opportunity to be creative and learn is the most precious gift a parent can give their child. Knowledge provides choice, freedom and an abundance of opportunity to make a difference – go ahead and make a difference!

National Institute of Health Research Funding Statement

This report is independent research arising from a Clinical Doctoral Research Fellowship supported by the National Institute of Health Research (reference CAT CDRF 10-057). The views expressed are those of the author(s) and not necessarily those of the NHS, the National Institute of Health Research and Department of Health.

Abstract

Bronchiolitis is a viral lower respiratory tract infection of infancy and a major cause of infant morbidity. Respiratory syncytial virus is the most common cause of bronchiolitis. The majority of infants infected with bronchiolitis will have mild symptoms, lasting up to five days with the infant being successfully managed at home. However, up to 3% of all infants will be admitted to hospital for supportive therapy, such as oxygen and/ or fluids. A small proportion of these hospitalised infants (10%) will rapidly deteriorate further and require critical care admission for either invasive or non-invasive ventilation.

Many clinical trials have been undertaken to evaluate a number of pharmaceutical interventions used to treat bronchiolitis. However, no treatment intervention has been proven to be effective. A large proportion of these clinical trials used clinical severity scores as an outcome measure. These clinical severity scores had not undergone any rigorous development and validation as recommended by the Food and Drug Agency (FDA) when developing an outcome measure for clinical trials.

This thesis sets out the psychometric methods used to develop and validate the Liverpool Infant Bronchiolitis Severity Score – Proxy Reported Outcome Measure (LIBSS-PRO). The premise of the LIBSS-PRO is two-fold. Firstly, the LIBSS-PRO has been primarily developed for use in daily clinical management to identify infant improvement or deterioration. This will contribute to the standardisation of patient care and facilitate clinical decision making. Secondly, by fulfilling the FDA criteria as an outcome measure the LIBSS-PRO will improve the quality of future clinical trials of treatment interventions for bronchiolitis. The study was divided into three phases over three bronchiolitis seasons.

The first phase was concerned with the development of the LIBSS-PRO. Items were identified from the literature and through stakeholder group workshops. A conceptual framework of bronchiolitis severity was developed. Consensus methods were used to identify which items were considered the most important and to develop criteria for mild, moderate and severe bronchiolitis.

The second phase determined the content validity of the LIBSS-PRO. The LIBSS-PRO was evaluated by a range of health care professionals working in a variety of clinical environments by applying the score to eligible infants. Cognitive interviewing of health care professionals was used to assess comprehension and interpretation of each section of the LIBSS-PRO.

Finally, in phase three, clinical field testing was undertaken in a variety of clinical locations by health care professionals to establish construct and criterion validity and reliability of the LIBSS-PRO. Responsiveness to change and cross cultural validation will be assessed in future clinical trials.

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Chapter One

1 Introduction

1.1 Bronchiolitis

Bronchiolitis is a common lower respiratory tract infection and a significant cause of morbidity within the first 12 months of life (1). There is a spectrum of disease from mild lower respiratory tract symptoms to respiratory failure requiring mechanical ventilation (2). Most infants experience mild symptoms and can be successfully managed in a community setting (3). However, approximately 3% of all infants (defined as a child less than one year) are admitted to hospital with bronchiolitis, usually during the seasonal epidemic over the Christmas period in the Northern hemisphere (4, 5). Hospitalisation with bronchiolitis peaks between three and six months of life for most infants (6). Epidemiological studies show that it is a leading cause of morbidity amongst infants less than one year of age in the developed world (7-11).

1.2 Respiratory syncytial virus

Respiratory syncytial virus (RSV) is the most common cause of bronchiolitis in infants, and is the single most common cause of hospital admissions in infancy (6). In 2005, it was estimated that 33.8 (95% Confidence Intervals (CIs) 19.3-46.2) million new episodes of RSV associated respiratory infection occurred worldwide in children younger than five years with associated mortality ranging between 66, 000 – 199, 000 deaths (12). Hospitalisation rates for RSV infection have steadily increased over the past few decades

(13). About 28 per 1000 children in the United Kingdom (UK) are admitted to hospital with RSV bronchiolitis and RSV accounts for up to 45% of all hospital admissions for lower respiratory tract infections in children younger than two years of age, with inpatients tending to be younger and experiencing greater disease severity (14, 15). RSV is contagious and is thought to be spread by large droplets of secretions from an infected person, either via contamination of surfaces or hand-to-hand transfer (16). Viral replication is greatest and most prolonged in infants with viral shedding being detected in infants for up to 21 days (7). In the UK, surveillance data suggests that bronchiolitis and RSV have similar winter seasonal trends with infection rates peaking during the coldest months (November-March) (6, 17). These trends are consistent with the rest of Europe (18), although the exact timing and duration of RSV seasons vary by region and year (19). Adenovirus, bocavirus, rhinovirus (RV) and human metapneumovirus (hMPV) are all viral pathogens that also cause bronchiolitis (10, 20). A large prospective study found that infants and children can be infected with more than one virus with a co-infection rate of approximately 6% (21). Laboratory tests for viral diagnosis include viral cultures, rapid antigen detection tests, polymerase chain reaction (PCR) and measurements of acute and convalescent antibody titres (22). Establishing the causative viral pathogen can be useful with respect to the management of these infants. This information enables healthcare professionals to consider the need for isolation, cohorting and other infection control measures to limit nosocomial infection and may help to reduce the need for other costly diagnostic investigations and antibiotic use (7, 23, 24).

1.3 Diagnosis

Bronchiolitis is characterised by acute inflammation, oedema and necrosis of epithelial cells lining small airways, increased mucous production, and bronchospasm (25). The degree of airway obstruction due to mucous varies as these areas are cleared, resulting in rapidly changing clinical signs that confound an accurate assessment of the severity of illness (26). Diagnosis of bronchiolitis is not straightforward as RSV also is an important cause of croup and is responsible for a significant proportion of exacerbations of asthma in young children (27). Diagnosis is usually based on recent medical history and clinical findings on examination (22). Typical clinical features include coryza, difficulties in breathing, tachypnoea, recession, low oxygen saturations, cough, poor feeding, apnoea, irritability, low grade temperature, and on auscultation, wheeze and widespread crepitation (17, 22, 28). Although a number of these features are common to other lower respiratory tract infections for instance, bacterial infections, acute viral infections, viral induced wheeze, bronchitis and asthma (22, 27), there is currently no test available to help discriminate between bronchiolitis and these other clinically similar pathologies (22, 27).

Studies have emphasized variations in terms of diagnosis, hospital admission, hospital length of stay, treatment interventions and management worldwide for bronchiolitis (29-33). In the UK, a 15 fold variation was found for children under the age of two years for hospital admission rates and a six fold variation for mean length of hospital stay (34). It was suggested that these variations were partly due to epidemiological factors, such as, socio-economic deprivation, maternal tobacco smoking during pregnancy, household tobacco

smoking and partly due to patient management, assessment or clinical admission criteria in the emergency department (2, 30).

There is poor agreement between physicians worldwide on how to differentiate bronchiolitis from other early childhood wheezing phenotypes (27). This lack of a standard definition can impact on bronchiolitis treatment interventions and research recommendations. Definitions for bronchiolitis varied in terms of age, clinical findings and viral aetiology (35). Furthermore, if children with wheeze are enrolled into studies, it is likely that they will represent a spectrum of wheezing phenotypes with treatment response dependent on the specific phenotype (36). In the UK, bronchiolitis diagnosis tends to be restricted to the first 12 months of life to avoid misdiagnosis with early presentations of asthma and viral wheeze (17, 37).

1.4 Treatment

Despite these variations in diagnosis and management the mainstay of treatment is supportive care through nasal suction, oxygen therapy, fluid management, and in severe cases, ventilation (invasive or non-invasive (NIV)) (17, 25, 38). Due to perceived clinical similarities between asthma and bronchiolitis, treatments typical for asthma such as, inhaled bronchodilators, epinephrine, glucocorticoids and inhaled corticosteroids are often used in clinical practice to treat bronchiolitis. The effectiveness of these interventions has been assessed in clinical trials and systematic reviews. A Cochrane overview of 11 systematic reviews examined the efficacy and safety of a different bronchiolitis treatment interventions including: antibiotics, bronchodilators, chest physiotherapy, epinephrine, extra-thoracic pressure,

glucocorticoids, heliox, hypertonic saline, immunoglobulin, inhaled corticosteroids and oxygen therapy (35). The findings of this overview concluded nebulised epinephrine may be useful in outpatients to avoid hospitalisation, and nebulised 3% hypertonic saline may help reduce length of hospitalisation. Since the publication of this overview three of the included systematic reviews have been updated (39-41). Despite identifying and incorporating more recently published trials into these reviews the conclusions remain largely unchanged. Hypertonic 3% saline was found to be the only intervention to show any benefit by significantly reducing length of hospital stay, clinical scores and having no significant adverse events (41). However, a recent large randomised controlled trial (RCT) undertaken in the UK, investigating the effectiveness of 3% hypertonic saline compared with standard care, found no difference between the two arms for the primary outcome: time for being declared fit for discharge (hazard ratio (HR): 0.95, 95% confidence intervals (CIs) [0.75−1.20]) (42).

Several other Cochrane systematic reviews, not included in the aforementioned overview, found insufficient evidence for the routine use of recombinant deoxyribonuclease (rhDNase) (43), steam inhalation and humidity (44), exogenous surfactant (in mechanically ventilated infants) (45), immunoglobulins (46), nasal continuous positive airway pressure (nCPAP) (47) and high flow nasal cannula (HFNC) (48). All of these reviews concluded that further research in the form of large multi-centred RCTs is required. Finally, one systematic review and network meta-analysis demonstrated a benefit for adrenaline on clinically relevant outcomes amongst outpatients and there may

be a beneficial synergistic effect between adrenaline and dexamethasone although further research was required (49).

1.5 Outcome measures

A heterogeneous group of outcomes were used to evaluate the effectiveness of bronchiolitis treatment interventions within the aforementioned systematic reviews. These include: rate of hospital admission; length of stay (either hospital or paediatric intensive care unit (PICU)); change in clinical severity score; hospital re-admissions; need for ventilation (invasive or NIV); oxygen saturation; pulmonary markers; wheeze; adverse events (35). These outcomes were found to be inconsistently measured. For instance, admission and length of stay could be influenced by external factors, such as, individual decision making or daily volume of patient admissions as opposed to the treatment under investigation (35, 50). Clinical scores were found to be limited by their inconsistency and have unknown clinical relevance (50). The absence of standardised and validated patient important outcomes has been considered a serious threat to bronchiolitis trial validity (50).

Given the reliance on clinical judgement for referral and admission to hospital, bronchiolitis should be an ideal condition for a clinical severity scoring instrument to aid clinical decision making. However, two literature reviews undertaken as part of the development of bronchiolitis guidelines (17, 25), found neither good quality evidence of validated clinical scoring instruments in infants with acute bronchiolitis, nor any good quality studies on the effectiveness of indicators for referral from primary to secondary care, or for admission to the PICU. This was further supported by a more recent overview

of systematic reviews which highlighted the need for a validated, reliable scoring instrument that is sensitive to important clinical changes in patients with bronchiolitis (35). Furthermore, it was found that clinical trials using unpublished outcome measures were more likely to report the treatment under investigation as being more effective than the comparison group suggesting detection bias (51).

1.6 Critical appraisal of bronchiolitis scoring instruments

Prior to developing a new outcome measure, a search of the literature and critical appraisal of existing outcome measures for their measurement properties (validity, reliability and responsiveness to change) is recommended (52, 53). This has become a prerequisite due to the burgeoning number of health outcome measures used in clinical practice and research (54). However critical appraisal of existing instruments is often poorly undertaken (53).

An electronic search to identify validated, published severity scoring instruments for use in infants with bronchiolitis was undertaken in the following databases; Medline, EMBASE, CINAHL and Cochrane Library. Seven studies that developed and validated a bronchiolitis scoring instrument were identified (1, 33, 55-60). The COSMIN (Consensus Based Standards for the Selection of Health Measurement Instruments) checklist was modified and adapted for use together with the Food and Drugs Administration (FDA) criteria for the development to facilitate critical appraisal of these seven instruments (54, 61).

Of these seven studies, four developed scoring instruments for use in generic childhood respiratory conditions (56, 58, 60, 62), and three were specific for bronchiolitis (1, 33, 59). The development and validation of these

instruments were undertaken in the following countries: Canada (58, 60); United States of America (USA) (33, 55, 56); UK (1); Republic of Ireland (59). The clinical settings in which these instruments were developed included: primary care (60); emergency department (ED) (1, 63); hospital (secondary or tertiary) (33, 55, 56, 58). As can be seen, the generalisability of these instruments may be limited to certain countries and clinical settings.

Jacobs *et al* (2000) developed the Canadian Acute Respiratory Infection and Flu Scale (CARIFS) in Canada (60). This instrument was developed for use by parents at home, with children up to 12 years of age with an acute respiratory infection. This instrument consisted of 18 items, responses to which used a four point ordinal scale: 0=no problem; 1=minor problem; 2=moderate problem; 3=major problem. The score for each item is summed and interpreted as 0 (best possible health) to 54 (worst possible health). Psychometric testing was undertaken on 206 children with 65 children falling within the 0-2 year age group. RSV was isolated in 29 children. Independent assessments for mild, moderate and severe illness were undertaken by either a physician or a nurse. The CARIFS score was validated using construct validity and responsiveness to change. Construct validity was determined by comparing the CARIFS with an assessment by either a health care professional (HCP) or a parent. The CARIFS score was also compared with the Yale Observation score. The authors reported good correlation between the CARFIS and physician assessment (0.36), nurse assessment (0.44) and Yale Observation score (0.48). The CARIFS mean score changed from 28.0 (10.3) on day one to 2.5 (5.7) on day 14.

Lui *et al* (2004) developed a four item instrument respiratory score for use by HCPs with children who are diagnosed with asthma, bronchiolitis or other wheezing phenotypes (55). Each item in the instrument was answered using a scale ranging between 0 and 3 points. These were then summed together to provide an overall score total. There was no instruction provided on how to interpret the score total. Fifty-five children participated with the inter-rater reliability testing. Of these 55 children, 28 children were aged below 24 months and 17 were diagnosed with bronchiolitis. The overall agreement for the rater pairs was 84% with a weighted kappa of 0.62 (95% CIs not provided). For the age group below 24 months the agreement was 80% with a weighted kappa of 0.39 (95% CI, 0.12-0.72).

Lowell *et al* (1987) developed the Respiratory Distress Assessment Instrument (RDAI) as an outcome measure for clinical trial of nebulised epinephrine (56). The instrument was developed for use by HCPs in children below 24 months of age with a diagnosis of asthma, bronchiolitis or other wheezing phenotypes. The instrument comprised three items that were answered using a scale from 0 to 4 points with the score for each item being summed. There was no instruction on how to interpret the summed score. The results for the overall inter-rater reliability were not presented. Results for inter-rater reliability were only presented for wheezing (96% agreement; weighted kappa 0.9) and retractions (96% agreement; weighted kappa 0.64).

Marlais *et al* (2011) developed an instrument to predict hospital admission (Bronchiolitis Risk of Admission Scoring System) (1). This instrument was developed for use by HCPs in infants with a clinical diagnosis of bronchiolitis in the ED. The authors identified 29 items for inclusion from a literature review. A

logistic regression analysis was used to determine which items were significant in predicting admission. Five items were included in the final instrument. Each item was answered with either a score of 0 or 1, with the score for each item being summed. A cut-off value of three or greater indicated that the infant being assessed required admission.

Walsh *et al* (2006) developed an instrument to predict hospital admission (63). The instrument was developed for use by HCPs in children up to 18 months of age with a clinical diagnosis of bronchiolitis in the Republic of Ireland. It contained four items. Two items were answered with a dichotomous answer response: present (1) or absent (0). One item was answered by using their age in months and the final item was answered by deciding whether the infant had mild, moderate or severe dehydration. The score for each item was then multiplied with a number unique to that item then summed together. The cut-off values suggested a score less than -0.645 indicated the child had 'mild' disease, whereas a score greater than 1.866 indicated 'severe' disease. Inter-rater reliability was assessed in a cohort of children in the USA. There was good agreement for severity of illness (actual agreement, 91.3%; (kappa =0.676). (59)

Wang *et al* (1992) modified an existing scoring instrument (58). The instrument was developed for use by HCPs in children up to the age of two years of age with a clinical diagnosis of bronchiolitis or pneumonia. The finalised instrument had four items with each item being scored on a scale from 0 to 3. The score of each item was summed together. For inter-rater reliability the Kappa was 0.48 for general assessment, 0.38 for respiratory rate, 0.31 for wheeze and 0.25 for retractions.

Wilson *et al* (2000) evaluated the paediatric component of the Comprehensive Severity Index (CSI) in a group of children who had been coded with ICD-9 codes for bronchiolitis (33). This score had been modified from the adult CSI. This instrument comprised seven domains and 27 items. Each item is answered using a four point scale: level 1 through to level four. The score total was a composite of the scores for each item. There was no instruction on how to interpret the summed score. To validate the score the authors appear to have applied the instrument retrospectively to the charts of the children included in the cohort. The CSI scores were more strongly correlated than the Paediatric Risk of Mortality (PRISM) III scores (24 hours) for costs CSI (r^2 =0.23) versus PRISM III (r^2 =0.07); p<0 .0001 and length of stay CSI (r^2 = 0.23) versus PRISM III (r^2 = 0.07) p<0 .0001.

Overall, there was minimal conceptual work undertaken within the studies to identify all important domains and items relevant to bronchiolitis. Furthermore, there was limited consultation with key stakeholder groups such as, nurses, physiotherapists and parents and/or carers. Four of these instruments require the user to be able to auscultate the chest for wheeze (33, 55, 56, 63). In the UK, this requirement immediately excludes a large number of HCPs as chest auscultation is not a skill routinely taught to nurses (though, it is debatable how much auscultation actually adds to clinical severity assessment as inter-rater reliability between physicians has been proven to be poor) (64). None of the studies evaluated instrument face validity or acceptability. There was limited evidence presented to indicate that rigorous psychometric testing had been fully undertaken to establish both validity (content, construct and criterion) and reliability (61). For instance, the RDAI was developed and *"validated"* in

tandem with its use as the primary outcome measure in a randomized controlled trial investigating the use of epinephrine in infants with bronchiolitis (56). Three studies provided fair evidence of content validity testing (1, 60, 63). Two studies provided fair evidence for construct validity (1, 60) and four studies provided fair evidence for reliability testing (33, 55, 56, 63). No study undertook cognitive interviews or cross-cultural validation. No study calculated sample size or any of the psychometric tests. Similarly, information on percentage of missing data was not provided or a description of how missing items were handled **(Appendix 1)**.

1.7 Why is it important to develop and validate a bronchiolitis severity score?

There is a very real clinical need for the development of a robust clinical severity scoring instrument with broad application for infants with bronchiolitis. Assessment and early detection of changes in clinical condition would facilitate decisions such as; admission to hospital, escalation of treatment, weaning treatment and discharge. Furthermore the instrument may help to reduce the number of unplanned admissions to critical care and cardiopulmonary arrest. Integration of a clinical severity scoring instrument within current bronchiolitis care pathways would assist with the standardisation of patient care and reduce variation in clinical management. Moreover, a clear and effective gauge of clinical severity in bronchiolitis is a prerequisite for RCTs of therapeutic interventions.

1.8 Aims and objectives

This thesis seeks to describe in detail the methods used to develop and rigorously validate the Liverpool Infant Severity Score-Proxy Reported Outcome (LIBSS-PRO) Measure. The principle function of the LIBSS-PRO measure is to assess severity of illness and evaluate treatment interventions in infants up to twelve months of age with a clinical diagnosis of bronchiolitis. The LIBSS-PRO is intended for use by nursing staff in the daily care and management of these infants. However, the LIBSS-PRO has been designed in such a way that it could be used by any HCP caring for these infants, in any clinical location within secondary/tertiary care settings in the UK.

1.9 Plan of investigation

To facilitate understanding, an overview of the plan of investigation will be presented. A more detailed description of each aspect of the LIBSS-PRO development will be reported and discussed within each discrete chapter. An overview of the study methods have been published in the Journal of Advanced Practice and on-line in the Core Outcome Measures in Effectiveness Trials (COMET) Initiative database (http://www.comet-initiative.org/) (65). The methods will be covered briefly in this thesis. The development and validation of the LIBSS-PRO was undertaken in three linked phases **(Figure 1)** over a 36-month period, using a mixed methods study design.

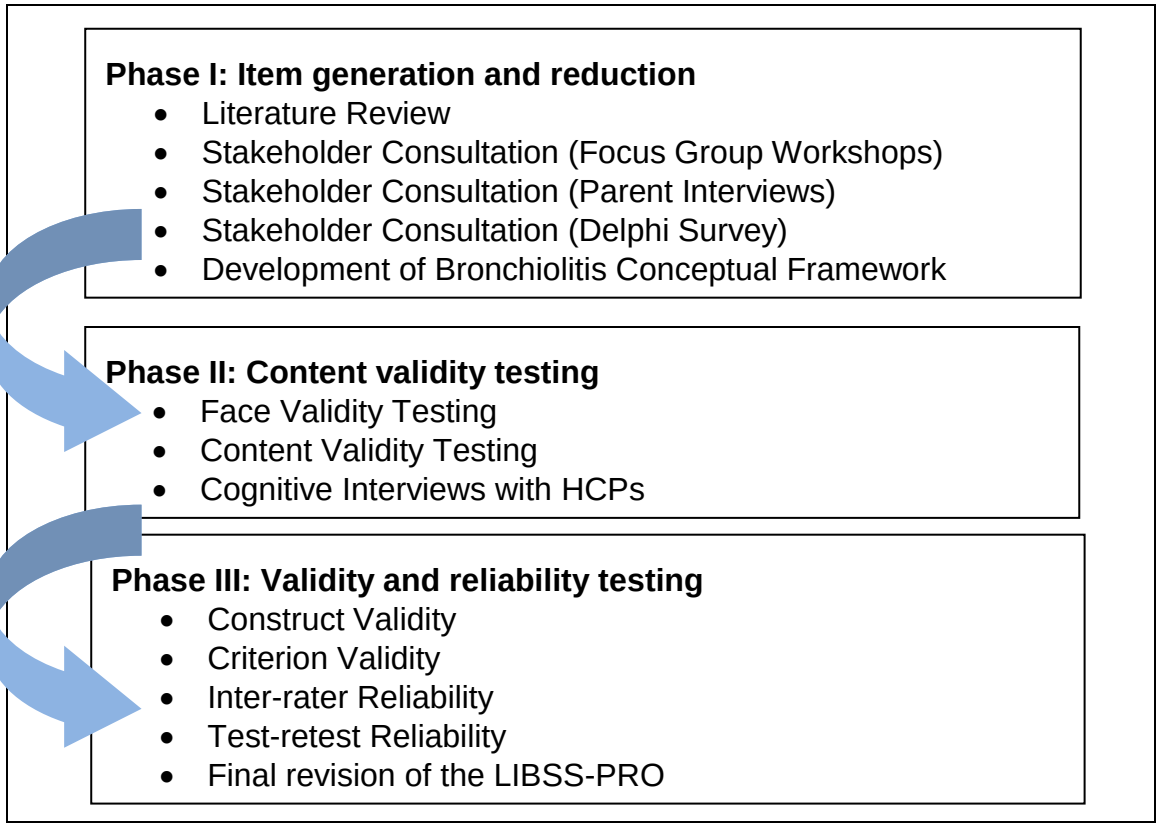


Figure 1: Study overview flow diagram

The aim of phase one was to generate a pool of domains and items for potential inclusion into the LIBSS-PRO. These domains and items were identified using *top-down* (literature review) and *bottom-up* (stakeholder consultation) approaches (Chapters 2-5). The Delphi survey of HCPs provided expert consensus over which of the identified items should be included in the LIBSS-PRO and which items were redundant (Chapter 6). A conceptual framework of bronchiolitis severity was formed based on the agreed domains and items. This framework was used to develop the LIBSS-PRO.

The purpose of phase two was to assess the content validity of the LIBSS-PRO within the clinical environment. The LIBSS-PRO was applied to infants with bronchiolitis. Included domains and items were assessed for relevance. The domains and items were also assessed to ensure they covered the

concept of bronchiolitis severity. In addition to this, response burden and acceptability was assessed and redundant items identified (Chapter 7). Cognitive interviews were used to assess comprehension and identify issues with answer responses (Chapter 8).

Finally, phase three was concerned with developing cut-off values to determine ‘mild’, ‘moderate’ and ‘severe’ bronchiolitis (construct validity), with examining the agreement between the LIBSS-PRO and a clinically agreed reference standard (criterion validity), and with assessing LIBSS-PRO score agreement between HCP dyads at two different time points (reliability) (Chapter 9). As with phase two, response burden and acceptability were also assessed. Items which performed poorly in field-testing were considered for removal. Following field-testing, the LIBSS-PRO was further revised ready for final validation (responsiveness to change and cross-cultural validity) in a future RCT.

The study protocol was reviewed and approved by the National Health Service (NHS) National Research Ethics Service, January 2011 (10/H1002/76). The study was funded through a National Institute of Health Research (NIHR) Clinical Academic Training Doctoral Fellowship CAT CDRF 10-057).

Chapter Two

2 Literature review

A preliminary step in devising items for a new scoring instrument is to examine those used in previously developed scoring instruments (52). In this chapter the literature review methods used to identify signs, symptoms and risk factors of bronchiolitis are described, and a narrative synthesis of the results, with a particular focus on risk factors, have been presented.

2.1 Aims

Phase one aimed to identify signs, symptoms and risk factors of bronchiolitis to be considered for inclusion into a bronchiolitis severity score.

2.2 Methods

2.2.1 Criteria for considering studies for this review

2.2.1.1 Types of studies

Guidelines, RCTs, systematic reviews of observational studies and observational studies (cohort or case control), specifically investigating bronchiolitis, were included.

2.2.1.2 Types of participant

Studies that included infants up to the age of 12 months with a clinical diagnosis of bronchiolitis were eligible for inclusion. Bronchiolitis was defined using the SIGN (2006) criteria, i.e. *an infant with nasal discharge and a wheezy cough, in the presence of fine inspiratory crackles and/ or high pitched expiratory wheeze, with or without apnoea* (17).

2.2.1.3 Exclusion criteria

Studies were excluded if they:

- Were not published in English
- Included animal subjects
- Did not present bronchiolitis data separately from other lower respiratory tract infections
- Comprised reviews, letters, commentary or case reports

2.2.2 Search methods for identifying studies

Studies were identified through searching the following databases: Cochrane Central Register of Clinical Trials (CENTRAL) (The Cochrane Library 2015, Issue 9); OvidSP MEDLINE (2000 to January 2015); OvidSP EMBASE (2000 to January 2015) and NHS Evidence CINAHL (2000 to January 2015). The search was initially undertaken in January 2011 and was updated in January 2015. All index terms were exploded. Due to the volume of research published, the electronic search for observational studies examining risk factors for severe bronchiolitis and signs and symptoms was restricted by date: year 2000 to 2015. However, there was no date restriction imposed on published or unpublished clinical scores used to assess severity of illness in bronchiolitis. The search strategy used can be found in **Appendix 2**.

2.2.3 Selection of studies

All the titles and abstracts from the search results were scrutinized against the inclusion criteria described above to identify potentially eligible studies from

the search. Full publications were obtained for those studies that appeared to meet the inclusion criteria.

2.2.4 Data extraction and management

The following data were extracted from the included studies and tabulated: first author, reference, country, population, sample size, exposure, outcomes, signs, symptoms, risk factors and outcome measure effect estimates. Data were also extracted on how bronchiolitis severity was defined and measured. A quality assessment was not undertaken and was considered unnecessary due to individual study outcomes not being included in a statistical synthesis. A narrative synthesis was used to summarise the results of the included studies in this review.

2.3 Results

2.3.1 Signs and symptoms for bronchiolitis

One hundred and ninety six bronchiolitis signs and symptoms were extracted from guidelines, observational studies and from existing scoring instruments (published and unpublished) **(Appendix 3)**. The included scoring instruments comprised generic respiratory scores and asthma scores as well as bronchiolitis scores. All of these instruments had been used as outcome measures within bronchiolitis research.

2.3.2 Risk factors for bronchiolitis

The yield from the electronic database search was 2,887 studies. 2,779 studies were excluded due to overlap between databases or did not fulfil the

review inclusion criteria. A full publication was obtained for 108 studies. Following further scrutiny, an additional 58 studies were excluded, as they did not meet the inclusion criteria. Fifty studies with a sum total of 166,4938 participants were included in this review **(Figure 2)**.

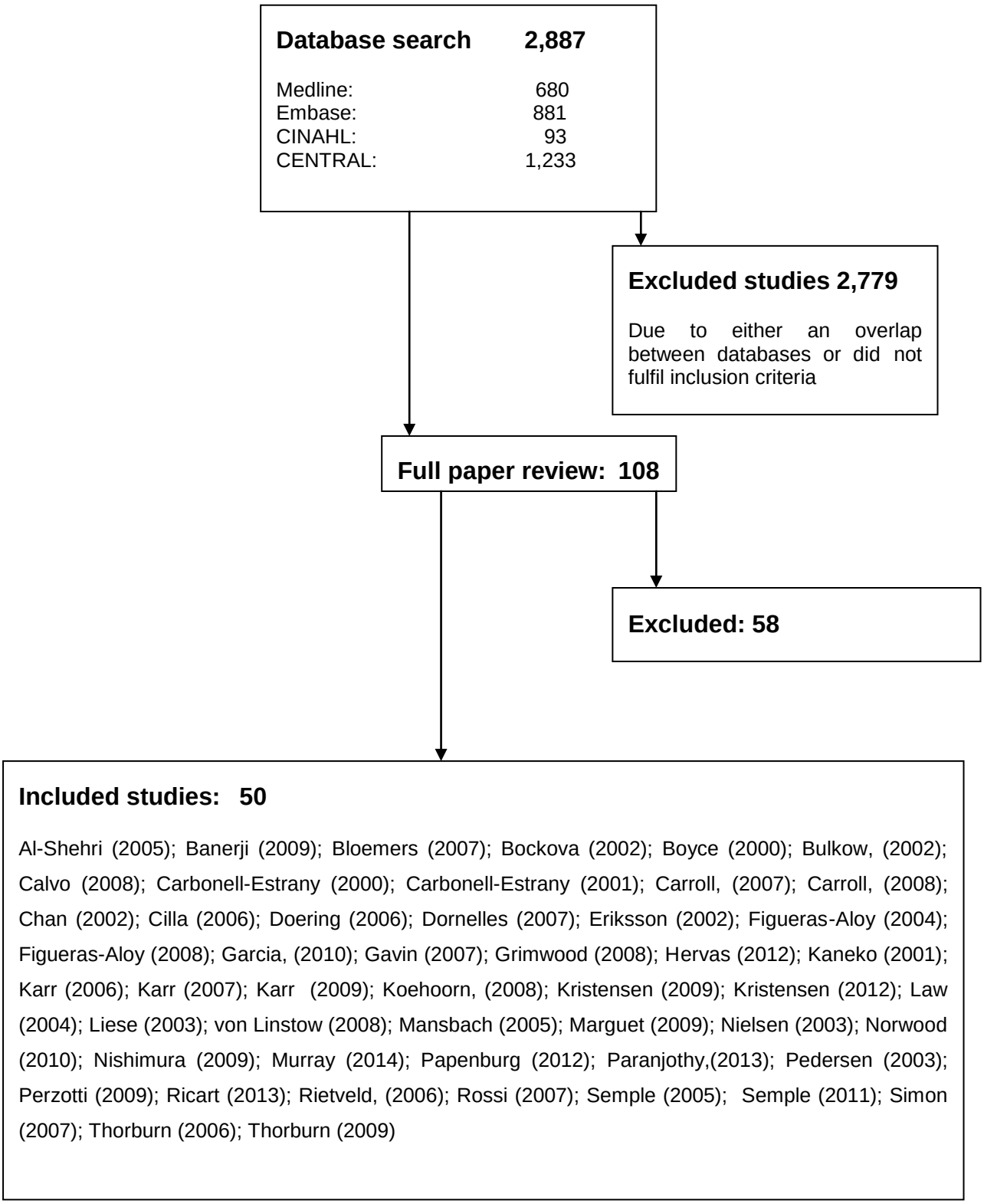


Figure 2: Search flow diagram

The included studies were undertaken in the following countries: Brazil (66); Canada (67-70); Denmark (71-75); France (76); Germany(77-79); Italy (80, 81); Japan (82); Malaysia(83); Netherlands (84, 85); New Zealand (86); Saudi Arabia (87); Spain(88-93); Sweden (94); UK (2, 95-99); and USA (38, 100-110).

2.3.3 Participants

Seven studies included otherwise healthy full term infants (38, 66, 73, 76, 103, 104, 111). Eleven studies included only infants born pre-term (69, 75, 77-80, 89, 90, 92, 93, 106). One study included infants born with Downs' Syndrome (84). One study included infants born with congenital heart disease (71). Thirty studies included infants with or without any co-morbidity (2, 30, 68, 70, 72, 74, 81, 82, 86, 94-99, 105, 107-110, 112-114). Three studies only included infants from particular ethnic communities: Inuit (67); Navajo and White Mountain Apache (100); and Alaskan Native (102).

2.3.4 Outcomes for severe bronchiolitis

The outcomes reported within these studies included: hospital admission (38, 67-73, 75, 77, 78, 80-82, 84-87, 89, 91-96, 100-104, 106-112, 115); duration of supplemental oxygen (66); supplemental oxygen requirement (91, 105, 111); clinic visit (103); emergency department visit (103, 110); PICU requirement (99, 105, 112); mechanical ventilation (79, 97, 105); hospital length of stay (70, 76, 88, 105); clinical severity score (70, 113); apnoea (79); death (79, 98); fever (88); hypoxia (116); and respiratory failure (116).

2.3.5 Risk factors for severe bronchiolitis

The following 23 risk factors for severe bronchiolitis were identified from fifty observational studies: atopy (69, 81, 87, 92, 104); chronic lung disease (CLD) (72, 75, 78, 80, 85, 87, 89, 94, 95, 101, 105, 113, 117); congenital heart disease (CHD) (71, 72, 79, 80, 82, 87, 91, 95, 99, 101, 105, 112, 113); day-care attendance (69, 81, 92, 93); Downs' Syndrome (71, 72, 84, 95, 105); environmental air pollution (107-109); ethnicity (38, 67, 86, 101, 104, 105, 110); gender (38, 68, 69, 71, 75, 77, 78, 80, 85, 86, 91, 96, 99-101, 104, 106, 110, 112); immunodeficiency (95); infection (viral or bacterial) (70, 76, 88, 97-99, 105); low birth weight (2, 68, 74, 79-81, 85, 91, 104, 106); month of birth (38, 69, 73, 86, 91, 96, 106); neuromuscular disorders (72, 95, 105); non-breast fed (66-68, 70, 73, 81, 87, 92, 93, 96, 102, 111); overcrowding (67, 69, 92, 102); parental age (68, 80, 91, 96, 104); parental education (68, 80, 92, 101, 104); prematurity (2, 70, 71, 73, 74, 79-81, 83, 85-87, 89-91, 95, 96, 99-101, 105, 110, 112, 113); previous episode of bronchiolitis (81, 110); siblings (68-70, 78, 81, 86, 89, 92, 93, 104, 106); residence (68, 91, 101, 104); tobacco smoke exposure (2, 67-69, 73, 81, 86, 87, 90, 92, 93, 96, 101, 103, 104, 106); young age (70, 80, 81, 87, 89, 90, 92, 93, 99, 100, 110). Outcome data from all of these studies were extracted for each risk factor and tabulated.

2.3.5.1 Atopy

Five studies, (69, 81, 87, 92, 103) with a sum total of 106,665 participants examined atopy as a risk factor for bronchiolitis **(Appendix 4)**. One study found maternal asthma increased the risk of hospital admission for an otherwise healthy infant with RSV positive bronchiolitis (Odds Ratio (OR): 1.45,

95% CIs [1.33–1.59]) (104). Conversely, another study did not find having an atopic parent significantly increased hospital admission (87). However, this study did find a significant increase in hospital admissions if there was an atopic child in the family (OR: 4.75, 95% CIs [3.98-5.16]) (87). There was also an increase in hospital admissions for pre-term infants with a family history of wheezing (OR: 1.83, 95% CIs [1.21–2.77]) or eczema (OR: 1.68, 95% CIs [1.08–2.63]) (92). Two studies found no significant difference in hospital admission for either eczema or a family history of allergy (69, 81).

2.3.5.2 Chronic lung disease (CLD)

Thirteen studies (72, 75, 78-80, 85, 87, 89, 94, 95, 101, 105, 113) with 706,702 participants examined the effects of CLD as a risk factor for severe bronchiolitis **(Appendix 5)**. Seven studies found an increased risk of hospital admission for those infants with CLD of prematurity (72, 78, 87, 89, 94, 95, 101). It was also found that CLD of prematurity also significantly increased the risk of supplemental oxygen requirement (OR: 1.88, 95% CIs [1.32–2.67]); PICU admission (OR: 1.80, 95% CIs [1.12–2.89]); length of hospital stay (OR: 1.47, 95% CIs [1.30–1.67]); apnoea (OR: 4.53, 95% CIs [2.19-8.92]); death (OR: 19.60, 95% CIs [2.96-104.3]) (79, 105); and clinical severity score (OR: 7.2, 95% CIs [1.2–43.3]) (113). However, two studies failed to demonstrate that CLD of prematurity increased the risk of intubation or mechanical ventilation (79, 105).

Two studies suggested that cystic fibrosis (CF) was a risk factor for hospital admission (72, 95).

2.3.5.3 Congenital heart disease (CHD)

Thirteen studies with 704,994 participants examined the relationship between CHD and severe bronchiolitis **(Appendix 6)** (71 72, 79, 80, 82, 87, 91, 95, 99, 101, 105, 112, 113). Five studies indicated that CHD was a significant risk factor for hospital admission, (71, 72, 80, 95, 101) but two studies did not (87, 112). CHD was also found to increase hospital length of stay; clinical severity scores (105, 113); supplemental oxygen (91, 105); PICU admission (79, 112); mechanical ventilation (OR: 2.77, 95% CIs [1.89-4.05]) (105) and mortality (RR: 2.98, 95% CIs [2.16-4.12]) (99).

2.3.5.4 Day care attendance

Four studies with a total of 8,270 participants investigated day care attendance as a risk factor for severe bronchiolitis **(Appendix 7)** (81, 92, 93, 118). Two studies found that day care attendance increased hospital admission, (69, 81) whilst two studies did not detect a difference (92, 93).

2.3.5.5 Down's syndrome

Five studies with a total of 694,235 participants investigated Down's syndrome as a risk factor for severe bronchiolitis **(Appendix 8)** (71, 72, 84, 95, 105). Four studies demonstrated an increased risk of hospital admission (71, 72, 84, 95). Furthermore, one study found a significant increase in supplemental oxygen requirement (OR: 2.32, 95% CIs [1.27–4.21]) (105).

2.3.5.6 Environmental air pollution

Three studies examined the effect of air pollution on bronchiolitis **(Appendix 9)** (107-109). It was unclear as to whether these three studies were presenting

data from the same study or for three individual studies. Therefore the number of participants for each study has not been summed. One study found an increased risk of hospital admission with an increase in fine particulate matter (Sub-chronic: OR: 1.09, 95% CIs [1.04-1.14]; Chronic: OR: 1.09, 95% CIs [1.04-1.14]) (107). One study found no significant increase in hospital admissions with increased ambient air pollution (108). One study found no significant association between bronchiolitis hospital admissions and distance between household residence and main transportation routes (109).

2.3.5.7 Ethnicity

Seven studies with over 112,582 participants investigated the role of ethnicity as a risk factor for severe bronchiolitis **(Appendix 10)** (38, 67, 86, 101, 104, 105, 110). One study did not provide data on the number of included participants (38). Infants who were of full Inuit ethnicity had an increased risk of hospital admission (OR: 3.77, 95% CIs [1.12-12.75]) (67). Caucasian infants were found to have an increased risk of hospital admission (Incidence Rate Ratio (IRR): 1.3, 95% CIs [1.2-1.4]) (101). One study found no increased risk of hospital admission for black (OR: 0.66, 95% CIs [0.61–0.71]) or Latino (OR: 0.87, 95% CIs [0.67–1.13]) infants (104). There was an increased risk of hospital admission for infants who were Maori (RR: 3.64, 95% CIs [2.27–5.85]), Pacific island (RR: 3.60, 95% CIs [2.14–6.06]) or of ‘other’ ethnicity (RR: 1.09, 95% CIs [0.52–2.25]) (86). There was a reduced requirement for supplemental oxygen in black infants (OR: 0.49, 95% CIs [0.41–0.60]) (105). There was an increased intubation requirement for Hispanic infants (OR: 2.17, 95% CIs [1.32–3.58]) (105). For those infants with an unspecified ethnicity

there was an increase in intubation requirement (OR: 2.37, 95% CIs [1.06–5.29])) and PICU admission (OR: 1.59, 95% CIs [1.03–2.44]) (105).

2.3.5.8 Gender

Twenty studies with over 449,637 participants examined gender as a risk factor for severe bronchiolitis **(Appendix 11)** (38, 68, 69, 71, 75, 77, 78, 80, 85, 86, 91, 96, 99-101, 104, 105, 110, 112). One study did not provide data on the number of included participants (38). Nine studies found male gender to be a significant risk factor for hospital admission (68, 69, 77, 78, 80, 85, 101, 104, 110). One study found male gender reduced hospital admission (OR: 0.68, 95% CIs [0.51-0.91]) (105), whilst another study found a reduction in hospital admissions for female infants (HR: 0.77, 95% CIs [0.75–0.80]) (96). There was a reduction in supplemental oxygen requirement in male infants (OR: 0.80, 95% CIs [0.71–0.91]) (105). There was an increase in unscheduled ED visits for male infants (OR: 1.7 95% CIs [1.1-2.5]) (110). Although it was found that male infants did not have an increased risk of mortality (RR: 1.02, 95% CIs [0.75-1.4]) (99).

2.3.5.9 Immunodeficiency

One study with a total of 296,618 participants found no increased risk of hospital admission for bronchiolitis, in infants who had immunodeficiency (RR: 1.69 95% CIs [0.80 to 3.58]) **(Appendix 12)** (95).

2.3.5.10 Infection (viral and bacterial)

Seven studies with 7,020 participants investigated the effect of viral and bacterial infections on bronchiolitis severity **(Appendix 13)** (70, 76, 88, 97-99,

105). The viruses isolated within these studies included: adenovirus (88); RV (76, 88); hMPV (76, 88); influenza A (88); influenza C (88); parainfluenza (88); enterovirus (88); coronavirus (88); cytomegalovirus (88); RSV (70, 76, 88, 97-99, 105).

Two studies compared infants with RSV to infants without RSV (70, 105). Both studies found that RSV infection significantly increased hospital length of stay (70, 105). Furthermore, it was found that RSV increased clinical severity score (RR: 4.04, 95% CIs [1.32–12.31]) (70); supplemental oxygen requirements (OR: 1.60, 95% CIs [1.40–1.82]) (105); and PICU admission (OR: 1.57, 95% CIs [1.25–1.98]) (105). One study compared infants infected with RSV to infants infected with either RV, hMPV or both (76). There was a reduction in length of hospital stay for those infants infected with RV (OR 0.13, 95% CIs [0.03-0.57]) and hMPV (OR: 0.09, 95% CIs [0.01-0.69]) (76). Two studies compared infants with RSV to infants with RSV plus a viral co-infection (76, 88). One study found those infants with a co-infection had an increased hospital length of stay (OR: 1.12, 95% CIs [1.0-1.23]) (88). Conversely, one study found a reduction in length of stay in the co-infected group (OR: 0.26, 95% CIs [0.09-0.76]) (76). Viral co-infections were also associated with increased fever (OR 2.36, 95% CIs [1.35–4.12]) and increased antibiotic therapy (OR: 2.3, 95% CIs [1.05–2.27]) (88). Finally, two studies did not detect a significant result for either PICU admission (99) or death (98) for those infants with RSV and a bacterial co-infection.

2.3.5.11 Low birth weight

Ten studies with 122,604 participants investigated low birth weight as a risk factor for severe bronchiolitis **(Appendix 14)** (2, 68, 74, 79-81, 85, 91, 104, 106). Six studies found that infants born with a birth weight below 3.0kg was a significant risk factor for hospital admission (68, 74, 80, 81, 85, 91). One study found that low birth weight did not increase the need for supplemental oxygen (OR: 0.94, 95% CIs [0.83-1.06]) or mechanical ventilation (OR: 0.48, 95% CIs [0.36-0.64]) (2). Another study found an increase in apnoea (OR: 3.73, 95% CIs [2.28 to 5.96]) and mortality (OR: 11.34, 95% CIs [2.09 to 61.65]) (79).

2.3.5.12 Month/ season of birth

Seven studies with over 323,258 participants investigated month or season of birth as a risk factor for severe bronchiolitis **(Appendix 15)** (38, 69, 73, 86, 91, 96, 106). One study did not provide data on number of participants (38).Six studies were undertaken in the northern hemisphere (38, 69, 73, 91, 96, 106). One study found increased hospital admissions for those infants born in the months November, December and January (OR: 4.88, 95% CIs [2.57-9.29]) (69). Another study found hospital admissions were higher for those infants born in April and June (HR: 1.05, 95% CIs [1.03–1.08]), July and September (HR: 1.19, 95% CIs [1.17–1.22]) and October and December (HR: 1.22, 95% CIs [1.19–1.25]) compared with infants born between January and March.(96) One study found increased hospital admissions for those infants born between July to November (OR: 3.00 95% CIs [1.86-4.84]). None of the remaining three studies reached statistical significance. (38, 73, 91) One study was undertaken in the southern hemisphere (New Zealand) and found an increase in hospital

admissions for babies born between February and July (OR: 1.23 95% CIs [0.97-1.56]) (86).

2.3.5.13 Neuromuscular disorders

Three studies with 692,886 participants investigated neuromuscular disorders as a risk factor for severe bronchiolitis **(Appendix 16)** (72, 95, 105). Two found an increased risk of hospital admission for those infants with a neuromuscular disorder (72, 95). One study found an increased risk of PICU admission (OR: 2.79, 95% CIs [1.43–5.46]) and length of stay in (OR: 1.69, 95% CIs [1.42–2.02]) (105).

2.3.5.14 Breast feeding

Twelve studies with more than 329,153 participants examined the relationship between breast feeding and severe bronchiolitis **(Appendix 17)** (66-68, 70, 73, 81, 87, 92, 93, 96, 102, 111). Two studies found non-breast fed infants had a significantly increased risk of hospital admission (67, 87). Furthermore, another study found an elevated risk of hospital admission for those infants whose mothers did not initiate breastfeeding in hospital (hazard rate ratio (HRR): 1.33, 95% CIs [1.14–1.54]) (68). Six studies found a reduced risk of hospital admission in infants and children who had been breast fed (70, 73, 81, 92, 96, 102). Conversely, three studies found no difference in rates of hospital admission (87, 93, 111). Three studies examined the effect of breast feeding duration had on hospital admission (81, 92, 93). Only one study demonstrated a statistically significant difference which indicated infants who had breast fed for less than two months were more likely to have a hospital admission than those who breast fed for greater than two months (OR: 3.26,

95% CIs [1.96 to 5.42]) (92). One study found that for each month of exclusive breastfeeding, infants had an 11 hour reduction in oxygen use when admitted to hospital with bronchiolitis (p=0.011) (66). One study observed a significant reduction in oxygen requirement in fully (OR: 0.25, 95% CIs [0.07-0.89]) and partially (OR: 0.61, 95% CIs [0.20-1.87]) breast fed infants (111).

2.3.5.15 Overcrowding

Five studies with 8,586 participants investigated overcrowding as a risk factor for severe bronchiolitis **(Appendix 18)** (67, 69, 92, 93, 102). Three found overcrowding to be a significant risk factor for hospital admission (67, 92, 102).

2.3.5.16 Parental age

Five studies with 426,635 participants investigate parental age as a risk factor for severe bronchiolitis **(Appendix 19)** (68, 80, 91, 96, 104). Four studies found an increased risk of hospital admission for infants whose parents were aged below 25 years of age (68, 91, 96, 104).

2.3.5.17 Parent education

Five studies with 111,778 participants investigated parent education as a risk factor for severe bronchiolitis **(Appendix 20)** (68, 80, 92, 101, 104). Three studies found a significantly increased risk of hospital admission for those infants whose mothers had less than 12 years education (92, 101, 104). One study investigated the risk of hospital admission associated with maternal educational quartiles based on census data: high (greater than 44% of neighbourhood residents with postsecondary education); medium high (36% to 44%); medium low (28% to 36%); and low (less than 28%) (68).There was an

increased hospital admission risk for three education quartiles: medium high (OR: 1.25, 95% CIs [1.08–1.46]); medium- low (OR: 1.41, 95% CIs [1.22–1.64]); low (OR: 1.78, 95% CIs (1.55–2.06)) (68). One study observed significantly higher incidence rates of hospital admission for children born to mothers with less than eight years education when compared to those with greater than eight years education (p = 0.02) (80).

2.3.5.18 Prematurity

Twenty-four studies with in excess of 648,402 participants examined prematurity as a risk factor for severe bronchiolitis **(Appendix 21)** (2, 70, 71, 73, 74, 79-81, 83, 85-87, 89-91, 95, 96, 99-101, 105, 110, 112, 113). Eleven studies found that those infants born before 37 weeks gestation were at increased risk of hospital admission (74, 80, 81, 85-87, 91, 95, 96, 100, 101). A further study also found an increased risk of hospital admission (OR: 3.44 95% CIs [2.27-4.33]) but did not provide a definition of prematurity (87). Prematurity was also found to be a risk factor for supplemental oxygen requirement (OR: 1.36, 95% CIs [1.17–1.59]) (105); increased hospital length of stay (OR: 1.16, 95% CIs [1.11–1.22]) (105); PICU admission (79, 105, 112); mechanical ventilation (2, 105); and increased clinical severity scores (70, 113). One study did not find prematurity was a risk factor for increased unscheduled ED visits (OR: 1.6, 95% CIs [0.8-3.2]) (110).

2.3.5.19 Previous episode of bronchiolitis

Two studies with 1,159 participants examined whether having a previous episode of bronchiolitis as a risk factor for severe bronchiolitis **(Appendix 22)** (81, 110). Having a previous episode of bronchiolitis was found to increase

hospital admission (OR: 1.85, 95% CIs [1.02-3.36]) (81) and unscheduled ED visits (OR: 1.7, 95% CIs [1.1-2.8]) (110).

2.3.5.20 Siblings

Eleven studies with 117,569 participants investigated siblings as risk factor for severe bronchiolitis **(Appendix 23)** (68-70, 78, 81, 86, 89, 92-94, 104). Nine studies found that having one or more siblings significantly increased hospital admission (68, 69, 78, 81, 89, 92-94, 104). Multiple births did not significantly increase hospital admissions (70, 86).

2.3.5.21 Tobacco smoke exposure

Sixteen studies with 541,384 participants examined the effect of exposure to household tobacco smoke as a risk factor for severe bronchiolitis **(Appendix 24)** (2, 67-69, 73, 81, 86, 87, 90, 92, 93, 96, 101, 103, 104, 106). Eleven studies found that household tobacco smoke exposure significantly increased hospital admissions (67, 68, 73, 87, 90, 92, 93, 96, 101, 103, 104). One study found a significant increase in clinic visits (OR: 1.06, 95% CIs [1.01–1.12]) and ED visits (OR: 1.22, 95% CIs [1.13–1.31]) (103). Another study found an increase in supplemental oxygen requirement (OR: 2.23, 95% CIs [1.21-4.10]) and mechanical ventilation (OR: 2.23, 95% CIs [1.21- 4.10]) (2).

2.3.5.22 Residence (suburban or rural)

Four studies with 109,168 participants examined the impact place of residence had on severe bronchiolitis **(Appendix 25)** (68, 91, 101, 104). Three studies found living in a rural residence significantly increased hospital admission (91, 101, 104). Whereas one study found living in a rural residence

did not significantly impact on hospital admissions (68). In addition, two studies found living in a suburban residence also significantly increased hospital admissions (91, 104).

2.3.5.23 Young age (less than 12 months)

Eleven studies with 14,655 participants investigated whether young age (less than 12 months) was a risk factor for severe disease **(Appendix 26)** (70, 80, 81, 87, 89, 90, 92, 93, 99, 100, 110). Seven studies found infants below the age of 12 months were at increased risk of hospital admission (70, 80, 81, 87, 92, 93, 100). Whilst one study found hospital admissions reduced with increasing gestational age (OR: 0.85, 95% CIs [0.72-0.99]) (89). There was an increase in unscheduled ED visits for infants less than two months of age (OR: 2.1, 95% CIs [1.1-4.3]) (110). Mortality increased for infants less than six weeks of age (RR: 2.98, 95% CIs [2.16-4.12]) (99).

2.4 Conclusion

In summary, 196 signs and symptoms and 23 risk factors were identified from the literature to be considered for inclusion as items into a bronchiolitis severity score. To date, there is no published comprehensive review that has summarised all the risk factors for severe bronchiolitis. Considerable heterogeneity was observed amongst the included studies in terms of geographical location, bronchiolitis definition, outcomes, and how outcomes were measured. Therefore it is questionable as to whether all the results of all these studies could be generalisable to a UK bronchiolitis population. The strengths of this review include pre-defining inclusion/exclusion criteria, and the rigorous methods used to search and identify studies for inclusion from

electronic databases. Despite this, there were a number of methodological limitations. The search was restricted by English language and date. Furthermore unpublished studies were not sought. These restrictions may have introduced publication bias and important studies may have been excluded. To reduce bias it is recommended to have two researchers independently assess studies for inclusion, extract data using a specifically developed data extraction sheet and appraise the quality of each included study (119). A meta-analysis to provide a pooled estimate for each of the risk factors was not undertaken either. This literature review was chosen to be pragmatic at the expense of using a more robust systematic review methodology. The reason for this was that undertaking a systematic review is time consuming and would have been difficult to complete within the allocated time. Critical time points for completion of the review were imposed to prevent the next stage of the study being delayed. Any delays with completion would have had a knock on effect with the rest of the study. It was crucial that delays in the development of the LIBSS-PRO were not incurred due to the number of discrete research projects planned within the overall study and more importantly with bronchiolitis being a seasonal condition.

Chapter Three

3 Family stakeholder group workshop

Parents (including carers or legal guardians) of infants with bronchiolitis can offer a unique insight into the condition and therefore their perspectives should not be overlooked as a source of items for a potential severity score. Parents can facilitate with item wording, suggest general themes, evaluate completeness of item coverage and perform initial assessment of clarity and readability (52, 61). This chapter outlines a stakeholder group workshop with parents using nominal group technique (NGT) to elicit signs, symptoms, important outcomes and potential items. Focus groups enable data to be collected on ideas, attitudes, understandings and perceptions from a target population (120). Unique data are generated from dynamic group interactions which may not be achieved through other data collection methods, such as one-to-one interviewing (120, 121). The purpose of using NGT was to achieve a degree of consensus as to which domains or items should be included in the LIBSS-PRO. NGT uses democratic methods allowing all ideas to be presented and discussed before facilitating consensus prioritisation (122).

3.1 Aims

The aims of the family stakeholder group workshop were to:

i) To identify signs and symptoms of bronchiolitis for potential inclusion as items in a bronchiolitis severity score.

ii) To identify outcomes important to parents

3.2 Sample and setting

Recruitment for the family stakeholder group workshop took place during February 2011. Participants were identified from four hospitals sites (one paediatric tertiary centre and three district general hospitals (DGH)) through the Cheshire and Merseyside Comprehensive Local Research Network (CLRN). Workshop participants were parents (including carers or legal guardians) of an eligible infant who had been recently discharged from hospital (within two weeks) with a clinical diagnosis of bronchiolitis. A purposive sample frame was devised **(Appendix 27)** to ensure representation of individuals with a wide range of personal experience. Families of eligible infants were stratified by their infant's age, gender and severity of illness. CLRN research nurses initially approached parents with information on the workshop event during the infant's hospital stay. Parents who expressed an interest in participating were contacted via telephone by Clare van Miert (CvM) and provided with further verbal and written information about the workshop event. The workshop was planned for approximately two weeks following hospital discharge to reduce the possibility of recall bias. It was held at a local family friendly attraction (Blue Planet Aquarium) in the North West of England. Crèche and play facilities were provided for infants and siblings. To facilitate family participation, travel expenses were reimbursed and each family was provided with an entry ticket for the aquarium and a £20 shopping voucher as per INVOLVE guidance (123).

3.3 Informed consent

Written and verbal information was provided to parents prior to attending the workshop and again on the day of the workshop. Written informed consent was obtained from all participating parents on the day of the workshop.

3.4 Methods

Two researchers (CvM & Bernie Carter (BC)), trained in qualitative research methods, facilitated the workshop. Two research nurses (Janet Clark (JSC) & Julie Cummings (JC)) and a research administrator (Sarah Olsen (SO)) provided additional support. Informed written consent was obtained from all participants prior to the start of the workshop. CvM provided a brief introduction to the workshop and to outline the research aims and workshop schedule. The workshop lasted approximately three hours and was digitally audio recorded (Tascam DR-100). The recordings were transcribed verbatim and anonymised for analysis (CvM). JSC, JC & SO acted as observers throughout the workshop and recorded handwritten notes. These notes were used to document salient points made during the workshop, non-verbal communication/behaviour, issues which created tensions and the group dynamics. Spatial maps of the room layout and where participants and researchers were located were also included within the notes.

At the beginning of the workshop the first NGT question **(Table 1)** was posed to the parents. Each parent was asked to silently reflect on the signs and symptoms their infant had displayed and which ones had given them cause for concern. This period of individual reflection was shortly followed by a

round-robin exercise whereby each parent was asked to share a sign or symptom to the group. This exercise continued around the group until no further new signs or symptoms were identified. All identified signs and symptoms were recorded on flip-charts. The group then discussed each of these signs and symptoms to clarify meaning, and to rationalise and condense similar signs and symptoms. Parents were then asked to group related signs and symptoms together, categorise them under an overarching heading (domain) and develop a statement(s) for each domain. Finally, parents were asked to rank each of the statements in order of importance. This process was repeated for the second NGT question which aimed to identify improving signs and symptoms. The rationale for identifying signs and symptoms of deterioration (question 1) and improvement (question 2) in infants with bronchiolitis was to ensure that the finished scoring instrument was responsive to change in clinical condition.

The final NGT question was used to explore parental experiences of their infant having bronchiolitis. The structured NGT process that was used to elicit answers for the first two questions (individual silent reflection and sharing) was not used for final NGT question. Instead parents were asked to freely describe their experiences: the researcher's followed their responses up by using additional probing questions.

Table 1: NGT Questions (family stakeholder group workshop)

NGT Question 1: What prompted you to seek medical help when your baby became unwell? NGT Question 2: How did you know when your baby was improving? NGT Question 3: What could have improved your experience of having a baby with bronchiolitis?

3.5 Analysis

All audio-recorded discussions were transcribed by CvM. The NGT ranking process by the participants within the group provided an initial form of data analysis. CvM analysed the other data sources derived from the workshop. These data sources included the audio-recorded discussions that had taken place. The lists of words and phrases written down by the parents, words and phrases recorded on flip charts, and field-notes made by the observers during the workshop, and those made by CvM and BC, were also analysed. The workshop transcript and these extra data sources were examined iteratively several times during the course of the analysis. Initial examination of the collected data was used to obtain an overview of the data and to record any general impressions, key ideas, themes and concepts arising from the content. Following on from this a descriptive thematic analysis was undertaken (124). This process involved manually coding the raw data then collapsing the coded data under broader themes. Codes and themes were inductively derived from the data. As new codes emerged, these were applied iteratively to the whole data set in subsequent examinations of the data sources until no new codes or themes were identified. Finally, a descriptive account was produced for each theme. QRS NVIVO (Version10) software was used to support the coding and

synthesis of the collected data. Field notes were used to support the analysis through describing the environmental geography, participant interaction, group dynamics, behaviour and non-verbal communication. Field notes also enabled the lead researcher to reflect on the workshop and record any meaningful thoughts and insights.

3.6 Results

The aim was to recruit ten families to participate with the workshop. However due to the short two-week timeframe between hospital discharge and the workshop event, fewer families (n=7) than anticipated agreed to participate. Ultimately, only five families (nine parents) attended the workshop event on the day. Family names were anonymised with the following labels F 01, F 02, F 03, F 04 and F 05. For the purpose of anonymity, all infant names used within the narrative have been changed. Family characteristics are described in **Table 2**.

