The University Of Sheffield.

Measuring Respiratory Rate in Children

By:

Dr William James Daw

A thesis submitted in fulfilment of the requirements for the degree of Doctor of Medicine

The University of Sheffield

Department of

Oncology and Metabolism

August 2017

"Thus says the Lord God to these bones: Behold, I will cause breath to enter you, and you shall live. And I will lay sinews upon you, and will cause flesh to come upon you, and cover you with skin, and put breath in you, and you shall live, and you shall know that I am the Lord."

Ezekiel 37:5-6

THESIS TABLE OF CONTENTS

I. DECLARATION

This research has been completed whilst in post as Clinical Research Fellow in Paediatrics for the University of Sheffield. The views expressed are those of the author and not those of any other body or organisation that the author is affiliated with. The author also received additional funding support from the Children's Hospital Charity which is stated in the relevant sections of this thesis. The author has no competing interests to declare.

The author declares that this thesis is his original work and that none of the material contained within this thesis has been previously submitted for a degree to any awarding institution. The work contained in this thesis has been undertaken by myself, with the support from those individuals mentioned in the acknowledgements section. Their contribution is also acknowledged in published papers cited in the Research Achievements section.

II. ACKNOWLEDGEMENTS

I would primarily like to thank my supervisor, Professor Heather Elphick for all her hard work and support whilst I've been studying for this MD. In particular I would like to thank her for giving me the opportunity to work in such an interesting area of research, for devising many of the studies and for her help and support whenever I needed it. I would also like to thank Professor Nick Bishop for his supervision throughout this MD and for allowing me this research opportunity within my career.

I would like to thank Dr Ruth Kingshott for her assistance with so many aspects of each of these research studies. Her knowledge, advice, support and words of wisdom have greatly enhanced this work.

I would like to thank the staff and patients at Sheffield Children's Hospital where the majority of this research was conducted and the research and innovation department for implementing many of these studies. I would also like to thank Dr Mark Boon, Mike Lee and Fiona Bell for being so accommodating and enabling us to test with them.

I would also like to thank staff from the faculty of ACES at Sheffield Hallam University and in particular Professor Reza Saatchi for all his work on the CPRM and constant modifications and improvements along the way.

Finally I would like to thank my wife Kate and our girls Arabella and Florence. You have made these years of research so much fun and I have loved going on this adventure with you.

III. RESEARCH ACHIEVEMENTS

Peer reviewed publications

Daw W, Kingshott R, Elphick H. Poor inter-observer agreement in the measurement of respiratory rate in children: a prospective observational study. BMJ Paediatrics Open. 2017;0:e000173. doi: 10.1136/ bmjpo-2017-000173.

Daw W, Kingshott R, Saatchi R, Burke D, Holloway A, Travis J, Evans R, Jones, A, Hughes B, Elphick H. Medical Devices for Measuring Respiratory Rate in Children: a Review. *Journal of advances in biomedical engineering and technology*. 2016. 3. 21-27.

Published abstracts

Daw W, Kingshott R, Elphick H. Variation in respiratory rate measurements in children. *Arch Dis Child* 2017;102:A168.

Daw W, Kingshott R, Saatchi R, Elphick H. Contactless portable respiratory rate monitor (CPRM) accurately measures respiratory rate in children. *European Respiratory Journal.* 2016 Vol 48 suppl 60.

Daw W, Kingshott R, Saatchi R, Elphick H. Contactless portable respiratory rate monitor accurately measures respiratory rate in sleeping children. *Arch Dis Child* 2016;101:A290-A291.

Daw W, Kingshott R, Scott A, Saatchi R, Elphick H. Development of the 'BreathEasy' Contactless Portable Respiratory Rate Monitor (CPRM). *European Respiratory Journal*. 2015; Vol 46 suppl 59.

Invited oral conference presentations

Daw W, Kingshott R, Saatchi R, Elphick H. Variation in respiratory rate measurements in children. Royal College of Paediatrics annual conference, 2017.

Daw W, Kingshott R, Elphick H. Contactless portable respiratory rate monitor accurately measures respiratory rate in sleeping children. Royal College of Paediatrics annual conference, 2016.

Invited conference poster presentations

Daw W, Kingshott R, Elphick H. Ordinal scales are not accurate to assess and measure respiratory rates in children. King's John Price Paediatric Respiratory Conference 2018.

Daw W, Kingshott R, Elphick H. Wide variation in practices for measuring respiratory rate in children. King's John Price Paediatric Respiratory Conference 2018.

Daw W, Kingshott R, Elphick H. Interobserver variation in the measurement of respiratory rate in children. European Respiratory Society Congress 2017.

Daw W, Kingshott R, Saatchi R, Elphick H. Contactless portable respiratory rate monitor (CPRM) accurately measures respiratory rate in children. European Respiratory Society Congress 2016.

Daw W, Kingshott R, Scott A, Saatchi R, Elphick H. Development of the 'BreathEasy' Contactless Portable Respiratory Rate Monitor (CPRM). European Respiratory Society Congress 2015.

Other research contributions

I have supervised two second year medical students (Rena Kaur and Mollie Delaney) in completing their SSC projects investigating the role of respiratory rate in predicting clinical deterioration in children.

IV. LIST OF TABLES

V. LIST OF FIGURES

VI. LIST OF ABBREVIATIONS

RR	Respiratory Rate
HR	Heart Rate
BP	Blood Pressure
PEWS	Paediatric Early Warning Systems
WHO	World Health Organisation
NICE	National Institute for Clinical Excellence
APLS	Advanced Paediatric Life Support
EPLS	European Paediatric Life Support
ATLS	Advanced Trauma Life Support
PALS	Paediatric Advanced Life Support
ED	Emergency Department
ECG	Electrocardiogram
ICC	Intraclass Correlation Coefficient
CI	Confidence Interval
RSV	Respiratory Syncytial Virus
EDR	Electrocardiogram Derived Respiration
PPG	Photoplethysomography
FDA	Food and Drug Administration
RIP	Respiratory Inductance Plethosomography
HCP	Healthcare professional
ST	Specialist Trainee
BPM	Breaths Per Minute
REC	Regional Ethics Committee
PICU	Paediatric Intensive Care Unit

HDU	High Dependancy Unit
eDMS	Electronic Document Management System
PPV	Positive Predictive Value
NPV	Negative Predictive Value
CPRM	Contactless Portable Respiratory Rate Monitor
NIHR	National Institute for Health Research
PSG	Polysomnography
MRA	Multi-Resolution Analysis
RCPCH	Royal College of Paediatrics and Child Health
NIHR	National Institute for Health Research

VII. ABSTRACT

Respiratory rate is an important vital sign used in the initial and ongoing assessment of all children in hospital. It is also used as a predictor of serious deterioration in a patient's clinical condition. Measuring respiratory rate in children can be difficult to perform and time consuming, especially in an uncooperative child. Convenient electronic devices exist for the measurement of many of the vital signs yet no device is currently available that can give an accurate and rapid assessment of respiratory rate in clinical practice.

In this thesis we have examined the current practices of local paediatric healthcare professionals in measuring respiratory rate and explored the levels of agreement that exist in measurements obtained. We have assessed the value of a respiratory rate measurement in detecting and identifying children at risk of clinical deterioration, comparing and contrasting it with the other vital signs. Finally we have developed a contactless portable respiratory rate monitor (CPRM) and evaluated the agreement in respiratory rate measurements between existing methods and our device.

Our work has added considerably to the overall body of evidence regarding respiratory rate measurements in children. We have provided clear evidence that there are a large variety of practices used by paediatric healthcare professionals in measuring respiratory rate. We have shown an inherent variability in respiratory rate measurements between observers and firmly established that respiratory rate is a powerful predictor of clinical deterioration in children, superior to other vital signs. Finally we successfully measured respiratory rates in both adults and children using the CPRM. Our device offers a promising alternative to current methods. In its present form it does not appear accurate enough to be used in clinical practice, however plans are underway to develop the device further with revisions informed by the research in this thesis. A contactless device for accurately and quickly measuring respiratory rate could be an important tool in the assessment of unwell children in the near future.

CHAPTER 1

REVIEW OF THE LITERATURE

1.1 Introduction

The measurement of a child's vital signs including heart rate, temperature, blood pressure and respiratory rate is routine practice to all those who attend emergency departments and paediatric assessment units (Cooper et al., 2002). The National Institute for Clinical Excellence (NICE) also recommends that these signs are recorded for all children presenting with a fever (NICE, 2007a). Respiratory rate is an important vital sign and is used in the initial and ongoing assessment of unwell children (Gandevia and McKenzie, 2008). It can be used to assess a child's clinical status and potentially as a predictor of serious deterioration (Subbe et al., 2003).

The World Health Organisation (WHO) recommends that a respiratory rate is counted or auscultated over 60 seconds. (WHO, 2002) However, measuring respiratory rate in children can be difficult to perform and time consuming especially in an uncooperative child. This may lead to inaccuracies in its measurement or it not being taken at all (Edwards and Murdin, 2001, Cretikos et al., 2008, Leuvan and Mitchell, 2008). There are also concerns of inconsistencies in measurements between observers, with studies citing a high degree of inter-observer variability (Chan et al., 2001, Liu et al., 2004).

Convenient electronic devices exist for the measurement of pulse, blood pressure, oxygen saturation and temperature. These provide accurate and prompt measures of vital signs. Devices for monitoring respiratory rate have entered the commercial market (Al-Khalidi et al.,2011a) but there is no device currently available that gives an accurate and rapid assessment of respiratory rate in clinical practice.

1.2 Aims

The aims of this review of the literature are to firstly assess how a respiratory rate should be measured and recorded in a child and evaluate what a normal respiratory rate is. The review will then address the evidence of how accurate and reliable these measurements are in terms of the method used and variability between different measurers. The usefulness of a respiratory rate measurement will then be analysed along with whether it appears to be a good indicator of disease severity and a predictor of patient deterioration. Finally the review will appraise different devices for measuring respiratory rate, both contact and non-contact methods, along with their suitability to enter clinical practice. Using the evidence gathered through this review of the literature we will then set out the research questions and aims and objectives that will be addressed through the rest of this thesis.

1.3 Measuring respiratory rate

Measurement of the respiratory rate is an important part of the assessment of the sick child. It plays a vital part in assessment of severity at triage and also as part of the monitoring response to treatment (Cooper et al., 2002). It is included in many childhood disease management guidelines,

including the integrated management of childhood illness manual from the WHO (WHO, 2002). Respiratory rate can be measured by observing abdominal or chest movements or by auscultation. Both methods have been shown to provide similar results in children (Singhi et al., 2003). However, in babies auscultation of breath sounds can yield a higher rate (Rusconi et al., 1994). This is most likely due to breaths being heard that may have been missed on observation.

The current WHO standard for a respiratory rate measurement is a count over a full minute by observing abdominal and chest movements (WHO, 2002). In practice however, it is usual for a direct observation of respirations to take place over a shorter period of 15, 20 or 30 seconds. The value then being multiplied up to give a rate per minute. This method has been shown to lead to inaccuracies (Berman et al., 1991, Simoes et al., 1991). Quadrupling a 15 second count showed up to 50% inaccuracy when compared with pneumogram measurements (Simoes et al., 1991). Similarly, counting for 30 seconds and doubling the value has shown to result in a higher mean count by two to four breaths per minute (BPM) (Berman et al., 1991).

When measuring respiratory rate it is also important to be aware that it can be subject to voluntary control, more so than any of the other vital signs (Lovett et al., 2005). When a subject is aware that their respiratory rate is being counted, the respiratory rate may change, although this may only be applicable for children over a certain age.

1.4 Recording respiratory rate

Along with national guidance, (NICE, 2007b) key findings from the Report of the National Confidential Enquiry into Patient Outcome and Death (NCEPOD, 2005) state that respiratory rate should be highlighted and recorded at any point that other observations are being made. However this does not appear to be happening in clinical practice.

The recording of vital signs in the hospital setting appears to be subject to a high degree of error (Schmidt et al., 2015). Studies suggest a number of reasons for this including, inadequate monitoring frequency (Buist and Stevens, 2013), poor legibility of recordings (Preece et al., 2012), incomplete data entry (Chen et al., 2009) and inaccurate calculations of early warning signs (Edwards et al., 2010). All of which have major implications on the recognition and response to patient deterioration.

Of the four vital signs, respiratory rate appears to be the least often recorded and most often completely omitted from hospital documentation (Gandevia and McKenzie, 2008). Hogan identified in adult nursing staff that the respiratory rate was the one parameter that was recorded less than 50% of the time (Hogan, 2006). Thompson et al in a study of 700 children referred to a paediatric assessment unit observed that RR was recorded in 85% of children (Thompson et al., 2009). Whereas other vital signs were recorded more frequently; temperature 98.6%, heart rate

98.4%, oxygen saturations 96.0%. Respiratory rate has also been shown to be poorly recorded locally (Burke, 2007). In 2007, an audit of feverish children against the NICE standard in the emergency department at Sheffield Children's NHS Foundation Trust revealed that RR was only recorded in 58% of children on arrival, (Burke, 2007) compared to the NICE standard of 100%. Of a total of 2755 patients with moderate or severe illness, RR was measured in 70.3%, as compared to temperature, pulse and oxygen saturation measurements of 85.7%, 86.7% and 83.5% respectively (Burke, 2007).

The reason behind this may be down to the method required to measure RR as well as staff awareness and perception of its significance. Within a busy clinical environment, a vital sign that requires direct observation for a full minute, is more likely to be estimated, inaccurately measured or even omitted in order to save time. In unwell and distressed children this may be even more the case where more skill and patience is required to obtain the measurement.

1.5 Normal respiratory rates in children

In order to interpret respiratory rate appropriately in children it is important to be clear of the normal ranges. An accurate reference range allows practitioners to assess whether a respiratory rate is normal or abnormal and identify children who are unwell. Respiratory rate ranges have been attempted to be studied from as early as 1849 (Hutchinson, 1849). However, there is still no clear consensus as to the correct reference ranges for respiratory rate. A number of international bodies have published reference ranges for respiratory rate, yet these are often consensus based (APLS, 2016, ATLS, 2004, Biarent D, 2006, Wardlaw TM, 2006, PALS, 2015, WHO, 2002). Table 1.1 summarises these ranges.

Table 1.1: Respiratory rate reference ranges from international bodies

Age Range (Years)	APLS	EPLS	ATLS	WHO	PALS
Neonate	25-50	30-40	<60	<60	-
0-1	20-40	30-40	<60	<50	30-53
1-2	20-35	26-34	<40	<40	22-37
2-3	20-30	26-34	<40	<40	20-28
3-4	20-30	26-34	<40	<40	20-28
4-5	20-30	26-34	<40	<40	20-28
5-6	20-30	26-34	<40	-	18-25
6-12	15-25	26-34	<40	-	18-25
12-13	12-24	26-34	<40	-	12-20
13-18	12-24	12-20	<30	-	12-20

There are three large scale studies looking at age-specific centiles for respiratory rate in children. Fleming et al presented a systematic review of all studies reviewing RR in healthy children (Fleming et al., 2011). Bonafide and colleagues performed an analysis of RR in paediatric inpatients, (Bonafide et al., 2013) and O'Leary et al analysed well children attending a paediatric emergency department (O'Leary et al., 2015). Figure 1.1 shows a comparison of their centile charts.

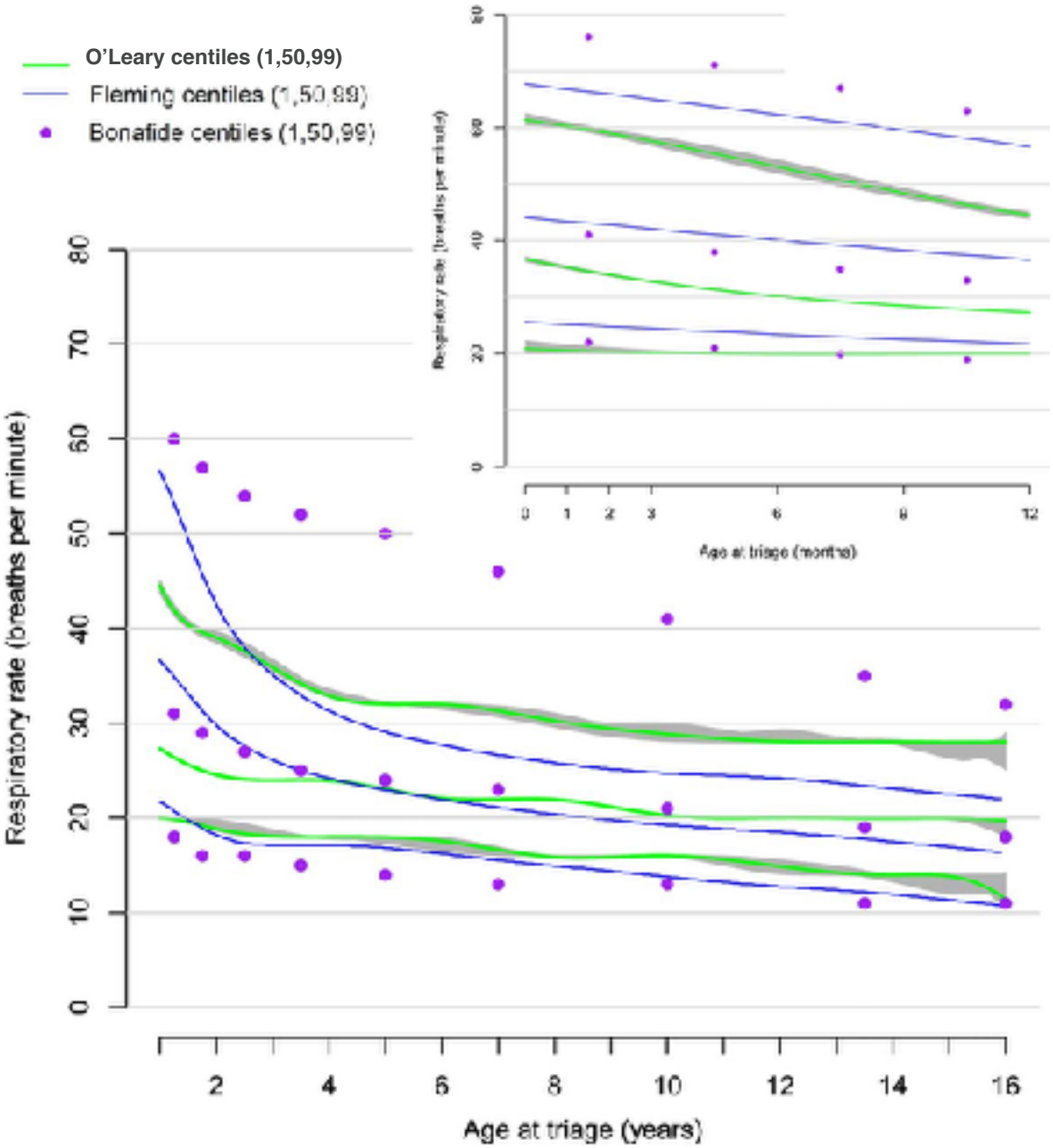


Figure 1.1: Centile charts for respiratory rate in infants and children from 3 studies. Adapted from O'Leary et al. (O'Leary et al., 2015) Adapted with permission.

Each of the studies produced quite differing centile charts for RR. However, all studies showed the respiratory rate declining from birth to adolescence with the steepest decline observed in infants less than 2 years. Importantly, when comparing the 1st and 99th centiles with APLS ranges there is marked disagreement, with the respiratory rate lying outside these ranges in all

age groups. This is of particular importance when interpreting respiratory rates and applying them to a paediatric scoring system.

There may be multiple reasons for the difference in RR ranges found by these studies. Each study has examined a different cohort of children, from healthy children to inpatients and those presenting to the emergency department. Also, in the study by O'Leary et al there is a large discrepancy in the age distribution of children, with five times as many patients in the 0-24 months group than in the over 12 years group (O'Leary et al., 2015). The reliability of measurements may also play a part in the difference observed. It is unclear in many of the studies how healthcare providers measured respiratory rate. O'Leary et al (O'Leary et al., 2015) found that 96% of respiratory rate values were even numbers. If a full count over one minute was made then there should be an equal split of odd and even measurements. These findings would however suggest that the measurement was made over a shorter counting period and multiplied up. A method which is known to be inaccurate (Berman et al., 1991).

Despite a growing body of evidence it is still not clear what constitutes a normal respiratory rate. RR is subject to voluntary control and in children appears to differ between populations and within different settings, whilst still being in the normal range. It is important therefore to ensure that RR is being recorded accurately and interpreted in light of the full clinical context of the child.

1.6 Variability in respiratory rate measurements

Variability can be expected from subjective assessments. It is important to understand the extent to which respiratory rate measurements may vary from one measurer to the next. A high degree of variability will call into question the reliability of the measurement and discrepancies could lead to delays in the recognition of patients with life threatening conditions.

There are multiple studies assessing the inter-observer agreement for RR measurements in both adults (Edmonds et al., 2002, Lim et al., 2002, Worster et al., 2003, Nielsen et al., 2015) and children (Wang et al., 1992, Wang et al., 1996, Chan et al., 2001, Liu et al., 2004, Gajdos et al., 2009, Lanaspa et al., 2014). They report a wide range of inter-observer variability and reliability of RR measurements. In children, it may be postulated that variability may be higher as children may not be as cooperative during the measurement, they may be agitated and in younger children their RR may vary quickly between breaths.

Studies assessing inter-observer agreements of RR measurements in adults have shown contrasting results. Edmunds et al found that from 140 independently measured RR by two trained observers, RR may differ by more than 35% (Edmonds et al., 2002). Worster et al compared triage nurse measurements with criterion standard measurements in 78 adult patients and found no significant differences (Worster et al., 2003). However, Nielsen et al showed a high

inter-observer agreement (Intraclass correlation coefficient (ICC): 0.99, 95% confidence interval (CI): 0.97-1.00) for 38 different nurses measuring the RR of an adult volunteer from a video recording (Nielsen et al., 2015). When the same group used a pre-defined scale to rate the RR the agreement was also substantial (Fleiss Kappa coefficient: 0.75).

Lim et al assessed the RR measurements when taken twice on 245 adult patients by the same and different observers (Lim et al., 2002). They also reported good agreement between observers. With 95% limits of agreement between -4.86 to 4.94 breaths/min for the same observer and -5.7 to 5.7 breaths/min for different observers. However it must be noted that in some situations there could be a difference in RR measurements as high as 6 breaths/min. With such a discrepancy there may be a risk that some patients could be wrongly classified as being more or less unwell than they actually are. This therefore could have an affect on the treatment they subsequently receive.

The reported inter-observer variability of RR measurements in children varies greatly between studies. Many of the studies looked at the variability in RR measurements as part of a wider clinical score, and in specific cohorts of patients. Table 1.2 summarises these studies and their relevant key results.

There are wide ranging degrees of reliability reported from these studies. Chan et al (Chan et al., 2001) found agreement between triage nurses, Emergency department (ED) nurses and ED physicians in children with croup to be fair to poor with a weighted Kappa statistic of 0.15-0.24. Similarly only fair agreement was demonstrated by Wang et al in infants under 2 years with lower respiratory tract infections, with a weighted Kappa score of 0.38 (Wang et al., 1992). Liu et al also observed agreement between respiratory therapists, physicians and nurses, in children admitted with asthma bronchiolitis or wheeze, as fair with weighted Kappa scores of 0.36 (95% CI 0.26-0.46) (Liu et al., 2004). However Gajdos et al found significantly better agreement between physicians, nurses and respiratory therapists in infants with bronchiolitis (Gajdos et al., 2009). Weighted Kappa values ranged from 0.76-0.97, with the highest agreement between physicians.

It is important to note that each of these studies relied upon converting each RR measurement into a discrete pre-defined category. The inter-observer variability was then calculated based upon the variation in categories assigned to. Thus a difference of even 1 breath/min could change the category a RR was assigned to, and as such increase the variability between observer measurements. Alternatively a large discrepancy in RR measurement, providing it remained within the defined category, would not be seen as a variability in measurement.

Table 1.2: Inter-observer variability in the measurement of respiratory rate in children

Citation	Study Group	Study Type	Methods	Relevant Key Results	Comments
Chan et al. Interobserver variability of croup scoring in clinical practice. Paediatric Child Health. 2001	158 Children aged 3 months - 5 years presenting with viral croup	Prospective cohort study	Child assessed by triage nurse, ED nurse and ED physician within 1 hour for clinical signs associated with croup - including RR	Weighted Kappa score for RR agreement: Traige nurse v ED nurse: 0.17 ED Nurse v Physician: 0.15 Traige nurse v ED Physician: 0.24	- Only accounts for children presenting with viral croup - 1 hr window may lead to variation in clinical status. - RR converted to categorical score - Large cohort studied - RR counted over 30 seconds then doubled
Wang et al. Observer agreement for respiratory signs and oximetry in infants hospitalised with lower resp infections. Am Rev Respir Dis. 1992	56 infants <2yrs hospitalised with bronchiolitis or pneumonia	Prospective cohort study	Assessed by Paediatric infectious disease consultant + Infectious disease nurse or infectious disease fellow. RR measured within 20 minutes	Kappa score for RR agreement: 0.38	- Small convenience sample - RR counted over 30 seconds - -RR converted to categorical score - Study ran over two 3 month periods 2 years apart
Wang et al. Study of observer reliability in clinical assessment of RSV lower respiratory illness (PICNIC). Paediatric Pulmol. 1996.	137 infants with RSV respiratory illness across 8 centres	Prospective cohort study	Two blinded observers: Research nurse + nurse or Paediatrician	Pearson correlation coefficient for RR agreement = 0.42 - 0.97	-RR counted over a full minute -Some assessments took place 6 hrs later with mean = 90 mins -Highest agreement seen in centre with fewest recruits
Liu et al. Use of a respiratory clinical score among different providers. Pediatr Pulmonol. 2004.	55 patients <1yr-19yrs admitted with asthma bronchiolitis or wheezing	Prospective cohort study	Physicians, nurses and respiratory therapists simultaneously assessed RR	Kappa score (unweighted) 0.36 (95% CI 0.26-0.46)	- Small convenience sample - RR converted to categorical score - No details of how RR measured given - Large age range of children studied
Gajdos et al. Inter-observer agreement between physicians, nurses and respiratory therapists for respiratory clinical evaluation of bronchiolitis. Pediatr Pulmonol. 2009.	180 infants under 18 months hospitalised with 1st episode of bronchiolitis	Prospective cohort study	Physicians, nurses and respiratory therapists. Two providers assessed child's RR at same time	Weighted Kappa score : 0.76 - 0.97. Highest agreement seen between 2 physicians	- Only accounts for infants with bronchiolitis - Narrow age range of children studied - No details of how RR measured - Minimum of 8hrs between each assessment - RR converted to categorical score
Lanaspa et al. High reliability in respiratory rate assessment in children with resp symptomatology in a rural area in Mozambique. J Trop Pediatr. 2014	55 children <10 years with cough, fever, or breathing difficulties in developing country setting	Prospective cohort study	RR measured 3 times by different observers in 30 min period	Agreement in RR count Intraclass Correlation Coefficient of 0.95 (95% CI: 0.93-0.97)	- RR counted over 60 seconds - Observers - medical agent + 2 study health assistants - Small sample size - Children from developing country

Two studies however assessed the variation between the actual continuous data of the RR measurements between observers (Wang et al., 1996, Lanaspa et al., 2014). Wang et al, in a study of infants with respiratory syncytial virus (RSV) respiratory infections, reported a large variation in agreement, with a Pearson correlation coefficient ranging from 0.42-0.97 (Wang et al., 1996). In a smaller study of 55 children presenting with respiratory illnesses, Lanaspa et al (Lanaspa et al., 2014) reported a substantial agreement in RR count with an Intraclass correlation coefficient (ICC) of 0.95 (95% CI: 0.93-0.97) between observers. However they did note that a single respiratory rate reading could have misclassified 5–11% of their participants as non-tachypneic.

The wide range of inter-observer variability reported may reflect the heterogeneity of the studies. It is difficult to ascertain the extent of any inter-observer variability when comparing studies of such different patient groups and contrasting methodologies. Variation in assessments may also exist due to changes in the clinical status of the patient over short periods of times, which many of the studies do not account for. However clinicians should recognise the inherent variability that can exist with subjective measurements and therefore interpret single respiratory rate measurements with caution.

1.7 Respiratory rate as a predictor of clinical deterioration

In respiratory illness, alveolar ventilation is altered. Alveolar ventilation is a product of respiratory rate and tidal volume and is controlled by chemoreceptors and driven by the arterial partial pressures of oxygen and carbon dioxide. In disease, when the body attempts to correct hypoxia and hypercarbia both tidal volume and respiratory rate increase (West, 1990). Therefore the presence of tachypnoea can indicate a number of severe and emergency diagnoses in different body systems, not just the respiratory system. However it is unclear the extent to which this vital sign can be used alone as a discriminator of disease severity and predictor of clinical deterioration.

Evidence from the adult literature shows a high prevalence of abnormal vital signs in the hours leading up to an inpatient cardiac arrest (Kause et al., 2004, Andersen et al., 2016). Further studies indicate that respiratory rate may be the most important predictor of cardiac arrest, and if detected at an early stage can be prevented by early therapeutic interventions (Fieselmann et al., 1993). Cretikos et al (Cretikos et al., 2007) found that over half of all adult patients they studied who were admitted to the intensive care unit or suffered cardiac arrest could have been identified as high risk up to 24 hours earlier based on their respiratory rate. Respiratory rate has also been shown to be superior to pulse and blood pressure in discriminating between stable patients and patients at risk, with a high association with mortality rate (Subbe et al., 2003, Goldhill et al., 2005). However, Anderson et al found the relationship between respiratory rate and adults suffering an in hospital cardiac arrest to be not be as robust as the other vital signs (Andersen et al., 2016).

In the Paediatric literature it is harder to see such a clear correlation. Van den Bruel et al identified tachypnoea as a strong red flag in predicting severe illness in children (Van den Bruel et al., 2010). Opiyo et al suggested a respiratory rate of greater than 60 breaths/minute was one of 8 clinical signs that were most likely to be of value in resource poor countries in identifying sick children (Opiyo and English, 2011). However, assessments of tachypnoea appear to display a greater predictive value when combined with other clinical signs and symptoms, rather than when used in isolation (Usen and Webert, 2001). Thompson et al supported this, adding that the presence of one or more of fever, tachycardia, tachypnoea and decreased oxygen saturations was moderately sensitive (80%) for identifying children with serious or intermediate infection, but still had limited specificity (39%) (Thompson et al., 2009).

In certain conditions such as asthma, heart failure and pneumonia, RR is an important prognostic parameter. The link between tachypnoea and pneumonia is well established (Margolis and Gadomski, 1998, Lynch et al., 2004, Nijman et al., 2013). Tachypnoea with a RR > 50 breaths/min, can be a useful discriminator of children less than 5 years with or without pneumonia (Rambaud-Althaus et al., 2015). However a subjective clinical impression of tachypnoea appears to be far less reliable (Shah et al., 2010).

Respiratory rate is also the most commonly used criteria within Paediatric Early Warning Scoring (PEWS) systems (Roland et al., 2014). PEWS are a set of predefined alert criteria that are incorporated into observation charts which are used to act as a trigger that a child may be deteriorating and require further medical or nursing input. Roland et al found that respiratory rate was a part of almost 90% of the scoring systems used across the U.K., and along with heart rate was the most commonly used criteria (Roland et al., 2014). Thus potentially indicating the importance of respiratory rate in identifying unwell children and those at risk of deterioration. There are however no randomised controlled trials evaluating the effectiveness of PEWS and there is still much debate as to how beneficial these scoring systems actually are (Winberg et al., 2008, Chapman et al., 2010).

1.8 Devices for measuring respiratory rate

Respiratory rate is one of the few signs that relies on clinical observation and not electronic conformation. It has been suggested that RR is not always measured because there is no automated respiratory measuring device available (Lim et al., 2002). Many electronic devices to monitor RR exist however none are in use within the triage and everyday clinical setting. These devices use multiple different methods to ascertain the RR of a subject and can be divided into contact and non-contact methods (Al-Khalidi et al., 2011a).

1.8.1 Contact based respiratory rate monitoring

Contact respiratory rate monitors make direct contact with the patient's body and make use of a number of different methods to obtain a respiratory rate. These include measuring chest and abdominal movements, acoustic sounds and airflow, exhaled carbon dioxide and calculating the RR from the electrocardiogram (ECG) or oxygen saturation (Al-Khalidi et al., 2011a). The main disadvantage of such contact methods is that in children they may be less well tolerated, potentially causing stress to the child altering their respiratory rate. Table 1.3 summarises the various contact methods available.

1.8.1.1 Movement detection

This is one of the most commonly used form of contact based respiratory rate monitoring in clinical practice. It is widely used in the intensive care and post-operative setting, where the RR is calculated by monitoring the distance between ECG electrodes placed on a patient's chest. An extension of this is the placing of bands around the subject's chest and abdominal wall, which measure the thoracic impedance changes associated with respiration (Freundlich and Erickson, 1974). These methods provide continuous RR measurements in a controlled environment and are also the recommended method for the monitoring of sleep disorders in infants and children (RCPCH, 2002). However, when applied to adults in the acute setting this method has had mixed results (Lovett et al., 2005, Bianchi et al., 2013). Its application to the paediatric population in the acute setting may also be difficult. The time taken to set up the equipment may delay assessment and the ECG leads or thoracic and abdominal bands may not be well tolerated in younger children.

1.8.1.2 Airflow methods

Various methods that detect airflow can be used to measure respiratory rate. These include using thermistors placed in the nose of the patient to detect changes in air temperature, (Storck et al., 1996) nasal pressure transducers to measure the volume of exhaled air (Al-Khalidi et al., 2011a) and sensors detecting expired carbon dioxide (capnometry) (Folke et al., 2002). These methods are used primarily in controlled environments and in the post-operative setting. Although potentially accurate they require sensitive equipment to be attached to the subject. This may not be well tolerated in children and as these devices can only be used once per patient there may be large cost implications if they are being used for one off RR measurements in a clinical setting.

2.8.1.3 Acoustic methods

Acoustic methods analyse respiratory vibrations to detect inspiratory and expiratory flow. The acoustic signal is then converted to a respiration rate. This method can provide an accurate measurement of RR and can also monitor for apnoeas (Werthammer et al., 1983, Mimoz et al., 2012, Patino et al., 2013, Frasca et al., 2015). One study conducted in post-operative children showed the acoustic method (Rainbow acoustic monitoring - RRa™) had a good agreement and a similar accuracy when compared to capnography (Patino et al., 2013). This method is not affected by subjects breathing through their mouth or nose and appears to be well tolerated by patients in

the post-operative setting. However swallowing, coughing, speaking and background noise can lead to large inaccuracies in measurements.

Table 1.3: Contact methods of measuring respiratory rate

Method	Mechanism	Application areas	Advantages	Disadvantages
Movement detection	Mercury strain gauge or impedance methods detect chest and abdominal wall movements through bands or electrodes placed on or around the subject.	Polysomnography sleep studies. Intensive care settings. Post operative settings.	-Continuous accurate measurements. -Can detect subtle thoraco-abdominal asynchrony related to specific respiratory disorders.	-May not be well tolerated by younger children. -Can be subject to motion artefact.
Airflow measurements	Air temperature, pressure and $C0_2$ measurement of exhaled air.	Post operative setting.	-Potentially very accurate method of monitoring RR. -Provides a continuous method of monitoring.	-Expensive equipment. -Probe has to be positioned in the exhaled airflow. -Easily dislodged, may not be well tolerated in children.
Acoustic Method	Analyses respiratory vibrations to detect inspiratory and expiratory flow. The acoustic signal is converted to a respiration rate.	Controlled environments. Post operative setting.	-Good accuracy when compared to capnography. -Better tolerated than other contact methods in the post-operative cohort. -Not affected by mode of breathing. -Small patch devices now in development.	-Few studies in children. All on post-operative patients. -May not be well tolerated by the awake or agitated child. -Reading altered by swallowing and other noises, therefore child would have to be silent.
Respiratory rate derived from electrocardiogram	Small morphological changes occur on the ECG during respiration. From these the respiration rate can be derived.	Intensive care setting. Remote monitoring of patients in community.	-Low cost alternative when ECG monitoring already in use. -Avoids high frequency currents and frequent recalibration.	-Readings often disrupted by motion artefact. -Lacking in accuracy when compared with more established contact methods.
Respiratory rate derived from photoplethyso-mography (PPG)	Pulse oximeter is based on PPG where red and infrared frequencies detect blood oxygen saturation level. RR can be monitored by looking at respiratory induced intensity variations contained within the PPG signal.	Intensive care setting. Post operative setting. Sleep studies. Triage setting along with oxygen saturations.	-Small probe size which may be better tolerated especially in infants and children. - Allows for continuous monitoring.	-Motion disturbances can lead to inaccuracies in measurements. -Risk of autonomic nerve activity influencing PPG signal.

1.8.1.4 Electrocardiogram derived measurements

This method relies on attaching ECG electrodes to the subject and measuring the fluctuation associated with respiration to derive a respiratory rate. This is known as ECG derived respiration (EDR) (G. Moody, 1986). This method has now been reported using a single-channel ECG (S. Ding, 2004) and can detect obstructive apnoea and changes in tidal volume (Babaeizadeh et al.,

2011). However it still appears less accurate when compared to airflow and movement methods of RR measurement (Helfenbein et al., 2014).

A further development on this method is a small wireless patch sensor from Vital Connect (Chan et al., 2013b). The HealthPatch MD consists of 2 ECG electrodes, a tri-axial accelerometer, micro-controller, and transceiver within a patch that straps like a bandage over the heart (Figure 1.2). The device measures heart rate, respiratory rate, steps and posture and connects wirelessly to a smartphone via bluetooth.

Figure 1.2: The HealthPatch MD - consisting of a patch sensor and reusable electronics module. Taken with permission of Vital Connect. www.vitalconnect.com/healthpatch-md

Respiratory rate is calculated by combining information from the ECG derived respiratory signal as well as chest movement signals from the accelerometer. The device has been given FDA approval but has only been tested on 25 healthy adults against RR data from capnography. The mean absolute error between respiratory rates was 1.0 ± 0.1 breaths/min, however it is difficult to draw any statistical conclusions from this data (Chan et al., 2013a). Although in its early phase this device offers the potential for long-term remote monitoring of RR. No testing on children has taken place to validate the device in this population.

As with the other contact methods, this device may cause distress to the small child due to its contact with the chest. It also does not appear appropriate for use in the ED triage setting but more as an option for longer term remote monitoring. The cost of applying a single use patch to each patient presenting to ED may not be feasible and the time delay in obtaining a reading may be significant.

1.8.1.5 Photoplethysomography derived measurements

Photoplethysomography (PPG) utilises a monitoring system that is already widely used in measuring patient's oxygen saturation levels. Leonard et al (Leonard et al., 2003) described using pulse oximeters in 10 healthy adults to extract respiratory waveforms to determine respiratory rates. This method has also been widely tested in newborn infants (Johansson et al., 1999,

Olsson et al., 2000, Wertheim et al., 2009). Olson et al reported a high degree of association between PPG and thoracic impedance measurements in 10 newborn infants (r= 0.99) (Olsson et al., 2000). Wertheim et al have shown they were able to reliably monitor respiratory rates from a commercially available pulse oximeter in term and preterm infants (Wertheim et al., 2009, Wertheim et al., 2014). This method has also been extended into children with preschool wheeze (Wertheim et al., 2013). 18 acutely wheezy children had their RR derived from pulse oximetry plethysmogram and compared against clinical assessment. The plethysmogram analysis was within 10 breaths/min of the clinical assessment during the acute episode. Clearly the accuracy of this method would need to be improved before it could be considered as an acceptable alternative for measuring respiratory rate in the acute setting.

1.8.2 Non-contact based respiratory rate monitoring

With non-contact respiratory rate monitors the device does not make contact with the patient's body. This method may be more suitable in the acute setting and also in children, where a contact method may not be tolerated and also unintentionally alter the respiratory rate. Table 1.4 summarises the non-contact methods.

1.8.2.1 Infrared thermography

Infrared thermography can be used to monitor fluctuations in facial skin surface temperature using an infrared detection device. During exhalation the skin temperature on the tip of the nose increases and a respiratory signal and rate can be extracted (Hsu CH, 2005). Abbas et al (Abbas et al., 2011) were able to detect respiration in preterm infants on a neonatal unit based on a 0.3 - 0.5^0C temperature difference between inspiration and expiration. This technique has also been demonstrated to work well in resting children, and when compared with conventional contact methods a close correlation was seen (correlation coefficient = 0.994) (Al-Khalidi et al., 2011b). However this technique requires complex equipment and detailed calibration to set up, and in its current form would not be a viable option to be used in clinical practice.

1.8.2.2 Video data

Video images have also been shown to provide RR measurements. The differences between video frames can be used to estimate movements and provide a RR (Koolen et al., 2015). Alternatively a RR and HR can be derived from analysing the video for skin colour changes observed in a subjects face (Aarts et al., 2013). These techniques may provide an accurate measurement of respiratory rate but require good illumination of the face and are not appropriate for sleep monitoring.

Aoki et al projected infrared light spots onto subjects chests and used cameras to determine the distance these light spots moved with respiration to derive a RR (Aoki H et al., 2001). Whilst this method could be used in the sleep study setting the projected light spots can be distracting for children. Also the accuracy of this method is affected by large movements and different sleeping positions. A further development of this method used a Eulerian video magnification to amplify

respiratory movements (Koolen et al., 2015). They used this to analyse the RR in 7 neonates, including those in dark settings, and were able to detect the RR on 94% of occasions.

Table 1.4: Non-contact methods of respiratory rate measurement

Method	Mechanism	Application areas	Advantages	Disadvantages
Infrared thermography	Detects fluctuations in skin surface temperature created by exhaled air and converts this to a respiratory signal.	Neonatal intensive care setting Sleep study setting	-Extremely accurate method, comparable to available contact methods. -Useful application in a sleep study setting.	-Long processing time to convert images and derive RR. -Difficulties when subjects breathe through both nose and mouth. -Head movements cause large inaccuracies. -Complex expensive equipment with long set up times.
Video data	RR derived through analysing video data. By detecting movement changes of subject, or infrared light, magnification of movements, or changes in skin colour.	Intensive care environment Neonatal intensive care environment Triage and ward setting	-Simple cameras using standard resolution images can be used. -Some methods are easy to use, could be used in ward or home environment.	-Some cameras will not work in poor light. -Measurement may be inaccurate if subject makes large or frequent movements.
Humidity detection	Device quantifies humidity of exhaled air. Derived signal is transmitted to monitor that calculates RR breath-by-breath.	Post operative setting Intensive care	- Provides continuous RR data useful in post operative or intensive care setting. - Small, mobile device.	-Device placed inside face mask, will not work unless subjects wear face mask. -Readings affected by low expiatory flow rates and water condensation.
Ultrasound	Can detect small body movements in respiration. Can also utilise doppler affect to detect velocity difference in exhaled air and environment.	Sleep study setting Intensive care setting	- Easier detection of sleep apnoea. - May be well suited for continuous monitoring in preterm infants.	- Inaccuracies with movement or if subject has nasal cannula in situ - Potentially expensive and difficult to set up.
Radar	Detects breathing movements of the chest using the doppler phenomenon.	Sleep study setting Intensive care setting	-Can be used at long distances. -Possibility of wireless transfer of RR data to central unit.	-Movement creates artefact which alters RR signal. -Currently expensive and difficult to set up.
Mobile phone applications	1.Detection of chest movement through mobile phone camera (Philips Vital Sign).		- Portable, quick and easy to use. Very user friendly.	-Not yet validated clinically. Measurements may be very inaccurate.
	2.RR derived from mean time interval between breaths by tapping on mobile device (RRate).		- Portable, easy to use and reduces time taken to measure RR. - Could be used in resource limited settings.	- Still requires subjective assessment of RR. - Time of measurement may affect accuracy.

More recently research groups have successfully adapted the Microsoft Kinect video gaming system, originally used with Microsoft Xbox, to track chest wall movement and obtain a respiratory rate measurement. The Kinect uses infrared laser light to continually calculate distances to different surfaces and has been shown to be capable of measuring RR during medical imaging procedures (Noonan et al., 2012). Current studies are ongoing to assess the use of the Kinect system in providing continual measurements of respiratory rate in the Paediatric intensive care setting. Further validation of this method is required, however it does potentially offer a cheaper, simpler alternative that could also be trialled in the triage and ward setting.

1.8.2.3 Humidity detection

This method is based on the measurement of the humidity of exhaled air which is then converted to a respiratory rate reading. Niesters et al (Niesters et al., 2012) have utilised this method by placing such a device within a facemask. They validated this in 28 healthy adults and found close agreement when compared with capnometry and the standard visual counting method (limits of agreement ±1 bpm). Their method of measurement may be of use in the post-operative setting however it requires further testing and validation in children and in other clinical settings before it can be adopted more widely.

1.8.2.4 Ultrasound

Ultrasound has been used to measure respiratory rate in a number of different ways (Min et al., 2007, Arlotto et al., 2014). Firstly by ultrasound wave telemeters that detect small body movements associated with respiration (Min et al., 2007). More recently Arlotto et al have developed an ultrasonic contactless sensor that measures the frequency shift produced by the velocity difference between the exhaled air flow and the ambient environment to derive a RR (Arlotto et al., 2014). This method is yet to be validated in the clinical setting and measurements appear to be affected by movement of the subject. However it may have applications in continuous RR monitoring in neonates and infants in an intensive care environment and also in the diagnosis of sleep apnoea.

1.8.2.5 Radar

Radar methods offer another option for the contactless measuring of RR. Greneker first utilised this method in monitoring the performance of Olympic athletes from distances of over 10 meters (Greneker, 1997). More recently Droitcour et al (Droitcour et al., 2009) developed a low powered doppler radar system and compared measurements of RR in 24 hospitalised adults against a standard contact method. The 95% limits of agreement fell within −4.5 and 1.8 breaths/min. This method has also been extended for use in babies. By using continuous wave doppler radars Hefner et al (Hafner et al., 2007) were able to measure the RR of preterm infants on a neonatal intensive care unit. However, these options remain complex to set up and potentially costly and at present may not offer a better alternative to current monitoring methods.

1.8.2.6 Mobile applications

Mobile applications provide a portable way of measuring RR. Philips vital sign mobile application measures both heart rate and respiratory rate using the built-in camera on a mobile device (Philips, 2015). By detecting facial flushing with each heart beat and chest movement, an estimation of HR and RR is given. The device has not been clinically tested and caution must be taken in bringing such an application into the clinical setting before it has been rigorously tested and validated. Figure 1.3 shows an image of the working application.

Karlen et al (Karlen et al., 2011) have produced another mobile application to measure RR (Figure 1.4). The RRate mobile application estimates the RR of the subject by measuring the median time interval between breaths obtained from tapping on the touch screen of a mobile device (Karlen et al., 2014). They obtained data from 30 subjects estimating the RR from 10 standard videos. They observed that the efficiency (time to complete a RR measurement) was improved by using this device however, by increasing the efficiency of the measurement accuracy was lost. They suggested the most balanced optimisation resulted in the measurement taking 9.9 seconds to complete, which corresponded to an error of 2.2 breaths/min at a RR of 40 breaths/min (Karlen et al., 2011).

This application again needs further testing within a clinical setting, and on subjects of different ages. Although it does offer a potential improvement in the efficiency of measuring RR, the application still relies upon a subjective assessment which could lead to further inaccuracies.

Figure 1.3: Screenshot of Philips vital sign mobile application.

Figure 1.4: Screenshot of the RRate mobile application.

1.9 The research questions

Respiratory rate is used every day in clinical practice and is heavily relied upon by many clinicians. However, from this review of the literature it is clear that there are still many gaps in our knowledge and this thesis aims to address these gaps, add to the overall body of evidence, and in turn influence future research pathways.

To explore respiratory rate in children this thesis will comprise of four main research questions, these are:

1. How well is respiratory rate measured in children?
2. Is there variability in respiratory rates measured in children?
3. Is respiratory rate a good predictor of deterioration in children?
4. Can a novel contactless device accurately measure respiratory rate in children?

In chapters two and three of this thesis I will analyse how respiratory rate is measured by healthcare professionals (HCP). I will examine their individual practices and preferences and assess the affect any differences may have on the reliability of the measurement obtained. I will then move on to determine the reliability of these respiratory rate counts. Establishing whether any variability is encountered between measurements taken by different observers. These two chapters will provide a greater knowledge and insight into our current practice of measuring respiratory rate in everyday clinical practice. It will inform us as to how much confidence we should have in respiratory rate measurements obtained in clinical practice.

In chapter four I will analyse the clinical importance of a child's respiratory rate. I will investigate the usefulness of respiratory rate measurements in predicting children that may deteriorate and its value compared to both heart rate (HR) and blood pressure (BP). The information gained from this will help put into context the importance of obtaining an accurate and reliable respiratory rate measurement in a child.

In chapter five I will explore an alternative option for measuring respiratory rate in children. This will be in the form of a contactless, portable, handheld device. The device will be tested against both a standard visual counting method and an established contact method of measurement. The clinical validation of this device will inform us as to whether such a device could improve the accuracy and reliability of respiratory rate measurements, reduce variability between measurements, and potentially supersede current methods of measurement used in clinical practice.

1.10 Aims and objectives

Outlined below are the aims and objectives of each of the different chapters of this thesis.

1.10.1 Respiratory rate measurements in children

The aims of this chapter are as follows:

- To establish local paediatric healthcare professionals' practices when measuring respiratory rate in children of different ages, including:
    - Method of measurement
    - Method of timing
    - Duration of measurement
- To compare different paediatric healthcare professionals' practices in measuring respiratory rate in children.
- To analyse the differences in practice amongst paediatric healthcare professionals of different roles and experience levels.

1.10.2 Variability in respiratory rate measurements in children

The aim of this chapter is to determine the level of agreement and correlation of a visual respiratory rate count taken on children when assessed by different observers. Further aims include:

- To determine the level of agreement of respiratory rate measurements when taken simultaneously using the recommended method of a visual count over 60 seconds.
- To determine the level of agreement of respiratory rate measurements when taken by different observers using different methods of visual count measurement.
- To determine the level of agreement in respiratory rate assessment when a predefined scale is used rather than an actual count.
- To explore the differences in the agreement of respiratory rate measurements between paediatric healthcare professionals of differing roles and experience levels.

1.10.3 Respiratory rate as a predictor of clinical deterioration in children

The aims of this chapter are to assess the value of respiratory rate in predicting clinical deterioration in children. Further aims include:

- To determine whether there is a significant change in a child's respiratory rate prior to their admission to the paediatric high dependancy or intensive care unit.
- To calculate the sensitivity, specificity, predictive values and odds ratios of respiratory rate in predicting children who may deteriorate.
- To compare respiratory rate against other vital signs including heart rate and blood pressure in predicting clinical deterioration in children.
- To determine particular threshold levels at which respiratory rate may be a good predictor of deterioration.
- To ascertain the time period before deterioration in which there may be a change in a child's respiratory rate.

1.10.4 Testing and development of a contactless device to measure respiratory rate

This final chapter will describe the clinical testing of a novel, newly developed, contactless portable respiratory rate monitor device. The aims of this chapter include:

- To analyse the accuracy of the device against an established contact method of respiratory rate measurement in both adults and children.
- To analyse the accuracy of the device against the visual counting method of respiratory rate measurement in both adults and children.
- To assess the accuracy of the device in a number of different clinical settings both in and out of hospital.
- To assess the usability and reliability of the device in a variety of different settings.
- To assess the accuracy of different funnel attachments to the device.
- To assess the reproducibility of measurements.
- To make recommendations for the modification and development of the device that can be used to take the device forward as part of further grant applications or with a commercial partner.

1.11 Summary

Respiratory rate is an important vital sign used for diagnosing illnesses in children as well as prioritising patient care (Cooper et al., 2002). However, measuring respiratory rate remains a subjective assessment and is liable to measurement error (Simoes et al., 1991) as well as inter-observer variability (Chan et al., 2001). Respiratory rate does appear to play a role as an indicator in predicting and diagnosing serious illnesses in children (Cretikos et al., 2007). However, it still remains unclear if repeated RR measurements can predict the deterioration of a child.

Devices to measure respiratory rate exist (Al-Khalidi et al., 2011a) but many provide only an estimate of RR due to the associated methodological complexities. Some devices are used within the intensive care, post-operative or more specialised investigatory settings none however have made their way into the everyday clinical setting for acute rapid assessments of RR.

The subsequent chapters of this thesis will further our knowledge of respiratory rate and its measurement in children. It will walk through many aspects of this vital sign from how it is measured, how varied its measurement can be, its accuracy and its usefulness as a vital sign. It will also provide comprehensive data and evidence for an alternative method for respiratory rate measurement in children and analyse its suitability to supersede current measurement methods used in clinical practice.

CHAPTER 2

RESPIRATORY RATE MEASUREMENTS IN CHILDREN

2.1 Introduction

Before any analysis of respiratory rate measurements in children can be completed it is important to assess how respiratory rate measurements in children are being taken by healthcare professionals in everyday clinical practice. We know from the literature that the recommended current standard for a respiratory rate measurement is a count over a full minute by observing abdominal and chest movements (WHO, 2002). We also know that using different measurements methods to this can lead to inaccuracies (Berman et al., 1991, Simoes et al., 1991). By analysing practices of local paediatric healthcare professionals we can begin to understand how much deviation there is from recommendations and the impact that this may have on the accuracy of measurements obtained.

2.2 Aims

To establish local paediatric healthcare professionals practices when measuring respiratory rate in children of different ages. To analyse the differences amongst paediatric healthcare professionals of different roles and experience levels.

2.3 Methods

2.3.1 Study design and population

This was a qualitative study using questionnaires. Paediatric healthcare professionals in a tertiary children's hospital in Sheffield and paediatricians working across the Yorkshire region were approached to answer the questionnaire.

2.3.2 Data collection

A questionnaire (Appendix 8.1) was developed and pilot tested on a range of healthcare professionals prior to distribution. This was to ensure that there was no ambiguity in the questions and that the right information was captured. The questionnaire had seven questions and took two to three minutes to complete. The questionnaire could be completed electronically via an online survey platform or by hand. The paediatric healthcare professionals at the tertiary children's hospital were approached through two different routes; the internal hospital email system and in person. Paediatricians were contacted by email using a database of paediatricians in the Yorkshire region. All paediatric healthcare professionals who measured respiratory rate as part of their role were invited to complete the questionnaire.

2.3.3 Data analysis

All data was collated in an Excel spreadsheet and results were presented as percentages using simple bar and pie charts. Data was also analysed separately for the different healthcare professionals roles and grades. The Mann-Whitney U test was used to determine any statistically

significant difference between data provided from the healthcare professionals of differing roles. All results were analysed using SPSS, version 22.0 for Mac.

2.3.4 Ethical approval

There was no ethical approval required for this study. According to the National Research Ethics Service it is not necessary to gain consent from the healthcare professionals who decided to complete the questionnaire. This questionnaire falls under normal employer/employee relationship and is in accordance with routine practice for staff surveys. Staff were not obliged to take part and confidentiality was ensured throughout.

2.3.5 Funding

This study received no specific grant from any funding agency.

2.4 Results

2.4.1 Participants

A total of 164 paediatric healthcare professionals completed the questionnaire. 82 (50%) of the participants completed their questionnaires via the online survey platform. The majority of respondents were specialist trainee (ST) paediatric doctors (69%), with paediatric nurses the next most common respondent (27%). The full breakdown of the roles of respondents is shown in Table 2.1.

Table 2.1: Role of respondent (n=164)

Nurse Band 5	19 (13%)
Nurse Band 6	15 (9%)
Nurse Band 7	6 (4%)
Nurse Band 8	2 (1%)
Doctor F1/F2	4 (2%)
Paediatric specialist trainee grade 1-3	41 (26%)
Paediatric specialist trainee grade 4-8	54 (34%)
Consultant Paediatrician	11 (7%)
Healthcare worker	6 (4%)
Paediatric Physiotherapist	2 (1%)
*Percentages rounded to nearest whole number	

2.4.2 Length of respiratory rate measurement

All respondents answered this question with 28% indicating they measured a respiratory rate over a full minute, while 44% measured over a period of 30 seconds (Figure 2.1).

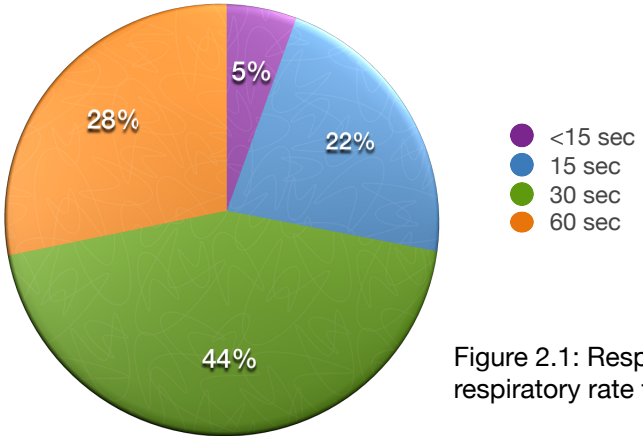


Figure 2.1: Responses to question 2: How long do you measure respiratory rate for?

When separating out the different healthcare professionals and their levels of experience differences were observed. In comparing the responses from doctors and nurses there was no

statistically significant difference in their responses (p=0.384). Doctors however showed a predominance to measure the RR over a 30 second period (49%) whereas nurses showed a similar distribution for measuring RR over 15, 30 or 60 seconds (Figure 2.2).

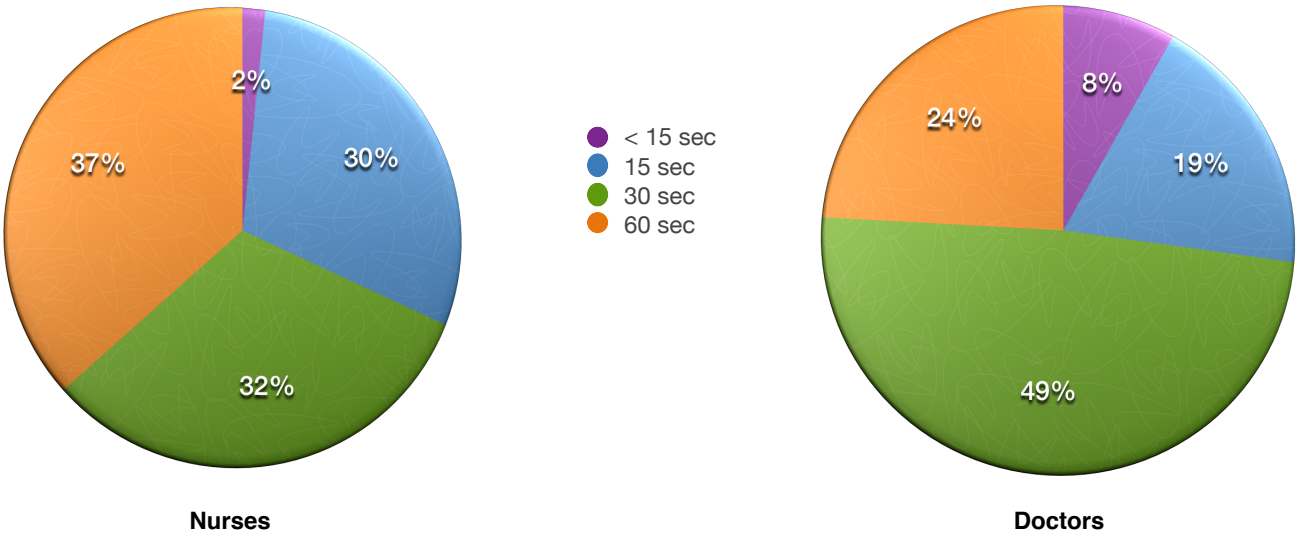


Figure 2.2: Nurses and doctors responses to question 2

There was a statistically significant difference seen when Band 5 nurses and healthcare workers responses were compared with consultant paediatricians (p=0.011). Band 5 nurses and healthcare workers were more likely to measure the RR over 60 seconds (42%) and none of this group reported measuring the RR over less than 15 seconds. However consultant paediatricians reported measuring RR over less than 15 seconds (56%) the most frequently (Figure 2.3). Senior nurses (Band 6 and above) and paediatric specialist trainee doctors showed very similar distributions to that seen overall.

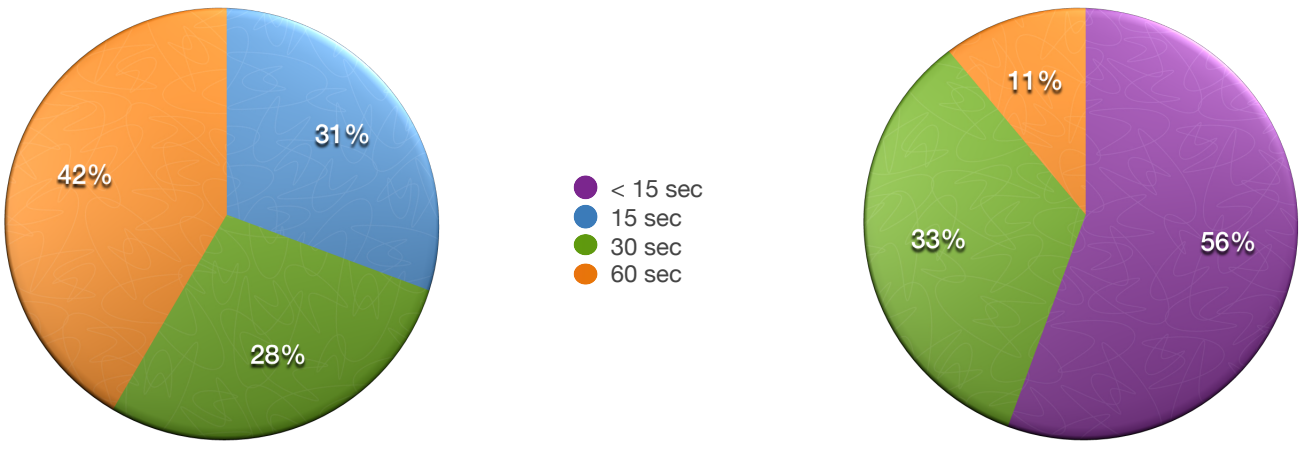


Figure 2.3: Band 5 nurses and healthcare workers and consultant paediatricians responses to question 2

2.4.3 Method of timing used

All respondents answered this question, with the most common method of timing being both a wall clock and a wrist/fob watch (Figure 2.4).

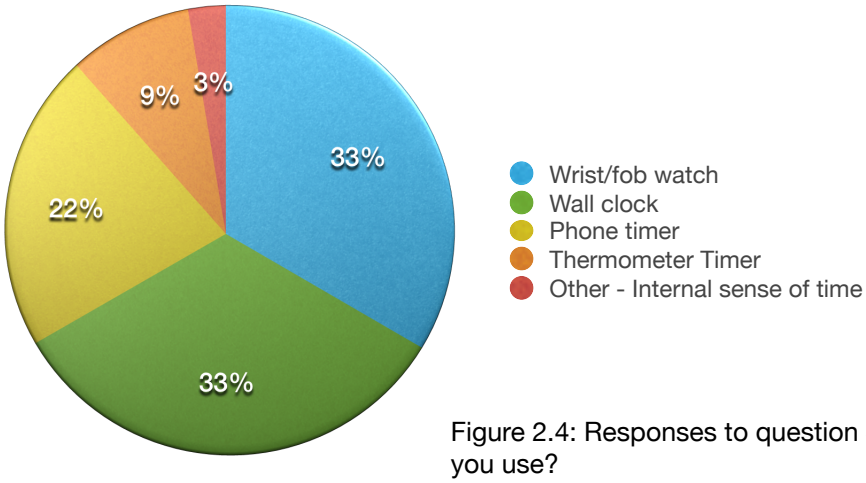


Figure 2.4: Responses to question 3: Which method of timing do you use?

There was no difference seen amongst nurses of different bands or doctors of different levels. However only the senior paediatricians (ST4-8) and consultants described an internal sense of time that they used to time the count of the respiratory rate. The main differences observed in the methods of timing used was seen between nurses and doctors (p=0.049). Nurses would most commonly use a wrist or fob watch (50%) and also made use of the timer located on the axillary thermometer (23%). However the doctors responses were more varied and shared between wrist/ fob watch, wall clock and phone timer (Figure 2.5).

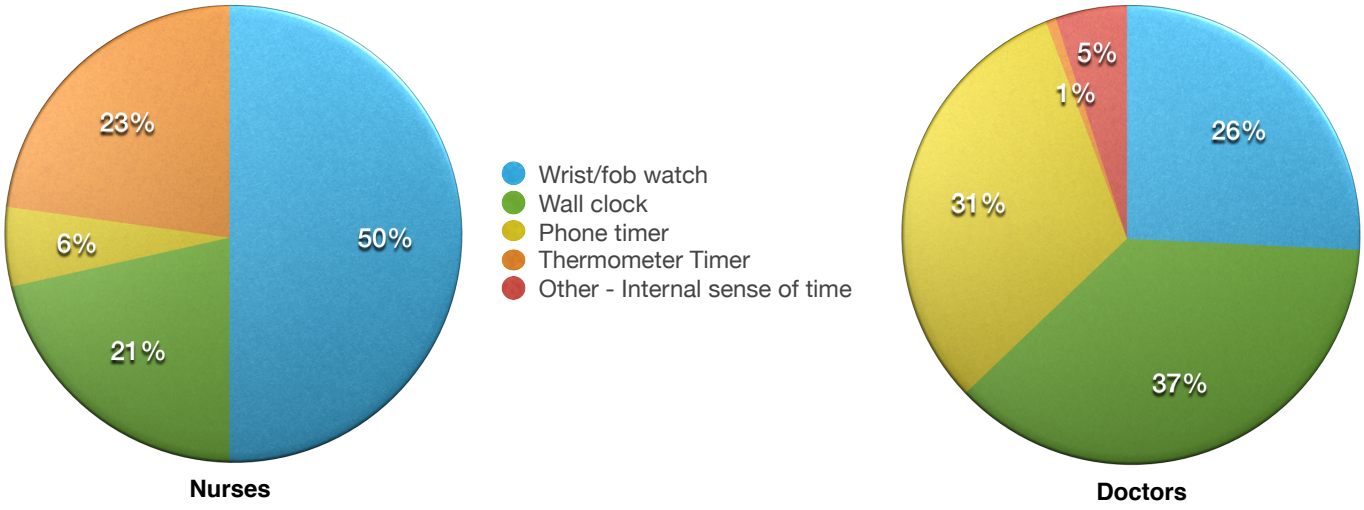


Figure 2.5: Nurses and doctors responses to question 3

2.4.4 Method of measurement used in different aged children

All respondents answered each part of this question and were also given the opportunity to select more than one option if they used a variety of methods. Figure 2.6 shows the overall frequency of methods used for each of the different age groups.

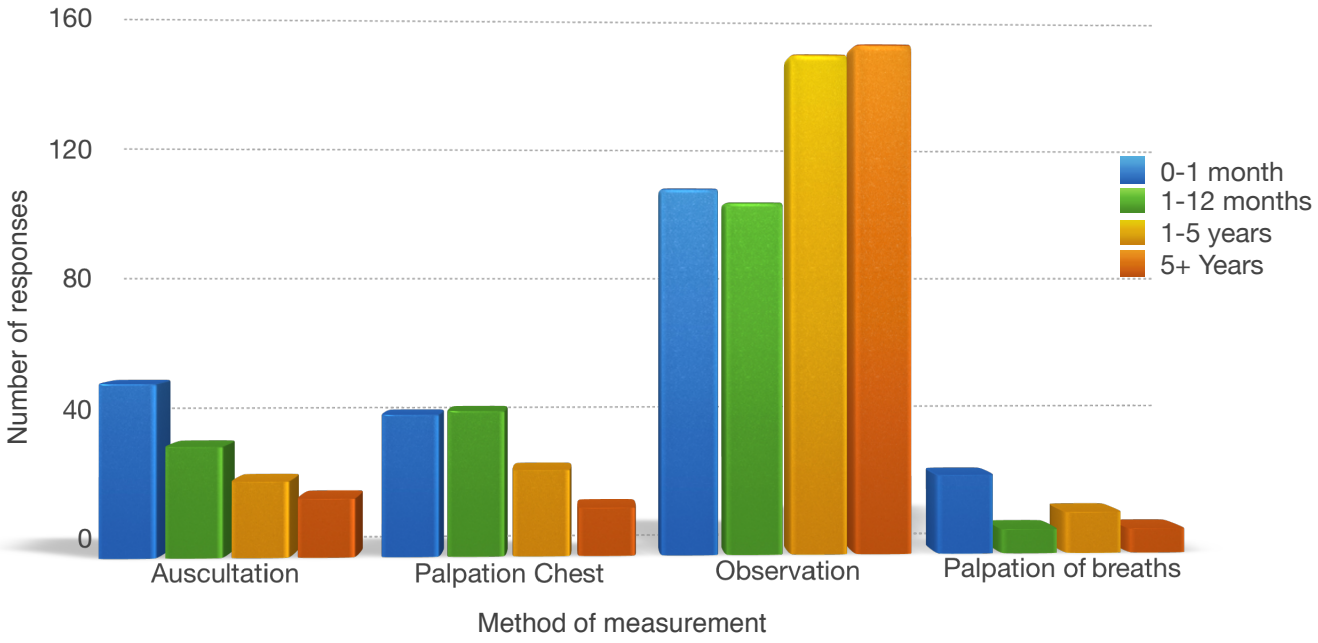


Figure 2.6: Responses to question 4-7: Which method of measurement do you use?

For all age groups the most popular method of measurement was the observation of chest and abdominal movements (63%). The method of palpating breaths was the least frequently used method of measurement (6%). Methods such as palpation of the chest (15%) and auscultation (15%) were still secondary to observation but were most frequently used in the younger children up to one year of age.

There was little difference in responses when comparing staff of different training levels and experience. However, there were significant differences when comparing the practices of both doctors and nurses (p=0.003). Overall, both doctors and nurses preferred the method of observation to measure respiratory rate (Figure 2.7). Doctors would use the method of observation more commonly than nurses (66% v 56%). However it was the methods of palpation of both chest (22%) and breaths (16%) that then predominated for nurses whereas doctors preferred to auscultate as a secondary method of measurement (19%).

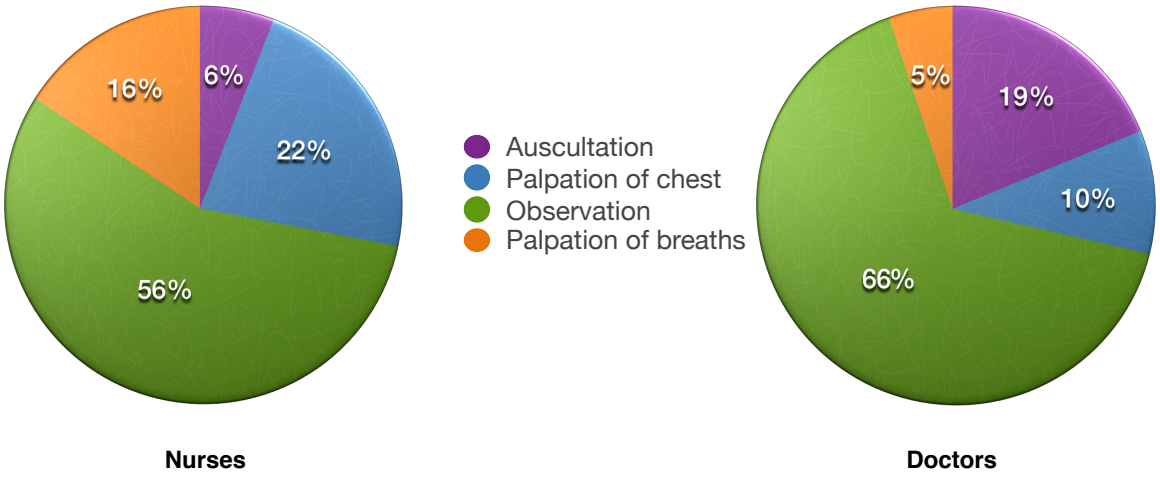


Figure 2.7: Method of measuring respiratory rate by doctors and nurses

In the younger age groups of 0-1 month and 1-12 months the greatest difference in methods of measurement was observed between nurses and doctors. In the 0-1 month age group this difference was statistically significant (p=0.046) however there was not a statistically significant difference seen in responses in the 1-12 month age group (p=0.076). From 12 months onwards there is little difference seen in responses from different healthcare professionals. Observation of RR is increasingly the preferred method and other methods of measurement are less frequently used. Figure 2.8 shows the comparison between doctors and nurses methods of measurements in the 0-1 month age group, whilst Figure 2.9 shows the comparison in children aged 1-12 months.

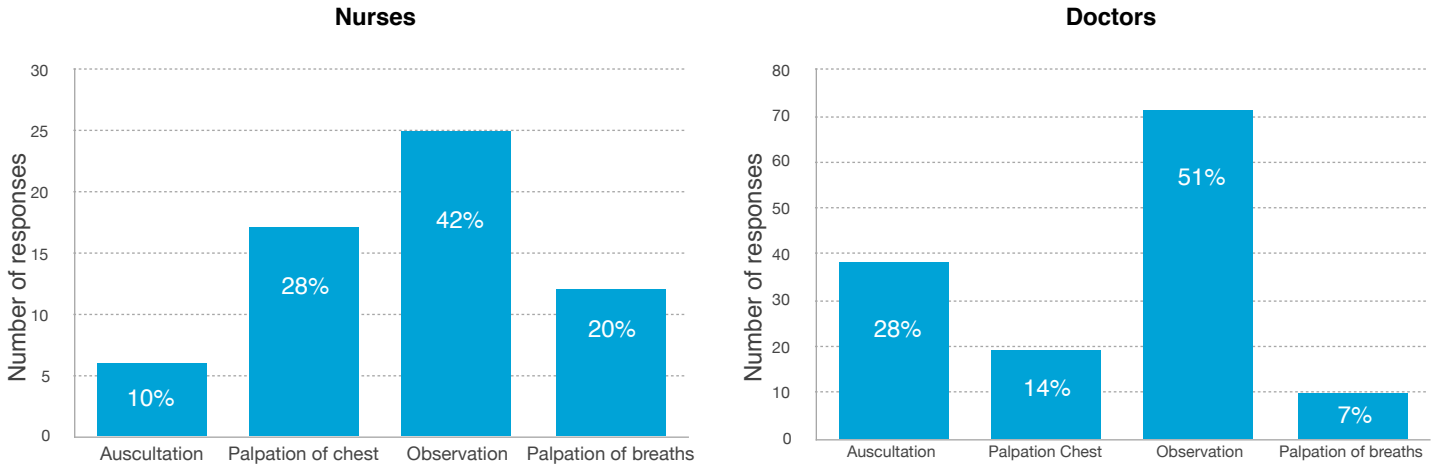


Figure 2.8: Method of measuring respiratory rate in 0-1 month age group by nurses and doctors. Percentages also shown.

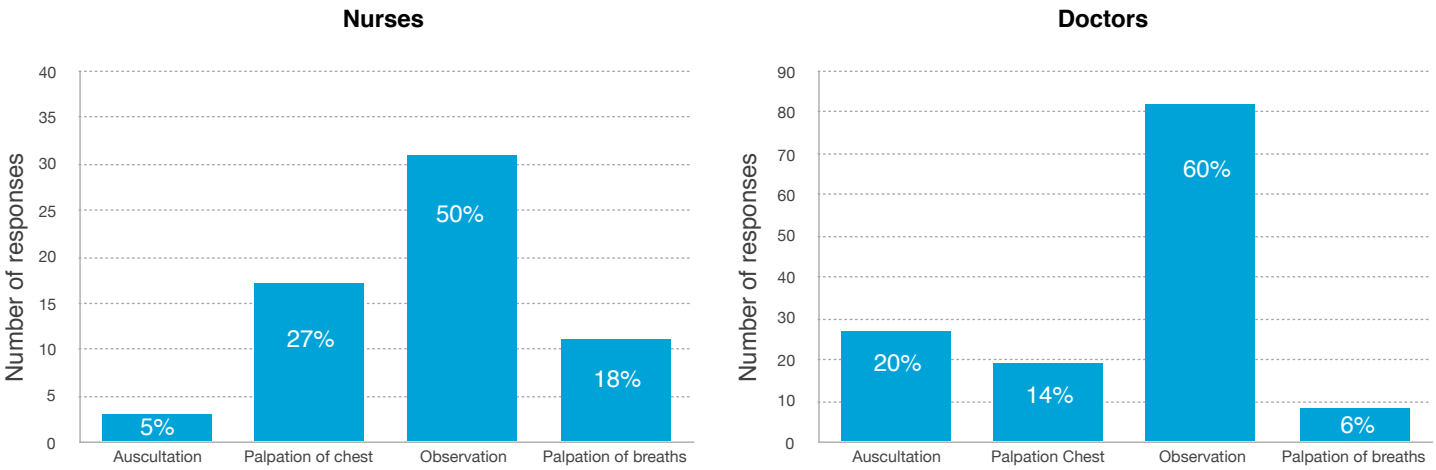


Figure 2.9: Method of measuring respiratory rate in 1-12 months age group by nurses and doctors. Percentages also shown.