Table 2: Family stakeholder group workshop - characteristics

Characteristics	Families (n=5); Parents (n=9); Infants (n=5)
Families with previous experience of bronchiolitis	No previous experience (n=2) Infant with more than one episode of bronchiolitis (n=2) Sibling with previous diagnosis of bronchiolitis (n=1)
Gender (parent/carers)	Female (n=5) Male (n=4)
Number of parent smokers	Non-smokers (n=8) Smoker (n=1)
Gender (infant)	Female (n=3) Male (n=2)
Ethnicity (infant)	White British (n=4) Mixed race (n=1)
Prematurity (infant)	<37 weeks (n=2) >37 weeks (n=3)
Co-morbidity (infant)	Yes (n=0) No (n=5)
Severity of illness (infant)	Severity of Illness (infant) Mild (n=1) (no hospital admission) Moderate (n=1) (hospital admission for oxygen/ feeding support) Severe (n=3) (required non/invasive ventilation)
Number of children in household	Family F 01 (n=1) Family F 02 (n=2) Family F 03 (n=3) Family F 04 (n=1) Family F 05 (n=3)

3.6.1 NGT questions one and two: round robin exercise

A sum total of 91 *'worsening'* and 27 *'improving'* signs and symptoms were identified from the round robin exercise, and a further 17 *'worsening'* and 12 *'improving'* signs and symptoms identified from transcribed workshop discussions **(Table 3)**. These signs and symptoms were broadly related to changes in vital signs, appearance/behaviour, and feeding. Particular signs and symptoms were highlighted on more than one occasion during the process, with parents using different adjectives (e.g., *"floppy"* and *"lifeless"*) and synonyms (e.g., *"lethargic"* and *"sleeping a lot"*) to describe them. During

the round-robin exercise a parent from each family took turns to suggest a sign or symptom of bronchiolitis. As the exercise advanced it became apparent that individual parents were disclosing explicit and related details of their own individual family experience. Their accounts were corroborated and sometimes elaborated upon by their partner. If other parent's had similar experiences then they sometimes verbalised agreement and wanted to discuss their experiences. Although this part of the NGT process does not require parents to engage in discussion, CvM allowed these conversations to take place and reach their natural conclusion. Throughout the NGT process it was noted that three family dyads (F 01, F 02 & F 03) were more confident in sharing their experiences than F 04 and F 05 and they were apt to dominate group discussions at times. This was particularly so for fathers from F 01 and F 03. Family dyad (F 04) and F 05 (a single parent family) required CvM and BC (facilitator) to provide opportunities for them to contribute towards the general discussions. Sensitive probing questions specifically directed toward these two families were used to encourage them to share their own individual experiences.

Table 3: Signs and symptoms identified from round–robin exercise (presented in chronological order)

***'Worsening'* signs and symptoms listed on flip charts (n=74)**
Irregular breathing; not taking feeds; cough & cold; slept a lot, colour changed; constant crying; not taking fluids – no wet nappies; feed – cough so hard made him vomit; stopped feeding; lethargic and dead weak; crackly; bit clammy looking especially in the face; restless and crying when she was awake; he lost his voice; grey green colour; wasn't himself; sucking in his stomach; breathing got worse crackling; turned blue; very lethargic; been sleeping a lot – not taking feeds this didn't bother me too much and then his colour changed and that triggered things; floppy; lifeless; no interaction; hear him breathing; sounded like an old man; like breathing through bubbles; popping sound; couldn't make her laugh or smile; you just know when they are not themselves; kept having to check she was still breathing; nostrils were flaring; sniffles and snuffles to begin with; vomiting; about two days from knowing they were ill; weight loss; diarrhoea – browny yellowy water; didn't poo; constipated; crying was hoarse; lower pitch; whiney cry – like was in pain; mouth got sore and sore throat; dry lips; trying to breathe through his neck muscles; sucking in his stomach to breathe; breathing set my alarms off; went downhill quite fast; really bad cough; bringing up phlegm and swallowing it; she was choking; nappies were dry; mum in law could see he wasn't himself; snuffly; personality change; like a really bad hangover; can't be bothered; temperature – felt hot but did not have a temperature when we took it; mottled - all over her especially her chest deep purple; first few days okish but just not right then things got worse; breathing was rapid and quite deep; working hard with breathing; using whole body to breathe; head bobbing breathing; stomach expanding – like a pot belly; sometimes very rapid – then sometimes a pause – stopping when went to sleep- sometimes slowed down

***'Worsening'* signs and symptoms discussed but not listed on flip charts (n=17)**
Recession; limp; very pale and grey; look really unwell and sick; temperature was really high; using muscles all over her body especially her chest; felt hot; breathing difficulties lasted for ages; apnoea; loud breathing; low oxygen levels; laboured breathing; deep breathing; struggling to breathe; press the skin – it takes longer for the colour to come back; colour drained; sleeping pattern; mucous
***'Improving'* signs and symptoms listed on flip charts (n=15)**
Colour returned; stopped vomiting; kept feeds down; perk up/ interact more; more alert; breathing got better; normal looking nappies (soiled); lest restless/more settled; no longer mottled; complexion better; oxygen levels rising on machine; needs less oxygen; weaning off CPAP; visitors saying he looks better; taken off antibiotics and iv fluids
***'Improving'* signs and symptoms discussed but not listed on flip charts (n=12)**
Appearance returns to normal (4/5 days); behaviour and interaction (2 days); more interactive – smiling/eye contact; eating properly; breathing improved with oxygen and/or CPAP; gradual improvement; less pain killers; less medical treatment; handling it herself better; cough doesn't clear up straight away; stopped being dead wheezy; breathing less noisy

Following the round-robin exercise parents were asked to group together signs and symptoms that they thought were related to each other. One father (F 01) suggested starting with *"the breathing thing"*. Collectively the parents went through words and terms on the flip charts to identify signs and symptoms related to *'worsening breathing'*. Parents were then asked to clarify some of the terminology they used to describe particular signs and symptoms. For example, with regards to the *"popping sound",* CvM asked parents to elaborate on what they perceived caused the *"popping sound"*. *"Was it bubbles going pop or was the infant making this noise with their little mouth?"* This process was repeated for *'improving breathing'* and the other three concepts identified by the parents; colour change, cough and body language. These concepts were assigned as domain headings within a conceptual framework **(Table 4)**.

Table 4: Conceptual framework of bronchiolitis based on parents' synthesis

	Domains	Sub-domains: associated signs and symptoms	
		'Worsening'	***'Improving'***
Bronchiolitis	**Breathing**	Irregular breathing (fast, slow, pauses) Hearing them breathe (crackly, quite loud, popping) Using stomach more than chest Their stomach was going in and out a lot and this made their head seem to bob Head bobbing Nostrils were flaring, Breathing through neck muscles Using muscles (all over body especially chest) Working hard it was a struggle and it was laboured	Breathing got better – gradually Less noisy
	Colour change	My baby's colour was ok to begin with and then as they got worse around the second day they looked pale and drained When their colour changed and they became very pale, mottled, grey or blue, they were at their worst. Crying Choking	Colour returns quickly (with oxygen)
	Cough	Cough (chesty, bad) Cough up phlegm/mucous and swallowing Makes them vomit Choking Snuffly	
	Body language	Slept a lot Feeding stopped Lethargic/weak Wasn't themselves Routine was off Floppy, lifeless, no interaction Couldn't make them laugh or smile Personality change (bad hangover) Can't be bothered Cry/pitch Family noticed not themselves Nothing we could do helped them *Temperature *Dry lips	Feeding improved No longer vomited Appearance returns to normal gradually (4/5 days) More interactive – smiling/making eye contact

*These signs and symptoms were included under the domain of "body language" during the NGT ranking exercise.

3.6.2 Domain one: breathing

This domain describes parents' observations of their infants' breathing *'worsening'* and *'improving'* during the course of the illness.

3.6.2.1 *'Worsening'* breathing

Parents noted that it was approximately two days between their infants developing cold-like symptoms to their breathing becoming laboured, with one mother describing:

> *"…by Sunday that was when the irregular breathing and when she started to go down-hill…the second day I would say…"* (Mother, F 02).

Parents identified several changes to their infants' breathing pattern, rate and noise, which they associated with *'worsening breathing'*. These changes included rate irregularity which varied between being *"very rapid and deep"* to *"slow"* [with occasional] *"pauses"*. Parents perceived the slowing of breathing or *"pauses"* to be connected with their infant becoming fatigued:

> *"…but when he got really tired it would slow down"* (Father, F 01);

and/ or sleeping:

> *"…especially if she went to sleep… she was like…she'd be stopping breathing wouldn't it? [checks with partner]…"* (Mother, F 02).

Furthermore, *"slow"* breathing rate or *"pauses"* were such a concern for parents that it prompted increased watchfulness of their infant:

> *"…yeah it's like we had to keep checking to make sure they were still breathing … it was fast and slow…"* (Father, F 04).

Parents commented on the additional effort their infant had to make in order to take a breath. They referred to this *"effort"* or *"work"* of breathing using the

following terms; *"sucking in"* the stomach and/or neck, *"using muscles all over the body but especially the chest"*, *"nostrils flaring"* and *"head bobbing"*. In addition, parents remarked that the breathing had become more audible. One father stated:

> *"You don't even have to get that close and you can hear from just being in the room"* (Father, F 03).

Adjectives the parents used to describe breath sounds included; *"crackly"*, *"popping"*, *"breathing through bubbles"*, *"like they have been smoking"* and *"sounding like an old man"*. One parent considered *"worsening breathing"* to be associated with a sudden deterioration in their infant's general condition:

> *"…that's when you start looking at their breathing and all that sort of stuff…they go downhill quite fast"* (Father, F 03).

3.6.2.2 *'Improved'* breathing

Parents noticed that *"breathing got better"* as their infant improved. In spite of this, they did not really specify in what way or how the breathing improved other than being *"less noisy"*. One mother (F 03) commented on how *"she [her infant] just stopped being dead wheezy"*. Although the wheeze was mentioned within *'improving breathing'*, it was not suggested as a worsening symptom. For those parents whose infant had been admitted to hospital, they took their cues for improvement from clinical monitoring, for example:

> *"…his oxygen erm well when they had him on the machine his oxygen levels were rising on their own…"* (Father, F 01);

and also through the weaning of the respiratory support their infant required, as one mother explained:

"…the CPAP is it...getting weaned off it...coming off for a couple of hours each day" (Mother, F 02).

However, although *'worsening breathing'* was talked of as being of sudden onset, the parents described *'improving breathing'* as being a gradual process. Breathing improved over a few days or over a more extended period with *"difficulties last[ing] for ages".* One father talked about his son's experience, saying:

"...like for Thomas he has only started to get better now [time of workshop] and you think how long is it…two weeks...three weeks..." (Father, F 01).

3.6.3 Domain two: colour change

This domain describes parents' observations of changes to their infants' colour *'worsening'* and *'improving'* during the course of the illness.

3.6.3.1 *'Worsening'* colour change

Colour change was another sign which triggered concerns of deterioration, as the mother in the following quote explains:

"…just the colour...that triggers a lot of stuff, you know, a baby isn't supposed to look like that..." (Mother, F 03).

Parents reported how the colour would *"drain"* from the infant and described a range of colours associated with the *'worsening'* infant: *"pale and grey"*, *"grey green"*, *"blue"* and *"mottled and deep purple"*. Parents' understanding of colour change was quite nuanced and they presented different explanations to account for particular colour changes. Crying was implicated as one father (F 02) noted *"constant crying changed their colour"*. Another father reflected on other reasons for colour change:

"Depends on the colour…if they are pale, obviously it could be that they are a bit queasy or ill…phlegm on the stomach...blue they obviously… they are not getting enough oxygen are they…" (Father, F 03).

Deterioration in their infants' colour was often the key prompt for parents to seek medical help. One father described their response to his infant's *'worsening'* colour:

"He went that grey colour and we took him to the hospital…" (Father, F 03).

3.6.3.2 *'Improving'* colour change

When asked *"How did they know their baby was getting better?"* parents recalled how *"their [infant's] colour returned"* or their *"complexion was better"*: these were reported as being amongst the first signs and symptoms which suggested improvement. One father noticed a rapid colour change following the administration of oxygen therapy:

"The colour comes back quite quickly once they start getting oxygen so…you know how they get over that hump erm they get the colour back quite soon…" (Father, F 03).

The *'improving'* appearance of the infant was also observed by visitors and other family members, *"…coming to see him as well saying doesn't he look better today…"* (Mother, F 01).

3.6.4 Domain three: cough

This domain describes parents' observations of their infants' *'worsening'* and *'improving'* cough during the course of the illness.

3.6.4.1 *'Worsening'* cough

In the early stages of bronchiolitis, parents described how the infant exhibited coryzal symptoms, such as *"sniffles"* together with a cough. At this point in their infants' illness the parents did not appear to be overly concerned, as one father explained:

> *"The first few days they are not too bad they just seem as though they are not quite right"* (Father, F 03).

However, some parents did seek a medical opinion:

> *"On the Friday…I noticed she was not well…she had like the sniff…snuffles and a crackly cough so I took her to the Walk-in and I took her to the Doctors and they both said that she was fine"* (Mother, F 05).

Parents described a *'worsening'* cough as being *"bad"*, *"crackly"*, *"choking"* and *"chesty"*. Parents remembered how the cough induced mucous expectoration:

> *"She would cough that hard that she would be bringing phlegm up, and she would be trying to swallow it and choke"* (Father, F 02);

and/ or vomiting:

> *"It got worse and made them vomit and bring up their bottles…"* (Mother, F 04).

3.6.4.2 *'Improving'* cough

Although cough was a prominent feature of *'worsening'* bronchiolitis no signs or symptoms were included under the domain of *'improving cough'*.

Parents noted that as their infant improved, the cough was one of the final symptoms to resolve and could potentially last for up to several weeks:

> *"The cough was still there like but when Thomas was coughing…after he coughed he would go Ahhh! As if it was hurting him…and that seemed to lessen…but he still had a cough for a week or two afterwards…"* (Father, F 01).

3.6.5 Domain four: body language

This domain describes parents' observations of their infants' *'worsening'* and *'improving'* body language during the course of the illness.

3.6.5.1 *'Worsening'* body language

Within this domain parents reported observed changes with their infants' behaviour and routine. Parents found these changes difficult to describe at times, often summing up their concern by saying their infant "*wasn't themselves"*, as one father explained:

> *"It is hard to describe you just know they are not them self..."* (Dad, F 03).

Parents discussed altered feeding and sleeping patterns and changes to their infants' general disposition. Infants' reduced or inability to feed was of considerable concern to their parents. Parents commented on how their infants either did not wake for feeds:

> *"…he had been sleeping a lot, not waking up and not taking feeds…"* (Mother, F 03),

or would vomit after feeding provoking parents to seek medical advice:

"The first time I took him because he wasn't keeping his feeds down...he hadn't kept a full bottle down within 24 hours, so that's why we took him…" (Mother, F 01).

Parents considered the impact poor feeding had on their infants' overall hydration status and were aware of the link between poor feeding and signs of dehydration:

"…if they are not feeding they are not going to create wet nappies are they…" (Father, F 03).

Dry nappies over a period of time were clearly a concern to the parents as this mother described:

"She was not taking her feeds and no wet nappies, her nappies were still dry" (Mother, F 04).

Parents described strategies to try and manage their infants' hydration. For instance, small volumes of milk feed were offered more frequently or additional fluids such as water or juice were offered to either supplement or as a substitute for milk feeds. Although juice was not necessarily seen as a good milk substitute it was used, as one father described when his daughter:

"She wasn't even taking a bottle so even if she has juice to keep her hydrated" (Father, F 04).

These strategies were developed through intuition, previous experience or on the advice of a HCP. Drawing on his previous experience with his infant's elder sibling, one father explained:

"What I'd try to do last time is like, with the previous one [elder sibling], when he started to show the same symptoms […] between every say

two or three bottles...a tiny bit of water in a erm bottle just to try and re-hydrate him and that helped a lot…" (Father, F 03).

Advice from HCPs guided some parents' actions, for example:

"…we were told essentially with feeds...two ounces at a time […] she would get nauseous with a full stomach and have difficulty in breathing" (Father, F 02).

One mother recalled the medical intervention required when her daughter stopped feeding:

"…Molly stopped feeding so they had to give her a drip [...] an IV thing erm I would say that she stopped feeding totally...she couldn't take nothing at all..." (Mother, F 05).

Other feeding related issues the parents briefly discussed included diarrhoea, constipation, sore throat and weight loss. During the *'worsening'* phase of bronchiolitis parent's observed a number of key differences to their infants' personality, behaviour and routine. Parents reported an increase in lethargy describing how their infant would sleep for extended periods:

"…will wake two hours, they will be awake for a little and then go back to sleep...it is offset a little..." (Father, F 03).

Words such as, *"floppy", "limp"* and *"lifeless"* became part of the lexicon parents used to describe their infants' *'worsening'* body language. Parents detected subtle changes to their infants' personality. Infants ceased to interact with their parents and appeared unhappy as one father summed up:

"With her she is normally dead happy, always smiling, but she was not like that at all, ...couldn't make her laugh couldn't make her smile" (Father, F 02).

Poor interaction was suggested by parents who used phrases, such as, *"they can't be bothered"* or were *"quiet"* or likened the change in their infants' behaviour to having a *"bad hangover"*. Whilst some parent's reported their infant as being *"quiet"*, other parent's reported *"constant crying"* and described the quality of their infants' cry as either *"whining"*, *"hoarse"* or *"low pitched"*. This change in quality of cry also triggered concern as one father explained:

> *"Yeah whining more than a cry… like he was in pain"* (Father, F 01).

3.6.5.2 *'Improving'* body language

As the infant recovered, parents reported that their infants' feeding *"improved"*, they became more *"alert"*, *"less restless"*, *"smiling"* and returned to their usual routines. This return to usual feeding regimes was perceived as a good sign:

> *"…as soon as they […] start eating properly again they start getting more alert, that's when you know they are getting better and you can see it in them..."* (Father, F 03).

One of the mothers explained how her daughter became more interactive as her condition *'improved'* and interventions were reduced:

> *"…when she was off the oxygen… the CPAP… and feeding more...she started to be more interactive...I noticed she was smiling again...it was the best thing ever...she just smiled at you...you know when they normally look at you and smile at you...she was more interactive [...] she was actually making eye contact with you…"* (Mother, F 02).

3.6.6 NGT ranking exercise

Collectively, the parents were invited to produce one or two statements for each of the previously identified four domains written in *"layman's terms"*. The purpose of this exercise was to prioritise statements related to *'worsening'* and *'improving'* bronchiolitis in order of importance. To assist the parents with creating these statements CvM suggested the parents consider how they would describe each domain to a doctor or nurse or alternatively, to imagine they were writing an information sheet for other parents to read. It was also suggested that each statement started with the opening phrase *'My baby…'.'* The parents made the following refinements when developing the statements; the term *"crackly"* was preferred over *"popping"* as was *"more of a generalisation"* of the breath sound heard. One father (F 03) suggested including *"short"* into the description of *'pauses in breathing'* as opposed to just pauses, *"…'cause it [pauses] was about ten or 15 seconds"* in length. As with the changes reported with breathing the parents stated that their infants' colour changed *"around the second day"*. Although parents did not object to saying the word *"phlegm"*, it was felt that mucous was preferable *"…'cause it [phlegm] is spelt quite weird […] people may not know what it is…"* if written down in a leaflet. The parents decided to include *"temperature"* and *"dry lips"* under the domain of body language. Only one family (F 01) reported their infant had a high temperature their infants' temperature was initially *"normal"* although *"felt hot to the touch"*. Following hospital admission the father (F 01) reported that his infants' *"temperature did elevate to about 39 degrees"*. Although, *"dry lips"* was included with the statement on feeds, the parents had primarily associated *"dry lips"* as being a side effect of *"oxygen"*. Parents initially included "lifeless"

in the statement about their infant being *“floppy”*. However, the parents decided to exclude the word *“lifeless”* as it made the statement *“a bit scary”*. The finalised statements are listed in **Tables 5 & 6**. Each statement was assigned a letter. Using the ‘letter’ the parents in each family worked together to rank the letters in order of their perception of importance with 1 being most important.

Table 5: NGT ranking exercise (worsening bronchiolitis statements and results)

	***'Worsening'* bronchiolitis statements**
A	My baby was working harder than usual to breathe. Their breathing was a struggle and they used their stomach to help them. Their stomach went in and out a lot and this made their head bob. Their breathing was irregular and mostly faster than usual but sometimes it slowed down and there were some short pauses. Their breathing sounded crackly.
B	My baby started with a chesty cough and cold which got worse. Sometimes their cough made them vomit after feeding. They may cough up mucous.
C	My baby's colour was ok to begin with and then as it got worse – around the second day – they looked pale and drained. As they became worse they became very pale or mottled or grey or blue
D	My baby was sleeping a lot and did not seem like themselves. Their routine was 'off'.
E	My baby seemed very floppy and didn't interact with me.
F	My baby stopped taking their usual feeds. They did not have as many wet nappies. They got dry lips. Some babies got diarrhoea.
G	My baby felt hot and had a temperature
H	You know your own baby – look out for differences in their personality, cry and sleeping patterns.
I	We could not make them smile or laugh.

Ranking Order	**Family 01**	**Family 02**	**Family 03**	**Family 04**	**Family 05**
1	A	A	D	B	A
2	B	F	E	A	F
3	F	B	C	C	G
4	G	C	F	F	D
5	E	E	A	D	B
6	D	G	H	E	E
7	C	I	B	G	I
8	I	D	G	Missing data	I
9	H	H	I	Missing data	H

For the top three ranking categories for *'worsening bronchiolitis'*, four out of five families considered statement 'A' (breathing) as being most important. Statements 'B' (cough) and 'F' (feeding) were also considered important with three out of five families including them in their top three rankings. Family F 03

stood out as an outlier for this part of the ranking exercise as their top three rankings statements were ‘C’ (colour change), ‘D’ (lethargic) and ‘E’ (floppy/poor interaction). This family described how they called for an ambulance after their infant *“suddenly changed very rapidly”* at home; their infant required a period of time on nCPAP. When an infant is *in extremis*, these three symptoms (C, D, and E) may be of more concern for parents than breathing, cough and feeding, as described by families whose infants had been less acutely ill. Statements, ‘H’ (different to usual) and ‘I’ (not smiling or laughing) were included in the three lowermost rankings (least important) of four out of five families. Data were missing from family F 04 for statements ‘H’ and ‘I’. Even if these data were available they could only have been included in the two lowermost rankings, concurring with the other four families.

Table 6: NGT ranking exercise *('improving'* bronchiolitis statements and results)

	***'Improving'* bronchiolitis statements**
A	My baby returned to a normal routine.
B	My baby wanted to feed and no longer vomited.
C	My baby's appearance returned to normal.
D	My baby became more interactive and less restless and more settled. My baby smiled. Other relatives noticed my baby looked better.
E	My baby's breathing improved gradually over a few days.
F	My baby's cough started to get better but it took longer to get better than the breathing.
G	My baby's breathing got less noisy and more regular.
H	My baby needed less medical care.

Ranking Order	**Family 01**	**Family 02**	**Family 03**	**Family 04**	**Family 05**
1	D	E	B	B	D
2	C	B	C	C	E
3	G	C	A	E	B
4	E	D	E	G	A
5	H	H	H	A	C
6	B	G	D	D	C
7	A	F	G	F	H
8	F	A	F	H	F

The top three ranking categories for improving bronchiolitis - statements 'B' (feeding) and 'C' (appearance normal) -.were both jointly ranked as being most important by four out of five families **(Table 6)**. Statement 'F' (cough) was ranked as being the least important by all five families.

3.6.6.1 NGT question three: what could have improved your experience of having a baby with bronchiolitis?

Throughout the various workshop discussions the parents identified a number of key issues that could have improved their experience of having an infant with bronchiolitis. For this exercise the parents were asked to consider

"What could have improved your experience?" and *"How could HCPs have helped you?"* Their responses are listed in **Table 7**.

Table 7: What could have improved your experience of having a baby with bronchiolitis?

What could have improved your experience?	How could HCPs have helped you?
Comfier mattress Once in [admitted to hospital] everyone good Took two hours to get seen, palmed off with Calpol – which didn't do nothing What is bronchiolitis? Just say its bronchiolitis This is what is going to happen Will she get worse or better Nurses/doctors should tell us Should talk to you Health visitors and midwives should know Leaflets, bullet points (e.g. meningitis) Hadn't heard of it before but kept hearing it was very common We know some wards/beds were empty – should open these up instead of sending home	Leaflets on early signs and symptoms Lots of kids get it but parents don't know much about it Had to stay on a ward – not go to intensive care Nurses expect it at particular times of the year Sending him home to come back then he'd got worse – up to mum to make judgement – felt a bit not enough room at hospital to take babies in Shouldn't say is this your first baby and then give you a 'look' Asking if you smoke (even if you don't) makes me feel guilty Hospital should get geared up for the expected influx – needs to plan

Parents reported finding that their infant having bronchiolitis to be frightening and confusing; they felt unprepared to deal with the situation. The reasons they gave for their fear included the sudden deterioration and young age of the infant:

> *"It was a shock that a six week old baby got bronchiolitis."* (Mother, F 02);

and a lack of knowledge of bronchiolitis and associated signs and symptoms:

"It was quite frightening for us first time […] we did not know what was going on at all…we didn't even know what bronchiolitis was until he got it…" (Father, F 03).

Confusion occurred when they were seeking help due to unsatisfactory information and advice from HCPs. Additionally there was a perceived lack of forward planning from secondary/tertiary health services. When the infant displayed signs and symptoms that were a cause for concern, parents initially sought medical help from either a primary care setting (General Practitioner (GP) or Walk-in Centre) or ED. Parents reported that some of their initial interactions with HCPs were at times, inadequate and unhelpful. Bronchiolitis was not always mentioned as the diagnosis. Instead parents were often provided with what they perceived to be a nebulous diagnosis such as *"viral infection"*. Information about managing the condition was sometimes vague with suggestions, such as, *"come back if they get worse"*. This advice was not usually qualified with what the HCP meant by *'getting worse'*. Parents reported seeking medical help on more than one occasion with similar information and advice being provided. This process left some parents questioning their own judgement on being able to assess how sick their infant was. Moreover, parents were made to feel like they were being overly anxious; they felt their parenting ability and knowledge was being brought into question. As one mother explained:

"We got sent home saying it was a viral infection... and then they say 'Is that your first baby?' and I say 'yeah' and then they look at you and go [parent rolls eyes] as if to say...your crazy...you don't know" (Mother, F 01).

The lack of guidance coupled with the expectation that their infant might get worse, often left parents feeling helpless and abandoned, as one mother explained:

> *"…especially when I got sent home the second time, and the doctor said he was just going to get worse […] I felt that I was just left on my own"* (Mother, F 03).

Another mother experienced similar feelings of being out of her depth and felt rejected:

> *"...the doctor said we expect him to come back but until he is worse you will have to go home…so we did and it was basically it was up to me to judge when he was bad enough... so I felt a bit kicked out really…"* (Mother, F 01)

The parents of those infants eventually admitted to hospital appeared surprised by the number of infants hospitalised with bronchiolitis during the seasonal epidemic. Furthermore, as parents became aware of the prevalence of bronchiolitis, they remarked upon the lack of knowledge of bronchiolitis amongst other parents, as one mother noted:

> *"There does seem to be lots of kids that get it and yet there are a lot of people that still don't know what it is..."* (Mother, F 03).

One mother commenting on the lack of preparation by the health services to cope with the increased seasonal demand made a comparison to the lack of preparedness for snow, saying:

> *"It's like every year when the snow comes and it's such a surprise and there is no grit..."* (Mother, F 03).

Whilst understanding the pressures on the health service, the perceived lack of preparation surprised parents as, one father noted:

> *"You can understand that they are short staffed and that they have a lot of work on, there's not a lot of money to go around, not enough room and all the rest of it, that's fair enough, I guess maybe a better priority system. It's this time of year… it's going to happen let's think ahead maybe if they opened up another ward..."* (Father, F 03).

Another father described how the lack of resources impacted on his son's care:

> *"...they [HCPs] said that Thomas was meant to be in intensive care…but because there was no room they just kept him on this ward…it was only supposed to be a 24 hour ward…they had to keep him there as there was no room"* (Father, F 01)

One key feature all the parents felt would have enhanced their experience was more verbal or written information. The parents contrasted the lack of information for bronchiolitis with other illnesses, for example, *"meningitis"* where more information was available. The parents gave consideration to the timing of the information and felt it should be given prior to the infant becoming ill with health visitors as possible informants:

> *"Maybe when the health visitor came around maybe have leaflets on it to look out for the early signs and symptoms so you can get them in earlier…"* (Father, F 01)

3.7 Conclusion

A group of nine parents identified 91 '*worsening'* and 27 *'improving'* signs and symptoms of bronchiolitis to be considered for potential inclusion into the LIBSS-PRO. Furthermore the parents developed a bronchiolitis conceptual framework incorporating four domains characterising *'worsening'* or *'improving'* bronchiolitis. *'Difficulties with breathing'*, *'cough'* and *'poor feeding'* were ranked as the most concerning characteristics of *'worsening'* bronchiolitis. The parents reached consensus on improvement and this was judged through the infants' *'routine returning to normal'* and *'improved feeding'*.

Parents, irrespective of their infants' age or number of children in the family, appeared to develop instinctive knowledge of what is considered *'normal'* in terms of their infants' appearance and behaviour when well. This knowledge seemed to enable the parent to observe both subtle and more obvious changes which occurred in their infant during an episode of acute illness such as bronchiolitis. The parents were able to identify most of the signs and symptoms that typically characterise bronchiolitis. However, at times parents would find it quite difficult to articulate these differences and would refer back to their instinctive knowledge of their infant.

> *"…you know your baby isn't supposed to look like that…"* (Mum FW3)

Parents rapidly learned and adopted medical vocabulary to describe their infants' symptoms through their encounters with HCPs.

> *"I referred to his breathing like, it is called recession but I said he was breathing with his stomach"* (Mum FW3).

Having a young infant with bronchiolitis was perceived to be a frightening experience by all the parents. All the parents' reported that their experience

could have been greatly improved with accessible, good quality information (written and/or verbal) on bronchiolitis including guidance on severe symptom recognition.

The strength of this group workshop was the use of a democratic method (NGT) to identify and achieve consensus on signs and symptoms perceived as important to parents. NGT enabled all parents to present their opinions throughout the group. Holding the group in a family friendly venue with childcare provision facilitated parental engagement with the research. However, there were a number of limitations. The small number of family participants may impact on the findings being generalisable to the wider community of parents with infants clinically diagnosed with bronchiolitis. In particular, ethnic minority families were under-represented within the sample. To address these issues, an ethics amendment for the study was successfully submitted to undertake parent interviews by telephone. The data collected during the group workshop were analysed by one researcher (CvM) and therefore bias could possibly be introduced. However, the data were partially analysed by the parents themselves within the group workshop and a second researcher (BC) reviewed the data following the analysis.

Chapter Four

4 Health Care Professional (HCP) stakeholder group workshop using NGT

4.1 Introduction

Through their clinical experience and observations, HCPs provide in depth knowledge of bronchiolitis. This chapter describes the HCP stakeholder group workshop, which used NGT to identify signs, symptoms and risk factors of bronchiolitis. In addition, HCPs were also asked to critically appraise existing scoring instruments and develop criteria statements for classifying infants as either ‘mild’, ‘moderate’ or ‘severe’ bronchiolitis. This critical appraisal was used to inform the development and layout of the LIBSS-PRO. Furthermore, criteria statements for ‘mild’, ‘moderate’ and ‘severe’ bronchiolitis and severity criteria extracted from the literature were collated to form the Delphi consensus survey. These criteria were also used in subsequent construct and criterion validity testing.

4.2 Aims

i) To identify signs and symptoms of bronchiolitis for potential inclusion as items in a bronchiolitis severity score.

ii) To critically appraise scoring instruments that have currently been used in bronchiolitis research

iii) To develop criteria for mild, moderate and severe bronchiolitis

iv) To develop a conceptual framework of bronchiolitis

4.3 Sample and setting

Recruitment for the HCP workshop was undertaken during March 2011. All participants were identified through the CLRN. Workshop participants were doctors, nurses or physiotherapists with recent experience of managing infants with bronchiolitis. HCPs came from one paediatric tertiary and three DGHs and represented a range of specialities including ED, critical care, and general medical wards. A purposive sample frame was devised **(Appendix 28)** to ensure adequate representation of individuals with a wide range of professional clinical experience. Eligible HCPs were stratified by profession type, employment grade and clinical speciality. CLRN research nurses approached eligible HCPs with information on the workshop event. The workshop was held at Alder Hey Children's Hospital in Liverpool. HCPs were reimbursed with travel expenses and given a certificate of participation.

4.4 Informed consent

Written and verbal information was provided to HCPs prior to attending the workshop and again on the day of the workshop. Written informed consent was obtained from all participating HCPs on the day of the workshop.

4.5 Methods

Two researchers (CvM & BC) trained in qualitative research methods, facilitated the workshop. One research nurse (JSC) and a research administrator (SO) provided additional support. Informed written consent was obtained from all participants at the beginning of the workshop. CvM provided a brief introduction to the workshop to outline the research aims and workshop

schedule. The workshop lasted approximately three hours and was digitally audio recorded (Tascam DR-100). The recordings were transcribed verbatim and anonymised for analysis (CvM). JSC & SO acted as observers throughout the workshop and composed handwritten notes. These notes were used to document salient points made during the workshop, non-verbal communication/behaviour, issues which created tensions and the group dynamics. Spatial maps of the room layout and where participants and researchers were located were also included with the notes.

During the workshop the HCP participants were given a series of group exercises **(Figure 3)** to facilitate with the development and design of the bronchiolitis scoring instrument.

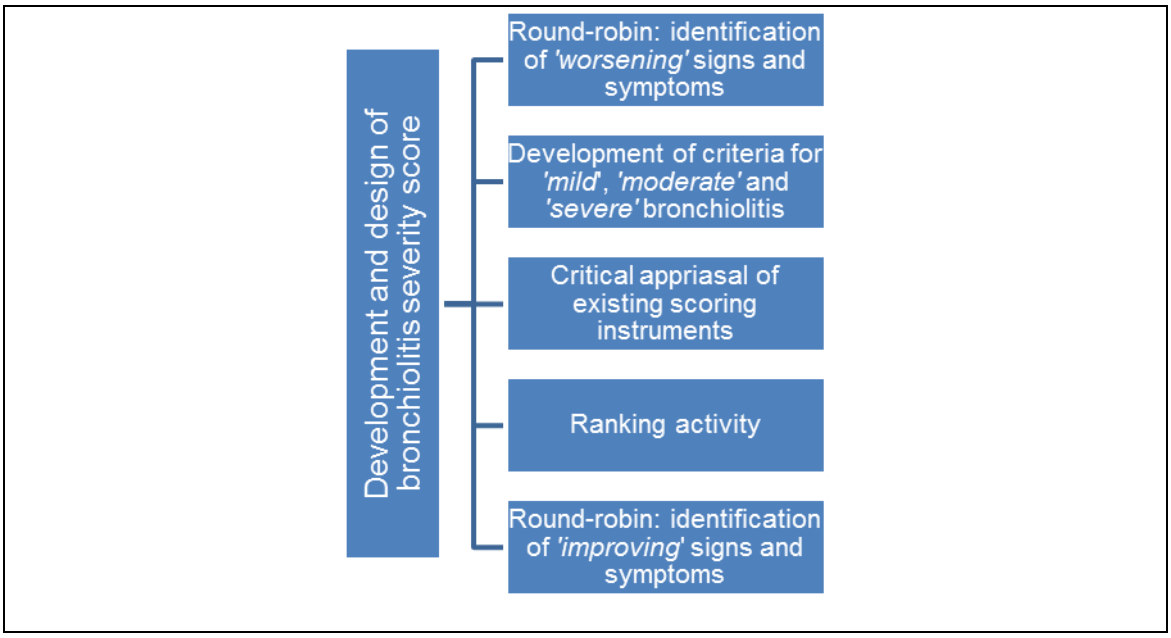


Figure 3: Flow chart illustrating HCP workshop group exercises

4.5.1 Round-robin exercise to identify *'worsening'* signs and symptoms of bronchiolitis

The purpose of this exercise was to identify *'worsening'* signs and symptoms for potential inclusion into the scoring instrument. At the beginning

of the workshop, NGT question one (**Table 8**) was posed to the HCPs. Each HCP was asked to silently reflect on *'worsening'* signs and symptoms. This period of individual reflection was shortly followed by a round-robin exercise. Each HCP was asked to share a *'worsening'* sign or symptom to the group. This exercise continued around the group until no further new signs or symptoms were identified. All identified signs and symptoms were recorded on to flip-charts. The HCPs discussed each of the recorded signs and symptoms to clarify meaning.

4.5.2 Development of criteria for 'mild', 'moderate' and 'severe' bronchiolitis

The purpose of this exercise was to develop criteria for 'mild', 'moderate' and 'severe' bronchiolitis:

- To enable the development of thresholds for 'mild', 'moderate' and 'severe' bronchiolitis within the scoring instrument and,
- To assist with the standardisation of the reference standard (clinical assessment by senior HCP) when used to evaluate criterion validity.

The HCPs were split into three smaller groups approximately containing six participants. Each group was allocated one of the three bronchiolitis severity categories: 'mild', 'moderate' or 'severe'. Using the identified signs and symptoms from task one; the HCPs were asked to produce criteria for their particular category. Each group presented their statements to the whole group for further discussion and clarification.

4.5.3 Critical appraisal of existing scoring instruments

The purpose of this exercise was to critically appraise the content and design of existing bronchiolitis scoring instruments. The results of this exercise helped to inform the design of a new scoring instrument. Six scoring instruments used as outcome measures in bronchiolitis research were identified for use in this exercise (33, 55, 56, 58, 63, 125). Each of the three small groups was provided with two of the six scoring instruments. The HCP participants in each group were asked to critically appraise the two scoring instruments for content and layout. Each of the three small groups fed back their scoring instrument appraisals to the whole group. A power point slide of each instrument was shown to the whole group during the feedback. The group as a whole also discussed each scoring instrument.

4.5.4 Ranking activity: prioritisation of *'worsening'* signs and symptoms

The purpose of this exercise was to prioritise which *'worsening'* signs and symptoms to include in the scoring instrument. Using the information and discussions from the previous group exercises, the HCPs were asked to design their '*perfect'* bronchiolitis severity score/instrument. HCPs were required to individually choose up to ten signs and symptoms and rank them in order of importance (one being most important and ten being least). The HCPs were asked to discuss signs and symptoms and rankings with the other small group members. A final group decision was made for the top ten signs and symptoms for their particular bronchiolitis severity category. The group ranked these signs and symptoms in order of importance. The three individual groups

fed back their prioritised *'worsening'* signs, symptoms and group rankings to the entire group for further discussion.

4.5.5 Round-robin exercise to identify *'improving'* signs and symptoms of bronchiolitis

The purpose of this exercise was to identify *'improving'* signs and symptoms to ensure that the developed score is responsive to clinical change. NGT question two **(Table 8)** was posed to the HCPs. Each HCP was asked to silently reflect on *'improving'* signs and symptoms for their pre-allocated *'severity'* category. This period of individual reflection was shortly followed by a round-robin exercise. Each HCP was asked to share an *'improving'* sign or symptom with the group. This exercise continued around the group until no further new signs or symptoms were identified. All identified signs and symptoms were recorded on flip-charts. The HCPs discussed each of the recorded signs and symptoms to clarify meaning.

Table 8: NGT questions (HCP workshop)

NGT question 1: What signs and symptoms characterise an infant with worsening bronchiolitis?
NGT question 2: What signs and symptoms characterise and infant with improving bronchiolitis?

4.6 Analysis

Initial data analysis was undertaken by the participants themselves during the workshop though the NGT ranking process. CvM analysed other data sources derived from the workshop (124). These included audio-recorded discussions that had taken place, all transcribed by CvM. The lists of words and phrases written down by HCPs, the words and phrases recorded on flip

charts, and field notes made by the observers during the workshop, and those made by CvM and BC, were also analysed. The workshop transcript and these extra data sources were examined several times during the course of the analysis. Initial examination of the collected data was used to obtain an overview of the data and to record general impressions, key ideas, themes and concepts arising from the content. Following on from this a descriptive thematic analysis was undertaken. This process involved manually coding the raw data then collapsing the coded data under broader themes. Codes and themes were inductively derived from the data. As new codes emerged these were applied iteratively to the whole data set in subsequent examinations of the data sources until no new codes or themes were identified. Finally, a descriptive account was produced for each theme. QRS NVIVO (Version 10) software was used to code and synthesise the data. Field notes also enabled the researchers to reflect on the workshop and record any meaningful thoughts and insights.

4.7 Results

The aim was to recruit 15 HCPs to participate in the workshop. In total, 18 HCPs attended the workshop. The HCPs characteristics are described in **Table 9**.

Table 9: HCP Workshop participant characteristics

HCP	Doctors	(n=8)
	Consultant	(n=5)
Groups/grades	ST3 and above	(n=3)
	Nurses	(n=9)
	Band 7	(n=1)
	Band 6	(n=1)
	Band 5	(n=6)
	Student	(n=1)
	Physiotherapist	(n=1)
	Band 8	(n=1)
Medical specialties	General medical	(n=13)
	A&E	(n=3)
	PICU	(n=2)

4.7.1 Round-robin exercise to identify *'worsening'* signs and symptoms of bronchiolitis

To maintain anonymity the HCPs were allocated an identification number from one to eighteen. When transcribing the workshop it was difficult at times to identify the speaker. In these instances, the HCP was referred to as unidentified male or female (UIM/F). During the round-robin exercise each HCP took it in turns to suggest a sign or symptom of bronchiolitis. As the exercise progressed, individual HCPs started to provide additional information and context, and highlight key issues with particular signs and symptoms to support their inclusion/exclusion into the scoring instrument. This prompted other HCPs to contribute to the discussion. Although this part of the NGT process does not require the HCPs to engage with discussion, CvM allowed these conversations to take place and reach their natural conclusion. Throughout the workshop the senior doctors had a tendency to dominate some of the group discussions, most notably HCPs 05, 14 and 15. The HCPs

identified 66 *'worsening'* signs and symptoms from the round-robin exercise. A further seven *'worsening'* signs and symptoms, not listed on flip charts, were identified from the transcribed workshop discussions **(Table 10)**.

A number of these signs and were repeated during the exercise or discussed in different contexts. During the thematic analysis related signs and symptoms were collapsed together and broadly grouped under the following five major themes: respiratory, feeding/hydration, appearance/ behaviour, risk factors and miscellaneous symptoms **(Table 11)**.

Table 10: Group Task 1-Signs and symptoms identified from round-robin exercise

***'Worsening'* signs and symptoms as listed on flip charts (n=66)**
Respiratory rate (slight, moderate, desperate, about to stop); apnoeas; cyanosed; low sats; lethargic; irritable; low GCS; worsening ability to feed; nasal flare; increased work of breathing with NG feeds; tracheal tug; tachycardia; poor perfusion (cap refill); getting tired; poor laboured breathing; increased oxygen need; increased recession at rest; getting tired and reduced air entry; complete inability to feed; any of these getting worse – TREND; instability on handling; desaturation on handling; wet nappy; increased PcO_2; head bobbing; grunting; pyrexia; increased subcostal recession; vomiting; decreased urine output; respiratory arrest; no improvement with suction; generally looking unwell; late fever; gut feeling; parental concern; dependent on child & threshold (prem, cardiac, chronic respiratory, Downs, underlying muscle disorder); day of illness; social background; secondary infections; increased work of breathing- breakdown into components and weighted (e.g. recession, tracheal tug); and change from increased work to more shallow breathing/effort →exhaustion; what baby is doing (sleep, feed etc context) – when would you do an assessment (e.g. x minutes post feed/handling); link breathing and other components (e.g. cyanosis & increased/decreased effort); ?what is baseline – then weight score re: 20%, 30% etc over baseline; many items but need to include these; transient nature of S&S – re: feeds etc then score to see if increased/decreased has been maintained; like PEWS – if 2+ borderline – review, if massively high then needs immediate review; increased oxygen demands & big jumps; ?quantify or look for trends in increased oxygen demands; will tool work on admission & in-patient tool – can it cover both; admission linked to softer factors (not bronch related) e.g. presenting at 2am – then increased likelihood of admission; SpO_2 may be ok when awake but dips when asleep; is baby feeding 100mLs/kg - as this may be appropriate if baby overfed; is nappy wet; generally look unwell (pale, mottled, floppy, posture, glassy eyed, lethargy, difficult to handle, clammy, sweaty, don't care – being handled (stopped screaming/crying/coughing)); don't mind being handled; unstable (??septic); resisting & screaming) – if all of these then maybe not

bronchiolitis but septic; pink & apnoeic; 'septic'; apnoea – little pauses, self-correcting (not quite sure if they are apnoeas), increased frequency, increased concern, "real" apnoea, apnoea definition – bradycardia + apnoea; pre-apnoea breathing; context – need to see trends – graphs, trend over time, (e.g. resp (tug & recession), oxygen requirement, effort, heart rate, GCS (irritable/floppy), central cyanosis); well - obvious, very severe – obvious, middle group – harder; would want to predict differently for admission/transfer (PICU/HDU) as consequences would be different; GCS – maybe hard to get a full assessment – (reduced handling); PEW triggers for most bronchs; pathway should have guidance for 'juniors'- prompt – should explain these are the signs…beware of 'red flag' boxes; score could be included into a pathway – score x then do A, score y then do B; aiming not to reinvent the PEW – so tool could be linked to this (overlap) – what would be different as most is relevant to sick child
***'Worsening'* symptoms discussed but not listed on flip charts (n=7)**
Iv fluids; intercostal recession; hospital re-attendance; length of cough; oral/NG feeding; day of illness; fluey looking

Table 11: Bronchiolitis conceptual framework (HCP workshop)

Major themes	*'Worsening'* signs and symptoms
Respiratory	Respiratory rate (slight, moderate, desperate, about to stop) Breathing (laboured/shallow/exhausted) Apnoea (little pauses self-correcting, increasing frequency, apnoea + bradycardia) Cyanosis Increased work of breathing (nasal flare, tracheal tug, head bobbing, grunting) Recession (intercostal/subcostal) Respiratory arrest Increased oxygen requirements Reduced air entry Increased PcO2 Reduced SpO2 Cough
Feeding/hydration	Worsening ability to feed Vomiting Feeding support (NG feeds/IV fluids) Poor perfusion (cap refill) Decreased urine output
Appearance/behaviour	Lethargic GCS (irritable/floppy) Instability on handling Generally looking unwell (pale, mottled, posture, glassy eyed, clammy, sweaty, fluey) don't care-being handled (stopped screaming, crying, coughing) Resisting and screaming
Risk factors	Prematurity Cardiac Chronic respiratory Down's Underlying muscular disorder Social background Secondary infection Hospital re-attendance
Miscellaneous	Pyrexia No improvement with suction Trends-over time Gut feeling Parental concern Day of illness Heart rate

The HCPs initially considered diagnosis and identification of the worsening infant through observing trends with certain signs and symptoms, with one HCP describing:

> *"The question is asking how can you tell that they are worsening [...] you are absolutely right it is the trend […] none of them tell you that the child has got bronchiolitis ...some don't really tell you that it is getting worse whilst some clearly tell you that it is getting worse…"* (HCP 14).

In addition to trends, the HCPs commented on the inclusion of thresholds to indicate normal and/or abnormal ranges, as one HCP explained:

> *"I suppose you would need kind of parameters as well so respiratory rate within normal range...respiratory rate slightly tachypnoeic...respiratory rate absolutely desperate...about to collapse...."* (HCP 15);

One HCP suggested thresholds could be standardised through calculating a percentage above the infant's baseline:

> *"The only other way you could try and standardise is perhaps to percentage over their baseline...everybody had a different baseline resp rate aren't they so if their resp rate is 20% higher than normal...would that score you anything ...than 40% higher than normal"* (HCP 06);

The practicalities of undertaking this calculation were questioned by another HCP:

> *"…have you got time to stand there and work out a percentage?…"* (HCP UIF).

The HCPs discussed the possibility of lowering thresholds for hospital admission for infants with risk factors, such as prematurity, with one HCP stating:

> *"I suppose if you were looking for admission criteria [...] you have a lower threshold for admitting things like prems [premature infants]…kids with lung disease...kids with cardiac complaints...you will always have a lower threshold to admit..."* (HCP UIF).

The HCPs also thought social circumstances and/or the parental educational level should be taken in to account when considering admission:

> *"The other thing I suppose you kind of judge when admitting a child is the social background and the understanding of parents […] you don't really want to send a child […] who ordinarily with sensible parents you might send home but parents who may have learning difficulties or it's a child in need or a child in an unstable family..."* (HCP 15).

Feed intake thresholds were also discussed in the context of admission. One HCP described how it can be difficult to gauge an accurate volume intake from the parents as some infants were perceived to be *"overfed"*. Another HCP suggested that fluid intakes 50% of normal volume were their local threshold for admission. In order to achieve a more truthful reflection of hydration status, in addition to feeding, HCPs advised evaluating urine output, one HCP noted:

> *"…you have got a wet nappy and you just think that's a miracle […] you start losing your bit of faith in the amount of feeding […] you watch them guzzle and you think things are looking up…"* (HCP 01).

When asked to clarify the concept of *"increased work of breathing"* HCPs felt it encompassed a number of individual signs and symptoms listed on the

flip charts, for example, *"recession"*, *"increased respiratory rate"*, *"grunting"*, *"head bobbing"* and *"nasal flare"*. Furthermore, HCPs felt *"increased work of breathing"* within the score would be more objective if broken down into individual components with different weightings. It was suggested that increasing oxygen requirements were also related to *"increased work of breathing"* as one HCP recounted:

> *"…when there is increased work of breathing…your oxygen requirement would be increasing and there would be desats [oxygen desaturations] that are fleeting"* (HCP 07);

Another HCP suggested quantify these changes by documenting trends of oxygen percentage increase:

> *"…you are looking for predominantly is your change in oxygen so if you have like a 5 % increase or something then that can also score… so you can sort of see the trend of oxygen getting worse...if you have got a baby ticking along quite well in 35% ...40% head box that's fine but if it is suddenly going ...you know ...up sort of hour by hour"* (HCP 15).

Some HCPs felt certain actions, such as *"feeding"* and/or *"crying"* or becoming *"pyrexial"* could trigger the infant to have a temporary episode of *"increased work of breathing"*. The group reflected on their experience of obtaining abnormal paediatric early warning scores (PEWS) following an episode of *"crying"* or *"feeding"* and how this would trigger a medical review:

> *"…you do this with PEWS […] if there is a massively high score then they need immediate review […] even if it is just after them feeding but the baby looks knackered"* (HCP 15).

The group felt these anomalies should be documented at the time of scoring the infant and reassessed within a short timeframe. *"Increased work of breathing"* following a feed was reported to potentially indicate the need to pass a nasogastric tube. The HCPs discussed how inserting a nasogastric tube could also *"tip them [the infant] over the edge"* if they put up a *"fight"*. Conversely, one HCP suggested that *"increased work of breathing"* may be misleading in certain circumstances:

> *"…increased work of breathing can be a bit of a false sign you can actually get very shallow breathing ...exhausted looking baby who has been working very hard [...] so actually not very much increased work of breathing…"* (HCP 15);

especially if there was a reduction in the *"work of breathing"*:

> *"…if you see reduced effort but increased cyanosis clearly you would be very worried..."* (HCP 05);

with potentially important nuanced clinical changes not being captured by a score:

> *"…tying that up with a score that gives you a total may mean you miss some of those subtleties..."* (HCP 14).

When asked to explain the notion of the infant *"generally looking unwell"*, adjectives used included; *"mottled"*, *"floppy"*, *"pale"*, *"fluey looking"* and *"glassy eyed"*. The HCPs perceived the infant being *"irritable"* and *"don't like being handled"*. However, the HCPs agreed that it was more concerning if an infant became *"quiet"* and/or *"unresponsive"*. One HCP described:

> *"It's when they don't mind...when they have got to the stage actually they don't care what you do to them...you drip them and you get nothing*

at all […] they are completely passed the stage of caring...they have stopped screaming and they have stopped crying […] it's a progression downhill" (HCP 01).

In this situation the HCPs recalled how they would initiate a septic screen to exclude *"a secondary bacterial infection"*. The HCPs also discussed how the appearance of the infant would differ between seasons. Some seasons they would appear *"septic"* whilst at other times they would *be "pink and apnoeic"* or *"milder"*:

"That's where you get the variation with the winters like this year we have a lot of those [septic and floppy] where as last year they tend to be much milder…" (HCP 01).

The group participants were asked to further describe and clarify what was meant by the term *"apnoea"*. The HCPs reported how respiratory rate may noticeably decrease. Although, it was questionable as to whether the infant was having a *"self-correcting apnoea"* or a *"normal pause"*.

"...they might be self-correcting apnoeas...you know the ones where you are not quite sure and you just look and you watch and you wonder if they are going to and then they don't and they carry on…" (HCP 02)

The HCPs proposed these pauses would gradually become longer and more frequent until they require an intervention:

"You wonder to begin with then gradually they get longer […] and then it gets to the stage that you feel you need to encourage them a bit and then they get more frequent and then you get to the stage where they need bagging..." (HCP 01).

A conversation ensued over using the traditional medical definition to classify apnoea as described by one HCP:

> *"…they [apnoeas] should be associated with bradycardias and only when the heart rate is going down for 30 seconds…20 seconds then they are called apnoeas"* (HCP 07).

Some of the HCPs disagreed with the use of the aforementioned definition in the context of bronchiolitis:

> *"…they have got increased recession and then all of a sudden they start having briefer pauses and their respiratory rate is slowing down ...in the context of their oxygen requirements staying high...you probably don't need to wait […] until they meet the official definition of apnoeas before you increase their score...so it is context that is really important…"* (HCP 14).

Neurological assessment in the worsening infant was perceived to be an important factor when assessing a deteriorating infant. Signs of neurological deterioration identified by the group included*: "irritability"*, *"more floppy"*, and *"less responsive"*. Commonly used neurological scoring instruments, such as, the Glasgow Coma Scale (GCS) and Alert, Verbal, Pain, Unresponsive (AVPU) were discussed. One HCP reported difficulties in obtaining a GCS score on an infant:

> *"I don't know whether you will be able to get a definitive GCS on a bronchiolitis because you don't tend to do sort of neuro obs on them ...you don't tend to touch them […] I don't know if you would be able to get proper 15, 14 ...."* (HCP 10).

Finally, the HCPs debated the need for a bronchiolitis score when PEWS are currently being used in clinical practice. They drew attention to the fact a number of aforementioned signs and symptoms are generic to *"all sick children"* and included in the PEWS, for instance, *"work of breathing"* and *"trends in observations"*. To prevent reinvention of the PEWS it was suggested having bronchiolitis specific criteria especially for admission and guidance on *"red flag symptoms"* for more junior HCPs. The sensitivity of the PEWS was brought into question as it was emphasised that most infants with bronchiolitis will unnecessarily *"trigger the PEW"*:

> *"Most bronchs [bronchiolitis] that will sit above that trigger [...] you will be constantly triggering a PEW [...] they have always been at that level...it's not like they are getting worse but they are just sitting at that level anyhow..."* (HCP UIF).

4.7.2 Development of criteria for 'mild', 'moderate' and 'severe' bronchiolitis

Using the pre-identified *'worsening'* signs and symptoms of bronchiolitis, HCPs created statements they felt characterised 'mild', 'moderate' and 'severe' bronchiolitis **(Table 12)**.

Table 12: Characteristics of 'mild', 'moderate' and 'severe' bronchiolitis

'Mild' bronchiolitis	'Moderate' bronchiolitis	'Severe' bronchiolitis
Generally doesn't require admission Increased work of breathing – recession, respiratory rate (<60 bpm/age appropriate), no grunting/head bobbing Acceptable coughing spasms (no apnoeas/cyanosis) Sats >92% in air and heart rate <150 bmp when settled Feeding – 2/3 of appropriate intake for weight Well hydrated – wet nappies mucous membranes Alert and active "grumpy" no irritability Improvement with simple measures Duration and underlying chronic conditions/social circumstances	Child has at least one of the following:- Low saturations <92% in room air/maybe fleeting Feeding less than 50% of required amount 150mL/kg Signs of moderate respiratory distress; subcostal/intercostal recession; tracheal tug; mild/audible at close distance grunt Normal neurological status; alert (maybe tired); normal responsiveness; normal tone; consolable by parents < one year old HR $\leq$ 160 bpm	A child with severe bronchiolitis is likely to have significant hypoxia, with increasing oxygen requirements, have apnoeas that require stimulation (with or without bradycardia) and have not responded to interventions given. **Moderate/severe (HDU)** Deteriorating despite interventions Increased oxygen requirements >60% Increasing apnoeas requiring stimulation and respiratory support Interventions Decreasing saturations despite increasing oxygen Hydration – IV Positioning Difficult to include signs of respiratory distress as so variable between patients **Severe/life threatening (PICU)** Continuing or prolonged apnoeas despite NIV Cardiorespiratory arrest

4.7.2.1 'Mild' bronchiolitis group

When considering infants with 'mild' bronchiolitis, the HCPs commented on what point should the scoring instrument *"come in to play"*. Would the infant require a positive diagnosis of RSV? Furthermore, they queried if based on

clinical symptoms alone, how would you make a robust clinical diagnosis? One HCP remarked:

> *"I bet you a load of those kids are called bronchiolitis but they have a variety of other respiratory tract infections…"* (HCP 14).

4.7.2.2 'Moderate' bronchiolitis group

The HCPs acknowledged that *'moderate'* bronchiolitis covered a wide spectrum of disease severity and found it difficult to encapsulate:

> *"I suppose moderate covers a wide range doesn't it...you get your mild to moderate ones that just about fit the criteria on the board and then you get the moderate to severe ones that you kind of keeping a closer eye on but we could sort of define it as anything that could be kept comfortable on the ward without danger of needing further intervention or didn't need admission at all [...] they all overlap slightly, the mild, moderate & severe…"* (HCP 15).

It was felt that *'moderate'* was a combination of at least three of the statements listed, particularly; *"low sats below 92 in air"*, *"feeding less than 50% of required amount"* or *"moderate respiratory distress"*. Defining *"moderate respiratory distress"* was found to be difficult but the group settled on: *"subcostal/intercostal recession"*, *"tracheal tug"* and *"mild grunt"*.

4.7.2.3 'Severe' bronchiolitis group

Similarly to the *'moderate'* group the *'severe'* group decided to divide this category into moderate/severe (PHDU patients) and severe/life threatening (PICU patients). They deliberately did not include a statements relating to *"respiratory distress"* as they thought this to be *"variable"* between patients and

"difficult to measure". Level of consciousness was also omitted as it was considered subjective:

> *"…we've seen very severe bronchiolitis could actually be quite alert and a lot of not that unwell ones could be quite sleepy and we didn't feel that it was…a good objective criteria"* (HCP 14).

More emphasis was placed on apnoea requiring intervention. It was noted that some *'worsening'* infants are managed on the wards due to the lack of available critical care beds. It was postulated whether earlier intervention would reduce length of stay in critical care areas such as PHDU. It was also highlighted that perceptions of *'severity'* can differ between HCP experience and clinical environment. For instance a paediatric intensivist may consider an infant on nCPAP to be *"not that severe"* whereas a paediatrician from a district general hospital may think "*if they are on nCPAP they are still pretty severe"*.

4.7.3 Critical appraisal of existing scoring instruments

A summary of each group's critical appraisal of scoring instruments can be found in **Table 13**.