In children from 0-1 months 28% of nurses opted for palpation of the chest whereas only 14% of doctors would use this method. Doctors were more likely to auscultate (28%) in these children, however this was nurses least chosen method (10%). With children up to 12 months of age a similar distribution was seen amongst doctors and nurses as was seen in the 0-1 month group. Observation of RR increased in both however, 27% of nurses still opted for palpation of the chest as a secondary method. Auscultation by doctors in this age group was now less commonly used (20%).

2.5 Discussion

Understanding the way paediatric healthcare professionals measure respiratory rate is vitally important. It gives us an insight into the different practices used and also the impact this could have on the accuracy and potential variability of measurements obtained.

2.5.1 Participants

The questionnaire captured a range of paediatric healthcare professionals who take children's respiratory rate. Over half of the respondents were doctors and just over a quarter were nurses. There was also a wide range of experience levels captured. This sample however was not representative of day to day clinical practice where nurses will usually measure RR more often than their doctor colleagues.

2.5.2 Length of measurement

The current WHO standard for a respiratory rate measurement is a count over a full minute (WHO, 2002). However we know that in practice many healthcare professionals may make a count over a shorter period of time (15, 20, or 30 seconds) and this is known to lead to inaccuracies (Berman et al., 1991, Simoes et al., 1991). Only 28% of the paediatric healthcare professionals who answered the questionnaire stated that they measured RR over a full minute. Doctors were less likely to measure over a full minute than their nursing colleagues. The more junior nurses and healthcare workers were the most likely to complete a measurement over one minute.

These differences may be explained by how often each professional is required to carry out a RR measurement as part of their role and at what point during the patient journey this occurs. Nurses will often take a RR multiple times during their shift and may also be the first healthcare professional to measure the RR on the child. As such a nurse may be more thorough in their assessment, spending a longer time taking the measurement. Doctors however may measure a respiratory rate less frequently within their role. They may also see the patient after another healthcare professional has already taken a RR, and rely on this measurement. As such the length of time taken for their own measurement may become shorter.

Consultant paediatricians reported taking the least amount of time to measure the RR. This could be explained by a longer time since they were trained and a lack of awareness of the current standard required for measuring a RR. However it is more likely that they are making a rapid overall assessment of the child and their clinical state, of which RR is only one part of their assessment.

2.5.3 Method of timing

A variety of timing methods were reported with clear distinctions seen between doctors and nurses. The majority of nurses would use a fob/wrist watch or the timer on the axillary thermometer. Doctors would rely on a phone timer or wall clock. Nurses are more likely to wear a

fob watch as part of their standard uniform. However, doctors tend not to wear these and with trusts requiring staff to be 'bare below the elbows' for infection control purposes, doctors will therefore rely on alternative methods of timing.

An interesting finding in this section was some doctors describing an 'internal sense of time' that they used to measure respiratory rate. This method of timing has not been previously described and is likely to be extremely inaccurate for the majority of RR measurements.

2.5.4 Method of measurement

The WHO standard for RR measurement states that the count should be performed by observing abdominal or chest wall movements (WHO, 2002). Auscultation, palpation of the chest and palpation for breaths are other methods used. Our data showed that the observation of breathing movements was the most common method of measurement across all paediatric healthcare professionals. Observation is the simplest and most straight forward method of RR measurement. It is non-contact and does not risk agitating the child and altering their RR. This is likely to account for the high numbers of healthcare professionals that we see opting to use this method.

However, in neonates and younger children (up to 12 months) there is an increased use of the other methods of measurements by all professionals regardless of experience. This is potentially due to observed movements being less obvious and harder to measure in these children. The professional, by using a different method, may be attempting to negate the difficulty encountered and use other methods that feel more reliable in this age group. It was only when analysing nurses and doctors methods in this cohort that significant differences were seen. After observation nurses would prefer to palpate for breaths and chest movements. However doctors would use the method of auscultation. This may be due to the differences in the training of doctors and nurses and their respective roles. Doctors are more practiced in using auscultation as part of their clinical examination and as such may be more likely to opt for this method. This may however have implications to the accuracy of measurements obtained. In babies auscultation of breath sounds has been shown to yield a higher rate to that obtained by observation (Rusconi et al., 1994).

2.6 Limitations

This questionnaire study had some limitations that must be taken into account when analysing the findings. This was an observational study and was not powered to show any statistical differences. Also although the sample size was large there was not an even distribution of paediatric healthcare professionals, with almost twice the number of doctors to nurses responding. There was also a small number of consultant paediatricians that responded, and caution must be taken in interpreting their responses.

As this data was gathered using a questionnaire, respondents were unable to freely express their opinions and were forced to choose their answers based upon pre-defined options. This may have led to answers being selected even if they did not reflect the respondent's true practices. Also, even though this was an anonymous questionnaire there was still a potential for respondents to give answers based on what they thought reflected best practice rather than what was their actual practice.

2.7 Conclusions and implications for remainder of thesis

There are wide ranging practices used by paediatric healthcare professionals to measure respiratory rate in children, from different measurement times to a variety of measurement methods. These vary between doctors, nurses and other healthcare professionals. Differences also exist between professionals of different experience levels. It is clear from the literature that these different practices will have an impact on the accuracy of measurements obtained.

These findings must therefore be taken into account when assessing respiratory rate measurements obtained by healthcare professionals in the clinical setting. This is of particular importance for subsequent chapters of this thesis where respiratory rate measurements obtained from clinical practice are used for comparison and to also draw conclusions from. Healthcare professionals across the paediatric specialty must therefore work to standardise practice, following national and international recommendations, in order to ensure there is accuracy and validity in their respiratory rate measurements.

CHAPTER 3

VARIABILITY IN RESPIRATORY RATE MEASUREMENTS IN CHILDREN

3.1 Introduction

Variation in the measurement of respiratory rate can be expected due to the subjective nature of its measurement. In children this variability may be higher than in adults as they may not be as cooperative during the measurement and their respiratory rate may also vary quickly between breaths. If high levels of inconsistencies in respiratory rate measurements exist then this could call into question the reliability of such an important vital sign. It may also impact greatly on the child, their clinical assessment and accurate identification of possible deterioration.

3.2 Aims

The aim of this study was to determine the degree of inter-observer agreement in respiratory rate measurements of children when assessed by different observers. The studied also aimed to assess the agreement in respiratory rate assessment when a predefined ordinal scale was used.

3.3 Methods

The study consisted of two strands: the assessment of the agreement in respiratory rate measurements by three independent observers and a questionnaire based assessment of respiratory rate from video recordings of children breathing.

3.3.1 Agreement in respiratory rate measurements by different observers

3.3.1.1 Study design and setting

This section of the study was a prospective observational study conducted at Sheffield Children's Hospital across all areas of the hospital.

3.3.1.2 Participants and eligibility criteria

Participants were children between the ages of 0-16 years with any clinical condition who had had their respiratory rate measured as part of their routine care within the previous 30 minutes. All children were clinically stable on one of the hospital wards and had already had at least one respiratory rate measurement taken during their admission. Criteria for exclusion were:

- Children whose respiratory rate had not been measured in the previous 30 minutes.
- Children who had had any clinical intervention in the period between the initial RR measurement and the planned simultaneous measurements by the research team.
- Children whose clinical condition deteriorated and they required immediate clinical intervention or children who were already seriously unwell requiring continual intervention.
- Parents and children who were unable to speak or read English as this would delay the consenting process.

Participants were recruited between the months of August and October 2016.

3.3.1.3 Sample size

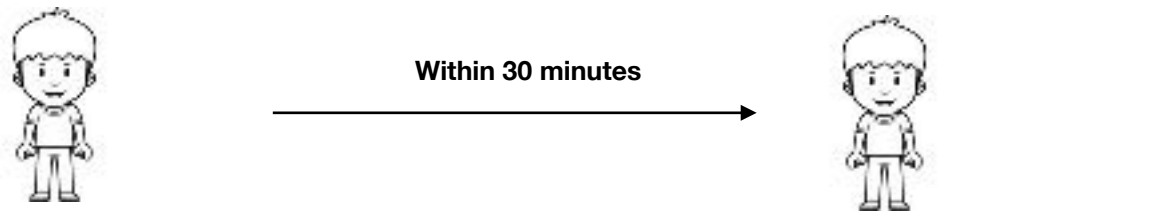
The sample size was calculated based on a previous pilot study completed in 2015 (Daw, W. 2015). In this pilot study two healthcare professionals measured the RR on 60 children. Based on the data from this study the sample size was calculated to detect an expected difference between the two means of ± 2.0 breaths/minute. The standard deviation was the pooled value of standard deviation from both groups (11.3 breaths/minute) and was derived from the 95% range of RR measurements obtained from the pilot study. Using these values we used the statistical package Statulator (Dhand and Khatkar 2014) to calculate a sample size to achieve a 90% power (Z value 1.645) and a significance level of 5%. A sample size of 169 children was required. In total 169 children were recruited to the study.

3.3.1.4 Recruitment

Potential participants were recruited from all areas of the hospital. They were approached by members of the research team and information was given to both parents and their child. There were no incentives offered to take part in the study.

3.3.1.5 Data collection and procedure

Each participant was assigned a unique identifying number based on the order in which they were recruited. Data on the participants age, sex, presenting complaint/diagnosis and activity status (asleep/active/awake) at the time of the measurements was collected. The first respiratory rate taken by the healthcare professional (RR1) was noted along with their role and the method and timing period that they used for that measurement. A further count of respiratory rate was then taken by two different observers simultaneously within 30 minutes of the first measurement. These observers were members of the research team and consisted of a Paediatric Doctor (RR2) and Paediatric Respiratory Physiologist (RR3). They measured the respiratory rate using the WHO recommended method of measurement (WHO, 2002), a count over a full minute by the observation of abdominal and chest movements. All observers were blinded to each of the others measurements. Figure 3.1 shows this process.



RR measurement 1 (RR1)
- Performed routinely by HCP
- HCP preferred method used

RR measurement 2 (RR2)
- Performed by Researcher A
- WHO method of measurement

RR measurement 3 (RR3)
- Performed by Researcher B
- WHO method of measurement

Figure 3.1: The process by which three RR measurements were taken on each child.

3.3.1.6 Statistical analysis

The inter-observer variability was assessed by the mean difference between respiratory rate measurements from the three different observers with 95% limits of agreement (mean ± the standard deviation of the difference). Intraclass correlation coefficients (ICC) with 95% confidence intervals were also reported. To assess any significant difference between ICC of different groups a Fisher r-to-z transformation was performed and differences expressed as p-values. All results were analysed using SPSS, version 22.0 for Mac.

The level of agreement was also assessed for those children with a normal respiratory rate and for those who had a respiratory rate in the tachypnoeic range for their age. A child was classified as tachypnoeic when one or more of the observers measured a respiratory rate at or above the tachypnoeic range. Tachypnoea for children up to 5 years of age was defined as per the age-related WHO proposed definitions (WHO 2002). Above this age, definitions were based upon data from the resuscitation councils Advanced Paediatric Life Support guidelines and recently published systematic reviews of normal age-specific respiratory rate ranges (APLS 2016, O'Leary et al., 2015). This is shown in Table 3.1.

Table 3.1: Respiratory rates classified as tachypnoeic by age group

Age range	< 2 months	2 - 12 months	1 - 5 years	5 - 12 years	12 years +
Respiratory rate (bpm)	> 60	> 50	> 40	> 30	> 20

* If the child 's age was at the upper limit of an age range then they were assessed based on the higher age range category

3.3.2 Questionnaire study of video recordings

3.3.2.1 Study design and setting

This section was a prospective questionnaire study based on video recordings of five different children.

3.3.2.2 Participants and eligibility criteria

Participants for this study were healthcare professionals from within the South Yorkshire region. To be eligible to take part in the questionnaire all healthcare professionals must regularly measure children's respiratory rates as part of their normal working role.

3.3.2.3 Sample size

A convenience sample of 100 healthcare professionals was selected. There are no established criteria for sample size calculations for this type of study.

3.3.2.4 Video recordings

The videos showed five different children of varying ages breathing at different rates. Video recordings were taken from selected children at Sheffield Children's Hospital using a Polaroid

IX828 camera. Each video recording lasted 60 seconds and only the thorax and neck of the child was shown. Participants could also hear any sounds that the child was making. The participants were only given information on the age and sex of the child but not their underlying diagnosis. Table 3.2 gives a description of each of the videos including the child's diagnosis and their observed counted respiratory rate over the 60 second period and Figure 3.2 shows a screenshot from each of the video recordings.

Table 3.2: Description of videos

Video number	Child's details	Underlying diagnosis	Counted RR
Video 1	3 year old girl	Viral induced wheeze	48 bpm
Video 2	3 month old boy	Bronchiolitis	69 bpm
Video 3	15 year old boy	Hand abscess	15 bpm
Video 4	2 week old girl	Bronchiolitis	53 bpm
Video 5	8 year old boy	Apnoeic episodes (Cerebral palsy)	20 bpm

3.3.2.5 Data collection and procedure

Each participant was assigned a unique identifying number based on the order that they were recruited. Data on the participant's sex and role was collected. Participants were given a summary of the child's age and sex before each of the videos commenced. Participants were then asked to use a predefined scale of very slow, slow, normal, fast and very fast to grade the child's respiratory rate. The participants were not given an indication of where a given respiratory rate should be on the scale and all participants were blinded to the answers of others.

3.3.2.6 Statistical analysis

Analysis of the agreement between participants rating of respiratory rate was assessed by Fleiss Kappa statistic. A Fleiss Kappa statistic between 0.61-0.80 was used to indicate substantial agreement, 0.41-0.60 moderate agreement, 0.21-0.40 fair agreement and <0.2 slight agreement. Comparisons were also made between different groups of healthcare professionals including doctors and nurses and between healthcare professionals with different levels of experience. The Mann-Whitney U test was used to assess any significant difference between different groups of healthcare professionals, with a p-value of <0.05 indicating a significant difference between groups. All results were analysed using SPSS, version 22.0 for Mac.

3.3.3 Ethical approval

The study received a favourable ethics opinion by the NRES committee Yorkshire and the Humber on 21/7/2016, REC reference 16/YH/0262 (Appendix 8.2). For the first section of the study, analysing the agreement of RR measurements by different observers, written informed consent was obtained from the participant or the parents of each participant prior to participation. For the

video questionnaire section of the study written informed consent was obtained from the participant or the parents of each participant who were recorded on video. It was not necessary to gain consent from the healthcare professionals completing the questionnaires as this fell under normal employer/employee relationship and is in accordance with routine practice for staff surveys. Staff were not obliged to take part and confidentiality was ensured throughout.

3.3.4 Funding

This study was funded by The Children's Hospital Charity and was granted £3,465.00 in April 2016.

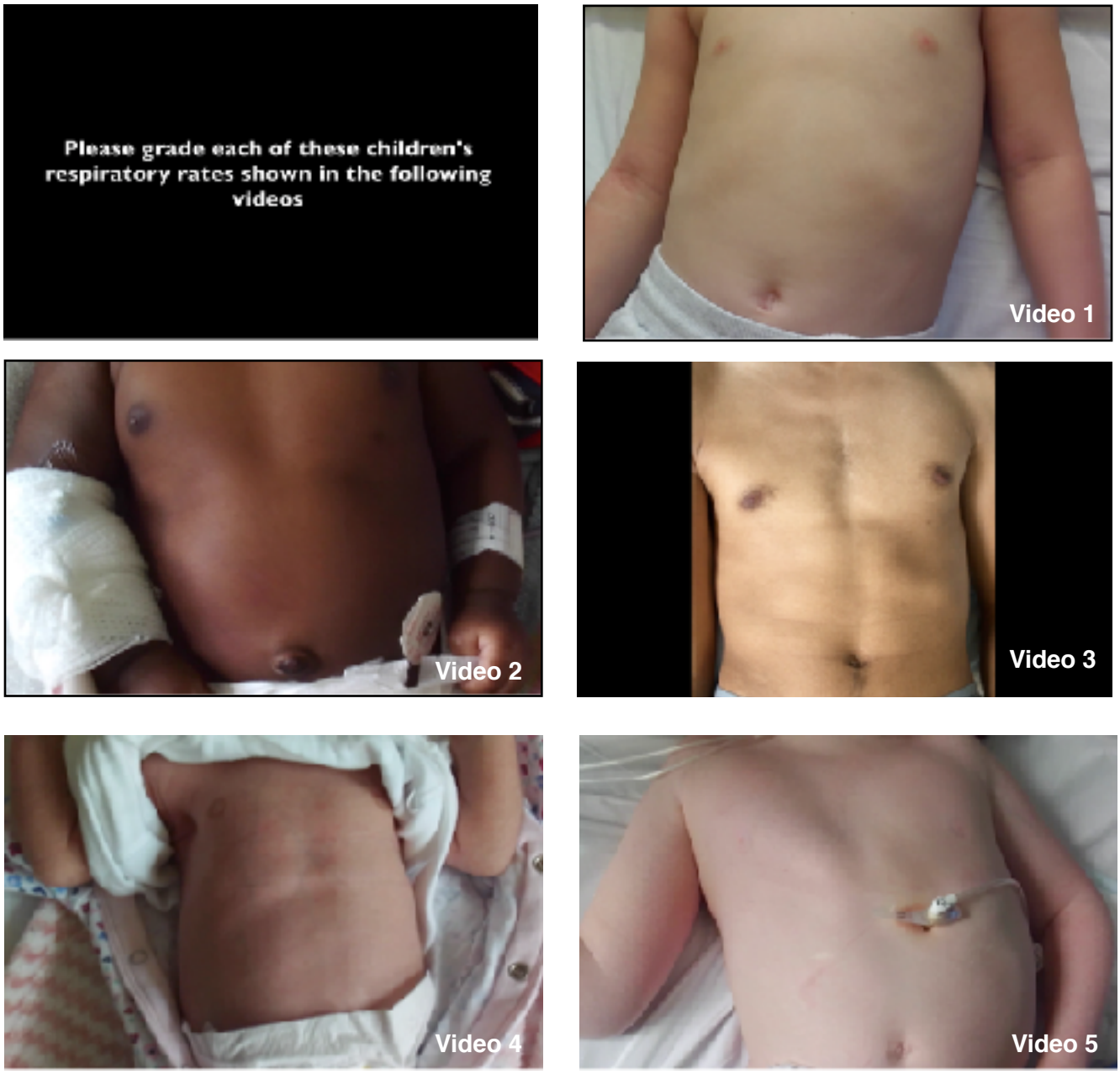


Figure 3.2: Screen shots of participant instructions and each of the five videos.

3.4 Results

3.4.1 Agreement in respiratory rate measurements by different observers

3.4.1.1 Participants

A total of 507 respiratory rate measurements were taken on 169 children. 53% of the participants were male and the median age was 29 months. The youngest participant was 3 days and the oldest was 15 years and 11 months. The median time between the RR1 and RR2/RR3 measurements was 16 minutes (range 1 to 30 minutes). Table 3.3 shows the patient characteristics and primary presenting complaint and Table 3.4 the age range of children studied.

Table 3.3: Patient Characteristics (n=169)

Age in months, median, range	29 (0.1 - 192)
Male gender, n (%)	90 (53%)
Primary presenting complaint, n (%)	
Increased work of breathing	39 (23.1%)
Fever	22 (13.0%)
Cough	16 (9.4%)
Vomiting	20 (11.8%)
Diarrhoea and vomiting	9 (5.3%)
Skin complaint	8 (4.7%)
Feeding difficulty	4 (2.4%)
Headache	3 (1.8%)
Burns	3 (1.8%)
Surgical problem	9 (5.3%)
Head injury	2 (1.2%)
Seizure	5 (3.0%)
Pain	5 (3.0%)
Constipation	2 (1.2%)
Planned admission/procedure	16 (9.4%)
Other*	6 (3.5%)

*Included - Anaphylaxis, accidental ingestion, animal bite, eye complaint and rheumatological complaint.

Table 3.4: Age range of participants	n (%)
0 -1 years	47 (28%)
1 - 2 years	29 (17%)
2 - 5 years	46 (27%)
5 - 12 years	30 (18%)
12 + years	17 (10%)

3.4.1.2 Respiratory rate 1 (RR1) measurement

The initial respiratory rate (RR1) was most often measured and recorded by a nurse (88%), who had varying levels of experience. Table 3.5 shows the breakdown of healthcare professionals taking the first respiratory rate and Table 3.6 shows the method of measurement that they used.

Table 3.5: Healthcare professionals	n (%)
Paediatric Nurse Band 5	82 (49%)
Paediatric Nurse Band 6	57 (34%)
Paediatric Nurse Band 7	9 (5%)
Paediatric Healthcare worker	7 (4%)
Student nurse	14 (8%)

Table 3.6: Method of measurement	n (%)
Observation 10 seconds	11 (7%)
Observation 15 seconds	125 (74%)
Observation 30 seconds	16 (9%)
Observation 60 seconds	12 (7%)
Palpation 30 seconds	4 (2%)
Palpation 60 seconds	1 (<1%)

*Observation/palpation of chest and abdominal movements

3.4.1.3 Respiratory rates

Respiratory rate measurements ranged from 11 to 65 breaths/min. Figure 3.3 shows the variability between measurements for the three observers. RR1 had a median of 32 bpm (interquartile range 24-40 bpm), RR2 a median of 28 bpm (interquartile range 21-37 bpm) and RR3 a median of 28 bpm (interquartile range 21-36 bpm). The respiratory rate for some individual subjects was highly variable. The largest difference in a subject's RR from a measurement taken simultaneously (RR 2 and RR 3) was 14 bpm. The largest subject discrepancy between a first (RR 1) and second (RR 2/3) measurement was 33 bpm.

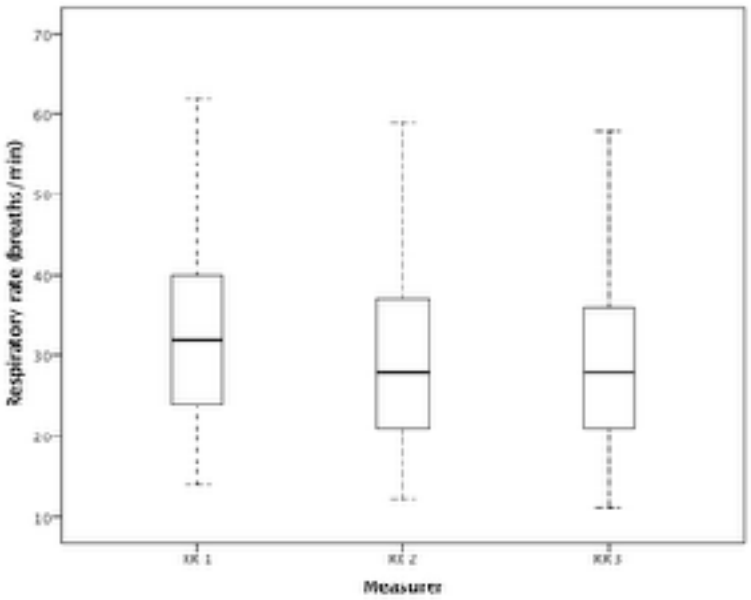


Figure 3.3: Box plot showing the variability of RR measurements for each observer (RR1, RR2, RR3). The solid line in the middle of the box represents the median. The boxes span the interquartile range and the whiskers extend to ±1.5 the interquartile range.

3.4.1.4 Agreement and correlation between measurements

When the respiratory rate measured by the healthcare professional (RR 1) was compared with the RR measured by the first observer (RR 2, Paediatric Doctor) Bland-Altman analysis showed a mean difference of 3.763 with 95% limits of agreement of -10.151 to 17.677. The correlation was high with an intraclass correlation coefficient of 0.864 (95% CI 0.736 - 0.921). When the respiratory rate measured by the healthcare professional (RR 1) was compared with the RR measured by the second observer (RR 3, Paediatric Respiratory Physiologist) Bland-Altman analysis showed a mean difference of 3.687 with 95% limits of agreement of -11.357 to 18.730. The correlation was again high, with an intraclass correlation coefficient of 0.845 (95% CI 0.726 - 0.904).

When the respiratory rate measured by the simultaneous observers (RR 2 and RR 3) was compared, Bland-Altman analysis showed a mean difference of -0.077 with 95% limits of agreement of -7.108 to 6.954. The correlation was excellent, with an intraclass correlation coefficient of 0.974 (95% CI 0.964 - 0.980). Figure 3.4 shows the Bland-Altman plots and scatterplots for each of these and Table 3.7 shows the agreement and correlation of measurements by age range.

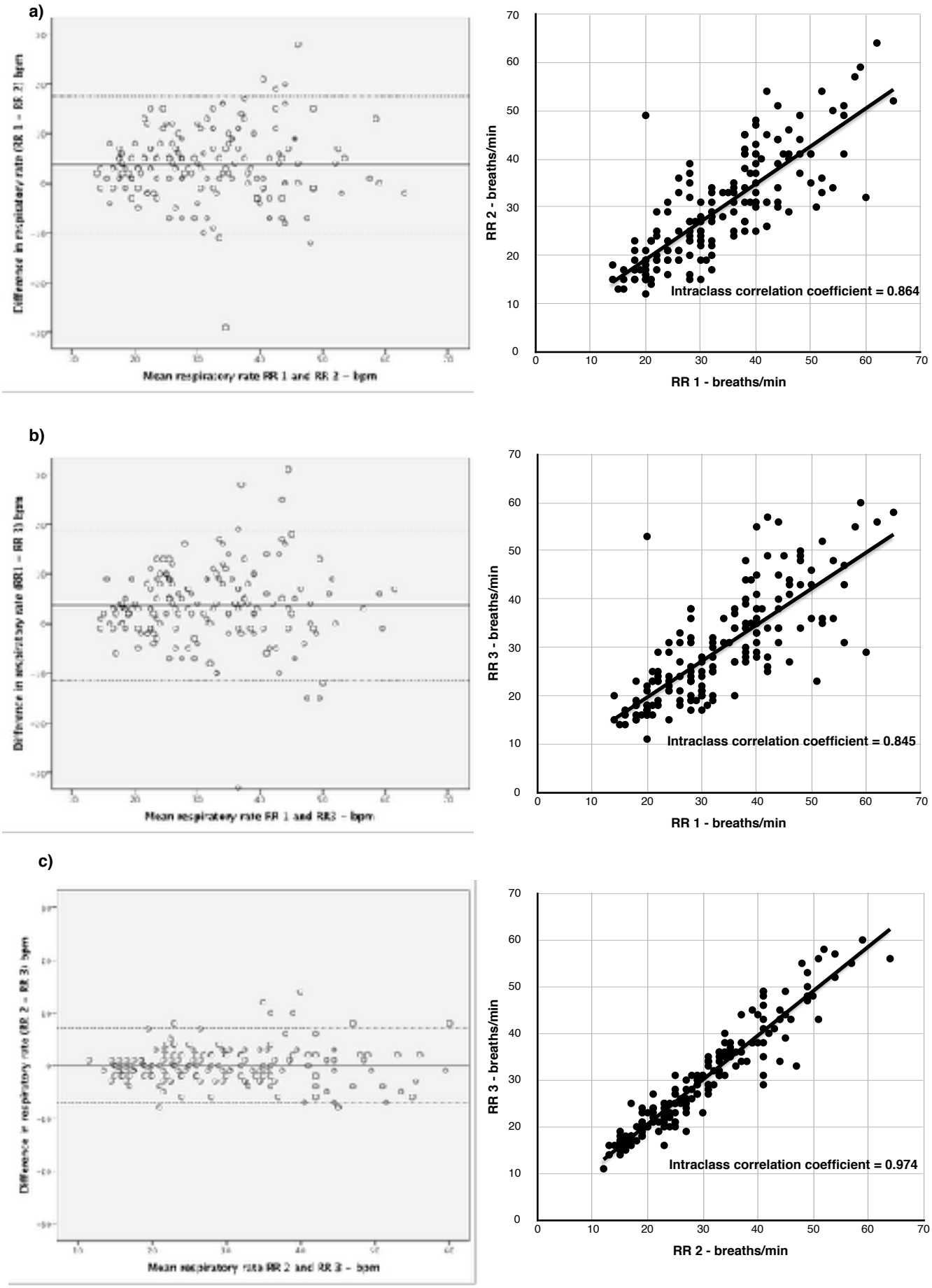


Figure 3.4: Bland-Altman plots and scatterplots assessing pairwise agreement and correlation for respiratory measurements by a) RR 1 and RR 2 b) RR 1 and RR 3 c) RR 2 and RR 3.

Table 3.7: Agreement and correlation of measurements by age			
Age group	**Measurers**	**95% Limits of Agreement (Mean Difference)**	**Intraclass correlation coefficient (95% CI)**
0 - 1 years	RR 1 v RR 2	-10.028 - 21.736 (5.854)	0.640 (0.186 - 0.701)
(47 subjects)	RR 1 v RR 3	-12.102 - 24.519 (6.208)	0.552 (0.119 - 0.764)
	RR 2 v RR 3	-7.956 - 8.665 (0.354)	0.951 (0.913 - 0.973)
1 - 2 years	RR 1 v RR 2	-16.191 - 18.191 (1.000)	0.675 (0.304 - 0.848)
(29 subjects)	RR 1 v RR 3	-18.211 - 20.211 (1.000)	0.584 (0.107 - 0.806)
	RR 2 v RR 3	-9.282 - 9.282 (0)	0.940 (0.872 - 0.972)
2 - 5 years	RR 1 v RR 2	-9.473 - 16.473 (3.500)	0.679 (0.365 - 0.831)
(46 subjects)	RR 1 v RR 3	-8.388 - 15.301 (3.457)	0.758 (0.471 - 0.789)
	RR 2 v RR 3	-6.719 - 6.631 (-0.044)	0.934 (0.880 - 0.963)
5 - 12 years	RR 1 v RR 2	-4.124 - 14.190 (5.033)	0.459 (-0.188 - 0.759)
(30 subjects)	RR 1 v RR 3	-5.141 - 13.941 (4.400)	0.406 (-0.163 - 0.711)
	RR 2 v RR 3	-4.502 - 3.235 (-0.633)	0.928 (0.846 - 0.966)
12 + years	RR 1 v RR 2	-5.931 - 9.578 (1.824)	0.898 (0.709 - 0.963)
(17 subjects)	RR 1 v RR 3	-8.242 - 11.065 (1.412)	0.841 (0.573 - 0.942)
	RR 2 v RR 3	-3.437 - 2.613 (-0.412)	0.982 (0.950 - 0.993)
Overall	RR 1 v RR 2	-10.151 - 17.677 (3.763)	0.864 (0.736 - 0.921)
(169 subjects)	RR 1 v RR 3	-11.357 - 18.730 (3.687)	0.845 (0.726 - 0.904)
	RR 2 v RR 3	-7.108 - 6.954 (-0.077)	0.974 (0.964 - 0.980)

3.4.1.5 Effect of time taken between first and second measurements

There was no significant difference observed in the pairwise agreements and intraclass correlation coefficients between measurements taken closer in time (RR1 - RR2/3 within 0-10 minutes) and those taken further apart (RR1 - RR2/3 within 20-30 minutes). Table 3.8 shows the ICC and mean difference with 95% limits of agreement along with the associated p-values for measurements taken early or late within the 30 minute measurement period.

Table 3.8: Agreement and correlation of measurements by time taken				
Measurers	**Time period**	**95% Limits of Agreement (Mean Difference)**	**Intraclass correlation coefficient (95% CI)**	**Significance (p-value)**
RR 1 v RR 2	**Early** - within 0-10 minutes (49 measurements)	-9.011 - 16.929 (3.959)	0.872 (0.681-0.939)	
	Late - within 20-30 minutes (69 measurements)	-9.623 - 15.652 (3.015)	0.899 (0.801-0.944)	p= 0.516
RR 1 v RR 3	**Early** - within 0-10 minutes (49 measurements)	-9.986 - 17.374 (3.694)	0.863 (0.697-0.931)	
	Late - within 20-30 minutes (69 measurements)	-9.790 - 17.123 (3.667)	0.869 (0.721-0.931)	p= 0.905

3.4.1.6 Effect of child's activity on measurements

For 26 participants (15%) the subjective assessment of the child's activity status during the measurement was different between the first and second/third RR measurements. However there was no significant difference observed in the pairwise agreements and ICC in measurements performed in children whose activity status differed between the three measurements compared with those whose activity status remained the same (Table 3.9).

Table 3.9: Agreement and correlation of measurements based on child's activity status				
Measurers	**Activity status**	**95% Limits of Agreement (Mean Difference)**	**Intraclass correlation coefficient (95% CI)**	**Significance (p-value)**
RR 1 v RR 2	**Same activity status** (143 measurements)	-10.221 - 18.165 (3.972)	0.866 (0.728 - 0.924)	
	Discrepancy in activity status (26 measurements)	-9.658 - 14.899 (2.615)	0.827 (0.604 - 0.923)	p=0.269
RR 1 v RR 3	**Same activity status** (143 measurements)	-11.392 - 19.028 (3.812)	0.849 (0.728 - 0.924)	
	Discrepancy in activity status (26 measurements)	-11.329 - 17.252 (2.962)	0.790 (0.528 - 0.906)	p=0.210

3.4.1.7 Correlation and agreement by seniority level of RR 1 measurer

There was a slight difference noted when assessing the seniority of the HCP taking the first RR measurement (RR1). A marginally higher correlation and agreement was seen with respiratory rates measured by a more senior nurse (Band 6 and 7) when compared with both RR 2 and RR 3, however this difference was not statistically significant (Table 3.10).

Table 3.10: Agreement and correlation of measurements by level of seniority				
Measurers	**Level of seniority**	**95% Limits of Agreement (Mean Difference)**	**Intraclass correlation coefficient (95% CI)**	**Significance (p value)**
RR 1 v RR 2	Band 5, HCW, Student nurse	-8.744 - 18.530 (4.893)	0.841 (0.570-0.923)	
	Band 6 and Band 7 nurse	-11.735 - 15.735 (2.000)	0.897 (0.827-0.938)	p= 0.150
RR 1 v RR 3	Band 5, HCW, Student nurse	-9.795 - 19.426 (4.816)	0.821 (0.576-0.908)	
	Band 6 and Band 7 nurse	-13.244 - 17.092 (1.924)	0.876 (0.796-0.925)	p= 0.219

3.4.1.8 Assessment of tachypnoea

A total of 30% (51 children) of all the measurements would have been classified as tachypnoeic (Table 4.1), by one or more of the three observers. Of these children in only 18% (9 children) did all three observers agree on the presence of tachypnoea and in only 33% (17 children) did the simultaneous research observers agree. Notably, in these children the agreement was statistically significantly different from the children whose respiratory rate was classified as being within the normal range by all of the observers.

This indicated that at higher respiratory rates less agreement between measurements was seen. Table 3.11 shows the 95% limits of agreement for the different groups along with the p-values indicating the significance in the difference in agreement and Figure 3.5 shows the associated Bland-Altman plots.

Table 3.11: Agreement and correlation of measurements based on RR range				
Measurers	**RR range (number)**	**95% Limits of Agreement (Mean Difference)**	**Intraclass correlation coefficient (95% CI)**	**Significance (p value)**
RR 1 v RR 2	Tachypnoiec (51)	-14.752 - 23.811 (4.529)	0.720 (0.557-0.830)	
	Normal range (118)	-7.417 - 14.282 (3.432)	0.859 (0.670-0.926)	p=0.013
RR 1 v RR 3	Tachypnoiec (51)	-17.112 - 26.641 (4.765)	0.645 (0.451-0.780)	
	Normal range (118)	-7.625 - 14.066 (3.220)	0.864 (0.702-0.926)	p=0.001
RR 2 v RR 3	Tachypnoeic (51)	-8.786 - 9.256 (0.235)	0.938 (0.894-0.964)	
	Normal range RR (118)	-6.210 - 5.786 (-0.212)	0.970 (0.957-0.979)	p=0.015

a) Tachypnoeic RR

b) RR in normal range

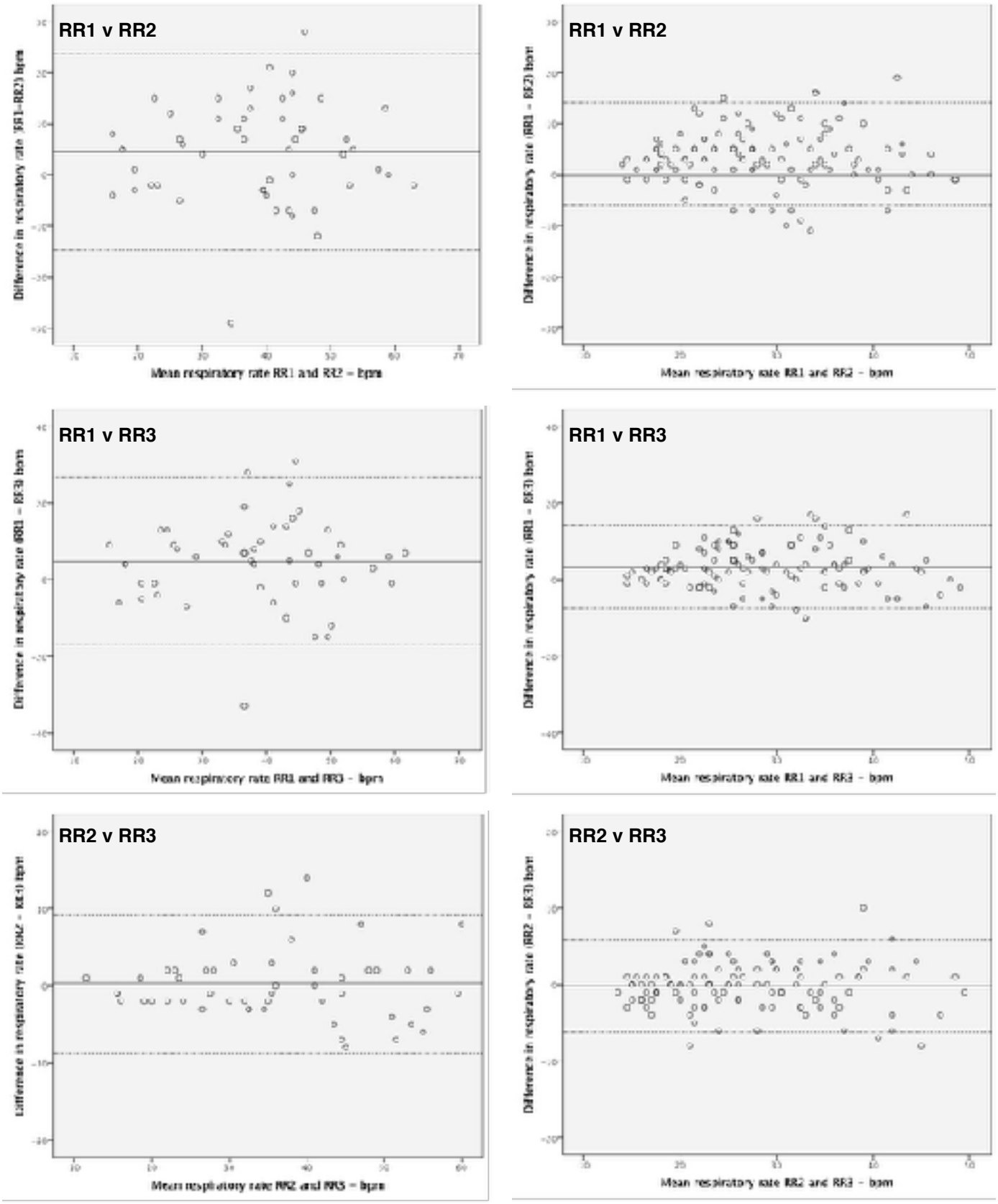


Figure 3.5: Bland-Altman plots assessing pairwise agreement for measurements for children who were assessed as tachypnoeic (a) and those whose RR was within the normal range (b).

Figures 3.6 and 3.7 depict these differences for two different age categories as would be seen on a Paediatric early warning score (PEWS) chart. Figure 4.6 shows this for children aged 2-12 months and shows that in 10 out of 12 of these children, the HCP (RR1) would have classified them as tachypnoeic. Both of the other observers would however have classified these children as having a normal RR.

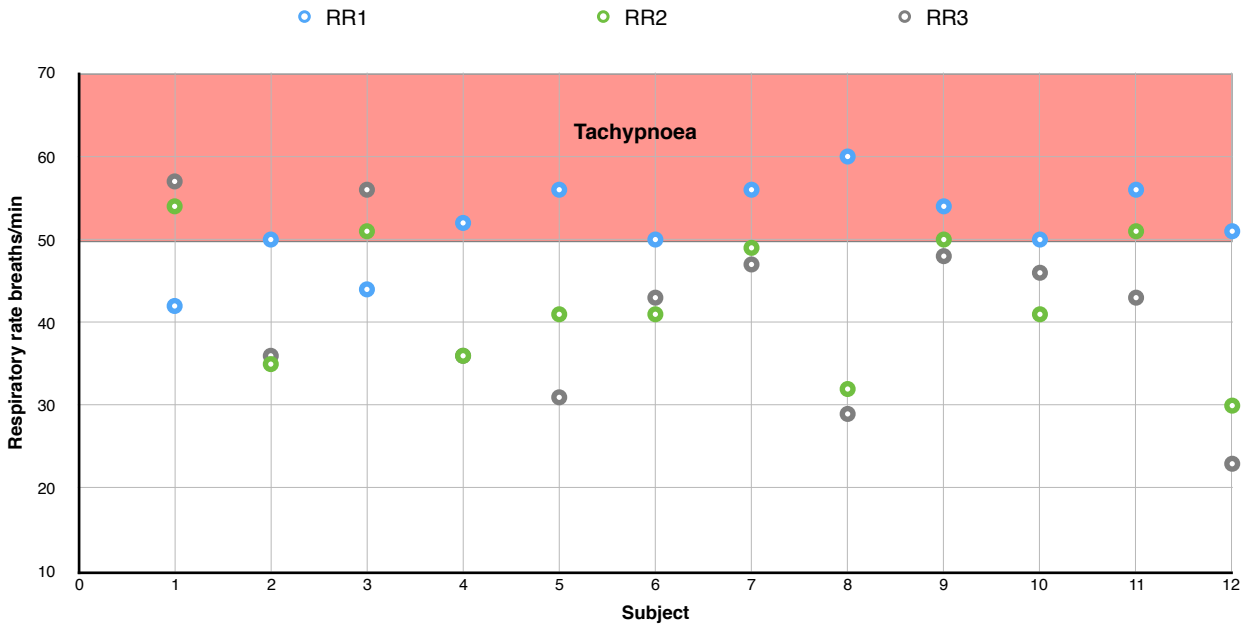


Figure 3.6: Subjects aged 2 -12 months who were assessed as being tachypnoeic by one or more observers.

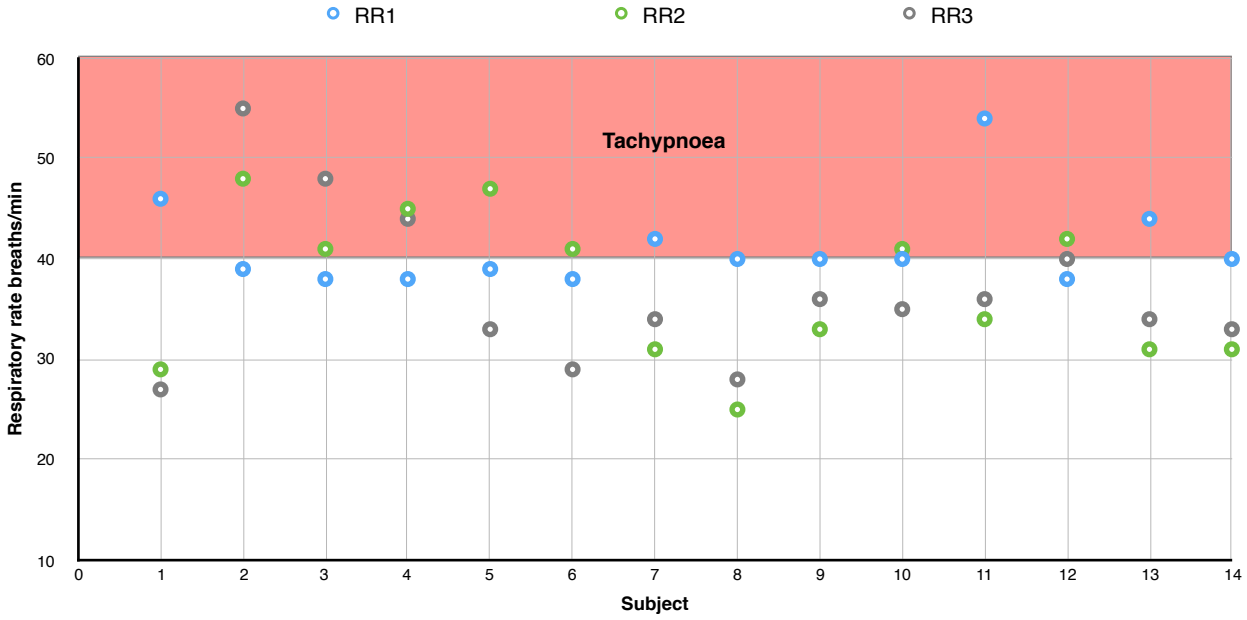


Figure 3.7: Subjects aged 1 - 5 years who were assessed as being tachypnoeic by one or more observers.

3.4.2 Questionnaire study of video recordings

3.4.2.1 Participants

In total 100 healthcare professionals participated in the study. 35% were paediatric trained doctors and 36% paediatric trained nurses. 26% of participants treated children as part of their day to day job but were not solely paediatric trained. The full breakdown of participants is shown in Table 3.12.

Table 3.12: Participant Characteristics (n=100)

Female gender, n	84
Role of participant, n	
Paediatric Nurse Band 5	15
Paediatric Nurse Band 6	10
Paediatric Nurse Band 7 and 8	11
Advanced Nurse Practitioner	19
Emergency Nurse Practitioner	5
Paediatric Specialist Trainee 1-3	15
Paediatric Specialist Trainee 4-8	13
Paediatric Consultant	7
Paramedic	2
Paediatric Healthcare Worker	3

3.4.2.2 Overall agreement

Overall the results showed a fair agreement between observers when a pre-defined ordinal scale was used to assess respiratory rate, with a Fleiss Kappa statistic of 0.333. Within different groups of healthcare professionals there was a similar level of agreement seen, with a Fleiss Kappa statistic for paediatric nurses of 0.334, paediatric doctors 0.365 and other healthcare professionals 0.318.

3.4.2.3 Agreement by video

When analysing the agreement in ratings by video, video 1 and video 2 had the highest level of agreement with a Fleiss Kappa of 0.661 and 0.501 respectively, indicating a moderate level of agreement. Video 4 showed poor agreement with a Fleiss Kappa of 0.176. Figure 3.8 shows the breakdown of responses and Fleiss Kappa statistic for each of the videos.

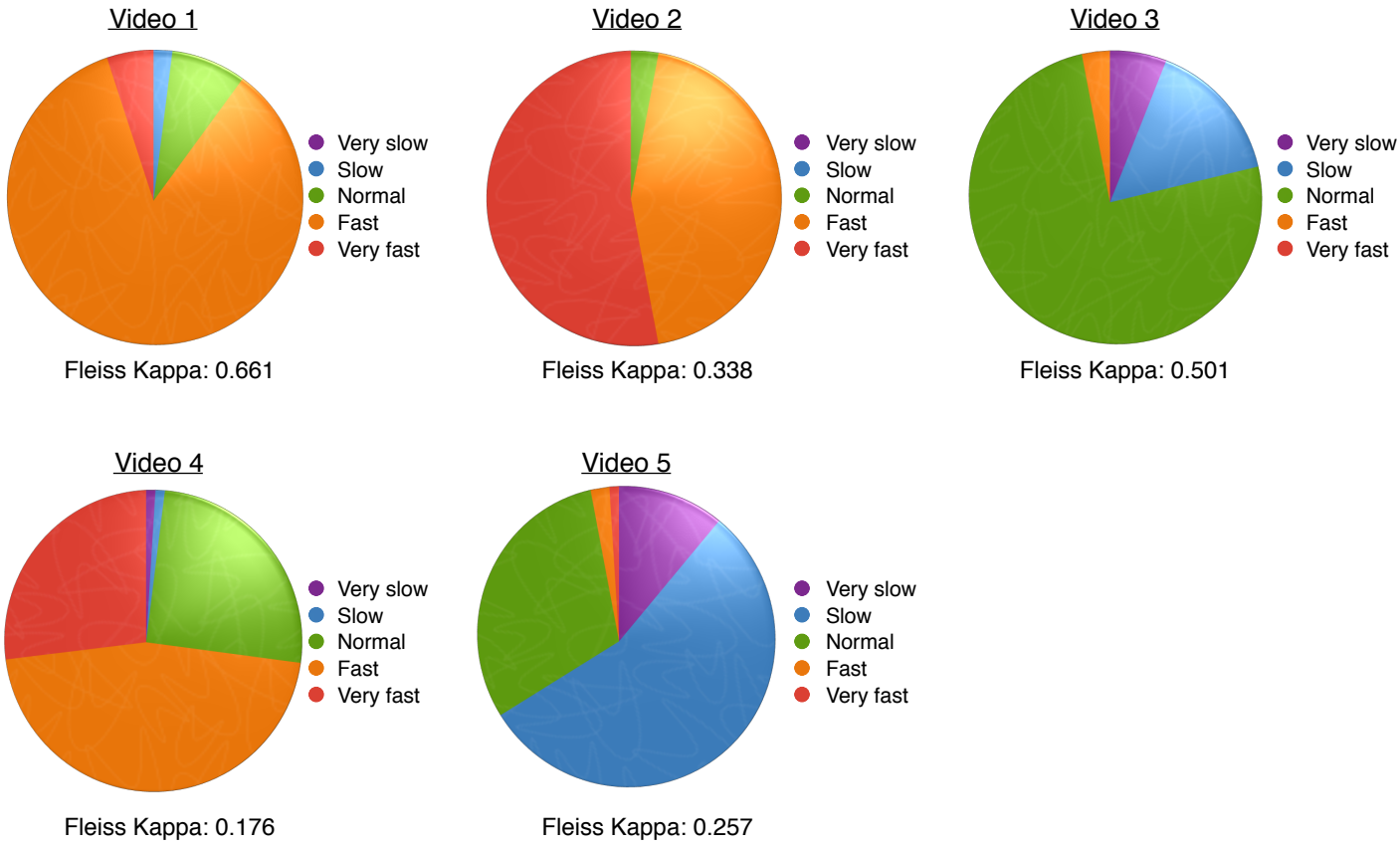


Figure 3.8: Pie charts showing the breakdown of responses for each video with Fleiss Kappa statistic.

3.4.2.4 Difference between healthcare professionals' responses

When analysing the difference in responses based on the healthcare professionals' role there was little difference seen. There was no statistical difference seen between responses from paediatric doctors and paediatric nurses for each of the videos, with all p-values >0.05 (Table 3.13). When analysing responses from HCP with formal paediatric training to those without, there was no significant difference seen in responses to the first four videos (Table 3.14). However there was a statistically significant difference seen in the responses to video 5 (p = 0.010).

Table 3.13: Difference in responses between paediatric doctors and nurses

Video number	p-value
Video 1	0.470
Video 2	0.427
Video 3	0.969
Video 4	0.555
Video 5	0.442

Table 3.14: Difference in responses between paediatric HCP and other HCP

Video number	p-value
Video 1	0.444
Video 2	0.628
Video 3	0.205
Video 4	0.122
Video 5	**0.010**

3.5 Discussion

3.5.1 Agreement in respiratory rate measurements by different observers

This study is the first to exclusively examine the inter-observer agreement of respiratory rate measurements in all children as encountered in day to day clinical practice in the U.K. We have shown from 507 RR recordings that there is poor agreement between measurements when taken by a healthcare professional in usual clinical practice, compared with researchers using the WHO recommended method within 30 minutes. Median RR showed a 4 bpm difference with median measurement from the healthcare professional being 32 bpm and median for the researchers being 28 bpm. This could be explained by measurements often being taken over a duration of 15 seconds in clinical practice and being multiplied by 4, resulting in an overestimate of 4 bpm due to observers invariably rounding values up rather than down.

There was however a wide variability in agreement with 95% limits of agreement indicating that measurements in clinical practice may have varied from 11 breaths below to 18 breaths above the standardised WHO method. There was better agreement between the two researchers taking simultaneous measurements, but even then there was a difference of up to 14 bpm. In children with faster respiratory rates there was an even poorer level of agreement seen than in children whose RR was within normal range, and in only 18% of children did all three observers agree on the presence of tachypnoea.

The available studies to date report a wide range of inter-observer variability in both children and adults (Wang et al., 1992, Wang et al., 1996, Chan et al., 2001, Lim et al., 2002, Liu et al., 2004, Gajdos et al., 2009, Lanaspa et al., 2014). This may reflect the heterogeneity of the studies, with many assessing the variability in RR measurements as part of a wider clinical score. Some studies only looked at small convenience samples and some looked at very narrow age ranges or specific clinical conditions only. Variation in assessments may also exist due to changes in the clinical status of the patient over short periods of time, which many of the studies do not account for, comparing measurements taken up to six or even eight hours later (Wang et al., 1996, Gajdos et al., 2009). Most studies in children report good agreement on the presence of tachypnoea (Wang et al., 1996, Gajdos et al., 2009, Lanaspa et al., 2014) however they have also shown that a single respiratory rate reading can result in misclassifying children as non-tachypnoeic and thus potentially alter their management (Lanaspa et al., 2014). We have attempted to produce a study that could address these issues and bring a more conclusive answer.

Many previous studies analyse and present their data by assessing the correlation between different measurements. Correlation of RR measurements will estimate the degree to which each of the different respiratory rates are associated. However a high correlation does not automatically imply that there is a good agreement between each individual's measurements (Giavarina, 2015). It also does not reveal information about the individual differences between measures. To assess the agreement we conducted a Bland-Altman analysis and assessed the mean difference and

limits of agreement between measurements (Bland and Altman, 1986). We could then examine the extent to which two measurements agreed with each other and also how this level of agreement varied across the range of respiratory rates.

Correlation between the first and second, first and third and the simultaneous second and third RR measurements is high, suggesting that measurements correlate well and there is only a small degree of inter-observer variation between different observers. This is similar to other studies assessing the correlation of RR measurements (Wang et al., 1992, Lanaspa et al., 2014). However there are no such studies in children reporting the actual agreement in respiratory rate measurements. One study in adults (Lim et al., 2002) reported the limits of agreement in RR measurements for the same observer as being -4.86 to 4.94 breaths/min and -5.7 to 5.7 breaths/min for different observers. We report much wider limits of agreement in children. This may be due to the nature of measuring a RR in a child, where the measurement often involves the observation of complex respiratory patterns in uncooperative subjects.

Overall the first measurement appeared to overestimate the RR, reflected by the mean measurements from each observer. This was likely to be due to the method of measurement used. In only 7% of measurements by the first observer was a 60 second respiratory rate count used (WHO standard). These reported values differ significantly from what was reported in chapter 2 of this thesis, where only 30% of nurses reported taking a respiratory rate count over 15 seconds and 37% stated they counted a respiratory rate over 60 seconds.

It is widely known this leads to inaccurate measurements (Berman et al., 1991, Simoes et al., 1991). RR1 was often a nurse and, to save time, nursing staff will often observe a respiratory rate for 15 seconds and multiply the result by 4 to get a value of breaths per minute. This would inevitably lead to an error of up to 4 breaths per minute as the observer would naturally round up rather than down. The agreement between the first and second, and first and third measurements was poorer than that of the simultaneousness measurements. The difference in measurements between the count by the HCP and a WHO standard count could have been anything from 11 breaths less to 18 breaths more per minute. This is potentially a significant level of variation in the context of clinical practice and it may have had clear implications on the sickness score given to the child and also on their subsequent clinical management.

We also showed that the agreement between simultaneous measurements using the WHO recommended method of measurement could have been anything from 7 breaths less to 7 breaths more per minute. Previous studies have reported high correlation between measurements taken over one minute (Simoes et al., 1991, Lanaspa et al., 2014) but they have not explored the agreement. These limits of agreement are significantly better than that between the first and second, and first and third measurements. This once again reiterates the importance of using the correct method of measurement. However, RR remains a somewhat subjective measure and this level of agreement may still hold significance within clinical practice.

The correlation and agreement of measurements also varied within children of different ages. Unsurprisingly the largest difference in agreement in measurements was in children aged 1-2 years followed by children from 0-1 years. This is likely to be due to difficulties encountered in gaining cooperation of the child during the measurement period, resulting in a less accurate measurement and a higher variation.

Importantly, there was no statistical change seen in the agreement when comparing readings closer in time with readings over a longer time interval. The maximum time limit between the first and second/third measurements was 30 minutes, which could potentially produce a variation in measurements as the child's RR may change in this time. However, this upper time limit between measurements remains less than or equal to previous studies (Wang et al., 1996, Gajdos et al., 2009).

Also there was only a small proportion of measurements where the child's activity status changed between the first and second/third measurements. This is important as a change in the child's activity is likely to alter their respiratory rate. However, in those measurements where the child's activity status was reported as being different between measurements, there was no significant difference found in the correlation and agreement Therefore we do not believe that the time difference significantly affected our results.

Perhaps the most important finding from this study is the lack of agreement in the recognition of tachypnoea. 51 children were identified as being tachypnoeic by one or more of the observers but in only 18% of these did all three observes agree. This level of agreement is lower than reported in previous studies (Lanaspa et al., 2014). In these children with faster respiratory rates there was a statistically significant lower level of agreement seen than in children whose RR was within the normal range. Tachypnoea is a key criterion used in assessing the unwell child. This is especially important in developing countries where guidelines for key conditions such as pneumonia rely on tachypnoea in its diagnostic criteria. It is therefore clinically important that tachypnoea is recognised and can be identified accurately with a single RR measurement.

When transferring these RR measurements onto a PEWS chart, as is used in clinical practice, we showed that in children aged 2-12 months it was the HCP who classified the majority of the children as tachypnoeic whereas the other observers did not. This may have had an impact clinically on the child and possibly led to them receiving a higher PEW score. In turn this could have resulted in more intensive management strategies being started including more frequent observations, a medical review or specific treatment being implemented.

The results from this part of the study bring into question our reliance on the accuracy of a respiratory rate measurement, as it is currently measured in clinical practice. In the light of recent recommendations suggesting new reference ranges for respiratory rate (O'Leary et al., 2015) we must remember that this data comes from measurements obtained by healthcare professionals in

clinical practice performing an observed count. Even if many of these measurements were performed using the WHO recommended method there is still a degree of variation that may exist. A robust assessment of the impact that this variation may have on clinical assessment and management of children along with recommendations for improvement of its measurement are needed in the light of these results. A review of education tools and measurement techniques, including introduction of technological solutions is also required.

3.5.2 Questionnaire study of video recordings

This study was the first of its kind to evaluate the agreement in respiratory rate assessments in children between healthcare professionals using a predefined ordinal scale. We showed a moderate to poor agreement when raters used this scale with no difference observed between different groups of healthcare professionals. However at higher respiratory rates there was better agreement observed.

Predefined ordinal scales to assess respiratory rate may be used to increase the reporting of respiratory rate where a count is potentially deemed too time consuming and laborious. Other similar studies in children assessing the use of an ordinal scale have converted a measured RR into a categorical score and then compared the agreement of scores between raters (Wang et al., 1992, Chan et al., 2001, Liu et al., 2004, Gajdos et al., 2009). This does not however fully assess the agreement of individuals when a true ordinal scale is used. One previous study has been conducted in an adult model, and showed substantial agreement with a Fleiss Kappa of 0.750 (Nielsen et al., 2015). However, there was better agreement seen when the raters counted the respiratory rate rather than use the ordinal scale. Our study showed a substantially lower level of agreement than that reported by Nielsen et al. There was also no difference observed when analysing the agreement amongst different groups of healthcare professionals, indicating that not one group agreed with each other more than another.

When separately analysing agreement for each of the videos there were clear differences observed. Video 1, showing a 3 year old girl, showed substantial agreement in responses (Fleiss Kappas 0.661). However video 4 of a 2 week old girl had poor agreement (Fleiss Kappa 0.197). These differences could be due to a number of factors. Both children showed signs of respiratory distress however, only the child in video 1 had an increased respiratory rate outside the normal range. The increased work of breathing observed could have made some healthcare professionals assume that the child's respiratory rate was fast, therefore creating some confusion and less agreement in responses. In addition, the child in video 4 is the youngest shown. Some healthcare professionals may have had less experience in children of this age resulting in a wider variety of responses given.

We were also able to analyse the raters responses to assess the agreement in the recognition of tachypnoea. Tachypnoea is a key criterion used in assessing the unwell child and it is therefore vital healthcare professionals recognise these children. If a 60 second visual count was performed

on each of the videos, two (video 1 and 2) would have been classified as tachypnoeic as per the WHO definition (WHO 2002). Of all of the responses 90% of respondents rated video 1 as fast or very fast and 97% of respondents rated video 2 as fast or very fast. This is encouraging indicating that the majority of the healthcare professionals were able to recognise these children as having a RR above the normal range, and as such would have classified them as tachypnoeic.

Both video 3 and video 4 showed children with a respiratory rate within the normal range (if a 60 second visual count had been performed). For video 3 (15 year old boy), 76% of raters categorised the RR as normal. However, almost one quarter rated it as slow or very slow. This disagreement may in part be due to paediatric trained professionals having less experience with older children who have normal respiratory rates that are slower, and as such believing these are abnormally low. In video 4 the RR was within normal range but there were signs of increased work of breathing which could have influenced the rater when categorising the RR. Only 25% rated this RR as normal, with 73% rating it fast or very fast. This discrepancy is important as a predefined ordinal scale does not account for any signs of increased work of breathing that may be present.

This study has given valuable information about the agreement seen in rating respiratory rates when using a predefined ordinal scale, and in different groups of healthcare professionals. In our study the raters were given no guidance as to what levels of RR should be categorised into which groups, and with a wide age range of children shown, this may in part account for the low level of agreement seen. An ordinal scale may be of use where a standard visual count is not practicable, however the level of agreement found between healthcare professionals is unlikely to be high enough for this method of respiratory rate assessment to be taken and used regularly in clinical practice.

3.6 Limitations

These two studies assessing the reliability of the assessment of a child's respiratory rate had a number of limitations. Firstly both studies were conducted in just one region. Although an appropriate number of participants were selected, results could have been biased by local practices that were particular to the region.

A limitation of our study assessing the agreement in measurements by different observers is that all three measurements were not recorded simultaneously. This would have been possible, but we opted to delay the researchers' observations until the HCP measurement had taken place so that actual clinical practice could be recorded. If the HCP had been aware of the researchers taking the RR simultaneously with them this could have altered their method of measurement and would not have truly reflected their actual practice, leading to a bias in our results. Importantly, there was no statistical change seen in agreement when comparing readings closer in time with readings over a longer time interval.

Another important limitation to take into consideration is the type of children recruited. Although children were recruited from most areas of the hospital, and had a range of illnesses, children that were severely unwell were not included. Having included these children would have given an insight into the accuracy of a RR measurement in an acute setting, which may have differed from that found in those children who were less unwell.

The questionnaire study enabled the agreement of a different method of RR measurement to be assessed. However this study was immediately limited by participants being fully aware of the purpose of the study. Their subsequent assessment of the child's RR may then have been more thorough than used in their standard clinical practice. In addition, the videos shown to the participants did not truly represent a real life scenario. The child's face was not shown and the videos were also subject to lighting and blurring affects. These factors could have increased the difficulty in assessing the child's RR and may not have reflected the situations encountered in everyday clinical practice.

3.7 Conclusions and implications for remainder of thesis

Respiratory rate measurements in children vary significantly between different observers. This is likely to have clear consequences in clinical practice and needs further evaluation. Variability in measurements is even greater in children with high respiratory rates potentially impacting on the recognition and identification of tachypnoea. However, the use of an ordinal scale could potentially be more sensitive in identifying these children. The variability seen between HCPs in clinical practice and observers under research conditions highlights that the inaccurate methods that are being employed at the frontline of clinical care are affecting the reliability of an important vital sign that is relied upon to make critical clinical decisions. For such an important vital sign that is relied heavily upon in everyday clinical practice there clearly needs to be a minimum degree of reproducibility. Paediatric healthcare professionals may benefit from further education on their technique of measuring respiratory rate, with a particular emphasis being placed on performing a measurement over 60 seconds, however, even researchers using the recommended criteria achieved sub-optimal agreement.

These findings have added considerably to the body of evidence on the accuracy of respiratory rate measurements in children. They highlight the need for a robust review of what may constitute a normal respiratory rate and the clinical impact of these inconsistencies in measurements. In the next chapter of this thesis the potential inaccuracies in a respiratory rate measurement must be kept in mind when assessing our current reliance and interpretation of this vital sign. This study also supports the need for the introduction of more objective measures including the use of medical devices. Subsequent chapters of this thesis will explore the development of a novel device to measure a respiratory rate and the agreement reported here can be used to compare and assess the accuracy of this device and its suitability for being used in clinical practice.

CHAPTER 4

RESPIRATORY RATE AS A PREDICTOR OF CLINICAL DETERIORATION IN CHILDREN

4.1 Introduction

The regular measurement and monitoring of a child's vital signs upon admission to hospital is standard and accepted practice (Cooper et al., 2002). These measurements aid clinicians in assessing a child's clinical status and their response to treatment. Many of these vital signs are now incorporated into early warning scoring systems to help try and identify children who may be deteriorating and require intervention (Roland et al., 2014). It is unclear however the extent to which each of these vital signs can be a discriminator of disease severity and a predictor of clinical deterioration (Anderson et al., 2016, Goldhill et al., 2005). The presence of a raised respiratory rate can indicate a number of severe and emergency diagnoses however it still remains unclear if repeated measurements can predict the deterioration of a child.

4.2 Aims

The aim of this study was to assess the value of respiratory rate as a predictor of clinical deterioration in children with a range of clinical conditions. It also aimed to assess the sensitivity and specificity of respiratory rate in predicting deterioration when compared with other vital sign measurements.

4.3 Methods

4.3.1 Study design and setting

This was a retrospective case-control study conducted at a tertiary children's hospital. Children who had deteriorated on a medical or surgical ward and required admission to high dependency or intensive care areas were identified and data about their vital signs were collected.

4.3.2 Participants and eligibility criteria

Subjects were identified from a centrally held hospital database based on pre-defined inclusion criteria (see below). After identifying the subjects from the database each potential subject was further screened using these criteria to ensure they were eligible for inclusion. The study period spanned 24 months from January 2014 to December 2015.

4.3.2.1 Inclusion and exclusion criteria

Patients who were eligible to be subjects were between the ages of 0-16 years with any medical or surgical condition and had been admitted to the Paediatric Intensive Care Unit (PICU) or High Dependency Unit (HDU) following a period of 48 hours or more on an inpatient ward. During this period these children must have had their vital signs measured and recorded on hospital observation sheets. Patients who were admitted to PICU or HDU from another hospital, from the operating theatres, or from a ward area less than 48 hours following initial admission were excluded. Patients whose observation sheets were unavailable to be analysed were also excluded.

4.3.2.2 Control group

Patients were also selected from the hospitals' central patient database to form a control group. They were children (aged between 0-16 years) who were inpatients at the hospital during the same time period as the children who deteriorated. These patients had been admitted to hospital for a period of 48 hours or more and did not require admission to PICU or HDU. Suitable control patients were identified for each identified subject patient. They were matched with the subject patients as far as possible based on their age, gender, diagnosis and hospital ward location. A random number generator was then used to select the particular control patient and the 48 hour period during their admission which would be analysed.

4.3.3 Vital sign measurements

Vital sign measurements collected on each patient included, respiratory rate, heart rate, blood pressure, and PEWS (Paediatric Early Warning Score). All vital sign measurements had been taken by a trained paediatric healthcare professional and recorded on an age appropriate observation sheet. Heart rate and blood pressure were taken using the wards own automated devices. Respiratory rate was counted manually. The technique or method used for taking the respiratory rate measurement was not known. Paediatric early warning scores were calculated by the healthcare professional taking the observations and based on the scoring system stated on the child's observation sheet. Vital sign measurements on all children were taken at varying intervals from every 30 minutes up to every six hours.

The upper limit values used for respiratory rate, heart rate and systolic blood pressure for the different age groups are shown in Table 4.1. All upper limits were taken from the 95th centile values as described by the resuscitation council's Advanced Paediatric Life Support guidelines (APLS, 2016).

a) Respiratory rate 95th centile

Age range	< 3 mths	3-6 mths	6-18 mths	18-24 mths	24-96 mths	96-144 mths	144+ mths
RR (bpm)	50	45	40	35	30	25	24

b) Heart rate 95th centile

Age range	< 3 mths	3-18 mths	18-24 mths	24-36 mths	36-48 mths	48-72 mths	72-96 mths	96-144 mths	144+ mths
HR (bpm)	170	160	155	150	140	135	130	120	110

c) Systolic blood pressure 95th centile

Age range	< 18 mths	18 - 60 mths	60 -144 mths	144 + mths
BP (mmHg)	105	110	120	140

Table 4.1: 95th centile values for respiratory rate (a), heart rate (b) and systolic blood pressure (c) by age range.

4.3.4 Data collection and analysis

Data was gathered from the patients online medical records using the hospital's Electronic Document Management System (eDMS). If the information was unavailable through this source then the child's paper medical records were obtained and the information gathered from here. Data was then inputed into an Excel spreadsheet and included the child's age, gender, diagnosis, initial inpatient ward, admission outcome and each of the vital sign measurements over the particular 48 hour period.

For each patient, once all vital sign measurements were obtained, the 95th centiles for each vital sign, based on the child's age, were identified. Different upper limit thresholds were then calculated based upon the percentage above the 95th centile. For each vital sign upper limit thresholds of 5%, 10%, 15%, 20%, 25% and 30% above the 95th centile were chosen. The vital sign data was then analysed to ascertain if any of the measurements recorded had exceeded the 95th centile and if so by what percentage it had risen above this. The data was analysed in this way as children's RR varies with age and as such they have different 95th centile limits. Therefore, by assessing the percentage above the upper limit this ensured the data could be analysed and presented uniformly for children of all different ages.

4.3.5 Statistical analysis

For each of the vital sign measurements the usefulness of the different upper limit thresholds was examined by calculating the sensitivity, specificity and odds ratio. Positive predictive values (PPV) and negative predictive values (NPV) were also calculated. Sensitivity was the proportion of children who deteriorated requiring admission to PICU/HDU who were predicted to do so by reaching a particular vital sign threshold. Specificity was the proportion of children who did not deteriorate requiring admission to PICU/HDU who were predicted not to deteriorate as they did not reach a particular vital sign threshold level. PPV was the probability that children who reached a particular vital sign threshold would deteriorate and NPV was the probability that children who did not reach a particular vital sign threshold would not deteriorate. Logistic regression analysis was used to determine if the child's age, gender and primary presenting condition were associated with deterioration of the child. Mean PEWS at selected time intervals were also calculated and the Mann-Whitney U test was used to assess any significant difference between mean PEWS, with a p-value of <0.05 indicating a significant difference between groups. All results were analysed using SPSS, version 22.0 for Mac.

4.3.6 Ethical approval

There was no ethical approval required for this retrospective case-control analysis.

4.3.7 Funding

This study received no specific grant from any funding agency.

4.4 Results

4.4.1 The subject group

After an initial screening process of the hospital database 161 patient episodes (154 children) were identified. Following further screening for eligibility 111 patient episodes did not meet the inclusion criteria and were excluded. For a further 10 patient episodes the observation charts were unavailable for analysis from both the electronic and paper records. A total of 40 patient episodes (36 children) were identified for analysis (Figure 4.1).

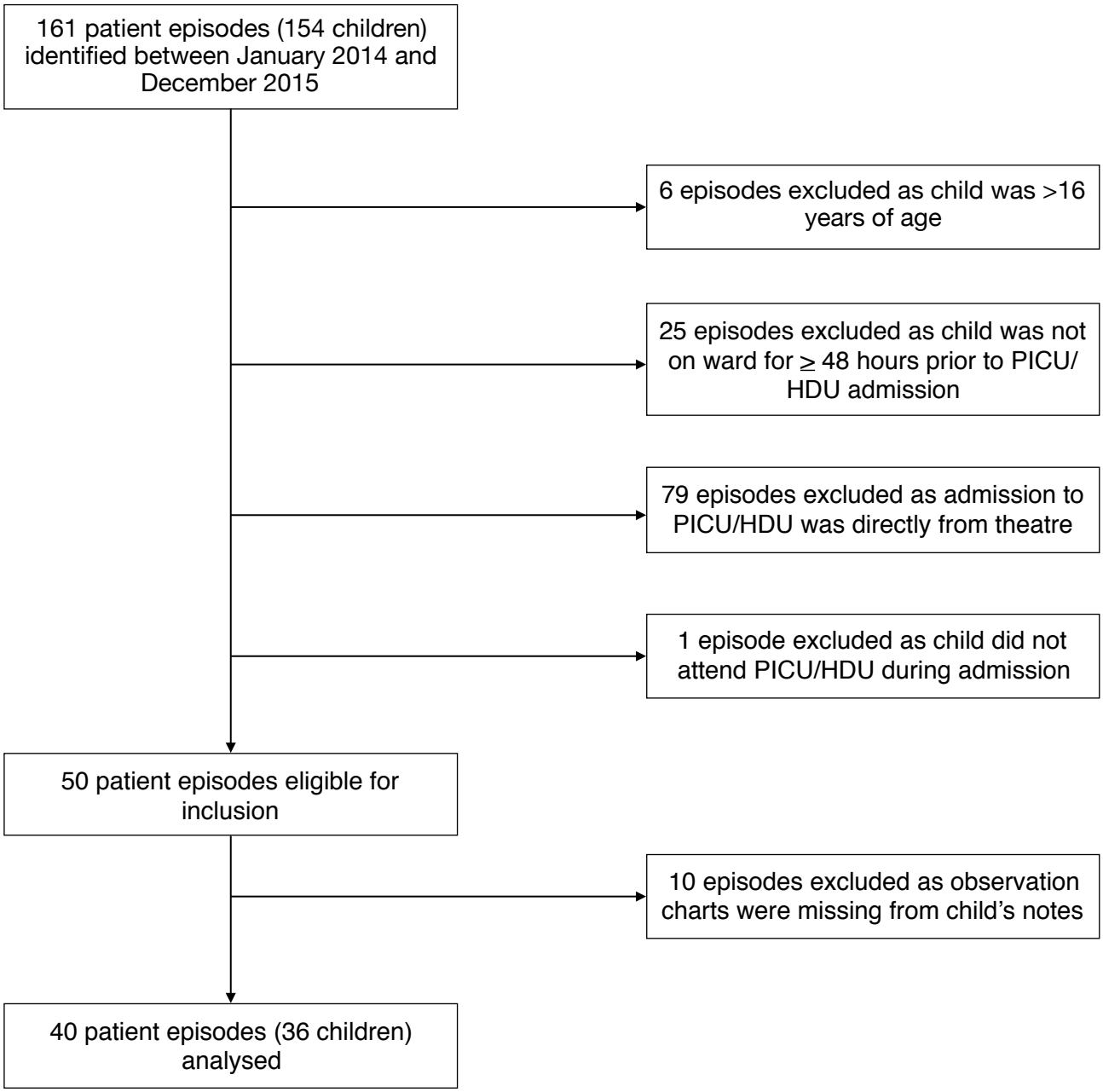


Figure 4.1: Flow diagram showing eligible patient episodes following initial screen.

4.4.2 Demographics

The mean age of subjects was 39 months (range: 7 weeks to 15 years) and the mean age of the controls was 41 months (range: 6 weeks to 15 years). There was a similar male to female ratio in both the subject and control groups of 45% and 47% respectively. The characteristics of the subjects and controls as well as their primary complaint are shown in Table 4.2. Table 4.3 shows the age ranges of the subjects and controls.

Table 4.2: Characteristics of subjects and controls

	Subjects (n=40)	Controls (n=40)
Mean Age (months)	39	41
Male (%)	18 (45%)	19 (47%)
Primary complaint		
Respiratory	25 (62.5%)	20 (50%)
Neurology	2 (5%)	1 (2.5%)
Infection	5 (12.5%)	8 (20%)
Haematology/Oncology	4 (10%)	4 (10%)
Gastrointestinal	0	2 (5%)
Metabolic	3 (7.5%)	2 (5%)
Orthopaedic	1 (2.5%)	3 (7.5%)

Table 4.3: Age range of subjects and controls

Age range	Subjects n (%)	Controls n (%)
0 - 12 months	15 (37.5%)	15 (37.5%)
1 - 5 years	11 (27.5%)	11 (27.5%)
5 - 12 years	13 (32.5%)	13 (32.5%)
12 + years	1 (2.5%)	1 (2.5%)

Of the subject group, 17 (42.5%) were transferred to HDU and 23 (57.5%) were transferred to PICU, four children (10%) died following admission to PICU/HDU. All of the control group survived to discharge. Table 4.4 shows the initial ward areas children were admitted to.