Table 13: Critical appraisal of existing scoring instruments

No.	Author	Comments	
1.	**Walsh *et al* 2006**	Likes	Struggled Not to many things to calculate/ simple
		Dislikes:	Thee decimal places (bad) Not user friendly Too simple Fair amount of subjectivity It is retrospective – not helpful/don't know who came back Use of centile chart Doesn't take into account other resp Not very intuitive how you work it out Could have a programme that enters absent/present
2.	**Wang *et al* 1992**	Likes:	Easy Nicely laid out Could use to calculate trends
		Dislikes:	Not sure how to calculate score? RR – age dependent Not convinced that wheezing is a good indicator Didn't talk of sub costal Is this a viral wheeze score (USA) or appropriate for European bronchiolitis? Nurses now getting trained for auscultation (not routine) – ok for nurses in MAU – not all Scoring has to be universal – e.g. for non-trained, paed nurses, Walk-in Centres Oximetry in title but no oximetry in table Layout good
3.	**Wilson *et al* 2000**	Likes:	Lots of criteria – some useful
		Dislikes:	Some un-useful criteria Lab values not useful – anyone should be able to assess – especially more junior/inexperienced people Sputum Frank haemoptysis Fever not so useful Had to look for trends Doesn't tell you how to score Busy Ranges are strange Overwhelming – can't be bothered
4.	**Liu *et al* 2004**	Likes:	Age related criteria - could be more specific Easier on the eyes Easier than '3' to use
		Dislikes:	Some elements - wheeze – not relevant Too simplistic – doesn't included HR etc

5.	**Lowell *et al* 1987**	Likes:	Simple to look at Clear scoring Could score change Retraction scoring good Layout simple
		Dislikes:	Very specific – e.g. expiration ¼, ½ - need consistent person to score Not particularly useful Zones would be more useful than segments – no good for nursing Supraclavicular retractions – hard to see on babies (short necks) Wheezing not a useful thing to be scoring and very subjective
6.	**Kerem *et al* 1991**	Likes:	Simple – not overpowering Not operator dependent – could be used by relatively inexperienced staff Didn't need auscultation Easy to interpret
		Dislikes:	Is age taken into account 'for asthma' Should identify what's happening – e.g. feeds, handling

Walsh *et al* (2004) developed a score which included four items (retractions, HR>97 centile, age and hydration) (63). When assessing an infant, a numerical value would be determined for each item. Each individual item value would then be multiplied by an additional numerical value (three decimal places). The values for the four items would then be summed together. Cut-offs values were developed for 'mild', 'moderate' and 'severe' bronchiolitis. This instrument was found to be *"complicated"* and *"off putting"* by the HCPs. An instrument which enabled you to calculate to three decimal places was considered a *"bad thing"*. Calculating the score was difficult and not *"intuitive"* to use. It was felt there was a *"fair amount of subjectivity"* when assessing hydration with hydration scores being more *"heavily weighted"* than heart rate, retractions and age. There were concerns with the instrument being developed

using a retrospective group of patients. Having to obtain information from percentile charts in order to *"score"* was considered an additional burden. Finally, the instrument did not take into account other clinical symptoms such as *"retractions"*, *"saturations"* and *"respiratory distress"*.

Wang *et al* (1992) developed an instrument which enabled the user to score an infant on four items (respiratory rate, retractions, wheeze, and general appearance) using a scale from *'0'* to *'3'* (58). The HCPs liked the lay out of this instrument and found it *"easy to use"*. However they did question its relevance to the UK definition of bronchiolitis. They considered the score was more suited to the North American definition of bronchiolitis, which include viral wheeze. They were not convinced that *"wheezing"* was particularly useful in assessing severity of illness. For respiratory rate $\leq$ 30 the infant would get a score of *'0'*. This scoring was perceived inappropriate for this age group with a score of *'3'* deemed more appropriate in certain situations. It was also noted there was a lack of guidance on how to calculate and interpret the score. Ultimately, the HCPs believed that a score should have *"universal"* use. For this score the user would have to be competent in auscultation therefore certain HCPs may be excluded from its use.

Wilson *et al* (2000) developed an instrument with seven items (digestive, lab-arterial blood gases, lab-haematology, neurology, radiology, respiratory and vital signs) (33). The respiratory item was further sub-divided into cyanosis, sputum/secretions, apnoea, dyspnoea, rales, breath sounds, nasal flare, retractions, expiratory grunt, wheeze and oxygen saturation. Each item would be assessed using a scale from '*level one'* to *'level four'*. It was felt that this instrument was *"too busy"* with superfluous criteria and was found to be

"too difficult and too hard to follow". Some criteria were perceived to be useful but required *"further clarification"*. The instrument includes criteria that prevent universal use. There was no guidance on how to calculate and interpret this score.

Liu *et al* (2004) (55) developed an instrument with four items (respiratory rate, retractions, dyspnoea and wheeze) (55). The instrument is divided into age groups from new-born to five years of age. Each item is scored on a scale from '0' to '3'. In general this score was *"liked better"* by the HCPs. It was felt that it was *"easier to use"*. They liked how the instrument was divided into age categories. Criticisms of this instrument were that it was generic and could be used for a number of respiratory conditions. Its *"criteria could be more specific"*, "*wheeze not helpful*", *"a little bit too simplistic"* and it omitted the following; heart rate, colour, neurological status and feeding.

Lowell *et al* (1987) (56) developed the RDAI which includes two items (wheeze (expiration/inspiration/location) and retractions (supraclavicular/intercostal/subcostal)) (56). Each item scored on a scale from *'0'* to *'4'*. The HCPs found this *"simple to look at"* and would be able to *"score a change"* in condition. However, it was perceived that the wheeze item was *"too specific"* and could lead to *"subjective scoring"*. The user had to assess whether wheeze occurred in either a half or three quarters of the expiration. In addition the location of the wheeze was required to be identified ($\underline{\leq}$ two or $\underline{\geq}$ three of four lung fields). It was felt that these assessments were operator dependent and could lack consistency. Assessing location of wheeze was also considered difficult to undertake and would prevent universal uptake.

Kerem *et al* (1991) developed an instrument for use in acute childhood asthma. This instrument contained five items (heart rate, respiratory rate, wheezing, skin colour/feeding, oxygen saturations) (125). The items would be scored on a scale from '1' to '3'. The HCPs found this instrument to be *"nice and simple"*, not *"operator dependent"*, provided objective values and was *"easy to interpret"*. Age was raised as a concern and whether this was taken into account with criteria such as heart/respiratory rate. Documenting activity, for example asleep or crying, at the time of using the instrument was also discussed and considered important to include.

4.7.4 Ranking activity: prioritisation of *'worsening'* signs and symptoms

4.7.4.1 'Mild' bronchiolitis group

The 'mild' HCP group considered signs and symptoms for those infants who could be managed at home or improving hospitalised infants who were being considered for discharge **(Table 14)**. They decided that they could not rank these items in order of importance as they all had *"equal significance"*. The 'mild' HCP group suggested that if the infant was being considered for hospital discharge: information on oxygen requirements would be required. History of apnoea was believed to be definite admission criteria. *"Work of breathing"* was considered *"relative to what they were doing at the time"*. They felt that oxygen saturation thresholds should be greater than 92% in air. An exception to this would be if the infant looked unwell then this might trigger them to consider admission. The example they gave would be an infant who looked *"mottled"*, with *"heart rate up"* but with *"good saturations"*. The HCPs felt they *"would want to know the day of illness"* to help decide if the infant was going to

improve or worsen. Although, they felt this information *"might not stop us [HCPs] from necessarily sending them [infant] home"*. One HCP from one of the other two groups disagreed with the 'mild' group's inability to rank the signs and symptoms. This HCP felt saturations and feeding should be prioritised:

> *"I would put saturations and feeding as the top two regardless of all the others if I was thinking of sending them home...they didn't need oxygen and they were feeding ok then there would be absolutely nothing that I would be doing in hospital that I wouldn't be doing at home"* (HCP 14).

A discussion arose amongst the whole group over the benefits and consequences to prioritising saturations and feeding over other signs and symptoms. Increased heart rate was argued for as being *"a good red flag"* indicator. Although, one of the 'mild' group HCPs suggested when assessing an infant you *"look at the all over picture"* which makes it difficult to prioritise particular signs and symptoms.

4.7.4.2 'Moderate' bronchiolitis group

The 'moderate' bronchiolitis group considered signs and symptoms for those infants who required hospital admission. The reported that the 'moderate' group *"covered"* everything that was discussed with the 'mild' [group] but being more *"specific"* for example, HCP 15 described:

> *"…oxygen […] saturations less than 92% in air …'cause you are going to admit them …but probably requiring less [than] 50 [percent oxygen] to maintain saturations greater than 92%..."* (HCP 15).

Important negatives, which could mark "severe" work of breathing included: no head bobbing, nasal flare, sternal recession or audible grunt heard. Apnoeas

were thought to indicate that the infant is *"getting knackered"* and may need intervention. Feeding was thought to be *"difficult"* and should be considered in conjunction with age. The 'moderate' group suggested that an infant less than six months they would be taking 75mL/kg/day whilst infants aged over six months would take 500mL/day. It was thought that nasogastric (NG) feeds and intravenous (IV) fluids may be used to *"differentiate the severity"* within the moderate category but does not necessarily *"differentiate between 'moderate' and 'severe'"*. An upper threshold limit of 60 was used for respiratory rate based on Advanced Paediatric Life Support (APLS) criteria. Whilst the upper threshold limit decided for heart rate was 160 beats per minute (bpm). It was noted by one HCP (HCP 05) from the main group that respiratory rate may increase if the infants' nose is obstructed with either *"vomit"* or *"snot"* and the respiratory rate will *"drop back down"* following removal of the obstruction. Consciousness level was included and considered important, particularly for less experienced HCPs. However, the HCPs found it difficult to *"differentiate"* which items were *"more important"* when assessing level of consciousness. During the whole group discussion HCP 15 suggested including a comments box to document whether the infant has had an intervention. Overall assessment was still felt to be *"quite subjective"* by one HCP (UIF). Whereas HCP 15 suggested:

> *"…if you scored for all of these …in theory it's supposed to make it less subjective and more objective…"* (HCP 15).

4.7.4.3 ‘Severe’ bronchiolitis group

The ‘severe’ group found it difficult to decide which sign or symptom should be ranked first so presented the signs and symptoms which they had ranked second, third, and fourth initially. Hypoxia despite supplemental oxygen was ranked second, reduced respiratory rate ranked third and abnormal blood gas results ranked fourth. The general consensus was *“general appearance”* should be ranked first although it was thought not *“particularly helpful”* for an *“objective”* instrument. Although HCP 14 explained:

> *“…you look at them […] and think I am worried about this one …”* (HCP 14).

The ‘severe’ group proceeded to try and objectify *‘general appearance’* by including *“colour”*, *“activity”*, *“tone”* and *“consciousness level”,* but thought the instrument could become *“busy”*. During the general discussion HCP 02 commented on how PEW scores only pick up *“50% of cardiac arrest calls”* whilst 50 percent of the time HCPs will rely on their *“gut instinct” […] no matter how good it [LIBSS-PRO] is…”*. Furthermore, it was suggested that *‘gut instinct’* should be included at the beginning of the scoring instrument. *“Parental concern”* and using *“mum as the expert”* was also suggested for inclusion, although HCP 15 felt this needed to be qualified by *“sensible parents”*. The researchers observed that wheeze had not been included by the HCPs as a symptom for consideration into the scoring instrument in spite of being included as an item within the six scoring instruments in the previous exercise. When asked to confirm whether wheeze should be excluded from the scoring instrument the whole HCP group were unanimous. Wheeze was considered helpful for diagnosis but not for assessing severity of bronchiolitis.

Table 14: HCP Workshop NGT Ranking Exercise

‘Mild’ bronchiolitis group	‘Moderate’ bronchiolitis group	‘Severe’ bronchiolitis group
“Fit to go home” Overall picture Saturations >92% in air and not requiring oxygen (review of recent oxygen requirement) Apnoeas Work of breathing Perfusion/heart rate Feeding in/out AVPU Day of illness (consider for discharge and discuss with parents) Underlying medical condition Social circumstances	Oxygen saturations: <92% in air requiring <50% oxygen Respiratory effort: intercostal/subcostal recession, tracheal tug without head bob/nasal flare, sternal recession. No audible grunt at the end of the bed. No apnoeas Feeding: < 50% 150mL/kg – < 75mLs/kg/day orally. NG requirements – able to tolerate. > 6 months old – 500mL/day (on diet) plus wet nappies Respiratory rate: new-born – 1 year 40-60 bpm. > 1 year 55bpm HR/circulation: new-born to 1 year 120-160 bpm. >1 year 100-140. CRT $\underline{<}$2 seconds Conscious level: consolable, spontaneous movements, normal posture, alert, interested in surroundings	General appearance (colour, activity, tone, ?AVPU) Hypoxia in spite of supplemental oxygen Reduced respiratory rate/apnoeic spells +/- bradycardia Increasing or persistent pCO_2 Work of breathing Risks (ex prem, CLD, neuromuscular)

4.7.5: Round-robin exercise to identify *‘improving’* signs and symptoms of bronchiolitis

The feedback from the ‘improving’ round robin exercise identified n=7 ‘mild’, n= 5 ‘moderate’ and n=8 ‘severe’ signs and symptoms **(Table 15)**.

Table 15: Improving signs and symptoms

‘Mild’ bronchiolitis group (n=7)	‘Moderate’ bronchiolitis group (n=5)	‘Severe’ bronchiolitis group (& getting better) (n=8)
Less nurse interaction – mum etc can care Less effort Probably at home so don’t see them Parents get confident Less medical intervention Less disturbed sleep Hardly any suction	Not requiring oxygen Feeding better Normal behaviour Better colour Less suction	Reduced oxygen requirements Increasing oxygen saturations Respiratory rate returns towards normal Increasing blood gases Looks better Coping without respiratory support Feeding recommenced and tolerated Parents happier

HCP 14 (from the ‘severe’ group) suggested it was the *“opposite of everything else”* that was discussed for ‘severe’ in the previous exercise, although additional items were suggested such as: *“not requiring interventions”*; *“feeding commenced”* and *“happier parents”*. One HCP (UIF), from the ‘mild’ group, described how there would be *“less nursing interaction”* and the *“parents getting confident”* in taking over the care of the infant. A discussion ensued over discharge criteria, particularly with regards to oxygen saturation thresholds and at what point oxygen saturations should stop being measured as HCP 14 explained:

> *“…you have these babies that are feeding fine…they are not working particularly hard with their breathing…but their [oxygen] saturations are kind of 90…91% when they are asleep…eventually the go home a couple of days later and you haven’t done anything to them…”* (HCP 14).

Other HCPs reported how the parents become reliant on the oxygen saturation monitor, would be *"looking at the numbers"* and become *"freaky"* if the monitors were switched off. The oxygen saturation thresholds were contrasted to the lower thresholds accepted for infants with CHD as HCP 15 described:

> *"…we let cardiac babies run at eighty five…acceptably for months and months if not years on end"* (HCP 15).

Having different thresholds for supplemental oxygen requirement and discharge criteria may lead to confusion with the parents as one HCP (UIF) noted:

> *"…the trouble is that we have spent how many days telling parents we want their sats to be above 92 and then we are then saying no…now you can go home at 91…"* (HCP UIF).

Another HCP reflected on how historically clinicians would gauge the infant being fit for discharge based on the infant's appearance:

> *"I mean what did we do years ago before we got obsessed with looking at sats? […] you would look at their colour"* (HCP 03).

4.8 Conclusion

A group of HCPs (n=18) identified a total of 73 *'worsening'* and 20 *'improving'* signs and symptoms for potential inclusion into the LIBSS-PRO. When appraising scoring instruments the HCPs wanted an instrument that was simple, easy to calculate, could score a change, age specific and easy to interpret the score. The HCPs also obtained consensus over criteria for an infant with 'mild', 'moderate' or 'severe' bronchiolitis.

The strength of this group workshop was the diverse group of HCPs of different grades and from different clinical settings, which should make the findings generalisable to the wider HCP population. As with the family group, using NGT to identify and achieve HCP consensus on signs, symptoms and severity criteria, increases the validity of the data collected. Furthermore the data obtained from the HCPs compliments the data from the family stakeholder group workshop. The bronchiolitis signs and symptoms identified from both workshops were broadly similar with significant overlap.

However, the large sample size of the group was also found to be a limitation. Transcribing the audio recordings proved difficult as distinguishing voices especially when more than one person was speaking at the same time was troublesome. In respect to this problem, the field notes made by the observer assisted with the transcription and analysis.

Chapter Five

5 Parent interviews

5.1 Introduction

This chapter describes the methods used and the results obtained from undertaking semi-structured interviews (telephone or face-to-face) with parents (including carers or legal guardians) of infants with bronchiolitis. In-depth key informant interviews are recommended to exploit the unique knowledge and experience of important stakeholders (52). These semi-structured interviews aimed to add a greater depth to and corroborate the findings from the family workshop, particularly as the sample size of the family workshop was smaller than anticipated.

5.2 Aims

The main aims of these interviews were:

- To identify signs and symptoms of bronchiolitis for potential inclusion as items in a bronchiolitis severity score;
- To contribute towards the development of a bronchiolitis conceptual framework.

5.3 Sample and setting

Recruitment for the interviews was undertaken over two bronchiolitis seasons: 2011/12 and 2012/13. Participants were identified from five hospital sites (one paediatric tertiary centre and four DGHs) through the Cheshire and Merseyside CLRN. Participants were parents (including carers or legal

guardians) of an eligible infant who had been recently discharged from hospital (within two weeks) with a clinical diagnosis of bronchiolitis. A purposive sample frame was devised **(Appendix 29)** to ensure adequate representation of individuals with a wide range of experience. Eligible infants were stratified by age, gender and severity of illness. CLRN research nurses initially approached parents during their infants' hospital stay with information about the research. Parents or carers who expressed an interest in participating were contacted via telephone by CvM and provided with further verbal information about the interviews. Interviews were arranged to take place within two weeks of hospital discharge. The short two week time period between hospital discharge and interviews was chosen to reduce the possibility of recall bias.

5.4 Informed consent

Information (written and verbal) was provided to parents prior to the infant being discharged from hospital. Parents were given time to consider this information before written informed consent was obtained by either CvM or from a CLRN research nurse. At the beginning of each interview CvM went through the consent process again and obtained an audio-recorded verbal consent off the parent.

5.5 Methods

One researcher (CvM) conducted all of the interviews. Parents were offered the option of either a telephone or face-to-face interview arranged at their convenience. Either a CLRN research nurse or CvM obtained informed written consent from all participants prior to the interview. At the beginning of each

interview CvM provided brief information on the research aims and checked that the parent still gave consent for the interview to proceed. The interviews lasted between 20-60 minutes. All interviews were digitally audio recorded (Tascam DR-100). The recordings were transcribed verbatim and anonymised prior to analysis (CvM). The interview schedule was based on the findings from the family workshop **(Table 17)**. Probe questions were used in addition to the questions contained in the interview schedule. CvM took handwritten notes during the interview.

Table 16: Parent interview schedule

Question 1	Who is in your family?
Question 2	What prompted you to seek medical help when your baby became unwell?
Question 3	How could you tell your baby was improving?
Question 4	What is your previous experience/knowledge of bronchiolitis? What information would you have liked? What format/provision?
Question 5	What could have improved your experience of having a baby with bronchiolitis?

5.6 Analysis

The process of analysis was iterative and the interview transcripts were examined and re-examined several times during the course of the analysis. An initial examination of the transcripts provided an overview of what the parents talked about and any general impressions, key ideas or potential concepts. Following this a descriptive thematic analysis was undertaken (124). This process involved manually coding the raw data then collapsing the codes into broader themes. Codes and themes were inductively derived from the data. As new codes emerged, these were applied iteratively, as appropriate, to the whole data set in subsequent examinations of the data sources until no new

codes or themes were identified. As data analysis progressed some codes were merged or discarded and themes were further developed, refined and some discarded. This resulted in a final set of codes and themes. A descriptive memo was produced for each of the final themes that summarised what the theme represented. QRS NVIVO (Version10) software was used to support the coding and synthesis of the data. Field notes were used to support the analysis and enabled the researcher to reflect on the interviews and record any thoughts and insights.

5.7 Results

The aim was to recruit approximately 15 parent participants. Informed consent was obtained from 22 parent participants. However, CvM was unable to make contact with six parents by telephone to arrange the interviews within the time period of two weeks, therefore it was assumed that these parents were either unavailable or no longer wished to participate with the study and they were classed as withdrawals. Interviews were obtained from the remaining 16 participants (one face-to-face interview and 15 telephone interviews). Technical problems with the audio recorder occurred with two interviews (P 05 and P 06). One interview (P 05) was partially recorded and one interview recording (P 06) failed completely. Parent names were anonymised with the following labels P 01, P 02, P 03…etc. For the purpose of anonymity all given names of family members have been changed within the narrative. The data generated from these interviews were used to support the development of the scoring instrument. The presentations of themes have been structured under the following headings*: 'worsening signs and*

symptoms', *'improving signs and symptoms'*, *'parental knowledge of bronchiolitis'* and *'parent experience'*.

5.8 Family demographics

Parent and family characteristics are presented in **Table 18**. The sample comprised one father and 15 mothers. The predominant ethnicity amongst the families was White British (n=9) with the remaining families being of mixed race (n=2). There were no data available on ethnicity for five families. Most of the families consisted of parents who were either married or cohabiting (n=15). Two of these families were blended and included children from a previous relationship. There was one single parent family. The number of children within each family varied. Four families had either one (n=4) or two (n=8) children. There were four larger with either three (n=1), four (n=2) or six (n=1) children. The majority of the infants admitted to hospital were aged below three months (n=10). There were five infants aged three months and older; data were missing for the age of one infant. Gender was evenly split between male (n=8) and female (n=8) infants. There were three sets of twins with bronchiolitis. Most infants had been categorised as having 'moderate' (n=9) bronchiolitis. Five infants were categorised as 'severe' and only two infants were categorised as 'mild'. Four infants had one or more risk factor for 'severe' bronchiolitis (prematurity (n=3), chronic lung disease (n=1), congenital heart defect (n=2)). Two infants had had more than one bronchiolitis episode.

Table 17: Parent or carer characteristics

Parent	Marital status	Infant age	Infant gender	Bronchiolitis severity	Infant ethnicity	Number of children in family	Risk factors
P 01 (Father)	Married	>3 months	Female	Moderate	*m/d	Two	Premature *CLD *PBE
P 02 (Mother)	Cohabiting	<3 months	Male	Moderate	*m/d	One	
P 03 (Mother)	Married	<3 months	Female (twins)	Severe (HDU)	*m/d	Three	
P 04 (Mother)	Married	<3 months	Male	Moderate	*m/d	Two	
P 05 (Mother)	Married (blended)	<3 months	Male (twins)	Severe (PICU)	White British	Six	
P 06 (Mother)	Married	>3 months	Male (twins)	Mild	*m/d	Two	Premature
P 07 (Mother)	Married	<3 months	Female	Severe (HDU)	Mixed race	Two	
P 08 (Mother)	Single	*m/d	Female	Severe (HDU)	White British	Two	
P 09 (Mother)	Cohabiting	>3 months	Female	Moderate	White British	Two	
P 10 (Mother)	Cohabiting	<3 months	Male	Severe (PICU)	White British	Four	
P 11 (Mother)	Married	<3 months	Female	Moderate	White British	One	
P 12 (Mother)	Married	<3 months	Female	Mild	Mixed race	One	
P 13 (Mother)	Married	>3 months	Male	Moderate	White British	One	*CHD
P 14 (Mother)	Married	<3 months	Male	Moderate	White British	Two	
P 15 (Mother)	Married	<3 months	Male	Moderate	White British	Two	
P 16 (Mother)	Cohabiting (blended)	>3 months	Female	Moderate	White British	Four	Premature *CHD *PBE

*m/d: missing data; *CLD: chronic lung disease; *CHD: congenital heart disease; *PBE: previous bronchiolitis episode

5.8.1 *'Worsening'* bronchiolitis signs and symptoms

This theme describes *'worsening'* bronchiolitis signs and symptoms as identified by the parents. This theme has been divided into two sub-themes*: 'seeking help'* when the parent first suspects the infant is unwell and *'hospital admission'* where parents observe signs of further deterioration during hospital admission. The *'worsening'* bronchiolitis signs and symptoms were broadly related to changes in physiology, appearance and behaviour.

5.8.1.1 'Seeking help'

Several parents often reported a family member (parent/sibling), having a *"cough"* or *"cold"* that preceded the infant becoming unwell. In the early stages of bronchiolitis, parents noticed signs and symptoms attributable to a common cold: *"cough"*; *"runny"/"blocked nose"* and *"snuffly"*. The *"cough"* appeared to be of particular concern for parents. This symptom alone was significant enough for thirteen parents to decide to *'seek help'*. The *"cough"* was characterised as being *"noisy"*, *"bad"*, *"nasty"*, *"chesty"*, *"wet"*, *"irritating"* and *"wheezy"*. Parents likened the sound of the *"cough"* to *"an orchestra"* or to *"smoking 60 fags a day"*. Furthermore, parents reported how the infant would have *"coughing fits"* with *"a lot more effort going into the cough"* than usual causing the infant to go *"bright red and purple"*. In addition to these cold-like symptoms parents witnessed the infant not seeming themselves explaining that the infants were: *"unsettled"* and *"irritable"*, *"not feeding well"* and had altered sleeping patterns. Five parents reported measuring their infant's temperature in the early stages of bronchiolitis although all reported that the infant's temperature initially fell within the normal range. One parent, who had previously heard of bronchiolitis, incorrectly assumed her infant did not have bronchiolitis *"because she didn't have a temperature"*. A small proportion of these infants went on to develop a high temperature as the illness progressed, usually after the infant had been admitted to hospital. Other early signs and symptoms observed were related to changes in the infants' breathing. Parents recalled how their infant was *"wheezing"* (n=6), *"finding it difficult to breathe"* (n=8) and had *"mucous coming out of their mouth and their nose"* (n=4). These signs and symptoms prompted parents to *'seek help'* and advice from a HCP

usually based in a primary care setting (GP surgery, GP out of hours, Walk-in Centre). The timing of *'seeking help'* varied between parents. Some parents would *'seek help'* soon after the infant became unwell:

> *"…at first it was just a little cough […] now and again […] it was getting a little bit worse so I took her to the out of hours…"* (Mother, P 08)

However, others were not overly concerned initially, choosing to delay *'seeking help'* until the signs and symptoms were perceived to have *'worsened'* over a period of time:

> *"…the baby started having a cough and a runny nose and it didn't worry me too much…it was just like an occasional cough […] then […] after three days she got like really ill like from the morning when we woke up she couldn't breathe very well and she had stopped feeding…"* (Mother, P 07).

When *'seeking help',* a diagnosis or a differential diagnosis of bronchiolitis in a primary health care setting was not often provided by HCPs. Parents reported receiving nebulous diagnoses such as *"it's a cough"*, *"just a cold"*, *"catarrh"*, *"chest infection" or "virus"*. Furthermore, parents reported receiving a limited explanation as one mother recalled:

> *"He [the GP] didn't explain what sort of virus he just said it was a virus…"* (Mother, P 13).

Treatment, management advice and guidance were also found to be inconsistent. Some parents received prescriptions for antibiotics or salbutamol inhalers, some were provided with limited advice on *'worsening'* signs and symptoms, whilst others were just told to *"come back if they [their infant] gets*

worse" without explaining what was meant by getting *"worse"*. However, one parent did ask for clarification from her GP:

> *"I sort of said 'What am I looking out for?' …thinking that this was a straight cold at this stage […] he said 'If she doesn't feed….you know the key things are if she stops feeding well and if she becomes less alert' …so those were the things I was looking out for from the point of view of expecting a cold"* (Mother, P 11).

As the illness progressed, parents noted continued deterioration in breathing difficulties, feeding, appearance and behaviour. Parents reported their infants' breathing was *"really fast"* or *"laboured"*. Some parents spotted a change in the breathing pattern with it becoming more *"irregular"* or *"pausing"* for a few seconds. This increased effort of breathing was characterised by the parents explaining how the infant's *"chest would "suck in"* as would the area *"between his collar bones",* the *"stomach seemed to be going in and out a lot"*, the *"head was sort of going up and down",* and the *"nostrils were going"*. One parent witnessed her daughters' lips turn *"blue"*. Feeding continued to be problematic with feeding patterns changing in terms of volume and frequency; milk was taken *"little and often"*. Feed intake was significantly *"reduced"* or the infant *"stopped"* feeding completely. Feeding difficulties were perceived to be related to either a *"stuffy nose"* or the infant not being able to *"suck well enough to feed"*. Parents suggested increased vomiting was a particular issue as infants' were not *"keeping bottles down"*. A general perception amongst parents was that feeding appeared to make the infant *"struggle to breathe"*. Parents whose ethnicity were white/British described how the infant would appear *"pale"* and/or *"grey"* as they worsened. In general infants who were

worsening were described as *"limp"*, *"lethargic"*, *"unresponsive"* and having *"reduced activity"*. *"Dull"* appearance, *"sunken eyes"* and *"eye rolling"* were also seen. One mother described how her twin boys *"wanted to be held a lot"* and *"kept upright"*. These *'worsening'* signs and symptoms caused concern and prompted parents to *'seek help'* either from their GP surgery, Walk-in Centre, ED, or consult an NHS website or NHS Direct. At this stage in the illness, parents who *'sought help'* from a primary care setting or NHS Direct were referred to ED. Two parents *'sought help'* directly from ED. One parent described her daughter's deterioration and her journey to ED:

> *"…she just become […] not hungry and sleeping a lot […] then she missed her 11 o'clock feed at night […] I kept an eye on her and within two hours she had gone completely grey and her lips were going blue […] I noticed her breathing… she was breathing from her stomach and her head was bobbing so I got straight up to hospital by taxi…not realising how ill she was….and within an hour she deteriorated […] she was […] on cpap in erm ICU…"* (Mother, P 16).

This parent did not appear to appreciate that the *'worsening'* signs and symptoms she observed indicated severe respiratory distress and were potentially life threatening. This mother reflected back on her own lack of knowledge and the inappropriate use of a taxi to get to the ED. For those parents who attended ED, the infants were triaged and either admitted to hospital for treatment or monitored in an observation area prior to being either admitted or discharged. Three infants were discharged home. In all three cases the infants deteriorated further, re-attended ED and were admitted to

hospital within a 24-hour period. One mother describes her apprehension at returning home with her sick infant:

> *"…I was very anxious about that actually because of how long they had monitored him for …it was six or seven hours […] the triage nurse […] said he'd almost definitely be admitted with the way he was breathing and obviously when the Walk-in centre had called an ambulance that was quite a dramatic thing to do really […] to hang around for six or seven hours just to be sent home …and the doctor…her words were 'he is on the cusp of being admitted'…and I felt that with such a small baby he shouldn't have been on the cusp of being admitted […] I felt that he should have stayed in"* (Mother, P 13).

Another mother, with previous bronchiolitis experience, felt more confident in returning home with her sick infant but reflected on how she may have felt if she had not had prior experience:

> *"I felt alright because I'd had a child who'd had bronchiolitis before and he was premature and in and out of SCBU [special care baby unit] […] so felt quite confident about the things that I needed to look out for […] I think maybe if I hadn't of had that experience […] I probably would have done one of two things…I'd either of felt very uncomfortable taking him home or the next morning maybe not reacted when I should have done…"* (Mother, P 15).

Some parents recounted how certain risk factors such as young age, were also taken into consideration when HCPs were deciding to admit to hospital as illustrated by one mother:

"…and then they decided to admit him because he was so small…" (Mother, P 04).

5.8.1.2 'Hospital admission'

For most parents, bronchiolitis was diagnosed at hospital using clinical signs and symptoms. HCPs obtained nasal pharyngeal aspirates from infants to look for the virus that was causing the signs and symptoms. Some were told their infant was:

"…positive for the RSV virus…" (Mother, P 13).

Once admitted, parents became aware of other *'worsening'* signs and symptoms from conversations with HCPs including reduced oxygen saturation levels, increased heart rate, increasing oxygen requirements, capillary blood gas results and exhaustion:

"…Monday night they were just monitoring him […] they were just checking his sats every hour […] Tuesday morning they put him on oxygen […] the oxygen levels were supposed to be above 92 and they kept dropping…" (Mother, P 04).

Some infants were admitted for observation whilst others required respiratory and/or feeding support. The type of respiratory support received would depend on the severity of symptoms but included oxygen therapy via nasal cannula, face mask or head box or NIV/invasive ventilation. Irrespective of the type of supportive therapy, parents found these therapies to be *"horrible"* as they acted as a barrier between them and their infant. Parents felt they were unable to *"touch"* (n=2) their infant and felt *"completely helpless"* (n=1);

"…it doesn't mean that it is any less terrifying to see your tiny baby with a tube down and when she is in a head box you can't touch them…" (Mother, P 11);

and reported experiencing a loss of control;

"…when they did the blood oxygen levels again […] they found that the levels had dropped […] they made the decision […] to put her on the CPAP ventilator […] I was absolutely heartbroken because I thought that was it and they did try and explain it the best they could but obviously it was still very hard because you just feel like you are losing complete control of everything…" (Mother, P 03).

5.9 *'Improving'* signs and symptoms

Similarly to *'worsening'* bronchiolitis *'improving'* signs and symptoms were related to changes in vital signs, appearance and behaviour. Parents primarily took their cues for improvement from either HCPs or from the technology used to monitor their child:

"…you are clearly very led by the doctors […] I mean you can tell from the monitor […] but there were lots of updates I felt like the nurses and the doctors were quite good at keeping me informed about progress" (Mother, P 11).

One parent commented on how they became *"too* reliant*"* on the monitors for information and how they then had to revert to using physical signs when the monitoring was discontinued:

"…you do almost become a bit too reliant on...staring at what their sats are or what the pulse rate is...I mean eventually when we obviously

didn't have their sats monitors I would look at the effort they were making in terms of their breathing, looking at whether they were tired or whether they were coping with their feeds the same sort of physical signs…" (Mother, P 03).

Other observations reported by parents included improved breathing, the infants required *"less effort"* to take a breath and had improved blood gas results, and a return to the infants' *"normal routine"* particularly with regards to sleep patterns and feeding. The infant appeared more *"alert"* and *"active"*, *"smiling"*, *"less irritable"* and their colour had improved. Parents noticed that as the aforementioned signs and symptoms *'improved'* their infant required less supportive therapy: non-invasive/invasive ventilation and oxygen would be weaned. Parents reported their infant would start to become more "*demanding"*, *"difficult to look after"* and less tolerant of supportive therapies. Cough was reported to be one of the last symptoms to improve, and although it became less *"distressing"*, *"frequent"* and *"noisy",* it could still disrupt sleep.

5.10 Bronchiolitis conceptual framework

Using the conceptual framework created in the family workshop: the *'worsening'* and *'improving'* bronchiolitis signs and symptoms identified from the interviews with the parents and carers were condensed and included under the relevant domains **(Table 19)**.

Table 18: Conceptual framework of bronchiolitis (parent interviews)

	Domains	Sub-domains: associated signs and symptoms	
		***'Worsening'* n=41**	***'Improving'* n=18**
Bronchiolitis	**Breathing**	**n=15**	**n=4**
		Wheezy and crackly Chest in-drawing Tracheal tug Grunting noise Oxygen levels dropping Increased respiratory rate Blood oxygen levels dropping Pulling right under his ribs to breathe Laboured breathing Nasal flare Noisy breathing High carbon dioxide Head nodding Protruding stomach Pauses in breathing	Sats [oxygen saturations] had improved No chest in-drawing Not as wheezy Breathing: not struggling; improved; not heavy; less noisy; less effort
	Colour change	**n=4**	**n=1**
		Grey Pale Coughing (bright red & purple) Blue lips	Colour as well picked up (pink)
	Cough	**n=6**	**n=1**
		Cough (chesty, wet, rattly, nasty) Snuffly/snotty/mucous/phlegm Cold symptoms Runny nose Blocked nose Sneezing	Still coughing
	Body language	**n=16**	**n=12**
		Listless/lifeless/lethargic/quiet Clingy Not them self Poor feeding Feeding: little and often Niggly/grumpy/unsettled/inconsolable Vomiting Limp Not as active Worse at night Not responding to pain Exhausted Increased heart rate Weight loss Sunken fontanelle Eyes (rolling/red/sunken)	General manner/appearance Smiling More active Gradually weaned treatment Improved feeding Information from monitoring Alert Sleeping less/more awake Less irritable/more content More demanding Return to normal routine Bright eyes

The data from the parent interviews was compared and contrasted with the data from the family workshop to assess for concordance. Overall the parent descriptions of *'worsening'* and *'improving'* bronchiolitis signs and symptoms were broadly similar and could be categorised under the four domains identified in the family workshop: breathing; colour change; cough; body language. This similarity between the family stakeholder workshop and the parents interviews provides confirmatory evidence to suggest the experience of the family workshop parents However, a small number of additional signs and symptoms were identified from the parent interviews and have been included into the conceptual framework these being: breathing (wheeze, grunting, altered oxygen saturations, carbon dioxide levels); and body language (clingy, worse at night, weight loss, sunken fontanelle, eyes (rolling/red/sunken)). With the exception of weight loss and worse at night these additional signs and symptoms were previously identified from the either the literature or the HCP stakeholder workshop.

5.11 Conclusion

The parent interviews identified a total of 41 *'worsening'* and 19 *'improving'* signs and symptoms. These signs and symptoms have been included as items under the domains of the conceptual framework developed from the data generated by the parents who attended the family workshop. There was significant overlap between the signs and symptoms identified from the family workshop and parent interviews although a small number of additional signs and symptoms were identified. The parent interviews were a later addition to the study following the small number of parents who attended the family

stakeholder group workshop. Due to having to submit an ethics amendment the parent interviews were not completed and analysed prior to Phase II of the study. Therefore it was not possible to incorporate the two additional symptoms identified (weight loss and worse at night) for consideration as items into the LIBSS-PRO. This could be considered a study limitation.

The strength of this study was with the sampling strategy. The strategy ensured there was a cross-section of parents' with infants of varying age, gender and severity. Furthermore, some infants had risk factors for severe disease. Recruiting parents from five study sites across the Northwest of England ensured parent perspectives were obtained from different localities and social groups. However, similar to the family workshop, an identified limitation of the sampling strategy was the under-representation of ethnic minority groups. Therefore these findings may not be generalisable to other population groups. Furthermore, mothers were the dominant parent and/or carer participating with the interviews. The inclusion of more fathers may have provided a different perspective on having an infant with bronchiolitis. In addition, the majority of included parents had infants classified as having 'moderate' bronchiolitis. Consequently, there may be important missing signs and symptoms, pertinent to 'mild' and 'severe' bronchiolitis groups. Parent experience of infants with bronchiolitis in these two groups may also differ resulting in important outcomes not being captured.

Chapter Six

6 Delphi consensus survey

6.1 Introduction

The signs, symptoms and risk factors identified from the literature review, stakeholder workshops and parent interviews were reviewed. Similar signs and symptoms were collapsed and merged together and listed under the domains contained in the bronchiolitis conceptual framework previously devised by the HCP stakeholder workshop. A final list was created consisting of 101 signs, symptoms and risk factors identified as potential items for inclusion into the LIBSS-PRO. Incorporating all 101 signs, symptoms and risk factors into the LIBSS-PRO would lack clinical utility: the instrument would be too long to complete in a timely manner by HCPs in a clinical environment so a process was identified to reduce the number. This chapter describes the methods used to obtain consensus over which of the 101 pre-identified signs, symptoms and risk factors to include in the LIBSS-PRO to assess severity of bronchiolitis.

The Delphi technique is an iterative process, which aims to seek consensus from a group of ‘experts’ through a series of structured questionnaires (rounds) (122, 126, 127). For each Delphi round the questionnaires are completed anonymously, the responses collated and fed back to the Delphi panel members until consensus is achieved (126). The Delphi survey has been found to be particularly useful when the included panel members are located across a large geographic region (127).

6.2 Aims

i) To obtain consensus over which of the pre-identified signs/symptoms should be usefully included as items in the scoring instrument.

ii) To obtain consensus definitions for ‘mild’, ‘moderate’ and ‘severe’ bronchiolitis.

iii) To obtain consensus criteria for hospital referral, admission and discharge.

6.3 Sample and setting

HCPs located across the UK and Ireland was invited to participate in a four round Delphi survey. Eligible participants were identified through five hospital study sites (one paediatric tertiary centre and four DGHs) via the Cheshire and Merseyside CLRN. In addition, emails were sent to the corresponding author for bronchiolitis Cochrane reviews and SIGN guidelines. Members of the following professional organisations were emailed: Medicine for Children’s Research Network (MCRN) General Paediatrics Clinical Studies Group; Paediatric Intensive Care Nursing Group; Acute Paediatric Emergency Medicine; Royal College of Nursing Children and Young Peoples Forum. The Delphi survey was also advertised through newsletters to HCPs working for Wirral and Liverpool Primary Care Trusts. There is no statistical method to determine the size of the Delphi panel. A pragmatic decision to recruit between 50-70 participants was based on the sample size reported in other studies (127).

6.4 Informed consent

Written information about the study was included as a separate attachment in the email with the hyperlink for the Delphi survey. The written information was also embedded into the first page of the electronic survey. The electronic survey was designed so that participants had to initially go through a formal procedure to indicate consent with participation otherwise they could not proceed to the next section of the survey.

6.5 Methods

The 101 signs and symptoms, criteria for hospital referral, admission and discharge and criteria for 'mild', 'moderate' and 'severe' bronchiolitis, identified from the literature and stakeholder consultation, were included into an electronic survey. The electronic survey was developed using SurveyMonkey® software and distributed to potential participants between May and October 2011. A hyperlink to the survey was embedded into an email and forwarded to the potential participants with an information sheet. The information sheet provided details of the study, notified potential participants that participation was voluntary and that they could withdraw at any point during the Delphi process. All HCPs who accessed the survey were asked to electronically sign an informed consent form prior to completing the survey. Participants were asked to complete all four rounds. As an incentive to reduce attrition bias, participants were advised following completion of all four rounds they would be entered into a prize draw to win one of three prizes: shopping vouchers to the value of either £100 (x 1) or £50 (x 2). All participants, irrespective of their participation in the previous round, were sent emails inviting them to

participate with each of the four rounds. Follow-up emails were sent out to participants on days seven and fourteen reminding them to complete the survey. Participants were given three weeks to complete each survey round. Withdrawals were classed as those participants who either contacted CvM directly or wrote a comment in the comment box to indicate they did not want to participate with any further Delphi survey rounds.

6.6 Delphi rounds one and two

The aim of round one was to gain consensus over which of the pre-determined signs and symptoms should be included in the scoring instrument. These signs and symptoms were grouped as items under the following domain headings: respiratory; feeding and hydration; level of consciousness; miscellaneous symptoms and risk factors. For each section the following question was posed:

"In an otherwise healthy infant with a clinical diagnosis of bronchiolitis, how important are the following items when assessing severity of illness?"

The participants were asked to rank each item using a Likert scale which ranged between 1 (extremely important) and 5 (completely unimportant). A *'don't know'* answer option was also provided. Participants were asked to supply details of other signs and symptoms not currently listed in the survey that should be considered for inclusion into a scoring instrument. At the end of each section a free text box was offered for any additional comments. Prior to distribution, the survey was peer reviewed and amended by the study steering group members. The survey was pilot tested with ten participants to determine any technical issues with the software, clarity of wording, time taken to

complete the survey and ease of use. The survey was further refined in light of the pilot test. The Delphi survey was not anonymous: a name and email address was required so surveys for subsequent Delphi rounds could be forwarded to participants. This information was kept on a secure password protected NHS computer. However, the data from the returned surveys were anonymised by CvM with the use of identification codes.

The questionnaire data were analysed using SPSS software (Version 22). Demographic data were collected and analysed using descriptive statistics for each participant on profession type, grade, NHS institution and area of clinical practice. An aggregate of the group Likert scores were collated and a percentage, mean (SD) and median (range) was determined for each item score. Consensus was determined *a priori* and considered achieved when greater than 80 percent of participant ratings fell into either the 1-2 (important) or 4-5 (unimportant) categories. Free text comments were saved verbatim into a word document and analysed using a descriptive thematic analysis.

The purpose of round two was to complete the consensus process by providing the participants with the opportunity to re-rank those items which had not achieved consensus in round one. These items were revised in light of the survey comments and included into a second survey for distribution to the Delphi panel members in round two. The question posed to the HCPs for each section was changed to:

> *'Which of the following respiratory items should be usefully included in a clinical severity scoring instrument for infants with bronchiolitis?'*

As for round one Delphi panel members were asked to rank each item on a Likert scale. The Likert scale responses were changed and ranged between

1(strongly agree) to 5 (completely disagree). In addition to the revised survey the Delphi participants were also provided with a summary report of the anonymised collated results (frequencies and percentages) for each included item and free text comments from round one. The Delphi participants were asked to re-rank the items in light of this information.

6.7 Delphi rounds three and four

In round three, Delphi panel members were asked to rate agreement using the same methods as described for rounds one and two, for the following: hospital referral/admission and discharge criteria and 'mild', 'moderate' and 'severe' bronchiolitis. The response categories ranged between 1 (strongly agree) to 5 (completely disagree) and 6 (don't know). In round four, those items which did not achieve consensus criteria in round three, were revised in light of the survey comments and re-distributed to the Delphi participants with the anonymised summary report. The Delphi participants were asked to re-appraise these items in view of this information.

6.8 Results

The questionnaire was emailed to over three hundred HCPs across the UK and Ireland. The aim was to recruit between 50-70 HCPs to act as Delphi participants. One hundred and ninety five HCPs responded to participate with round one. Over the four rounds there was noticeable attrition with each subsequent round **(Table 20)**. Response rates comprise: round two 136 out of 195 (70%); round three 103 out of 195 (53%) and round four 96 out of 195 (49%). The paediatrician HCP group had the least amount of attrition with only a 34% decrease in respondents between rounds one and four. Attrition rates

for the remaining HCP groups rose by 50% or greater by round four. Despite the attrition rate, recruitment for round four still exceeded the original recruitment target.

Table 19: Characteristics of Delphi participants by round

	Round 1 (n=195)	**Round 2 (n=136)**	**Round 3 (n=103)**	**Round 4 (n=96)**
Profession/Role	n (%)	n (%)	n (%)	n (%)
Paediatrician	53 (27.2)	48 (34)	39 (37.9)	35 (36.5)
Children's nurse	101 (51.8)	65 (46.1)	45 (43)	41 (42.7)
Children's nurse specialist/advanced nurse practitioner	16 (8.2)	14 (9.9)	7 (6.8)	7 (7.3)
Physiotherapist	9 (4.6)	4 (2.8)	4 (3.9)	3 (3.1)
Assistant practitioner	1 (0.5)	0 (0)	0 (0)	0 (0)
General practitioner	6 (3.1)	2 (1.4)	2 (1.9)	2 (2.2)
Student (nurse/medical)	2 (1.0)	0 (0)	0 (0)	1 (1.0)
Other	6 (3.1)	3 (2.1)	3 (2.9)	3 (3.3)
Missing data	1	5	3	4

The largest group of HCP participants recruited were children's nurses (51.8%) with 46% of these nurses falling into Agenda for Change pay bands 5 and 6. The next largest group of HCPs were paediatricians (27.2%) who were mostly either consultants (16.9%) or specialty training registrars (8.2%) **(Figures 4 & 5)**. The category *'other'* was made up of, nurse consultant, associate professor, senior lecturer, staff grade, locum, GP partner, research fellow and specialty doctor. Most HCPs (47.2%) were employed in a paediatric tertiary centre. The remaining HCPs were employed by district general hospitals (32.3%), primary care trusts (13.3%) or other healthcare settings (1%) **(Figure 6)**. For the most part, HCP participants principally worked on paediatric medical wards (43.1%) Other clinical environments included: PICU

(19.7%); PHDU (12%); ED (8.2); acute admissions (6.6%) and GP surgery (2.7%) **(Figure 7)**. In addition, 4.9% of HCPs reported working in *'other'* clinical environments such as, community children's nursing, hospital at home, adult ICU (receiving children), clinical lead for deteriorating patients, critical care outreach, paediatric respiratory medicine and regional transport team.

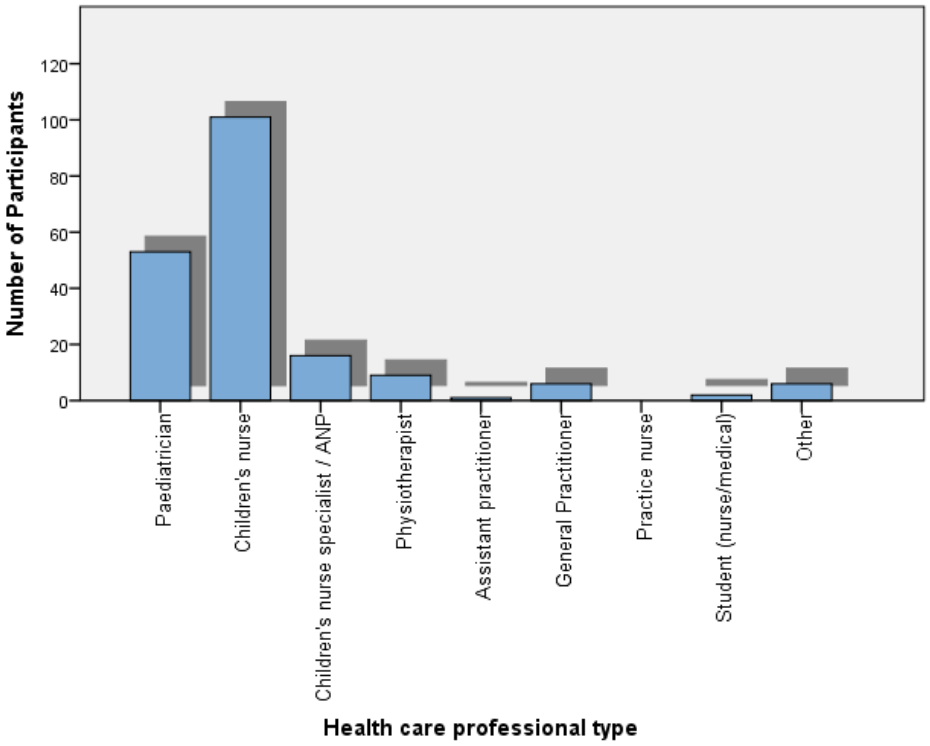


Figure 4: Distribution of HCPs by Profession Type

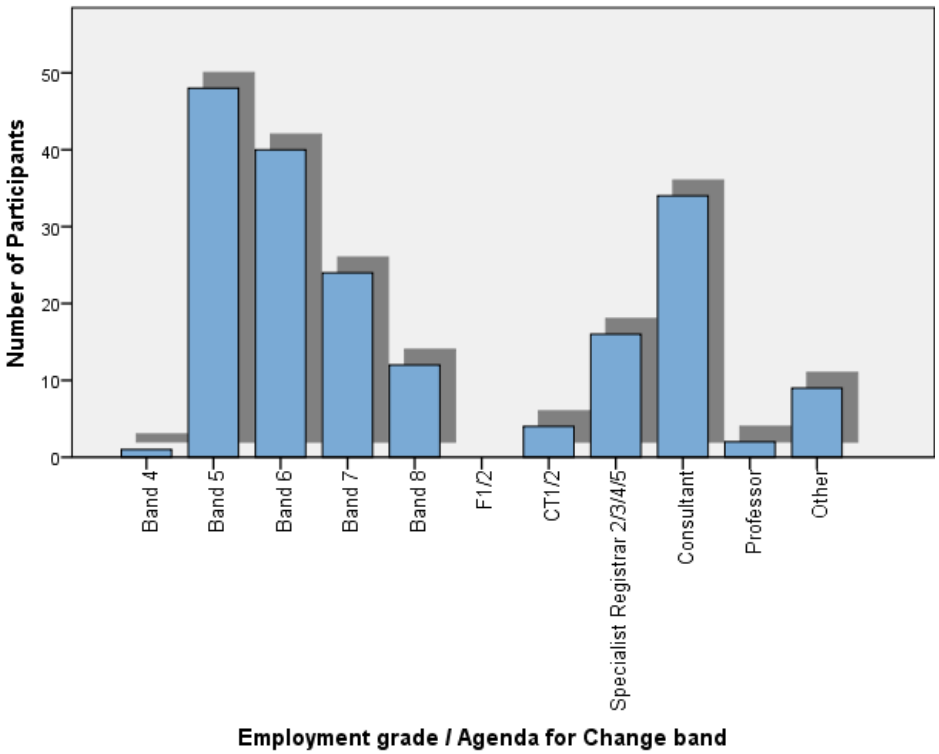


Figure 5: Distribution of HCPs by Grade

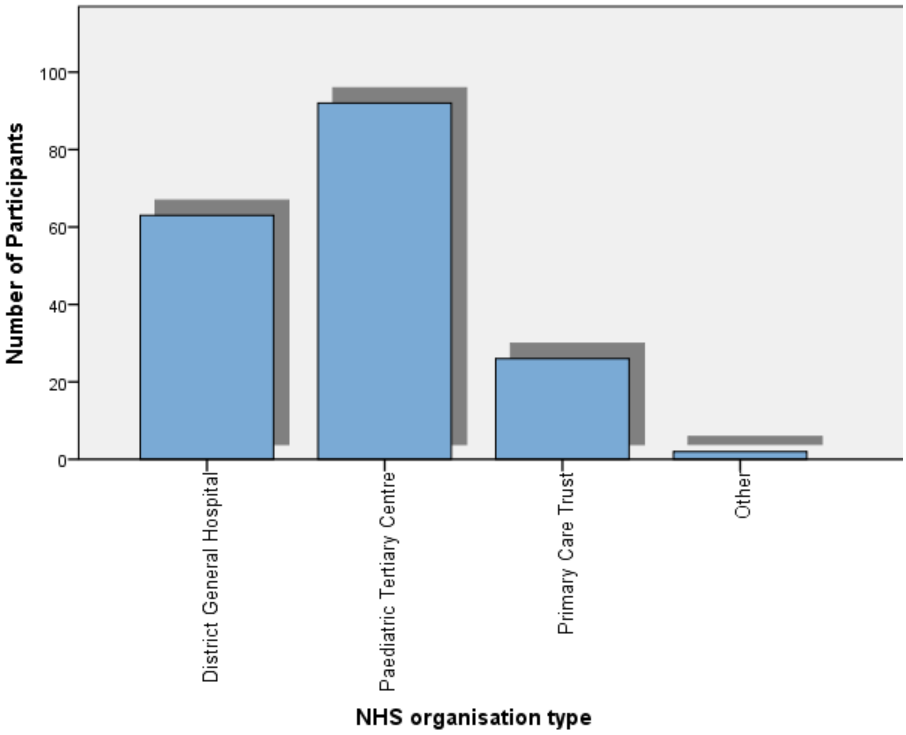


Figure 6: Distribution of HCPs by NHS Organisation Type

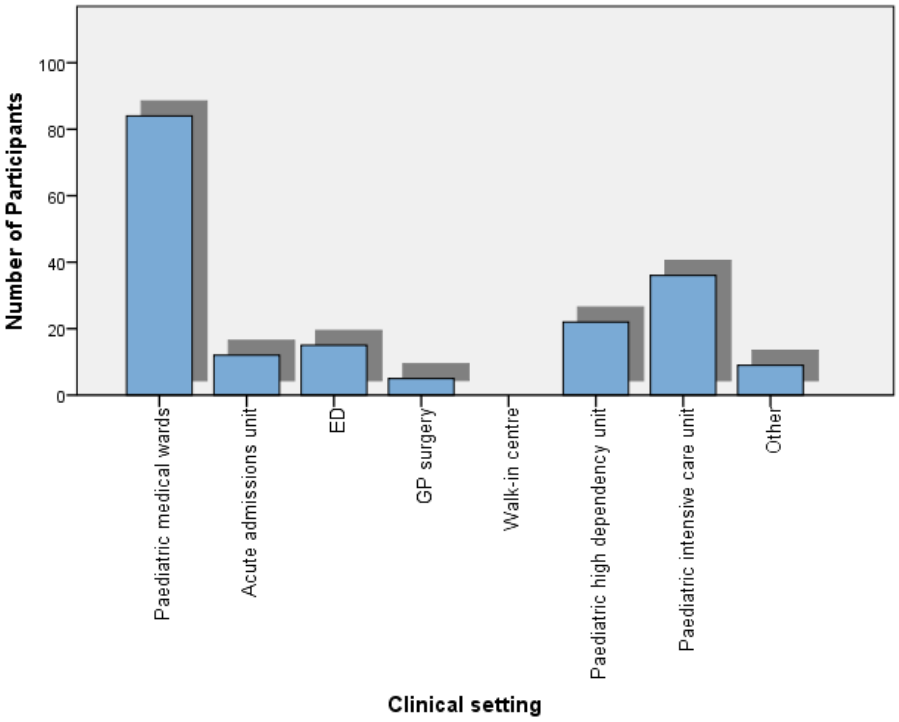


Figure 7: Distribution of HCPs by Clinical Setting

6.9 Delphi rounds one and two

Of the 101 items in round one the item with lowest mean item score was '*unresponsive'* (mean 1.12 [SD 0.36]) whereas the item with highest mean score was for *'suburban residence'* (mean 3.61 [SD 0.98]). Forty four of 101 items achieved consensus criteria of 80 percent or greater for importance (categories 1 & 2), whilst no items achieved consensus for unimportance (categories 4 & 5) in round one following preliminary analysis **(Appendix 30)**. A further three items (clammy skin, convulsion, and altered behaviour), initially met the 80 percent criteria for consensus in the preliminary data analysis, but fell short of meeting the criteria for importance after the data was cleaned and further analysed. Nevertheless, as these three items originally met the criteria and were not included in the round two Delphi survey for re-ranking, they were still classified as meeting the consensus criteria for important. The outstanding 54 items that did not achieve consensus were revised and included into round two **(Appendix 31).**

A descriptive thematic analysis of round one participant comments highlighted a number of issues with trying to rank individual items for *'importance'*. It was felt that it was *"difficult to quantify"* the importance of some individual items in isolation. It was perceived more important to regard combinations of symptoms and how they interact, for example, the effect of feeding on the effort of breathing. Subsequently for the round two Delphi the question was changed from assessing items for *'importance'* or *'unimportance'* to *'agreement'* or *'disagreement'* for inclusion into a bronchiolitis severity score. It was noted that context, history, duration, stage and direction of illness, HCP

experience, HCP type, and clinical setting were additional factors that should be taken into consideration when assessing severity of bronchiolitis. A number of items were challenged as to whether they actually assessed bronchiolitis severity. Some items were thought to contribute more to diagnosis, such as, secretion colour, cough or chest radiograph findings, whilst other items were perceived as being more of a *"complication"* of bronchiolitis, for instance, signs of dehydration. It was suggested that if one item *'stridor'* was present then the diagnosis of bronchiolitis *"must be questioned"*. A number of HCPs recounted poor comprehension of particular terminology, for example, *"air hunger"* and *"rhonchi"*. These items were consequently left unanswered by some HCPs.

Participants were asked to identify additional items not listed in the Delphi survey. Suggestions included PEW scores, trends, type of oxygen support required (for example, HFNC, nCPAP), age, pain score, response to treatment and previous admission to PICU/PHDU. After some consideration by CvM, none of these identified items were included in the round two Delphi survey. This was because:

- Items *'pain'* and *'increasing oxygen requirements'* had been included in the round one Delphi survey.
- Only a very small proportion of infants will have had a previous bronchiolitis episode with a critical care admission and the item *'previous admission/ episode of bronchiolitis'* had been included in round one
- *'Age'* and *'response to treatment'* were both included as criteria statements in round three.

- For PEW score and trends, it was deemed unnecessary to include these as items for consideration in the round two Delphi because the premise of a PEW score is to identify a deteriorating child with any medical or surgical condition. The LIBSS-PRO has a similar premise to the PEW score in identifying deterioration but is bespoke to infants with a clinical diagnosis of bronchiolitis. Including a PEW score within a bronchiolitis score would create some degree of overlap and repetition. Regular use and documentation of the bronchiolitis score would provide information on *'trends'*.

The results for the 54 items included into the round two Delphi found the lowest mean score was for wheezy/noisy breathing (mean 2.11 [SD 0.96]) and the highest mean score was for cervical adenopathy (mean 3.86 [SD 1.08]). Following re-ranking, none of the 54 items achieved the consensus criteria for agreement (categories 1&2) or disagreement (categories 4&5). Therefore none of these items were subsequently considered for inclusion into the LIBSS-PRO. In general the descriptive analysis of the round two comments was similar to and confirmatory of the comments in round one. For example, a lot of the items again were considered as *"diagnostic criteria not indicators of severity",* and highlighted issues of comprehension with certain terms. The AVPU score was generally perceived to be *"the appropriate tool"* for assessing *"level of consciousness"* by HCPs for use in this patient group as opposed to the Glasgow Coma Scale. In addition there were a number of other suggestions such as, changing *"pitch of cry"* to *"strength of cry"*, and separating *"risk factors"* from *"clinical features"* within the score. It was thought that *"risk factors"* could be *"legitimately used to identify which infants to monitor*

more closely […] but they do not measure disease severity". Finally, it was noted that the item *"born second half of the year"* would *"depend upon which hemisphere you were born in"*.

6.10 Delphi rounds three and four

The results of rounds three and four will be presented together under the following headings: Criteria for Referral and/or Admission to Hospital; Criteria for 'mild' bronchiolitis; Criteria for 'moderate' bronchiolitis, Criteria for 'severe' bronchiolitis and Criteria for hospital discharge. The criteria included under these headings were identified from bronchiolitis publications including guidelines and from the criteria developed within the HCP stakeholder workshop.

6.10.1 Criteria for referral and/ or admission to hospital

The following question was posed:

'Which of the following criteria should be used when considering referral or admission to hospital for an otherwise healthy infant, up to 12 months of age, with bronchiolitis...?'