Table 4.4: Initial ward of admission for subjects and controls

Ward area	Subjects n (%)	Controls n (%)
Medical ward 1 (0-4 years)	15 (37.5%)	16 (40%)
Medical ward 2 (4-16 years)	9 (22.5%)	13 (32.5%)
General surgical ward	4 (10%)	2 (5%)
Haematology + Oncology ward	5 (12.5%)	4 (10%)
Neurosciences ward	2 (5%)	1 (2.5%)
Orthopaedics + Plastic Surgery ward	5 (12.5%)	4 (10%)

4.4.3 Vital signs

All children analysed in this study had respiratory rate and heart rate measurements recorded throughout the 48 hour period. However, 12 subjects and 18 controls had no blood pressure measurements recorded during the 48 hour period.

Of the children who deteriorated 3 (7.5%) had a RR that remained within normal limits and 15 (37.5%) had a HR that remained within normal limits throughout the 48 hour period. Of the control group 13 children (32.5%) had a RR that remained within normal limits and 18 children (45%) had a HR that remained within normal limits in the chosen 48 hour period. Figure 4.2 shows bar charts for the percentage of subjects and controls with a RR and HR that stayed within the normal range and reached above certain percentage thresholds.

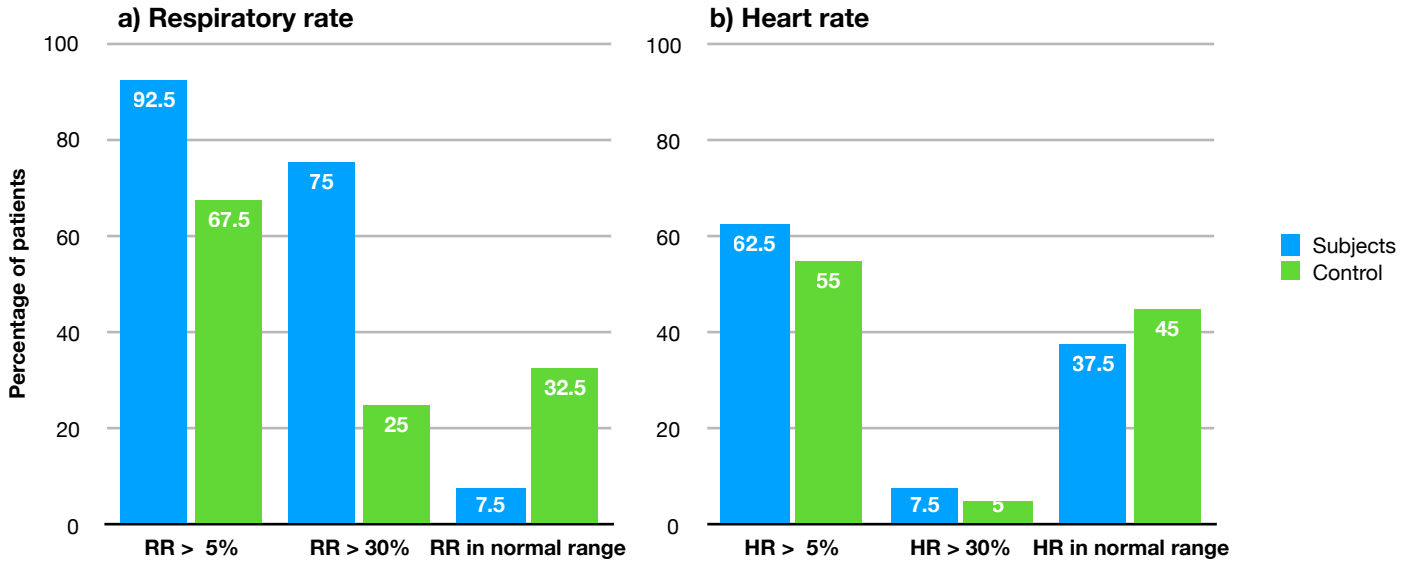


Figure 4.2: Bar charts showing percentage of children with (a) RR and (b) HR within normal limits and above certain threshold levels.

4.4.4 Sensitivity, specificity, odds ratios and predictive values

For each of the vital signs, as the threshold (percentage above the 95th centile) increased the sensitivity decreased and the specificity increased. That is, at a lower threshold limit the majority of the subjects were captured however, many of the controls were also captured. At higher threshold limits very few controls were captured (i.e. 25% at a RR of ≥30% above 95th centile), this was however at the expense of a lower sensitivity. Table 4.5 outlines the sensitivity, specificity, odds ratio and positive and negative predictive values for each of the three vital signs.

Table 4.5: Sensitivity, specificity, odds ratio and positive and negative predictive values for vital sign thresholds

Vital Sign	No. of patients		Sensitivity	Specificity	PPV	NPV	Odds Ratio (95% CI)
	Subjects	Controls					
Respiratory rate (% above 95th centile)							
≥ 5%	37	27	0.925	0.325	0.578	0.813	5.938 (1.540 - 22.904)
≥ 10%	37	24	0.925	0.400	0.607	0.842	8.222 (2.162 - 31.271)
≥ 15%	36	21	0.900	0.475	0.632	0.826	8.143 (2.440 - 27.173)
≥ 20%	35	17	0.875	0.576	0.673	0.821	9.471 (3.067 - 29.242)
≥ 25%	33	14	0.825	0.650	0.702	0.788	8.755 (3.086 - 24.839)
≥ 30%	30	10	0.750	0.750	0.750	0.750	9.000 (3.271 - 24.763)
Heart rate (% above 95th centile)							
≥ 5%	25	22	0.625	0.450	0.532	0.545	1.364 (0.558 - 3.331)
≥ 10%	21	15	0.525	0.625	0.583	0.568	1.842 (0.755 - 4.493)
≥ 15%	13	8	0.325	0.800	0.619	0.542	1.926 (0.695 - 5.335)
≥ 20%	10	6	0.250	0.850	0.625	0.531	1.889 (0.613 - 5.818)
≥ 25%	7	3	0.175	0.925	0.700	0.529	2.616 (0.625 - 10.950)
≥ 30%	3	2	0.075	0.950	0.600	0.507	1.541 (0.243 - 9.755)
Blood pressure (% above 95th centile)							
≥ 5%	12	7	0.429	0.682	0.632	0.484	1.607 (0.499 - 5.170)
≥ 10%	9	4	0.321	0.818	0.692	0.486	2.132 (0.557 - 8.162)
≥ 15%	6	0	0.214	1	1	0.500	13.000 (0.691 - 244.741)
≥ 20%	2	0	0.071	1	1	0.458	4.245 (0.194 - 93.110)
≥ 25%*	1	0	0.036	1	1	0.449	2.455 (0.095 - 63.228)

*BP analysis only completed up to ≥ 25% as no measurements in either group were ≥ 30%

The odds ratios for each of the respiratory rate thresholds were all greater than 1 and the 95% confidence intervals all excluded 1. This indicated that for each of the threshold levels respiratory rate was a significant predictor of deterioration. The odds ratios for heart rate and blood pressure thresholds did not appear to be predictive of deterioration. Although all of the odds ratios were greater than 1, for each of these the 95% confidence intervals all included 1.

There was a clear increase in PPV and a decline in NPV as the RR threshold increased. When a child's RR reached a level ≥30% above the 95th centile for their age there was a 75% chance that the child would deteriorate. Alternatively if a child's RR did not rise ≥30% above the 95th centile for their age then there was a 75% chance that they would not deteriorate. The predictive values for HR were lower for all of the thresholds, in comparison to those for RR, and the NPV all remained around 50 to 55% for each of the thresholds. The PPV for blood pressure increased as the threshold above the upper limit increased, however the NPV all remained between 40% to 50%.

4.4.5 Timing of respiratory rate elevation

For the 37 subjects whose RR did become elevated, this occurred more than 24 hours prior to admission to HDU/PICU for each of the set threshold levels. However, the maximal respiratory rate of the subject during this period was often observed within 24 hours of admission to HDU/PICU. Table 4.6 shows the mean number of hours prior to admission to HDU/PICU that the subjects' RR reached the certain percentage levels above the 95th centile.

Table 4.6: Timing of respiratory rate elevation

Respiratory rate (Percentage above 95th centile)	Mean time before deterioration that elevated respiratory rate first occurred
≥ 5%	39.8 hours
≥ 10%	38.2 hours
≥ 15%	37.2 hours
≥ 20%	36.1 hours
≥ 25%	35.3 hours
≥ 30%	33.9 hours
Maximal respiratory rate	16.8 hours

4.4.6 Confounding factors

It was also important to analyse whether any other factors such as age, sex or primary condition were associated with deterioration of the child. These factors may have confounded the possibility of the association between a raised respiratory rate and the subsequent deterioration of the child.

4.4.6.1 Age and sex

To determine if age and sex were associated with deterioration of the child we performed a logistic regression analysis (Table 4.7) entering age, sex and a RR threshold of ≥30% above the 95th centile. This respiratory rate threshold level was chosen as at this level false positives were limited without a significant drop in the sensitivity.

Table 4.7: Logistic regression predicting deterioration of a child from age, sex and a RR ≥30%

Variable	Beta coefficient	Standard error	p-value	Odds Ratio (95% CI)
Age	-0.001	0.006	0.903	0.999 (0.988 - 1.011)
Gender (female)	-0.782	0.552	0.157	0.458 (0.155 -1.351)
Respiratory rate ≥30% above 95th centile	2.275	0.554	<0.001	10.756 (3.632 - 31.856)

From the regression analysis only respiratory rate was a significant independent predictor of deterioration (p-value <0.001). Both age and gender were not significant in predicting the deterioration of a child and as such did not confound our results.

4.4.6.2 Primary condition

We also performed a logistic regression analysis to establish whether the primary condition of the child predicted subsequent deterioration. There were 25 subjects who deteriorated due to a primary respiratory condition (mean age 37.8 months). In the control group there were 20 children who had a primary respiratory condition (mean age 23.5 months). On performing logistic regression analysis (Table 4.8) the clinical condition of the child (respiratory condition or not) was not a significant independent predictor of deterioration (p-value 0.260). A respiratory rate ≥30% above 95th centile remained a significant predictor of deterioration (p-value <0.001).

Table 4.8: Logistic regression predicting deterioration of a child from clinical condition and RR ≥ 30%

Variable	Beta coefficient	Standard error	p-value	Odds Ratio (95% CI)
Clinical condition (respiratory)	0.413	0.590	0.484	1.511 (0.476 - 4.798)
Respiratory rate ≥30% above 95th centile	2.370	0.586	<0.001	10.699 (3.395 - 33.714)

4.4.7 Paediatric early warning scores

Eight children (3 subjects and 5 controls) did not have a paediatric early warning score recorded during the 48 hour period of observations that were analysed. The mean PEWS for subjects increased as the time to admission to PICU/HDU reduced. The mean PEWS for controls did not change significantly during the 48 hour period. There was a statistically significant difference in

the mean PEWS at each of the selected time intervals apart from the initial PEWS. Table 4.9 shows the mean PEWS at these different time periods.

Table 4.9: Mean paediatric early warning score at different times during admission

	Subject	Control	Significance (p value)
Overall mean PEWS	4.51	1.57	<0.001
Initial mean PEWS	3.29	2.13	0.066
Mean PEWS at 24 hours	4.39	1.44	0.010
Mean PEWS at 48 hours	7.17	1.00	<0.001

4.5 Discussion

This study provides significant evidence that changes in respiratory rate can identify and predict children that may be at risk of deterioration, and is superior to other vital signs. Of the subjects who deteriorated requiring admission to HDU or PICU 75% had at least one recorded respiratory rate that was ≥30% above the 95th centile for their age. An elevated respiratory rate was the only vital sign whose odds ratios was significant at each threshold level above the 95th centile, with any rise in RR often occurring more than 24 hours prior to the child's deterioration. Neither the age, sex or primary condition of the child were significantly associated with deterioration.

The results from our study support the findings of other such studies performed in adults (Fieselmann et al., 1993, Subbe et al., 2003, Goldhill et al., 2005, Cretikos et al., 2007). Fieselmann et al reported that 54% of adults requiring cardiopulmonary resuscitation (CPR) had a RR that was >27 breaths/min (35% above adult upper limit) in the preceding 72 hours (Fieselmann et al., 1993). Schein et al reported similar findings where new-onset tachypnoea preceded a cardiac arrest in 33-55% of adult patients (Schein et al., 1990). However, although evidence from the paediatric literature has also suggested an important role for respiratory rate in predicting deterioration in children (Van den Bruel et al., 2010, Opiyo and English, 2011), none of these studies have shown such clear associations as those demonstrated in our study.

4.5.1 Sensitivity, specificity and odds ratios

When comparing respiratory rate with both heart rate and blood pressure there was a clear difference in the sensitivities, specificities, positive and negative predictive values and odds ratios. All of the odds ratios for the differing respiratory rate thresholds were significant (95% confidence intervals >1). The odds ratios for BP and HR were all greater than 1, however the 95% confidence all crossed 1 and for BP they were extremely wide.

In analysing the different respiratory rate threshold levels, a cut off of ≥30% above the 95th centile appeared significant. At a RR above this level 75% of the children who would deteriorate would be detected and 25% of children would be falsely identified as going to deteriorate (specificity: 75%). These children whose RR exceeded ≥30% above the 95th centile were nine times more likely to deteriorate than children whose RR did not rise this high. In comparison, Fieselmann et al recommended a RR threshold of >27 breaths/min to identify adult patients who may arrest (Fieselmann et al., 1993). Comparatively the sensitivity at this threshold was only 54% however, the specificity was 89% and the odds ratio six. Despite this poor sensitivity the false positive rate was only 11%, meaning at this level only 11% of patients would be falsely identified as potentially deteriorating, which may be more acceptable if used in clinical practice.

Heart rate threshold levels were significantly worse at predicting patients' deterioration than those for RR. For each of the different heart rate threshold levels the sensitivities were lower than those for respiratory rate. However the specificity at the higher threshold values were higher than those

seen for RR, and as such there were minimal false positives. However this was at the detriment of a significantly reduced sensitivity, and at a HR ≥30% above the 95th centile only 7.5% of those children who were going to deteriorate would be identified. The odds ratio for the heart rate thresholds were also a lot lower than those for RR, with the highest odds ratio showing just over a two and a half fold increase in the likelihood of deterioration when the HR increased to a level ≥25% above the 95th centile. The confidence intervals also all crossed 1 at every threshold level. This therefore questions the significance of any rise in heart rate predicting deterioration in children. In a previous adult study a heart rate >100 bpm (above normal adult upper limit) was present in 36% of adults who went on to suffer cardiac arrest (Castagna et al., 1974). Our study showed greater sensitivity levels than this when the heart rate rose above the upper limit of normal, however it is difficult to fully make comparisons between such varied data sets from both adults and children.

Blood pressure was the least well documented of all of the vital signs with 45% of controls and 30% of subjects not having a single blood pressure measurement taken. This may reflect the difficulties encountered when trying to obtain a BP reading on a child, or possibly the healthcare professionals under reliance or perceived lack of importance of this particular vital sign. The BP in both controls and subjects was rarely measured ≥20% above the 95th centile. The sensitivity of BP was poor at all threshold levels and although the specificity was high, this reflects the limited number of measurements obtained. The odds ratios varied at each threshold level with wide 95% confidence intervals that all overlapped 1. This suggests that a rise in BP was not statistically significant in predicting deterioration in children. However, with such limited documentation of blood pressure measurements, these results must be interpreted with caution.

4.5.2 Confounding factors

Neither age, sex or clinical presentation of the child were associated with the risk of deterioration. This is likely to be due to the mechanism by which illness induces a raised respiratory rate. Many disease states such as acidosis, sepsis, hypovolaemia and raised intracranial pressure, induce hypoxia and hypercarbia which in turn leads to an increase in tidal volume and respiratory rate (West, 1990). Therefore many serious disease states, not only primary respiratory conditions, may induce tachypnoea prior to the deterioration of the child which will also be unaffected by the age and sex of the child.

4.5.3 Timing of elevation

The timing of the elevation of the child's respiratory rate was also of importance. For each of the set RR thresholds the child's RR reached this more than 24 hours prior to admission to HDU/PICU. Although the mean time to reach the peak RR was 16.8 hours prior to HDU/PICU admission, this is still of clinical significance. These findings are similar to that of Fieselmann et al (Fieselmann et al., 1993) who found that in 88% of their adult patients who deteriorated requiring CPR, the first significantly elevated RR occurred over 24 hours prior to their arrest. This gives

further evidence that there is a rise in respiratory rate a considerable time before the child deteriorates. Therefore there may be time leading up to deterioration, during which further evaluation and intervention may be taken, based on an elevated RR, that could potentially prevent this subsequent deterioration.

4.5.4 Paediatric early warning scores

In many hospitals, respiratory rate is incorporated into an early warning scoring system along with other vital signs. Respiratory rate is the most commonly used criteria within paediatric early warning scoring systems (Roland et al., 2014). However, on many occasions PEWS was not calculated at each set of observations, and for eight children there was no PEWS calculated at all during the 48 hour recording period. The mean PEWS for subjects was statistically significantly higher over the 48 hour period than for the controls. The mean PEWS was also higher for subjects at 24 hours and 48 hours (just prior to admission to HDU/PICU), however there was no statistically significant difference in scores at the start of the analysis period (48 hrs prior to deterioration). This gives further indication of the value of a PEWS system in identifying children who may deteriorate. However, again caution must be taken in drawing too many conclusions from this data due to the number of episodes where a PEWS was not documented at the point of taking the child's observations.

4.6 Limitations

Our study had a number of limitations which need to be taken into account when interpreting these results. Firstly this was a retrospective analysis with no calculated sample size. The end point of admission to HDU/PICU which was used to identify subject patients could also have been misleading. This is potentially quite subjective as there were no specific criteria for admission to HDU/PICU and this was decided upon solely by the accepting intensive care team. However, using a definitive end point such as cardiac or respiratory arrest would not have captured as many subjects during the specified time period.

The quality of the recording and documenting of observations may also have influenced the results. Not all observations were documented for each patient during the 48 hour recording period and many measurements were omitted. Also, particularly relevant to RR, errors in measurement techniques could have reduced the accuracy of the measurement obtained and again affected the data collected.

Finally, this was a single centre study at a tertiary hospital and our reported results may not be generalisable to other hospitals. Also the selected 48 hour recording period for the control group may have unintentionally not been representative of the paediatric population as a whole. Ideally a multi-centre prospective study where controls could be more thoroughly matched would be needed to further validate our findings.

4.7 Conclusions and implications for remainder of thesis

Respiratory rate is a powerful predictor of clinical deterioration in children. Despite concerns about the subjective nature of its measurement, respiratory rate appears to be superior to both heart rate and blood pressure in identifying and detecting children at risk of deterioration. The age and sex of a child does not confound this association and the clinical presentation of a child does also not appear to predict deterioration. A raised respiratory rate also occurs well in advance of the child being admitted to a high dependency setting and therefore if targeted early, through more frequent clinical reviews or more aggressive medical management, could prevent subsequent deterioration. Respiratory rate is already included in many paediatric early warning scoring systems but it is clear from our study that a greater weighting and importance should be placed on this vital sign.

However, caution must be taken in responding to every raised RR in a child. A respiratory rate greater $\geq$30% above the 95th centile could identify a significant number of children who are going to deteriorate without capturing many children who will not. Future prospective studies are needed to further validate such threshold levels that may identify children at risk of deterioration early, target resources better, and ultimately lead to improved patient outcomes.

The data presented in this chapter further emphasises the importance of respiratory rate measurements in clinical practice. It also increases the importance of the findings from the two previous chapters and should make us more intent on gaining accurate and reproducible respiratory rate measurements. One solution to this is by the introduction of a medical device that could replace current measurement methods, increasing accuracy, reducing variability and enabling us to place more reliance upon this vital sign.

CHAPTER 5

TESTING AND DEVELOPMENT OF A CONTACTLESS DEVICE TO MEASURE RESPIRATORY RATE

5.1 Introduction

There are convenient electronic devices for the measurement of many of the vital signs. Not only do these provide accurate measures, they also provide healthcare professionals with a prompt to measure. Although devices for measuring respiratory rate exist (Al-Khalidi et al., 2011a), they are used mainly in the intensive care, post-operative or sleep study setting, none have entered everyday clinical practice in the acute assessment of patients. Many of these devices require body contact, (Freundlich and Erickson, 1974, G. Moody, 1986, Wertheim et al., 2009) which may not be practical and could be distressing to the patient, and inadvertently increase their RR. Non-contact devices have also been developed but can require complex equipment, (Abbas et al., 2011) be expensive to use and set up and impractical for most clinical settings (Droitcour et al., 2009, Arlotto et al., 2014). Devices using wireless technology have also been developed (Chan et al., 2013b) but these have focused on continuous monitoring of RR rather than acute assessment, and most are yet to be evaluated in the clinical setting.

5.2 Aims and hypothesis

The aims of this section are to test and develop a non-contact device to measure respiratory rate, the Contactless Portable Respiratory Rate Monitor (CPRM). The pilot studies contained within this section aim to provide information on the accuracy, reliability and usability of this device in a variety of settings and on different subject groups. We hypothesise that the device will be more effective and reliable in measuring respiratory rate than the existing available methods.

5.3 The contactless portable respiratory rate monitor

The contactless portable respiratory rate monitor is a non-contact, hand-held respiratory rate monitor. It is a small battery powered unit that contains a temperature sensing self-heating thermistor and consists of two parts, an interface unit and base unit. The device has two patent applications (GB application and PCT application).

5.3.1 Development and funding

The CPRM was developed by a collaborative group from Sheffield Hallam University and Sheffield Children's Hospital. A clinical problem was identified from an audit of practice at Sheffield Children's NHSFT against NICE standards in 2007. Only 58% of children presenting to the Emergency department with fever had a RR recorded on arrival (Burke 2007), compared to the NICE standard of 100% (NICE, 2007a).

In order to establish why RR was not recorded, a focus group was held with nurses from the emergency department, who highlighted the difficulties and perceived inaccuracies in recording RR in the triage setting. It was suggested that due to the variety of the manual methods used and the nature of work in the department, the recording of RR may not be accurate. The observation

that all other physiological parameters were measured using a portable device except RR was made.

A collaboration between Sheffield Hallam University and Sheffield Children's Hospital that had been ongoing for 6 years working in transitional research then set about to develop a non-contact device to record RR in the triage setting. The CPRM prototype was based on novel technology incorporating a self-heating ultra-sensitive thermistor and was designed and manufactured at Sheffield Hallam University within the department of arts, computing, engineering and science led by Professor Reza Saatchi. The development of the device was supported by a National Institute for Health Research (NIHR) Invention for Innovation grant (II-LB-0712-20004) for £180,000, which was awarded in November 2012.

Described in this section of the thesis is the clinical validation phase of the project to inform on the further future development of the device.

5.3.2 The interface unit

This section of the device converts the exhaled airflow to an electrical signal. It consists of a detachable air inlet funnel, a heat chamber containing a self-heating thermistor and a switch to start recording (Figure 5.1).

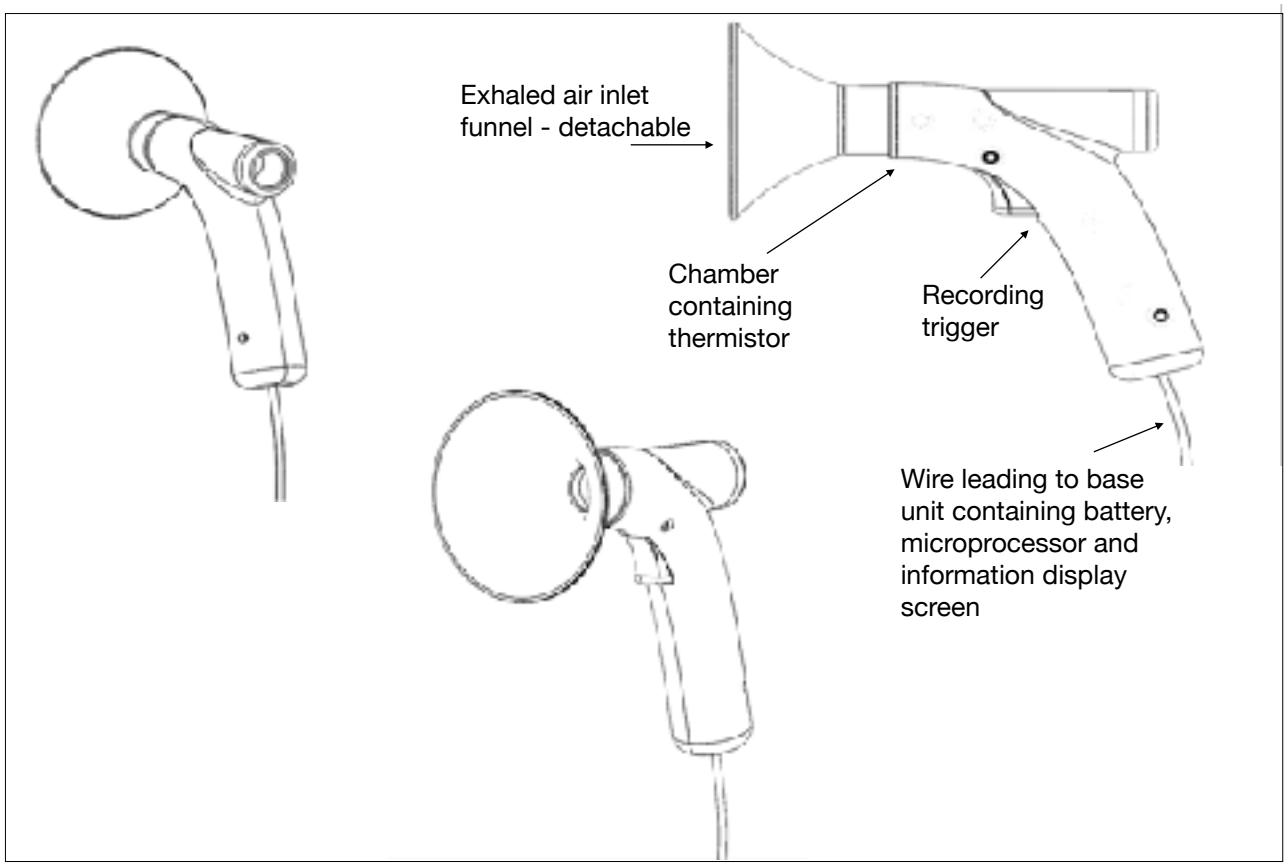


Figure 5.1: Diagram of the CPRM interface section

5.3.3 The base unit

This unit receives the electrical signal from the interface unit and converts it to a respiration rate that is then displayed on its screen. It contains a rechargeable battery, an electronic circuit to filter and amplify the respiration signal, a microprocessor board to digitise the amplified signal and perform the respiration rate calculation and a liquid crystal display unit to display the information (Figure 5.2).

5.3.4 The CPRM components

The casing of the device is made from a tough PVC material (Figure 5.3). The unit has a commercially available rechargeable battery housed within the base unit. The battery lasts up to five hours and is charged using a commercial battery charger. The electronic components of the unit are all widely available commercial components used extensively in the electronic industry. The software is written in C-language.

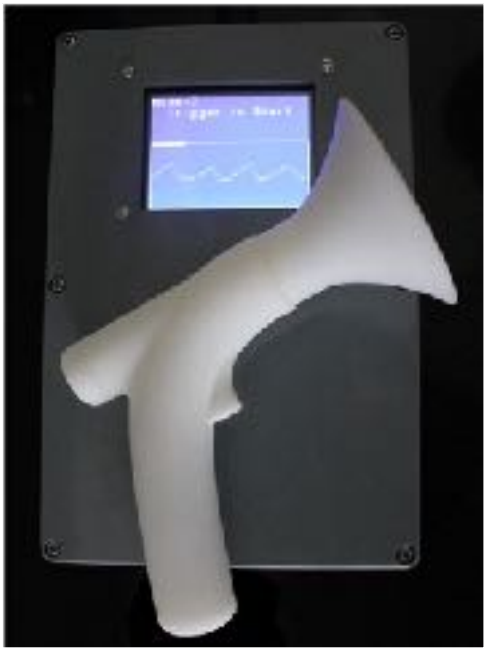


Figure 5.2: CPRM interface and base unit

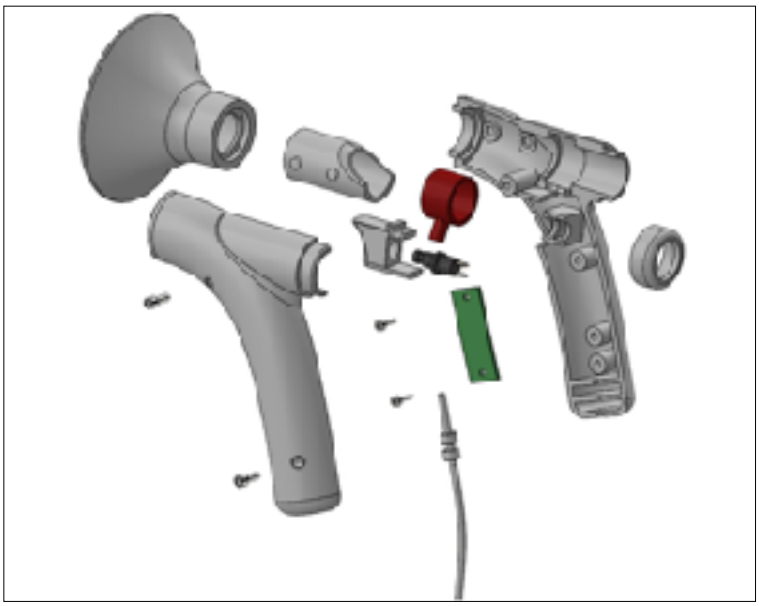


Figure 5.3: CPRM components

5.3.5 The CPRM funnels

During the manufacturing and development process of the CPRM a number of funnels were produced and tested in the laboratory setting. The funnels were designed to enhance the respiration signal from the subject by channeling the subject's breath to the thermistor more effectively. Four funnels were selected to be taken forward to the clinical validation phase of testing and are described within the individual pilot studies.

5.3.6 Obtaining a respiratory rate measurement

The CPRM uses thermal anemometry to measure instantaneous fluid velocity. The funnel attached to the device assists in guiding the subject's breath into the unit. The thermistor within the device detects the rate of heat loss by a change in resistance and this forms the measurement signal. This signal is passed through signal processing software to exclude background noise and to derive a signal which indicates the variation in fluid velocity. Within a micro-controller the analogue signal is digitised and passed through a signal processing algorithm. This extracts the dominant frequency and passes it as a numerical value that is displayed on the integrated screen. The measurement is taken over 52 seconds and the respiration rate in breaths per minute is calculated and displayed.

5.3.7 Using the CPRM

The device is switched on from a switch on the side panel of the base unit. The interface is then held up to 15 centimetres from the subject's face, in front of the nose or mouth (Figure 5.4). The display screen on the base unit shows the respiration signal being picked up. The interface is then moved around in front of the subject's face until a regular consistent waveform is seen on the base unit display screen (Figure 5.5). Once an adequate respiration signal is established the start button on the interface unit is pressed once and then released, the recording then starts. During the measurement period a message on the display indicates that a recording is in progress and a countdown timer indicates how long is left. Once the recording is complete a buzzer sounds and the respiration rate in breaths per minute is displayed on the screen.

Figure 5.4: The CPRM in use in a child

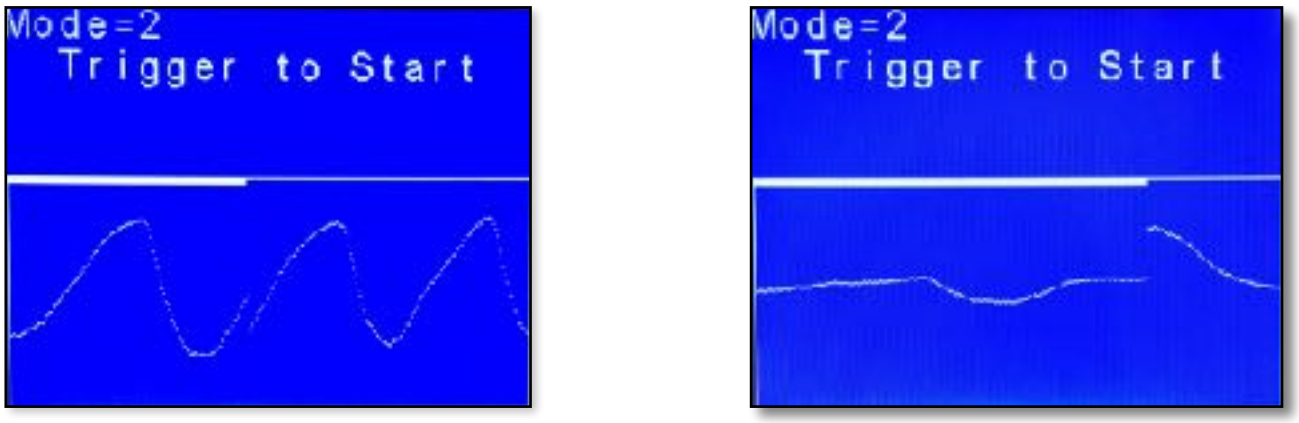


Figure 5.5: CPRM respiration signals. The image on the left shows a good respiratory signal with regular consistent waveforms. The image on the right indicates a poor respiration signal with no clear waveforms present.

5.4 The research questions

The research questions which these studies aim to answer include:

- Can the contactless portable respiratory rate monitor accurately measure respiratory rate in both adults and children?
  - What level of agreement and correlation is there between the CPRM and an established contact method of measuring respiratory rate?
  - What level of agreement and correlation is there between the CPRM and a visual counting method of measuring respiratory rate?
- Which funnel attachments for the CPRM are most accurate and in which subjects?
- Is there any variability seen between CPRM measurements taken by different users?
- How useable and reliable is the CPRM in different settings?
- What modifications and improvements are needed to further develop and enhance the CPRM?
- Can the CPRM supersede current methods for measuring respiratory rate?

In order to answer the research questions set out above we have designed a number of pilot studies, these are as follows:

1. Pilot study A: Analysis of the CPRM in healthy adults, including analysis of different funnel attachments.
2. Pilot study B: Analysis of the CPRM in healthy children, including analysis of different funnel attachments and assessment of reproducibility.
3. Pilot study C: Analysis of the CPRM in healthy children in a primary school.
4. Pilot study D: Analysis of the CPRM on sleeping children undergoing polysomnography sleep studies.
5. Pilot study E: Analysis of the CPRM in the pre-hospital setting including:
   i. Children attending a Paediatric Emergency Department
   ii. Children and adults attending a General Practice Surgery
   iii. Children and adults treated by the Yorkshire Ambulance Service

5.5 Pilot Study A

Analysis of the CPRM in healthy adults including funnel analysis

5.5.1 Aims

To evaluate the agreement in respiratory rate measurements between the contactless portable respiratory rate monitor and existing methods in healthy adult volunteers. To also analyse different detachable funnels that connect to the CPRM.

5.5.2 Methods

5.5.2.1 Study design and setting

This was a prospective feasibility pilot study conducted at Sheffield Children's Hospital.

5.5.2.2 Participants and eligibility criteria

We enrolled a convenience sample of 20 healthy adult volunteers working at Sheffield Children's Hospital. The inclusion criteria for participants was any adult working at Sheffield Children's Hospital who was available to participate at a designated time. The only exclusion criteria was if the participant was unable to speak or read English.

5.5.2.3 Methods of measurements

The respiratory rate of each participant was measured simultaneously by three different methods. Respiratory inductance plethysmography (RIP) was used as the established contact method and our gold standard. Visual counting of chest movements represented the established non-contact method, and method used in most clinical settings. The contactless portable respiratory monitor (CPRM), which is the new method, was the experimental method. Seven to eight data sets were collected for each participant.

5.5.2.4 Instruments

5.5.2.4.1 Contactless portable respiratory rate monitor

The CPRM (described in Section 5.2) was held at a distance of 10 to 15 centimetres from the participant's face and positioned so that maximal exhaled breath was collected and an adequate signal obtained. Four differently shaped funnels (Figure 5.6) were attached to the CPRM and two measurements were made with each funnel.

Funnel A

Funnel B

Funnel C

Funnel D

Figure 5.6: The 4 detachable funnels used with the CPRM.

5.5.2.4.2 Respiratory inductance plethysmography

Thoracic and abdominal respiratory inductance plethysmography bands (zRIP inductance effort belts) were used to capture and record respiratory signals from the participants. Data was recorded on the SOMNOtouch RESP portable screening device (S-Med, Birmingham, UK) and downloaded for visual analysis. To determine the RIP respiratory rate, the number of observed respiration cycles from this respiratory signal was counted manually during the time period at which the simultaneous measurements were taken.

Respiratory inductance plethysmography was chosen as our gold standard measurement as it remains the recommended method used in monitoring sleep disorders in children (RCPCH, 2002), it has also been used as the comparative method of RR measurement in many previous studies validating RR devices (Olsson et al., 2000, Droitcour et al., 2009, Al-Khalidi et al., 2011c).

5.5.2.4.3 The visual counting method

Visual counting of respiratory rate was performed by a separate observer. A count of observed chest movements over the same time period as the other measurements were being taken was made.

5.5.2.5 Data collection and procedure

Each participant was assigned a unique identifying number based on the order that they were recruited. Data on the participants age and sex was collected. Measurements were made at rest with subjects sitting upright comfortably in a chair. At a defined starting time the respiratory rate was simultaneously taken by each of the three methods for a period of 52 seconds. One observer measured RR with the CPRM, and another observer measured using the visual counting method. Figure 5.7 summarises this process. All measurements were converted to breaths per minute and this data was then entered into an Excel spreadsheet.

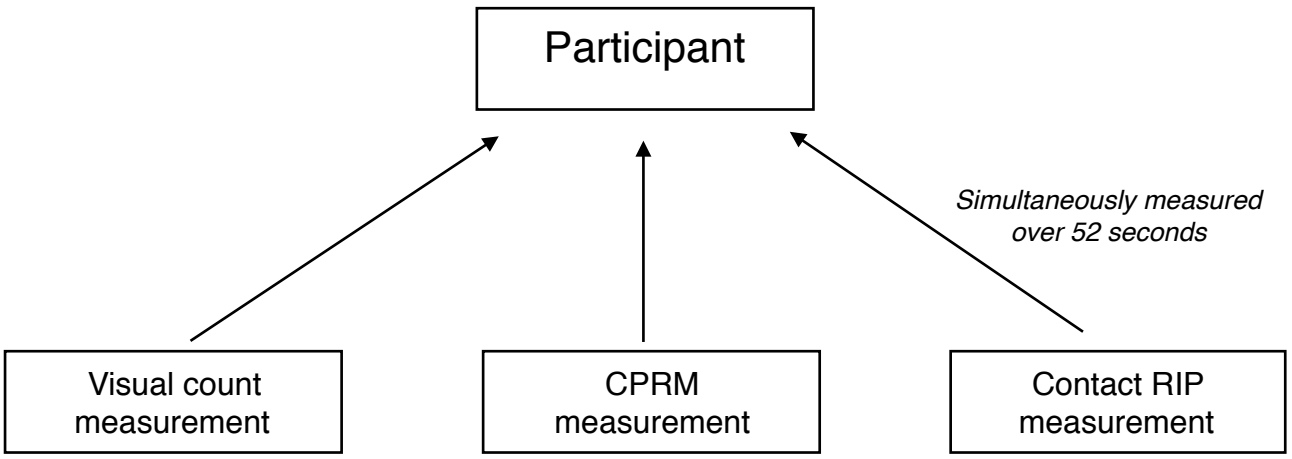


Figure 5.7: Summary of the measurement process for each participant.