Eighteen different criteria statements were presented under this section. These statements covered thresholds for oxygen saturations in air, respiratory rate and heart rate, presence of specific signs which indicate respiratory distress, fluid intake and output, consideration of risk factors/social issues, duration of symptoms and age at presentation of the infant. The statement with the lowest mean score was *'frequent apnoea'* (mean 1.03 [SD 0.23]) whereas the statement with the highest mean score was *'oxygen saturations less than 97% in air'* (mean 3.98 [SD 0.83]). Six statements achieved consensus for

agreement (categories 1&2) in round three. These included: *'oxygen saturations less than either 92%* (93.2%) or *90%* (95.0%) *in air'*; *'respiratory rate greater than 70 bpm'* (96.1%); *'presence of nasal flare or grunting'* (98%); *'frequent apnoea'* (99%) and *'less than 50% feeds in preceding 24 hours'* (91.2%) **(Appendix 32)**. A further statement *'moderate to severe intercostal or sub-sternal recession'* initially achieved consensus following the preliminary analysis but fell short of the consensus criteria following data cleaning. As this statement was not included into the round four Delphi survey for re-ranking it has been classified as meeting the consensus criteria for agreement. This left 11 statements that did not achieve the consensus criteria for either agreement (categories 1&2) or disagreement (categories 4&5).

Comments from round three proposed the consideration of *"the whole clinical picture"* when contemplating referral or admission to hospital. It was noted that the respiratory rate threshold (greater than 70 bpm) would set *"the bar too high"* for older infants and that respiratory rate *"varied with age"*. *"Duration of illness"* was considered to provide important context when assessing the infant. One participant suggested that they would be less worried if oxygen saturations were "*89% on day 10 of illness"* than if they were *"89% on day 1".*

In round three, consensus for agreement (categories 1&2) was obtained for oxygen saturation thresholds (90% and 92%) and respiratory rate ($\geq$70 bpm) to be considered for inclusion into the bronchiolitis score. It was therefore judged unnecessary to re-rank oxygen saturation and respiratory rate threshold statements, which did not achieve the consensus criteria for agreement (categories 1&2) or disagreement (categories 4&5) in round four. Based on the

round three comments all the other remaining statements that did not achieve consensus were either changed or merged together. Four criteria statements were included in round four*:*

'Raised heart rate at rest greater than 150bpm'; *'parents report a noticeable reduction in number of wet nappies and/or urine output in preceding 12 hours'*; *'consideration of other risk factors, such as, young age, chronic lung disease and congenital heart disease'*; *'duration of symptoms less than three days in combination with other symptoms*'.

After re-ranking in round four a further two statements achieved consensus for agreement **(Appendix 33)**:

'Parents report a noticeable reduction in number of wet nappies and/or urine output in preceding 12 hours' (80%; mean 2.06 [0.64]); *'consideration of other risk factors, such as, young age, CLD and CHD'* (96.8%; mean 1.52 [SD 0.59]).

6.10.2 Criteria for 'mild' bronchiolitis

The following question was posed to the Delphi panel members:

'Do you agree or disagree with the following statements that describe an otherwise healthy infant, up to 12 months of age, with 'mild' bronchiolitis...?'

Twenty different 'mild' criteria statements were developed. These statements covered a range of symptoms related to oxygen requirements, work of breathing, cardiovascular function, hydration and perfusion and neurology. The statement with the lowest mean score was *'will not have cyanosis'* (mean 1.43 [SD 0.74]) and whilst the statement with the highest mean score was *'duration of illness'* (mean 2.70 [SD 1.07]). Of these

statements, 17/20 met the consensus criteria for agreement (categories 1&2) following the round three rankings **(Appendix 32)**. One statement initially achieved consensus in the preliminary analysis but fell short of the criteria following data cleaning: *'may show some signs of improvement following administration of paracetamol or nasal pharyngeal suctioning'*. As this statement was not included into the round four Delphi survey for re-ranking, it has been classified as meeting the consensus criteria for agreement (categories 1&2). This leaves two statements which did not achieve the consensus criteria and were included into round four **(Appendix 33)**. The comments were mostly similar to what had been voiced previously in terms of assessing symptoms in combination. However it, was suggested the infant maybe *"alert but not necessarily active"* and for those infant's being looked after at home, parents would need to be *"alerted to deteriorating symptoms"*. After consideration, one statement, *'will have near normal wet nappies/urine output over preceding 12 hours'*, was included into the round four Delphi survey but failed to meet the consensus criteria for either agreement (categories 1&2) or disagreement (categories 4&5).

6.10.3 Criteria for 'moderate' bronchiolitis

The following question was posed to the Delphi panel members:

'*Do you agree or disagree with the following statements that describe an otherwise healthy infant, up to 12 months of age, with 'moderate' bronchiolitis...?'*

Fourteen 'moderate' criteria statements were developed and included into the round three Delphi survey **(Appendix 32)**. As with 'mild' bronchiolitis, these

statements covered a range of signs and symptoms related to oxygen requirements, work of breathing, cardiovascular functions, hydration and perfusion and neurology. The statement with the lowest mean score was *'may have moderate subcostal and or/intercostal recession'* (mean 1.77 [SD 0.57]) and the statement with the highest mean score was *'may have increasing oxygen requirements (oxygen up to 50-60%) to maintain oxygen saturations >92%'* (mean 2.72 [SD1.22]). One statement initially achieved consensus in the preliminary analysis but fell short of the criteria following data cleaning: *'may have < four wet nappies in preceding 24 hours or urine output <2mLs/kg/hr'*. As this statement was not included into the round four Delphi survey for re-ranking it has been classified as meeting the consensus criteria for agreement (categories 1&2). Eight out of the 14 'moderate' statements achieved the consensus criteria. Within the comments it was felt that an oxygen requirement greater than 50% would constitute *"severe"* bronchiolitis. Whilst *'grunting'* and *'tracheal tug'* was perceived to be either absent or present rather than being on a continuum between *'mild'* and *'severe'*. Measuring urine output was thought to be more accurate than counting number of wet nappies. *'Unwell appearance'* was considered *"too subjective"*. As with previous Delphi rounds, context and constellation of symptoms were emphasized as important when assessing for 'moderate' bronchiolitis.

Eight criteria statements for 'moderate' bronchiolitis were developed for the round four Delphi survey **(Appendix 33)**. These statements were based on the statements which did not achieve the consensus criteria for agree or disagreement (categories 1&2; 4&5) and the participant comments from round three. The statement with the lowest mean score was *'may be irritable/restless'*

(mean 2.05 [SD 0.73]) and the highest mean score *'may have self-correcting apnoea'* (mean 2.78 [SD 1.18]). Four of these eight statements achieved the consensus criteria for agreement (categories 1&2) in round four, whilst the remaining four statements did not achieve the consensus criteria for either agreement or disagreement (categories 1&2; 4&5).

6.10.4 Criteria for 'severe' bronchiolitis

The following question was posed to the Delphi panel members:

'Do you agree or disagree with the following statements that describe an otherwise healthy infant, up to 12 months of age, with 'severe' bronchiolitis...?'

Twenty-seven 'severe' criteria statements were developed for round three **(Appendix 32)**. As with previous rounds, they were broadly related to: oxygen requirements, work of breathing, cardiovascular functions, hydration and perfusion and neurology. The statement with the lowest mean score was *'apnoea (+/- bradycardia) increasing in frequency & duration, requiring bag and mask intervention*' (mean 1.20 [SD 0.40]), whilst the statement with the highest mean score was *'alert but inactive and or/ passive'* (mean 1.97 [SD 1.01]). All the statements with one exception (*'alert but inactive and or/ passive'*) met the consensus criteria for agreement (categories 1&2). There were a minimal number of comments for the 'severe' criteria in comparison to the other criteria. It was felt that *"signs of exhaustion need to be objective"*, the term *'toxic'* brought to mind the *"toxic shock look"* and finally there was poor comprehension of the following statement: *'alert but inactive and or/ passive'*. In round four, the Delphi participants were asked to vote on which adjective they preferred to describe the appearance of an infant with 'severe'

bronchiolitis **(Appendix 33)**. The adjectives provided were either *'toxic'*, extracted from the literature, or *'lifeless'* which was a term used by parents participating with the family workshop. A total of 79.7% of respondents preferred the adjective *'lifeless'* (mean 1.79 [SD 0.40]) to describe the appearance of 'severe' bronchiolitis.

6.10.5 Criteria for hospital discharge

The following question was posed:

'Which of the following hospital discharge criteria, should be used for an otherwise healthy infant, up to 12 months of age, with bronchiolitis...?'

Twelve 'hospital discharge' criteria statements were developed for the round three Delphi survey **(Appendix 32)**. The hospital discharge criteria covered monitoring frequency, last documented apnoea, oxygen saturation thresholds in air, work of breathing, hydration and neurology. The lowest mean score was for the statement *'infant is alert and active'* (mean 1.53 [SD 0.53]) and the highest mean score was for the statement *'greater than 12 hours since last documented apnoea'* (mean 3.48 [SD 1.14]). Three of the 12 statements achieved the consensus criteria for agreement (categories 1&2): *'mild respiratory recession may be observed but acceptable'* (90.3%; mean 1.84 [SD 0.76]); *'tolerating 50-75% of oral feeds during preceding 24 hours'* (84.5%; 1.94 [0.89]); *'infant is alert and active'* (98.1%; mean 1.53 [SD 0.53]). Within the comments it was suggested that in an improving infant *"one accepts different endpoints"* in comparison to an infant in the early stages of the disease course. When deciding to discharge a clinically stable infant there was disagreement with regards to the minimum length of observation time with

suggestions ranging between 12 and 24 hours. A further consideration highlighted was the type or quality of care available following discharge. For example, would the infant be discharged home solely into the parents' care or with support from an NHS community service?

The statements from round three were revised and included in to the round four Delphi survey **(Appendix 33)**. Statements for oxygen saturation thresholds were separated into whether the infant was asleep or awake and settled. The statement relating to the time period of observation for oxygen saturations in air before considering discharge was changed from a Likert scale to choosing one of five time periods. Similarly to oxygen saturation thresholds, the statements for last documented apnoea were separated into whether the apnoea was self-correcting or required intervention. The statement with the lowest mean score and the only one to achieve consensus for agreement (categories 1&2) was *'saturations >94% in room air – asleep'* (81.2%; mean 1.81 [SD 1.04]). The statement with the highest mean score and the only one to achieve consensus for disagreement (categories 4&5) was *'>12 hours since last documented apnoea – requiring intervention'* (88.2%; mean 4.20 [SD 1.09]).

6.11 Conclusion

A total of 195 multi-disciplinary stakeholders participated with a four round Delphi questionnaire as *'expert'* panel members. Following the first two Delphi rounds 47 out of 101 signs symptoms and risk factors achieved consensus for importance when assessing bronchiolitis severity. These 47 signs, symptoms and risk factors were incorporated into the LIBSS-PRO ready to be further

assessed in clinical field-testing. Criteria achieving consensus in rounds three and four for ‘mild’, ‘moderate’ and ‘severe’ bronchiolitis, were included into a proforma. This proforma will be used by the clinically agreed reference standard in the construct and criterion validity and paediatrician inter-rater reliability testing in Chapter 9.

The strength of the Delphi questionnaire was the engagement of a comprehensive group of experts located across the UK and Ireland to ensure the applicability of the LIBSS-PRO for use in a variety of healthcare contexts. However, a limitation of the expert group was that a large proportion of the Delphi panel members were nursing staff (AfC pay bands 5 or 6). There was an under-representation of other HCP groups or pay grades. Furthermore, parents were not included in the Delphi questionnaire. This could have been a missed opportunity to further engage with this important stakeholder group. The reason for not including parents was to do with the timing of the study in respect to the bronchiolitis season. The study commenced towards the end of the bronchiolitis season. The Delphi questionnaire was conducted outside the bronchiolitis season, which made recruitment of parents or carers more difficult and also raised issues around recall bias.

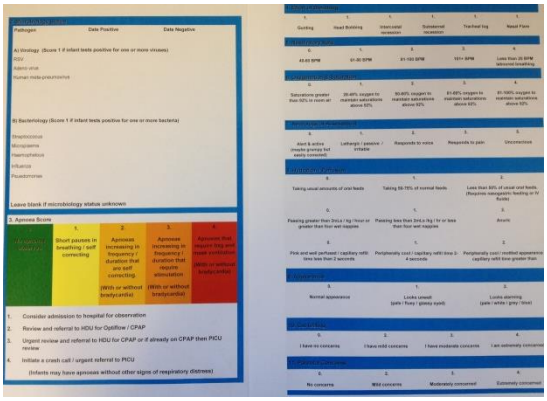
Another limitation was with the amount of attrition observed between Delphi rounds one and four especially amongst nursing staff. These attrition rates may have been due to the length of survey and the number of rounds resulting in survey fatigue. Some of the participants may not have appreciated fully the commitment involved in becoming a Delphi panel member and having to complete all the Delphi rounds. With hindsight it may have been beneficial to have undertaken a consensus meeting with stakeholders involved in the two

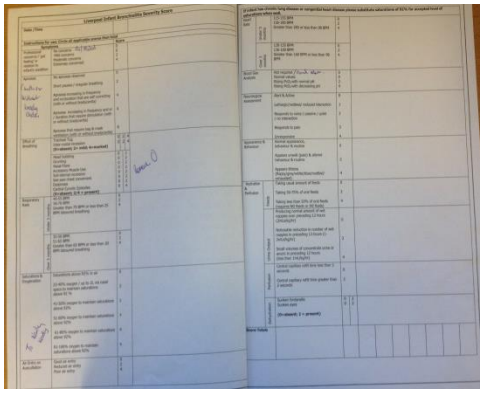
focus groups and the study steering group members prior to the Delphi survey. A consensus meeting could have been used to further reduce and achieve a level of agreement over which items and domains to include into the Delphi survey. This would have made the survey less burdensome for Delphi panel members and may have led to a reduction in attrition rates. Furthermore, having a degree of prior agreement over items and domains may make it more likely that that those included will achieve the Delphi consensus criteria for importance. Moreover, increased consensus could have also possibly improved the development of the reference standard used within the construct and criterion validity testing.

Chapter Seven

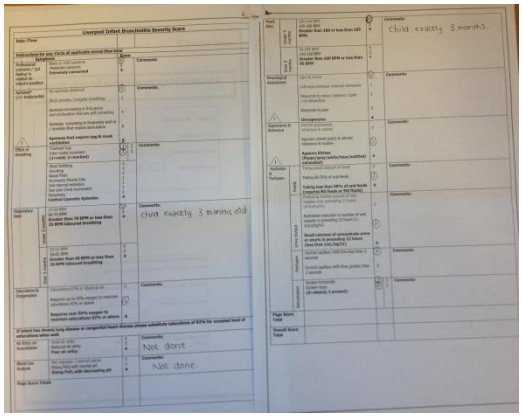
7 Content validity

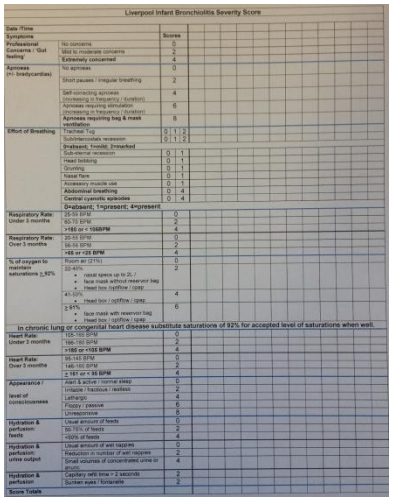
The 47 items that achieved consensus in the Delphi survey were included in the LIBSS-PRO instrument. Various iterations of the instrument were developed and shown to the study steering group and several HCP groups for comment to establish face validity. It was confirmed that the LIBSS-PRO appeared to measure bronchiolitis severity. The LIBSS-PRO instrument was revised further based on suggestions to improve clarity and the layout prior to content validity testing **(Figure 8)**. Content validity is the extent to which the instrument measures the concept of interest (61). It had partly been established during phase one of this study through the identification of important items underlying the concept of bronchiolitis. This chapter describes the methods used to confirm content validity of the LIBSS-PRO (Version 7.0) **(Appendix 34)** in clinical practice. Through this, the relevance of the domains and items contained in the LIBSS-PRO will be determined in a clinical setting.





…





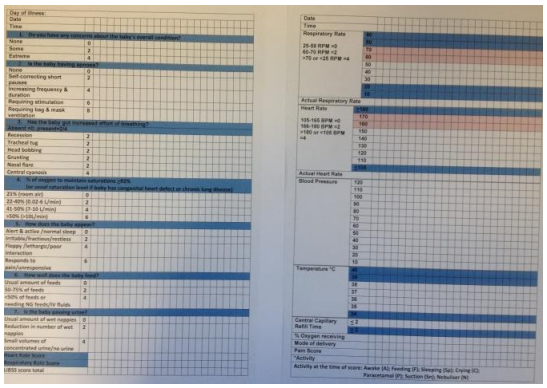


Figure 8: Various iterations of the LIBSS-PRO

7.1 Aims

i) To evaluate whether the domains and items contained within the LIBSS-PRO (Version 7.0) were representative of the concept bronchiolitis severity.

ii) To identify redundant domain and/or items for removal from the LIBSS-PRO.

7.2 Methods

Eligible HCPs located within five study sites (one paediatric tertiary centre and four DGHs) were identified via the Cheshire and Merseyside CLRN to participate with the content validity testing. The HCPs were asked to administer the LIBSS-PRO (Version 7.0) instrument to eligible infants whose parents (including carers or legal guardians) had previously signed informed consent to participate with the clinical testing. The LIBSS-PRO (Version 7.0) had 12 domains: risk factors; professional concern/'gut' feeling; apnoea; effort of breathing; respiratory rate; saturations and supplemental oxygen requirement; air entry on auscultation; blood gas analysis; heart rate; neurological assessment; appearance and behaviour; hydration and perfusion (feeds, urine output, perfusion, dehydration). Using a structured evaluation form **(Appendix 35)**, HCPs were asked to rate each domain/item on a Likert scale from one to four for clinical relevance, with one being extremely relevant and four being completely irrelevant. HCPs were also asked to provide additional information on ease of administration, interpretation, layout and timeliness, and to identify redundant domains/items. The completed LIBSS-PRO was assessed for completeness of data and score distributions. Criteria

for acceptability included missing data for summary scores of less than 5% and even distribution of endorsement frequencies across response categories. Items were considered for elimination if judged clinically impractical by five or more HCPs. HCPs were encouraged to make suggestions on how to improve the LIBSS-PRO (Version 7.0). The *'rule of thumb'* used to determine sample size was between 10 and 15 participants for each included domain/item (52). The LIBSS-PRO contained 12 domains therefore a minimum sample size of n=120 infants was required for the content validity testing.

7.3 Results

Content validity testing was undertaken during the 2011/12 bronchiolitis season. 114 content validity tests were undertaken. The characteristics of participating HCPs and infants can be found in **Table 20**. 62.8% of participating HCPs were nurses, whilst 37.2% were doctors. Nearly half of the nurses were AfC band 5 staff nurses. There were slightly more males (54.0%) compared to female infants (46.0%). There were more infants aged under three months of age (53.1%). The mean time for HCPs to complete the LIBSS-PRO (version 7.0) was 9.47 (SD 4.79) minutes. The mean LIBSS-PRO (version 7.0) score total was 10.5 (SD 6.75).

Table 20: Content validity – participant characteristics (HCPs and infants)

Professional role	**n (%)**
Nurse	68 (60.2)
Doctor	42 (37.2)
Assistant Practitioner	2 (1.8)
HCA	1 (0.9)
Missing data	1
Clinical grade	**n (%)**
Consultant	7 (6.3)
Associate specialist	3 (2.7)
SpT 4/5/6/7	5 (4.5)
SpT 1/2/3	15 (13.4)
F1/2	11 (9.8)
AfC 8a/b	3 (2.7)
AfC 7	4 (4.5)
AfC 6	8 (7.1)
AfC 5	52 (46.4)
AfC 4	2 (1.8)
AfC 3	1 (0.9)
Infant age	**mean (SD)**
Under three months age	60 (53.1)
Three months and over	53 (46.5)
Infant gender	**n (%)**
Male	61 (54.0)
Female	52 (46.0)

Of the 114 completed tests, two evaluation forms were not completed due the staff being busy. A further six evaluation forms were excluded from the analysis because six HCPs completed an evaluation form on two separate occasions thus providing duplicate data. This left 106 evaluation forms included in the analysis. All domain and items, with the exception of one (reduced air entry (79.7%)), achieved consensus of 80% or greater for clinical relevance for assessment of bronchiolitis severity **(Appendix 36)**. In spite of this, a significant amount of missing data was noted for two domains on the completed LIBSS-PRO scores: air entry on auscultation and blood gas

analysis. The collated free text comments for each of these domains are summarised below.

7.3.1 Professional concerns / 'gut' feeling

'Free text' opinion was divided on the professional concerns/ 'gut' feeling domain. Some HCPs thought professional concerns/ 'gut' feeling to be *"subjective"* and dependent on *"experience",* and that *"concern"* could be determined by *"clinical signs"*. Others thought the usefulness of this domain would be limited. Conversely, other HCPs reported how they *"trust their gut"* even if there were no obvious concerning clinical signs as they believed it to be more *"reliable"*.

7.3.2 Apnoea

One HCP queried whether this domain was referring to apnoea *"observed"* at the time of the score or a *"history"* or apnoea. Another HCP recommended apnoea being a *"red flag"* with apnoea of any description requiring a *"senior review"*. Two HCPs felt that infants who have apnoea requiring bag and mask ventilation should not be nursed on a ward but looked after in a critical care area.

7.3.3 Effort of breathing

Four HCPs suggested there should be an option to score zero for *'effort of breathing'*. One HCP recommended the domain of *'apnoea'* should have a higher weighting than the items contained under the domain of *'effort of breathing'*. Three HCPs were unsure as to how *'dyspnoea'* differed from *"work of breathing"* and reported that this was a *"subjective symptom"*. One HCP

believed that *'see saw chest movement'* should have a higher weighting whilst another HCP felt it was *"subjective*" and *"non-specific"*. One HCP advised including an instruction to indicate more than one item can be circled. One HCP thought the domain of *'effort of breathing'* was *"useful to think through all aspects of increased WOB [work of breathing]"*.

7.3.4 Respiratory rate

Three HCPs commented on how *'respiratory rate'* being divided into two age categories was *"confusing"*. Furthermore, the age category labels being written vertically were *"unclear"* and caused HCPs to circle the incorrect age group for *'respiratory rate'.* It was also noted by five HCPs that *'respiratory rate'* could be affected by *"crying"*, *"activity"* or *"fever"*. One HCP thought that the range 20-55 for the three months and older age group was *"slightly inaccurate"* and believed *"30-56 would provide a far more accurate picture"*.

7.3.5 Oxygen and saturations

Five HCPs reported this domain to be *"confusing"*. One HCP thought they could only score the infant if the infant was receiving 50% oxygen or greater. Other HCPs reported only being familiar with recording oxygen in litres as opposed to percentage. Two HCPs recommended including oxygen ranges to improve clarity and one HCP suggested further training may be required.

7.3.6 Air entry on auscultation

Within the free text comments a large proportion of nurses (n=37) reported they were not trained in undertaking auscultation. This domain within the LIBSS-PRO was either left blank or the nurses reported obtaining the

information from either consulting the medical notes or a HCP trained in auscultation. One HCP felt that it was unlikely that air entry assessment would change the *"management [of the infant] in isolation unless there was significant poor air entry".* However, other HCPs (n=7) reported that changes to *'air entry'* may indicate *"infection"*, *"worse disease"* or the need to *"escalate care"*. Finally, one HCP suggested that *"prolonged expiration"* may be a finding that was not currently covered by the score.

7.3.7 Blood gas analysis

There was missing data from 31 LIBSS-PRO scores for this domain. Twelve nurse HCPs reported either not being trained in blood gas analysis or it was not considered part of their role. There were missing data from a further seven HCPs who did not comment as to why they did not complete this domain. Three HCPs stated that they did not understand the question. The remaining nine HCPs felt this domain was not *"relevant"* to the particular infant under assessment. Sixteen HCPs remarked on how blood gas analysis was only *"relevant"* and clinically indicated in *"severe"* bronchiolitis. To improve the clarity of this domain it was suggested by eight HCPs to provide a range of *"values"* to make blood gas results *"easier to interpret"*.

7.3.8 Heart rate

The majority of comments were related to either how heart rate is a good indicator of the *"patients' condition"* or how the heart rate was obtained (palpation or monitor) and the result. Seven HCPs highlighted that an elevated heart rate may be linked to activities such as feeding and/or crying or when an infant has a *"fever"*.

7.3.9 Neurological assessment

In most cases the comments described observations of what the infant was doing at the time of the score, for example, *"they were alert and playful"*. It was thought by some HCPs (n=5) that neurology was difficult to assess due to their young age or when the infant was asleep. Three HCPs reported obtaining information on neurology from parents or family members when the infant was asleep. One HCP was unsure how *"lethargic differed from quiet"*. One HCP proposed merging neurological assessment with appearance. Whereas another HCP thought there was an *"overlap with 'gut' feeling"*. One HCP noted that *"irritability"* was missing from the score and that *"bronchs"* were are *"often irritable"*.

7.3.10 Appearance and behaviour

The majority of the comments described the appearance and behaviour of the infant. Four HCPs suggested merging appearance and behaviour with neurology as it was felt to be *"repetitious"*. One HCP believed *"paleness doesn't tell you a baby is sick"*. Two HCPs felt that this domain included *"subjective assessments"* which could change *"quickly"* and would only be helpful when the infant was *"severe"*. Finally, one HCP reported that it *"provides a quick assessment which can be done at the end of the bed"*.

7.3.11 Hydration and perfusion

This was split into four sub-domains: feeds; urine output; perfusion; dehydration. A large proportion of comments were associated with the mode of feeding and urine volumes of individual infants. 'Hydration and perfusion' was

regarded as an important domain by six HCPs to assess the need for admission to and discharge from hospital or clinical improvement or deterioration. Eight HCPs reported involving parents with the assessment of this domain, although one HCP acknowledged *"there may be a discrepancy between what mum is actually telling you and the clinical picture"*. Urine output was considered *"subjective"* (n=1); *"difficult to assess"* (n=1); and the score of two was *"too high"* (n=1). Two HCPs queried the value of including "2mLs/kg/hr" in the score as it is not always calculated. One HCP recommended by removing *"2mL/kg/hr"* would *"simplify"* the score. Three HCPs noted there was no zero score option for perfusion and dehydration. Furthermore, two HCPs suggested removing the wording *"greater than"* from the perfusion sub-domain and substituting it with the following *"<2 or >2"*. One HCP advised including an instruction as to where capillary refill time (CRT) should be taken, whilst another HCP suggested the CRT score should have a greater weight than a score of two. The sub-domain dehydration was considered irrelevant by one HCP due to the *"age of the child"*. Furthermore another HCP proposed that *"skin turgor"* should be included in the assessment as *"research indicates poor inter-rater reliability between sunken eyes /fontanelle – whereas skin turgor was good"*.

When asked if the LIBSS-PRO was easy or hard to complete only five HCPs reported difficulties. One HCP thought it was hard because *"subjective symptoms are difficult while ticking boxes"*. Another HCP found it difficult due to the fact that the infant did *"not just have bronchiolitis"*. The scoring for the 'effort of breathing domain' was found *"confusing"* by one HCP. It was judged

that *"repeated assessments"* of the LIBSS-PRO may be *"time consuming"*. The LIBSS-PRO was felt to be *"too wordy"*.

When asked if the LIBSS-PRO was clear or confusing 24 HCPs reported some domains that were confusing. Five HCPs were confused by the respiratory and heart rate domains being divided by age. Other domains identified as being confusing included: 'oxygen and saturations' (n=1); 'blood gas analysis' (n=1); 'effort of breathing' (n=1); 'appearance and behaviour' (n=1). In addition, it was felt that 'young age' and 'gestational age less than 37 weeks' in the 'risk factor' box were unclear. The shading of the font to indicate severity and the *"time period"* over which to undertake the score were also found confusing.

When asked which domains and/or items should be removed from the LIBSS-PRO the following eight domains/items were recommend: 'professional concerns/'gut' feeling' (n=1); 'air entry on auscultation' (n=10); 'blood gas analysis' (n=5); 'neurology' (n=1); 'appearance and behaviour' (n=2); 'dehydration' (n=2); 'dyspnoea' (n=1); 'see saw chest movement' (n=1). It was suggested that 'neurological assessment' and 'appearance and behaviour' were merged together by five HCPs. When asked about the layout of the LIBSS-PRO most of the HCPs reported to like it. Five HCPs did not like the font size or how the font was shaded to indicate increasing severity of bronchiolitis. This caused reading difficulties. Furthermore, it was postulated that the font may be more *"difficult to see at night"* during night shifts. Other suggestions to improve the layout included: a legend for symbols; more colour; fitting the LIBSS-PRO onto one page; using both percentage and litres for oxygen and linking to a treatment pathway. The following four items were

suggested for consideration for inclusion into the LIBSS-PRO: subcostal recession, skin turgor, social and family history.

7.4 Conclusion

Most of the domains and items were considered clinically relevant for the concept of bronchiolitis severity. Furthermore, most HCPs were able to complete the LIBSS-PRO but a number of issues with the content were identified. Following clinical testing two domains (air entry on auscultation and blood gas analysis) were deemed impractical by more than five HCPs and were removed from the LIBSS-PRO. Based on HCP comments 'dyspnoea' and 'see saw chest movement' were also removed. Two domains ('neurological assessment' and 'appearance and behaviour') were merged together to become a new domain i.e. 'appearance' and 'level of consciousness'. Two sub-domains within the domain of 'hydration and perfusion' were merged together i.e. 'perfusion' and 'dehydration'. Of the four items suggested for inclusion, one further item was included into the LIBSS-PRO: 'subcostal recession'.

There were limitations with regards to the sampling strategy. Firstly, the sample size of 120 infants was not achieved. The majority of HCPs who were involved with the content validity testing were nursing staff. Therefore, including other HCP groups may have discerned different insights. It became apparent that some nursing staff when approached was reluctant to participate with the content validity testing. Further inquiry found they perceived their knowledge and skills of bronchiolitis and clinical assessment were under

scrutiny as opposed to the LIBSS-PRO being evaluated. Reassurance was provided to inform these nurses that this was not the case.

Chapter Eight

8 Cognitive interviews

Cognitive psychology challenges the assumption that respondents understand the questions being asked of them and can provide accurate responses when completing health measurement instruments (128-130). (130). The social knowledge and cultural models to which an individual is exposed determines cognitive processes and these directly influence interpretation of the questions posed (131). Cognitive interviewing reveals that participants may not understand questions or may interpret them differently from how they were intended. Respondents may also interpret questions differently to other respondents or be unable or unwilling to complete questions (129, 132). For example, one study reported that respondents, when asked about the type of “work” engaged with during the previous week, failed to report activities such as voluntary work and/or casual work such as babysitting (133). Cognitive interviews were used to pre-test the LIBSS-PRO to expose issues which could lead to measurement error if not identified and adequately addressed (130). This chapter describes the cognitive interview methods used to identify potential problems with the LIBSS-PRO prior to clinical field-testing.

8.1 Aims

The overall aim of cognitive interview testing was to investigate the likelihood of response error with the bronchiolitis scoring instrument and specifically to:

i) To evaluate how HCPs comprehend, interpret and respond to each section of the scoring instrument.

ii) To check understanding of medical terminology used within the scoring instrument.

8.2 Sample and setting

Recruitment of HCPs was undertaken between May and September 2012. All participants were identified through the Cheshire and Merseyside CLRN. Interview participants were doctors, nurses or health care assistants (HCAs) who had recent experience in caring for infants with bronchiolitis. HCPs were identified from five hospitals (one paediatric tertiary and four DGHs). These hospitals represent a range of specialities including; accident and emergency, critical care, and general medical wards. A purposive sample frame was devised **(Appendix 37)** to ensure adequate representation of a wide range of professional clinical experience. Eligible HCPs were stratified by profession type, employment grade and hospital. CLRN research nurses approached eligible HCPs with information about their potential involvement in a cognitive interview.

8.3 Informed consent

Written information about the study was provided to participants prior to the interviews and either CvM or a CLRN research nurse obtained informed written consent. At the beginning of each interview CvM went through the consent process again to obtain verbal consent which was audio recorded.

8.4 Methods

The method chosen was audio-recorded, semi-structured cognitive interviews using a *'think aloud'* technique (128, 132). These interviews focused on the recent version of the scoring instrument (LIBSS-PRO 7.7) **(Appendix 38)**.

8.5 Development of the vignettes

Four hypothetical vignettes were developed and used as part of the cognitive interview process (128, 133). The purpose of the vignettes was twofold. Firstly, the vignettes provided contextual information on infant behaviour with bronchiolitis as an *aide memoir*. This was particularly important as the interviews were conducted outside the bronchiolitis seasonal epidemic. Secondly, the vignettes were used to prompt discussion in order to explore cognitive processes when participants considered how they would arrive at their response for each domain and item. The vignettes were developed through examining the patient data collected during content validity testing. Each vignette contained a scenario that described varying severities, signs and symptoms of disease, risk factors, interventions and clinical settings **(Table 22)**. The table with all four vignettes were given to the participants at the beginning of the interview.

Table 21: Bronchiolitis vignettes

Vignette one
Four week old male infant with a two day history of cough and runny nose was diagnosed in A&E with bronchiolitis. Past Medical History (PMH): previously fit and well; normal vaginal delivery at term. On examination: Respiratory: saturations high 90's in air, respiratory rate 55 BPM, wheeze on auscultation Cardiovascular System (CVS): heart rate 150 BPM, capillary refill less than 2 seconds, apyrexial. Neurology: alert but irritable Fluids: noticeably reduced amount of oral intake and has vomited feeds. Passing urine. Senior House Officer decides to admit for observation
Vignette two
Two week old female infant on medical ward who is RSV positive. Parents report infant has been unwell for approximately three days. PMH: previously fit and well, normal vaginal delivery at term On examination: Respiratory: Requires oxygen to maintain saturations above 92%. Oxygen has recently increased to one litre via nasal cannula. Increased work of breathing, respirations around 60 BPM, mild intercostal recession. Nasal suction has helped. CVS: tachycardic after feeds. Capillary refill less than two seconds. Temperature 37.9C Neurology: alert but irritable at times especially after feeds. Fluids: 3 hourly tube feeds, wet nappies
Vignette three
Six month old male infant in HDU who is RSV positive with a two day history of decreased feeds and snuffles. PMH: atrial septal defect. On examination: Respiratory: requiring CPAP for apnoea. Positive End Expiratory Pressure (PEEP) 4-6 cms H_2O, 50% oxygen to maintain saturations above 92%. Continues to have self-correcting apnoea that does not require stimulation. Increased respiratory rate at times. Blood gases satisfactory. Tolerating 5 minute pressure relief off NCPAP. CVS: tachycardic at times, apyrexial, Fluids: on intravenous fluids, nil by mouth, passing good amounts of urine
Vignette four
Six week old female infant, born via caesarean section, at 32 weeks gestation. Diagnosed with RSV positive bronchiolitis. Weight 2.4kg. History of apnoea requiring 24 hours of CPAP on HDU. Currently in the process of being discharged from HDU to the medical ward Respiratory: 31% humidified oxygen via incubator to maintain saturations high 90's. No increased work of breathing, respiratory distress or apnoea. Respiratory rate 22-52 BPM CVS: Heart rate 140-165 BPM, apyrexial, capillary refill time less than 2 seconds Neurology: behaving appropriately for age Fluids: tolerating NG feeds, passing normal amount of urine

8.6 Undertaking the Interviews

A *"think aloud"* technique was employed during the interview to further explore cognitive thought processes (128, 132). As the name suggests participants were asked to *"think aloud"* when they reflected on each section and when considering their answers/responses. This technique enabled participants to verbalise their thoughts whilst they were problem solving or responding to questions. A standard set of probe questions **(Table 23)** were developed and used to supplement the *"think aloud"* technique.

Table 22: Cognitive interview probe questions

	Probe questions	Exemplars
Comprehension/Interpretation probe	What do you believe this section to be asking of you?	*"Basically it is asking you whether this is a […] a baby with any underlying health conditions" (*HCP-N09)
Comprehension/Interpretation probe	What do you think is meant by the following term(s)...?	*"tracheal tug is erm the collapsing of the trachea as the baby's breathing hard"* (HCP-N07)
General probe	How do you think you would assess for this and arrive at your response?	"*You would look at the chest movement and feel for the chest movement […] you can do it […] with a stethoscope erm so you can hear the breaths going in and out or just do it with your eyes…"* HCP-N14
General probe	How sure are you of your answer?	"I think I am pretty sure…all four of them are in different stages of their illness and that's pretty obvious" (HCP-D02)
General probe	Based on your experience what would make this section easy or difficult to complete?	*"I think it's subjective and it depends on peoples' experience…"* (HCP-N09)
Specific probe	Does the question have any particular features that would make it likely not to be understood?	*"that is quite a tricky one especially with the differential between the short pauses then apnoeas"* (HCP-H01)

All interviews were arranged at the convenience for the participant. At the beginning of each interview CvM provided information on the overall research aims and the purpose of the interview. Participants were supplied with the four vignettes and the most recent version of the LIBSS-PRO (Version 7.7 **(Appendix 38)**). This version contained nine domains: 'risk factors', 'professional concerns/ 'gut' feelings', 'apnoea', 'effort of breathing', 'respiratory rate', 'oxygen requirements', 'heart rate', 'appearance and level of consciousness' and 'hydration and perfusion'. One domain 'professional concerns/ 'gut' feelings' covered a subjective concept only relevant to the individual respondent completing the LIBSS-PRO (Version 7.7). The remaining eight domains were related to a physical reality observed in an infant with bronchiolitis. There were two response formats. The first section, 'risk factors' provided an option for the respondent to tick all applicable 'risk factors' the infant may have. The remaining eight sections provided a numerical response option. The scores for these eight sections were then summed together to obtain a score total. Following the first six interviews, Version 7.7 was revised in light of participant comments. LIBSS-PRO (Version 8.0 **(Appendix 39)**) was used with the remaining ten cognitive interviews. CvM conducted all of the interviews (either telephone or face-to-face) in a standardised manner. All interviews were digitally audio recorded (Tascam DR-100). The recordings were transcribed verbatim and anonymised for analysis (CvM).

8.7 Analysis

Cognitive interviewing falls within the paradigm of qualitative research and a qualitative analysis approach was used (124). As with the workshops and

parent interviews, the process of analysis was iterative and the interview transcripts were examined and re-examined several times during the course of the analysis. Initial examination of the transcripts was used to obtain an overview – at the content level – of what the HCPs talked about and to record any general impressions, key ideas, themes and concepts arising from the content. A modified data coding scheme was developed *a priori* and manually applied to the raw data **(Table 24)** (128). Categories 1-3 were concerned with comprehension, whilst category 4 was concerned with retrieval, decision making/judgement or response. A descriptive thematic analysis of the data was then undertaken. QRS NVIVO (Version10) software was used to support the coding and synthesis of the data. Field notes were used to support the analysis and enabled the researcher to reflect on the interviews and record any thoughts and insights.

Table 23: Data coding scheme

1.	The participant has difficulty understanding the section
2.	The participant has difficulty understanding the meaning of particular words or concepts
3.	Different participants have different understandings of the section
4.	The participants have difficulty in recalling, formulating or reporting an answer

8.8 Results

The interviews lasted 30-60 minutes. The target was to recruit 15 participants to take part with the cognitive interviews; 16 HCPs consented to participate (see **Table 25** for HCP characteristics). The sample comprised doctors (n=7), nurses (n=7) and HCAs (n=2). The majority of participating

doctors were speciality trainees in paediatrics. Of the two consultants, one was a general paediatrician and one a paediatric intensivist. Most nurses (n=4) worked on paediatric general medical wards, although there was one ED nurse, one ANP and one PHDU nurse. Twelve interviews were conducted face-to-face and three over the telephone. Technical problems with the audio recorder meant that one interview was only partially recorded (HCP-N14). Quotations are linked to generic labels to increase anonymity: HCP-H01, HCP-D02, through to HCP-D16.

Table 24: Cognitive interviews – HCP characteristics

HCP ID	HCP Gender	HCP Profession	HCP Grade	Interview Type	Hospital
HCP-H01	Male	HCA*	Band 3	Telephone	DGH* 1
HCP-D02	Male	Doctor	>ST4	Face	DGH* 1
HCP-D03	Male	Doctor	Consultant	Face	DGH* 1
HCP-D04	Female	Doctor	<ST4	Telephone	DGH* 3
HCP-N05	Female	Nurse	Band 6	Face	DGH* 3
HCP-N06	Female	Nurse	Band 5	Telephone	DGH* 3
HCP-N07	Male	Nurse	Band 7	Face	DGH* 2
HCP-A08	Female	ANP*	Band 8	Face	DGH* 2
HCP-N09	Female	Nurse	Band 6	Face	PTC*
HCP-D10	Male	Doctor	Consultant	Face	PTC*
HCP-D11	Female	Doctor	<ST4	Face	DGH* 2
HCP-H12	Female	HCA	Band 3	Face	DGH* 4
HCP-N13	Female	Nurse	Band 5	Face	DGH* 4
HCP-N14	Female	Nurse	Band 5	Face	DGH* 4
HCP-D15	Female	Doctor	<ST4	Face	PTC*
HCP-D16	Male	Doctor	>ST4	Face	PTC*
*HCA: Health Care Assistant; *ANP: Advanced Nurse Practitioner; *DGH: District General Hospital; *PTC: Paediatric Tertiary Centre					

The results for the cognitive interviews were aggregated under the nine domain headings which reflect those found on the LIBSS-PRO (Versions 7.7 and 8.0): ‘risk factors’, ‘professional concerns/ ‘gut’ feelings’, ‘apnoea’, ‘effort of breathing’, ‘respiratory rate’, ‘oxygen requirements’, ‘heart rate’, ‘appearance and level of consciousness’ and ‘hydration and perfusion’.

8.8.1 Risk factors

This domain asks the participant *‘Does the infant have any of the following* ‘risk factors’ *for severe disease?’.* The participant has to tick either the ‘yes’ or ‘no’ box and is then asked to tick all applicable ‘risk factors’ from the following options: ‘CLD’; ‘CHD’; ‘neurological disorder’; ‘immunodeficiency’; ‘Down’s Syndrome’; ‘gestational age less than 37 weeks’; ‘low birth weight <2.5kg’ or

'young age (corrected age less than six weeks)'. In general, HCPs considered the purpose of this domain was *"to identify a group of children who […] are at high risk of having severe disease"* which may lead to *"poor outcomes"* (HCP-D10). HCPs reported 'risk factors' could be easily identified from past medical history, by asking the parents and/or carer or by reading the infant's clinical documentation. For those HCPs working in either the medical profession or ANP roles, certain 'risk factors' may also be discerned following a clinical examination. Participants highlighted specific comprehension issues with a number of the 'risk factors' listed. Participants considered whether CLD was restricted to *"chronic lung disease of prematurity"* or whether this term encompassed other chronic respiratory diseases such as *"cystic fibrosis"* or *"bronchiectasis"*. 'Gestational age less than 37 weeks' was found to be *"not specific enough"* and should be accompanied with a *"definition"*. One HCP questioned whether this referred to the infants' age at the time of the score only or whether this also applied to older infants whose gestational age was less than 37 weeks. If this applied only to infants who were less than 37 weeks gestation at the time of the score it was felt this would be covered by 'prematurity'. It was felt that an infant with a gestational age of 36 weeks may not have any more *"increased risk"* of severe bronchiolitis than an infant with a gestational age of 37 weeks. Lower thresholds for gestational age were suggested. Participants commented on there being an overlap between a number of 'risk factors' such as 'CLD', 'gestational age less than 37 weeks', 'low birth weight' and 'prematurity'. Despite this overlap, HCP (HCP-D03) felt by keeping these 'risk factors' separate it would make HCPs *"assess the patient more closely"*. It was felt that 'neurological disorders' covered a *"broad*

spectrum" including *"developmental delay"* or *"epilepsy"*. It was suggested it should be changed to *"neuromuscular disorders"* as one participant recalls:

> *"…children with cerebral palsy or muscular skeletal problems […] are more prone to developing severe bronchiolitis…"* (HCP-H01)

Other suggestions to improve the 'risk factor' domain included: list the 'risk factors' in order of importance; include a box under 'CLD' to document home oxygen requirements and include a box to indicate whether the infant met the criteria for and received Palivizumab. Overall, the participants found this section *"easy to complete"* although it was proposed that junior staff, HCAs and adult trained HCPs working in DGHs may find this section difficult to complete.

8.8.2 Professional concerns/ 'gut' feelings

For the 'professional concerns/ 'gut' feelings' domain, participants had to choose one of three categories: 'no concerns: (0)'; 'mild to moderate concerns: (2)'; 'extremely concerned: (4)'. 'Professional concerns/ 'gut' feelings' were largely thought to be a culmination of HCP experience together with initial thoughts or impressions following a quick assessment of the infant. It was further suggested that the level of concern might prompt an urgent action or intervention. Overall, 'professional concerns/ 'gut' feelings' was considered to be a *"subjective"* assessment.

The use of the four vignettes highlighted particular features of concern for the HCPs. The vignettes also emphasised difficulties with comprehension and response categories. For vignette one, increased concern was related to the young age of the infant, day of illness and reduced oral intake. Some of the

HCPs reported that the 'SHOs' decision to admit the infant' increased concern. This might indicate that concern could also be influenced by the decision making of others, introducing a response bias. Overall, HCPs were not unduly concerned with this infant but acknowledged that they had the potential to deteriorate. This infant was scored as 'mild to moderate concerns: (2)' by all HCPs: with some HCPs stating their concerns to be more *"mild"*.

HCPs identified the following features as being of concern for vignette two: RSV positive diagnosis, young age, increased oxygen requirements, increased effort of breathing, tachycardia and naso-gastric feeds. When looking at vignette two, the term 'concern' was questioned by two of the HCPs. One proposed the term 'concern' was not *"the right word"* and should be replaced with *"level of severity",* whilst another HCP queried what was meant by the term 'concern':

> *"…when we say concerned…is it concerned with my ability to care for the child or concerned about how unwell the child is…"* (HCP-N07).

This response uncertainty indicates that further clarification of the term 'concern' may be required. HCPs perceived the infant in vignette two as having more severe bronchiolitis than the infant in vignette one. Despite this the HCPs generally scored this infant as 'mild to moderate concerns: (2)'. Thirteen HCPs declared their level of 'concern' for this infant to be *"moderate"*, whilst one HCP, who worked within critical care, reported having *"mild"* concerns. However, two HCPs (HCP-N13; HCP-N14) were 'extremely concerned: (4)'. One of these HCPs (HCP-N13) wanted to score the infant *"severe"* even though this category was not available, whilst the other HCP found it difficult to use the score with the vignettes provided, as she explained:

"…it's hard though isn't it without the baby in front of you…" (HCP-N14).

When determining the level of 'concern' an important consideration discussed was with supportive therapies received and the perceived stability of the infant, as HCP-A08 described:

"…I mean technically this child is sicker than child [in vignette] one but sort of has more things in place like a bit of oxygen so you'd be happy […] so again I wouldn't be desperately concerned…" (HCP-A08).

Vignette three appeared to be more of a challenge for HCPs to come up with a definitive response. Three HCPs gauged their level of 'concern' for this infant to be 'mild to moderate concerns: (2)' whilst the remaining 13 HCPs opted for 'extremely concerned: (4)'. Despite recognising the infant in vignette three was more severe than the previous two infants, the three HCPs who scored 'mild to moderate concerns: (2)' felt the infant was receiving appropriate supportive therapy, was clinically stable and was being cared for in a safe environment. Several HCPs who scored 'extremely concerned: (4)' stated they would have liked an additional response category between the second and third response categories, as HCP-D11 explained:

"…I think that one's difficult…they don't sound mild or moderate but they don't sound like… you know… really severe…life threatening kind of category…" (HCP-D11).

One of the primary characteristics identified to cause 'concern' was with the infant still having a degree of self-correcting apnoea in spite of receiving CPAP. Other attributes deemed 'concerning' by the HCPs included: CHD, day of illness, being cared for in a critical care environment and high oxygen

requirements. HCP-H01 conceded having a knowledge deficit with regards to CPAP and found it problematic to provide a *"better answer"*.

Finally, most HCPs (n=11) appraised vignette four as 'mild to moderate concerns: (2)'. The rationale for this score was that despite having a number of 'risk factors' the baby appeared to be improving and care was being *"stepped down"*. HCP-D15 scored 'no concerns: (0)' again for the same reasons previously stated by those HCPs who scored 'mild to moderate concerns: (2)'. HCP-N07, who scored the infant 'extremely concerned: (4)', reasoned that this was due to the infant being born preterm, having a corrected age of 38 weeks gestation with the infant requiring a period of CPAP to treat apnoea. In light of vignette four, HCP-A08 wanted to revise the score for the first vignette from 'mild to moderate concerns: (2)' to 'no concerns: (0)'.

It was highlighted during the interviews that the term 'professional concerns' was found to be *"nebulous"* and could be confused with other 'concerns' such as *"safeguarding"*. It became apparent that some HCPs responses were influenced by external factors other than how the infant presented in the vignette. For example, some HCPs appeared to be swayed by the clinical setting where the infant was situated as HCP-D11 explained:

> *"…because they're in HDU […] I supposed your gut feeling would be extremely concerned…"* (HCP-D11).

When working through the vignettes, it became evident to HCPs that three infants were being largely categorised as 'mild to moderate concerns: (2)' in spite of HCPs perceiving them to have different severities of illness.

In order to capture these different severities HCPs suggested dividing the 'mild to moderate concerns: (2)' category in to two categories, although, it was

suggested there should be a maximum of three response categories. Regardless of some of the uncertainty around completing the response categories, the majority of HCPs reported to find this section *"easy"* to complete. Conversely, HCP-D16 described this section to be *"fake"* and *"difficult"* to complete. Furthermore, he described how he would probably *"ignore"* this section when assessing an infant.

8.8.3 Apnoea

The 'apnoea (plus or minus bradycardia)' section had five response categories to choose from: 'no apnoea: (0)'; 'short pauses/irregular breathing: (2)'; 'self-correcting apnoea (increasing in frequency and/or duration): (4)'; 'apnoea requiring stimulation (increasing in frequency and/or duration): (6)' and 'apnoea requiring bag and mask ventilation: (8)'. Response categories (4) and (6) were colour coded yellow: consider urgent review by a senior doctor and category (8) was colour coded red: issue an arrest call.

None of the HCPs experienced many difficulties in understanding what this section was asking of them or what was meant by the term 'apnoea'. The general opinion was this section expected HCPs to assess and score the infant on the presence and severity of apnoea observed, with *'apnoea'* being described by HCP-N09 as:

> *"…where […] the baby stops breathing for a period of time…some babies might be self-correcting and then they will start again…others might need a bit of stimulation and […] the worst one's are obviously when the babies stop breathing and doesn't start breathing…"* (HCP-N09).

Some HCPs (n=6) suggested the *"pause"* in breathing had to be a certain length of time before being considered an apnoea, with estimates ranging between five and 20 seconds. Apnoea would be assessed either by: parental reports (although the accuracy of these reports were questioned), direct observation or the use of apnoea monitoring. When reflecting on the *"different stages"* of apnoea, HCPs reacted positively towards the five apnoea response categories presented in the LIBSS-PRO. They were asked to explain each of the response categories in turn to assess their understanding. The HCPs found the following categories: 'no apnoea: (0)'; 'apnoea requiring stimulation (increasing in frequency and/or duration) (6)'; and 'apnoea requiring bag and mask ventilation: (8)' were relatively objective and easy to complete. HCP-D10 queried the description in brackets, 'increasing frequency/duration', for category (6) and felt it required further clarification as he explained:

> *"…what do we mean by increasing frequency and duration […] so you could say more than two per hour or the chart …it's less than two at this hour and then they look at it the next hour […] so maybe define what that means …"* (HCP-D10).

Some HCPs suggested response categories (6) and (8) may not always be completed: in this scenario it was considered more important to *"get help"* than to *"add up a score"*. The response category that appeared to create the most difficulties was 'short pauses/irregular breathing: (2)'. HCP-N09 thought category (2) revealed possible impending respiratory failure. As she explained:

> *"…that could be an indication of increasing work of breathing […] the patient's finding it harder to get the oxygen and shift the CO_2."* (HCP - N09).

Six HCPs reported *"periodic"*, irregular breathing being part of the young infants *"normal breathing pattern"* but would *"take it seriously"* if associated with other symptoms such as *"desaturations"* or *"high temperature"*. It was suggested that *"periodic breathing"* could easily be *"misinterpreted as apnoea"* by inexperienced HCPs. Furthermore, it was suggested it may be difficult to differentiate between response categories 'short pauses/irregular breathing: (2)' and 'self-correcting apnoea (increasing in frequency and/or duration): (4)'. As HCP-D03 explained:

> *"…what's a short pause and when does it become a self-correcting apnoea?"* (HCP-D03).

HCP-A08 recommended that 'short pauses/irregular breathing: (2)' should be removed completely. Despite there being an overlap between these two response categories, HCP-D04 thought it to be acceptable to include both response categories in the context of bronchiolitis. With the exception of HCP - H01, all the HCPs found this section *"easy to complete"*.

8.8.4 Effort of breathing

For this section HCPs were provided with a list of symptoms associated with 'effort of breathing': tracheal tug, sub/intercostal recession, sub-sternal recession, head bobbing, grunting, nasal flare, accessory muscle use abdominal breathing and central cyanotic episodes (LIBSS-PRO Version 7.7). For the first two symptoms, HCPs had to decide between three response categories: 'absent: (0)'; 'mild: (1)'; or 'marked: (2)'. For the remaining seven symptoms there were two response categories: 'absent: (0)' or 'present: (1 or 4)'. 'Central cyanotic episodes' was given a greater score weighting for the

response category ‘present: (4)’ and colour coded red: issue an arrest call. For those HCPs who received Version 8.0 the following symptoms had been removed: accessory muscle use; abdominal breathing. The response categories had changed to: ‘absent: (0)’, ‘present: (1)’ for tracheal tug, sub-sternal recession, head bobbing, grunting and nasal flare. For central cyanotic episodes the answer responses were either: ‘absent: (0’), ‘present: (4). There were three answer options for sub/intercostal recession: ‘absent: (0)’; ‘present: (1)’ or ‘severe: (2)’.

‘Effort of breathing’ was described as *“how much extra work”* the infant had to undertake to maintain *“normal respiratory function”* using *“respiratory and accessory muscles”*. It was judged that collecting information on these symptoms would provide useful information on trends. Some of the symptoms were considered more important than others. HCP-D10 felt *“grunting”* was an *“important sign”* and not only should it be given a *“higher score”* but it should be removed from the ‘effort of breathing’ section and classified as a *“separate risk factor”*. Two HCPs found the term ‘sub-sternal recession’ difficult to comprehend and wanted further clarification. ‘Tracheal tug’ was believed to be difficult to detect in a young infant *“who doesn’t have a neck”*. It was suggested by HCP-D10 that the response category ‘present: (4)’ for ‘central cyanotic episodes’ should be weighted similarly to the response category ‘apnoea requiring bag and mask ventilation: (8)’ for ‘apnoea’.

The HCPs identified a number of areas of overlap within this section. It was thought that ‘accessory muscle use’ could be removed as this was already covered by ‘tracheal tug’ and ‘recession’. ‘Abdominal breathing’ was judged redundant for two reasons: firstly *“most neonates are abdominal breathers”*

and secondly it was deemed to *"overlap with accessory muscle use"*. Furthermore, it was considered that 'central cyanotic episodes' was partly covered by an alternative section in the scoring instrument (% of oxygen to maintain saturations >92%). Overall, the 'effort of breathing' section in Version 7.7 was found to be particularly confusing by HCPs. This was due to the response categories being inconsistent between the first two symptoms and the remaining seven symptoms. Changes were made to the score responses in Version 8.0 and in general HCPs found this section *"straight forward to complete"*.

8.8.5 Respiratory rate

The 'respiratory rate' section was sub-divided into two age groups each having three response categories: under three months '*'*25-59 bpm: (0)'; '60-70bpm: (2)'; '>70 or <25 bpm: (4)'; or three months and older '20-55 bpm: (0)'; '50-65: (2)'; '>65 or < 20 bpm: (4)'. The third response category for both age groups was colour coded yellow: consider urgent review by senior doctor. HCPs understood what this section was asking about and HCP-D04's response was typical:

> *"[this section is]…inquiring about the child's rate of breathing and how appropriate it is in relation to the child's age…" (*HCP-D04).

This domain was reported to be *"objective"* and the reference ranges were considered reasonable. It was noted by HCP-03 that respiratory rate is *"dynamic"* and is dependent on the activity of the infant at the time of the score. This section of the scoring instrument was found to be *"very easy to complete"*.

8.8.6 % Oxygen to maintain saturations ≥92%

This domain required HCPs to choose one of four response categories related to the infant's oxygen requirements as follows: 'room air (21%): (0)'; 22-40% (nasal cannula up to 2 litres; face mask without reservoir bag; head box; Optiflow; CPAP): (2)'; 41-50% (head box; Optiflow; CPAP), '6' ≥51% (facemask with reservoir bag; Optiflow; CPAP): (4)'. The fourth response category was colour coded yellow: consider urgent review by senior doctor. Underneath the response categories there was a box with the following caveat: 'In chronic lung or congenital heart disease substitute saturations of 92% for accepted level of saturations when well'. HCPs believed this section was asking them to assess whether the child needed supplemental oxygen to maintain oxygen saturations greater than 92%. HCP-D10 postulated:

> *"the more oxygen you need the more severe the illness is likely to be"* (HCP-D10).

'Optiflow' was the only term that a significant number of HCPs had difficulty in understanding. This was due to it being a relatively new intervention for oxygen therapy delivery: not all hospitals had introduced this intervention into clinical practice. HCP-D03 raised an issue of uncertainty as to how to score *"wafting"* oxygen. This is when an infant will not tolerate a mask or nasal specs being directly applied to the face and a mask is positioned a few inches away from the face. It is thus difficult to accurately assess how much oxygen the infant is actually receiving to provide a score. When asked how they think they might score an infant with *"wafting oxygen"* HCP-D03 stated:

> *"I would probably score that as a two"* (HCP-D03).

HCP-N06 raised an issue with how oxygen was usually recorded in litres as opposed to percentages in her clinical setting and how this may cause some difficulties with completing the score, as she explained:

> *"…for example, we've had one [infant] on cpap and a lot of people have been a bit unsure how to work out the litres to percentage […] so we would probably need a bit of training in that"* (HCP-N06).

Two HCPs (HCP-D03 and HCP-D16) suggested for infants with CLD you would be *"aiming for saturations at 92 plus"* and a lower cut-off value was considered *"more important"* for infants with CHD. Therefore it was suggested by one HCP (HCP-D16) that CLD should be removed from the caveat. A further HCP (HCP-A08) felt that including the caveat *"makes the whole section look a bit complicated"*. Whilst another HCP (HCP-D04) suggested the caveat should be moved to the beginning of the domain for clarity. All HCPs (n=16) felt overall this section was *"objective"* and *"easy"* to complete, although one HCP (HCP-A08) felt it was a little *"wordy"*.

8.8.7 Heart rate

'Heart rate' was sub-divided into two age groups each with three response categories: under three months '105-165 bpm: (0)'; '166-180 bpm: (2)'; '>180 or <105 bpm: (4)'and three months and over '95-145 bpm: (0)'; '146-160 bpm: (2)'; '>160 or <95 bpm: (4)'. The third response category for both age groups was colour coded yellow: consider urgent review by senior doctor. It was felt that heart rate was an *"important marker"* to determine how *"unwell"* an infant is. 'Heart rate' would be assessed either by *"monitoring"*, *"checking a pulse"* or *"listening at the apex with a stethoscope"*. HCP-D03 suggested 'heart rate'

should be *"measured directly"* at the apex and proposed adding the following instruction, *"taken at the apex"* as he described:

> *"…because when people are doing observations they should do them properly…"* (HCP-D03).

When this instruction was incorporated into LIBSS-PRO (Version 8.0) the response was unenthusiastic. Most of the HCPs (n=11) reportedly used monitoring to assess 'heart rate' and it was believed *"unrealistic"* to auscultate 'heart rate' at the apex. Furthermore, the accuracy of auscultation at the apex for 'heart rate' was questioned, especially when heart rates are greater than 166 beats per minute (bpm) as HCP-D11 explained:

> *"…it's very quick and you are never going to be so accurate…you're always going to be […] guestimating…"* (HCP-D11).

However, auscultation of 'heart rate' was considered useful to check the accuracy of the monitoring equipment. Most of the HCPs (n=9) judged the reference ranges within the three response categories to be reasonable. Yet HCP-D10 had a reservation about the upper threshold of 180 bpm for infants less than three months of age. He suggested having an additional category with an upper threshold of 200 bpm as he explained:

> *"…if you asked me to come and review a child and I see 185 [bpm] I wouldn't differentiate much with this group …but when I look at the child it might tell us a lot more […] if it's 200 [bpm]…my alarm bells will ring"* (HCP-D10).

A recommendation from HCP (HCP-A08) was to have a LIBSS-PRO instrument developed specifically for the two different age groups rather than having to *"ignore a section"* within the score because it is for a *"different age*

group". Another issue identified was with the use of *"adult probes"* for pulse oximetry in some clinical settings, for example, *"GP practices"*. HCP-N07 proposed:

> *"…this could produce a ridiculous set of observations which doesn't tally with the infant"* (HCP-N07).

It was also noted that 'heart rate', like 'respiratory rate', was dynamic and could alter significantly in relation to activity of the infant at the time. Overall the section on 'heart rate' was considered *"easy to complete"* by the HCPs.

8.8.8 Appearance/level of consciousness

For this section of the score HCPs were required to assess appearance, behaviour and neurology and score against one of four response categories: 'alert & active/normal sleep: (0)'; 'irritable/fractious/restless: (2)'; 'lethargic/floppy/no interaction: (4)'; 'unresponsive: (6)'. The third category was colour coded yellow: consider urgent review by senior doctor and the fourth category was colour coded red: issue an arrest call.

The HCPs were in agreement about what this section aimed to be assessing. HCP-D15's response was typical:

> *"…the consciousness level of the infant […] whether or not they [the infant] are irritable or […] not acting as they usually do or in extreme situations not responding at all…"* (HCP-D15).

Some HCPs (n=3) believed some response categories were objective whilst other categories appeared *"ambiguous"* or open to *"interpretation"*. It was proposed that *"outside influences"*, for example, painful procedures, could induce certain behaviour changes in infants. Furthermore, it was suggested

that there may be overlap between the response categories, which require further *"clarification"*, as HCP-D03 observed:

> *"…well 'no interaction' suggests to me that they are 'unresponsive' 'cause they are not interacting to anything that you are doing …so they are not responding…"* (HCP-D03).

HCP-N13 suggested merging the two middle categories so the 'appearance and behaviour' has a sum total of three categories. HCPs contrasted this section with other neurological scoring instruments that are widely used in clinical practice and considered objective, such as GCS and AVPU score. Although these scores were well received it was thought they may be *"too simplistic",* particularly AVPU for use in infants. HCP-N07 commented:

> *"…when we write out nursing kardex…you know… will write happy interactive baby…we don't just put the baby is alert…we make a comment on how they are actually handling…"* (HCP-N07).

Despite the identified issues with subjectivity this section of the LIBSS-PRO it was reported to be *"easy to complete"* and thought to be useful to identify *"trends"* with the illness progression.

8.8.9 Hydration and perfusion

The 'hydration and perfusion' section was sub-divided into 'feeds', 'urine output' and 'perfusion'. The 'feeds' section had three response categories: 'usual amount of feeds: (0)'; '50-75% of feeds: (2)'; '<50% of feeds: (4)'. The third category was colour coded yellow: consider urgent review by senior doctor. 'Urine output' had three response categories: 'usual amount of wet nappies: (0)'; 'reduction in number of wet nappies: (2)'; 'small volumes of

concentrated urine or anuric: (4)'. The third category was colour coded yellow: consider urgent review by senior doctor. 'Perfusion' had two response categories: 'central capillary refill time > 2 seconds: (2)' (colour coded yellow: consider urgent review by senior doctor) and 'sunken eyes/fontanelle: (2)'. HCPs reported understanding what this domain is asking them to assess, and HCP-H01 summed this up:

> *"…how much fluids they [the infants] are taking on board …how much they are passing out and whether their capillary refill is as you would expect…or whether they are dehydrated…"* (HCP-H01).

HCPs recounted how they would ask the parents for information on the amount of feed the infant usually takes and then estimate how much feed the infant was actually taking. An issue highlighted by this process was that parental reports were reported often to be *"unreliable"* or *"wrong"*. Detailed questioning of the parents may uncover infants are taking an adequate volume of feed over the day but are taking *"smaller amounts more frequently"*. It was suggested that *"explicit questioning"* of the parents is required to obtain an accurate reflection of feed intake. HCP-H01 noted the incongruity between the volume of feed provided by the parents at home and the volume of hospital maintenance feeds calculated by weight:

> *"…what we tend to do is work them out on the 150 or 120/kg […] per day […] the parents might think they're not taking their usual amount of fluids but as far as we're concerned their intake is absolutely perfect for their weight…"* (HCP-H01).

For those infants who are admitted to hospital, HCPs reported that hydration status becomes easier to assess as the infant has a *"fluid balance chart filled*

out". It was also reported that maintenance fluid intake would be restricted to 75% if the infant was thought to be *"working hard"* to breathe. It was suggested by one HCP that it may be difficult to use the score with an infant who is receiving either nasogastric (NG) feeds or intravenous (IV) fluids with the current response options, as he explained:

> *"…if you are being NG fed […] you are getting 100% of your feeds…do you score a zero or do you score a four…I think you should probably score a four […] so I would say less than 50% or requiring NG feeds stroke IV fluids […] the very fact that they are needing NG feeds would mean to me that they are more severe…"* (HCP-D03).

HCP-A08 highlighted that there was an *"expectation"* that those infants receiving IV fluids were sicker than those who receive NG feeds when the route of fluid administration is influenced by the personal preference of the HCP assessing the infant:

> *"…they may just have a penchant for IV fluids …somebody might have gone for an NG […] but doesn't mean the kid's any less sick…"* (HCP-A08).

In some circumstances an infant may receive both NG and IV fluids as HCP-N05 explained:

> *"…sometimes […] we feed them a smaller amount of feeds again so they get the calories and […] we give them a ratio of part IV fluids and part tube feed…"* (HCP-N05).

Furthermore, it was questioned whether the term *"oral feeds"* needs to be included into the wording of the response categories. It was suggested that including the term 'oral feeds' may cause some ambiguity for those infants who

are receiving percutaneous endoscopic gastrostomy (PEG) feeding tubes and not being fed orally. After some deliberation, HCP-D03 suggested including:

> *"…usual amount of feeds and usual route of feeding…"* (HCP-D03).

Urine output was initially assessed from taking a history from the parents and then for those infants admitted to hospital, urine output would be documented on the fluid balance chart. HCP-N07 suggested including a time frame when assessing urine output to improve clarity:

> *"…you could ask the question to someone… have they passed urine in the last four hours? and the answer is no…the level of concern would raise […] if you are putting a time frame that's black and white…not passing urine could be potentially interpreted different …by different people…"* (HCP-N07).

It became apparent that assessment of urine output differed depending on the clinical environment in which the infant was situated. HCPs on general medical wards recorded urine output in terms of number of wet nappies over 24 hours, whilst HCPs in critical care areas weigh the nappy to obtain a more accurate measure of urine (mLs/kg/hour). Three HCPs either reported that they did not understand the term *'anuric'* or highlighted that other HCPs may not necessarily understand this term. Although it was thought that 'feeds' and 'urine output' were both *"equally important",* it was judged they were both providing similar information on hydration status. HCPs contemplated whether these two sections could be merged together or whether one of these two sections should be removed. The general consensus was that both sections should remain unchanged with HCP-N14 explaining:

"I think even though one is dependent on the other they probably still need to be separate …'cause even the respiratory and heart rate are dependent on the other but they are very separate aren't they…"(HCP-N14).

Assessing capillary refill time (CRT) was considered to be straight forward and thought that, with training it could be undertaken by HCPs *"across the board"*. More senior HCPs recognised that to obtain an accurate CRT it should be taken over a bony prominence, on a central region of the body, such as the sternum. Some more junior HCPs reported assessing CRT by applying pressure at a peripheral location, a digit, for instance. It was suggested that the term *"central"* should be included as a prefix to CRT to avoid CRT being undertaken at a peripheral location. It was understood by some HCPs (n=5) that in addition to dehydration, a prolonged CRT could be due to a *"cold environment"*, *"sepsis"*, *"hypoxia"* or *"acidosis"*.

Sunken eyes and fontanelle were believed to be more difficult to assess, being not that *"accurate"* or *"subjective"*. Some HCPs (n=2) judged 'sunken eyes' and 'sunken fontanelle' as being a *"late sign"* of *"moderate to severe hydration"*. Despite indicating severe dehydration it was noted that that this section only scored a *'2',* the same as 'reduction in number of nappies': an early sign of dehydration. Conversely, one HCP (HCP-D02) preferred it to have a lower score as it was a subjective measure. To gauge whether the infants' eyes were sunken, HCP-D02 stated they would ask the parents *"does his eyes look normal to you?"* Other HCPs (n=7) reported looking for*: "dark circles"*, *"eyes look like they're going into the back of the head"*, *"eyes look tired"* or infants looking *"droopy"*, *"pinched"*, *"anxious"* or *"worried"*. Furthermore, HCP-

D03 described how sunken eyes may not be identified until the infant has improved:

> *"…I don't appreciate that a child has got sunken eyes or had sunken eyes until their better and you go back and see them again and you think you know he did have sunken eyes…"* (HCP-D03).

Two HCPs felt that there was *"a wide range"* in how a normal fontanelle feels making assessment difficult, especially for more junior HCPs. It was suggested by three HCPs that *'sunken eyes and fontanelle'* should be considered for removal from the final version of the LIBSS-PRO, although one HCP reported that sunken fontanelle should be included.

Finally, following completion of each of the sections, HCPs understood they had to add the scores together to arrive at a sum total. Other comments made to improve the score included: adding a section for parental concern and including assessment of skin turgor into the hydration and perfusion section.

8.9 Conclusion

In summary, the cognitive interviews identified a number of issues with regards to comprehension and terminology, which required further clarification and modification. It was also suggested that a number of domains and items should be either merged together or removed. A clearer definition of 'professional concerns/ 'gut' feeling' emerged although, external factors, such as clinical location of the infant and decision making by other HCPs, could influence responses. The LIBSS-PRO was revised and modified in light of these suggestions and identified issues (LIBSS-PRO Version 9.2) **(Appendix 40)**. The strength of these interviews was with the inclusion of a diverse range

of HCPs of varying experience and grades. These interviews highlighted the importance of including HCP stakeholders to aid further refinement of the LIBSS-PRO. The aim of cognitive interviews is to identify problems with questionnaires that can introduce error. Due to the subjective nature of cognitive interviews potential error can occur through the conduct of the interview (130). To increase objectivity and reduce the potential for error, each interview was conducted in a standardised manner using the same format by one interviewer. Although the vignettes were useful to help HCPs to help think about a child with bronchiolitis it may have been more useful to have shown videos. Having a video may have solved the issues raised with finding it *"hard"* not having a child in front of them.

Chapter Nine

9 Clinical field testing

9.1 Introduction

This chapter describes the methods used to establish construct and criterion validity and reliability of the LIBSS-PRO (Version 9.2). Construct validity aims to establish important relationships between the domains and items included in a scoring instrument and how they measure a hypothetical construct (52, 61, 134). For instance, the LIBSS-PRO purports to measure the construct of bronchiolitis severity. In order to gauge severity of illness in infants when using the LIBSS-PRO, cut-off values were determined for 'mild', 'moderate' and 'severe' bronchiolitis. However, construct validity cannot be proven definitively: continued testing is required to provide evidence in order to understand the underlying construct of interest (135).

Criterion validity testing assesses how well the new instrument correlates with another accepted measure, usually a reference 'gold' standard in the field (52). There is currently no instrument available that is widely accepted as being a reference standard to measure bronchiolitis severity. Therefore the reference standard used here was clinical examination by senior HCP, using guidelines/criteria that achieved consensus from the Delphi survey. Prior to using, the reference standard underwent inter-rater reliability testing for agreement to ascertain the level of objectivity.

Reliability testing establishes the amount of random and systematic measurement error that occurs when using the instrument (52). The reliability

of a measure can be assessed by the same rater applying the instrument at different time points (test–retest) (136), or by multiple raters applying the instrument at the same time point (inter-rater reliability) and obtaining similar scores (61, 136).

9.2 Aims

i) To develop cut-off values for a range of values within the score to classify ‘mild’, ‘moderate’ and ‘severe’ bronchiolitis.

ii) To determine whether there is good agreement between the LIBSS-PRO and the agreed clinical reference standard for bronchiolitis severity categories: ‘mild’, ‘moderate’, ‘severe’.

iii) To determine the inter-rater reliability of the LIBSS-PRO instrument

iv) To determine the test-retest reliability of the LIBSS-PRO instrument

9.3 Sample and setting

The field-testing was undertaken during two bronchiolitis seasons: 2011/12 and 2012/13. A convenience sample of eligible HCPs and infants located within 11 study sites (four paediatric tertiary centres and seven DGHs) were identified via the CLRN to participate. The ‘rule of thumb’ to determine sample size for each of the clinical field-tests is 10 and 15 participants for each included domain/item (52). The LIBSS-PRO contained 12 domains therefore a minimum sample size of n=120 infants was calculated for each of the three clinical field tests.

9.4 Informed consent

Informed consent was obtained from all participating HCPs and parents and/or carers of eligible infants prior to the clinical field-testing.

9.5 Methods

Prior to the clinical field-testing, all HCPs were provided with verbal training on how to complete the LIBSS-PRO. For all three clinical field-tests, HCPs were kept 'blind' to each other's LIBSS-PRO score or the assessment of 'mild', 'moderate' or 'severe'. Immediately following field-testing the completed paperwork was filed in an opaque folder until data entry and analysis.

9.6 Construct validity testing

The construct validity testing involved an HCP being asked to administer the LIBSS-PRO instrument to an eligible infant. The reference standard was a clinical examination, independently undertaken, by one or two senior HCPs (paediatrician ST3 or above and/or ANP). The clinical examination took place within 15 minutes of the HCP administering the LIBSS-PRO. It was recognised that clinical examination is subjective. Therefore, following the clinical examination the senior HCP was asked to complete a proforma **(Appendix 41)**. This proforma contained the definition/criteria for 'mild', 'moderate' and 'severe' bronchiolitis that had achieved expert consensus through the Delphi survey. The proforma was used to increase the objectivity of the reference standard. Where possible a second senior HCP was also asked to independently undertake a clinical examination of the eligible infant and complete a proforma. The purpose of the second examination was to enable inter-rater reliability testing to be undertaken to ascertain the level of

agreement for the bronchiolitis severity categories. The inter-rater reliability testing would provide evidence of consistency for the reference standard.

9.7 Criterion validity testing

Criterion validity of the LIBSS-PRO was assessed concurrently by comparing it to a clinically agreed reference standard: clinical examination by a senior HCP. HCPs were asked to administer the LIBSS-PRO instrument to eligible infants. The LIBSS-PRO summed score was calculated, placing the infants in one of the three pre-defined categories: ‘mild’, ‘moderate’ or ‘severe’. Within a 15 minute timeframe the infant was assessed using the clinically agreed reference standard as described in the construct validity testing **(Section 9.6)**. The senior HCP was asked to allocate the infant to one of the three bronchiolitis severity categories on the proforma.

9.8 Reliability Testing

Two HCP raters were invited to independently apply the LIBSS-PRO to the same eligible infant within 15 minutes of each other at two different time points. A time interval (minimum 30 minutes up to a maximum of two hours) was required between time points. Both sets of observations were undertaken in similar clinical conditions.

9.9 Analysis

Data analysis for all three clinical field tests was conducted using SPSS (Version 22). Frequencies were used to examine infant and HCP characteristics. Descriptive statistics (mean (SD)) were used to inspect the

time taken to complete the LIBSS-PRO, the total score values and day of illness.

Ordered categorical data (three categories) were collected for all three clinical field tests. The level of agreement was estimated using the weighted Kappa co-efficient. The Kappa coefficient measures the level of agreement between the screening tool and gold standard when the outcome is measured using either a binary or categorical scale. In the simplest case when there is a binary (yes/no) outcome exact agreement occurs when both the screening tool and gold standard identify the same response. Chance agreement occurs because there are limited (in this example 4) possible outcomes, so even using a random process, such as, tossing a coin some agreement would occur by chance. The kappa coefficient is designed to provide an estimate of the true agreement, which is the exact agreement adjusted for the chance agreement. In this application the outcome measure had three response categories, mild moderate and severe. Consequently the kappa coefficient is expanded to allow for full agreement, for example, mild/mild, disagreement by one category, for example, mild/moderate and full disagreement, for example, mild/severe. These responses are then weighted with full agreement having a weighting of one, disagreement by one category a weighting of 0.5 and full disagreement a weighting of zero. Chance agreement is also calculated in a similar manner. Intra-class Correlation Coefficient (ICC) was used to determine agreement for continuous data using a two-way mixed model for reliability testing. The weighted Kappa and the ICC were interpreted as follows: poor agreement (<0.20); fair agreement (0.21-0.40); moderate agreement (0.41-0.60); good

agreement (0.61-0.80); excellent agreement (0.81-1.0) (137). The weighted Kappa and the ICC co-efficient are presented with 95% CIs.

9.10 Results

9.10.1 Construct validity testing

One hundred and twenty eight construct validity tests were undertaken during the 2011/12 bronchiolitis season. The characteristics of the eligible infants are found in **Table 26**. The majority of HCPs who applied the LIBSS-PRO to infants were nurses (78.8%) with most being employed on AfC grades 5 (56.6%), 6 (14.8%) and 7 (18.9%). Thirteen (10.4%) clinical tests were undertaken either by CvM or a research nurse due to there being no available clinical HCP to apply the LIBSS-PRO. The characteristics of senior HCPs undertaking the first clinical examination were: consultant (60.6%); specialist trainee (31.3%); associate specialist (4.7%); staff grade (2.4%); ANP (0.8%). A total of n=128 clinical tests were undertaken. The mean time taken to complete the LIBSS-PRO was 7.6 (SD 5.4) minutes. The mean LIBSS-PRO score total was 10.5 (6.4). For the paediatrician inter-rater reliability testing n=75 second clinical examinations were undertaken. The characteristics of the senior HCPs undertaking the second clinical examination were: consultant (5.4%); specialist trainee (75.7%); associate specialist (5.4%); staff grade (1.4%); ANP (12.2).

Table 25 Construct validity testing – infant characteristics

Infant Gender	Male 76 (59.4%); Female 52 (40.6%)
Infant Ethnicity	White British 111 (87.4%) Asian or Asian British 2 (1.6%) White European 1 (0.8%) Black or Black British 5 (3.9%) Other 8 (6.3%)
Clinical Setting	Assessment unit 12 (9.4%) General medical ward 88 (68.8%) PHDU 15 (11.7%) PICU 6 (4.7%) Other 7 (5.5%)
Age group	Under three months 68 (53.1%) Three months and over 60 (46.9%)

There was agreement for 57/75 inter-rater reliability tests for 'mild', 'moderate' and 'severe' categories. Inter-rater reliability for the reference standard raters when assessing for 'mild', 'moderate' & 'severe' bronchiolitis showed good agreement (Weighted Kappa 0.61, 95% CIs [0.35-0.86]) **(Table 27)**. However, the 95% confidence intervals ranged between fair and excellent agreement. This imprecision was likely due to the small sample size and the low number of tests falling within the 'severe' category. The exact weighted agreement was 89% but chance agreement (how much agreement would be expected to be present by chance alone) was 73%. This was due to the sparse distribution of cases outside mild/mild and moderate/moderate categories.

Table 26: Paediatrician inter-rater reliability testing

	Mild	**Moderate**	**Severe**	**Totals**
Mild	23	9	0	32
Moderate	4	35	1	40
Severe	0	2	1	3
Totals	27	46	2	75

Prior to developing the cut-off values within the score a decision had to be made with regards to which severity category to use for the 16 clinical assessments where the reference standard raters disagreed. CvM and a second researcher (PM) independently scrutinised the patient data and comments on the LIBSS-PRO and both reference standard proformas. This information was used to decide which category the infant should fall into. The two researchers then compared results. There was agreement for 10/16 tests whilst 6/16 tests still disagreed. Of these six tests disagreements occurred in four tests due to the infant receiving respiratory support. One infant received 0.5L of oxygen via nasal specs. Three infants received NIV (nCPAP or HFNC) with two infants requiring less than 40% oxygen and one infant was in air. All four infants were in the improving phase of bronchiolitis with minimal symptoms. The remaining two infants did not require respiratory support but either had reduced feeds or tracheal tug. Following further discussion CvM and PM eventually agreed categories for the remaining six tests.

The final stage of the construct validity was to develop an optimum cut-off to classify infants as being either ‘mild’ or ‘moderate’, and then a second cut-off to classify patients as being either ‘moderate’ or ‘severe’. Sensitivity and specificity was calculated for a range of cut-off values. The sensitivity and specificity curves were then plotted on a single graph for a range of cut-off values **(Figure 8 & 9)**. Where the sensitivity and specificity curves crossed is the cut-off value which optimises sensitivity and specificity. The cut-off value for mild and moderate was a LIBSS-PRO score of 10, whilst the cut-off value for moderate and severe was a LIBSS-PRO score of 20.

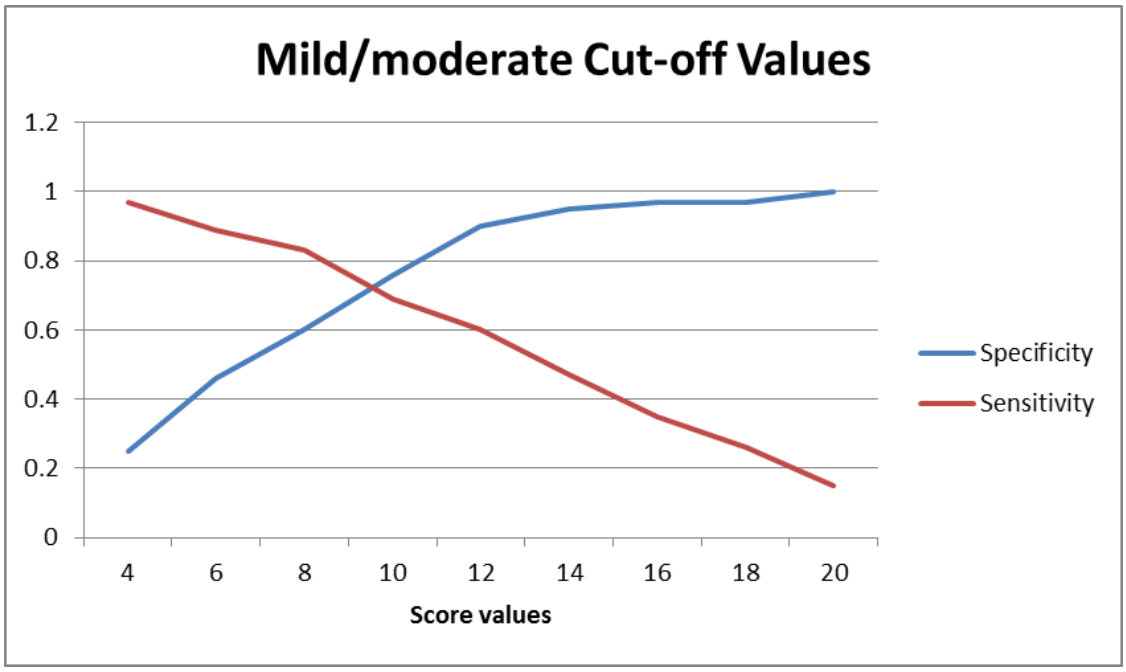


Figure 9: Mild/moderate sensitivity and specificity plotted for range of cut-off values

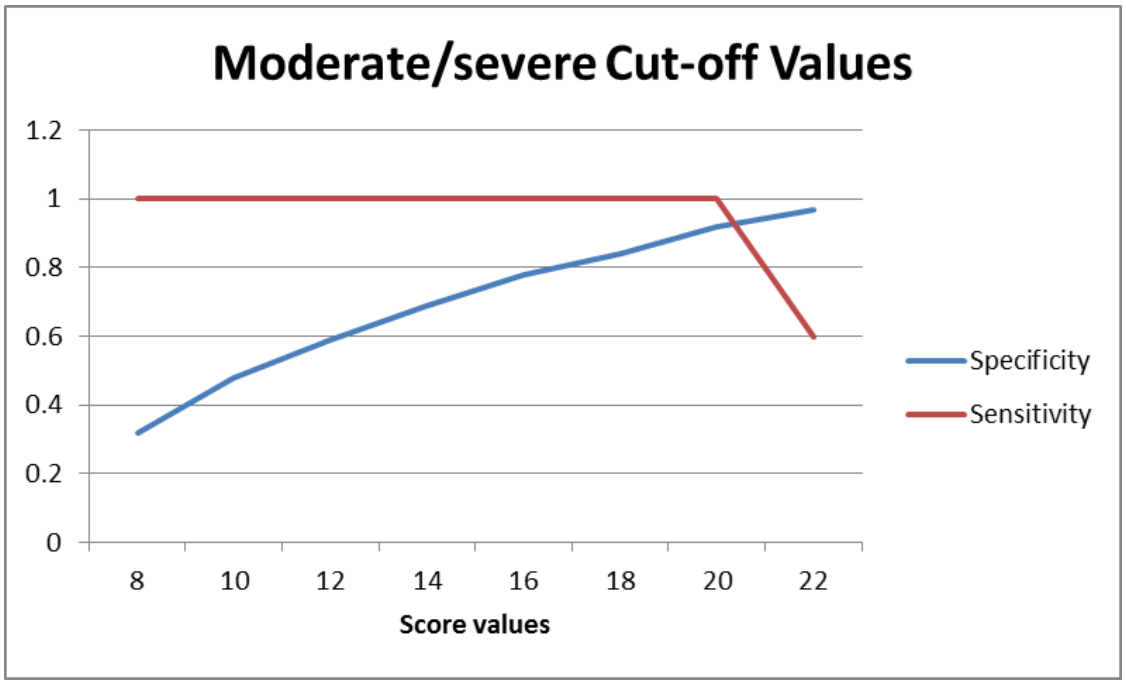


Figure 10: Moderate/severe sensitivity and specificity plotted for range of cut-off values

9.10.2 Criterion validity testing

One hundred and twenty three criterion validity tests were undertaken. The mean time taken to apply the LIBSS-PRO was 5.7 (3.10) minutes. The mean day of illness of the infant at the time of testing was 5.1 (2.4) days. Infant characteristics can be found in **Table 28**. The mean LIBSS-PRO score was 9.92 (8.14). The majority of HCPs who applied the score were nurses (70.7%), mainly AfC band 5 (61.8%); 6 (17.1%) or 7 (16.3%). Thirty (24.4%) tests were undertaken either by CvM or a research nurse because clinical HCPs were unavailable. The senior HCPs who undertook the clinical examination comprised consultants (34.1%), specialist trainees (40.7%), associate specialists (13.0%), staff grades (6.5%) and ANPs (5.7%).

Table 27: Criterion validity testing- infant characteristics

Gender	Male 65 (52.8%); Female 58 (47.2%)
Ethnicity	White British 112 (91.1%) Asian or Asian British 1 (0.8%) White European 1 (0.8%) Black or Black British 4 (3.3%) Other 5 (4.1%)
Clinical Setting	Medical assessment unit 27 (22.1%) General medical ward 55 (45.1%) PHDU 32 (26.2%) PICU 8 (6.6%)
Age group	Under three months 75 (61.0%) Three months and over 48 (39.0%)

Seventy-two out of 123 (58.5%) LIBSS-PRO scores agreed with the reference standard. The inter-rater reliability testing between the LIBSS-PRO and the reference standard indicated fair agreement. However, 95% CIs ranged between poor and moderate agreement (Kappa 0.38, 95% CIs [0.18-

0.59]) **(Table 29)**. The exact weighted agreement was 78% but chance agreement was high at 64%.

Table 28: Agreement between the LIBSS-PRO and the reference standard

	Mild	**Moderate**	**Severe**	**Totals**
Mild	45	30	3	78
Moderate	4	23	7	34
Severe	0	7	4	11
Totals	49	60	14	123

There are several possible explanations for this result. There were differences in recorded observations between the LIBSS-PRO and the reference standard for the following symptoms: recession; tracheal tug; respiratory rate; irritable and restless; feed volumes. This may highlight a training/education requirement. One of the proforma criteria for ‘moderate’ was: requiring supplemental oxygen to maintain saturations greater than 92%. From the documentation, it was observed that a number of infants who were improving had minimal symptoms but still required a small amount of oxygen (less than one litre) to maintain saturations above 92%. Despite the infant improving, the reference standard criteria categorised the infant as being ‘moderate’ whilst the LIBSS-PRO score categorised the infant as ‘mild’. It was also discerned that interventions such as, suctioning, feeding, CPAP or HFNC could greatly affect the severity of the symptoms. This could lead to discrepancy between the LIBSS-PRO and the reference standard. Finally, the clinical area in which the infant was situated may have influenced the reference standard assessment. For example, one senior HCP assessed an infant on PHDU as ‘severe’ in spite of the child being in head box oxygen with a plan for ward discharge.

9.10.3 Reliability testing

The number of eligible infants recruited to participate in the clinical testing of the LIBSS-PRO was 128. Their characteristics are in **Table 30**. The mean day of illness when the score was applied to the infant was 5.5 (4.7) days. Most HCPs participating as rater one were nurses (74%), mainly AfC band 5 (62.7%) or 6 (17.5%). 9.4% of participants were doctors and 7.9% were health care assistants. For ten tests (7.9%) either CvM or a research nurse acted as rater one if other clinical staff were unavailable. The mean time taken for rater one to apply the LIBSS-PRO was: test one 6.4 (3.2); test two 4.8 (2.4) minutes. The mean LIBSS-PRO score total for rater one was: test one 8.7 (6.8); test two 8.2 (6.7). Of those HCPs participating as rater two, nurses accounted for only 38.1% of participants (AfC band 5 (28.2%) and band 6 (38.7%)). The remaining HCP participants were doctors (5.6%) or student nurse (0.8%). For 70 (55.6%) tests, either CvM or a research nurse acted as the second rater due to clinical staff being unavailable. The mean time taken for rater two to apply the LIBSS-PRO was: test one 6.0 (2.7); test two 8.3 (7.0) minutes. The mean LIBSS-PRO score total for rater two was: test one 9.6 (7.2); test two 8.3 (7.0).

Table 29: Reliability testing – infant characteristics

Gender	Male 71 (55.5%); Female 57 (44.5%)
Ethnicity	White British 124 (96.9%) Asian or Asian British 2 (1.6%) Chinese or Chinese British 1 (0.8%) Black or Black British 1 (0.8%) Other 5 (4.1%)
Clinical Setting	Medical assessment unit 17 (13.3%) General medical ward 97 (78.8%) PHDU 6 (4.7%) PICU 6 (4.7%)
Age group	Under three months 71 (55.5%) Three months and over 57 (44.5%)

9.10.3.1 Inter-rater reliability

For inter-rater reliability, the ICC for the overall LIBSS-PRO score total at both time points showed excellent agreement, with 95% CIs ranging between good and excellent: Time point 1(T1) 0.83, 95% CIs [0.75-0.88]; Time point 2 (T2) 0.84, 95% CIs [0.77-0.89]. The scores for individual domains and items can be found in **Appendix 42**. Two domains had excellent agreement: 'saturations and oxygen supplementation' (T1 0.97, 95% CIs [0.96-0.98]; T2 0.97, 95% CIs [0.96-0.98]); 'feeding' (T1 0.80, 95% CIs [0.72-0.86]; T2, 95% CIs 0.80 [0.71-0.86]). Three domains had good agreement: 'effort of breathing' (T1 0.65, 95% CIs [0.50-0.75]; T2 0.67, 95% CIs [0.53-0.77]); 'heart rate' (T1 0.71, 95% CIs [0.59-0.79]; T2, 95% CIs 0.70 [0.57-0.79]); 'urine output' (T1 0.73, 95% CIs [0.62-0.81]; T2 0.72, 95% CIs [0.60-0.80]). Of the six items within the 'effort of breathing' domain only two items achieved good agreement: 'recession' (T10.61, 95% CIs [0.44-0.73]; T2 0.69, 95% CIs [0.56-0.78]); 'head bobbing' (T1 0.62, 95% CIs [0.46-0.73]; T2 0.71, 95% CIs [0.58-0.80]). Three domains had moderate agreement: 'professional concerns' (T1 0.49, 95% CIs [0.28-0.64]; T2 0.46, 95% CIs [0.23-0.62]); 'respiratory rate' (T1

0.43, 95% CIs [0.19-0.60]; T2 0.41, 95% CIs [0.41-0.41]); ‘appearance’ (T1 0.54, 95% CIs [0.35-0.68]; T2 0.41, 95% CIs [0.16-0.59]). Finally there was poor agreement for two domains: ‘apnoea’ (T1 -0.12, 95% CIs [-0.59-0.20]; T2 -0.97, 95% CIs [-0.56-0.23]); ‘CRT’ (T1 -0.14, 95% CIs [-0.63-0.19]; T2 0.22, 95% CIs [-0.11-0.45]).

The moderate agreement within the ‘respiratory rate’ domain was unexpected. There is a dynamic association between heart rate and respiratory rate. It was assumed that any increase or decrease in respiratory rate would have a similar effect on heart rate, and thus similar levels of agreement would be observed, but this was not the case. One explanation for this observed difference might be that respiratory rate was largely assessed manually whereas heart rate was more likely to be obtained from the monitoring equipment. This premise might also account for the poor agreement for CRT which also relied on manual assessment.

Agreement between the two raters at time point one for the categories ‘mild’, ‘moderate’ and ‘severe’ was moderate (weighted kappa 0.43, 95% CIs [0.22-65]). However the 95% CIs ranged between fair and good. The exact agreement was 0.83 and the chance agreement 0.69 **(Table 31)**.

Table 30: Agreement for LIBSS-PRO categories ‘mild’, ‘moderate’ and ‘severe’ (Time point 1)

	Mild	**Moderate**	**Severe**	**Totals**
Mild	64	13	3	80
Moderate	16	18	6	40
Severe	0	3	4	7
Totals	80	34	13	127

Agreement between the two raters at time point two for the categories ‘mild’, ‘moderate’ and ‘severe’ was moderate (weighted kappa 0.49, 95% CIs [0.27-0.72]). However 95% CIs ranged between fair and good. The exact agreement was 0.86 with chance agreement being 0.73 **(Table 32)**.

Table 31: Agreement for LIBSS-PRO categories ‘mild’, ‘moderate’ and ‘severe’ (Time point 2)

	Mild	**Moderate**	**Severe**	**Totals**
Mild	71	12	1	84
Moderate	14	15	5	34
Severe	0	1	4	5
Totals	85	28	10	123

Seventy tests were undertaken by a member of the research team (CvM or a research nurse) on more than one occasion. Therefore the research team members could be considered as being ‘expert’ in comparison to the clinical staff who were involved with the testing on one occasion. The data was further analysed to explore the differences between the tests undertaken by an ‘expert’ and a ‘novice’ rater and those tests undertaken by two ‘novice’ raters.

There was fair agreement between two ‘novice’ raters at time point one for the categories ‘mild’, ‘moderate’ and ‘severe’ although the 95%CIs ranged between poor and good agreement (weighted kappa 0.33 95%CIs [-0.03-0.69]). The exact agreement was 0.79 and the chance agreement was 0.69. Moderate agreement was found between the ‘novice’ and ‘expert’ raters with 95% CIs ranging between fair and good agreement (weighted kappa 0.51 95%CIs [0.25-0.77]). The exact agreement was 0.85 and the chance agreement was 0.69.

For time point two there was fair agreement between the two ‘novice’ raters for the categories ‘mild’, ‘moderate’ and ‘severe’ although the 95%CIs ranged between poor and good agreement (weighted kappa 0.31 95%CIs [-0.13-0.75]). The exact agreement was 0.84 and the chance agreement was 0.77. Whilst moderate agreement was found between the ‘novice’ and ‘expert’ raters with 95% CIs ranging between fair and excellent agreement (weighted kappa 0.51 95%CIs [0.25-0.77]). The exact agreement was 0.85 and the chance agreement was 0.69.

Although the ‘expert’/ ‘novice’ raters have a better weighted kappa compared to the ‘novice’/ ‘novice’ raters it would be difficult to draw a conclusion that this was largely due to expertise alone. Firstly, one half of the ‘expert’/ ‘novice’ dyad was a ‘novice’. Ideally, to make a clean comparison for agreement the dyads should not mix ‘expert’ and ‘novice’ raters. Secondly dividing these two groups for analysis reduces the sample size particularly for the ‘novice’/ ‘novice’ dyad group. The reduction in sample size for this group could account for the wide 95% CIs observed.

9.10.3.2 Test re-test reliability

For test re-test reliability, the ICC for the overall LIBSS-PRO score for both raters showed excellent agreement: rater one (R1) 0.92, 95%CIs [0.89-0.94]; rater two (R2) 0.93, 95%CIs [0.91-0.95]. The scores for individual domains and items can be found in **Appendix 43**. The test re-test reliability for the following domains was excellent for both raters: ‘professional concerns’ (R1 0.86, 95%CIs [0.80-0.90]; R2 0.86, 95%CIs [0.80-0.90]); ‘effort of breathing’ (R1 0.89, 95%CIs [0.85-0.92], R2 0.87, 95%CIs [0.82-0.91]); ‘saturations and

oxygen supplementation' (R1 0.95, 95%CIs [0.93-0.96], R2 0.95, 95%CIs [0.93-0.96]); 'feeding' (R1 0.96, 95%CIs [0.94-0.97], R2 0.94, 95%CIs [0.92-0.96]); 'urine output' (R1 0.93, 95%CIs [0.90-0.95]; R2 0.93, 95%CIs [0.90-0.95]). For one domain, 'apnoea', there was fair agreement for R1 (0.35, 95%CIs [0.07-0.54]) whilst R2 had excellent agreement (0.83, 95%CIs [0.76-0.88]). The following domains achieved good agreement: 'respiratory rate' (R1 0.62, 95%CIs [0.46-0.73], R2 0.68, 95%CIs [0.54-0.77]); 'appearance' (R1 0.72, 95%CIs [0.60-0.80], R2 0.69, 95%CIs [0.56-0.78]). One domain – 'CRT' – had good agreement for R1whilst there was fair agreement for R2 (0.26, 95%CIs [-0.04-0.48]). Finally one domain – 'heart rate' – had moderate agreement (R1 0.50, 95%CIs [0.28-0.65]; R2 0.50, 95%CIs [0.28-0.65]).

9.11 Conclusion

Following clinical field-testing, cut-off values were established for 'mild' (0-10); 'moderate' (11-20) and 'severe' ($\geq$21) bronchiolitis for the LIBSS-PRO. For criterion validity, the LIBSS-PRO was found to have fair agreement when compared to the reference standard. Although we attempted to employ rigorous methods to develop an objective reference standard it was still found to be subjective which more than likely affected the agreement. It became apparent during the clinical field testing there were problems with the reference standard proforma. A number of children who were improving and had 'mild' symptoms of bronchiolitis were being incorrectly classified as 'moderate'. This was due to them being on small amounts of oxygen (<0.5L/min) to maintain oxygen saturations at 92% or greater. Furthermore, a proportion of children would meet the criteria for oxygen saturations in air when awake but would

immediately drop their saturations to approximately 89-90% when asleep and would require oxygen. According to the reference standard proforma being on oxygen immediately categorises the child as being ‘moderate’ and did not take into account those children with improving symptoms. A further issue found with the reference standard was that it was operator dependent. The clinician completing the proforma was found to be influenced by the location of infant and their clinical experience. For example, a consultant intensivist assessed an infant located on PHDU on nCPAP as being ‘mild’. Whereas a general paediatrician assessed a similar infant as being ‘severe’ despite the infant being weaned from nCPAP with a plan for ward discharge.

The LIBSS-PRO was found to have good reliability (inter-rater and test-retest) for the overall score total. However, the agreement for individual domains and items ranged between excellent and poor. This is probably due to the subjective nature of some of the domains and items. In a future revision of the score those domains and items with less than good agreement may need to be considered for removal. For 70 (55.6%) of the tests CvM or a research nurse acted as rater 2 when no ward nurse was available. This may have introduced an element of bias. CvM and the research nurses were undertaking the testing on a regular basis. Therefore were more familiar and experienced with completing the LIBSS-PRO. In comparison to a clinical health care professional who may have completed the LIBSS-PRO once. In spite of this difference in experience the inter-rater agreement for the LIBSS-PRO score total between the ‘novice’ and ‘expert’ raters was still excellent. In spite of the excellent agreement for the LIBSS-PRO score total the agreement for individual items was variable. When looking at the paperwork for the construct

and criterion validity testing differences were also noted between what was scored on the LIBSS-PRO and what was recorded on the reference standard proforma. For example, the senior paediatrician may have recorded that recession was observed yet this may not have been scored on the LIBSS-PRO. These observed differences for individual items by the various health care professionals may highlight an educational or training need in clinical assessment.

In conclusion, the clinical field-tests were able to establish validity and reliability of the LIBSS-PRO particularly for those infants with ‘mild’ or ‘moderate’ bronchiolitis. Further evidence may be required to establish validity and reliability in the more ‘severe’ bronchiolitis group. Additional longitudinal research may be required to compare agreement between ‘novice’ and ‘expert’ raters to determine the variability between scores and how this impacts on the LIBSS-PRO as an outcome measure.

Chapter Ten

10 Discussion

10.1 Summary

Rigorous methods were used to develop and validate the LIBSS-PRO instrument to assess severity of illness in infants with a clinical diagnosis of bronchiolitis. A conceptual framework was derived from the literature and from stakeholder consultation using workshop groups with NGT and in-depth interviews. The conceptual framework comprised five domains: respiratory; feeding/hydration; appearance/behaviour; risk factors; miscellaneous signs and symptoms. A total of 101 signs, symptoms and risk factors were categorised under the five domain headings. Selection over which of the pre-identified signs, symptoms and risk factors to use as items in the LIBSS-PRO was obtained through Delphi expert consensus methods. Forty eight items achieved consensus and were included in the LIBSS-PRO. Various iterations of the LIBSS-PRO were shown to several HCP groups and the study steering group to establish face validity. Based upon comments and feedback from these groups, the LIBSS-PRO (Version 7.0) contained the following domains: 'risk factors'; 'professional concerns/'gut' feeling'; 'apnoea'; 'effort of breathing'; 'respiratory rate'; 'chest auscultation'; 'blood gas analysis'; 'supplemental oxygen requirements'; 'heart rate'; 'appearance/behaviour'; 'hydration/perfusion' (feeds, urine output, capillary refill, sunken eyes/fontanelle). Content validity field-testing was undertaken in eligible infants (n=114) and HCPs (n=6). All items were evaluated as being clinically relevant

but two items were removed due to substantial missing data: auscultation; blood gas analysis. The outcome of the cognitive interviews with HCPs (n=16) led to items being merged together, and changes to wording and answer responses. Furthermore a more objective definition of professional concerns/'gut' feeling was developed. The LIBSS-PRO (Version 8.0) was revised prior to the clinical field-testing. Construct validity testing (n=128) enabled cut-off values to be determined in the score for 'mild', 'moderate' and 'severe' bronchiolitis. Paediatrician inter-rater reliability testing (n=75) was undertaken to establish the level of agreement for the clinically agreed reference standard prior to criterion validity testing. Criterion validity testing (n=123) found good agreement between the LIBSS-PRO (Version 9.2) and the clinically agreed reference standard although the 95% CIs range between poor and excellent agreement. Finally there was excellent agreement for inter-rater reliability and test-retest reliability testing (n=128).

10.2 Challenges with developing and validating the LIBSS-PRO

There is no standardised definition of bronchiolitis. For this study we used the definition developed by the SIGN Bronchiolitis guideline group (17). This guideline limited bronchiolitis to infants up to 12 months of age to minimise bias from including older children with other wheezing phenotypes. The SIGN Bronchiolitis guideline was published in 2006 (17). This guideline has since been superseded by the National Institute for Health and Care Excellence (NICE) Bronchiolitis guideline (138). The definition of bronchiolitis proposed in the NICE guideline extends the age group beyond 12 months to include

children up to 24 months. The LIBSS-PRO will be restricted for use in infants aged up to 12 months. This change in definition by the NICE guideline may preclude the uptake of the LIBSS-PRO in clinical practice and restrict its use as an outcome measure in clinical research.

Bronchiolitis being a seasonal condition presented a challenge. Stakeholder groups and clinical field-testing could only be conducted during the bronchiolitis season (October to March). The study was carefully planned over a three year period. For each of the three phases, critical time points were identified to commence or complete key aspects of the study. This was to prevent study phases from over-running, and causing delays. It was anticipated that if delays occurred they may impact on achieving the study recruitment targets for the clinical field-testing. Bronchiolitis admissions peak during the months of November and December. To achieve the recruitment target during this short time period it became necessary to open other sites across England. CLRN research nurses facilitated with the recruitment and clinical field-testing to ensure recruitment targets were met. Over this period there were also increased admissions for other illnesses in addition to bronchiolitis, and increased staff sickness. These two factors created increased workload for clinical ward staff. At times it was difficult to get clinical staff to participate with field-testing because of this increased workload. Consequently, CvM or the CLRN research nurses would participate with the clinical testing instead.

To facilitate the involvement of doctors as the reference standard for criterion validity and the inter-rater reliability testing, clinical field-testing was undertaken during the morning ward rounds. However, this presented several

problems. Firstly, the morning ward rounds commenced between eight and nine in the morning. Some infants would have been in hospital for a few days and it was often possible for parents and/or carers to be approached the day before the ward round to obtain informed consent. However, for those infants admitted during the night, obtaining informed consent proved more difficult. The research team were mindful that these parents were potentially exhausted due to sleep deprivation and anxious with regards to their infants' acutely ill condition. Ward staff were consulted first to ascertain whether it was appropriate to approach these parents to provide information and obtain informed consent before the ward round. Due to bed shortages, severity of illness, infection control policy and volume of admissions, infants were placed in a wide variety of geographical locations across the hospital including general medical and surgical wards; neuro-medical ward; medical and surgical assessment units, ED; PHDU; PICU. The volume of infants and the distribution across such a large hospital as Alder Hey made obtaining informed consent prior to wards rounds difficult. Furthermore, several ward rounds would often be undertaken simultaneously making clinical field-testing difficult. These ward rounds did not have a set starting point or route around the hospital: it was down to individual preference and workload of the person leading the ward round. Additionally, it was common for two or more ward rounds to occur at the same time on the same ward or the same time on different wards, and to arrive at consented infants contemporaneously.

10.3 Study strengths

The study used rigorous methodology, not previously employed in the development and validation of any other bronchiolitis scoring instrument. The overall sample size exceeded 1,300 participants (infants, parents and/or carers, HCPs). The 11 hospital study sites were located across England and were a mix of paediatric tertiary centres and DGHs, to try and ensure a representative sample. No other study validating a bronchiolitis scoring instrument has compared the instrument to a clinically agreed reference standard where the reference standard was subjected to robust investigation to determine objectivity and standardisation. A range of different qualitative methods was used within the study. This triangulation of data increased the study validity and adds depth to the data collected. A unique aspect of this study was the involvement of a wide range of parent and HCP stakeholders in all aspects of the study. This study was pragmatic. Clinical staff rather than researchers participated with the clinical field-testing of the LIBSS-PRO. This engagement ensured the LIBSS-PRO was clinically relevant and acceptable to HCPs, which will aid future implementation into clinical practice. Moreover, the study sought to engage clinical staff with the research process with certificates of participation being provided for personal development portfolios. Stakeholders were not just involved with the development of the LIBSS-PRO and clinical field-testing. They were also involved in study design, reviewing the protocol, participating in the study steering group and advising on a stakeholder engagement newsletter.

10.4 Study limitations

Despite the number and location of the study sites, there was still an under-representation of infants and parents and/or carers from different ethnic backgrounds. HCPs applying the LIBSS-PRO to infants during clinical field-testing tended to be from the nursing profession. This was because nursing staff were more available than other HCP groups and the previously described seasonal pressures. The acute, labile nature of bronchiolitis rendered it difficult to identify, recruit and undertake clinical field-testing in the *'severe'* group of infants. To try and improve recruitment in this group, an ethics amendment was successfully submitted for deferred consent. Parents and/or carers of an infant *in extremis* were provided with a brief verbal explanation of the study and that observational data was being collected. At an appropriate time once the infant had been stabilised; parents were provided with detailed written and verbal information about the study. Parents were given time to consider the information and whether the collected data could be included into the study. If agreeable, parents and/or carers were asked to sign deferred consent. If they disagreed, the data collected would be destroyed. Even with deferred consent, capturing those *'severe'* infants remained difficult. It became apparent that some infants, transferred to either PICU or PHDU and commenced on either nCPAP or HFNC for their symptoms, would rapidly improve. The LIBSS-PRO would often categorise these infants as *'moderate'*.

The clinical premise of the LIBSS-PRO was to have thresholds for 'mild', 'moderate' and 'severe' bronchiolitis in order to standardise care, support clinical decision making, for example, escalation or weaning of treatment and be a mechanism to improve patient safety with the early detection of

deteriorating infants. Furthermore, these thresholds were to aid HCPs with interpretation of the score. However, through undertaking this research it has become apparent that a number of difficulties/tensions arose through trying to develop these thresholds. Particularly, tensions occurred with individual HCP perceptions of what constitutes ‘mild’, ‘moderate’ and ‘severe’ bronchiolitis and how this was influenced by factors, such as, level of seniority, clinical experience and clinical location of the infant. Due to these tensions, having thresholds for ‘mild’, ‘moderate’ and ‘severe’ bronchiolitis may be questionable and could be considered superfluous. An alternative to using thresholds to guide severity of illness and treatment decision making could be with the use of LIBSS-PRO score trends. For example, if the LIBSS-PRO score increases on two consecutive occasions maybe this would trigger the need for a medical review or an escalation in treatment.

The original objective of this study was to develop a scoring instrument which had both clinical utility and could be used as an outcome measure. It is debatable whether one scoring instrument can have a dual purpose within clinical practice and research. The LIBSS-PRO does have the potential to achieve this objective. The LIBSS-PRO is a standardised objective measure which can provide quantifiable data on trends in clinical condition to facilitate decision making. Furthermore, the LIBSS-PRO could be used to evaluate the effectiveness of treatment interventions given to individual patients as part of their management. This is particularly important when the treatment under investigation does not have a strong evidence base, such as, nCPAP and HFNC. However, the LIBSS-PRO may be perceived by HCPs as time consuming, burdensome and difficult to interpret, particularly if the thresholds

for ‘mild’, ‘moderate’ and ‘severe’ bronchiolitis are considered redundant. This may preclude the clinical uptake of the LIBSS-PRO and restrict its use to being a research outcome measure.

10.5 Comparison of the LIBSS-PRO with other scoring instruments

There are several differences between the content of the LIBSS-PRO (Version 9.2) and the seven scoring instruments which were appraised in Chapter 1 (1, 33, 56, 58-60, 62). None of these instruments considered risk factors, professional concerns, urine output or capillary refill time for inclusion. Interestingly, only one instrument included apnoea as an item despite apnoea being perceived by most HCPs as an important symptom of ‘severe’ bronchiolitis in young infants (33). Five instruments included items related to effort of breathing (33, 56, 58, 59, 62): this was usually restricted to recession. In addition to recession the LIBSS-PRO (version 9.2) also assessed for tracheal tug, nasal flare, head-bobbing, grunting and central cyanosis. Two instruments included oxygen saturation with thresholds of 90% (33) and 97% (1) to score an infant. The oxygen saturation threshold used within the LIBSS-PRO (Version 9.2) are 92% based on current UK guidance (17, 138), which is slightly higher than the thresholds of 90% recommended for use in American guidelines (139). Using higher saturation thresholds of 97% may skew the score total and lead to a greater number of hospital admissions and/ or prolonged length of hospital stay. Four instruments included respiratory rate (1, 33, 58, 62). Two instruments developed respiratory rate thresholds based on a review of clinical records (1, 33), whilst two instruments did not report how the

respiratory thresholds were developed (58, 62). Two instruments included thresholds for heart rate (1, 59). One instrument developed heart rate thresholds following a review of clinical records (1), whilst one instrument reported using a heart rate greater than 97th centile (59). The thresholds for respiratory rate and heart rate used in the LIBSS-PRO (Version 9.2) were based on a systematic review of observational studies of normal heart and respiratory rate ranges in children from birth to 18yrs (140). The upper thresholds were based on the 75th and 90th centiles whilst the lower threshold was based on the 10th centile. Four instruments included items related to appearance (33, 58, 60, 62) and used adjectives similar to those used in the LIBSS-PRO (version 9.2) to describe appearance. Four instruments included items related to feeding/fluid requirements (33, 55, 59, 60). Amongst these instruments the assessment for feeding was largely subjective with no clear thresholds describing poor fluid intake. The LIBSS-PRO provides objective thresholds for both fluid intake and urine output. The thresholds used for fluid intake were developed from the stakeholder consultation and are comparable to those thresholds recommended in the recently published UK bronchiolitis guidance (138). The thresholds for urine output were based on Advanced Paediatric Life Support guidance (141). This comparison of the LIBSS-PRO (Version 9.2) with other scoring instruments emphasises how the LIBSS-PRO (Version 9.2) provides a comprehensive assessment of an infant with bronchiolitis. Furthermore, objective threshold criteria based on research evidence or stakeholder consensus, where no evidence exists, were used to provide an overall objective score to assess severity of illness in infants with

bronchiolitis. This is particularly advantageous for use by those HCPs with less clinical experience of managing infants with bronchiolitis.

10.6 Research and innovation recommendations

Developing a measurement instrument is an iterative process (61) which involves testing the instrument, making changes then evaluating these changes (61). Although there was excellent agreement for LIBSS-PRO score total in the inter-rater reliability testing, agreement for individual items was variable. Further research may involve removing these poorly performing items from the LIBSS-PRO and re-evaluating its performance in clinical field tests. To facilitate implementation into clinical practice the LIBSS-PRO may need further development and evaluation in an older patient population group. Although the LIBSS-PRO has already undergone psychometric tests to confirm validity and reliability there are a number of other tests needed to fulfil the validation process. A longitudinal study is required to assess the LIBSS-PROs responsiveness to change. For instance, can the instrument detect improvement or deterioration over time or following a treatment intervention? Assessment of responsiveness is a prerequisite if the score is to be used as an outcome measure in clinical trials (52, 53). Despite the clinical field-testing being undertaken in sites across England, ethnic groups were under represented in the sample. Therefore more research needs to be undertaken to ensure the LIBSS-PRO has clinical relevance and is generalisable to these patient groups. Prior to being used in clinical practice outside the UK and/or as an outcome measure in international research, cross-cultural validation is essential to identify important differences in language and cultural practices

(53). The clinical field-testing of the LIBSS-PRO was restricted to secondary and tertiary health care settings. Research is required to validate its use in primary health care settings. The qualitative research with parents identified reduced knowledge of bronchiolitis, symptom recognition and when to appropriately seek help from HCPs. A future planned project will try to address this knowledge deficit. Parents will be consulted to identify the most effective methods to raise awareness and access health information. This will culminate with the development of an application for a phone or tablet for use by both parents and HCPs which will contain links to NICE bronchiolitis guidelines, parent information and video capture of infants displaying different bronchiolitis signs and symptoms.

Finally, a heterogeneous group of PEW scoring instruments are commonly used within clinical practice. The premise of these instruments is to help identify the deteriorating child, with any medical or surgical condition (including bronchiolitis), in order to respond quickly and escalate treatment to improve outcomes. It is therefore questionable as to whether the LIBSS-PRO is required in clinical practice if a generic instrument is available. Furthermore, it would become burdensome for HCPs if the LIBSS-PRO was introduced into clinical practice alongside the PEW scores. This is due to overlap and duplication of certain items and domains contained within both instruments. However, none of these PEW scoring instruments appear to have been rigorously developed and validated across diverse acute patient population groups. Hence, a single universal PEW score has not been implemented nationwide across the NHS. Moreover, a number of issues have been identified with the use of PEW scores through local audits. Firstly, a large

proportion of hospitalised children still have unplanned admissions to critical care and do not always ‘trigger the PEW’. This highlights either a HCP training need with the use of the PEW or the PEW is not sensitive enough to identify all deteriorating children. Secondly, particular groups of children will constantly trigger the PEW thresholds. For example, in children with cyanotic heart lesions accepted oxygen saturation thresholds are considerably lower than PEW oxygen saturation thresholds. This is due to PEW thresholds being based on data which comes from otherwise healthy children. This supports the argument for the need of sensitive, disease specific measurement instruments. Hospitals are starting to move more towards electronic patient documentation. A third way forward could be to have a standard electronic PEW where a disease specific component, such as bronchiolitis, could be activated as required. Further research is needed to help decide what would be the best way forward with regards to clinical severity score use. In particular, research is required in infants with bronchiolitis to evaluate the sensitivity of the LIBSS-PRO in comparison to a PEW scoring instrument to detect clinical deterioration and/or improvement.

In conclusion the LIBSS-PRO has been developed and validated as a standardised outcome measure to assess severity of illness for infants with bronchiolitis. Current Government policies focus on improving safety and outcomes for patients with the recognition of clinical deterioration of a child being a key safety indicator (142, 143). Incorporating the LIBSS-PRO into an evidence based care pathway might aid prompt detection of those infants at risk of developing severe bronchiolitis leading to early intervention, reducing harm and improving patient outcomes. Furthermore, a standardised measure

of bronchiolitis severity may reduce variation in clinical practice and has possible use as an outcome measure in clinical studies.