5.5.2.6 Statistical analysis

The pairwise agreement between RR counts from each of the three methods was assessed by calculating the mean difference and 95% limits of agreement (mean $\pm$ the standard deviation of the difference). These were charted using Bland-Altman plots (Bland and Altman, 1986). Intraclass correlation coefficients with 95% confidence intervals were also reported. All results were analysed using SPSS, version 22.0 for Mac.

5.5.2.7 Ethical approval

The study received a favourable ethics opinion by the NRES committee Yorkshire and the Humber on 15/9/14, REC reference 14/YH/1137 (appendix 8.3). Written consent was obtained from each individual prior to participation.

5.5.2.8 Funding

This study received no specific grant from any funding agency.

5.5.3 Results

5.5.3.1 Study subjects

A total of 159 respiratory rate measurements were made on 20 healthy adult subjects. Participants ages ranged from 20 to 42 years, with a mean age of 31 years. 14 subjects were female (70%).

5.5.3.2 CPRM compared with contact method

Bland-Altman plots were used to assess the pairwise agreement between measurements from the CPRM and RIP by analysing the mean difference and standard deviation of the difference (Figure 5.8a). The mean difference was -0.494 with 95% limits of agreement of -7.204 to 6.216. This suggests that the CPRM may read up to 7 breaths/min below and 6 breaths/min above the RIP method. The correlation of measurements was moderate, ICC: 0.568 (95% CI 0.453 - 0.664). Figure 5.8b shows the scatterplot of the correlation between CPRM and RIP measurements.

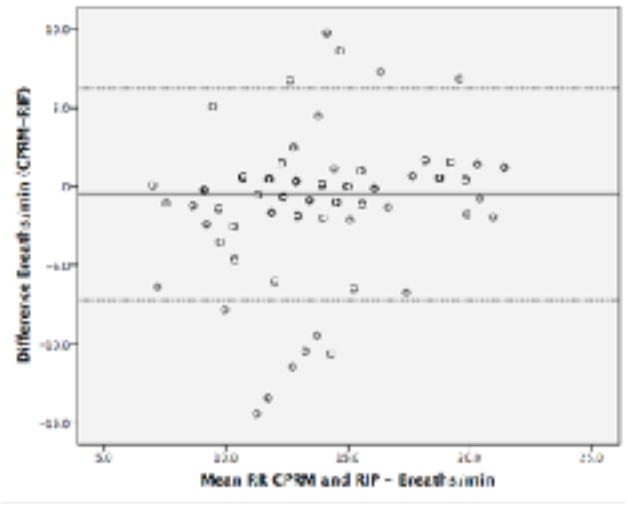


Figure 5.8a: Bland-Altman plot showing the pairwise agreement between CPRM and RIP measurements.

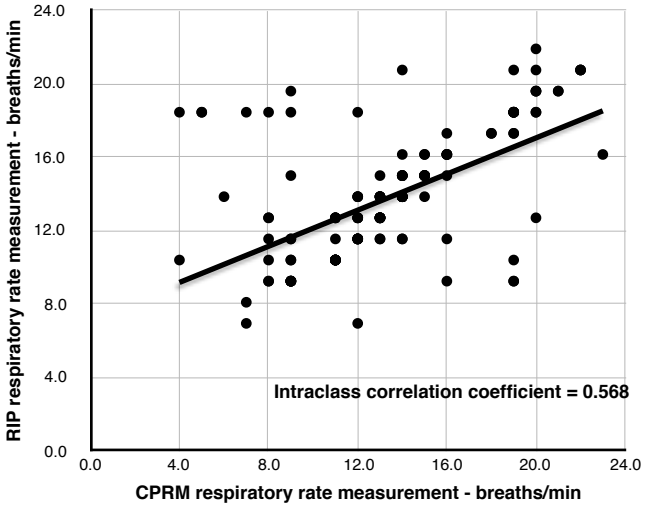


Figure 5.8b: Scatterplot of correlation between CPRM and RIP measurements. ICC also show.

5.5.3.3 CPRM compared with visual counting method

When the CPRM was compared with the visual counting method the mean difference was -0.632 with 95% limits of agreement between -7.333 and 6.068. There was again moderate correlation, ICC 0.560 (95% CI 0.443 - 0.659). Figure 5.9 shows the Bland-Altman plots and scatterplots assessing the agreement and correlation between CPRM and visual counting measurements.

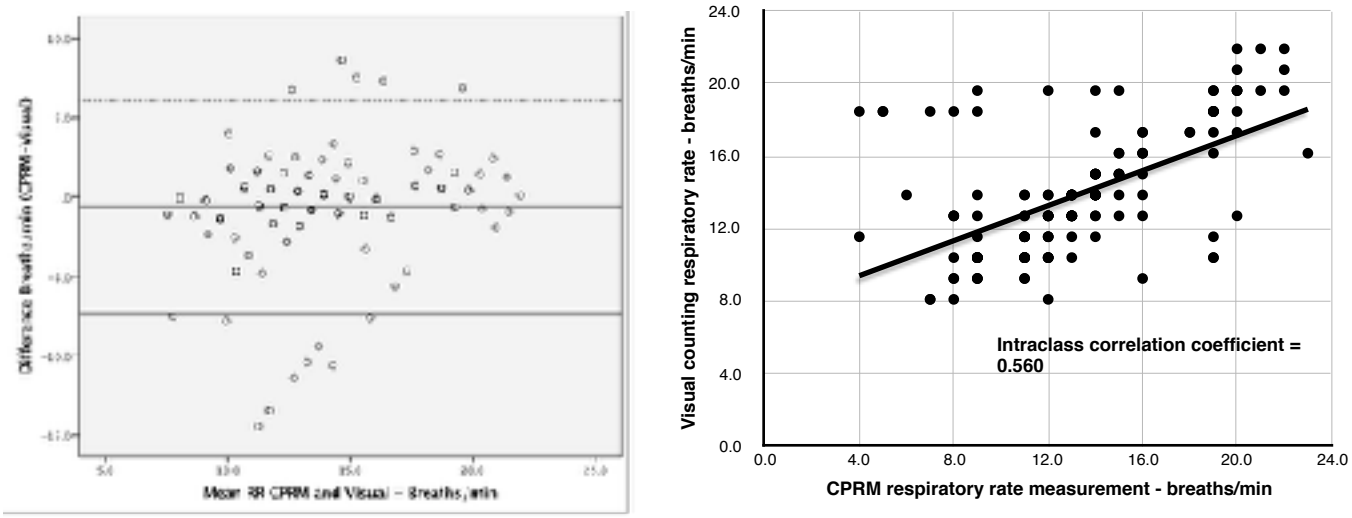


Figure 5.9: Bland-Altman plot and scatterplot of correlation and agreement between CPRM and visual count RR measurements.

5.5.3.4 Analysis of CPRM funnels

Data was also analysed separately for each air inlet funnels. Funnel C showed the highest agreement and correlation with both RIP and standard visual counting methods. The CPRM with Funnel C, when compared with RIP measurements, had a mean difference of -0.238 and 95% limits of agreement -3.941 to 3.465. The intraclass correlation coefficient was 0.841 (95% CI 0.720 - 0.912). Figure 5.10 shows Bland-Altman plots and scatterplots assessing the agreement and correlation between the CPRM and the RIP method for each of the detachable funnels.

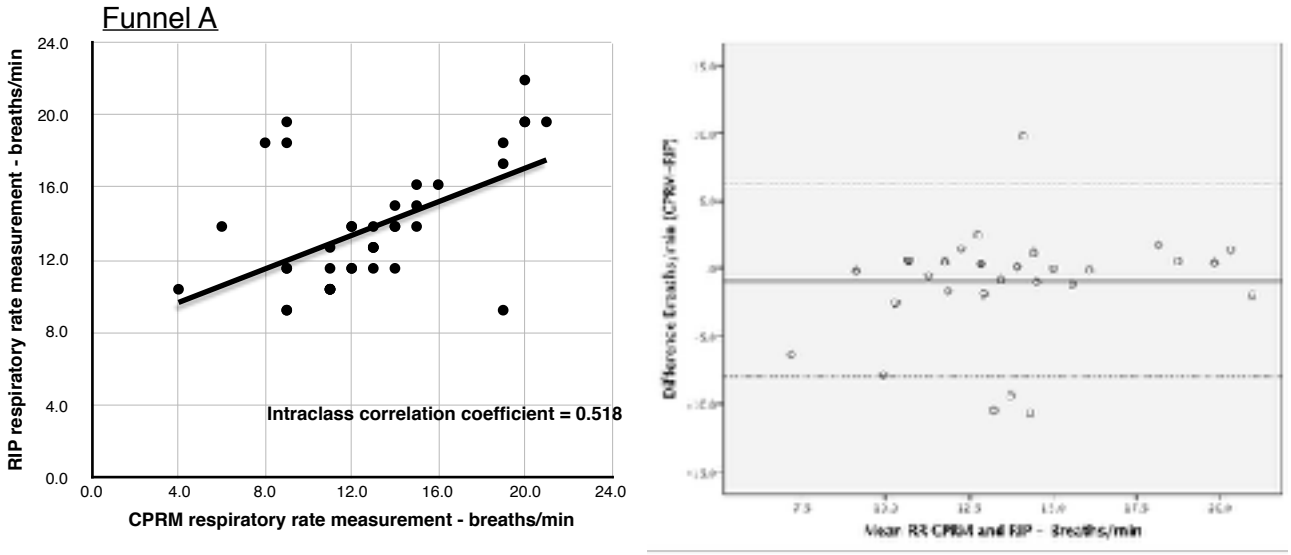


Figure 5.10: Bland-Altman plots and scatterplots of the agreement and correlation between CPRM and RIP measurements with different funnel attachments. Intra-class correlation coefficients also shown.

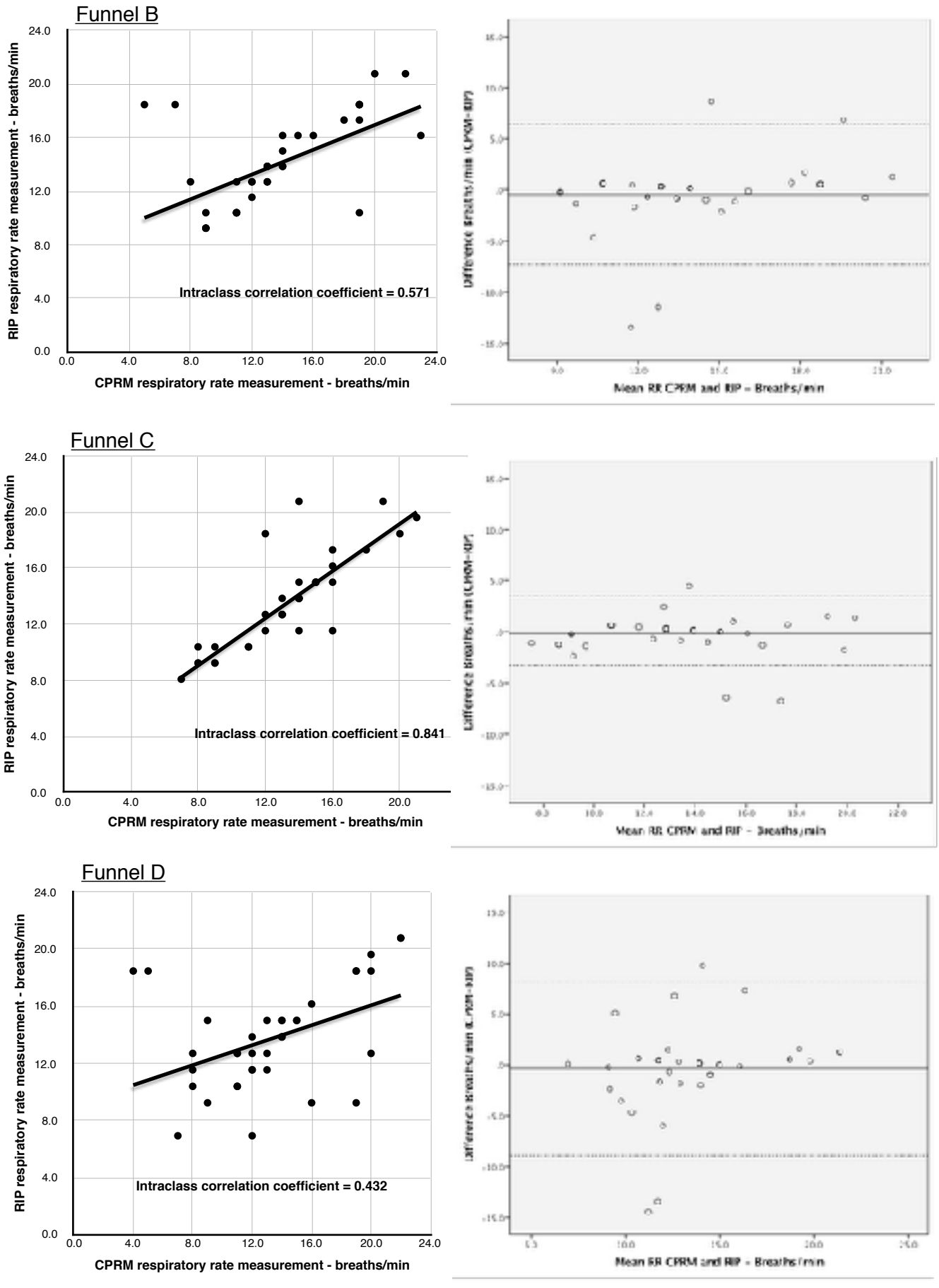


Figure 5.10: Bland-Altman plots and scatterplots of the agreement and correlation between CPRM and RIP measurements with different funnel attachments. Intra-class correlation coefficients also shown.

5.5.3.5 Further analysis of CPRM compared with contact method

On closer analysis of the data there were eight occasions where the CPRM gave dramatically different measurements to both contact and visual counting methods. On each occasion the CPRM did not appear to pick up a breath signal from the participant and as such read significantly lower than the other two measurements. These eight measurements occurred four times with Funnel A, twice with Funnel B and twice with Funnel D. Six of these readings were from the same participant, a 22 year old female who had a shallow breathing pattern. In clinical practice these eight measurements (0.05%) would have been repeated or abandoned. With these eight measurements removed the agreement of the CPRM with the RIP contact method is greatly improved with a mean difference of -0.084, 95% limits of agreement -4.480 to 4.648, and an ICC of 0.784 (95% CI 0.714 - 0.838) (Figure 5.11).

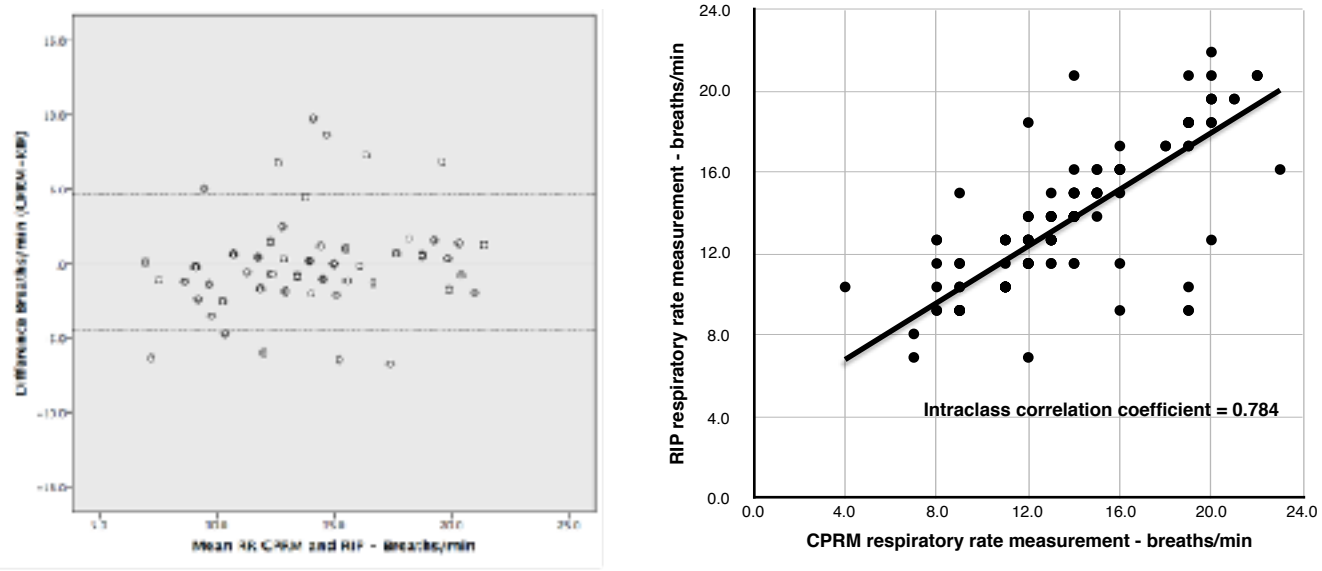


Figure 5.11: Bland-Altman plot and scatterplot of correlation and agreement between CPRM and RIP measurements with 8 outlying results removed.

5.5.3.6 Summary of results

Table 5.1 summarises all of the results for Pilot study A.

Table 5.1: Summary of results for Pilot study A

Methods of measurement	95% Limits of agreement (mean difference)	Intraclass correlation coefficient (95% CI)
CPRM v Contact method (all funnels)	-7.204 - 6.216 (-0.494)	0.568 (0.453 - 0.664)
CPRM v Visual count (all funnels)	-7.333 - 6.068 (-0.632)	0.560 (0.443 - 0.659)
CPRM v Contact method - Funnel A	-7.985 - 6.218 (-0.884)	0.518 (0.259 - 0.708)
CPRM v Contact method - Funnel B	-7.249 - 6.386 (-0.432)	0.571 (0.320 - 0.747)
CPRM v Contact method - Funnel C	-3.941 - 3.465 (-0.238)	0.841 (0.720 - 0.912)
CPRM v Contact method - Funnel D	-8.970 - 8.155 (-0.408)	0.432 (0.132 - 0.659)
CPRM v Contact method - Outliers removed	-4.480 - 4.648 (-0.084)	0.784 (0.714 - 0.838)

5.5.4 Discussion

This first pilot study of the contactless portable respiratory rate monitor successfully measured the respiratory rate of healthy adult volunteers. The CPRM was well tolerated by the adult participants, and there was minimal set up required. There was moderate correlation between the measurements from the CPRM device and that of the established contact method (RIP) and also the standard clinical method of visual counting of breaths. When taking into account the shape of the air inlet funnel a strong correlation was observed with Funnel C that had a circular upward pointing air inlet.

The CPRM, in this study showed 95% limits of agreement between -7.20 to 6.21 breaths/min when compared to the gold standard contact method. These limits of agreement appear to be close to what would be acceptable for clinical practice in adults. When Lim et al (Lim et al., 2002) assessed the RR measurements taken twice on 245 adult patients by the same and different observers they showed 95% limits of agreement between -4.86 and 4.94 breaths/min for the same observer and -5.7 and 5.7 breaths/min for different observers. Based upon this data the 95% limits of agreement for a respiratory rate measurement in an adult should therefore be less than ±4 to ±6 breaths/min. Currently the CPRM's measurements do not however fall within this potentially clinically acceptable range.

A major fault found with the CPRM during this pilot study was that on occasions the device discontinued its recording before the end of the analysis period, without giving a RR measurement. When this occurred the measurement was abandoned and subsequently retaken. This did not affect the results but led to multiple abandoned recordings for some participants and questioned the robustness and reliability of the device.

On occasions the CPRM would give a RR measurement far lower than expected. This appeared to be the main reason behind its reduced accuracy and suggested that it was not picking up and recording all of the subject's breaths. This was most apparent when the subject moved their head and it was clear from the signal display that a breath signal was not obtained. In clinical practice these measurements would have been repeated or the recording abandoned to be measured in a different way i.e. manually. A final clinically deployable device would hopefully exclude these measurements, disallowing spurious results. This occurred on eight occasions, 0.05% of the time. Taking this into account it was possible to exclude these results from the analysis. The accuracy of the CPRM was greatly improved with the 95% limits of agreement between -4.48 to 4.65. This level of accuracy is more acceptable in clinical practice and is comparative to that suggested by Lim et al (Lim et al., 2002).

This pilot study also analysed four separate funnel attachments for the CPRM. Funnel C showed the highest degree of accuracy with Funnel D being the least accurate. Measurements with Funnel C were also more reliable and there were no outlying results with this funnel. However Funnel C was notably larger than the other funnels. Once attached to the CPRM it significantly altered the

overall size and portability of the device. This could be a disadvantage when thinking about introducing the device into different clinical settings.

5.5.5 Conclusions and recommendations

Results obtained from the first testing of the contactless respiratory rate monitor were encouraging. In a controlled environment, on cooperative adult subjects the CPRM was able to measure respiratory rate. However, the accuracy of the device is not yet adequate for use in clinical practice, and fell below that of our gold standard contact method. This study also gained valuable information on the robustness and reliability of the device as well as the accuracy of four different detachable funnels.

From this first pilot study recommendations for development of the CPRM include:

- Engineers to examine the device and rectify the fault causing it to cut out before the end of a measurement.
- Funnel B and D to be excluded from further testing and a further funnel, Funnel E, to be developed based on a smaller version of Funnel C.
- To develop the CPRM so that it rejects poor respiration signals and will only analyse when an adequate signal is received.

5.6 Pilot Study B

Analysis of the CPRM in healthy children including funnel analysis and assessment of reproducibility

5.6.1 Aims

To evaluate the agreement in respiratory rate measurements between existing methods and the contactless portable respiratory rate monitor in healthy children. To also analyse different funnel shapes of the CPRM and perform an inter-observer analysis of measurements taken with the CPRM by different users.

5.6.2 Methods

5.6.2.1 Study design and setting

This was a prospective feasibility pilot study conducted at Sheffield Children's Hospital.

5.6.2.2 Participants and eligibility criteria

We enrolled a convenience sample of 11 healthy children whose parents worked at Sheffield Children's Hospital and Sheffield Hallam University. Participants were selected based on their availability to take part in the study and no other exclusion criteria were applied.

5.6.2.3 Methods of measurements

The respiratory rate of each participant was measured simultaneously by three different methods. Respiratory inductance plethysmography was used as the established contact method and as our gold standard. Visual counting of chest movements represented the established non-contact method, and method used in most clinical settings. The contactless portable respiratory monitor was the experimental method.

5.6.2.4 Instruments

5.6.2.4.1 Contactless portable respiratory rate monitor

The CPRM was held at a distance of 10 to 15 cm from the child's face and positioned so that maximal exhaled breath was collected and an adequate signal obtained. Three differently shaped funnels (Figure 5.12) were attached to the CPRM and two measurements were made with each funnel by two different observers.

Funnel A

Funnel C

Funnel E

Figure 5.12: The three detachable funnels used with the CPRM.

5.6.2.4.2 Respiratory inductance plethysmography

Thoracic and abdominal respiratory inductance plethysmography bands (zRIP inductance effort belts) were used to capture and record respiratory signals from the participants. Data was recorded on the SOMNOtouch RESP portable screening device (S-Med, Birmingham, UK) and downloaded for visual analysis. To determine the RIP respiratory rate, the number of observed respiration cycles from this respiratory signal was counted manually during the time period at which the simultaneous measurements were taken.

5.6.2.4.3 The visual counting method

Visual counting of respiratory rate was performed by a separate observer. A count of observed chest movements over the same time period as the other measurements were being taken was made.

5.6.2.5 Data collection and procedure

Each participant was assigned a unique identifying number based on the order that they were recruited. Data on the participants age and sex was collected. Measurements were made at rest with subjects sitting upright comfortably in a chair or on the lap of their parent. At a defined starting time the respiratory rate was simultaneously taken by each of the three methods for a period of 52 seconds. One observer measured RR with the CPRM, and another observer measured RR using the visual counting method. All measurements were converted to breaths per minute and the data was then entered into an Excel spreadsheet. Three differently shaped funnels were attached to the CPRM and two measurements were made with each funnel by two different observers, to assess user variation in measurements. A total of six recordings were taken if tolerated by the child.

5.6.2.6 Statistical analysis

The pairwise agreement between RR counts from each of the three methods was assessed by calculating the mean difference and 95% limits of agreement (mean $\pm$ the standard deviation of the difference). These were charted using Bland-Altman plots (Bland and Altman, 1986). Intraclass

correlation coefficients with 95% confidence intervals were also reported. All results were analysed using SPSS, version 22.0 for Mac.

5.6.2.7 Ethical approval

The study received a favourable ethics opinion by the NRES committee Yorkshire and the Humber on 15/9/14, REC reference 14/YH/1137 (appendix 8.3). Written consent was obtained from the parents of each child prior to participation.

5.6.2.8 Funding

This study received no specific grant from any funding agency.

5.6.3 Results

5.6.3.1 Study subjects

A total of 60 respiratory rate measurements were made on 11 healthy children. The age range of subjects was 1 to 12 years. The mean age of subjects was 96 months (8 years) (Table 5.2). Two subjects only tolerated one set of recordings with each funnel (one child with autism and a 1 year old child).

Table 5.2: Participant characteristics (n=11)

Age in months, mean, range	96 (12-144)
Male gender, n (%)	8 (73%)

It was noted that the two 5 year old children panted into the device thus artificially increasing their respiratory rate. The older children over 5 years of age (n=8) behaved in the same way as the adult volunteers in Pilot study A.

5.6.3.2 CPRM compared with contact method

When the CPRM was compared with RIP measurements Bland-Altman plots showed the mean difference was -4.112 with 95% limits of agreement of -23.608 to 15.385 (Figure 5.13). This suggests that the CPRM could read up to 24 breaths/min below and 15 breaths/min above the RIP method. The correlation was fair (ICC: 0.336; 95% CI 0.098 - 0.540).

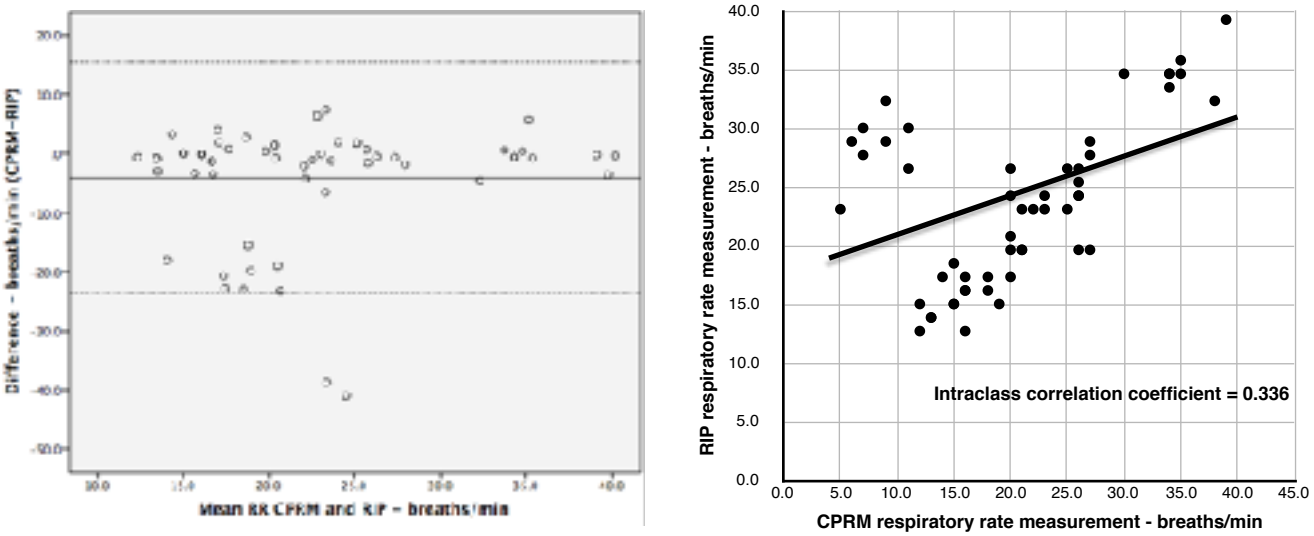


Figure 5.13: Bland-Altman plot and scatterplot of correlation and agreement between CPRM and RIP measurements.

5.6.3.3 CPRM compared with visual counting method

There was a similar level of correlation seen when the CPRM was compared with the visual counting method, ICC:0.353 (95% CI 0.119 - 0.552). Agreement was also poor with a mean difference of -3.188 and 95% limits of agreement of -22.794 to 16.419 (Figure 5.14).

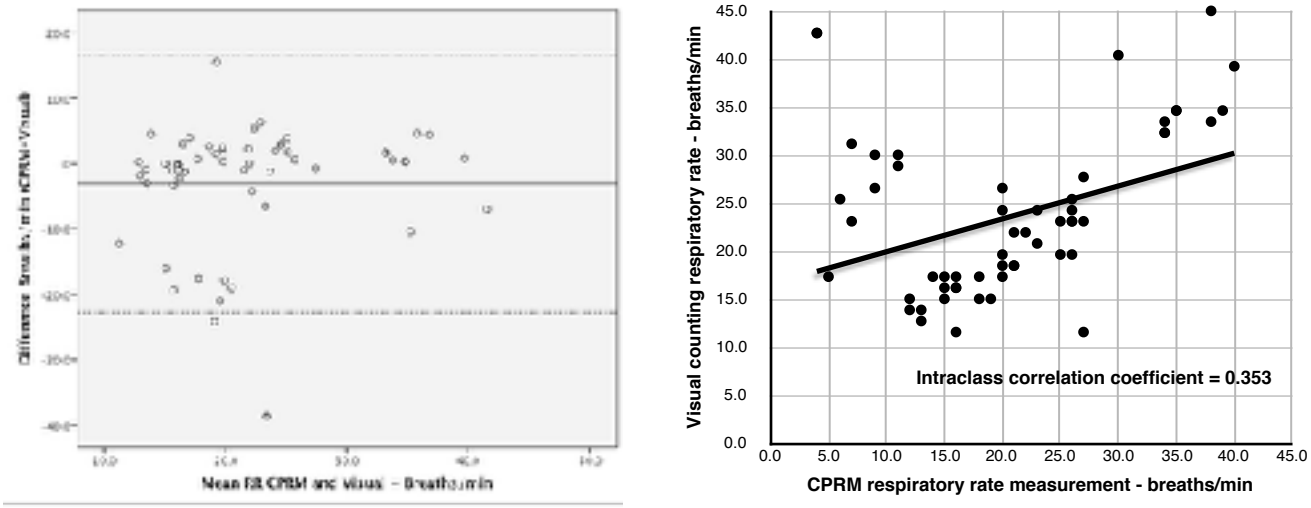
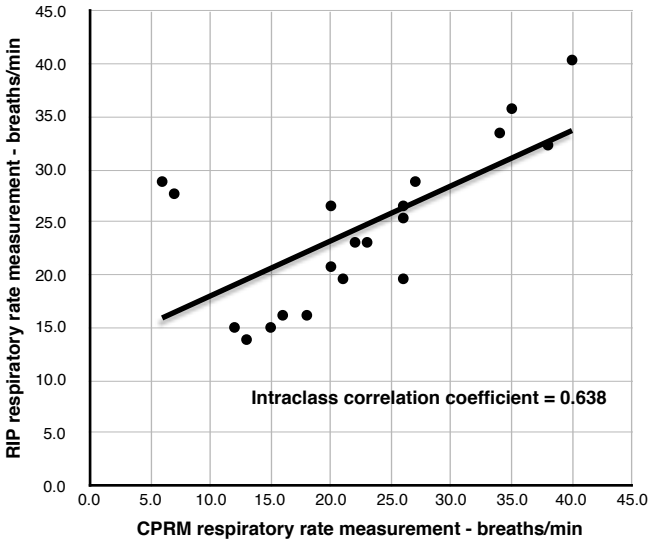


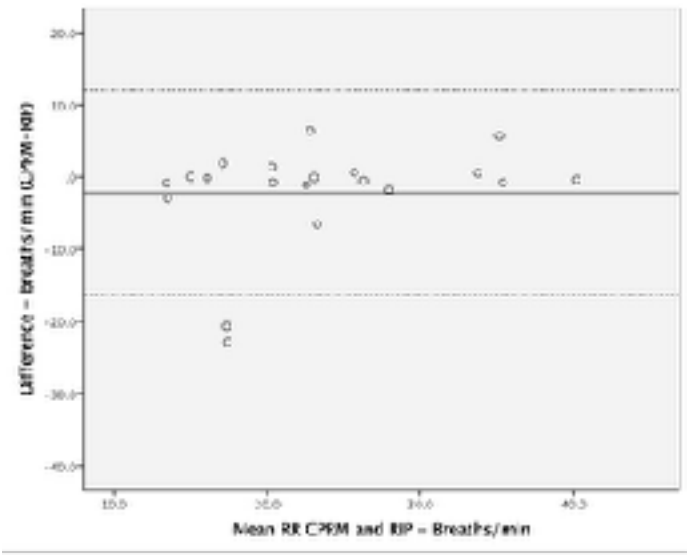
Figure 5.14: Bland-Altman plot and scatterplot of correlation and agreement between CPRM and visual count RR measurements.

5.6.3.4 Analysis of CPRM funnels

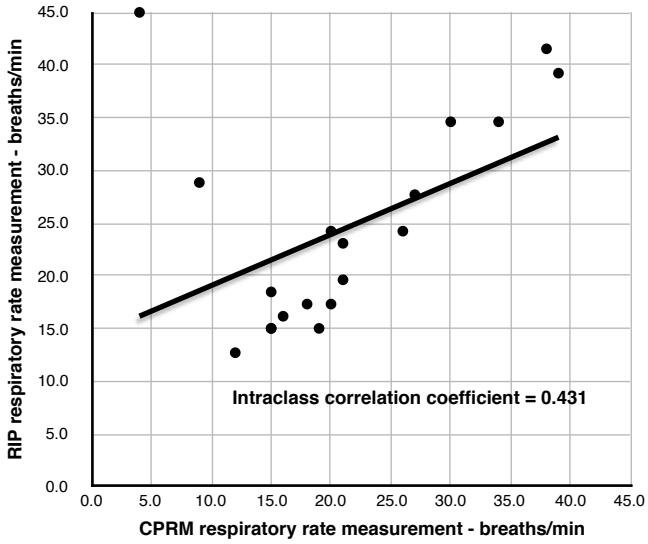
Further analysis of each air inlet funnels showed that Funnel A had substantially better agreement and correlation when compared with RIP measurements. The mean difference was -2.155 with 95% limits of agreement between -16.340 and 12.031. The ICC was 0.638 (95% CI: 0.296 - 0.837). Funnel C showed agreement which was similar to that seen overall, with a mean difference of -3.539 and 95% limits of agreement between -23.256 and 16.178. Correlation was less than Funnel A, ICC: 0.431 (95% CI: 0.025 - 0.723). Funnel E however showed extremely poor agreement and correlation, with a mean difference of -6.640 and 95% limits of agreement of -30.043 to 16.763. The ICC was 0.006 (95% CI -0.310 - 0.383). Figure 5.15 shows the Bland-Altman plots and scatterplots for each of the different funnels.

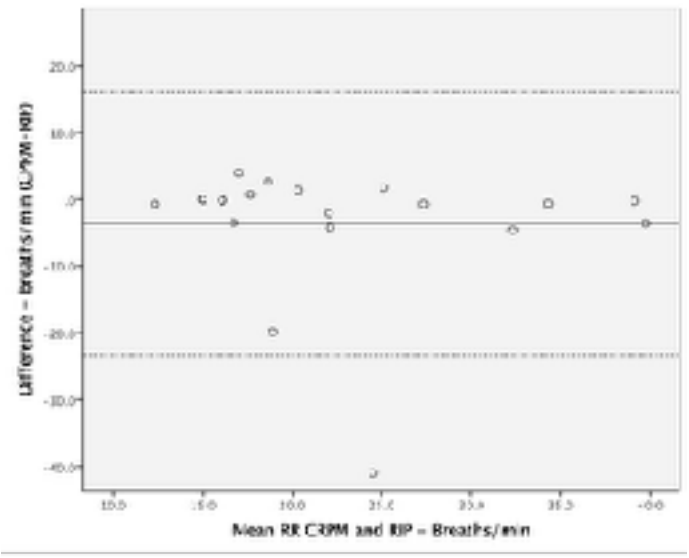
Funnel A



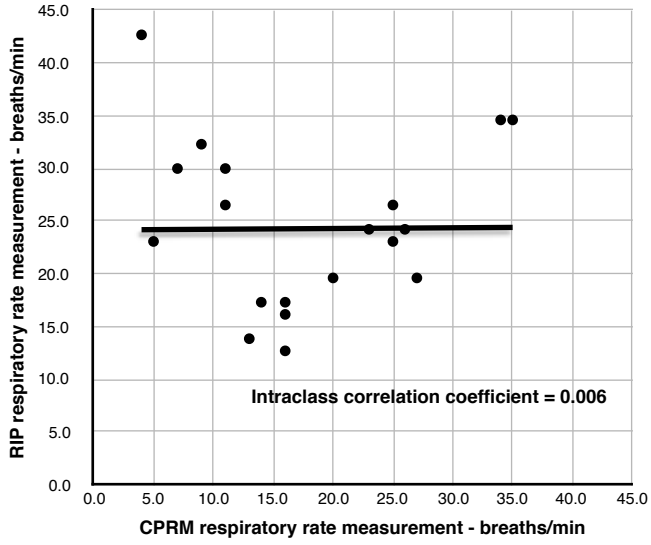


Funnel C





Funnel E



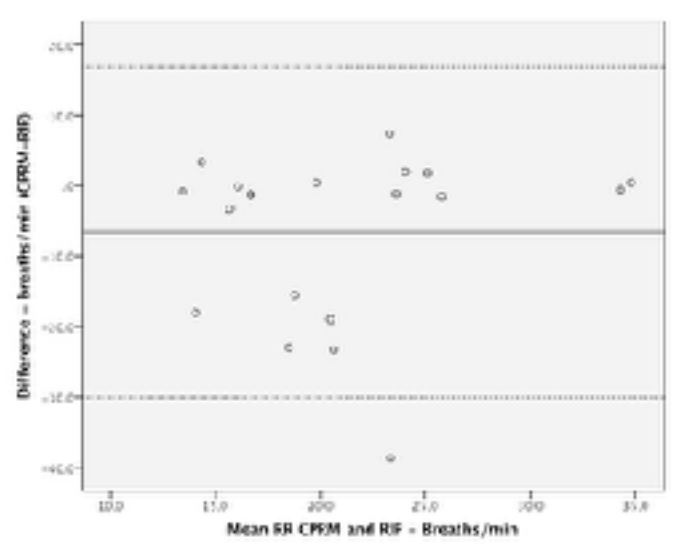


Figure 5.15: Bland-Altman and scatterplots showing the agreement and correlation between CPRM and RIP measurements with different funnel attachments.