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Appendix

Appendix 1: Summary of properties of published scoring instruments

	Jacobs (2000)	Liu (2004)	Lowell (1987)	Marlais (2011)	Walsh (2006)	Wang (1992)	Wilson (2000)
Setting	Canada/Primary Care	USA/hospital in-patients	USA/hospital in-patients	UK/ED	Republic of Ireland/ED	Canada/ Secondary care	USA/hospital in-patients
Population	Sample size: (n=206 0-12 years age Diagnosed with an acute respiratory infection	Sample size: n=55 0-19yrs Diagnosed with either asthma, bronchiolitis or other wheezing phenotypes	Sample size: not reported 0-24 months Diagnosed with either asthma, bronchiolitis or wheezing phenotype	Sample size: n=449 0-12 months Clinical diagnosis of bronchiolitis	Sample size: n=182 Clinical diagnosis of bronchiolitis	Sample size: n=56 2-24 months Diagnosed with bronchiolitis or pneumonia	Sample size: n=804 0-30 months Clinical diagnosis of bronchiolitis
Conceptual model	+	+	0	+	+	0	+
Face validity/ acceptability	0	0	0	0	0	0	
Stakeholder involvement	+	0	0	+	0	0	
Cognitive interviews	0	0	0	0	0	0	
Content validity	++	0	0	+	+	0	
Construct validity	++	0	0	+	0	0	
Criterion validity	0	0	0	0	0	0	
Inter-rater reliability	+	+	+	0	++	+	
Test-retest reliability	+	0	0	0	0	0	
Respondent	0	0	0	+	0	0	

burden							
Responsiveness to change	++	0	+	0	0	+	
Cultural/ language adaption	0	0	0	0	0	0	
0=poor evidence; + fair evidence; ++ good evidence; +++ excellent evidence							

Appendix 2: Search strategy

#1	expBRONCHIOLITIS/ OR bronchiolitis.ti,ab OR exp RESPIRATORY SYNCYTIAL VIRUS INFECTIONS/ OR exp RESPIRATORY SYNCYTIAL VIRUS, HUMAN/ OR exp RESPIRATORY SYNCYTIAL VIRUSES/ OR (respiratory adj3 syncytial adj3 virus).ti,ab OR rsv.ti,ab OR exp RESPIRATORY TRACT INFECTIONS/ OR (respiratory adj3 tract adj3 infection*).ti,ab OR (lower adj3 respiratory adj3 tract adj3 infection*).ti,ab OR exp METAPNEUMOVIRUS/ OR (human adj3 metapneumovirus).ti,ab OR exp ADENOVIRUS INFECTIONS, HUMAN/ OR adenovirus.ti,ab
#2	exp CHILD, PRESCHOOL/ OR exp INFANT/ OR infant*.ti,ab
#3	exp HEART DEFECTS, CONGENITAL/ or ((heart OR coronary OR cardiac) adj2 (defect* OR disease* OR disorder* OR abnormalit* OR congenital)).ti,ab OR exp INFANT, EXTREMELY LOW BIRTH WEIGHT/ OR exp INFANT, EXTREMELY PREMATURE/ OR exp INFANT, LOW BIRTH WEIGHT/ OR exp INFANT, NEWBORN/ OR exp INFANT, PREMATURE/ OR exp INFANT, PREMATURE, DISEASES/ OR exp INFANT, SMALL FOR GESTATIONAL AGE/ OR exp INFANT, VERY LOW BIRTH WEIGHT/ OR (premature adj3 infant).ti,ab OR exp BRONCHOPULMONARY DYSPLASIA/ OR(bronchopulmonary AND dysplasia).ti,ab OR chronic adj3 lung adj3 disease OR (chronic adj3 lung adj3 disease*).ti,ab OR exp SMOKING/ OR exp TOBACCO SMOKE POLLUTION/ OR smoking.ti,ab OR exp AIR POLLUTION/ OR exp AIR POLLUTION, INDOOR/ OR Medline exp BREAST FEEDING/ OR (breast adj3 f?ed*).ti,ab OR exp MULTIPLE BIRTH OFFSPRING/ OR exp SIBLING RELATIONS/ OR exp SIBLINGS/ OR sibling*.ti,ab OR exp ETHNIC GROUPS/ OR (ethnic adj3 group*).ti,ab OR ethnicity.ti,ab OR exp NURSERIES/ OR nurser*.ti,ab OR exp CHILD CARE/ OR exp CHILD DAY CARE CENTERS/ OR (child adj3 care adj3 cent*).ti,ab OR exp DOWN SYNDROME/ OR (down's adj3 syndrome).ti,ab OR (trisomy adj3 21).ti,ab OR (neuromuscular adj3 disorder*).ti,ab OR exp ASTHMA/ OR asthma.ti,ab OR exp ECZEMA/ OR eczema.ti,ab OR atopy.ti,ab OR
#4	#1 AND #2 AND #3
Title (ti); abstract (ab)	

Appendix 3: Signs and symptoms of bronchiolitis extracted from the literature (including existing published or unpublished clinical scoring instruments)

No.	Sign or Symptoms	References
1.	Abnormal chest radiograph findings	Norwood (2010); SIGN (2006); Wilson (2000); Lukić-Grlić (1999)
2.	Abnormal cry	Hewson (1990);
3.	Accessory respiratory muscles	Daugbjerg (1993); Dobson (1998); Roosevelt (1996); Schuh (1990); van Woensel (1997); Tal (1983); Bierman (1974); Wood (1972);
4.	Age	Walsh (2006); Marlais (2011); Wood (1972);
5.	Agitated	Lui (2004); Wood (1972);
6.	Air entry	Gadomski (1994a); Gadomski (1994b);
7.	Air hunger	Gadomski (1994a); Gadomski (1994b);
8.	Airway obstruction	Simon (2006); AAP (2006)
9.	Anxious	Gadomski (1994a);
10.	Apathetic	Gadomski (1994a);
11.	Apnoea	Papenberg (2012); Simon (2006); SIGN (2006); AAP (2006); Wilson (2000); Marlais (2011); Durani (2008); Lukić-Grlić (1999); Al-Sonboli (2006); Hewson (1990);
12.	Asleep	Dobson (1998);
13.	Auscultatory breath sounds	Kristjansson (1993); Wilson (2000);
14.	Blood in stools	Hewson (1990);
15.	Blood gases	SIGN (2006); Wilson (2000);
16.	Blood gases (PCO_2)	Marlais (2011);
17.	Blood gases (pH)	Marlais (2011);
18.	Blood gases (HCO_3)	Marlais (2011);
19.	Blue lips	Al-Sonboli (2006);
20.	Calm	Dobson (1998)
21.	Cannot be comforted	Gadomski (1994a);
22.	Cervical adenopathy	Durani (2008);
23.	Chest indrawing	Gadomski (1994b); Al-Sonboli (2006);
24.	Clingyness	Jacobs (1999);
25.	Conjunctivitis	von Linstow (2008); Chan (2006); Durani (2008); Chan (2007);
26.	Cold peripheries	Hewson (1990);

27.	Content	Dobson (1998); Gadomski (1994a);
28.	Congested pharynx	Chan (2007);
29.	Convulsions	Papenberg (2012); Meury (2004); Gombojav (2009); Hewson (1990);
30.	Coryza	Durani (2008);
31.	Cough	Marguet (2009); Norwood (2010); von Linstow (2008); Papenberg (2012); SIGN (2006); AAP (2006) Jacobs (1999); Chan (2006); Khuri-Burlos (2010); Marlais (2011); Meury (2004); Durani (2008); Al-Sonboli (2006); Hewson (1990); Chan (2007);
32.	Crackles	Dobson (1998); Al-Sonboli (2006);
33.	Cranky	Jacobs (1999);
34.	Crepitations	SIGN (2006); Goh (1997); Chan (2006); Chan (2007);
35.	Crying	Gadomski (1994a);
36.	Crying more than usual	Jacobs (1999); Hewson (1990);
37.	Cyanosis	SIGN (2006); Can (1998); Kristjansson (1993); van Woensel (1997); Wilson (2000); Tal (1983); Wood (1972); Al-Sonboli (2006); Gombojav (2009); Hewson (1990);
38.	Cyanosis (circumoral on crying)	Tal (1983);
39.	Cyanosis (circumoral at rest)	Tal (1983);
40.	Cyanosis (generalised)	Tal (1983);
41.	Decreased activity	Durani (2008); Hewson (1990);
42.	Decreased sleeping	Hewson (1990);
43.	Decreased vocalisations	Lui (2004);
44.	Dehydration	Walsh (2006); Marlais (2011);
45.	Diarrhoea	von Linstow (2008); Papenberg (2012); Chan (2006); Marlais (2011); Meury (2004); Hewson (1990); Chan (2007);
46.	Difficulty breathing	Durani (2008); Gombojav (2009); Hewson (1990); Khuri-Bulos (2010);
47.	Difficulty feeding	Lui (2004);
48.	Difficult to console	Dobson (1998);
49.	Difficulty waking	Al-Sonboli (2006);
50.	Drowsy	SIGN (2006); Marlais (2011); Hewson (1990);
51.	Duration of illness/symptoms	von Linstow (2008); Papenberg (2012); Gilca (2006); Khuri-Burlos (2010); Marlais (2011);
52.	Dyspnoea	Marguet (2009); SIGN (2006); Lui (2004); Wilson (2000); Meury (2004); Lukić-Grlić (1999)
53.	Dyspnoea (rest)	Wilson (2000);
54.	Dyspnoea (exertion)	Wilson (2000);
55.	Earache	Khuri-Bulos (2010);
56.	Ear problem	Gombojav (2009);
57.	Extremely irritable	Gadomski (1994a);
58.	Eye problem	Gombojav (2009);
59.	Febrile	Lukić-Grlić (1999)
60.	Feeding difficulties	SIGN (2006)

61.	Feels hot	Hewson (1990);
62.	Feels unwell	Jacobs (1999);
63.	Fever	von Linstow (2008); SIGN (2006); Jacobs (1999); Khuri-Burlos (2010); Durani (2008); Al-Sonboli (2006); Gombojav (2009);
64.	Fever/chills	Papenberg (2012)
65.	Fine inspiratory crackles	SIGN (2006)
66.	Flaring	Goebel (2000);
67.	Floppy	Gombojav (2009);
68.	Full blood count	Wilson (2000);
69.	Fussy	Jacobs (1999);
70.	General condition/appearance	Cengizlier (1997); Dobson (1998) Gadomski (1994a); Gadomski (1994b);
71.	Glascow Coma Score	Marlais (2011);
72.	Grunting	SIGN (2006); AAP (2006); Gadomski (1994a); Gadomski (1994b); Wilson (2000); Marlais (2011); Durani (2008);
73.	Grunting (intermittent)	Gadomski (1994a);
74.	Grunting (audible and persistent)	Gadomski (1994a);
75.	Haemoptysis	Wilson (2000);
76.	Happy	Dobson (1998); Gadomski (1994a);
77.	Headache	Jacobs (1999);
78.	Heart rate	Cade (2000); Walsh (2006); Marlais (2011)
79.	Hepatomegaly	Al-Sonboli (2006);
80.	Hoarseness	von Linstow (2008)
81.	Hoarse voice	Papenberg (2012)
82.	Hypoxia (O_2 saturations <94%)	Calvo (2008)
83.	Hyperactivity	Lui (2004);
84.	Hypoxaemia	Simon (2006)
85.	Ill at ease	Gadomski (1994a);
86.	Increased coughing after play	Lui (2004);
87.	Increased respiratory effort	AAP (2006)
88.	Increased sleep	Hewson (1990);
89.	Increased work of breathing	Papenberg (2012); SIGN (2006); Marlais (2011);
90.	Intravenous infusion	Goh (1997); Richter (1998);
91.	Interactive	Dobson (1998); Gadomski (1994a);
92.	Intercostal recession/retraction/in-drawing	SIGN (2006); AAP (2006) Can (1998); Dobson (1998); Gadomski (1994a); Gadomski (1994b); Lui (2004); Lowell (1987); Richter (1998); Schuh (1990a); Wang (1992); Wilson (2000);
93.	Intermittent crying	Gadomski (1994);
94.	Irritable	SIGN (2006); Cengizlier (1997); Jacobs (1999); Wang (1992); Wilson (2000); Gombojav (2009); Hewson (1990);
95.	Jaundice	Hewson (1990);

96.	Laboratory tests	Norwood (2010)
97.	Length of hospital stay	Calvo (2008)
98.	Less interactive	Dobson (1998); Gadomski (1994a);
99.	Less urine	Hewson (1990);
100.	Lethargy	Papenberg (2012); SIGN (2006); Cengizlier (1997); Gadomski (1994a); Wang (1992); Wilson (2000); Gombojav (2009);
101.	Loss of appetite	von Linstow (2008); Papenberg (2012)
102.	Low energy	Jacobs (1999);
103.	Malaise	von Linstow (2008)
104.	Mechanical ventilation	Evarard (2001); Khuri-Burlos (2010);
105.	Mildly irritated when touched	Dobson (1998); Gadomski (1994a);
106.	Moderately irritable	Dobson (1998); Gadomski (1994a);
107.	Mottled	SIGN (2006)
108.	Mucous plugging	AAP (2006)
109.	Muscle aches/pains	Jacobs (1999);
110.	Nasal congestion/runny nose	Jacobs (1999); Chan (2006); Khuri-Burlos (2010); Hewson (1990); Chan (2007);
111.	Nasal discharge	von Linstow (2008); SIGN (2006); AAP (2006); Lukić-Grlić (1999); Gombojav (2009);
112.	Nasogastric tube feeds	Richter (1998);
113.	Nasal flare	AAP (2006); Can (1998); Gadomski (1994a); Gadomski (1994b); Richter (1998); Schuh (1990a); Wilson (2000); Durani (2008);
114.	Nasal flow	Wang (1992);
115.	Nebulisation	Goh (1997);
116.	Needing extra care	Jacobs (1999);
117.	Neurology	Wilson (2000);
118.	Noisy breathing	Gombojav (2009); Hewson (1990);
119.	No symptoms	Everard (2001);
120.	Normal activity	Lui (2004);
121.	Normal play	Lui (2004);
122.	Normal vocalisations	Lui (2004);
123.	Not themselves	Hewson (1990);
124.	Not interactive	Gadomski (1994a);
125.	Not interested in what's going on	Jacobs (1999);
126.	Not playing well	Jacobs (1999);
127.	Not sleeping well	Jacobs (1999);
128.	Not quiet	Gombojav (2009);
129.	Obtunded	Wilson (2000);
130.	Occasional crying but consolable	Dobson (1998); Gadomski (1994a);

131.	Oral intake	Norwood (2010)
132.	Otitis media	Papenberg (2012); Khuri-Burlos (2010); Meury (2004); Durani (2008); Lukić-Grlić (1999);
133.	Oxygen duration	Khuri-Burlos (2010);
134.	Oxygen saturations	Norwood (2010); SIGN (2006); De Boeck (1997); Goebel (2000); Richter (1998); Wilson (2000); Dayan (2006); Marlais (2011); Wood (1972); Al-Sonboli (2006);
135.	Pale	SIGN (2006)
136.	Pallor	Kristjansson (1993); Hewson (1990);
137.	Pharyngitis	Meury (2004); Durani (2008); Lukić-Grlić (1999)
138.	Phlegm	Gombojav (2009);
139.	PICU admission	Gilca (2006);
140.	Poor feeding/appetite	Cengizlier (1997); Jacobs (1999); Wang (1992); Wilson (2000); Khuri-Burlos (2010); Marlais (2011); Meury (2004); Durani (2008); Gombojav (2009); Hewson (1990);
141.	Poor feeding due to tachypnoea	Wilson (2000);
142.	Post-tussive emesis	Khuri-Burlos (2010);
143.	Prolonged expiration	Daugbjerg (1993);
144.	Rales	Papenberg (2012); Kristjansson (1993); Wilson (2000); Durani (2008); Lukić-Grlić (1999)
145.	Rales ($\leq$50% or <3 lobes)	Wilson (2000);
146.	Rales (50% or $\geq$3 lobes)	Wilson (2000);
147.	Rash	von Linstow (2008); Chan (2006); Durani (2008); Al-Sonboli (2006); Gombojav (2009); Hewson (1990); Chan (2007);
148.	Recession	SIGN (2006); Kristjansson (1993); Richter (1998); Gombojav (2009);
149.	Recurrent wheeze	Calvo (2008)
150.	Resists comforting	Gadomski (1994a);
151.	Respiratory rate	Norwood (2010); SIGN (2006); AAP (2006); Bertrand (2001); Cade (2000); Can (1998); Kristjansson (1993); Can (1998); Cengizlier (1997); Goebel (2000); Goh (1997); Kristjansson (1993); Lui (2004); Richter (1998); van Woensel (1997); Wang (1992); Wilson (2000); Tal (1983); Bierman (1974); Dayan (2006); Marlais (2011); Al-Sonboli (2006); Gombojav (2009);
152.	Respiratory distress	SIGN (2006); AAP (2006)
153.	Retraction	Norwood (2010); Bertrand (2001); Cade (2000); Cengizlier (1997); Dobson (1998); Goebel (2000); Lui (2004); Lowell (1987); Wang (1992); Wilson (2000); Walsh (2006); Durani (2008);
154.	Rhinitis	Marguet (2009)
155.	Rhinorrhea	Papenberg (2012); SIGN (2006); AAP (2006); Meury (2004); Durani (2008);
156.	Rhonchi	Kristjansson (1993); Lukić-Grlić (1999)
157.	Seizures	Simon (2006); Chan (2006); Chan (2007);
158.	Serum CRP	SIGN (2006)
159.	Skin colour	Kristjansson (1993);
160.	Sleeping problem	Gombojav (2009);
161.	Sore throat	Papenberg (2012); Jacobs (1999); Khuri-Burlos (2010);

162	Sputum/secretions (white, thin, yellow, mucoid)	Wilson (2000);
163.	Sputum/secretions (blood tinged/purulent/frothy)	Wilson (2000);
164.	Sternal retractions	AAP (2006)
165.	Sternoclidomastoid muscles	Wilson (2000);
166.	Stridor	Durani (2008);
167.	Subcostal recession/retraction	SIGN (2006); AAP (2006); Can (1998); Dobson (1998); Goh (1997); Lui (2004); Lowell (1987); Wilson (2000);
168.	Supplemental oxygen requirement	Norwood (2010); Bertrand (2001); Cade (2000); Goh (1997); Lowell (1987); Richter (1998); Gilca (2006); Khuri-Burlos (2010); Marlais (2011); Meury (2004);
169.	Supraclavicular recession/retraction	SIGN (2006); Can (1998); Dobson (1998); Gadomski (1994a); Gadomski (1994b); Lui (2004);
170.	Substernal recession	Wilson (2000);
171.	Sweating	Hewson (1990);
172.	Tachycardic	SIGN (2006)
173.	Tachypnoea	von Linstow (2008); Simon (2006); AAP (2006); Al-Sonboli (2006);
174.	Temperature	Wilson (2000); Khuri-Burlos (2010); Marlais (2011); Al-Sonboli (2006);
175.	Temperature ≥38°C	Calvo (2008); Ricart (2013); Meury (2004);
176.	Temperature ≥39°C	Meury (2004);
177.	Tired	Jacobs (1999);
178.	“Toxic” appearance	SIGN (2006); Dayan (2006);
179.	Tracheosternal retractions	Richter (1998); Schuh (1990a); Wang (1992);
180.	Trouble breathing	Khuri-Burlos (2010);
181.	Unable to control secretions	Wilson (2000);
182.	Unable to get out of bed	Jacobs (1999);
183.	Unresponsive	Wilson (2000); Wood (1972);
184.	Vomiting	von Linstow (2008); Papenberg (2012); Jacobs (1999); Wilson (2000); Chan (2006); Marlais (2011); Meury (2004); Gombojav (2009); Hewson (1990); Chan (2007);
185.	Vomiting (persistent)	Wilson (2000);
186.	Vomiting (bilious)	Wilson (2000); Hewson (1990);
187.	Weight at presentation	Marlais (2011);
188.	Wheeze	Marguet (2009); Norwood (2010); von Linstow (2008); Papenberg (2012); SIGN (2006); AAP (2006); Bertrand (2001); Can (1998); Cengizlier (1997); Daugbjerg (1993); Dobson (1998); Gadomski (1994a); Gadomski (1994b); Goebel (2000); Goh (1997); Kristjansson (1993); Lui (2004); Richter (1998); Schuh (1990a); van Woensel (1997); Wang (1992); Wilson (2000); Tal (1983); Bierman (1974); Chan (2006); Khuri-Burlos (2010); Khuri-Burlos (2010); Durani (2008); Lukić-Grlić (1999); Al-Sonboli (2006); Al-Sonboli (2006); Chan (2007);
189.	Wheeze (audible without stethoscope)	Gadomski (1994a); Goebel (2000); Lowell (1987); Schuh (1990a); Wang (1992); Wang (1992); Tal (1983); Marlais (2011);

190.	Wheezing on auscultation	Papenberg (2012); Bertrand (2001); Can (1998); Cengizlier (1997); Goebel (2000); Wang (1992); Tal (1983); Bierman (1974);
191.	Wheezing (expiratory)	Can (1998); Cengizlier (1997); Dobson (1998); Gadomski (1994a); Goebel (2000); Lui (2004); Lowell (1987); Schuh (1990a); Tal (1983); Bierman (1974); Wood (1972);
192.	Wheeze (duration)	Gadomski (1994a);
193.	Wheeze (inspiratory)	Can (1998); Cengizlier (1997); Dobson (1998); Gadomski (1994a); Lowell (1987); Schuh (1990a); Wang (1992); Tal (1983); Bierman (1974);
194.	Wheeze location (segmental<2 of 4 lung fields)	Gadomski (1994a); Lowell (1987);
195.	Wheeze location (Diffuse >3 of 4 lung fields)	Gadomski (1994a); Lowell (1987);
196.	White blood cell/mm3	Calvo (2008)

Appendix 4: Atopy

Reference	Location	Design	Number of Participants	Population/age	Outcome(s)	Results [95% Confidence Intervals]
Al-Shehri *et al* (2005)	Saudi Arabia	Case control	Cases: n=51 Controls: n=115	< 5 years	Hospital admission	Atopic child OR: 4.75 [3.98-5.16] Atopic mother OR: 0.97 [0.84-1.72] Atopic father OR: 0.84 [0.65-1.23] Atopic parents OR: 1.02 [0.96-1.81]
Carroll *et al* (2008)	USA	Retrospective cohort	n= 103 670	healthy infants ≥ 37 weeks gestation 0-12 months >2500 g at birth	Hospital admission	Maternal asthma OR: 1.45 [1.33–1.59]

Figueras-Aloy *et al* (2004)	Spain	Prospective case-control	Cases: n=189 Controls: n=371	Ex pre-term infants 33-35 weeks gestation 0-12 months	Hospital admission for RSV	Asthma OR: 1.20 [0.81–1.78] Wheezing OR: 1.83 [1.21–2.77] Allergic rhinitis OR: 1.03 [0.72–1.48] Eczema OR: 1.68 [1.08–2.63]
Law *et al* (2004)	Canada	Prospective cohort	n=1832	Ex-pre-term infants 33-35 weeks gestation	Hospital admission for RSV	Family history of eczema OR: 0.44 [0.19-1.01]
Rossi *et al* (2007)	Italy	Case control	Cases: n=145 Controls: n=292	≤4 years RSV **Exclusion Criteria:** Received Palivizumab	Hospital admission	Family history of allergy OR: 1.57 [0.99-2.50]

Appendix 5: Chronic lung disease (including prematurity and cystic fibrosis)

Reference	Location	Design	Number of Participants	Population/age	Outcome(s)	Results [95% Confidence Intervals]
Al-Shehri *et al* (2005)	Saudi Arabia	Case control	Cases: n=51 Controls: n=115	< 5 years	Hospital admission	OR: 3.12 [2.19-3.78]
Boyce *et al* (2000)	USA	Retrospective cohort	n=3553	<3 years	Hospital admission	IRR: 10.7 [8.4-13.6]
Carbonell-Estrany *et al* (2000)	Spain	Prospective cohort	n= 680	Ex preterm infants born ≤32weeks 0-12 months	Hospital admission	OR: 5 3.1 [1.22-7.91]; P < 0.016
Eriksson *et al* (2002)	Sweden	Cohort	n=1503	RSV	Hospital admission	OR: 2.83 [1.08-7.42]
Garcia *et al* (2010)	USA	Retrospective case control	Cases: n=2840 Controls: n=1445	<2 years	Requirement of supplemental oxygen PICU Requirement Intubation Requirement Length of Stay	0R: 1.88 [1.32–2.67] OR: 1.80 [1.12–2.89] Not significant OR: 1.47 [1.30–1.67]
Kirstensen *et al* (2012)	Denmark	Retrospective cohort	n=391 983	0-23 months	RSV hospital admission	CLD Prematurity IRR: 2.58 [2.06–3.24] p<0.001 CF IRR: 4.32 [2.42–

						7.71]
Liese *et al* (2003)	Germany	Cohort	n=717	Ex preterm < 35 weeks gestation RSV	Hospital admission	OR: 3.99 [1.4-11.2]; p=0.009
Murray *et al* (2014)	UK	Prospective cohort	n= 296618	0-12 months	Hospital admission	CLD Prematurity RR: 1.6 [1.4-1.8] CF RR = 2.5 [1.4-4.4]
Pedersen *et al* (2003)	Denmark	Retrospective cohort	n=269	0-24 months	Hospital admission	OR: 2.2 [1.0-5.1]; p=0.06
Pezzotti *et al* (2009)	Italy	Retrospective cohort	n=2407	Ex-preterm infants born <36 weeks gestational age 0-18 months	Hospital admission	IRR: 1.70 [0.68 - 4.28] p=0.26
Ricart *et al* (2013)	Spain	Prospective cohort	n=484	0-12 months Positive virus detection	Bronchiolitis clinical score >11	OR: 7.2; [1.2–43.3]; P =0.031
Rietveld *et al* (2006)	Netherlands	Retrospective cohort	n=2469	0-24 months	Hospital admission	OR: 2.2 [not reported]
Simon *et al* (2007)	Germany	Prospective cohort	n=1568	Inpatients >24 hours RSV	Apnoea Death Mechanical ventilation	OR: 4.53 [2.19 to 8.92] p=0.0001 OR: 19.60 [2.96 to 104.3] p=0.0029 Not significant

Appendix 6: Congenital heart disease

Reference	Location	Design	Number of Participants	Population/age	Outcome(s)	Results [95% Confidence Intervals]
Al-Shehri *et al* (2005)	Saudi Arabia	Case control	Cases: n=51 Controls: n=115	< 5 years	Hospital admission	OR: 1.11 [0.85-1.95]
Boyce *et al* (2000)	USA	Retrospective cohort study	n=3553	<3 years	Hospital admission	IRR: 2.8 [2.3-3.3]
Cilla *et al* (2006)	Spain	Retrospective study	n=357	<2 years	Supplemental oxygen	OR: 12.77 (3.89 to 41.89)
Garcia *et al* (2010)	USA	Retrospective case control	Cases: n=2840 Controls: n=1445	<2 years	Hospital length of stay Supplemental oxygen PICU admission Mechanical ventilation	OR: 1.47 (1.30–1.67) OR: 1.88 [1.32 to 2.67 ns OR: 2.77 [1.89 to 4.05]
Hervas *et al* (2012)	Spain	Retrospective cohort	n=2384	0-24 months	Hospital admission PICU admission plus RSV	Not significant OR: 3.08 [1.14–8.3] p<0.0001
Kaneko *et al* (2001)	Japan	Retrospective cohort	n=157	RSV <4 years	Hospital admission	OR: 99.2 [8.5-1160.1]

Kristensen *et al* (2009)	Denmark	Retrospective case control	Cases: 313 Controls: 313	0-23 months RSV Congenital heart disease	Hospital admission	Cardiomyopathy OR: 5.84 [1.26-27.16] Haemodynamically significant heart disease OR: 1.53 [1.04-2.26]
Kirstensen *et al* (2012)	Denmark	Retrospective cohort	n=391 983	0-23 months	RSV hospital admission	IRR: 1.70 [1.45–1.99]
Murray *et al* (2014)	UK	Prospective cohort	N= 296618	0-12 months	Hospital admission	RR: 3.4 [2.9–3.8]
Pezzotti *et al* (2009)	Italy	Retrospective cohort	n=2407	Ex-preterm infants born <36 weeks gestational age 0-18 months	Hospital admission	Rate per 100 person years 7.58 [2.44 -23.50]
Ricart *et al* (2013)	Spain	Prospective cohort	n=484	0-12 months Positive virus detection	Bronchiolitis clinical score >11	4.7 [1.1 to 19.9]
Simon *et al* (2007)	Germany	Prospective cohort	n=1568	Inpatients >24 hours RSV	PICU admission Death	OR: 2.97 [1.81 to 4.82] p<0.001 OR: 3.69 [0.36 to 20.92] p=0.27
Thornburn *et al* (2009)	UK	Prospective cohort	n=406	RSV	Death	RR: 2.98 [2.16, 4.12]

Appendix 7: Day Care attendance

Reference	Location	Design	Number of Participants	Population/age	Outcome(s)	Results [95% Confidence Intervals]
Law *et al* (2004)	Canada	Prospective cohort	n=1832	Pre-term infants 33-35 weeks gestation	Hospital admission for RSV	OR: 12.32 [2.56-59.34]
Figueras-Aloy *et al* (2004)	Spain	Prospective case-control	Cases: n=189 Controls: n=371	0-12 months	Hospital admission	OR: 0.53 [0.15–1.95]
Figueras-Aloy et al (2008)	Spain	Prospective case-control	Cases: n=202 Controls: n=5239	0-12 months RSV	Hospital admission	OR: 1.25 [0.67 to 2.34]
Rossi *et al* (2007)	Italy	Case control	Cases: n=145 Controls: n=292	<4 years RSV	Hospital admission	OR: 4.17 [1.23-14.08]

Appendix 8: Down's syndrome

Reference	Location	Design	Number of Participants	Population/age	Outcome(s)	Results [95% Confidence Intervals]
Bloemers *et al* (2007)	Netherlands	Retrospective and prospective cohort	Retrospective: n=206 Prospective: Cases: n= 241 Controls:n=276	0-24 months	RSV hospital admission	Without CHD OR: 12.6 [2.9-54.5] With CHD OR: 10.5 [2.2-49.5]
Garcia *et al* (2010)	USA	Retrospective case control	Cases: n=2840 Controls: n=1445	<2 years	Oxygen requirement Length of Stay	OR: 2.32 [1.27–4.21] OR: 1.16 [0.98–1.37]
Kristensen *et al* (2009)	Denmark	Case control	Cases: n=313 Controls: n=313	RSV Heart disease 0-23 months	Hospital admission	OR: 3.24 [1.80-5.80]
Kirstensen *et al* (2012)	Denmark	Retrospective cohort	n=391 983	0-23 months	RSV hospital admission	IRR: 3.43 [2.66–4.42]
Murray *et al* (2014)	UK	Prospective cohort	n= 296618	0-12 months	Hospital admission	RR 2.5 [1.7–3.7]

Appendix 9: Air pollution

Reference	Location	Design	Number of Participants	Population/age	Outcome(s)	Results [95% Confidence Intervals]
Karr *et al* (2006a)	USA	Case control	Cases: 18595 Controls: 169472	0-12 months	Hospital admission	Fine particulate matter Sub-chronic OR: 1.09 [1.04-1.14] Chronic OR: 1.09 [1.04-1.14]
Karr *et al* (2006b)	USA	Case control	Cases: 19109 Controls: 169472	0-12 months	Hospital admission	10µg/m^3 increase in particulate matter Lagged 1-2 days OR: 0.96 [0.94-0.99 Lagged 3-5 days OR:0.98 [0.96-1.0] Lagged 6-8 days OR: 0.96 0.93-0.98]
Karr *et al* (2009)	USA	Case control	Cases: 2604 Controls: 23354	0-12 months	Hospital admission	Lives within 150m of highway OR: 1.07 [0.90-1.27] Lives within 150m of a designated truck route OR: 1.06 [0.91-1.23]

Appendix 10: Ethnicity

Reference	Location	Design	Number of Participants	Age	Outcome(s)	Results [95% Confidence Intervals]
Banerji *et al* (2009)	Canada	Prospective case-control study	Cases: n=110 Controls: n=101	Inuit 0-24 months RSV	Hospital admission	Full Inuit Race OR: 3.77 [1.12-12.75]
Boyce *et al* (2000)	USA	Retrospective cohort study	n=3553	<3 years	Hospital admission	White race IRR: 1.3 [1.2-1.4]
Carroll *et al* (2008)	USA	Retrospective cohort	n= 103 670	healthy infants ≥ 37 weeks gestation	Hospital admission	Black OR: 0.66 [0.61–0.71] Latino OR: 0.87 [0.67–1.13]
Garcia *et al* (2010)	USA	Retrospective case control	Cases: n=2840 Controls: n=1445	<2 years	Requirement of supplemental oxygen PICU Requirement Intubation Requirement Length of Stay	Black OR: 0.49 [0.41–0.60] OR: 0.89 [0.65–1.23] OR: 1.73 [0.93–3.19] OR: 0.95 [0.89–1.01]
Garcia *et al* (2010)	USA	Retrospective case control	Cases: n=2840 Controls: n=1445	<2 years	Requirement of supplemental	Hispanic OR: 1.12 [0.96–

					oxygen PICU Requirement Intubation Requirement Length of Stay	1.31] OR: 1.01 [0.79–1.31] OR: 2.17 [1.32–3.58] OR: 1.05 [1.00–1.11]
Garcia *et al* (2010)	USA	Retrospective case control	Cases: n=2840 Controls: n=1445	<2 years	Requirement of supplemental oxygen PICU Requirement Intubation Requirement Length of Stay	Other OR: 1.02 [0.76–1.39] OR: 1.59 [1.03–2.44] OR: 2.37 [1.06–5.29] OR: 1.04 [0.95–1.15]
Grimwood *et al* (2008)	New Zealand	Retrospective cohort	n=141	0-24 months	RSV Hospital admission	Maori RR: 3.64 [2.27–5.85] Pacific 3.60 [2.14–6.06] Other RR: 1.09 [0.52–2.25]
Mansbach *et al*	USA	Cohort	m/d	0-24 months	Hospital admission	Hispanic

(2005)						OR: 2.3 [1.1-5.0] Black OR: 1.6 [0.9-3.2] Other OR: 0.3 [0.03-3.4]
Norwood *et al* (2010)	USA	Prospective cohort	n=722	0-24 months	Unscheduled ED visit	African American OR: 0.6 [0.4-1.1] Hispanic OR: 1.3 [0.8-2.1] Other OR: 1.02 [0.4-2.7]

Appendix 11: Gender

Reference	Location	Design	Number of Participants	Population/age	Outcome(s)	Results [95% Confidence Intervals]
Boyce *et al* (2000)	USA	Retrospective cohort study	n=3553	<3 years	Hospital admission	Male IRR: 1.3 [1.2 to 1.4]
Bockova *et al* (2002)	USA	Prospective cohort	n=1837	Navajo and White Mountain Apache Children 0-24 months	Hospital admission	Male OR: 1.2 [0.6–2.2]
Carroll *et al* (2008)	USA	Retrospective cohort	n= 103 670	healthy infants ≥ 37 weeks gestation	Hospital admission	Male OR: 1.33 [1.26–1.41]
Cilla *et al* (2006)	Spain	Retrospective study	n=357	0-24 months	Hospital admission	Male OR: 1.07 [0.86–1.32]
Doering *et al* (2006)	Germany	Prospective cohort	n=1158	Ex preterm infants of 29–35 weeks	Hospital admission	Male OR: 2.8 [1.6 - 5.5]
Gavin *et al* (2007)	USA	Retrospective cohort	n=2098	Ex pre-term infants born 32 to 35 weeks of gestation 0-12 months	Hospital admission	Male OR: 1.07 (0.70 to 1.64)
Garcia *et al* (2010)	USA	Retrospective case control	Cases: n=2840 Controls: n=1445	<2 years	Supplemental oxygen	OR: 0.80 [0.71 to 0.91
Hervas *et al* (2012)	Spain	Retrospective cohort	n= 2889	0-24 months	Hospital admission	Male OR: 0.68 [0.51 to 0.91]
Koehoorn *et al* (2008)	Canada	Retrospective cohort	n=1588	0-12 months	Hospital admission	Male OR: 1.46 [1.32–

						1.62]
Kristensen *et al* (2009)	Denmark	Case control	Cases: n=313 Controls: n=313	RSV Heart disease 0-23 months	Hospital admission	Male OR: 1.14 [0.81-1.59]
Law *et al* (2004)	Canada	Prospective cohort	n=1832	Pre-term infants 33-35 weeks gestation	Hospital admission for RSV	Male OR: 1.91 [1.10-3.31]
Liese *et al* (2003)	Germany	Cohort	n=717	Ex preterm < 35 weeks gestation RSV	Hospital admission	Male OR: 8.7 [2.6-29.1]; p<0.001
Mansbach *et al* (2005)	USA	Cohort	m/d	0-24 months	Hospital admission	Male OR: 1.2 [0.7-2.3]
Norwood *et a*l (2010)	USA	Prospective cohort	n=722	0-24 months	Unscheduled ED visit	Male OR: 1.7 [1.1-2.5]
Paranjothy *et al* (2013)	UK	Cohort	n=318 613	Ex-preterm infants born <36 weeks gestational age	Hospital admission	Female HR: 0.77 [0.75–0.80]
Pedersen *et a*l (2003)	Denmark	Retrospective cohort	n=269	0-24 months	Hospital admission	Male OR: 1.4 [0.7-2.6]
Pezzotti *et al* (2009)	Italy	Retrospective cohort	n=2407	Ex-preterm infants born <36 weeks gestational age 0-18 months	Hospital admission	Rate per 100 person years Male 5.54 [4.48 -6.85]
Rietveld *et al* (2006)	Netherlands	Retrospective cohort	n=2469	0-12 months	Hospital admission	Male OR: 1.4 1.3–1.5
Thorburn *et al* (2009)	UK	Prospective cohort	n=406	RSV	Death	Male RR: 1.02 [0.75 to 1.4]

Appendix 12: Immunodeficiency

Reference	Location	Design	Number of Participants	Population/age	Outcome(s)	Results [95% Confidence Intervals]
Murray *et al* (2014)	UK	Prospective cohort	n= 296,618	0-12 months	Hospital admission	RR: 1.69 [0.80 to 3.58]

Appendix 13: Infection (viral and/or bacterial)

Reference	Location	Design	Number of Participants	Age	Outcome(s)	Results [95% Confidence Intervals]
Calvo *et al* (2008)	Spain	Prospective cohort	n= 749	RSV Includes infants with co-morbidity 0-24 months	 Hospital Length of Stay Fever	RSV vs RSV + co-infection OR: 1.12 [1.0-1.23] OR: OR: 2.90 [1.45-5.94]
Garcia *et al* (2010)	USA	Retrospective case control	Cases: n=2840 Controls: n=1445	0-24 months	 Requirement of supplemental oxygen PICU admission Hospital length of stay Mechanical ventilation	RSV infection OR: 1.60 [1.40–1.82] OR: 1.57 (1.25–1.98) OR: 1.18 (1.13–1.23) OR: 1.66 (1.06–2.59)
Marguet *et al* (2009)	France	Prospective cohort	n=209	0-12 months	Hospital duration >5 days	RSV vs RSV/RV OR: 0.26 [0.09-0.76] RSV vs RV OR: 0.13 [0.03-0.57]

						RSV vs hMPV OR: 0.09 [0.01-0.69]
Papenberg *et al* (2012)	Canada	Prospective cohort	n=>1000	0-36 months	Hospital vs clinic Hospitalization >5 days Severity score ≥2	RSV RR: 0.48 [0.30–0.78] RR: 2.79 [1.07–7.30] RR: 4.04 [1.32–12.31]
Semple *et al* (2005)	UK	Retrospective case control	Cases: n=196 Controls: n=10	0-24 months	Mechanical ventilation	RSV & hMPV RR: 10.99 [5.0–24.12]; P < .001
Thorburn *et al* (2006)	UK	Prospective cohort	n=165	0-12 months	Death	Bacterial co-infection OR:1.3 [0.57-2.95]
Thorburn *et al* (2009)	UK	Prospective cohort	n=406	RSV	PICU Admission	Bacterial co-infection OR: 0.66 [0.35 to 1.24]

Appendix 14: Low birth weight

Reference	Location	Design	Number of Participants	Population/age	Outcome(s)	Results [95% Confidence Intervals]
Carroll *et al* (2008)	USA	Retrospective cohort	n= 103 670	healthy infants ≥ 37 weeks gestation	Hospital admission	3001–3500 g HR: 0.86 [0.81–0.92] 3501–4000 g HR: 0.80 [0.75–0.87] 4001–4500 g HR: 0.76 [0.67–0.86]
Cilla *et al* (2006)	Spain	Retrospective study	n=357	0-24 months	Hospital admission	<2.0kg OR: 2.62 [1.50-4.49] 2.0-2.4 OR: 2.85 [2.02-4.01] 2.5-2.9 OR: 0.81 [0.61-1.09] ≥3.0 OR: 0.71 [0.57-0.89]
Gavin *et al* (2007)	USA	Retrospective cohort	n=2098	Ex pre-term infants born 32 to 35 weeks of gestation 0-12 months	Hospital admission	<2.5kg OR: 0.90 [0.56–1.45]

Koehoorn *et al* (2008)	Canada	Retrospective cohort	n=1588	0-12 months	Hospital admission	>4000g OR: 0.88 [0.75–1.02] 1500–2500g OR: 2.56 [2.12–3.08] 1500g 6.56 [4.82–8.92]
Nielsen *et al* (2003)	Denmark	Retrospective matched case control	Cases: 1272 Controls: 5 matched controls for every case	0-24 months RSV	Hospital admission	<3.0kg 1.42 [1.10-1.98] 3-3.5kg OR: 1.15 [0.90-1.51] 3.5-4.0kg OR: 1.06 [0.83-1.38]
Pezzotti *et al* (2009)	Italy	Retrospective cohort	n=2407	Ex-preterm infants born <36 weeks gestational age 0-18 months	Hospital admission	Rate per 100 person years <1000g 9.26 [5.58 -15.36] 1000-2000 6.58 [5.11 -8.48] >2000 3.37 [2.63 -4.32]
Rossi *et al* (2007)	Italy	Case control	Cases: n=145 Controls: n=292	<4 years RSV	Hospital admission	1.5-2.4kg OR: 1.96 [1.09-3.54] <1.5kg OR: 4.58 [0.83-25.39]
Rietveld *et al* (2006)	Netherlands	Retrospective	n=2469	0-12 months	Hospital admission	<2.5kg

		cohort				OR: 3.2 [2.1–4.8] 2.5–3.0kg OR: 1.3 [1.1–1.4]
Semple *et al* (2011)	UK	Prospective cohort	n=378	0-24 months	Oxygen supplementation Mechanical ventilation	OR: 0.94 [0.83-1.06] OR: 0.48 [0.36-0.64]
Simon *et al* (2007)	Germany	Prospective cohort	n=1568	Inpatients >24 hours RSV	Apnoea Death	Birth weight <1500 g OR: 3.73 [2.28 to 5.96] OR: 11.34 [2.09 to 61.65]

Appendix 15: Month/ season of birth

Reference	Location	Design	Number of Participants	Population/age	Outcome(s)	Results [95% Confidence Intervals]
Cilla *et al* (2006)	Spain	Retrospective study	n=357	<2 years	Hospital admission	Jan-March OR: 0.62 [0.47-0.83] Apr-June OR: 0.55 [0.40-0.73] July-Sept OR: 1.23 [0.97-1.56]
Gavin et al (2007)	USA	Retrospective cohort	n=2098	Ex pre-term infants born 32 to 35 weeks of gestation	Hospital admission	Born within 6 months of season OR: 1.99 [1.27–3.10] Born July to November OR: 3.00 [1.86–4.84]
Grimwood *et al* (2008)	New Zealand	Retrospective cohort	n=141	0-24 months	RSV Hospital admission	February–July OR: 1.62 [1.15–2.29]
Law *et al* (2004)	Canada	Prospective cohort	n=1832	Pre-term infants 33-35 weeks gestation	Hospital admission for RSV	Born November, December or January OR: 4.88 [2.57-9.29]
von Linstow *et al* (2008)	Denmark	Prospective cohort	n=217	0-12 months	Hospital admission	Spring OR: 0.63 [0.13-2.99] p=0.56 Summer

						OR: 0.96 [0.25-3.73] p=0.95 Fall OR: 0.81 [0.21-3.17] p=0.77 Winter OR: 2.29 [0.57-9.13] p=0.24
Mansbach *et al* (2005)	USA	Cohort	m/d	0-24 months	Hospital admission	Jan-March OR: 0.5 [0.2-1.6] April-June OR: 0.5 [0.1-1.6] October-December OR: 0.7 [0.2-2.1]
Paranjothy *et al* (2013)	UK	Cohort	n=318 613	Ex-preterm infants born <36 weeks gestational age	Hospital admission	April–June HR: 1.05 [1.03–1.08] July–September HR: 1.19 [1.17–1.22] October–December HR: 1.22 [1.19–1.25]

Appendix 16: Neuromuscular disorders

Reference	Location	Design	Number of Participants	Population/age	Outcome(s)	Results [95% Confidence Intervals]
Garcia *et al* (2010)	USA	Retrospective case control	Cases: n=2840 Controls: n=1445	<2 years	Oxygen requirement PICU Requirement Length of Stay	OR: 1.52 [0.87–2.64] OR: 2.79 [1.43–5.46] OR: 1.69 [1.42–2.02]
Kirstensen *et al* (2012)	Denmark	Retrospective cohort	n=391 983	0-23 months	RSV hospital admission	Encephalocele IRR: 1.54 [1.14–2.08] Spina bifida and malformations of the spinal cord IRR: 2.16 [1.31–3.55] Spinal muscular atrophy IRR: 1.0 [2 .24–4.27] Muscular dystrophy IRR: 2.49 [1.36–4.56] Cerebral palsy IRR: 1.59 [1.27–1.99]
Murray *et al* (2014)	UK	Prospective cohort	n= 296618	0-12 months	Hospital admission	cerebral palsy

						RR: 2.4 [1.5–4.0] nervous system congenital abnormalities RR: 1.7 [1.3-2.4]

Appendix 17: Breastfed infants

Reference	Location	Design	Number of Participants	Age	Outcome(s)	Results [95% Confidence Intervals]
Al-Shehri *et al* (2005)	Saudi Arabia	Case control	Cases: n=51 Controls: n=115	< 5 years	Hospital admission	Exclusive breast-fed OR: 0.43 [0.22-1.13] Mixed fed OR: 4.15 [3.68-5.24] Non-breast fed OR: 2.51 [2.11-3.73]
Banerji *et al* (2009)	Canada	Prospective case-control study	Cases: n=110 Controls: n=101	Inuit 0-24 months RSV	Hospital admission	Non-breast fed OR: 3.64 [1.16, 11.46]
Bulkow *et al* (2002)	USA	Retrospective case-control	Cases: n=204 Controls: n=338	Native Alaskan 0-36 months	Hospital admission	Ever been breastfed more than half of feedings (infants aged <6 months) OR: 0.33; P =0.001
Dornelles *et al* (2007)	Brazil	Prospective cohort	n=175	0-6 months	Length of oxygen use	For each month of exclusive breastfeeding infants had an 11 hour reduction in oxygen use (p=0.011).
Figueras-Aloy *et al* (2004)	Spain	Prospective case-control	Cases: n=189 Controls: n=371	0-12 months	Hospital admission	Breast fed <2 versus >2 months OR: 3.26 [1.96 to 5.42]
Figueras-Aloy *et al*	Spain	Prospective case-	Cases: n=202	0-12 months	RSV Hospital	Breast fed <2

(2008)		control	Controls: n=5239		admission	versus >2 months OR: 1.24 [0.89 to 1.72]
Koehoorn *et al* (2008)	Canada	Retrospective cohort	n=1588	0-12 months	Hospital admission	Breast feeding initiation at hospital HRR1.33 [1.14–1.54]
von Linstow *et al* (2008)	Denmark	Prospective cohort	n=217	0-12 months	Hospital admission	Exclusive breast feeding for first 14 days of life OR 0.21 [0.06-0.79]
Nishimura *et al* (2009)	Japan	Prospective cohort	n=203	≤4 months	Hospital admission Oxygen therapy	Not significant Full breast fed OR: 0.25 [0.07-0.89] Partial breast fed OR: 0.61 [0.20-1.87]
Paranjothy *et al* (2013)	UK	Cohort	n=318 613	Ex-preterm infants born <36 weeks gestational age	Hospital admission	HR: 0.89 [0.88–0.91]
Papenberg *et al* (2012)	Canada	Prospective cohort	n=>1000	0-36 months	Hospital vs clinic	OR: 0.55 [0.33–0.92]
Rossi *et al* (2007)	Italy	Case control	Cases: n=145 Controls: n=292	<4 years RSV	Hospital admission	Ref: none or <3 months 3-6 months OR: 1.22 [0.49-3.04] ≥7 months OR: 0.18 [0.02-1.44]

Appendix 18: Overcrowding

Reference	Location	Design	Number of Participants	Age	Outcome(s)	Results
Banerji *et al* (2009)	Canada	Prospective case-control study	Cases: n=110 Controls: n=101	Inuit 0-2 years RSV	Hospital admission	OR: 2.49 [1.01-6.14]
Bulkow *et al* (2002)	USA	Retrospective case-control	Cases: n=204 Controls: n=338	Native Alaskan 0-36 months	RSV hospital admission	Household crowding index >2 (<6 months of age) OR: 2.41; P=0.007
Figueras-Aloy *et al* (2004)	Spain	Prospective case-control	Cases: n=189 Controls: n=371	0-12 months	Hospital admission	OR: 1.79 [1.18–2.72]
Figueras-Aloy *et al* (2008)	Spain	Prospective case-control	Cases: n=202 Controls: n=5239	0-12 months RSV	Hospital admission	$\geq$ 4 adult residents OR: 1.37 [0.85 to 2.20]
Law *et al* (2004)	Canada	Prospective cohort	n=1832	Pre-term infants 33-35 weeks gestation	RSV hospital admission	>5 residents OR: 1.69 [0.93-3.10]

Appendix 19: Parental age

Reference	Location	Design	Number of Participants	Population/age	Outcome(s)	Results [95% Confidence Intervals]
Carroll *et a*l (2008)	USA	Retrospective cohort	n= 103 670	healthy infants ≥ 37 weeks gestation	Hospital admission	15–19 y OR: 1.15 [1.06–1.23] 30–39 y OR: 0.66 [0.60–0.73] 40–44 y OR: 0.43 [0.26–0.69]
Cilla *et al* (2006)	Spain	Retrospective study	n=357	0-24 months	Hospital admission	<25 years OR: 2.32 [1.62-3.32] 25-34.9 years OR: 0.08 [0.63-1.02] >35 years OR: 0.91 [0.69-1.20]
Koehoorn *et al* (2008)	Canada	Retrospective cohort	n=1588	0-12 months	Hospital admission	>29 y OR: 0.82 [0.74–0.91] <20 y OR: 1.58 [1.23–2.04]
Pezzotti *et al* (2009)	Italy	Retrospective cohort	n=2407	Ex-preterm infants born <36 weeks gestational age 0-18 months	Hospital admission	Rate per 100 person years <32 years 5.00 [3.94 -6.34] >32 years 4.44 [3.51 -5.63]
Paranjothy *et al*	UK	Cohort	n=318 613	Ex-preterm	Hospital admission	<20 years

(2013)				infants born <36 weeks gestational age		1.23 [1.19–1.27] 20–24 years 1.14 [1.11–1.17] 30–34 years 0.90 [0.88–0.92] 35–39 years 0.84 [0.82–0.87] ≥40 years 0.80 [0.76–0.85]

Appendix 20: Parent education

Reference	Location	Design	Number of Participants	Age	Outcome(s)	Results [95% Confidence Intervals]
Boyce *et al* (2000)	USA	Retrospective cohort study	n=3553	<3 years	Hospital admission	Maternal education <12 years IRR: 1.2 [1.1-1.3]
Carroll *et al* (2008)	USA	Retrospective cohort	n= 103 670	healthy infants ≥ 37 weeks gestation	Hospital admission	<12 y 1.15 (1.04–1.26) 12 y 1.02 (0.93–1.11)
Figueras-Aloy *et al* (2004)	Spain	Prospective case-control	Cases: n=189 Controls: n=371	0-12 months	Hospital admission	No school or primary OR: 1.48 [0.98–2.23]
Koehoorn *et al* (2008)	Canada	Retrospective cohort	n=1588	0-12 months	Hospital admission	Medium high OR: 1.25 [1.08–1.46] Medium low OR: 1.41 [1.22–1.64] Low OR: 1.78 (1.55–2.06)
Pezzotti *et al* (2009)	Italy	Retrospective cohort	n=2407	Ex-preterm infants born <36 weeks gestational age 0-18 months	Hospital admission	Rate per 100 person years <8 years 6.10 [4.90 -7.59] >8 years 3.51 [2.70 -4.56]

Appendix 21: Prematurity

Reference	Location	Design	Number of Participants	Population/age	Outcome(s)	Results [95% Confidence Intervals]
Al-Shehri *et al* (2005)	Saudi Arabia	Case control	Cases: n=51 Controls: n=115	< 5 years	Hospital admission	OR: 3.44 [2.27-4.33]
Bockova *et al* (2002)	USA	Prospective cohort	n=1837	Navajo and White Mountain Apache Children 0-24 months	Hospital admission	<36 weeks gestation OR: 1.8 [0.7–5.1]
Boyce *et al* (2000)	USA	Retrospective cohort study	n=3553	<3 years	Hospital admission	Gestational age in weeks ≤28 OR: 2.4 [1.8 to 3.3] 29 to <33 OR: 2.2 [1.8-2.7] 33 to <36 OR: 1.8 [1.6-2.1]
Carbonell-Estrany *et al* (2000)	Spain	Prospective cohort	n=680	0-12 months RSV Ex pre-term infants ≤32 weeks gestation discharged from hospital	Hospital admission	Increasing gestational age OR: 0.85 [0.72 to 0.99]; P<0.047
Carbonell-Estrany *et al* (2001)	Spain	Prospective cohort	n= 1206	Ex pre-term infants ≤32 weeks gestation discharged from NICU RSV 0-12 months	Hospital admission	Increasing gestational age OR: 0.87 [0.77 to 0.97]; P = 0.019

Chan *et al* (2002)	Malaysia	Retrospective cohort	n=216	RSV 0-24 months	Hypoxia Mechanical ventilation	OR: 1.17 [1.06-1.55] OR: 1.14 [1.02-2.07]
Cilla *et al* (2006)	Spain	Retrospective study	n=357	0-24 months	Hospital admission	<37 weeks gestational age OR: 1.61 [1.07–2.42]
Garcia *et al* (2010)	USA	Retrospective case control	Cases: n=2840 Controls: n=1445	0-24 months	Supplemental oxygen PICU admission Mechanical Ventilation Hospital length of stay	OR: 1.36 [1.17–1.59] OR: 1.63 [1.29–2.05] OR: 1.54 [1.02–2.33] OR: 1.16 [1.11–1.22]
Grimwood *et al* (2008)	New Zealand	Retrospective cohort	n=141	0-24 months	RSV Hospital admission	<37weeks gestational age OR: 2.29 [1.48–3.56]
Hervas *et al* (2012)	Spain	Retrospective cohort	n=2384	0-24 months	Hospital admission PICU admission	<32 weeks gestation age +/- RSV (result not significant) <32 weeks gestation OR: 5.6 [1.89–16.59]; p<0.01 <32 weeks gestation plus RSV (4.92 (1.95–12.40];

						p<0.001)
Kristensen *et al* (2009)	Denmark	Retrospective case control	Cases: 313 Controls: 313	0-23 months RSV Congenital heart disease	Hospital admission Disease severity	<37 weeks gestational age OR: 1.03 [0.65 to 1.64]
von Linstow *et al* (2008)	Denmark	Prospective cohort	n=217	0-12 months	Hospital admission	<38 weeks OR: 2.56 [0.32-20.57] p=0.38
Murray *et al* (2014)	UK	Prospective cohort	N= 296618	0-12 months	Hospital admission	RR: 1.9 [1.8–2.0]
Nielsen *et al* (2003)	Denmark	Retrospective matched case control	Cases: 1272 Controls: 5 matched controls for every case	0-24 months RSV	Hospital admission	Gestational age in weeks: <32 OR: 3.88 [2.74–7.75] 33–35 OR: 1.73 [1.20–2.82] 35-37 OR: 1.43 [1.10–1.97]
Norwood *et al* (2010)	USA	Prospective cohort	n=722	0-24 months	Unscheduled ED visit	OR: 1.6 [0.8-3.2]
Papenburg *et al* (2012)	Canada	Prospective cohort	n=>1000	<3 years	 Hospital admission Clinical score Hospital admission Clinical score	<37 weeks gestation hMPV OR: 2.31 [0.73–7.30] OR: 13.97 [1.50–130.0] RSV OR: 1.29 [0.68–

						2.43] OR: 3.08 (1.63–5.83)
Paranjothy *et al* (2013)	UK	Cohort	n=318 613	Ex-preterm infants born <36 weeks gestational age	Hospital admission	<33 HR: 2.18 [2.06–2.30] 33–34 HR: 1.59 [1.50–1.68] 35–36 HR: 1.39 [1.34–1.45]
Pezzotti *et al* (2009)	Italy	Retrospective cohort	n=2407	Ex-preterm infants born <36 weeks gestational age 0-18 months	Hospital admission	Rate per 100 person years <32 weeks 5.81 [4.15 -8.13] 32-35 weeks 4.43 [3.65-5.37]
Ricart *et al* (2013)	Spain	Prospective cohort	n=484	0-12 months Positive virus detection	Bronchiolitis clinical score >11	<37 weeks OR: 2.6 [1.3–5.1]; P= 0.005
Rietveld *et al* (2006)	Netherlands	Retrospective cohort	n=2469	0-12 months	Hospital admission	<28 weeks gestation OR: 3.2 [2.1–4.8] 29–32 weeks gestation OR: 2.8 [2.1–3.8] 33–34 weeks gestation OR: 2.3 [1.8–3.0]

						35–36 weeks gestation OR: 1.6 [1.3–1.9]
Rossi *et al* (2007)	Italy	Case control	Cases: n=145 Controls: n=292	<4 years RSV	Hospital admission	33-35 weeks OR: 1.22 [0.50-2.98] <33 weeks OR: 5.35 [1.45-15.89]
Semple *et al* (2011)	UK	Prospective cohort	n=378	0-24 months	Oxygen supplementation Mechanical ventilation	<37 weeks gestation, was significantly associated with need for mechanical ventilation (all p≤0.002).
Simon *et al* (2007)	Germany	Prospective cohort	n=1568	Inpatients >24 hours RSV	PICU admission Death	<37 weeks gestation OR:1.73 [1.08 to 2.72] OR: 2.88 [0.53 to 15.52]
Thorburn *et al* (2009)	UK	Prospective cohort	n=406	RSV	Death	RR: 0.46 [0.15 to 1.39]

Appendix 22: Previous RSV/ bronchiolitis episode

Reference	Location	Design	Number of Participants	Population/age	Outcome(s)	Results [95% Confidence Intervals]
Norwood *et al* (2010)	USA	Prospective cohort	n=722	0-24 months	Unscheduled ED visit	OR: 1.7 [1.1-2.8]
Rossi *et al* (2007)	Italy	Case control	Cases: n=145 Controls: n=292	<4 years RSV	Hospital admission	OR: 1.85 [1.02-3.36]

Appendix 23: Siblings

Reference	Location	Design	Number of Participants	Population/age	Outcome(s)	Results [95% Confidence Intervals]
Carbonell-Estrany *et al* (2000)	Madrid	Prospective cohort	n= 680	Ex preterm infants born ≤32weeks 0-12 months	Hospital admission	OR: 1.86 [1.01-3.4]; P < 0.048
Carroll *et al* (2008)	USA	Retrospective cohort	n= 103 670	healthy infants ≥ 37 weeks gestation	Hospital admission	1 sibling HR: 1.38 [1.29–1.49] >2 siblings HR: 1.64 [1.51–1.78]
Gavin *et al* (2007)	USA	Retrospective cohort	n=2098	Ex pre-term infants born 32 to 35 weeks of gestation 0-12 months	Hospital admission	OR: 1.98 [1.18–3.32]
Grimwood *et al* (2008)	New Zealand	Retrospective cohort	n=141	0-24 months	RSV Hospital admission	Multiple birth RR:1.25 (0.62–2.54)
Figueras-Aloy *et al* (2004)	Spain	Prospective case-control	Cases: n=189 Controls: n=371	0-12 months	Hospital admission	>1 School age siblings OR: 2.40 [1.61–3.57]
Figueras-Aloy *et al* (2008)	Spain	Prospective case-control	Cases: n=202 Controls: n=5239	0-12 months RSV	Hospital admission	OR: 1.96 [1.47 to 2.60]
Law *et al* (2004)	Canada	Prospective cohort	n=1832	Pre-term infants 33-35 weeks gestation	Hospital admission for RSV	OR: 2.76 [1.51-5.03]
Liese *et al* (2003)	Germany	Cohort	n=717	Ex preterm < 35 weeks gestation RSV	Hospital admission	OR: 3.9 [1.9-8.3]; p<0.001
Papenberg *et al* (2012)	Canada	Prospective cohort	n=>1000	0-36 months	Hospital vs clinic	Multiple birth HR: 0.83 [0.79–

						0.87]
Rossi *et al* (2007)	Italy	Case control	Cases: n=145 Controls: n=292	<4 years RSV	Hospital admission	≥2 children OR: 1.83 [1.16-2.88]
Koehoorn *et al* (2008)	Canada	Retrospective cohort	n=1588	0-12 months	Hospital admission	OR: 2.04 [1.83–2.04]

Appendix 24: Tobacco smoke exposure

Reference	Location	Design	Number of Participants	Population/age	Outcome(s)	Results [95% Confidence Intervals]
Al-Shehri *et al* (2005)	Saudi Arabia	Case control	Cases: n=51 Controls: n=115	< 5 years	Hospital admission	OR: 2.51 [2.11-3.73]
Banerji *et al* (2009)	Canada	Case control	Cases: n=110 Controls: n=101	Inuit 0-24 months RSV	Hospital admission	Smoking during pregnancy OR: 4.04 [1.12-14.64]
Boyce *et al* (2000)	USA	Retrospective cohort study	n=3553	<3 years	Hospital admission	Maternal smoking (IRR: 1.3 [1.2-1.4])
Carroll *et al* (2007)	USA	Retrospective cohort	n= 101 245	healthy infants ≥ 37 weeks gestation	Clinic visit ED visit Hospital admission	Maternal smoking OR: 1.06 [1.01–1.12] OR: 1.22 [1.13–1.31] OR: 1.28 [1.20–1.36]
Carroll *et al* (2008)	USA	Retrospective cohort	n= 103 670	healthy infants ≥ 37 weeks gestation	Hospital admission	1–9 cigarettes per d HR: 1.14 [1.03–1.27] ≥10 cigarettes per d HR: 1.28 [1.20–1.36]
Carbonell-Estrany *et al* (2001)	Spain	Prospective cohort	n= 1206	Ex pre-term infants ≤32 weeks gestation discharged from	Hospital admission	Tobacco smoke exposure OR: 1.63; [1.05 to 2.56]; P=0.031