5.6.3.5 Further analysis of CPRM compared with contact method

As was with Pilot Study A the CPRM on some occasions gave dramatically different measurements when compared with both contact and visual count methods, reading significantly lower. Again the CPRM did not appear to pick up a respiration signal from the subject. This occurred a total of eight times. Three times from a 7 year old girl, three from a 5 year old boy, once from a 8 year old boy, and once from a 1 year old girl. Four of these readings were taken with Funnel E, two with Funnel C and two with Funnel A. From our data 13% of measurements would have been repeated or abandoned. With these eight measurements removed the agreement improved with a mean difference of -0.754 and 95% limits of agreement -9.076 to 7.568. Correlation between the CPRM and the RIP contact method was then substantial with an ICC of 0.859 (95% CI 0.767 - 0.916) (Figure 5.16).

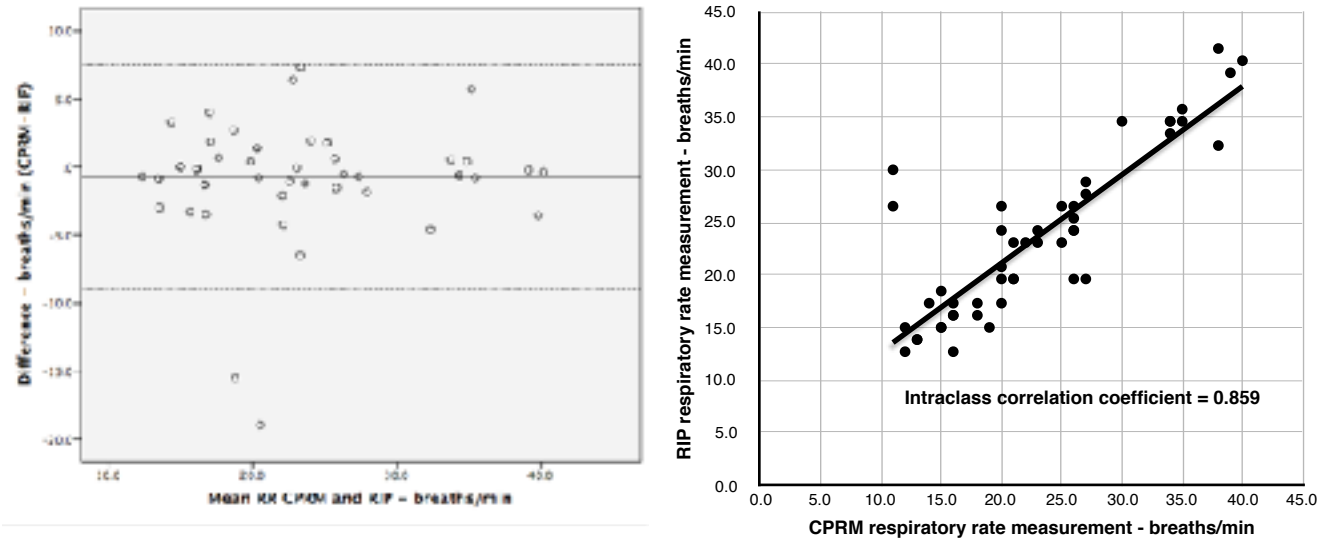


Figure 5.16: Bland-Altman and scatterplot plot of agreement and correlation between CPRM and RIP measurements with 8 outlying results removed.

5.6.3.6 Variability of CPRM measurements between users

The reproducibility of measurements from two different users was assessed on nine of the children. Two children were discounted from this analysis as they only tolerated one set of readings from one observer. A total of 24 paired measurements were assessed. The mean difference was -0.500 with 95% limits of agreement between -13.463 and 12.463. Correlation was assessed as substantial with an ICC of 0.724 (95% CI: 0.458 - 0.871) (Figure 5.17).

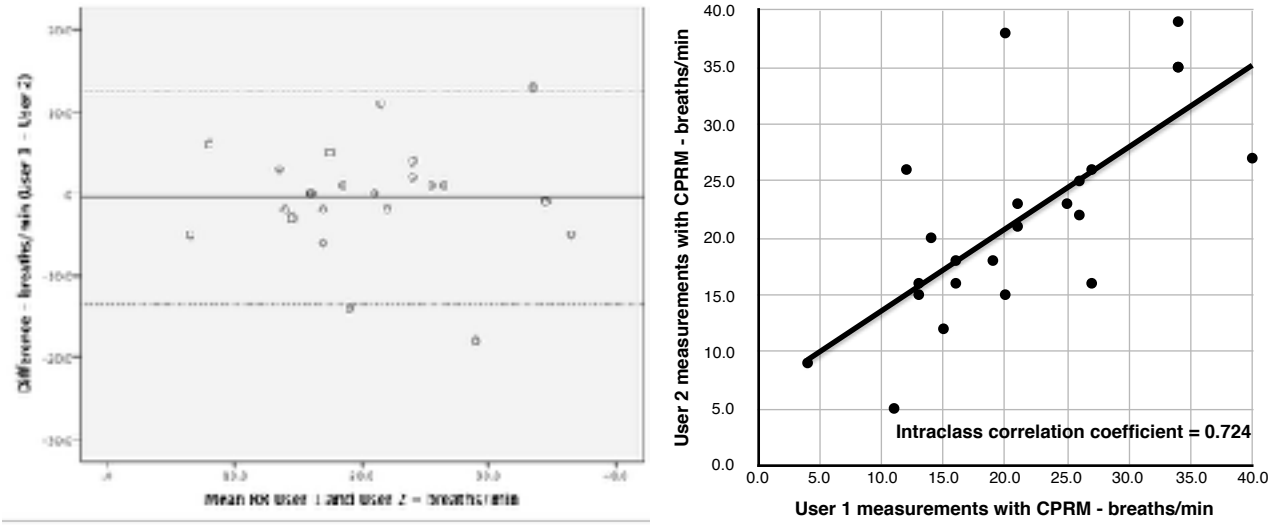


Figure 5.17: Bland-Altman plot and scatterplot of the agreement and correlation between CPRM measurements taken by two different users.

5.6.3.7 Summary of results

Table 5.3 summarises the results for Pilot study B.

Table 5.3: Summary of results for Pilot study B

Methods of measurement	95% Limits of agreement (mean difference)	Intraclass correlation coefficient (95% CI)
CPRM v Contact method (all funnels)	-23.608 - 15.385 (-4.112)	0.336 (0.098 - 0.540)
CPRM v Visual count (all funnels)	-22.794 - 16.419 (-3.188)	0.353 (0.119 - 0.552)
CPRM v Contact method - Funnel A	-16.340 - 12.031 (-2.155)	0.638 (0.296 - 0.837)
CPRM v Contact method - Funnel C	-23.256 - 16.178 (-3.539)	0.431 (0.025 - 0.723)
CPRM v Contact method - Funnel E	-30.043 - 16.763 (-6.640)	0.006 (-0.310 - 0.383)
CPRM v Contact method - Outliers removed	-9.076 - 7.568 (-0.754)	0.859 (0.767 - 0.916)

5.6.4 Discussion

This was the first study testing the CPRM in children. The technical difficulties with the CPRM cutting out before the end of the measurement period had been resolved and new and existing funnel shapes were trialled. The overall accuracy of the device fell below that seen in Pilot study A, however there was vital information gathered.

Chapter 3 of this thesis showed 95% limits of agreement to be between -7.11 and 6.95 breaths/min for simultaneous measurements taken by two observers using a 60 second visual count and -11.36 to 18.73 breaths/min for measurements performed by different observers within 30 minutes. The CPRM in this study showed wider limits of agreement than these, however there were reasons to account for this. On a number of occasions the CPRM did not pick up a respiration signal from the subject. This led to the CPRM producing a number of measurements that were far lower than that expected and lower than that obtained from visual or contact methods. This occurred in 13% of the measurements. In clinical practice these spurious readings would have been repeated or measured manually. When these measurements were discounted the accuracy of the CPRM improved greatly and the limits of agreement were closer to that described within Chapter 3 and seen within clinical practice.

From the information gained on the different funnels in Pilot study A a further funnel was developed, Funnel E. This was designed based on Funnel C but had a smaller inlet area so that the overall portability of the CPRM could be maintained. Funnel A and C were also chosen for testing in these subjects. When analysing the results separately for each funnel it was clear that Funnel E was extremely inaccurate. There was poor agreement seen with both contact and visual methods of measurement. The funnel did not channel the subjects breath to the CPRM effectively and as such the CPRM missed multiple breaths. Conversely to the study in healthy adults, Funnel A proved the most accurate funnel in child subjects, appearing to be more effective in channeling the child's breath into the device.

An interesting finding in two of the subjects, both aged 5 years, was that measuring with the CPRM led these children to alter their respiratory rate. On placing the device in front of their face these children panted into the device thus increasing their respiratory rate for the period of measurement. In clinical practice this would have implications as the reading would not be their true respiratory rate and not reflect their current clinical status.

The sampling time required for the CPRM to measure a RR was also problematic in these children. In its prototype phase the CPRM requires 52 seconds of data recording to analyse and measure the subject's respiratory rate. In healthy adults in Pilot study A this was not problematic as participants were compliant and able to sit still for this period of time. However, the child participants were less cooperative for the measurement period. They moved their head from the device, talked or pushed the device away. This made the RR measurement more difficult to obtain and resulted in breaths being missed and meant the overall measurement obtained was less

accurate. As the recording time went on the younger children became less cooperative and the measurement became increasingly difficult to obtain.

This study also assessed the reproducibility of measurements by different users. If the device was to be used in clinical practice by different healthcare professionals it would be important to ensure that there was little variability in measurements taken by different users. The agreement found between measurements was better than that found overall but would still not be acceptable in clinical practice. However only 24 paired measurements were assessed and different funnel types were used which required slightly different techniques to obtain a measurement. To further validate the usability of the CPRM it would be worth extending the inter-user analysis to a larger number of subjects using a standard funnel shape.

5.6.5 Conclusions and recommendations

This study has demonstrated that the CPRM is able to measure respiratory rates in healthy children of various ages. Although the accuracy of the CPRM was lower in this study, there are a number of factors that can account for this. We have also gained valuable information on the reproducibility of measurements, the accuracy of different funnel shapes and also the behaviour of different aged children towards the CPRM. It is possible that modifications to the device and measuring procedure can be made to reduce these factors and improve the overall accuracy of the CPRM.

Further recommendations for development of the CPRM include:

- Development of the device to reduce the sampling time without compromising on the accuracy of measurements.
- Funnel C and E to be discontinued and Funnel A to be used in future pilot studies of children.
- Strategies to be developed to gain the attention of children of different ages to ensure an adequate respiration signal is collected throughout the measurement period. These may include modifications to the CPRM to make it more appealing and capture the child's attention, or distraction techniques with other devices to bring a child's attention towards the CPRM.

5.7 Pilot Study C

Analysis of the CPRM in healthy children in a primary school

5.7.1 Aims

To evaluate the agreement and correlation in respiratory rate measurements between existing methods and the contactless portable respiratory rate monitor in healthy child volunteers from a local primary school.

5.7.2 Methods

5.7.2.1 Study design and setting

This was a prospective feasibility study conducted at a local Sheffield primary school.

5.7.2.2 Participants and eligibility criteria

We enrolled a convenience sample of 19 children from a year 3 class of a local primary school. All 32 children in the class had information leaflets and consent forms sent home to their parents. Those parents who were happy for their child to take part in the study completed a consent form and returned it to the school. 19 children returned their forms and all were eligible to take part in the study.

5.7.2.3 Methods of measurements

The respiratory rate of each child was measured simultaneously by three different methods. Respiratory inductance plethysmography, the established contact method and our gold standard. Visual counting of chest movements, the established non-contact method, and the contactless portable respiratory monitor, the new method.

5.7.2.4 Instruments

5.7.2.4.1 Contactless portable respiratory rate monitor

The CPRM was held at a distance of 10 to 15 cm from the child's face and positioned so that maximal exhaled breath was collected and an adequate respiration signal obtained. Only one detachable funnel (Funnel A) was used throughout the study.

5.7.2.4.2 Respiratory inductance plethysmography

Thoracic and abdominal respiratory inductance plethysmography bands (zRIP inductance effort belts) were used to capture and record respiratory signals from the participants. Data was recorded on the SOMNOtouch RESP portable screening device (S-Med, Birmingham, UK) and downloaded for visual analysis. To determine the RIP respiratory rate, the number of observed respiration cycles from this respiratory signal was counted manually during the time period at which the simultaneous measurements were taken.

5.7.2.4.3 The visual counting method

Visual counting of respiratory rate was performed by a separate observer. A count of observed chest movements over the same time period as the other measurements were being taken was made.

5.7.2.5 Data collection and procedure

Each participant was assigned a unique identifying number based on the order that they were recruited in their particular setting. Data on the child's age and sex was collected. Measurements were made at rest with the participant sitting upright comfortably in a chair. At a defined starting time the respiratory rate was simultaneously taken by each of the three methods for a period of 52 seconds. One observer measured RR with the CPRM, and another observer measured using the visual counting method. All measurements were converted to breaths per minute and the data was then entered into an Excel spreadsheet. Two data sets were taken for each child

5.7.2.6 Statistical analysis

The pairwise agreement between RR counts from each of the three methods was assessed by calculating the mean difference and 95% limits of agreement (mean $\pm$ the standard deviation of the difference). These were charted using Bland-Altman plots (Bland and Altman, 1986). Intraclass correlation coefficients with 95% confidence intervals were also reported. All results were analysed using SPSS, version 22.0 for Mac.

5.7.2.7 Ethical approval

The study received a favourable ethics opinion by the NRES committee Yorkshire and the Humber on 5/10/15 REC reference 15/YH/0297 (appendix 8.4). Written consent was obtained from the parent of each child participant prior to participation.

5.7.2.8 Funding

This study was funded by The Children's Hospital Charity and was granted £15,138.53 in March 2015.

5.7.3 Results

5.7.3.1 Study subjects

A total of 38 recordings were obtained from the 19 children. Each child had 2 readings taken. The age range of subjects was 7 to 8 years. 11 of the children (58%) were female.

5.7.3.2 CPRM compared with contact method

When the CPRM was compared with RIP measurements Bland-Altman analysis showed a mean difference of -1.893 with 95% limits of agreement of -16.198 to 12.412. The correlation was fair with intraclass correlation coefficient 0.409 (95% CI 0.116 - 0.639) (Figure 5.18).

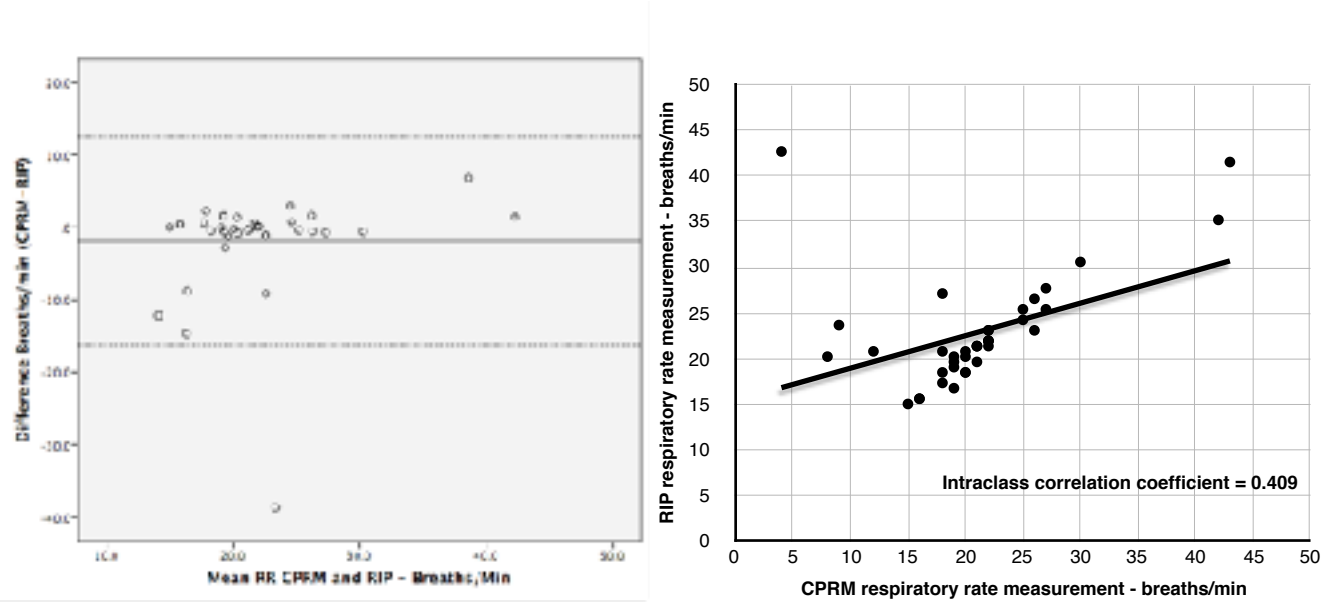


Figure 5.18: Bland-Altman plot and scatterplot of correlation and agreement between CPRM and RIP measurements.

5.7.3.3 CPRM compared with visual counting method

There was a similar level of agreement and correlation seen when the CPRM was compared with the visual counting method with an intraclass correlation coefficient of 0.325 (95% CI 0.03 - 0.583). Bland-Altman analysis showed a mean difference of -0.122 with 95% limits of agreement of -15.222 to 14.976 (Figure 5.19).

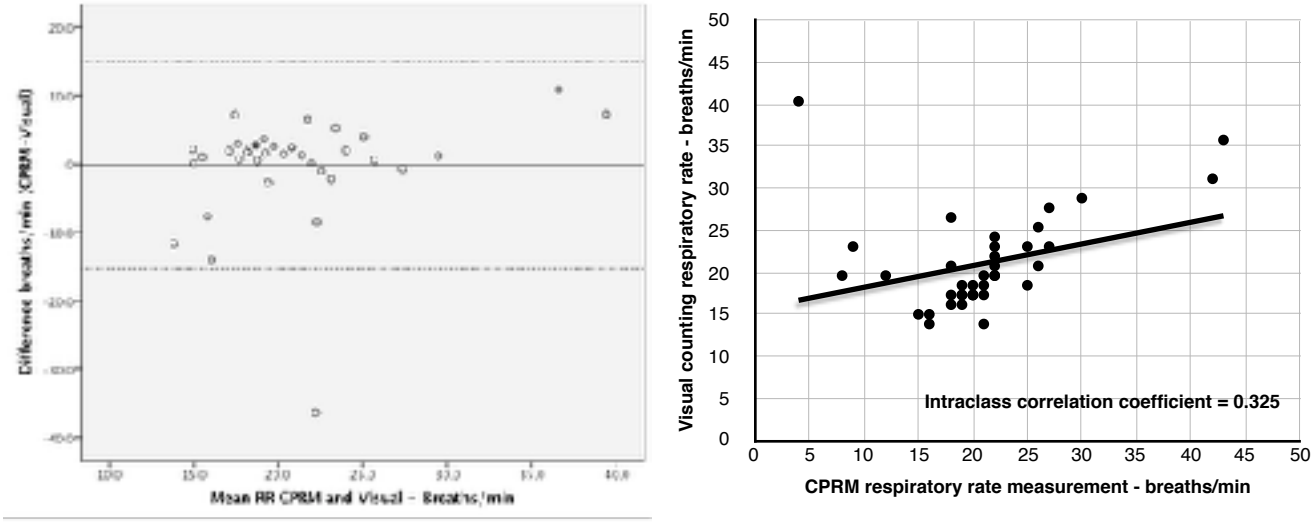


Figure 5.19: Bland-Altman plot and scatterplot of agreement and correlation between CPRM and visual count respiratory rate measurements.

5.7.3.4 Further analysis of CPRM compared with contact method

On further analysis of the data there were three occasions from three different subjects where the CPRM did not appear to pick up a RR signal and measured significantly lower than both the visual and contact methods. On removing these results the agreement between the CPRM and RIP was greatly improved with mean difference -0.1886 and 95% limits of agreement of -5.465 to 5.089. Correlation was also substantial, ICC: 0.897 (95% CI 0.805 - 0.946) (Figure 5.20).

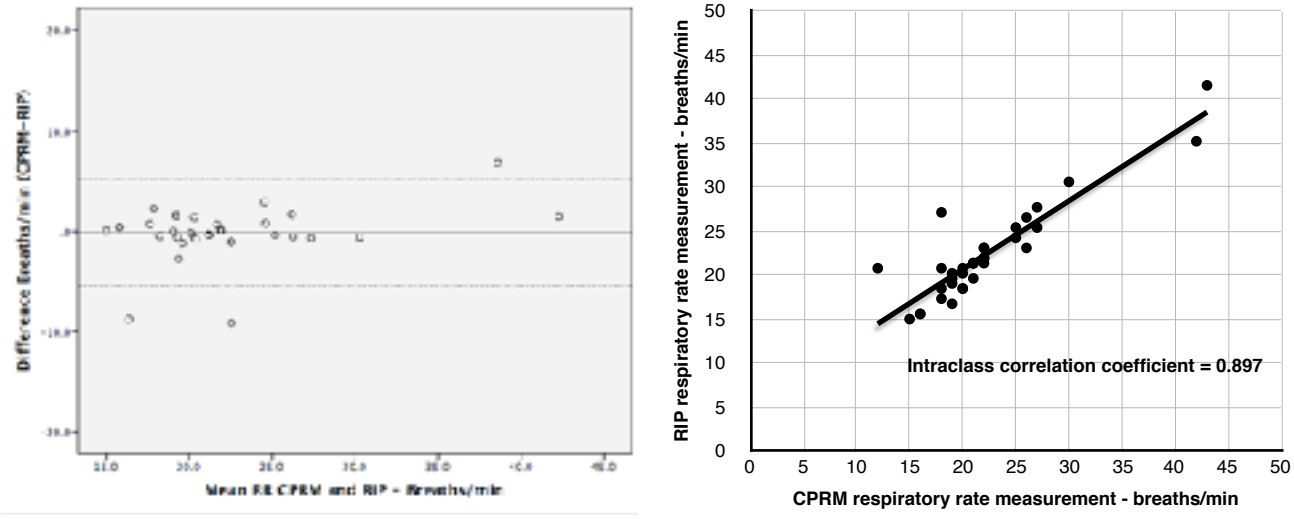


Figure 5.20: Bland-Altman plot and scatterplot of correlation and agreement between CPRM and RIP measurements with three measurements removed.

5.7.4 Discussion

This pilot study gained further data on the accuracy and usability of the CPRM in healthy children. All children were cooperative and tolerated the CPRM measurement well. The agreement with both visual and contact methods of measurements was only fair on initial analysis however when three measurements were discounted the agreement was substantial.

From Chapter 3 of this thesis the inter-observer agreement of RR measurements in this age group (5-12 years) was shown to be much better than what we have demonstrated with the CPRM (-4.50 to 3.24 breaths/min for simultaneous observers). However when the three spurious measurements are discounted the agreement moves a lot closer to this, -5.47 to 5.09 breaths/min. These spurious measurements accounted for 8% of the total measurements taken and again were related to the CPRM not gaining an adequate signal during the recording process, resulting in breaths missed and a falsely low value being obtained. It was unclear if the respiration signal was not picked up due to the subject moving, user error, or a poor quality signal being obtained. However, in practice if this device was to be used clinically these results would be discarded and the user would re-take the measurement.

An interesting finding in this age group was the child's response to being told they were having their breathing/respiratory rate measured. By giving the child this information they immediately focused on how they were breathing and breathed into the device, most often at an increased rate. They did not pant as was seen in the younger children in Pilot study B but their RR did become falsely elevated. When the child's focus was taken away from the measurement their respiratory rate returned to its previous rate. This is of importance when considering the CPRM for clinical use. Any artificial alteration in rate produced by the CPRM could result in false readings that may alter the assessment of the child's clinical condition and also their subsequent management.

5.7.5 Conclusions and recommendations

This study successfully measured the RR of well children in a primary school setting. It was found that this group of children needed distracting from the measurement process to ensure they did not artificially change their respiratory rate. The accuracy of measurements was substantial once spurious readings were discounted. There was however a very narrow age range studied here and despite important findings in this age group it would be necessary to extend testing to a wider age range of children.

Recommendations for further development of the CPRM include:

- Development of the CPRM to reject sections of poor respiration signal.
- Improvement in the extraction of the respiration signal obtained so that only the best sections of signals are analysed.
- Further work to be carried out looking into distraction techniques that could be used in different age groups to improve compliance and improve accuracy during the measurement process.

5.8 Pilot Study D

Analysis of the CPRM on sleeping children undergoing polysomnography sleep studies

5.8.1 Aims

To evaluate the agreement in respiratory rate measurements between existing methods and the contactless portable respiratory rate monitor in children undergoing polysomnography sleep studies. To assess the usability and accuracy of the CPRM in children in this specialist investigatory setting.

5.8.2 Methods

5.8.2.1 Study design and setting

This was a prospective feasibility pilot study conducted at Sheffield Children's Hospital.

5.8.2.2 Participants and eligibility criteria

We enrolled a convenience sample of 30 children undergoing polysomnography (PSG) sleep studies at Sheffield Children's Hospital. Children aged between 0-16 years with a range of sleep and breathing disorders who were seen in the sleep clinic at Sheffield Children's Hospital were approached to take part. Children were selected based on their availability to take part in the research study whilst undergoing PSG. We excluded families whom English was not their first language for ease of consent, and those children who it was thought that taking part in the research study could adversely affect the results of their PSG.

5.8.2.3 Methods of measurements

The respiratory rate of each participant was measured simultaneously by three different methods. Respiratory inductance plethysmography, the established contact method, visual counting of chest movements, the established non-contact method, and the CPRM. Two data sets were taken for each participant.

5.8.2.4 Instruments

5.8.2.4.1 Contactless portable respiratory rate monitor

The CPRM was held at a distance of 10 to 15 cm from the child's face as they were sleeping and positioned so that maximal exhaled breath was collected and an adequate signal obtained. One detachable funnel (Funnel A) was used throughout the study.

5.8.2.4.2 Respiratory inductance plethysmography

Thoracic and abdominal respiratory inductance plethysmography bands (zRIP inductance effort belts) were used to capture and record respiratory signals from the participants. These were part

of the PSG equipment already in use for the sleep study. Data was recorded on the Alice 5 diagnostic sleep system (Philips, Respironics, Chichester, UK) and downloaded for visual analysis. To determine the RIP respiratory rate, the number of observed respiration cycles from this respiratory signal was counted manually during the time period at which the simultaneous measurements were taken.

5.8.2.4.3 The visual counting method

Visual counting of respiratory rate was performed by the same observer taking the CPRM measurement. A count of observed chest or abdominal movements over the same time period as the other measurements were being taken was made.

5.8.2.5 Data collection and procedure

Each participant was assigned a unique identifying number based on the order that they were recruited. Data on the participants age and sex was collected. Measurements were made once the child was asleep and the sleep study recording had been initiated. At a defined starting time the respiratory rate was simultaneously taken by each of the three methods for a period of 52 seconds. One observer measured RR using both the CPRM and visual counting method. All measurements were converted to breaths per minute and this data was then entered into an Excel spreadsheet.

5.8.2.6 Statistical analysis

The pairwise agreement between RR counts from each of the three methods was assessed by calculating the mean difference and 95% limits of agreement (mean $\pm$ the standard deviation of the difference). These were charted using Bland-Altman plots (Bland and Altman, 1986). Intraclass correlation coefficients with 95% confidence intervals were also reported. All results were analysed using SPSS, version 22.0 for Mac.

5.8.2.7 Ethical approval

The study received a favourable ethics opinion by the NRES committee Yorkshire and the Humber on 15/9/14 REC reference 14/YH/1137 (appendix 8.3). Written consent was obtained from the parent of each participant prior to participation.

5.8.2.8 Funding

This study received no specific grant from any funding agency.

5.8.3 Results

5.8.3.1 Study subjects

A total of 61 recordings were obtained from 30 children all of whom had a range of sleep and breathing disorders and one child breathed through a tracheostomy. Each child had two readings taken and one child had an extra reading taken over their tracheostomy. The age range of subjects was 8 months to 15 years. The mean age of subjects was 53.4 months (4 yrs 4 months) (Table 5.4).

Table 5.4: Participant characteristics (n=30)

Age in months, mean, range	53.4 (8-180)
Male gender, n (%)	18 (60%)

5.8.3.2 CPRM compared with contact method

When the CPRM was compared with RIP measurements Bland-Altman plots showed a mean difference of -0.212 with 95% limits of agreement of -6.842 to 6.419 (Figure 5.21). This suggests that the CPRM could read up to 7 breaths/min below and 6 breaths/min above the RIP method in this cohort of children. The correlation was substantial with intraclass correlation coefficient 0.762 (95% CI 0.633 - 0.850).

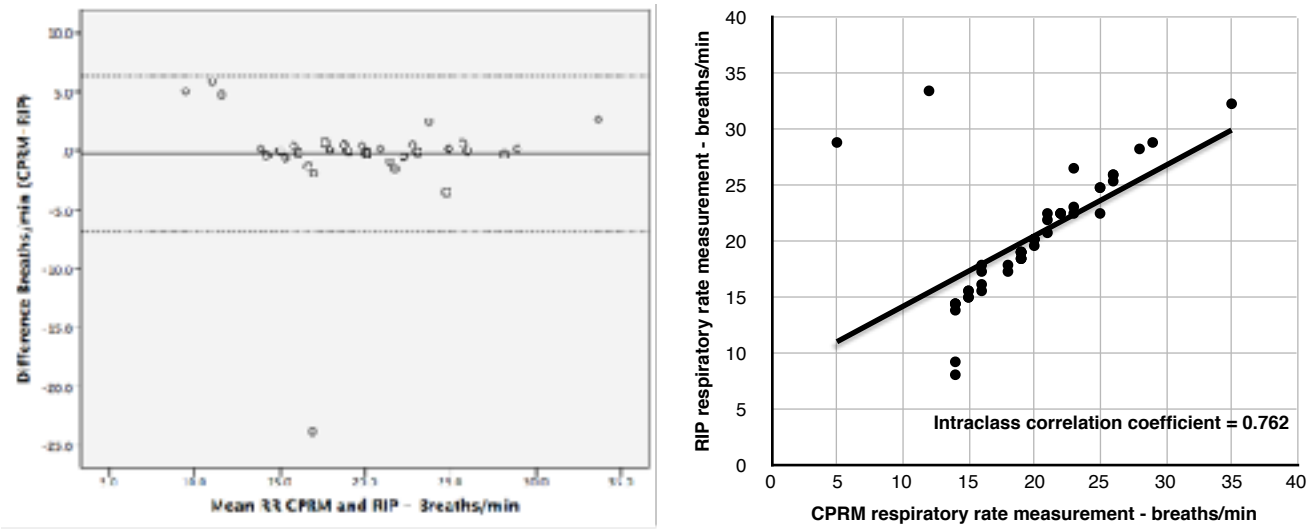


Figure 5.21: Bland-Altman plot and scatterplot of correlation and agreement between CPRM and RIP measurements.

5.8.3.3 CPRM compared with visual counting method

When the CPRM was compared with the visual counting method agreement was slightly less with a mean difference of -0.123 and 95% limits of agreement of -7.009 to 6.763. There was a similar level of correlation with ICC: 0.729 (95% CI 0.586 - 0.828) (Figure 5.22).

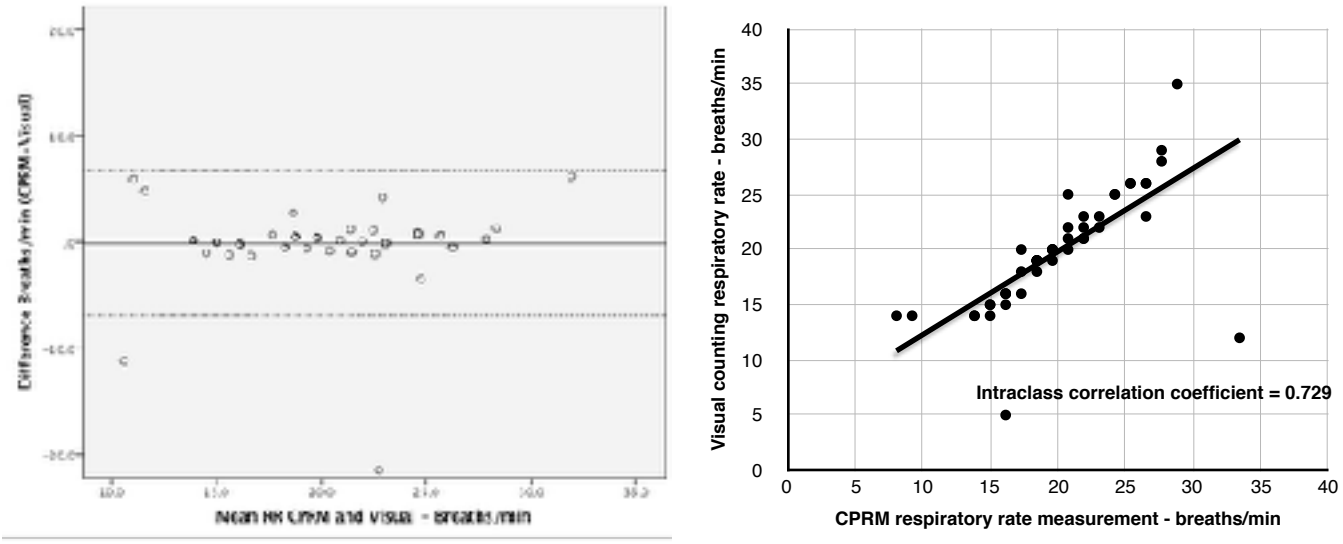


Figure 5.22: Bland-Altman plot and scatterplot of agreement and correlation between CPRM and visual count respiratory rate measurements.

Interestingly though, when the visual count was compared with the contact method the agreement was not as high as that seen between the CPRM and the contact method. The mean difference was 0.089 with 95% limits of agreement -7.551 to 7.728. Correlation was also less, ICC: 0.674 (95% CI 0.509 - 0.791).

5.8.3.4 Further analysis of CPRM compared with contact method

On further analysis of the data there were two subjects (four readings) where the CPRM measurements were significantly different to that of the RIP contact method. The two subjects had sleep disordered breathing with long pauses between breaths followed by periods of short shallow fast breaths. The CPRM was unable to pick up some of these breaths and added in extra breaths during the long pauses. The visual counting method was also inaccurate in these subjects.

If these measurements are removed from the analysis the correlation between the CPRM and contact method is almost perfect with ICC:0.981 (95% CI 0.968 - 0.989). Bland-Altman plots showed a mean difference of -0.086 with 95% limits of agreement of -1.716 to 1.544 (Figure 5.23). This suggests that the CPRM could read up to 2 breaths/min below and 2 breaths/min above the RIP method.

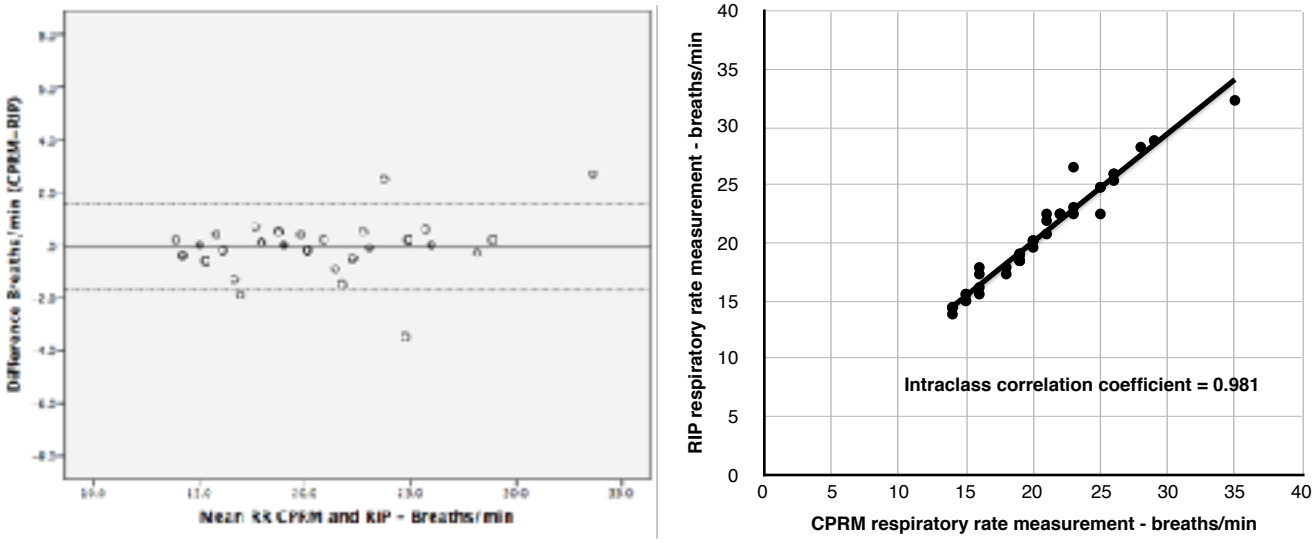


Figure 5.23: Bland-Altman plot and scatterplot of correlation and agreement between CPRM and RIP measurements with two participants removed.

5.8.4 Discussion

This study in sleeping children showed substantial agreement between the CPRM and the contact method of respiratory rate measurement. It also gave a valuable insight into the usability of the device in this particular clinical setting.

In the initial analysis of results the CPRM showed substantial agreement with both visual and contact methods. This level of agreement was similar to that described in chapter 3 (-7.11 to 6.95 breaths/min), when two observers measured a child's RR simultaneously, and so could therefore be classified as being within an acceptable range for clinical practice. On removal of two children with sleep-disordered breathing, where even a visual count was highly inaccurate, the accuracy of the CPRM was significantly increased and the level of agreement surpassed that shown in chapter 3.

Further benefits of the device were also found in this particular setting. In a darkened environment a visual RR count is difficult to complete as the observation of breaths can be challenging. This was reflected in the accuracy of the visual count compared to the contact method, which was only moderate and below that of the CPRM. The CPRM was able to be operated in the dark without compromising on accuracy. Also once a RR signal was obtained from the child the device could be left by the bedside for the duration of the recording. Thus the child was not disturbed or woken and their RR not altered.