				NICU RSV +ve 0-12 months		
Gavin *et al* (2007)	USA	Retrospective cohort	n=2098	Ex pre-term infants born 32 to 35 weeks of gestation 0-12 months	Hospital admission	OR: 0.78 [0.38–1.61]
Grimwood *et al* (2008)	New Zealand	Retrospective cohort	n=141	0-24 months	RSV Hospital admission	Maternal smoking (in pregnancy) RR: 1.41 [0.95–2.10]
Figueras-Aloy *et al* (2004)	Spain	Prospective case-control	Cases: n=189 Controls: n=371	0-12 months	Hospital admission	Tobacco smoke at home OR: 0.95 [0.66–1.36] Maternal smoking OR: 1.49 [1.01–2.18] >2 smokers OR: 1.41 [0.92–2.14] Smoking during pregnancy OR: 1.62 [1.08–2.42]
Figueras-Aloy *et al* (2008)	Spain	Prospective case-control	Cases: n=202 Controls: n=5239	0-12 months RSV	Hospital admission	Maternal smoking (in pregnancy) OR: 1.62 [1.17 to 2.24]
Koehoorn *et al* (2008)	Canada	Retrospective cohort	n=1588	0-12 months	Hospital admission	Maternal smoking (in pregnancy) OR: 1.78 [1.55–2.04]
Law *et al* (2004)	Canada	Prospective cohort	n=1860	Preterm infants born at 33-35 weeks gestation	Hospital admission	≥2 smokers in the home OR: 1.71 [0.97-3.00]

von Linstow *et al* (2008)	Denmark	Prospective cohort	n=217	0-12 months	Hospital admission	OR: 5.06 [1.36-18.76] p=0.015
Paranjothy *et al* (2013)	UK	Cohort	n=318 613	Ex-preterm infants born <36 weeks gestational age	Hospital admission	HR: 1.04 [1.01–1.06]
Rossi *et al* (2007)	Italy	Case control	Cases: n=145 Controls: n=292	≤4 years RSV	Hospital admission	OR: 0.81 [0.54-1.12]
Semple *et al* (2011)	UK	Prospective cohort	n=378	0-24 months	 Oxygen supplementation Mechanical ventilation	Household tabacco smoker (OR: 2.23 [1.21, 4.10]) (OR: 7.19 (2.28, 22.60)

Appendix 25: Residence (suburban or rural)

Reference	Location	Design	Number of Participants	Population/age	Outcome(s)	Results [95% Confidence Intervals]
Carroll *et al* (2008)	USA	Retrospective cohort	n= 103 670	healthy infants ≥ 37 weeks gestation	Hospital admission	Suburban HR: 1.28 [1.18–1.39] Rural HR: 1.87 [1.74–2.02]
Cilla *et al* (2006)	Spain	Retrospective study	n=357	<2 years	Hospital admission	Rural-suburban OR: 1.33 [1.06-1.67]
Boyce *et al* (2000)	USA	Retrospective cohort study	n=3553	<3 years	Hospital admission	Rural residence IRR: 1.3 [1.2-1.4]
Koehoorn *et al* (2008)	Canada	Retrospective cohort	n=1588	0-12 months	Hospital admission	Small town OR: 1.30 [0.84–1.99] Rural fringe OR: 1.15 [0.98–1.36] Rural OR: 1.20 [0.87–1.66]

Appendix 26: Young age (less than 12 months)

Reference	Location	Design	Number of Participants	Population/age	Outcome(s)	Results [95% Confidence Intervals]
Al-Shehri *et al* (2005)	Saudi Arabia	Case control	Cases: n=51 Controls: n=115	≤ 5 years	Hospital admission	< 1 year OR: 3.44 [2.27 to 4.33]
Bockova *et at* (2002)	USA	Prospective cohort	n=1837	Navajo and White Mountain Apache Children 0-24 months	Hospital admission	< 6 months OR: 6.6 [3.0–14.4]
Carbonell-Estrany *et al* (2000)	Madrid	Prospective cohort	n= 680	Ex preterm infants born ≤32weeks 0-12 months	Hospital admission	Increase in gestational age OR: 0.85 [0.72 to 0.99]; P < 0.047]
Carbonell-Estrany *et al* (2001)	Spain	Prospective cohort	n= 999	Ex preterm infants born <32weeks 0-12 months	RSV hospital admission	< 3 months OR: 0.44 [0.25 to 0.77]
Figueras-Aloy *et al* (2004)	Spain	Prospective case-control	Cases: n=189 Controls: n=371	0-12 months	Hospital admission	<10 weeks 3.75 [2.59–5.45]
Figueras-Aloy *et al* (2008)	Spain	Prospective case-control	Cases: n=202 Controls: n=5239	0-12 months	RSV Hospital admission	≤10 weeks OR: 2.81 [2.10 to 3.75]
Norwood *et al* (2010)	USA	Prospective cohort	n=722	0-24 months	Unscheduled ED visit	≤ 2 months OR: 2.1 [1.1-4.3]
Papenburg *et al* (2012)	Canada	Prospective cohort	n=>1000	0-36 months	Hospital admission RSV	< 6 months OR: 2.26 [1.31–3.89]
Perzotti *et al* (2009)	Italy	Retrospective cohort	n=2407	Ex-preterm infants born <36 weeks gestational age	Hospital admission	IRR: 5.98 [2.68 to 13.35]

				0-18 months		
Rossi *et al* (2007)	Italy	Case control	Cases: n=145 Controls: n=292	<4 years RSV	Hospital admission	≥12 months OR: 2.53 [0.99-6.48] 6-11 months OR: 4.52 [1.80-11.33] 3-5 months 7.87 [3.13-19.75] <3 months 1.98 [1.28-3.05]
Thorburn *et al* (2009)	UK	Prospective cohort	n=406	RSV	Death	<6 weeks RR: 2.98 [2.16, 4.12]

Appendix 27: Family group workshop – sample frame

		Hospital 1		Hospital 2		Hospital 3		Hospital 4		
		Boy	Girl	Boy	Girl	Boy	Girl	Boy	Girl	Totals
Mild	**<3/12**							*	*	**N=2**
	>3/12				*					**N=1**
Moderate	**<3/12**					*				**N=1**
	>3/12	*	*							**N=2**
Severe	**<3/12**			*			*			**N=2**
	>3/12	*	*							**N=2**
Totals		**N=2**	**N=2**	**N=1**	**N=1**	**N=1**	**N=1**	**N=1**	**N=1**	**N=10**

Mild: minimal interventions, short admission to hospital
Moderate: NG feeds / IVI fluids + oxygen via head box / nasal specs
Severe: none invasive ventilation (ncpap/HFNC) + NG feeds / IVI fluids

Appendix 28: HCP group workshop – sample frame

Nursing Staff

	Hospital 1				Hospital 2				Hospital 3				Hospital 4			
Nurse Band	**5**	**6**	**7**	**8**	**5**	**6**	**7**	**8**	**5**	**6**	**7**	**8**	**5**	**6**	**7**	**8**
A&E/ Short Stay				*					*					*		
Medical Wards	*				*											
Critical Care	*	*														

Medical Staff

	Hospital 1			Hospital 2			Hospital 3			Hospital 4		
Grade	**ST 1/2**	**ST 3/4**	**Cons**	**ST 1/2**	**ST 3/4**	**Cons**	**ST 1/2**	**ST 3/4**	**Cons**	**ST 1/2**	**ST 3/4**	**Cons**
A&E			*									
Critical Care			*									
Medical	*					*		*				

Appendix 29: Parent interviews – sample frame

		Hospital 1		Hospital 2		Hospital 3		Hospital 4		Hospital 5		
		Boy	Girl	Boy	Girl	Boy	Girl	Boy	Girl	Boy	Girl	Totals
Mild	<3/12								*	*		N=2
	>3/12					*					*	N=2
Moderate	<3/12				*			*				N=2
	>3/12		*						*	*		N=3
Severe	<3/12			*	*		*					N=3
	>3/12	*	*			*						N=3
Totals		N=1	N=2	N=1	N=2	N=2	N=1	N=1	N=2	N=2	N=1	N=15

Mild – minimal interventions, short admission to hospital
Moderate – NG feeds / IVI fluids + oxygen via head box / nasal specs
Severe – none invasive ventilation (nCPAP/HFNC) + NG feeds / IVI fluids

Appendix 30: Delphi round one

Item No.	Item	Response n/N (missing data))	1 Very Important n (%)	2 Important n (%)	3 Neutral n (%)	4 Unimportant n (%)	5 Completely unimportant n (%)	6 Don't know n (%)	Consensus % (category)	Mean (SD)	Median (range)
1.	Respiratory Rate	180/195 (15)	114 (63.3)	65 (33.3)	1 (0.6)	0 (0)	0 (0)	0 (0)	99.4 (1&2)	1.37 (0.49)	1.0 (2.0)
2.	Grunting	182/195 (13)	147 (80.8)	33 (18.1)	2 (1.1)	0 (0)	0 (0)	0 (0)	98.9 (1&2)	1.20 (0.43)	1.0 (2.0)
3.	Nasal Flaring	182/195 (13)	87 (47.8)	88 (48.4)	7 (3.8)	0 (0)	0 (0)	0 (0)	96.2 (1&2)	1.5 (0.57)	2.0 (2.0)
4.	Air Hunger	177/195 (18)	74 (41.8)	47 (26.6)	26 (14.7)	4 (2.3)	2 (1.1)	24 (13.6)	68.4 (1&2)	2.35 (1.67)	2.0 (5.0)
5.	Recession	182/195 (13)	109 (59.9)	70 (38.5)	2 (1.1)	1 (0.5)	0 (0)	0 (0)	98.4 (1&2)	1.42 (0.54)	1.0 (3.0)
6.	Accessory Muscle Use	182/195 (13)	106 (58.2)	73 (40.1)	2 (1.1)	1 (0.5)	0 (0)	0 (0)	98.4 (1&2)	1.43 (0.55)	1.0 (3.0)
7.	Dyspnoea	181/195 (14)	86 (47.5)	83 (45.9)	10 (5.5)	2 (1.1)	0 (0)	0 (0)	93.4 (1&2)	1.60 (0.64)	2.0 (3.0)
8.	Tracheal Tug	182/195 (13)	107 (58.8)	73 (40.1)	0 (0)	1(0.5)	0 (0)	1 (0.5)	98.9 (1&2)	1.44 (0.62)	1.0 (5.0)
9.	Nasal Discharge	178/195 (17)	6 (3.4)	40 (22.5)	73 (41.0)	46 (25.8)	12 (6.7)	1(0.5)	25.8 (1&2)	3.11 (0.96)	3.0 (5.0)
10.	Respiratory Secretion Colour	180/195 (15)	11 (6.1)	54 (30.0)	68 (37.8)	39 (21.7)	7 (3.9)	1 (0.6)	36.1 (1&2)	2.88 (0.97)	3.0 (5.0)
11.	Cough	180/195 (15)	14 (7.8)	62 (34.4)	79 (43.9)	24 (13.3)	1 (0.6)	0 (0)	42.2 (1&2)	2.64 (0.82)	3.0 (4.0)
12.	Respiratory Pattern	181/195 (14)	82 (45.3)	79 (43.6)	16 (8.8)	2 (1.1)	0 (0)	2 (1.1)	89.0 (1&2)	1.70 (0.82)	2.0 (5.0)
13.	PaCo2 on BGA	179/195 (16)	103 (57.5)	56 (31.3)	12 (6.7)	2 (1.1)	2 (1.1)	4 (2.2)	88.8 (1&2)	1.63 (1.0)	1.0 (5.0)
14.	HCo3 on BGA	172/195 (23)	36 (20.9)	58 (33.7)	53 (30.8)	11 (6.4)	3 (1.7)	11 (6.4)	54.7 (1&2)	1.63 (1.0)	2.0 (5.0)
15.	pH on BGA	170/195 (25)	93 (54.7)	53 (31.2)	15 (8.8)	2 (1.2)	2 (1.2)	5 (2.9)	85.9 (1&2)	2.53 (1.29)	1.0 (5.0)
16.	Apnoeas	182/195 (13)	153 (84.1)	27 (14.8)	1 (0.5)	1 (0.5)	0 (0)	0 (0)	98.9 (1&2)	1.17	1.0 (3.0)

										(0.43)	
17.	Stridor	182/195 (13)	85 (46.7)	60 (33.0)	29 (15.9)	5 (2.7)	2 (1.1)	1 (0.5)	79.7 (1&2)	1.8 (0.94)	2.0 (5.0)
18.	Wheeze/ Noisy Breathing	182/195 (13)	31 (17.0)	79 (43.4)	51 (28.0)	18 (9.9)	3 (1.6)	0 (0)	60.4 (1&2)	2.35 (0.93)	2.0 (4.0)
19.	Location of Wheeze	181/195 (14)	16 (8.8)	47 (26.0)	70 (38.7)	41 (22.7)	4 (2.2)	3 (1.7)	34.8 (1&2)	2.88 (1.03)	3.0 (5.0)
20.	Duration of Wheeze	180/195 (15)	23 (12.8)	70 (38.9)	63 (35.0)	19 (10.6)	2 (1.1)	3 (1.7)	51.7 (1&2)	2.53 (0.99)	2.0 (5.0)
21.	Wheeze Volume	177/195 (18)	11 (5.6)	54 (30.5)	72 (40.7)	23 (13.0)	9 (5.1)	8 (4.5)	36.7 (1&2)	2.9 (1.13)	3.0 (5.0)
22.	Chest Xray	176/198 (22)	10 (5.7)	50 (28.4)	75 (42.6)	35 (17.7)	4 (2.3)	2 (1.1)	33.5 (1&2)	2.8 (0.93)	3.0 (5.0)
23.	Head Bobbing	182/195 (13)	114 (62.6)	64 (35.2)	3 (1.6)	0 (0)	0 (0)	1 (0.5)	97.8 (1&2)	1.41 (0.62)	1.0 (5.0)
24.	Using Stomach to breathe	180/195 (15)	61 (33.9)	89 (49.4)	22 (12.2)	6 (3.3)	2 (1.1)	0 (0)	83.3 (1&2)	1.88 (0.82)	2.0 (4.0)
25.	Cyanosis	181/195 (14)	156 (86.2)	23 (12.7)	2 (1.1)	0 (0)	0 (0)	0 (0)	98.9 (1&2)	1.14 (0.38)	1.0 (2.0)
26.	Effort of Breathing	181/195 (14)	147 (81.2)	34 (18.8)	0 (0)	0 (0)	0 (0)	0 (0)	100 (1&2)	1.18 (0.39)	1.0 (1.0)
27.	Air Entry	177/195 (18)	100 (56.5)	62 (35.0)	11 (6.2)	3 (1.7)	1 (0.6)	0 (0)	91.5 (1&2)	1.54 (0.73)	1.0 (4.0)
28.	Oxygen Requirement	181/195 (14)	128 (70.7)	50 (27.6)	2 (1.1)	0 (0)	0 (0)	1 (0.6)	98.3 (1&2)	1.32 (0.59)	1.0 (5.0)
29.	Oxygen Saturation	181/195 (14)	128 (70.7)	47 (26.0)	5 (2.8)	0 (0)	0 (0)	1 (0.6)	96.7 (1&2)	1.34 (0.62)	1.0 (5.0)
30.	Respiratory Crackles	181/195 (14)	20 (11.0)	75 (41.4)	62 (34.3)	23 (12.7)	(0)	1 (0.6)	52.5 (1&2)	2.50 (0.87)	2.0 (4.0)
31.	Rhonchi	175/195 (20)	10 (5.7)	55 (31.4)	62 (35.4)	23 (13.1)	4 (2.3)	21 (12.0)	37.1 (1&2)	3.10 (0.87)	3.0 (5.0)
32.	See Saw Chest Motion	181/195 (14)	97 (53.6)	55 (30.4)	22 (12.2)	1 (0.6)	2 (1.1)	4 (2.2)	84.0 (1&2)	1.71 (1.02)	1.0 (5.0)
Hydration and Perfusion											
33.	Feeding	176/195 (19)	64 (36.4)	101 (57.4)	10 (5.7)	1 (0.6)	0 (0)	0 (0)	93.8 (1&2)	1.7 (0.59)	2.0 (3.0)

34.	Blowing bubbles through mouth	175/195 (20)	6 (3.4)	40 (22.9)	78 (44.6)	34 (19.4)	13 (7.4)	4 (2.3)	26.3 (1&2)	1.7 (0.59)	3.0 (5.0)
35.	Urine output	176/195 (19)	58 (33.0)	100 (56.8)	15 (8.5)	2 (1.1)	0 (0.0)	1 (0.6)	89.8 (1&2)	1.8 (0.71)	2.0 (5.0)
36.	Capillary Refill Time	176/195 (19)	69 (39.2)	89 (50.6)	18 (10.2)	0 (0)	0 (0)	0 (0)	89.8 (1&2)	1.71 (0.64)	2.0 (3.0)
37.	Peripheral perfusion	176/195 (19)	87 (49.4)	74 (42.0)	14 (8.0)	1 (0.6)	0 (0)	0 (0)	91.5 (1&2)	1.59 (0.66)	2.0 (3.0)
38.	Mottled appearance	176/195 (19)	104 (59.1)	64 (36.4)	7 (4.0)	0 (0)	0 (0)	0 (0)	95.5 (1&2)	1.47 (0.66)	1.0 (5.0)
39.	Skin Turgor	176/195 (19)	44 (25.0)	90 (51.1)	39 (22.2)	3 (1.7)	0 (0)	0 (0)	76.1 (1&2)	2.0 (0.73)	2.0 (3.0)
40.	Sunken Eyes	176/195 (19)	57 (32.4)	88 (50.0)	27 (15.3)	3 (1.7)	0 (0)	1 (0.6)	82.4 (4&5)	1.88 (0.79)	2.0 (5.0)
41.	Sunken fontanelle	176/195 (19)	67 (38.1)	87 (49.4)	20 (11.4)	1 (0.6)	0 (0.6)	1 (0.6)	87.5 (1&2)	1.76 (0.74)	2.0 (5.0)
42.	Vomiting	175/195 (20)	21 (12.0)	84 (48.0)	65 (37.1)	4 (2.3)	1 (0.6)	0 (0)	60.0 (1&2)	2.31 (0.73)	2.0 (4.0)
43.	Diarrhoea	173/195 (22)	3 (1.7)	40 (23.1)	94 (54.3)	33 (19.1)	3 (1.7)	0 (0)	24.9 (4&5)	2.95 (0.74)	3.0 (4.0)
44.	Clammy skin	178/195 (21)	48 (27.6)	89 (51.1)	31 (17.8)	6 (3.4)	0 (0)	0 (0)	78.7 (1&2)	1.97 (0.77)	2.0 (3.0)
45.	Heart Rate	176/195 (19)	95 (54.0)	80 (45.5)	1 (0.6)	0 (0)	0 (0)	0 (0)	99.4 (1&2)	1.46 (0.51)	1.0 (2.0)
46.	Temperature	176/195 (19)	35 (19.9)	92 (52.3)	45 (25.6)	4 (2.3)	0 (0)	0 (0)	72.2 (1&2)	2.10 (0.73)	2.0 (3.0)
Neurology Items											
47.	Alertness	175/195 (20)	108 (61.7)	63 (36.0)	3 (1.7)	1 (0.6)	0 (0)	0 (0)	97.7 (1&2)	1.41	1.0

										(0.55)	(3.0)
48.	Smiling	173/195 (22)	30 (17.3)	59 (34.1)	57 (32.9)	22 (12.7)	5 (2.9)	0 (0)	51.4 (1&2)	2.49 (1.01)	2.0 (4.0)
49.	Curious	172/195 (23)	16 (9.3)	57 (33.1)	65 (37.8)	27 (15.7)	4 (2.3)	3 (1.7)	42.4 (1&2)	2.73 (1.02)	3.0 (5.0)
50.	Crying/ consolable	173/195 (22)	21 (12.1)	79 (45.7)	59 (34.1)	13 (7.5)	0 (0)	1 (0.6)	57.8 (1&2)	2.39 (0.83)	2.0 (5.0)
51.	Inconsolable	173/195 (21)	32 (18.4)	86 (49.4)	49 (28.2)	6 (3.4)	0 (0)	1 (0.6)	67.8 (1&2)	2.18 (0.81)	2.0 (5.0)
52.	Irritability	174/195 (21)	64 (36.8)	86 (49.4)	24 (13.8)	0 (0)	0 (0)	0 (0)	86.2 (1&2)	1.77 (0.67)	2.0 (2.0)
53.	Drowsiness	175/195 (20)	92 (52.6)	69 (39.4)	12 (6.9)	0 (0)	1 (0.6)	1 (0.6)	92.0 (1&2)	1.58 (0.75)	1.0 (5.0)
54.	Responds to pain	172/195 (23)	77 (44.8)	70 (40.7)	21 (12.2)	2 (1.2)	1 (0.6)	1 (0.6)	85.5 (4&5)	1.73 (0.83)	2.0 (5.0)
55.	Un-responsive	173/195 (22)	153 (88.4)	18 (10.4)	2 (1.2)	0 (0)	0 (0)	0 (0)	98.8 (1&2)	1.12 (0.36)	1.0 (2.0)
56.	Glasgow Coma Scale	174/195 (21)	49 (28.2)	47 (27.0)	47 (27.0)	24 (13.8)	5 (2.9)	2 (1.1)	55.2 (1&2)	2.39 (1.18)	2.0 (5.0)
57.	AVPU scale	174/195 (21)	125 (71.8)	40 (23.0)	7 (4.0)	2 (1.1)	0 (0)	0 (0)	94.8 (4&5)	1.34 (0.61)	1.0 (3.0)
58.	Muscle Tone	174/195 (21)	29 (16.7)	99 (56.9)	34 (19.5)	10 (5.7)	2 (1.1)	0 (0)	73.6 (1&2)	2.1 (0.81)	2.0 (4.0)
59.	Convulsion	173/195 (22)	75 (43.4)	62 (35.8)	27 (15.6)	6 (3.5)	2 (1.2)	1 (0.6)	79.2 (1&2)	1.84 (0.95)	2.0 (5.0)
Risk Factors and Miscellaneous Items											
60.	Pitch of Cry	173/195 (22)	42 (24.3)	81 (46.8)	40 (23.1)	7 (4.0)	1 (0.6)	2 (1.2)	71.1 (1&2)	2.13 (0.92)	2.0 (5.0)
61.	Altered	170/195 (25)	41 (24.1)	93 (54.7)	31 (18.2)	4 (2.4)	0 (0)	1 (0.6)	78.8 (1&2)	2.01	2.0

	Behaviour									(0.78)	(5.0)
62.	Pain	170/198 (28)	19 (11.2)	70 (41.2)	59 (34.7)	17 (10.0)	3 (1.8)	2 (1.2)	52.3 (1&2)	2.52 (0.97)	2.0 (5.0)
63.	Con-junctivitis	173/195 (22)	0 (0)	23 (13.3)	81 (46.8)	57 (32.9)	10 (5.8)	2 (1.2)	60.1 (1&2)	3.34 (0.82)	3.0 (4.0)
64.	Sore Throat	170/195 (25)	7 (4.1)	43 (25.3)	81 (47.6)	28 (16.5)	9 (5.3)	2 (1.2)	29.4 (1&2)	2.97 (0.95)	3.0 (5.0)
65.	Otitis Media	172/195 (23)	3 (1.7)	28 (16.3)	78 (45.3)	48 (27.9)	11 (6.4)	4 (2.3)	34.3 (4&5)	3.27 (0.95)	3.0 (5.0)
66.	Hoarseness	174/195 (21)	12 (6.9)	46 (26.4)	75 (43.1)	32 (18.4)	6 (3.4)	3 (1.7)	33.3 (1&2)	2.90 (1.15)	3.0 (5.0)
67.	Rash	172/195 (23)	44 (25.6)	45 (26.2)	57 (33.1)	18 (10.5)	6 (3.5)	2 (1.2)	51.7 (1&2)	2.43 (1.15)	2.0 (5.0)
68.	Cervical Adenopathy	171/195 (24)	6 (3.5)	23 (13.5)	68 (39.8)	37 (21.6)	11 (6.4)	26 (15.2)	28.0 (4&5)	3.59 (1.33)	3.0 (5.0)
69.	Hepato-megaly	171/195 (24)	22 (12.9)	63 (36.8)	55 (32.2)	14 (8.2)	2 (1.2)	15 (8.8)	49.7 (1&2)	2.74 (1.32)	3.0 (5.0)
70.	Laboratory Tests	174/195 (21)	19 (10.9)	77 (44.3)	51 (29.3)	22 (12.6)	4 (2.3)	1 (0.6)	55.2 (1&2)	2.52 (0.96)	2.0 (5.0)
71.	Day of Illness	175/195 (20)	41 (23.4)	104 (59.4)	24 (13.7)	4 (2.3)	2 (1.1)	0 (0)	82.9 (1&2)	1.98 (0.75)	2.0 (4.0)
72.	Personal Concerns/ Gut feelings	174/195 (21)	68 (39.1)	94 (54.0)	11 (6.3)	0 (0)	1 (0.6)	0 (0)	93.1 (1&2)	1.68 (0.64)	2.0 (4.0)
73.	Parental concerns	174/195 (21)	52 (29.9)	102 (58.6)	20 (11.5)	0 (0)	0 (0)	0 (0)	88.5 (1&2)	1.81 (0.61)	2.0 (2.0)
74.	General Condition	174/195 (21)	73 (42.0)	94 (54.0)	7 (4.0)	0 (0)	0 (0)	0 (0)	96.0 (1&2)	1.62 (0.56)	2.0 (2.0)

75.	Pallor	173/195 (22)	47 (27.2)	95 (54.9)	26 (15.0)	3 (1.7)	3 (1.8)	1(0.6%)	82.1 (1&2)	1.95 (0.79)	2.0 (5.0)
76.	Born second half of year	163/195 (32)	7 (4.3)	51 (31.3)	60 (36.8)	34 (20.9)	9 (5.5)	2 (1.2)	35.6 (1&2)	2.95 (1.01)	3.0 (5.0)
77.	Suburban Residence	159/195 (36)	0 (0)	13 (8.2)	73 (45.9)	42 (26.4)	24 (15.1)	7 (4.4)	41.5 (4&5)	3.61 (0.98)	3.0 (4.0)
78.	Household Crowding	161/195 (34)	7 (4.3)	44 (27.3)	65 (40.4)	33 (20.5)	10 (6.2)	2 (1.2)	31.7 (1&2)	3.0 (1.0)	3.0 (5.0)
79.	Chronic Lung Disease	172/195 (23)	117 (68.0)	54 (31.4)	1 (0.6)	0 (0)	0 (0)	0 (0)	99.4 (1&2)	1.32 (0.48)	1.0 (2.0)
80.	Congenital Heart Disease	172/195 (23)	123 (71.5)	48 (27.9)	1 (0.6)	0 (0)	0 (0)	0 (0)	99.4 (1&2)	1.29 (0.46)	1.0 (2.0)
81.	Neurological disorder	169/195 (26)	34 (20.1)	91 (53.8)	35 (20.7)	6 (3.6)	2 (1.2)	1 (0.6)	74.0 (1&2)	2.13 (0.85)	2.0 (5.0)
82.	Immuno-deficiency	170/195 (25)	68 (40.0)	87 (51.2)	11 (6.5)	2 (1.2)	1 (0.6)	1 (0.6)	91.2 (1&2)	1.72 (0.76)	2.0 (5.0)
83.	Downs' Syndrome	171/195 (24)	34 (19.9)	86 (50.3)	44 (25.7)	5 (2.9)	1 (0.6)	1 (0.6)	70.7 (1&2)	2.15 (0.83)	2.0 (5.0)
84.	Gestational Age <37weeks	171/195 (24)	34 (19.9)	115 (67.3)	16 (9.4)	5 (2.9)	1 (0.6)	0 (0)	87.1 (1&2)	1.97 (0.68)	2.0 (4.0)
85.	Low birth weight	170/195 (25)	38 (22.4)	111 (65.3)	14 (8.2)	4 (2.4)	1 (0.6)	2 (1.2)	87.6 (1&2)	1.97 (0.80)	2.0 (5.0)
86.	Previous admission/ episode of bronchiolitis	162/195 (33)	27 (16.7)	96 (59.3)	34 (21.0)	2 (1.2)	2 (1.2)	1 (0.6)	75.9 (1&2)	2.12 (0.78)	2.0 (5.0)
87.	Parental smoking	170/195 (25)	31 (18.2)	94 (55.3)	30 (17.6)	10 (5.9)	4 (2.4)	1 (0.6)	73.5 (1&2)	2.20 (0.92)	2.0 (5.0)
88.	Number of siblings in household	170/195 (25)	3 (1.8)	26 (15.3)	80 (47.1)	48 (28.2)	12 (7.1)	1 (0.6)	35.3 (4&5)	3.25 (0.88)	3.0 (5.0)
89.	Day-care attendance	166/195 (24)	4 (2.4)	32 (18.7)	74 (43.3)	46 (26.9)	15 (8.8)	1 (0.6)	35.7 (4&5)	3.23 (0.93)	3.0 (5.0)
90.	Environment -al Air Pollution	171/195 (24)	5 (2.9)	51 (29.8)	64 (37.4)	33 (19.3)	15 (7.7)	3 (1.8)	32.7 (1&2)	3.06 (1.05)	3.0 (5.0)
91.	Ethnicity	171/195 (24)	2 (1.2)	9 (5.3)	78 (45.6)	53 (31.0)	26 (15.2)	3 (1.8)	46.2 (4&5)	3.59	3.0

										(0.911)	(5.0)
92.	Bacterial or viral co-infection	169/195(26)	44 (26.0)	98 (58.0)	23 (13.6)	2 (1.2)	1 (0.6)	1 (0.6)	84.0 (1&2)	1.94 (0.76)	2.0 (5.0)
93.	Gender	170/195 (25)	0 (0)	9 (5.3)	68 (40.0)	62 (36.5)	31 (18.2)	0 (0)	54.7 (1&2)	3.67 (0.83)	4.0 (3.0)
94.	Infection with RSV	171/195 (24)	40 (23.4)	78 (45.6)	35 (20.5)	8 (4.7)	7 (4.1)	3 (1.8)	69.0 (1&2)	2.25 (1.10)	2.0 (5.0)
95.	Infection with Adenovirus	171/195 (24)	36 (21.6)	81 (47.4)	30 (17.5)	10 (5.8)	4 (2.3)	9 (5.3)	69.0 (1&2)	2.35 (1.24)	2.0 (5.0)
96.	Infection with HMPV	171/195 (24)	37 (21.6)	68 (39.8)	36 (21.1)	9 (5.3)	4 (2.3)	17 (9.9)	61.4 (1&2)	2.56 (1.45)	2.0 (5.0)
97.	Parental age	170/195 (25)	0 (0)	28 (16.5)	73 (42.9)	43 (25.3)	25 (14.7)	1 (0.6)	40.0 (4&5)	3.4 (0.95)	3.0 (4.0)
98.	Breastfed	171/195 (24)	2 (1.2)	35 (20.5)	84 (49.1)	42 (24.6)	7 (4.1)	1 (0.6)	28.7 (4&5)	3.11 (0.83)	3.0 (5.0)
99.	Educational needs of parents	169/195 (26)	10 (5.9)	79 (46.7)	57 (33.7)	16 (9.5)	7 (4.1)	0 (0)	52.7 (1&2)	2.59 (0.89)	2.0 (4.0)
100.	Family transport issues	171 /195 (24)	1 (0.6)	38 (22.2)	74 (43.3)	37 (21.6)	19 (11.1)	2 (1.2)	22.8 (4&5)	3.23 (0.97)	3.0 (5.0)
101.	Family history of Atopy	171/195 (24)	5 (2.9)	51 (29.8)	63 (36.8)	27 (15.8)	13 (7.6)	12 (7.0)	32.7 (1&2)	3.16 (1.22)	3.0 (5.0)

Appendix 31: Delphi round two

Item Number	Item	Response n/N (missing data)	1 Strongly agree Frequency (%)	2 Agree Frequency (%)	3 Neutral Frequency (%)	4 Disagree Frequency (%)	5 Completely disagree Frequency (%)	6 Don't know Frequency (%)	Consensus % (categories)	Mean (SD)	Median (range)
1.	Air Hunger	131/136 (6)	41 (31.3)	40 (30.5)	22 (16.8)	12 (9.2)	8 (6.1)	8 (6.1)	61.8 (1&2)	2.46 (1.47)	2.0 (5.0)
2.	Nasal Discharge	134/136 (2)	9 (6.7)	41 (30.6)	40 (29.9)	33 (24.6)	11 (8.2)	0 (0)	37.3 (1&2)	2.97 (1.07)	3.0 (4.0)
3.	Respiratory Secretion Colour	134/136 (2)	3 (2.2)	35 (26.1)	48 (35.8)	43 (32.1)	5 (3.7)	0 (0)	35.8 (4&5)	3.08 (0.90)	3.0 (4.0)
4.	Cough	134/136 (2)	20 (14.9)	56 (41.8)	30 (22.4)	28 (20.9)	0 (0)	0 (0)	56.7 (1&2)	2.49 (0.98)	2.0 (3.0)
5.	HCo3 on BGA	133/136 (3)	14 (10.5)	45 (33.8)	39 (29.3)	25 (18.8)	3 (2.3)	7 (5.3)	44.4 (1&2)	2.84 (1.22)	3.0 (5.0)
6.	Stridor	131/136 (5)	35 (26.7)	33 (25.2)	26 (19.8)	28 (21.4)	7 (5.3)	2 (1.5)	51.9 (1&2)	2.58 (1.31)	2.0 (5.0)
7.	Wheeze/Noisy Breathing	134/136 (2)	36 (26.9)	64 (47.8)	17 (12.7)	16 (11.9)	1 (0.7)	0 (0)	74.6 (1&2)	2.11 (0.96)	2.0 (4.0)
8.	Location of Wheeze	133/136 (3)	6 (4.4)	36 (26.3)	39 (28.5)	45 (32.8)	11 (8.0)	0 (0)	42.1 (4&5)	3.15 (1.04)	3.0 (4.0)
9.	Duration of Wheeze	134/136 (2)	12 (9.0)	43 (32.1)	48 (35.8)	29 (21.6)	2 (1.5)	0 (0)	41.0 (1&2)	2.74 (0.94)	3.0 (4.0)
10.	Wheeze Volume	133/136 (3)	10 (7.5)	37 (27.8)	43 (32.3)	34 (25.6)	5 (3.8)	4 (3.0)	35.3 (1&2)	2.99 (1.12)	3.0 (5.0)
11.	Chest Xray	(133/136 (3)	8 (6.0)	27 (20.3)	47 (35.3)	39 (29.3)	12 (9.0)	0 (0)	38.3 (4&5)	3.15 (1.04)	3.0 (4.0)
12.	Respiratory Crackles	133/136 (3)	23 (17.3)	59 (44.4)	25 (18.8)	26 (19.5)	0 (0)	0 (0)	61.7 (1&2)	2.40 (0.99)	2.0 (3.0)
13.	Rhonchi	132/136 (4)	9 (6.8)	36 (27.3)	45 (34.1)	30 (22.7)	2 (1.5)	10 (7.6)	34.1 (1&2)	3.07 (1.23)	3.0 (5.0)
14.	Blowing bubbles through mouth	134/136 (2)	3 (2.2)	23 (17.2)	50 (37.3)	46 (34.3)	9 (6.7)	3 (2.2)	41.0 (4&5)	3.32 (0.98)	3.0 (5.0)
15.	Skin turgor	133/136 (3)	17 (12.8)	70 (52.6)	30 (22.6)	15 (11.3)	1 (0.8)	0 (0)	65.4 (1&2)	2.35	2.0 (5.0)

										(0.89)	
16.	Vomiting	133/136 (3)	14 (10.5)	57 (42.9)	38 (28.6)	23 (17.3)	1 (0.8)	0 (0)	53.4 (1&2)	2.54 (0.92)	2.0 (4.0)
17.	Diarrhoea	134/136 (2)	1 (0.7)	21 (15.7)	48 (35.8)	54 (40.3)	10 (7.5)	0 (0)	47.8 (1&2)	3.38 (0.86)	3.0 (4.0)
18.	Temperature	133/136 (6)	19 (14.3)	68 (51.1)	30 (22.6)	16 (12.0)	0 (0)	0 (0)	65.4 (1&2)	2.32 (0.86)	2.0 (3.0)
19.	Smiling	131/136 (5)	14 (10.7)	50 (38.2)	39 (29.8)	24 (18.3)	3 (2.3)	1 (0.8)	48.9 (1&2)	2.65 (1.02)	3.0 (5.0)
20.	Curious	130/136 (6)	10 (7.7)	31 (23.8)	42 (32.3)	40 (30.8)	4 (3.1)	3 (2.3)	33.9 (4&5)	3.04 (1.09)	3.0 (5.0)
21.	Crying but consolable	132/136 (4)	14 (10.6)	64 (48.5)	35 (26.5)	15 (11.4)	3 (2.3)	1 (0.8)	59.1 (1&2)	2.48 (0.96)	2.0 (5.0)
22.	Inconsolable	130/136 (6)	23 (17.7)	68 (52.3)	25 (19.2)	13 (10.0)	0 (0)	1 (0.8)	52.3 (1&2)	2.24 (0.91)	2.0 (5.0)
23.	Glasgow Coma Scale	129/136 (7)	15 (11.6)	43 (33.3)	32 (24.8)	34 (26.4)	5 (3.9)	0 (0)	45.0 (1&2)	2.77 (1.08)	3.0 (4.0)
24.	Muscle tone	129/136 (7)	10 (7.8)	69 (53.5)	31 (24.0)	19 (14.7)	0 (0)	0 (0)	61.2 (1&2)	2.45 (0.83)	2.0 (3.0)
25.	Pitch of Cry	129 /136 (7)	9 (7.0)	53 (41.1)	33 (25.6)	29 (22.5)	4 (3.1)	1 (0.8)	48.1 (1&2)	2.75 (1.02)	3.0 (5.0)
26.	Pain	128/136 (8)	4 (3.1)	32 (25.0)	51 (39.8)	35 (27.3)	5 (3.9)	1 (0.8)	31.2 (1&2)	3.06 (0.93)	3.0 (5.0)
27.	Conjunctivitis	129/136 (7)	0 (0)	15 (11.6)	49 (38.0)	53 (41.1)	10 (7.8)	2 (1.6)	48.9 (4&5)	3.49 (0.85)	4.0 (4.0)
28.	Sore throat	127/136 (9)	1 (0.8)	19 (15.0)	46 (36.2)	49 (38.6)	10 (7.9)	2 (1.6)	46.5 (4&5)	3.42 (0.92)	3.0 (5.0)
29.	Otitis media	129/136 (7)	2 (1.6)	13 (10.1)	47 (36.4)	56 (43.4)	10 (7.8)	1 (0.8)	51.2 (4&5)	3.48 (0.86)	4.0 (5.0)
30.	Hoarseness	129/136 (7)	5 (3.9)	30 (23.3)	40 (31.0)	45 (34.9)	7 (5.4)	2 (1.6)	40.3 (4&5)	3.19 (1.03)	3.0 (5.0)
31.	Rash	129/136 (7)	9 (7.0)	15 (11.6)	47 (36.4)	48 (37.2)	10 (7.8)	0 (0)	45.0 (4&5)	3.27 (1.00)	3.0 (4.0)
32.	Cervical adenopathy	129/136 (7)	0 (0)	11 (8.5)	38 (29.5)	53 (41.1)	12 (9.3)	15 (11.6)	50.4 (4&5)	3.86 (1.08)	4.0 (4.0)
33.	Hepatomegaly	129/136 (7)	5 (3.9)	37 (28.7)	41 (31.8)	33 (25.6)	3 (2.3)	10 (7.8)	32.6 (1&2)	3.17 (1.21)	4.0 (4.0)
34.	Laboratory tests	127/136 (9)	14 (11.0)	47 (37.0)	31 (24.4)	29 (22.8)	6 (4.7)	0 (0)	48.0 (1&2)	2.73 (1.07)	3.0 (4.0)
35.	Born second half	129/136 (7)	5 (3.9)	32 (24.8)	44 (34.1)	32 (24.8)	15 (11.6)	1 (0.8)	36.4 (4&5)	3.17	3.0 (5.0)

	of year									(1.07)	
36.	Suburban residence	127/136 (7)	2 (1.6)	6 (4.7)	55 (43.3)	48 (37.8)	16 (12.6)	0 (0)	50.4 (4&5)	3.55 (0.83)	4.0 (4.0)
37.	Household crowding	128/136 (8)	6 (4.7)	26 (20.3)	48 (37.5)	39 (30.5)	9 (7.0)	0 (0)	37.5 (4&5)	3.14 (0.98)	3.0 (4.0)
38.	Neurological disorders	127/136 (9)	19 (15.0)	63 (49.6)	29 (22.8)	13 (10.2)	3 (2.4)	0 (0)	64.6 (1&2)	2.35 (0.93)	2.0 (4.0)
39.	Downs' Syndrome	129/136 (7)	9 (7.0)	58 (45.0)	39 (30.2)	18 (14.0)	5 (3.9)	0 (0)	51.9 (1&2)	2.62 (0.94)	2.0 (4.0)
40.	Parental smoking	129/136 (7)	21 (16.3)	59 (45.7)	26 (20.2)	17 (13.2)	6 (4.7)	0 (0)	62.0 (1&2)	2.44 (1.05)	2.0 (4.0)
41.	Previous bronchiolitis admission/episode	129/136 (7)	26 (20.2)	67 (51.9)	22 (17.1)	11 (8.5)	3 (2.3)	0 (0)	72.1 (1&2)	2.20 (0.94)	2.0 (4.0)
42.	Number of siblings	129/136 (7)	3 (2.3)	21 (16.3)	49 (38.0)	43 (33.3)	13 (10.1)	0 (0)	43.4 (4&5)	3.32 (0.94)	3.0 (4.0)
43.	Day care attendance	128/136 (8)	5 (3.9)	27 (21.1)	43 (33.6)	37 (28.9)	15 (11.7)	0 (0)	40.6 (4&5)	3.25 (1.06)	3.0 (5.0)
44.	Environmental air pollution	128/136 (8)	5 (3.9)	27 (21.1)	42 (32.8)	43 (33.6)	10 (7.8)	0 (0)	41.4 (4&5)	3.22 (1.02)	3.0 (5.0)
45.	Ethnicity	127/136 (9)	0 (0)	6 (4.7)	55 (43.3)	47 (37.0)	18 (14.2)	1 (0.8)	51.2 (4&5)	3.62 (0.81)	4.0 (4.0)
46.	Gender	129/136 (7)	1 (0.8)	12 (9.3)	48 (37.2)	49 (38.0)	19 (14.7)	0 (0)	52.7 (4&5)	3.56 (0.88)	4.0 (4.0)
47.	RSV infection	128/136 (8)	40 (31.3)	47 (36.7)	22 (17.2)	14 (10.9)	4 (3.1)	1 (0.8)	68.0 (1&2)	2.20 (1.13)	2.0 (5.0)
48.	Adenovirus infection	129/136 (7)	29 (22.5)	52 (40.3)	24 (18.6)	18 (13.2)	4 (3.1)	2 (1.6)	62.8 (1&2)	2.39 (1.16)	2.0 (5.0)
49.	HMPV infection	126/136 (10)	26 (20.6)	40 (31.7)	31 (24.6)	17 (13.5)	4 (3.2)	8 (6.3)	52.4 (1&2)	2.65 (1.36)	2.0 (5.0)
50.	Breastfed	129/136 (7)	5 (3.9)	19 (14.7)	57 (44.2)	33 (25.6)	13 (10.1)	2 (1.6)	35.7 (4&5)	3.27 (1.01)	3.0 (5.0)
51.	Parental age	127/136 (7)	2 (1.6)	12 (9.4)	52 (40.9)	44 (34.6)	17 (13.4)	0 (0)	48 (4&5)	3.48 (0.89)	3.0 (4.0)
52.	Educational needs of parents	128/136 (8)	2 (1.6)	38 (29.7)	46 (35.9)	32 (25.0)	9 (7.0)	1 (0.8)	32 (4&5)	3.08 (0.95)	3.0 (5.0)
53.	Family transport issues	128/136 (8)	0 (0)	31 (24.2)	43 (33.6)	40 (31.3)	14 (10.3)	0 (0)	42.2 (4&5)	3.28 (0.95)	3.0 (3.0)
54.	Family history of atopy	129/136 (7)	4 (3.1)	29 (22.5)	51 (39.5)	30 (23.3)	8 (6.2)	7 (5.4)	29.5 (4&5)	3.23 (1.12)	3.0 (5.0)

Appendix 32: Delphi round three

Item No.	Item	Response n/N (missing data)	1 Strongly agree Frequency (%)	2 Agree Frequency (%)	3 Neutral Frequency (%)	4 Disagree Frequency (%)	5 Completely disagree Frequency (%)	6 Don't know Frequency (%)	Consensus % (categories)	Mean (SD)	Median (range)
Criteria for referral/admission to hospital											
1.	Oxygen saturations less than 97% in air	102/103 (1)	1 (1.0)	4 (4.9)	18 (17.6)	52 (51.0)	27 (26.5)	0 (0)	77.5 (4&5)	3.98 (0.83)	4.0 (4.0)
2.	Oxygen saturations less than 95% in air	102/103 (1)	9 (8.8)	18 (17.6)	22 (21.6)	38 (37.3)	15 (14.7)	0 (0)	52 (4&5)	3.31 (1.18)	4.0 (4.0)
3.	Oxygen saturations less than 94% in air	102/103 (1)	21 (20.6)	42 (41.2)	18 (17.6)	14 (13.7)	7 (6.9)	0 (0)	61.8 (1&2)	2.45 (1.16)	2.0 (4.0)
4.	Oxygen saturations less than 92% in air	103/103 (0)	67 (65.0)	29 (28.2)	4 (3.9)	3 (2.9)	0 (0)	0 (0)	93.2 (1&2)	1.44 (0.71)	1.0 (3.0)
5.	Oxygen saturations less than 90% in air	101/103 (2)	84 (83.2)	12 (11.9)	2 (2.0)	2 (2.0)	1 (1.0)	0 (0)	95 (1&2)	1.25 (0.68)	1.0 (4.0)
6.	Respiratory rate >45bpm	101/103 (2)	11 (10.8)	25 (24.5)	34 (33.3)	27 (26.5)	5 (4.9)	0 (0)	35.3 (1&2)	2.90 (1.06)	3.0 (4.0)
7.	Respiratory rate >50bpm	103/103 (0)	32 (31.1)	47 (45.6)	15 (14.6)	8 (7.8)	1 (1.0)	0 (0)	76.7 (1&2)	2.01 (0.92)	2.0 (4.0)
8.	Respiratory rate >70bpm	103/103 (0)	82 (79.6)	17 (16.5)	2 (1.9)	1 (1.0)	1 (1.0)	0 (0)	96.1 (1&2)	1.27 (0.64)	1.0 (4.0)
9.	Presence of nasal flaring or grunting	102/103 (1)	77 (75.5)	23 (22.5)	2 (2.0)	0 (0)	0 (0)	0 (0)	98.0 (1&2)	1.26 (0.48)	1.0 (2.0)
10.	Moderate to severe intercostal or sub-sternal recession	103/103 (0)	78 (75.7)	25 (24.3)	0 (0)	0 (0)	0 (0)	0 (0)	75.7 (1&2)	1.24 (0.43)	1.0 (1.0)
11.	Frequent apnoeas	103/103 (0)	100 (97.1)	2 (1.9)	1 (1.0)	0 (0)	0 (0)	0 (0)	99 (1&2)	1.03 (0.23)	1.0 (2.0)
12.	Heart rate >155bpm	103/103 (0)	39 (37.9)	35 (34.0)	20 (19.4)	9 (8.7)	0 (0)	0 (0)	71.8 (1&2)	1.99 (0.96)	2.0 (3.0)
13.	<50% feeds in preceding 24 hrs	102/103 (1)	55 (53.9)	38 (37.3)	8 (7.8)	1 (1.0)	0 (0)	0 (0)	91.2 (1&2)	1.55 (0.68)	1.0 (3.0)
14.	< 4 wet nappies in preceding 24 hrs	103/103 (0)	12 (11.7)	46 (44.7)	33 (32.0)	11 (10.7)	0 (0)	1 (1.0)	56.3 (1&2)	2.45 (0.90)	2.0 (5.0)

15.	Consideration of other risk factors/social issues	103/103 (0)	19 (18.4)	46 (44.7)	30 (29.1)	8 (7.8)	0 (0)	0 (0)	44.7 (1&2)	2.26 (0.85)	2.0 (3.0)
16.	Duration of symptoms <5days	100/103 (3)	3 (3.0)	43 (43.0)	39 (39.0)	12 (12.0)	3 (3.0)	0 (0)	43 (1&2)	2.69 (0.83)	3.0 (4.0)
17.	Age at presentation <18 weeks	102/103 (1)	28 (27.5)	40 (39.2)	25 (24.5)	9 (8.8)	0 (0)	0 (0)	39.2 (1&2)	2.14 (0.92)	2.0 (3.0)
18.	Age at presentation < 6 months	103/103 (0)	7 (6.8)	37 (35.9)	37 (35.9)	19 (18.4)	3 (2.9)	0 (0)	35.9 (1&2)	2.74 (0.93)	3.0 (4.0)
Criteria for 'mild' bronchiolitis											
20.	Would generally not be admitted to hospital	103/103 (0)	35 (34.0)	59 (57.3)	6 (5.8)	2 (2.9)	1 (1.0)	0 (0)	91.3 (1&2)	1.78 (0.72)	2.0 (4.0)
21.	May have some increased work of breathing that would be acceptable	103/103 (0)	23 (22.3)	74 (71.8)	3 (2.9)	3 (2.9)	0 (0)	0 (0)	94.2 (1&2)	1.86 (0.59)	2.0 (3.0)
22.	May have mild recession	101/103 (2)	23 (22.8)	75 (74.3)	2 (2.0)	1 (1.0)	0 (0)	0 (0)	97.0 (1&2)	1.81 (0.50)	2.0 (3.0)
23.	Will not have grunting	103/103 (0)	57 (55.3)	34 (33.0)	5 (4.9)	7 (6.8)	0 (0)	0 (0)	88.3 (1&2)	1.63 (0.86)	1.0 (3.0)
24.	Will not have head bobbing	103/103 (0)	56 (54.4)	37 (35.9)	5 (4.9)	5 (4.9)	0 (0)	0 (0)	90.3 (1&2)	1.60 (0.79)	1.0 (3.0)
25.	Will not have cyanosis	103/103 (0)	70 (68.0)	27 (26.2)	1 (1.0)	5 (4.9)	0 (0)	0 (0)	94.2 (1&2)	1.42 (0.74)	1.0 (3.0)
26.	Will not have apnoeas or pauses in breathing	103/103 (0)	66 (64.1)	30 (29.1)	2 (1.9)	5 (4.9)	0 (0)	0 (0)	93.2 (1&2)	1.47 (0.76)	1.0 (3.0)
27.	May have an increased respiratory rate but will be no greater than 60bpm	103/103 (0)	28 (27.2)	56 (54.4)	8 (7.8)	11 (10.7)	0 (0)	0 (0)	81.6 (1&2)	2.01 (0.88)	2.0 (3.0)
28.	May have coughing spasms	103/103 (0)	25 (24.3)	67 (65.0)	8 (7.8)	2 (1.9)	1 (1.0)	0 (0)	89.3 (1&2)	1.90 (0.69)	2.0 (4.0)
29.	Will have oxygen saturations >92% in air	103/103 (0)	39 (37.9)	56 (54.4)	4 (3.9)	4 (3.9)	0 (0)	0 (0)	92.2 (1&2)	1.73 (0.71)	2.0 (3.0)
30.	Will have age appropriate heart rate <150 bpm	103/103 (0)	25 (24.3)	67 (65.0)	10 (9.7)	1 (1.0)	0 (0)	0 (0)	89.3 (1&2)	1.87 (0.60)	2.0 (3.0)
31.	Will be taking at least	103/103 (0)	26 (25.2)	63 (61.2)	10 (9.7)	4 (3.9)	0 (0)	0 (0)	86.4 (1&2)	1.92	2.0

	50-75% of an appropriate feed intake for weight									(0.70)	(3.0)
32.	May have an element of vomiting but clinically hydrated	103/103 (0)	27 (26.2)	65 (63.1)	7 (6.8)	3 (2.9)	1 (1.0)	0 (0)	89.3 (1&2)	1.90 (0.77)	2.0 (5.0)
33.	Will have warm peripheries	103/103 (0)	34 (33)	60 (58.3)	6 (5.8)	3 (2.9)	0 (0)	0 (0)	91.3 (1&2)	1.78 (0.68)	2.0 (3.0)
34.	Will have CRT <2 seconds	103/103 (0)	41 (39.8)	56 (54.4)	4 (3.9)	2 (1.9)	0 (0)	0 (0)	94.2 (1&2)	1.67 (0.64)	2.0 (3.0)
35.	Will have more than four wet nappies in preceding 24 hours	103/103 (0)	21 (20.4)	55 (53.4)	22 (21.4)	4 (3.9)	0 (0)	0 (0)	73.8 (1&2)	2.12 (0.84)	2.0 (5.0)
36.	Will be alert and active	103/103 (0)	39 (37.9)	52 (50.5)	10 (9.7)	2 (1.9)	0 (0)	0 (0)	88.3 (1&2)	1.75 (0.70)	2.0 (3.0)
37.	May be grumpy but not irritable	102/103 (1)	25 (24.5)	70 (68.6)	5 (4.9)	1 (1.0)	0 (0)	0 (0)	93.1(1&2)	1.86 (0.68)	2.0 (5.0)
38.	May show some signs of improvement following administration of paracetemol or nasal pharyngeal suctioning	102/103 (1)	21 (20.6)	59 (57.8)	15 (14.7)	4 (3.9)	0 (0)	0 (0)	78.4 (1&2)	2.11 (0.91)	2.0 (5.0)
39.	Duration of illness	101/103 (2)	10 (9.9)	37 (36.6)	35 (34.7)	13 (12.9)	0 (0)	0 (0)	46.5 (1&2)	2.70 (1.07)	3.0 (5.0)
Criteria for 'moderate' bronchiolitis											
40.	May have saturations <92% in room air requiring supplemental oxygen	103/103 (0)	20 (19.4)	73 (70.9)	4 (3.9)	6 (5.8)	0 (0)	0 (0)	90.3 (1&2)	1.96 (0.68)	2.0 (3.0)
41.	May have increasing oxygen requirements (oxygen up to 50-60%) to maintain oxygen saturations >92%	103/103 (0)	13 (12.6)	47 (45.6)	6 (5.8)	29 (28.2)	0 (0)	0 (0)	58.3 (1&2)	2.72 (1.22)	2.0 (4.0)
42.	May have moderate subcostal and or/intercostal recession	103/103 (0)	29 (28.2)	70 (68.0)	2 (1.9)	2 (1.9)	0 (0)	0 (0)	96.1 (1&2)	1.77 (0.57)	2.0 (3.0)
43.	May have moderate	103/103 (0)	25 (24.3)	62 (60.2)	3 (2.9)	13 (12.6)	0 (0)	0 (0)	84.5 (1&2)	2.03	2.0

	tracheal tug									(0.88)	(3.0)
44.	May have a mild grunt	103/103 (0)	19 (18.4)	61 (59.2)	7 (6.8)	16 (15.5)	0 (0)	0 (0)	77.7 (1&2)	2.19 (0.91)	2.0 (3.0)
45.	May have self-correcting apnoeas and/or pauses in breathing	103/103 (0)	13 (12.6)	49 (47.6)	13 (12.6)	20 (19.4)	8 (7.8)	0 (0)	60.2 (1&2)	2.62 (1.16)	2.0 (4.0)
46.	Will be alert but may be getting irritable or tired and or/exhausted	103/103 (0)	18 (17.5)	56 (54.4)	8 (7.8)	19 (18.4)	2 (1.9)	0 (0)	71.8 (1&2)	2.33 (1.03)	2.0 (4.0)
47.	May have normal responsiveness	103/103 (0)	21 (20.4)	72 (69.9)	4 (3.9)	6 (5.8)	0 (0)	0 (0)	90.3 (1&2)	1.95 (0.69)	2.0 (3.0)
48.	May have normal muscle tone	103/103 (0)	26 (25.2)	69 (67.0)	5 (4.9)	3 (2.9)	0 (0)	0 (0)	92.2 (1&2)	1.85 (0.63)	2.0 (3.0)
49.	May be consolable by parents	103/103 (0)	23 (22.3)	71 (68.9)	7 (6.8)	2 (1.9)	0 (0)	0 (0)	91.3 (1&2)	1.88 (0.59)	2.0 (3.0)
50.	May have a heart rate 160bpm or just over	102/103 (1)	18 (17.6)	70 (68.6)	12 (11.8)	2 (2.0)	0 (0)	0 (0)	86.3 (1&2)	1.98 (0.61)	2.0 (3.0)
51.	May be taking <50% oral feeds	102/103 (1)	20 (19.6)	68 (66.7)	11 (10.8)	3 (2.9)	0 (0)	0 (0)	86.3 (1&2)	1.97 (0.65)	2.0 (3.0)
52.	May have an 'unwell' appearance – pale/fluey/glassy eyed	103/103 (0)	15 (14.6)	56 (54.4)	9 (8.7)	17 (16.5)	0 (0)	0 (0)	68.9 (1&2)	2.45 (1.13)	2.0 (5.0)
53.	May have < four wet nappies in preceding 24 hours or urine output <2mLs/kg/hr	103/103 (0)	14 (13.6)	68 (66.0)	15 (14.6)	5 (4.9)	0 (0)	1 (1.0)	79.6 (1&2)	2.14 (0.78)	2.0 (5.0)
Criteria for 'severe' bronchiolitis											
54.	Significant hypoxia with increasing oxygen requirements >50%	102/103 (1)	79 (77.5)	23 (22.5)	0 (0)	0 (0)	0 (0)	0 (0)	100 (1&2)	1.22 (0.41)	1.0 (1.0)
55.	Apnoea (+/- bradycardia) increasing in frequency & duration, requiring bag and mask intervention	103/103 (0)	82 (79.6)	21 (20.4)	0 (0)	0 (0)	0 (0)	0 (0)	100 (1&2)	1.20 (0.40)	1.0 (1.0)
56.	Apnoea (+/-	103/103 (0)	75 (72.8)	27 (26.2)	0 (0)	1 (1.0)	0 (0)	0 (0)	99.0 (1&2)	1.29	1.0

	bradycardia) increasing in frequency & duration, despite non-invasive ventilation									(0.51)	(3.0)
57.	Respiratory rate >70 bpm	103/103 (0)	75 (72.8)	28 (27.2)	0 (0)	0 (0)	0 (0)	0 (0)	100 (1&2)	1.27 (0.44)	1.0 (1.0)
58.	Decreasing respiratory rate with bradycardia	103/103 (0)	75 (72.8)	26 (25.2)	1 (1.0)	1 (1.0)	0 (0)	0 (0)	98.1 (1&2)	1.30 (0.53)	1.0 (3.0)
59.	Increased recession and effort of breathing at rest and or/ following naso-gastric feeds	103/103 (0)	69 (67.0)	28 (27.2)	5 (4.9)	1 (1.0)	0 (0)	0 (0)	94.2 (1&2)	1.39 (0.63)	1.0 (3.0)
60.	Severe subcostal/intercostal/ sub-sternal recession	103/103 (0)	78 (75.7)	25 (24.3)	0 (0)	0 (0)	0 (0)	0 (0)	100 (1&2)	1.24 (0.43)	1.0 (1.0)
61.	Head bobbing	103/103 (0)	76 (73.8)	27 (26.2)	0 (0)	0 (0)	0 (0)	0 (0)	100 (1&2)	1.26 (0.44)	1.0 (1.0)
62.	Grunting	103/103 (0)	80 (77.7)	23 (22.3)	0 (0)	0 (0)	0 (0)	0 (0)	100 (1&2)	1.22 (0.41)	1.0 (1.0)
63.	Nasal flare	103/103 (0)	72 (69.9)	30 (29.1)	1 (1.0)	0 (0)	0 (0)	0 (0)	100 (1&2)	1.31 (0.48)	1.0 (2.0)
64.	Persistently raised or increasing carbon dioxide levels on blood gas analysis with decreasing pH	103/103 (0)	72 (69.9)	30 (29.1)	1 (1.0)	0 (0)	0 (0)	0 (0)	99.0 (1&2)	1.31 (0.48)	1.0 (2.0)
65.	Look exhausted	103/103 (0)	80 (77.7)	23 (22.3)	0 (0)	0 (0)	0 (0)	0 (0)	100 (1&2)	1.22 (0.41)	1.0 (1.0)
66.	Tire with poor laboured breathing	103/103 (0)	76 (73.8)	26 (25.2)	0 (0)	1 (1.0)	0 (0)	0 (0)	99.0 (1&2)	1.28 (0.51)	1.0 (3.0)
67.	Reduced air entry	103/103 (0)	62 (60.2)	33 (32.0)	7 (6.8)	1 (1.0)	0 (0)	0 (0)	92.2 (1&2)	1.48 (0.66)	1.0 (3.0)
68.	Not respond to previous treatment interventions	102/103 (1)	52 (51.0)	45 (44.1)	3 (2.9)	1 (1.0)	1 (1.0)	0 (0)	95.1 (1&2)	1.56 (0.69)	1.0 (4.0)
69.	A complete inability take oral feeds	103/103 (0)	67 (65.0)	33 (32.0)	0 (0)	2 (1.9)	0 (0)	1 (1.0)	97.1 (1&2)	1.42 (0.74)	1.0 (5.0)
70.	Clinical signs of	103/103 (0)	59 (57.3)	39 (37.9)	4 (3.9)	1 (1.0)	0 (0)	0 (0)	95.1 (1&2)	1.48	1.0

	dehydration									(0.62)	(3.0)
71.	Less an four nappies in preceding 24 hours or urine output <2mLs/kg/hr	103/103 (0)	55 (53.4)	38 (36.9)	8 (7.8)	1 (1.0)	1 (1.0)	0 (0)	90.3 (1&2)	1.60 (0.80)	1.0 (5.0)
72.	Toxic appearance (blue/white/grey/blue)	103/103 (0)	64 (62.1)	36 (35.0)	3 (2.9)	0 (0)	0 (0)	0 (0)	97.1 (1&2)	1.40 (0.55)	1.0 (2.0)
73.	No muscle tone/floppy	103/103 (0)	60 (58.3)	40 (38.8)	1 (1.0)	2 (1.9)	0 (0)	0 (0)	97.1 (1&2)	1.46 (0.62)	1.0 (3.0)
74.	Alert but inactive and or/passive	103/103 (0)	39 (37.9)	39 (37.9)	17 (16.5)	6 (5.8)	1 (1.0)	1 (1.0)	75.7 (1&2)	1.97 (1.01)	2.0 (5.0)
75.	Decreased level of consciousness or unresponsive	103/103 (0)	56 (54.4)	39 (37.9)	7 (6.8)	1 (1.0)		0 (0)	92.2 (1&2)	1.54 (0.66)	1.0 (3.0)
76.	Handling may cause cardiovascular instability	101/103 (2)	52 (51.5)	40 (39.6)	6 (5.9)	2 (2.0)	0 (0)	1 (1.0)	91.1 (1&2)	1.62 (0.82)	1.0 (5.0)
77.	Clammy, damp and sweaty	103/103 (0)	57 (55.3)	39 (37.9)	5 (4.9)	2 (1.9)	0 (0)	0 (0)	93.2 (1&2)	1.53 (0.68)	1.0 (3.0)
78.	Poor perfusion with mottled appearance	103/103 (0)	65 (63.1)	37 (35.9)	1 (1.0)	0 (0)	0 (0)	0 (0)	99.0 (1&2)	1.37 (0.50)	1.0 (2.0)
79.	Fever	103/103 (0)	38 (36.9)	49 (47.6)	13 (12.6)	2 (1.9)	0 (0)	1 (1.0)	84.5 (1&2)	1.83 (0.84)	2.0 (5.0)
80.	Cardio/respiratory arrest	103/103 (0)	67 (65.0)	34 (33.0)	1 (1.0)	1 (1.0)	0 (0)	0 (0)	98.1 (1&2)	1.37 (0.56)	1.0 (3.0)
Criteria for hospital discharge											
81.	Intermittent monitoring of saturations is acceptable as symptoms improve	101/103 (2)	27 (26.7)	50 (49.5)	13 (12.9)	10 (9.9)	1 (1.0)	0 (0)	76.2 (1&2)	2.08 (0.93)	2.0 (4.0)
82.	Saturations should be >90%	98/103 (5)	22 (22.4)	7 (7.1)	9 (9.2)	47 (48.0)	13 (13.3)	0 (0)	61.3 (4&5)	3.22 (1.39)	4.0 (4.0)
83.	Saturations should be >92%	101/103 (2)	33 (32.7)	20 (19.8)	13 (12.9)	29 (28.7)	6 (5.9)	0 (0)	52.5 (1&2)	2.55 (1.35)	2.0 (4.0)
84.	Saturations should be >93%	100/103 (3)	22 (22.0)	23 (23.0)	23 (23.0)	26 (26.0)	6 (6.0)	0 (0)	45 (1&2)	2.71 (1.24)	3.0 (4.0)
85.	Saturations should be >94%	102/103 (1)	38 (37.3)	37 (36.3)	19 (18.6)	6 (5.9)	2 (2.0)	0 (0)	73.5 (1&2)	1.99 (0.99)	2.0 (4.0)
86.	Oxygen saturations should be stable in	103/103 (0)	41 (39.8)	38 (36.9)	14 (13.6)	7 (6.8)	3 (2.9)	0 (0)	76.7 (1&2)	1.96 (1.03)	2.0 (4.0)

	room air 8-12 hrs minimum										
87.	Mild respiratory recession may be observed but acceptable	103/103 (0)	32 (31.1)	61 (59.2)	5 (4.9)	4 (3.9)	1 (1.0)	0 (0)	90.3 (1&2)	1.84 (0.76)	2.0 (4.0)
88.	>12 hrs since last documented apnoea	102/103 (1)	7 (6.9)	17 (16.7)	13 (12.7)	51 (50.0)	13 (12.7)	1 (1.0)	62.7 (4&5)	3.48 (1.14)	4.0 (5.0)
89.	>24 hrs since last documented apnoea	101/103 (2)	25 (24.8)	35 (34.7)	15 (14.9)	18 (17.8)	8 (7.9)	0 (0)	59.4 (1&2)	2.49 (1.26)	2.0 (4.0)
90.	>48 hrs since last documented apnoea	100/103 (3)	33 (33.0)	29 (29.0)	23 (23.0)	15 (15.0)	0 (0)	0 (0)	62.0 (1&2)	2.20 (1.06)	2.0 (3.0)
91.	Tolerating 50-75% of oral feeds during preceding 24 hours	103/103 (0)	32 (31.1)	55 (53.4)	8 (7.8)	6 (5.8)	2 (1.9)	0 (0)	84.5 (1&2)	1.94 (0.89)	2.0 (4.0)
92.	Infant is alert and active	103/103 (0)	50 (48.5)	51 (49.5)	2 (1.9)	0 (0)	0 (0)	0 (0)	98.1	1.53 (0.53)	2.0 (2.0)

Appendix 33: Delphi round four

Item No.	Item	Response n/N (missing data)	1 Strongly agree Frequency (%)	2 Agree Frequency (%)	3 Neutral Frequency (%)	4 Disagree Frequency (%)	5 Completely disagree Frequency (%)	6 Don't know Frequency (%)	Consensus % (categories)	Mean (SD)	Median (range)
Which of the following criteria should be used when considering referral/admission to hospital for an otherwise healthy infant with bronchiolitis…?											
1.	Raised heart rate at rest >150bpm	95/96 (1)	22 (23.2)	52 (54.7)	17 (17.9)	4 (4.2)	0 (0.0)	0 (0)	77.9 (1&2)	2.03 (0.76)	2.0 (3.0)
2.	Parents report a noticeable reduction in number of wet nappies/UOP in preceding 12 hrs	95/96 (1)	15 (15.8)	61 (64.2)	17 (17.9)	2 (2.1)	0 (0.0)	0 (0)	80 (1&2)	2.06 (0.64)	2.0 (3.0)
3.	Consideration of other risk factors, such as young age, chronic lung disease, congenital heart disease	95/96 (1)	49 (51.6)	43 (45.3)	2 (2.1)	1 (1.1)	0 (0)	0 (0)	96.8 (1&2)	1.52 (0.59)	1.0 (3.0)
4.	Duration of symptoms <3 days in combination with other symptoms	95/96 (1)	8 (8.4)	46 (48.4)	27 (28.4)	13 (13.7)	1 (1.1)	0 (0)	56.8 (1&2)	2.50 (0.87)	2.0 (4.0)
Do you agree or disagree with the following statement that describes an otherwise healthy infant with *'mild'* bronchiolitis…?											
5.	Will have near normal wet nappies/urine output over preceding 12 hours	96/96 (0)	14 (14.6)	62 (64.6)	17 (17.7)	3 (3.1)	0 (0)	0 (0)	62.1 (1&2)	2.09 (0.66)	2.0 (3.0)
Do you agree or disagree with the following statements that describe an otherwise healthy infant with *'moderate'* bronchiolitis…?											
6.	May require up to 50% oxygen to maintain saturations >92%	95/96 (1)	11 (11.6)	48 (50.5)	4 (4.2)	24 (25.3)	8 (8.4)	0 (0)	62.1 (1&2)	2.68 (1.21)	2.0 (4.0)
7.	May 'grunt'	94/96 (2)	12 (12.8)	47 (50.0)	6 (6.4)	26 (27.7)	3 (3.2)	0 (0)	62.8 (1&2)	2.58 (1.12)	2.0 (4.0)
8.	May breathe irregularly	94/96 (2)	8 (8.5)	55 (58.5)	8 (8.5)	20 (21.3)	3 (3.2)	0 (0)	67.0 (1&2)	2.52 (1.02)	2.0 (4.0)

9.	May have self-correcting apnoea	96/96 (0)	9 (9.4)	45 (46.9)	8 (8.3)	26 (27.1)	8 (8.3)	0 (0)	56.3 (1&2)	2.78 (1.18)	2.0 (4.0)
10.	May be irritable/restless	95/96 (1)	15 (15.8)	67 (70.5)	7 (7.4)	5 (5.3)	1 (1.1)	0 (0)	86.3 (1&2)	2.05 (0.73)	2.0 (4.0)
11.	May get tired	95/96 (1)	20 (21.1)	64 (67.4)	5 (5.3)	5 (5.3)	1 (1.1)	0 (0)	88.4 (1&2)	1.97 (0.75)	2.0 (4.0)
12.	May appear unwell (pale)	95/96 (1)	13 (13.7)	64 (67.4)	7 (7.4)	10 (10.5)	1 (1.1)	0 (0)	81.1 (1&2)	2.17 (0.83)	2.0 (4.0)
13.	May have altered behaviour/routine	95/96 (1)	15 (15.8)	66 (69.5)	7 (7.4)	5 (5.3)	2 (2.1)	0 (0)	85.5 (1&2)	2.08 (0.79)	2.0 (4.0)
In an otherwise healthy infant with bronchiolitis which of the following saturation levels should be used for hospital discharge?											
14.	Saturations >90% in room air – asleep	84/96 (12)	8 (9.5)	12 (14.3)	8 (9.5)	39 (46.4)	17 (20.2)	0 (0)	66.6 (4&5)	3.5 (1.23)	4.0 (4.0)
15.	Saturations >92% in room air – asleep	92/96 (4)	21 (22.8)	38 (41.3)	8 (8.7)	22 (23.9)	3 (3.3)	0 (0)	64.1 (1&2)	2.43 (1.17)	2.0 (4.0)
16.	Saturations >93% in room air – asleep	87/96 (9)	16 (18.4)	34 (39.1)	16 (18.4)	20 (23.0)	1 (1.1)	0 (0)	57.5 (1&2)	2.49 (1.07)	2.0 (4.0)
17.	Saturations >94% in room air – asleep	85/96 (11)	43 (50.6)	26 (30.6)	6 (7.1)	9 (10.6)	1 (1.2)	0 (0)	81.2 (1&2)	1.81 (1.04)	1.0 (4.0)
18.	Saturations >90% in room air – awake/settled	84/96 (12)	10 (11.9)	5 (6.0)	8 (9.5)	43 (51.2)	18 (21.4)	0 (0)	72.6 (4&5)	3.64 (1.22)	4.0 (1.5)
19.	Saturations >92% in room air – awake/settled	90/96 (6)	21 (23.3)	28 (31.1)	8 (8.9)	27 (30.0)	6 (6.7)	0 (0)	54.4 (1&2)	2.65 (1.30)	2.0 (1.7)
20.	Saturations >93% in room air – awake/settled	85/96 (11)	16 (18.8)	30 (35.3)	20 (23.5)	18 (21.2)	1 (1.2)	0 (0)	54.1 (1&2)	2.50 (1.06)	2.0 (1.1)
21.	Saturations >94% in room air – awake/settled	85/96 (11)	31 (36.5)	35 (41.2)	7 (8.2)	10 (11.8)	2 (2.4)	0 (0)	77.7 (1&2)	2.02 (1.06)	2.0 (1.1)
22.	>12 hours since last documented apnoea – self correcting	86/96 (10)	7 (8.1)	22 (25.6)	4 (4.7)	38 (44.2)	15 (17.4)	0 (0)	61.6 (4&5)	3.37 (1.26)	4.0 (4.0)
23.	>24 hours since last documented apnoea – self correcting	92/96 (11)	26 (28.3)	39 (42.4)	9 (9.8)	16 (17.4)	2 (2.2)	0 (0)	70.7 (1&2)	2.22 (1.11)	2.0 (4.0)
24.	>48 hours since last documented apnoea – self correcting	87/96 (9)	35 (40.2)	33 (37.9)	9 (10.3)	8 (9.2)	2 (2.3)	0 (0)	78.2 (1&2)	1.95 (1.04)	2.0 (4.0)
23.	>12 hours since last	85/96(11)	6 (7.1)	2 (2.4)	2 (2.4)	34 (40.0)	41 (48.2)	0 (0)	88.2 (4&5)	4.20	4.0

	documented apnoea – requiring intervention									(1.09)	(4.0)
21.	>24 hours since last documented apnoea – requiring intervention	89/96 (7)	13 (14.6)	23 (25.8)	13 (14.6)	28 (31.5)	12 (13.5)	0 (0)	45 (4&5)	3.03 (1.30)	3.0 (4.0)
23.	>48 hours since last documented apnoea – requiring intervention	91/96 (5)	27 (29.7)	41 (45.1)	13 (14.3)	8 (8.8)	2 (2.2)	0 (0)	74.7 (1&2)	2.08 (0.99)	2.0 (4.0)
In an otherwise healthy infant who has required oxygen during hospital admission, how long should their saturations be stable in room air before discharge is considered?											
			1. <8 hours	**2. 8-12 hours**	**3. 12-24 hours**	**4. 24-48 hours**	**5. >48 hours**				
18.		93/96 (3)	7 (7.5)	32 (34.4)	37 (39.8)	17 (18.3)	0 (0)		58.1 (4&5)	2.68 (0.85)	3.0 (3.0)
Which adjective best describes the appearance of a *'severe'* infant?											
		Response n/N (missing data)	**Toxic Frequency (%)**	**Lifeless Frequency (%)**						**Mean (SD)**	**Median (range)**
19.		79/96 (17)	16 (20.3)	63 (79.7)						1.79 (0.40)	2.0 (1.0)

Appendix 34: LIBSS-PRO (Version 7.0)

Liverpool Infant Bronchiolitis Severity Score

(Version 7.0)

Hospital:	**Test Number:**
Time Test Started:	
Time Test Completed:	
Total Time Taken:	

Does the infant have any of the following risk factors for severe disease? Please tick all applicable boxes	
Chronic Lung Disease	Congenital Heart Disease
Neurological Disorders	Immunodeficiency
Down's Syndrome	Gestational age less than 37 weeks
Low Birth Weight (less than 2.5kg or 5.5lbs)	Young Age

Date /Time				
Instructions for use: Circle all applicable scores then total				
Symptoms		**Score**		
Professional concerns / 'gut feeling' in relation to infant's condition	None or mild concerns Moderate concerns **Extremely concerned**	0 2 **4**		**Comments:**
Apnoeas (+/- bradycardia) 	No apnoeas observed Short pauses / irregular breathing Apnoeas increasing in frequency and or/duration that are self correcting Apnoeas increasing in frequency and or / duration that require stimulation **Apnoeas that require bag & mask ventilation**	0 2 4 6 **8**		**Comments:**
Effort of Breathing	Tracheal Tug Inter-costal recession **(2=mild; 4=marked)**	1 1	2 2	**Comments:**
	Head bobbing Grunting Nasal Flare Accessory Muscle Use Sub-sternal recession See saw chest movement Dyspnoea **Central Cyanotic Episodes**	1 1 1 1 1 1 1 **4**		
Respiratory Rate — Under 3 months	25-59 BPM 60-70 BPM **Greater than 70 BPM or less than 25 BPM laboured breathing**	0 2 **4**		**Comments:**
Respiratory Rate — Over 3 months	20-55 BPM 56-65 BPM **Greater than 65 BPM or less than 20 BPM laboured breathing**	0 2 **4**		
Saturations & Oxygenation	Saturations 92% or above in air Requires up to 50% oxygen to maintain saturations 92% or above **Requires over 50% oxygen to maintain saturations 92% or above**	0 2 **4**		**Comments:**
If infant has chronic lung disease or congenital heart disease please substitute saturations of 92% for accepted level of saturations when well.				
Air Entry on Auscultation	Good air entry Reduced air entry **Poor air entry**	0 2 **4**		**Comments:**
Blood Gas Analysis	Not required / normal values Rising PcO_2 with normal pH **Rising PcO_2 with decreasing pH**	0 2 **4**		**Comments:**
Page Score Totals				

Heart Rate	Under 3 months	105-165 BPM 165-180 BPM **Greater than 180 or less than 105 BPM**	0 2 **4**	**Comments:**
	Over 3 months	95-145 BPM 146-160 BPM **Greater than 160 BPM or less than 95 BPM**	0 2 4	
Neurological Assessment 		Alert & Active Lethargic/restless/ reduced interaction Responds to voice / passive / quiet / no interaction Responds to pain **Unresponsive**	0 1 2 3 **4**	**Comments:**
Appearance & Behaviour 		Normal appearance, behaviour & routine Appears unwell (pale) & altered behaviour & routine **Appears lifeless (floppy/grey/white/blue/mottled/ exhausted)**	0 2 **4**	**Comments:**
Hydration & Perfusion	Feeds	Taking usual amount of feeds Taking 50-75% of oral feeds **Taking less than 50% of oral feeds (requires NG feeds or IVI fluids)**	0 2 **4**	**Comments:**
	Urine Output	Producing normal amount of wet nappies over preceding 12 hours (2mLs/kg/hr) Noticeable reduction in number of wet nappies in preceding 12 hours (1-2mLs/kg/hr) **Small volumes of concentrate urine or anuric in preceding 12 hours (less than 1mL/kg/hr)**	0 2 **4**	**Comments:**
	Perfusion	Central capillary refill time greater than 2 seconds	2	**Comments:**
	Dehydration	Sunken fontanelle Sunken eyes	2 2	**Comments:**
Page Score Total				
Overall Score Total				

Day of Illness:													
Date/TIME													
	41.5												41.5
	41												**41**
	40.5												40.5
	40												**40**
	39.5												39.5
	39												**39**
	38.5												38.5
	38												**38**
Temperature													37.5
°C													**37**
	36.5												36.5
	36												**36**
	35.5												35.5
	35												**35**
	230												230
	220												220
	210												210
	200												200
	190												190
	180												180
	170												170
	160												160
	150												150
Blood	140												140
Pressure mmHg	130												130
	120												120
	110												110
	100												100
Pulse rate	90												90
	80												80
	70												70
	60												60
	50												50
	40												40
Respirations	30												30
	20												20
	10												10
	5												5
	0												0
O2 saturation %													
Administered O2 %													
Method of O2													
LIBS Score													
Apnoea Score													
*Activity													

***Activity at the time of score:** Awake (A); Feeding (F); Sleeping (Sg); Crying (C); Paracetamol (Pl); Suction (Sn); Nebuliser (Nr)
***Method of O2 delivery:** Nasal Spec (NS); Face Mask (FM); Head box (HB); Optiflow (OF); nCPAP (CP)

Appendix 35: Content validity evaluation form

Hospital:			**Test Number:**			
How relevant are the following domains and items, to you, when assessing and infant with bronchiolitis for severity of illness? Please circle applicable X.						
Domain		Items	Extremely relevant	Relevant	Irrelevant	Completely irrelevant
Professional concerns 'gut feeling'		None or mild concerns Moderate concerns Extremely concerned	X X X	X X X	X X X	X X X
If irrelevant or completely irrelevant why?						
Why did you assign the score that you did for this domain?						
Apnoea		No apnoea observed Short pauses/irregular breathing Apnoea increasing in frequency and or/ duration that are self-correcting (with or without bradycardia) Apnoea increasing in frequency and or/ duration that require stimulation (with or without bradycardia) Apnoea that require bag & mask ventilation (with or without bradycardia)	X X X X X	X X X X X	X X X X X	X X X X X
If irrelevant or completely irrelevant why?						
Why did you assign the score that you did for this domain?						
Effort of breathing		Tracheal tug Inter-costal recession Head bobbing Grunting Nasal flare Accessory muscle use Sub-costal recession See saw chest movement Dyspnoea Central cyanotic episodes	X X X X X X X X X X	X X X X X X X X X X	X X X X X X X X X X	X X X X X X X X X X
If irrelevant or completely irrelevant why?						
Why did you assign the score that you did for this domain?						
Respiratory rate	Under three months	25-59 bpm 60-70 bpm Greater than 70 or less than 25 bpm	X X X	X X X	X X X	X X X
	Three months and over	20-55 bpm 56-65 bpm Greater than 65 or less than 20 bpm/laboured breathing	X X X	X X X	X X X	X X X

If irrelevant or completely irrelevant why?						
Why did you assign the score that you did for this domain?						
Saturations & oxygenation		Saturations 92% and above in air	X	X	X	X
		Requires up to 50% oxygen to maintain saturations 92% or above	X	X	X	X
		Requires over 50% oxygen	X	X	X	X
If irrelevant or completely irrelevant why?						
Why did you assign the score that you did for this domain?						
Air entry on auscultation		Good air entry	X	X	X	X
		Reduced air entry	X	X	X	X
		Poor air entry	X	X	X	X
If irrelevant or completely irrelevant why?						
Why did you assign the score that you did for this domain?						
Blood gas analysis		Not required/normal values	X	X	X	X
		Rising PCO2 with normal pH	X	X	X	X
		Rising PCO2 with decreasing pH	X	X	X	X
If irrelevant or completely irrelevant why?						
Why did you assign the score that you did for this domain?						
Heart rate	Under three months	105-165 bpm	X	X	X	
		165-180 bpm	X	X	X	
		Greater than 180 or less than 95 bpm	X	X	X	
	Three months and over	95-45 bpm	X	X	X	X
		146-160 bpm	X	X	X	X
		Greater than 160bpm or less than 95bpm	X	X	X	X
If irrelevant or completely irrelevant why?						
Why did you assign the score that you did for this domain?						
Neurological assessment		Alert & active	X	X	X	X
		Lethargic/restless/reduced interaction	X	X	X	X
		Responds to voice/passive/quiet/no interaction	X	X	X	X
		Responds to pain	X	X	X	X
		Unresponsive	X	X	X	X
If irrelevant or completely irrelevant why?						
Why did you assign the score that you did for this domain?						
Appearance & behaviour		Normal appearance, routine & behaviour	X	X	X	X
		Appears unwell (pale), altered behaviour & routine	X	X	X	X
		Appears lifeless	X	X	X	X

		(floppy/grey/white/blue/ Mottled exhausted)				
If irrelevant or completely irrelevant why?						
Why did you assign the score that you did for this domain?						
Hydration & perfusion	Feeds	Taking usual amount of feeds	X	X	X	X
		Taking 50-75% of oral feeds	X	X	X	X
		Taking less than 50% of oral feeds (requires NG or IVI fluids)	X	X	X	X
	Urine output	Normal amount of wet nappies over preceding 12 hours (2mLs/kg/hr)	X	X	X	X
		Noticeable reduction in number of wet nappies in preceding 12 hours (1-2mLs/kg/hr)	X	X	X	X
		Small volumes of concentrate urine or anuric in preceding 12 hours (less than 1mL/kg/hr)	X	X	X	X
	Perfusion	Central capillary refill time greater than 2 seconds	X	X	X	X
	Dehydration	Sunken fontanelle	X	X	X	X
		Sunken eyes	X	X	X	X
If irrelevant or completely irrelevant why?						
Why did you assign the score that you did for this domain?						
Should any of the domains/items be removed from the score-if so which ones?						
How easy or hard was it for you to complete the scoring instrument? If hard – why?						
Did you find the scoring instrument to be clear or confusing? If confusing – why?						
Did you like or dislike the layout? If dislike – why?						
Do you feel the score can be completed in a reasonable amount of time?						
Do you have any suggestions that would help to improve the scoring instrument?						

Appendix 36: Content validity testing – evaluation analysis

No.	Domain	Item	Response n/N (missing data)	1 Extremely relevant n (%)	2 Relevant n (%)	3 Irrelevant n (%)	4 Completely irrelevant n (%)	Consensus % Categories	Mean (SD)
1.	Professional concerns/ 'gut feeling '	None or mild concerns	95/106 (11)	56 (58.9)	38 (40.0)	1 (1.1)	0 (0)	98.9 (1&2)	1.42 (0.51)
		Moderate concerns	90/106 (16)	56 (62.2)	34 (37.8)	0 (0)	0 (0)	100 (1&2)	1.38 (0.48)
		Extremely concerned	81/106 (25)	59 (72.8)	22 (27.2)	0 (0)	0 (0)	94.8 (1&2)	1.27 (0.44)
2.	Apnoea								
		No apnoea observed	103/106 (3)	74 (71.8)	27 (26.2)	2 (1.9)	0 (0)	98.0 (1&2)	1.30 (0.50)
		Short pauses/irregular breathing	87/106 (19)	64 (73.6)	23 (26.4)	0 (0)	0 (0)	100 (1&2)	1.26 (0.44)
		Increasing in frequency/duration	87/106 (19)	72 (82.8)	15 (17.2)	0 (0)	0 (0)	100 (1&2)	1.17 (0.38)
		Require stimulation	86/106 (20)	71 (82.6)	15 (17.4)	0 (0)	0 (0)	100 (1&2)	1.17 (0.38)
		Require bag and mask ventilation	86/106 (20)	71 (82.6)	12 (14.0)	2 (2.3)	1 (1.2)	96.6 (1&2)	1.22 (0.54)
3.	Effort of breathing	Tracheal tug	96/106 (10)	77 (80.2)	19 (19.8)	0 (0)	0 (0)	100 (1&2)	1.20 (0.40)
		Intercostal recession	101/106 (5)	77 (76.2)	24 (23.8)	0 (0)	0 (0)	100 (1&2)	1.24 (0.42)
		Head bobbing	93/106 (13)	75 (80.6)	18 (19.4)	0 (0)	0 (0)	100 (1&2)	1.19 (0.39)
		Grunting	91/106 (15)	75 (82.4)	16 (17.6)	0 (0)	0 (0)	100 (1&2)	1.18 (0.38)
		Nasal Flare	92/106 (14)	72 (78.3)	19 (20.7)	1 (1.1)	0 (0)	98.9 (1&2)	1.23 (0.44)
		Accessory muscle use	95/106 (11)	71 (74.5)	22 (23.2)	2 (2.1)	0 (0)	97.9 (1&2)	1.27 (0.49)
		Sub-costal recession	100/106 (6)	75 (75.0)	25 (25.0)	0 (0)	0 (0)	99 (1&2)	1.25 (0.43)
		See saw chest movement	91/106 (15)	71 (78.0)	19 (20.9)	1 (1.1)	0 (0)	98.9 (1&2)	1.23 (0.44)
		Dyspnoea	93/106 (13)	68 (73.1)	21 (22.6)	3 (3.2)	1 (1.1)	95.7 (1&2)	1.32 (0.59)
		Central cyanotic episodes	92/106 (14)	79 (85.9)	13 (14.1)	0 (0)	0 (0)	100 (1&2)	1.14 (0.35)
4.	Respiratory Rate	Under three months							
		25-59 bpm	88/106 (16)	61 (69.3)	25 (28.4)	2 (2.3)	0 (0)	97.7 (1&2)	1.33 (0.51)
		60-70 bpm	80/106 (26)	64 (80.0)	15 (18.8)	1 (1.3)	0 (0)	98.8 (1&2)	1.21 (0.44)
		>70 or <20 bpm	78/106 (28)	69 (88.5)	8 (10.3)	1 (1.3)	0 (0)	98.7 (1&2)	1.13 (0.37)
		Three months and over							
		20-55 bpm	76/106 (30)	53 (69.7)	21 (27.6)	2 (2.6)	0 (0)	97.4 (1&2)	1.33 (0.52)
		56-65 bpm	74/106 (32)	57 (77.0)	16 (21.6)	1 (1.4)	0 (0)	98.6 (1&2)	1.24 (0.46)
		>65 or < 20 bpm	75/106 (31)	64 (85.3)	10 (13.3)	1 (1.3)	0 (0)	98.7 (1&2)	1.16 (0.40)
5.	Oxygen & saturations (>92%)	Room air	95/106 (11)	70 (73.7)	24 (25.3)	1 (1.1)	0 (0)	98.9 (1&2)	1.27 (0.47)
		≤50% oxygen	91/106 (15)	76 (83.5)	14 (15.4)	1 (1.1)	0 (0)	98.9 (1&2)	1.18 (0.41)
		>50% oxygen	83/106 (23)	72 (86.7)	10 (12.0)	1 (1.2)	0 (0)	98.8 (1&2)	1.14 (0.38)

6.	Air entry	Good air entry Reduced air entry Poor air entry	83/106 (23) 73/106 (33) 70/106 (36)	35 (42.2) 35 (47.9) 34 (48.6)	32 (38.6) 23 (31.5) 22 (31.4)	14 (16.9) 13 (17.8) 12 (17.1)	2 (2.4) 2 (2.7) 2 (2.9)	80.7 (1&2) 79.5 (1&2) 80.0 (1&2)	1.80 (0.80) 1.75 (0.84) 1.74 (0.84)
7.	Blood gas analysis	Not required/normal values Rising PcO_2 with normal pH Rising PcO_2 with rising pH	80/106 (26) 70/106 (36) 70/106 (36)	34 (42.5) 36 (51.4) 39 (55.7)	39 (48.8) 28 (40.0) 25 (35.7)	6 (7.5) 5 (7.1) 5 (7.1)	1 (1.3) 1 (1.4) 1 (1.4)	91.3 (1&2) 91.4 (1&2) 91.4 (1&2)	1.68 (0.67) 1.59 (0.69) 1.54 (0.69)
8.	Heart rate	Under three months 105-165 bpm 165-180 bpm >180 or <95bpm Three months and over 95-45 bpm 146-160 bpm >160 or <95	 83/106 (23) 81/106 (25) 77/106 (29) 75/106 (31) 73/106 (33) 73/106 (33)	 53 (62.4) 58 (70.7) 61 (79.2) 53 (63.9) 58 (71.6) 61 (79.2)	 30 (35.3) 22 (26.8) 15 (19.5) 28 (33.7) 21 (25.9) 15 (19.5)	 2 (2.4) 2 (2.4) 1 (1.3) 2 (2.4) 2 (2.5) 1 (1.3)	 0 (0) 0 (0) 0 (0) 0 (0) 0 (0) 0 (0)	 97.7 (1&2) 97.5 (1&2) 98.7 (1&2) 97.6 (1&2) 97.5 (1&2) 98.7 (1&2)	 1.39 (0.53) 1.31 (0.51) 1.22 (0.44) 1.32 (0.52) 1.29 (0.51) 1.23 (0.45)
9.	Neurological assessment	Alert & Active Reduced interaction Responds to voice Responds to pain Unresponsive	96/106 (10) 92/106 (14) 85/106 (21) 85/106 (21) 85/106 (21)	70 (72.9) 70 (76.1) 66 (77.6) 67 (78.8) 70 (84.2)	23 (24.0) 20 (21.7) 17 (20.0) 16 (18.8) 13 (15.3)	3 (3.1) 2 (2.2) 2 (2.4) 1 (1.2) 1 (1.2)	0 (0) 0 (0) 0 (0) 1 (1.2) 1 (1.2)	96.9 (1&2) 97.8 (1&2) 97.6 (1&2) 97.6 (1&2) 97.6 (1&2)	1.30 (0.52) 1.26 (0.48) 1.25 (0.48) 1.25 (0.53) 1.21 (0.51)
10.	Appearance & behaviour	Normal Unwell altered behaviour/routine Appears lifeless	93/106 (13) 92/106 (14) 83/106 (23)	52 (55.9) 60 (65.2) 63 (75.9)	36 (38.7) 27 (29.3) 17 (20.5)	5 (5.4) 5 (5.4) 3 (3.6)	0 (0) 0 (0) 0 (0)	94.6 (1&2) 94.6 (1&2) 96.4 (1&2)	1.49 (0.60) 1.40 (0.59) 1.28 (0.52)
11.	Hydration & perfusion	Feeds Usual amount of oral feeds 50-75% oral feeds <50% oral feeds	 86/106 (20) 94/106 (12) 89/106 (17)	 58 (67.4) 65 (69.1) 73 (82.0)	 26 (30.2) 29 (30.9) 16 (18.0)	 2 (2.3) 0 (0) 0 (0)	 0 (0) 0 (0) 0 (0)	 97.7 (1&2) 100 (1&2) 100 (1&2)	 1.35 (0.52) 1.31 (0.46) 1.18 (0.38)
		Urine output Normal amount of nappies Reduction in nappies Small volumes/anuric	 89/106 (17) 93/106 (13) 82/106 (24)	 51 (57.3) 56 (60.2) 61 (74.4)	 37 (41.6) 37 (39.8) 21 (25.6)	 1 (1.1) 0 (0) 0 (0)	 0 (0) 0 (0) 0 (0)	 98.9 (1&2) 100 (1&2) 100 (1&2)	 1.44 (0.52) 1.40 (0.49) 1.26 (0.43)
		Perfusion CRT >2 seconds CRT <2 seconds	 85/106 (17) 89/106 (19)	 66 (77.6) 65 (73.0)	 18 (21.2) 23 (25.8)	 1 (1.2) 1 (1.1)	 0 (0) 0 (0)	 98.8 (1&2) 98.9 (1&2)	 1.24 (0.45) 1.28 (0.47)
		Dehydration Sunken fontanelle Sunken eyes	 87/106 (19) 86/106 (20)	 66 (75.9) 66 (76.7)	 20 (23.0) 18 (20.9)	 1 (1.1) 2 (2.3)	 0 (0) 0 (0)	 98.9 (1&2) 97.7 (1&2)	 1.25 (0.46) 1.26 (0.49)

Appendix 37: Cognitive interviews – sample frame

		Hospital 1	Hospital 2	Hospital 3	Hospital 4	Hospital 5	Totals
Paediatrician	Consultant			*			N=1
	≥ST4/ Associate specialist			*		*	N=2
	<ST4		*		*		N=2
Intensivist	Consultant	*					N=1
Nurse	ANP/ Consultant		*				N=1
	Band 7		*				N=1
	Band 6	*			*		N=2
	Band 5	*			*	*	N=3
	HCA 3/ AP			*		*	N=2
Totals		N=3	N=3	N=3	N=2	N=3	N=15

Appendix 38: LIBSS-PRO(Version7.7)

Alder Hey Children's NHS
NHS Foundation Trust

UNIVERSITY OF LIVERPOOL

uclan
University of Central Lancashire

Liverpool Infant Bronchiolitis Severity Score

Hospital: **Alder Hey** **Test Number:** ☐☐☐

Time Test Started: ☐☐ ☐☐ ☐☐

Time Test Completed: ☐☐ ☐☐ ☐☐

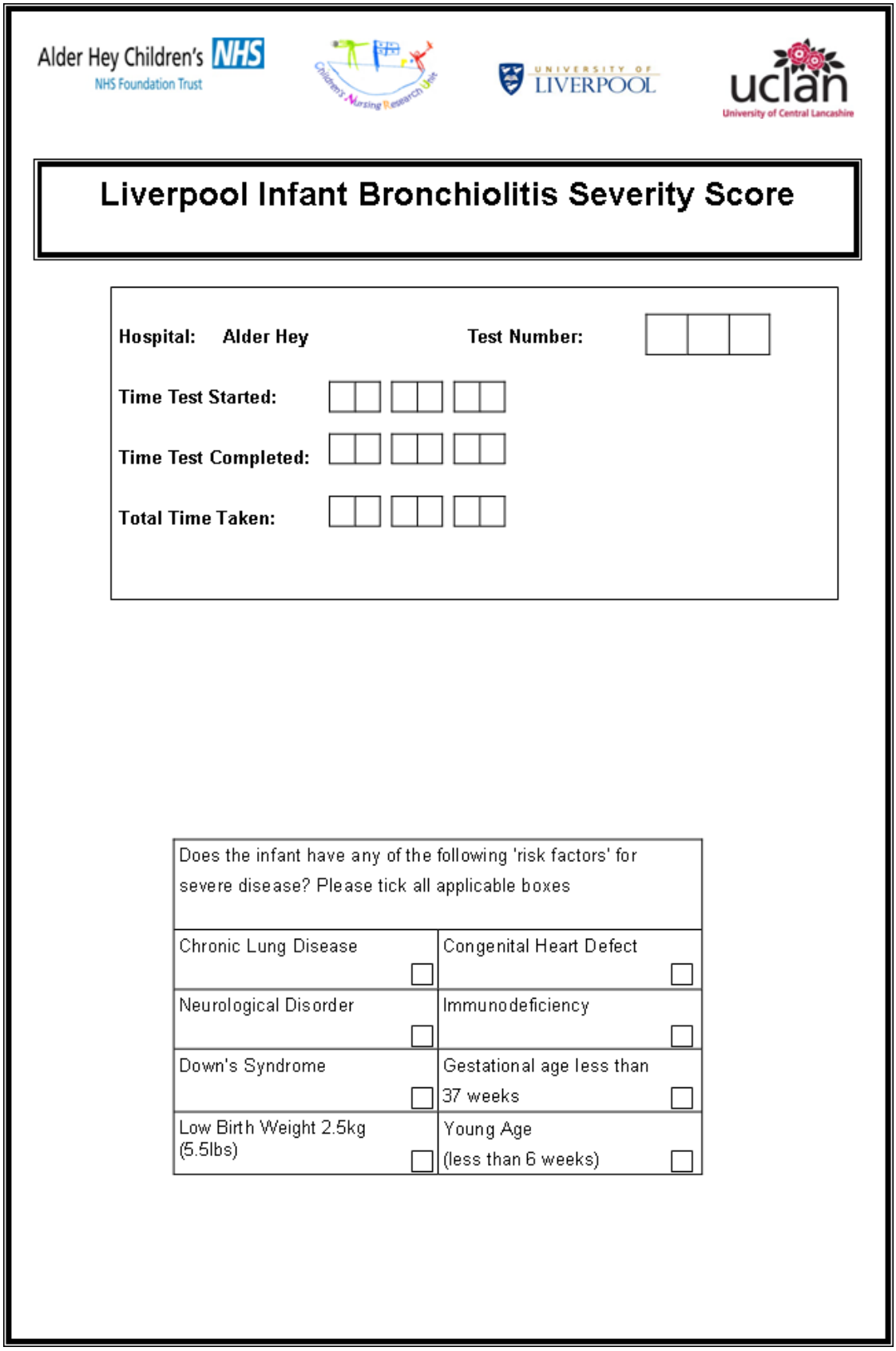
Total Time Taken: ☐☐ ☐☐ ☐☐

Does the infant have any of the following 'risk factors' for severe disease? Please tick all applicable boxes	
Chronic Lung Disease ☐	Congenital Heart Defect ☐
Neurological Disorder ☐	Immunodeficiency ☐
Down's Syndrome ☐	Gestational age less than 37 weeks ☐
Low Birth Weight 2.5kg (5.5lbs) ☐	Young Age (less than 6 weeks) ☐

Date /Time															
Symptoms		**Scores**													
Professional Concerns / 'Gut feeling'	No concerns	0													
	Mild to moderate concerns	2													
	Extremely concerned	4													
Apnoeas (+/- bradycardias)	No apnoeas	0													
	Short pauses / irregular breathing	2													
	Self-correcting apnoeas (increasing in frequency / duration)	**4**													
	Apnoeas requiring stimulation (increasing in frequency / duration)	**6**													
	Apnoeas requiring bag & mask ventilation	**8**													
Effort of Breathing	Tracheal Tug	0	1	2											
	Sub/intercostal recession	0	1	2											
	Absent = 0; Mild = 1; Marked = 2														
	Sub-sternal recession	0	1												
	Head bobbing	0	1												
	Grunting	0	1												
	Nasal flare	0	1												
	Accessory muscle use	0	1												
	Abdominal breathing	0	1												
	Central cyanotic episodes	0	**4**												
	Absent = 0; Present = 1 or 4														
Respiratory Rate: Under 3 months	25-59 BPM	0													
	60-70 BPM	2													
	>70 or < 25BPM	**4**													
Respiratory Rate: 3 months and over	20-55 BPM	0													
	56-65 BPM	2													
	>65 or <20 BPM	4													
% of oxygen to maintain saturations ≥ 92%	Room air (21%)	0													
	22-40% • Nasal cannula up to 2L • Face mask without reservoir bag • Head box / optiflow / CPAP	2													
	41-50% • Head box / Optiflow / CPAP	4													

	≥ 51% • Face mask with reservoir bag • Head box / Optiflow / CPAP)	**6**													
In chronic lung or congenital heart disease substitute saturations of 92% for accepted level of saturations when well.															
Heart Rate: Under 3 months	105-165 BPM	0													
	166-180 BPM	2													
	>180 or <105 BPM	**4**													
Heart Rate: 3 months and over	95-145 BPM	0													
	146-160 BPM	2													
	≥ 160 or < 95 BPM	**4**													
Appearance / level of consciousness	Alert & active / normal sleep	0													
	Irritable / fractious / restless	2													
	Lethargic / Floppy / No with parents	**4**													
	Unresponsive	**6**													
Hydration & perfusion: Feeds	Usual amount of feeds	0													
	50-75% of feeds	2													
	<50% of feeds (NG feeds or IVI fluids)	**4**													
Hydration & perfusion: urine output	Usual amount of wet nappies	0													
	Reduction in number of wet nappies	2													
	Small volumes of concentrated urine or anuric	**4**													
Hydration & perfusion	**Capillary refill time > 2 seconds**	0 **2**													
	Sunken eyes / fontanelle	0 2													
Score Totals															
	Consider urgent review by senior Dr														
	Issue an arrest call														

Appendix 39: LIBSS-PRO (Version 8.0)



Alder Hey Children's NHS
NHS Foundation Trust

Children's Nursing Research Unit

University of Liverpool

uclan
University of Central Lancashire

Liverpool Infant Bronchiolitis Severity Score

Hospital: **Alder Hey** **Test Number:** ☐☐☐

Time Test Started: ☐☐ ☐☐ ☐☐

Time Test Completed: ☐☐ ☐☐ ☐☐

Total Time Taken: ☐☐ ☐☐ ☐☐

Does the infant have any of the following 'risk factors' for severe disease? Please tick all applicable boxes	
Chronic Lung Disease ☐	Congenital Heart Defect ☐
Neurological Disorder ☐	Immunodeficiency ☐
Down's Syndrome ☐	Gestational age less than 37 weeks ☐
Low Birth Weight 2.5kg (5.5lbs) ☐	Young Age (less than 6 weeks) ☐

Date /Time																
Symptoms		**Scores**														
Professional Concerns / 'Gut feeling'	No concerns	0														
	Mild to moderate concerns	2														
	Extremely concerned	4														
Apnoeas	No apnoeas	0														
	Short pauses / irregular breathing	2														
	Self-correcting apnoeas • increasing frequency/duration • no bradycardia	**4**														
	Apnoeas • **requiring stimulation** • **increasing frequency/duration** • **+/- bradycardia)**	**6**														
	Apnoeas • **requiring bag & mask ventilation** • **+/- bradycardia**	**8**														
Effort of Breathing	Sub/intercostal recession	0	1	2												
	Tracheal tug	0	1													
	Sub-sternal recession	0	1													
	Head bobbing	0	1													
	Grunting	0	1													
	Nasal flare	0	1													
	Central cyanotic episodes (blue tongue/ mucous membranes)	0	**4**													
	Absent = 0; Present = 1 or 4; Severe = 2															
Respiratory Rate: Under 3 months	25-59 BPM	0														
	60-70 BPM	2														
	>70 or < 25BPM	**4**														
Respiratory Rate: 3 months and over	20-55 BPM	0														
	56-65 BPM	2														
	>65 or <20 BPM	4														
% of oxygen to maintain saturations ≥ 92% **(In chronic lung or congenital heart disease substitute saturations of 92% for**	Room air (21%)	0														
	22-40% • Nasal cannula up to 2L • Face mask without reservoir bag • Head box / Optiflow / CPAP	2														
	41-50% • Head box / Optiflow / CPAP	4														

accepted level of saturations when well.)	**> 50%** • Face mask with reservoir bag • Head box / Optiflow / CPAP)	**6**														
Heart Rate (at apex with stethoscope): Under 3 months	105-165 BPM	0														
	166-180 BPM	2														
	>180 or <105 BPM	**4**														
Heart Rate (at apex with stethoscope): 3 months and over	95-145 BPM	0														
	146-160 BPM	2														
	> 160 or < 95 BPM	**4**														
Appearance / level of consciousness	Alert & active / normal sleep	0														
	Irritable / fractious / restless	2														
	Lethargic / floppy / poor interaction	**4**														
	Responds to pain /unresponsive	**6**														
Hydration & perfusion: Feeds	Usual amount of feeds	0														
	50-75% of feeds	2														
	<50% of feeds or requiring nasogastric feeds / intravenous fluids	**4**														
Hydration & perfusion: urine output	Usual amount of wet nappies	0														
	Reduction in number of wet nappies	2														
	Small volumes of concentrated urine / not passing urine	**4**														
Hydration & perfusion	**Central capillary refill time > 2 secs**	0 **4**														
	Sunken eyes / fontanelle	0 2														
Score Totals																
	Consider urgent review by senior Dr															
	Issue an arrest call															

Appendix 40: LIBSS-PRO (Version 9.2): Under three months and Three months and over

Alder Hey Children's NHS Foundation Trust

Children's Nursing Research Unit

University of Liverpool

uclan University of Central Lancashire

Liverpool Infant Bronchiolitis Severity Score

Hospital: **Test Number:** ☐☐☐

Time Test Started: ☐☐☐☐☐☐

Time Test Completed: ☐☐☐☐☐☐

Total Time Taken: ☐☐☐☐☐☐

Does the infant have any of the following 'risk factors' for severe disease? Yes ☐ No ☐	
Please tick all applicable boxes	
Chronic Lung Disease ☐	Congenital Heart Defect ☐
Neuromuscular disorder ☐	Immunodeficiency ☐
Down's Syndrome ☐	Gestational age less than 37 weeks ☐
Low Birth Weight < 2.5 kg (5.5lb) ☐	Young Age (corrected age less than 6 wks) ☐

Liverpool Infant Bronchiolitis Severity Score: Infant aged under three months				
Day of illness:				
1. Do you have any concerns relating to the infant's overall condition?				
No concerns (condition is stable or improving)		**0**		**Comments:**
Some concerns (may become unstable/requires close observation)		**4**		
Extremely concerned (unstable requires immediate medical review)		**8**		
2. Apnoea				
None		**0**		**Comments:**
Occasional self-correcting apnoea / short pauses		**2**		
Apnoea's increasing frequency & duration		**4**		
Apnoea's requiring stimulation		**6**		
Apnoea's requiring bag & mask ventilation		**8**		
3. Increased work of breathing (Absent or Mild =0) Please complete all boxes				
Moderate/severe recession	**0**	**2**		**Comments:**
Moderate/severe tracheal tug	**0**	**2**		
Moderate/severe nasal flare	**0**	**2**		
Moderate/severe head bobbing	**0**	**4**		
Grunting	**0**	**4**		
Central cyanosis (blue lips / tongue)	**0**	**6**		
4. % oxygen to maintain saturations ≥92% (or usual saturation level if infant has congenital heart defect)				
21% (room air)		**0**		**Comments:**
22 - 40% (0.02 - 6L/min)		**2**		
41 - 50% (7 - 10L/min)		**4**		
>50% (>10L/min)		**6**		
Actual amount of oxygen administered				
Mode of oxygen delivery: Nasal specs (NS); Face Mask (FM); Head box (HB); HiFlow (HF); nCPAP (CP)				
5. Respiratory rate (breaths per minute)				
25 - 59		**0**		**Comments:**
60 - 70		**2**		
<25 or >70		**4**		
6. Heart rate (beats per minute)				
105 - 165		**0**		**Comments:**
166 - 180		**2**		
<105 or >180		**4**		
7. Appearance				
Alert & active / normal sleep		**0**		**Comments:**
Irritable / fractious / restless		**2**		
Floppy / lethargic / poor interaction		**4**		
Only responds to pain / unresponsive		**6**		
AVPU				
8. Feeding				
>75% or normal amount of feeds via usual route		**0**		**Comments:**
50 - 75% of feeds of normal feeds via usual route		**2**		
<50% of feeds or needing NG feeds / IV fluids		**4**		
9. Urine output				
Usual number of wet nappies (> 2 mLs /kg/hr)		**0**		**Comments:**
Reduction in number of wet nappies (1 - 2 mLs /kg/hr)		**2**		
Small volumes of concentrated urine / no urine (< 1mL/kg/hr)		**4**		
10. Central capillary refill time (preferably press on the sternum for 5 seconds)				
≤ 2 seconds		**0**		**Comments:**
> 2 seconds		**2**		
Actual capillary refill time in seconds				
LIBSS Score Total: **Mild (0-10); Moderate (11-20); Severe (≥ 21)**				**Comments:**

Liverpool Infant Bronchiolitis Severity Score: Infant aged three months and over				
Day of illness:				
1. Do you have any concerns relating to the infant's overall condition?				
No concerns (condition is stable or improving)		**0**		**Comments:**
Some concerns (may become unstable/requires close observation)		**4**		
Extremely concerned (unstable requires immediate medical review)		**8**		
2. Apnoea				
None		**0**		**Comments:**
Occasional self-correcting apnoea / short pauses		**2**		
Apnoea's increasing frequency & duration		**4**		
Apnoea's requiring stimulation		**6**		
Apnoea's requiring bag & mask ventilation		**8**		
3. Increased work of breathing (Absent or mild =0) Please complete all boxes in this section				
Moderate/severe recession	**0**	**2**		**Comments:**
Moderate/severe tracheal tug	**0**	**2**		
Moderate/severe nasal flare	**0**	**2**		
Moderate/severe head bobbing	**0**	**4**		
Grunting	**0**	**4**		
Central cyanosis (blue lips / tongue)	**0**	**6**		
4. % oxygen to maintain saturations ≥92% (or usual saturation level if infant has congenital heart defect)				
21% (room air)		**0**		**Comments:**
22 - 40% (0.02 - 6L/min)		**2**		
41 - 50% (7 - 10L/min)		**4**		
>50% (>10L/min)		**6**		
Actual amount of oxygen administered				
Mode of oxygen delivery: Nasal specs (NS); Face Mask (FM); Head box (HB); HiFlow (HF); nCPAP (CP)				
5. Respiratory rate (breaths per minute)				
20 – 55		**0**		**Comments:**
56 – 65		**2**		
<20 or >65		**4**		
6. Heart rate (beats per minute)				
95 – 145		**0**		**Comments:**
146 – 160		**2**		
<95 or >160		**4**		
7. Appearance				
Alert & active / normal sleep		**0**		**Comments:**
Irritable / fractious / restless		**2**		
Floppy / lethargic / poor interaction		**4**		
Only responds to pain/unresponsive		**6**		
AVPU Score				
8. Feeding				
>75% of feeds or normal amount of feeds via usual route		**0**		**Comments:**
50 - 75% of feeds via usual route		**2**		
<50% of feeds or needing NG feeds / IV fluids		**4**		
9. Urine output				
Usual number of wet nappies (> 2 mLs /kg/hr)		**0**		**Comments:**
Reduction in number of wet nappies (1 - 2 mLs /kg/hr)		**2**		
Small volumes of concentrated urine / no urine (< 1mL/kg/hr)		**4**		
10.Central capillary refill time (preferably press on the sternum for 5 seconds)				
≤ 2 seconds		**0**		**Comments:**
> 2 seconds		**2**		
Actual capillary refill time in seconds				
LIBSS Score Total **Mild (0-10); Moderate (11-20); Severe (≥21)**				**Comments:**

Appendix 41: Senior paediatrician assessment proforma

<table>
<tr><td colspan="2">Please assign a category which best describes the ‘severity’ of illness of the infants’ condition</td></tr>
<tr><td colspan="2">Criteria for ‘mild’ bronchiolitis</td></tr>
<tr><td>Would generally not be admitted to hospital
Some increased work of breathing
Mild recession
Respiratory rate ≤ 60 BPM
Oxygen saturations ≥92% in room air
Heart rate ≤ 150 BPM
Coughing spasms
Taking usual feeds or at least 50-75% of an appropriate feed for weight
Maybe vomiting but clinically hydrated
Peripherally warm
Central capillary refill < 2 seconds
Usual amount of wet nappies
Alert & active
Will not have grunting, head bobbing, cyanosis, apnoeas / irregular breathing</td><td>In your opinion does the infant have ‘mild’ bronchiolitis?

Yes No

Comments:</td></tr>
<tr><td colspan="2">Criteria for ‘moderate’ bronchiolitis</td></tr>
<tr><td>Saturations < 92% in room air – requiring supplemental oxygen
Moderate sub/inter-costal recession
Moderate tracheal tug
Mild grunt
Irritable / restless
Consolable by parents
Heart rate160 BPM or just over
Taking less than 50% of feeds orally (NG feeds / IVI fluids)
Reduction in urine output
Getting tired
Appears unwell
Altered behaviour routine
Normal responsiveness / muscle tone</td><td>In your opinion does the infant have ‘moderate’ bronchiolitis?

Yes No

Comments:</td></tr>
</table>

Criteria for 'severe' bronchiolitis	
• **Significant hypoxia with oxygen requirements > 50%** • **Apnoeas (+/- bradycardia), increasing in frequency, requiring stimulation and or bag and mask ventilation.** • **Apnoeas (+/- bradycardia) increasing in frequency and or duration despite non-invasive ventilation** • **Respiratory rate > 70 BPM** • **Decreasing respiratory rate with bradycardia** • **Increased recession and effort of breathing at rest and or / following NG tube feeds** • **Severe sub / inter-costal recession / sub-sternal recession** • **Head bobbing / grunting / nasal flaring** • **Persistently raised or increasing carbon dioxide level with decreasing pH** • **Exhausted** • **Appears lifeless** • **Getting tired with poor laboured breathing** • **Reduced air entry** • **No response to previous treatment interventions** • **Complete inability to take oral feeds** • **Clinical signs of dehydration** • **Passing small volumes of concentrated urine / anuric** • **No muscle tone / 'floppy'** • **Decreased level of consciousness / unresponsive** • **Cardiovascular instability on handling** • **Clammy / sweaty** • **Poor perfusion with mottled appearance** • **High temperature** • **Cardio/respiratory arrest**	**In your opinion does the infant have 'severe' bronchiolitis?** **Yes** **No** **Comments:**

Appendix 42: Inter-rater reliability testing

LIBSS-PRO Domains/items	n/N (missing data)	Time point one Intraclass Correlation Coefficient [95% CIs]	Mean (SD)	n/N (missing data)	Time point two Intra-class correlation Coefficient [95% CIs]	Mean (SD)
Professional Concerns	127/128 (1)	0.49 [0.28-0.64]	1.48 (1.93)	122/128 (6)	0.46 [0.23-0.62]	1.15 (1.81)
Apnoea	127/128 (1)	-0.12 [-0.59-0.20]	0.09 (0.42)	123/128 (5)	-0.97 [-0.56-0.23]	0.08 (0.39)
Effort of Breathing	123/128 (5)	0.65 [0.50-0.75]	2.52 (2.85)	120/128 (8)	0.67 [0.53-0.77]	2.32 (2.78)
Recession	125/128 (5)	0.61 [0.44-0.73]	1.20 (0.98)	120/128 (8)	0.69 [0.56-0.78]	1.17 (0.99)
Tracheal tug	123/128 (5)	0.36 [0.09-0.55]	0.36 (0.77)	119/128 (9)	0.32 [0.25-0.52]	0.27 (0.68)
Nasal flare	123/128 (5)	0.33 [0.43-0.53]	0.13 (0.49)	120/128 (8)	-0.12 [-0.60-0.21]	0.12 (0.47)
Grunting	123/128 (5)	-0.04 [-0.04-0.26]	0.13 (0.71)	120/128 (8)	-0.02 [-0.47-0.28]	0.10 (0.62)
Head bobbing	123/128 (5)	0.62 [0.46-0.73]	0.75 (1.56)	120/128 (8)	0.71 [0.58-0.80]	0.67 (1.49)
Cyanosis	123/128 (5)	0.00 [-0.42-0.30]	0.00 (0.00)	120/128 (8)	0.00 [0.00-0.00]	0.00 (0.00)
Respiratory rate	125/128 (5)	0.43 [0.19-0.60]	0.62 (1.09)	121/128 (7)	0.41 [0.41-0.41]	0.38 (0.90)
Saturations & supplemental oxygen	127/128 (1)	0.97 [0.96-0.98]	1.21 (1.28)	123/128 (5)	0.97 [0.96-0.98]	1.28 (1.23)
Heart rate	124/128 (4)	0.71 [0.59-0.79]	0.56 (1.03)	123/128 (5)	0.70 [0.57-0.79]	0.42 (1.00)
Appearance	126/128 (2)	0.54 [0.35-0.68]	0.44 (0.97)	123/128 (5)	0.41 [0.16-0.59]	0.28 (0.73)
Feeding	126/128 (2)	0.80 [0.72-0.86]	2.11 (1.68)	123/128 (5)	0.80 [0.71-0.86]	1.97 (1.63)
Urine Output	126/128 (2)	0.73 [0.62-0.81]	0.52 (0.95)	123/128 (5)	0.72 [0.60-0.80]	0.44 (0.83)
CRT	125/128 (3)	-0.14 [-0.63-0.19]	0.13 (0.49)	123/128 (5)	0.22 [-0.11-0.45]	0.05 (0.31)
LIBSS-PRO score Total	127/128 (1)	0.83 [0.75-0.88]	9.65 (7.25)	123/128 (5)	0.84 [0.77-0.89]	8.33 (7.03)

Appendix 43: Test-retest reliability

LIBSS-PRO Domains/items	n/N (missing data)	HCP One Intraclass Correlation Coefficient [95% CIs]	Mean (SD)	n/N (missing data)	HCP Two Intra-class correlation Coefficient [95% CIs]	Mean (SD)
Professional Concerns	123/128 (5)	0.86 [0.80-0.90]	1.20 (1.84)	124/128 (4)	0.86 [0.80-0.90]	1.16 (1.82)
Apnoea	124/128 (4)	0.35 [0.07-0.54]	0.10 (0.43)	124/128 (4)	0.83 [0.76-0.88]	0.08 (0.39)
Effort of Breathing	120/128 (8)	0.89 [0.85-0.92]	2.03 (2.40)	124/128 (4)	0.87 [0.82-0.91]	2.27 (2.75)
Recession	120/128 (8)	0.87 [0.82-0.91]	1.08 (1.00)	124/128 (4)	0.86 [0.81-0.90]	1.16 (0.99)
Tracheal tug	119/128 (9)	0.77 [0.68-0.84]	0.37 (0.78)	120/128 (8)	0.28 [-0.28-0.50]	0.37 (0.77)
Nasal flare	124/128 (4)	0.78 [0.69-0.84]	0.11 (0.46)	124/128 (4)	0.78 [0.69-0.84]	0.11 (0.46)
Grunting	120/128 (8)	-0.02 [-0.46-0.28]	0.03 (0.36)	124/128 (4)	0.71 [0.59-0.80]	0.10 (0.61)
Head bobbing	120/128 (8)	0.93 [0.91-0.95]	0.47 (1.28)	124/128 (4)	0.87 [0.81-0.91]	0.65 (1.47)
Cyanosis	120/128 (8)	0.00 [-0.43-0.30]	0.00 (0.00)	124/128 (4)	0.00 [0.00-0.00]	0.00 (0.00)
Respiratory rate	124/128 (4)	0.62 [0.46-0.73]	0.39 (0.83)	120/128 (8)	0.68 [0.54-0.77]	0.38 (0.90)
Saturations & supplemental oxygen	124/128 (4)	0.95 [0.93-0.96]	1.27 (1.28)	124/128 (4)	0.95 [0.93-0.96]	1.27 (1.23)
Heart rate	123/128 (5)	0.50 [0.28-0.65]	0.55 (1.12)	122/128 (6)	0.50 [0.28-0.65]	0.41 (0.99)
Appearance	123/128 (5)	0.72 [0.60-0.80]	0.28 (0.73)	124/128 (4)	0.69 [0.56-0.78]	0.27 (0.73)
Feeding	124/128 (4)	0.96 [0.94-0.97]	1.85 (1.61)	123/128 (5)	0.94 [0.92-0.96]	1.98 (1.65)
Urine Output	123/128 (5)	0.93 [0.90-0.95]	0.46 (0.84)	123/128 (5)	0.93 [0.90-0.95]	0.46 (0.84)
CRT	124/128 (4)	0.78 [0.68-0.84]	0.16 (0.54)	122/128 (6)	0.26 [-0.04-0.48]	0.05 (0.31)
LIBSS-PRO score Total	124/128 (4)	0.92 [0.89-0.94]	8.27 (6.73)	124/128 (4)	0.93 [0.91-0.95]	8.35 (7.01)

Publications arising from this thesis