Another important finding was that a facemask, nasal prongs or a child's dummy did not affect the RR signal from the subject. The device also accurately measured the RR from a child's tracheostomy and could detect RR signals from children as young as 8 months of age.

The CPRM clearly showed added benefits in this setting compared to the other methods of measurement and these could also be applied to the ward setting overnight. The device was easy to use and no spurious results were generated like those that were seen in the two previous studies. This was likely due to the controlled nature of the testing environment where the sleeping children did not frequently move and all their breaths could be captured. The CPRM was however unable to accurately measure the RR in those children with significant sleep-disordered breathing.

5.8.5 Conclusions and recommendations

The results obtained on children in this sleep study setting were excellent when compared with our gold standard method. They show that in a controlled setting the CPRM can accurately measure respiratory rate and can even obtain an accurate measurement when a dummy, nasal prongs or facemask is in place. Although unable to accurately measure the respiratory rate in children with sleep-disordered breathing, the CPRM is not intended for this purpose and this cohort of patient is not often encountered in everyday clinical practice. This study has also shown a clinical area where the CPRM has clear advantages over other methods of RR measurement. In dark ward areas overnight the CPRM can potentially measure a child's RR without disturbing or waking them.

Recommendations for further development of the CPRM include:

- The development of 'signal locking' so that when an adequate respiration signal is obtained the CPRM initiates the measurement process.
- The development of visual and audio user alerts to guide the user. This would not only enable measurements to be made more easily in darkened environments but it would also act to:
    - Notify the user when a strong signal is received and recording can be started.
    - Signal the end of a recording.
    - Notify the user that a RR measurement is within normal limits or not.

5.9 Pilot Study E

Analysis of the CPRM in the pre-hospital setting

5.9.1 Aims

To evaluate the agreement in respiratory rate measurements between existing methods and the contactless portable respiratory rate monitor within the pre-hospital setting, prior to admission to hospital. Three different pilot studies evaluated the accuracy, usability and robustness of the CPRM in a general practice surgery, a paediatric emergency department and with the Yorkshire ambulance service.

5.9.2 Methods

5.9.2.1 Study design and setting

5.9.2.1.1 General Practice Surgery

A prospective feasibility study conducted at a general practice surgery in the Doncaster area.

5.9.2.1.2 Paediatric Emergency Department

A prospective feasibility study conducted at Sheffield Children's Hospital in the emergency department.

5.9.2.1.3 Yorkshire Ambulance Service

A prospective feasibility study conducted with the Yorkshire ambulance service on patients who were seen by paramedics from across the South Yorkshire region.

5.9.2.2 Participants

5.9.2.2.1 General Practice Surgery

We enrolled a convenience sample of 20 patients who attended their general practice surgery on one set day. Participants were selected based on their availability to take part in the study after they had been seen for their specific appointment. Patients were approached by their GP or practice nurse. If willing, these patients were then approached by the research team. Patients were excluded if they were deemed too unwell or required emergency treatment. Patients who were unable to speak or read English were also excluded.

5.9.2.2.2 Paediatric Emergency Department

We enrolled a convenience sample of 30 children presenting to the emergency department at Sheffield Children's Hospital. Participants were selected based on their availability to take part in the study whilst waiting to be seen by a doctor. Children were excluded if they were deemed too unwell or required emergency treatment. Children whose parents were unable to speak or read English were also excluded.

5.9.2.2.3 Yorkshire Ambulance Service

We enrolled a sample of four patients who were seen by the paramedic first responder on two particular 12 hour shifts over a four month period. Participants were firstly approached by the paramedic and if willing they were then approached by the research team. If patients were deemed too unwell or taking part in the research could delay their treatment or transfer to hospital, then they were not approached. Patients who were unable to give consent due to their condition or were unable to speak or read English were also excluded from taking part.

5.9.2.3 Methods of measurements

The respiratory rate of each participant in each setting was measured simultaneously by three different methods. Respiratory Inductance plethysmography (RIP), the established contact method; visual counting of chest movements, which is the established non-contact method and the contactless portable respiratory monitor (CPRM), which is the new method.

5.9.2.4 Instruments

5.9.2.4.1 Contactless portable respiratory rate monitor

The CPRM was held at a distance of 10 to 15 cm from the participant's face and positioned so that maximal exhaled breath was collected and an adequate signal obtained.

5.9.2.4.2 Respiratory inductance plethysmography

Thoracic and abdominal respiratory inductance plethysmography bands (zRIP inductance effort belts) were used to capture and record respiratory signals from the participants. Data was recorded on the SOMNOtouch RESP portable screening device (S-Med, Birmingham, UK) and downloaded for visual analysis. To determine the RIP respiratory rate, the number of observed respiration cycles from this respiratory signal was counted manually during the time period at which the simultaneous measurements were taken.

5.9.2.4.3 The visual counting method

Visual counting of respiratory rate was performed by a separate observer. A count of observed chest movements over the same time period as the other measurements were being taken was made.

5.9.2.5 Data collection and procedure

Each participant was assigned a unique identifying number based on the order that they were recruited in their particular setting. Data on the participants age and sex along with their presenting complaint and triage RR, where applicable, was collected. Measurements were made at rest with the participant sitting upright comfortably in a chair or for a younger child on the lap of a parent.

At a defined starting time the respiratory rate was simultaneously taken by each of the three methods for a period of 52 seconds. One observer measured RR with the CPRM, and another observer measured using the visual counting method. All measurements were converted to breaths per minute and the data was then entered into an Excel spreadsheet. One detachable funnel (Funnel A) was used throughout the studies. Two data sets were taken for each participant, except in the study with the Yorkshire ambulance service where only one data set was taken for each participant.

5.9.2.6 Statistical analysis

The pairwise agreement between RR counts from each of the three methods was assessed by calculating the mean difference and 95% limits of agreement (mean $\pm$ the standard deviation of the difference). These were charted using Bland-Altman plots (Bland and Altman, 1986). Intraclass correlation coefficients with 95% confidence intervals were also reported. All results were analysed using SPSS, version 22.0 for Mac.

5.9.2.7 Ethical approval

The study received a favourable ethics opinion by the NRES committee Yorkshire and the Humber on 5/10/15 REC reference 15/YH/0297 (appendix 8.4). Further site specific ethical approval was obtained from both the Yorkshire Ambulance Service and the Doncaster Clinical Commissioning Group. Written consent was obtained from the participant or the parent of each child participant prior to participation.

5.9.2.8 Funding

This study was funded by The Children's Hospital Charity and was granted £15,138.53 in March 2015.

5.9.3 Results

5.9.3.1 General Practice Surgery

5.9.3.1.1 Study subjects

A total of 41 respiratory rate measurements were made on 20 adult subjects. Participant's ages ranged from 23 to 88 years, with a mean age of 58 years. 10 subjects (50%) were female. Each subject had two or three measurements taken.

5.9.3.1.2 CPRM compared with contact method

When the CPRM was compared with RIP measurements Bland-Altman analysis showed a mean difference of 0.376 with 95% limits of agreement of -5.129 to 5.880. The correlation was substantial with an Intraclass correlation coefficient of 0.723 (95% CI 0.538 - 0.842) (Figure 5.24).

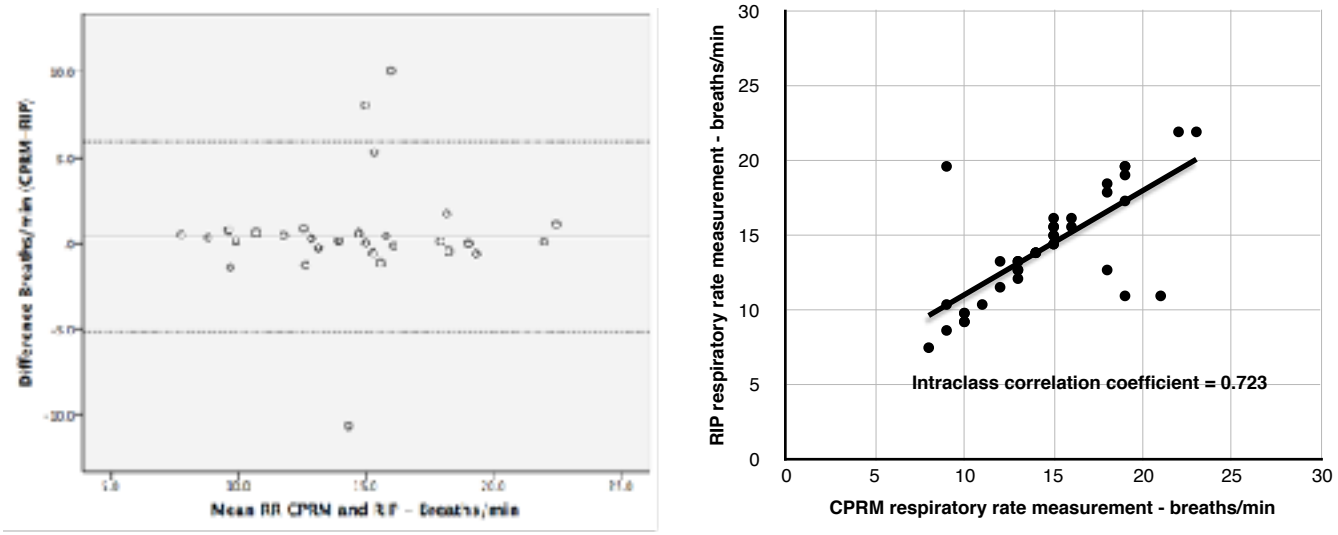


Figure 5.24: Bland-Altman plot and scatterplot of agreement and correlation between CPRM and RIP measurements.

5.9.3.1.3 CPRM compared with visual counting method

There was a slightly lower level of agreement seen when the CPRM was compared with the visual counting method, with a mean difference of 0.897 and 95% limits of agreement of -5.031 to 6.825. The correlation was also less with intraclass correlation coefficient of 0.653 (95% CI 0.436 - 0.799) (Figure 5.25).

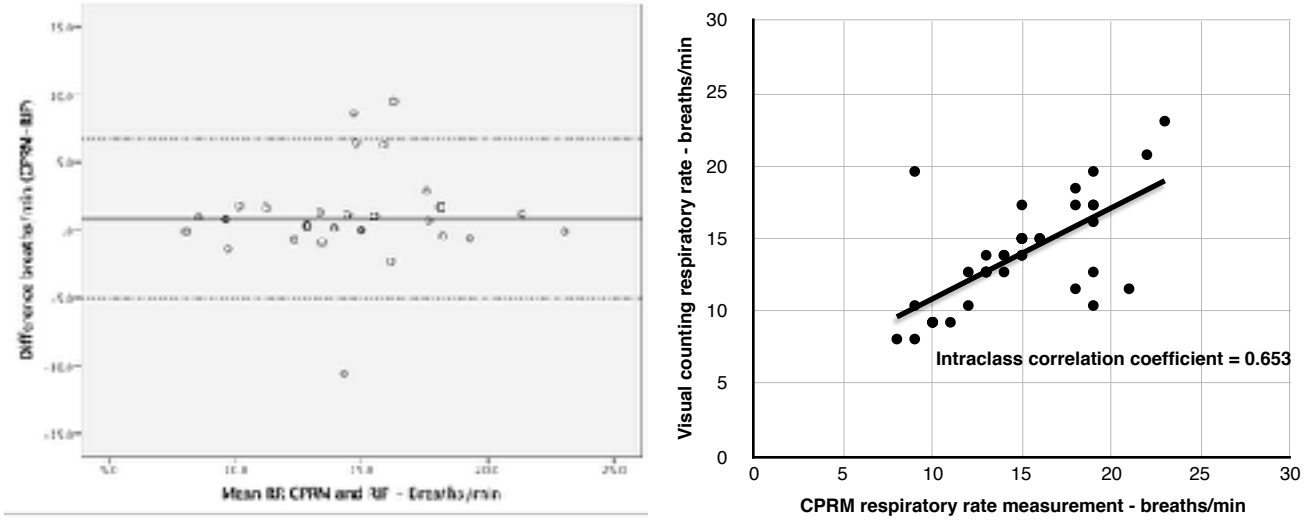


Figure 5.25: Bland-Altman plot and scatterplot of agreement and correlation between CPRM and visual count respiratory rate measurements.

5.9.3.1.4 Further analysis of CPRM compared with contact method

On four occasions there was difficulty in detecting the participant's breath with the CPRM, and measuring started before a respiratory breath signal was obtained. This occurred for three different participants. When these measurements were removed from analysis the agreement between the CPRM and the contact method was greatly improved with a mean difference of 0.072 and 95% limits of agreement of -1.181 to 1.891. Correlation was almost perfect with ICC: 0.985 (95% CI 0.971 - 0.992) (Figure 5.26).

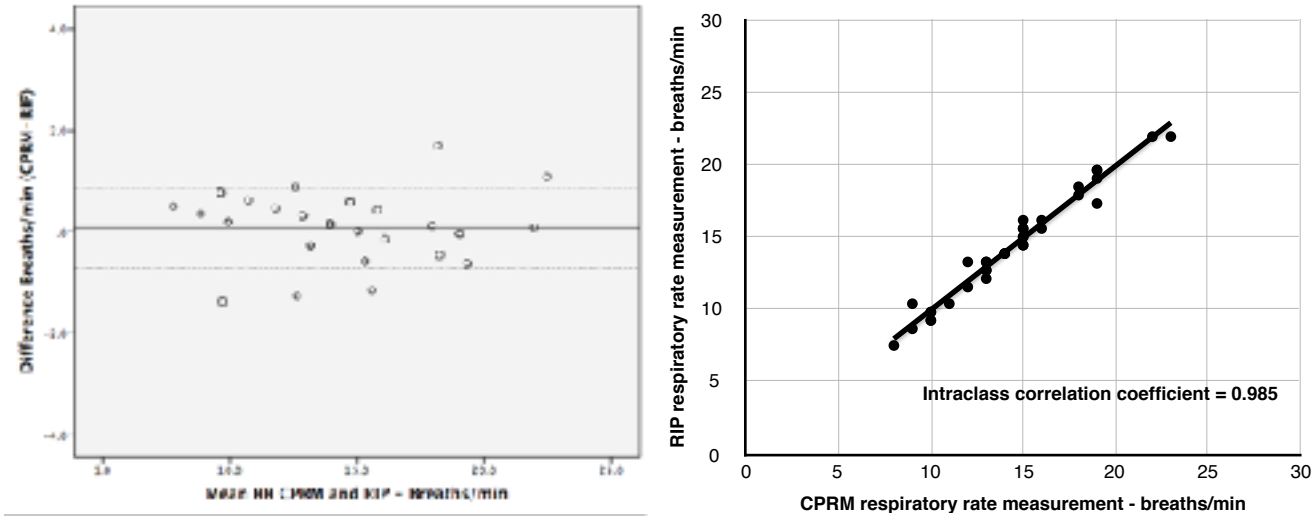


Figure 5.26: Bland-Altman plot and scatterplot of agreement and correlation between CPRM and RIP measurements with four outlying measurements removed.

5.9.3.2 Paediatric Emergency Department

5.9.3.2.1 Study subjects

A total of 59 recordings were obtained from the 30 children. On one occasion the CPRM failed and needed replacing, as such one child had only one measurement taken. Eight participants (27%) did not have a respiratory rate recorded in the Emergency Department triage. The participant characteristics are summarised in Table 5.5 along with their presenting complaints.

Table 5.5: Participant characteristics (n=30)

Age in months, mean, range	82.8 (24-168)
Male gender, n (%)	19 (63%)
Presenting complaint, n (%)	
Respiratory illness *	9 (30%)
Generally unwell/non-specific illness	7 (23%)
Head injury	4 (13%)
Limb injury	4 (13%)
Eye problem	2 (6%)
Ear problem	1 (3%)
Abdominal pain	1 (3%)
Burn	1 (3%)
Seizure	1 (3%)

*Included wheeze, increased work of breathing, cough and croup

5.9.3.2.2 CPRM compared with contact method

When the CPRM was compared with RIP measurements Bland-Altman analysis showed a mean difference of -4.571 with 95% limits of agreement of -24.310 to 15.167 (Figure 5.27). Correlation was also only fair with an intraclass correlation coefficient of 0.380 (95% CI 0.133 - 0.581).

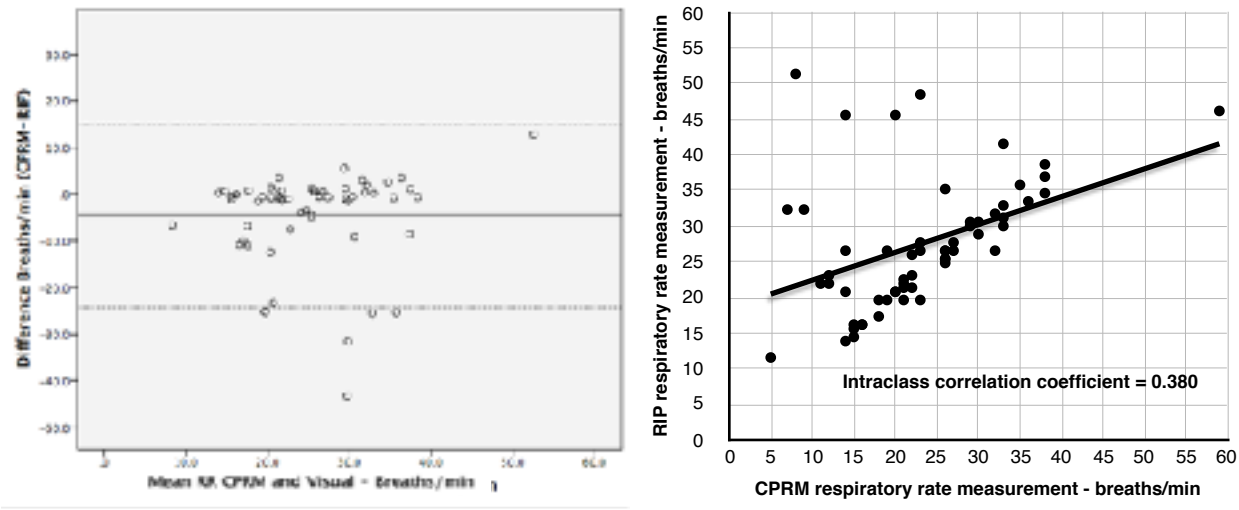


Figure 5.27: Bland-Altman plot and scatterplot of agreement and correlation between CPRM and RIP measurements.

5.9.3.2.3 CPRM compared with visual counting method

There was a similar level of agreement seen when the CPRM was compared with the visual counting method with a mean difference of -2.146 and 95% limits of agreement of -24.069 to 19.777. The intraclass correlation coefficient was 0.340 (95% CI 0.099 - 0.545) (Figure 5.28).

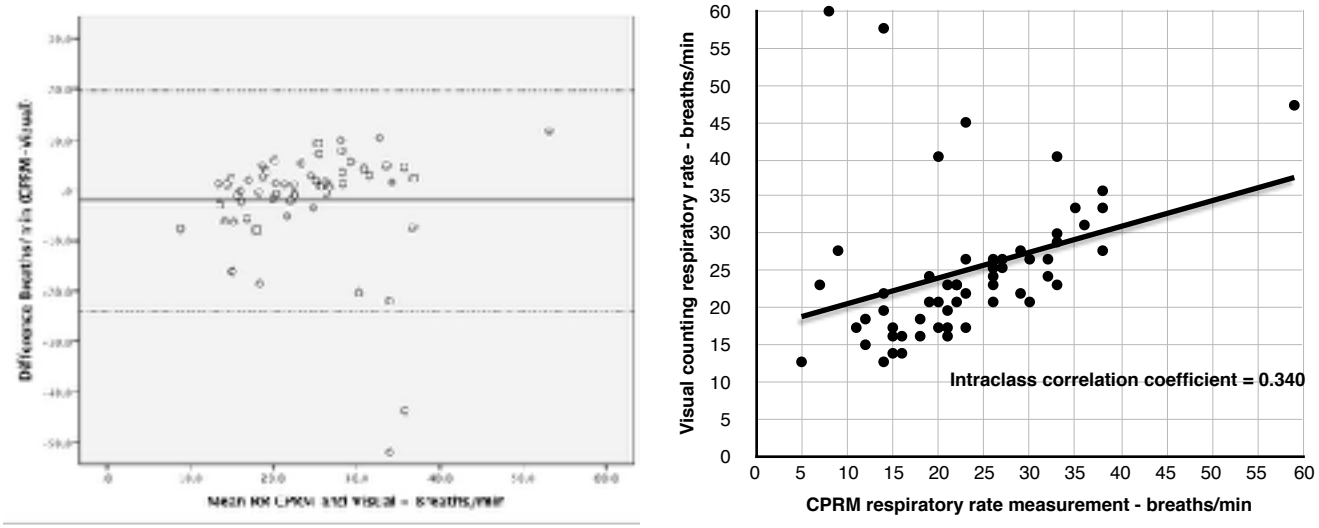


Figure 5.28: Bland-Altman plot and scatterplot of agreement and correlation between CPRM and visual count respiratory rate measurements.

5.9.3.2.4 Further analysis of CPRM compared with contact method

On further analysis of the data it was clear that the CPRM was less accurate than both visual and contact methods in children under 4 years of age. There were seven children under 4 years and when they were removed from analysis the agreement between the CPRM and the contact method was improved considerably with a mean difference of -1.334 and 95% limits of

agreement of -10.278 to 7.610. Correlation was also substantial with an ICC of 0.849 (95% CI 0.737 - 0.915) (Figure 5.29).

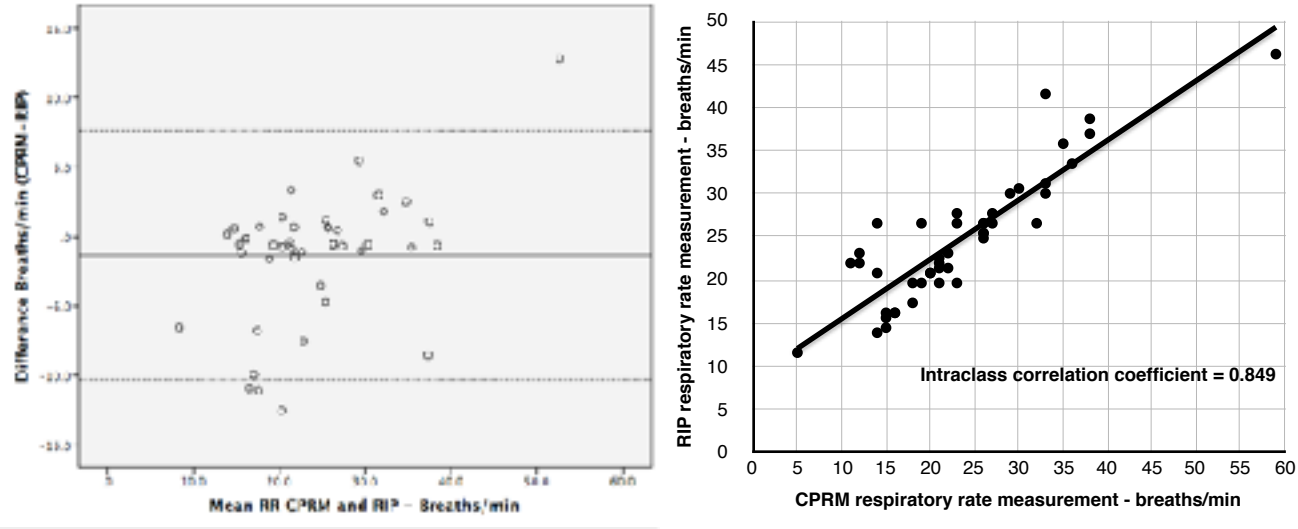


Figure 5.29: Bland-Altman plot and scatterplot of the agreement and correlation between CPRM and RIP measurements for participants over 4 years of age.

5.9.3.3 Yorkshire Ambulance Service

5.9.3.3.1 Study subjects

A total of four respiratory rate measurements were made, three on adult subjects and one on a child. Participant's ages ranged from 4 to 97 years. Each subject had only one measurement taken.

5.9.3.3.2 Agreement of CPRM with contact method and visual method

Although only 4 subjects were tested, agreement with both RIP measurements and visual measurements was almost perfect. Bland-Altman analysis showed a mean difference of -0.423 and 95% limits of agreement of -2.220 to 1.375 when compared with the contact method and a mean difference of 0.730 and 95% limits of agreement of -2.242 to 3.702 when compared with the visual method (Figure 5.30). Correlation was also excellent. When compared with the contact RIP method the ICC was 0.994 (95% CI 0.918 - 1.000) and when compared with the visual counting method the ICC was 0.982 (95% CI 0.753 - 0.999).

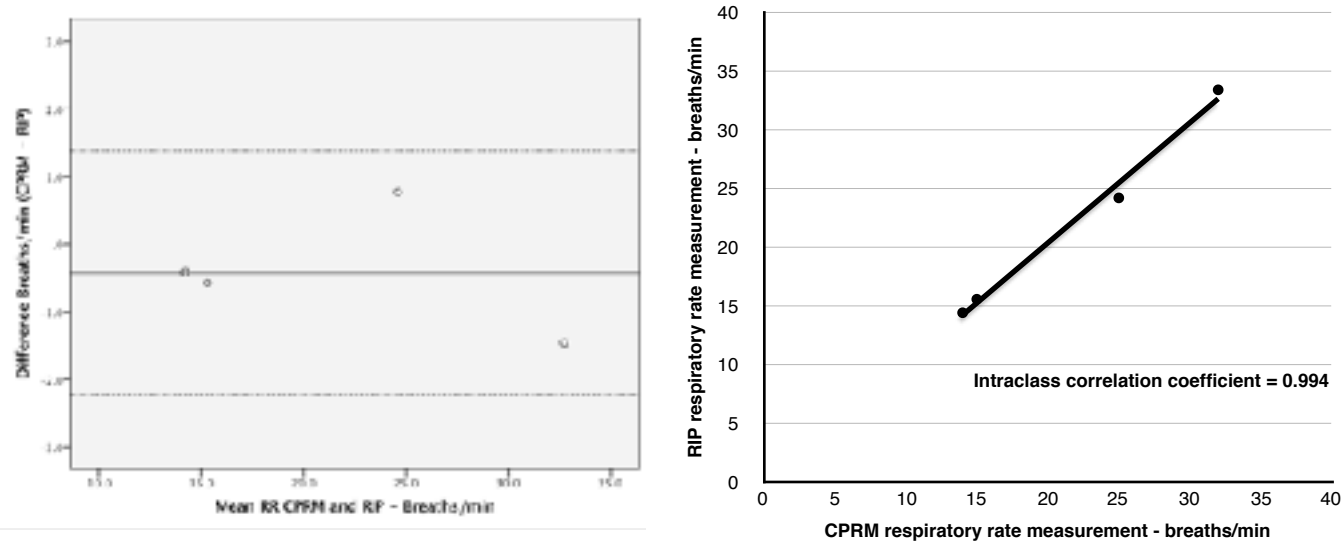


Figure 5.30: Bland-Altman plot and scatterplot of agreement and correlation between CPRM and RIP measurements.

5.9.3.4 Summary of results

Table 5.6 summarises the results for the CPRM in the pre-hospital setting.

Table 5.6: Summary of results for Pilot study F

Setting	Methods of measurement	95% Limits of agreement (mean difference)	Intraclass correlation coefficient (95% CI)
Emergency Department	CPRM v Contact method	-24.310 - 15.167 (-4.571)	0.380 (0.133 - 0.581)
	CPRM v Visual count	-24.069 - 19.777 (-2.146)	0.340 (0.099 - 0.545)
General Practice	CPRM v Contact method	-5.129 - 5.880 (0.376)	0.723 (0.538 - 0.842)
	CPRM v Visual count	-5.031 - 6.825 (0.897)	0.653 (0.436 - 0.799)
Yorkshire Ambulance Service	CPRM v Contact method	-2.220 - 1.375 (-0.423)	0.994 (0.918 - 1.000)
	CPRM v Visual count	-2.242 - 3.702 (0.730)	0.982 (0.753 - 0.999)

5.9.4 Discussion

5.9.4.1 General Practice Surgery

This study provided useful information on the accuracy and usability of the CPRM in a general practice setting and on participants with active illnesses and co-morbidities. All data was obtained from adult subjects and no children were tested. There were however a large age range of adult ages tested that had not previously been captured.

The accuracy of the CPRM was substantial in this setting and was higher than the previous pilot study that involved only adult participants (Pilot study A). The level of agreement was also likely to be close to that acceptable for clinical practice. The 95% limits of agreement were better than those we have described for a visual measurement in children (Chapter 3), and similar to those described in adults by Lim et al (Lim et al., 2002). This greater level of agreement than that described in Pilot study A is likely to be due to one consistent funnel being used, improved user accuracy in taking measurements and a more reliable device with technical faults now resolved.

There were four particular measurements (9.7% of all measurements) when the device had not gained an adequate respiration signal before the measurement started. This led to a period during the 52 seconds of sampling where the user had to move the device around the participants face to pick up the subject's breath signal again. Therefore some breaths were missed and also spurious breaths appeared to be added by the device. This accounted for outlying readings that could be above or below the actual measurement. When these were removed the correlation of the CPRM with the RIP contact method was almost perfect with excellent 95% limits of agreement. The CPRM measurement should not have started until the subject's respiration signal was obtained and confirmed. However, in clinical practice and in time pressured environments this problem could become more common. The user may be more rushed and lack experience using the device meaning less time is given to finding the respiration signal and the recording is started too soon leading to more inaccurate measurements being obtained.

Although a general practice surgery setting may not be as pressured as a hospital environment, GPs and nurses are still limited by consultation times. The average consultation time lasts between 10-12 minutes (RCGP, 2013). With a RR measurement by the CPRM taking up almost 10% of this time, the device in its current format may not be feasible to use in this setting. An option could be for the measurement to be made in the waiting room by a different healthcare professional or by the patient themselves. However the usability of the device would need to be improved before this was a viable option.

5.9.4.2 Paediatric Emergency Department

This was the first testing of the CPRM on unwell children. It captured children with a wide range of medical and surgical conditions. It was also the first time the CPRM had been used in an acute hospital clinical setting. Disappointingly, the overall accuracy of the CPRM was the lowest seen when compared with all of the previous pilot studies.

Poor agreement was seen on multiple occasions between the CPRM and both the RIP and visual count. This was seen most often in children with higher respiratory rates, above 40 breaths/ minute. The CPRM did not always capture all of these children's breaths and as such gave a lower reading. This is of concern as in the clinical setting it is the children with raised respiratory rates that need to be captured and identified earlier in order to instigate treatment promptly. The CPRM did not however over-measure a child's respiratory rate.

With further analysis of the data it was clear that the CPRM was less accurate in children under the age of 4 years. These children accounted for 23% of the cohort studied. Children under 4 years of age had higher respiratory rates and were less likely to cooperate with the measurement process. Also when the child was unwell they were again less likely to cooperate. They regularly moved their head away from the device, talked, coughed or pushed the device away. All of these actions meant that a number of breaths were not captured and the final measurement fell well below the respiratory rate as measured by the other methods. However if the child was sat still and cooperated, which was seen in many of the older children, the accuracy of the CPRM greatly increased.

The CPRM was again limited by its sampling time of 52 seconds. This became more evident in a busy triage setting where a quick and accurate assessment of the child is required. Of all the observations taken on the child a respiratory rate using the CPRM would be the most time consuming. Blood pressure can take up to 30 seconds to complete via the automated device but a heart rate and oxygen saturation level can be obtained almost instantaneously. Nurses in the emergency department triage and hospital managers may therefore be resistant to use such a device as it may increase the time taken to assess a child and reduce the number of children they could see within a given time.

Of the participants in this study 27% did not have a RR measured in triage. However, these children presented to the ED with injuries where departmental guidelines do not require a RR to be measured. Interestingly, of the respiratory rates taken in triage, 95% of these measurements were even number values. This suggests that the triage nurse may have taken a measurement over 15 or 30 seconds and multiplied the value up. This is a finding that has also been reported when looking at respiratory rate data (O'Leary et al., 2015) and as shown in chapter 3 of this thesis is far less accurate than a 60 second visual count.

5.9.4.3 Yorkshire Ambulance Service

In the four measurements taken in this setting the CPRM was extremely accurate, showing excellent agreement and almost perfect correlation. However, in this setting the recruitment of patients was difficult. A number of patients were unable to be recruited as they were deemed too unwell to undergo the measurement and others were unable to be consented due to lack of capacity or language barriers. Therefore due to the small number of participants, it is not possible to fully comment on the accuracy of the CPRM in this setting.

However, useful information was obtained on the usability of the CPRM. The CPRM could be used at the scene either at the patients home or at the roadside. The device in its current form with the base unit attachment could be carried from the vehicle to the patient with little difficulty. However, a paramedic may find this difficult when the device is added to the other equipment that has to be carried to the patient. At the patient side observations are taken by the Paramedic using medical devices to measure heart rate, oxygen saturations, temperature and blood pressure. A respiratory rate measurement with the CPRM could be incorporated into this process. However, the current sampling time could hinder a quick assessment by the Paramedic. If the measurement could be made simultaneously with other measurements then this would save time and enhance the devices' usability.

Another occasion in which a respiratory rate may be measured by the Paramedic is en-route to the hospital. A visual count in this environment can be challenging and potentially inaccurate. Measuring with the CPRM in this situation is also demanding, as holding the device still so that a good quality respiration signal is obtained is difficult. If the CPRM could be fixed within the ambulance on an extendable arm then the measurements may not be affected by movement within the ambulance.

Finally, in this setting multiple RR measurements are sometimes needed throughout the assessment and transport process. These readings however can be forgotten or misplaced if not recorded immediately. If the device was able to store or provide a print out of the most recent measurements then this would ensure all measurements are recorded accurately and promptly and can be recalled on arrival to hospital.

5.9.5 Conclusions and recommendations

This pilot study has provided useful information on the accuracy and usability of the CPRM in three very different clinical settings. The CPRM could be a useful addition to GP surgeries. However, adjustments to the device would need to be made to reduce sampling times so that measurements did not impact upon consultation times. There were also clear benefits found for Paramedics using the CPRM, with the device potentially making measurements en route to hospital easier and more accurate. However, the device would require miniaturising and strengthening for use in this setting.

Unfortunately the CPRM did not perform well in unwell children in the triage setting. The accuracy of the CPRM continued to be affected by interference including, coughing, talking, and movement, particularly in the younger child. This greatly affected the respiration signal received and therefore the accuracy of the measurement obtained. Therefore many alterations are needed to be made to the CPRM to improve it for use in younger children and to bring its accuracy in line with current methods of measurement.

From this pilot study the recommendations for further development of the CPRM include:

- Reduction in the sampling time.
- Enabling of sampling time to be adjusted based upon the respiration signal received.
- Signal lock to start a respiratory rate recording.
- Rejection of a poor respiration signal.
- Adjustments in signal amplification to enhance respiration signal received.
- Miniaturisation of the device to improve portability.
- Strengthening of the casing of the device to improve robustness.
- Facilities to store and download respiratory rate measurements made with the CPRM.

5.10 Discussion on the CPRM pilot studies

These four pilot studies have provided vital information on the accuracy, usability and feasibility of the CPRM in a number of different settings and on a variety of subject groups. We have firstly demonstrated that the CPRM can measure the respiratory rate in both adults and children. The accuracy of these measurements are however dependent upon a number of different factors. The sections below give an appraisal of the accuracy and usability of the device, its advantages and limitations, and recommendations for modifications and improvements that can be made to further develop the device.

5.10.1 Accuracy of the CPRM

The CPRM showed varying degrees of accuracy across each of the different pilot studies, these are summarised in Table 5.7. The greatest accuracy was demonstrated in the most controlled settings and in individuals who were the most cooperative. If a clear respiratory signal was obtained from the subject, and maintained throughout the measurement period, then the CPRM was highly accurate and comparable to the contact method of measurement, and in some instances, more accurate than a visual count.

Table 5.7: CPRM compared with the contact RIP method for each pilot study

Study	Subjects (Number of measurements)	95% Limits of Agreement (Mean Difference)	Intraclass correlation coefficient (95% CI)
Pilot study A	Healthy Adults (159)	-7.204 - 6.216 (-0.494)	0.568 (0.453-0.664)
Pilot study B	Healthy Children (60)	-23.608 - 15.385 (-4.112)	0.336 (0.098 - 0.540)
Pilot study C	Primary school - Children (38)	-16.198 - 12.412 (-1.893)	0.409 (0.116 - 0.639)
Pilot study D	Children undergoing sleep studies (61)	-6.842 - 6.419 (-0.212)	0.762 (0.633 - 0.850)
Pilot study E	a) Emergency Department - Children (59)	-24.310 - 15.167 (-4.571)	0.380 (0.133 - 0.581)
	b) General Practice - Adults (41)	-5.129 - 5.880 (0.376)	0.723 (0.538 - 0.842)
	c) Yorkshire Ambulance Service - Adults (3) & children (1)	-2.220 - 1.375 (-0.423)	0.994 (0.918 - 1.000)
Overall	Adult subjects (203)	-6.770 - 6.146 (-0.312)	0.619 (0.527 - 0.697)
	Child subjects (219)	-19.112 - 13.594 (-2.759)	0.437 (0.306 - 0.548)
	Total subjects (422)	-14.438 - 11.259 (-1.590)	0.626 (0.553 - 0.687)

However in many of the pilot studies there were episodes where a clear respiration signal was not obtained or it was not maintained throughout the measurement period. This was due to a variety of factors which are outlined later in this chapter. On these occasions it was clear that the RR

measurement was not accurate and in practice these measurements may have been discarded and retaken. When we accounted for these readings within the studies and removed them from analysis the accuracy of the CPRM greatly increased and moved towards ranges that could be deemed acceptable for use within a clinical setting.

The accuracy of measurements in Pilot study A and B were also affected by the different funnel attachments used. Some of the funnels used in these studies were extremely inaccurate and as such skewed the accuracy of the results. Overall though the CPRM showed a greater degree of accuracy in adult subjects. This is unsurprising as the cooperation of the subject had a great impact on the respiration signal obtained and as such the measured RR.

It is also useful to compare the accuracy of the CPRM against other devices that have been developed to measure respiratory rate. Table 5.8 summarises the different devices and their reported accuracy.

Table 5.8: Summary of the accuracy of devices for measuring respiratory rate

Device method	Subject's tested	Control	Reported accuracy
Acoustic *(Patino et al.,2013)*	40 Children	Capnography	95% limits: -7.3 - 6.6 bpm
ECG derived *(Chan et al., 2013a)*	15 Adults	Capnography	95% limits: -4.4 - 3.8 bpm
Photoplethosomography *(Olsson et al.,2000)*	10 Neonates	Thoracic impedance	Correlation coefficient (r) = 0.99
(Wertheim et al.,2013)	18 Children	60 sec visual count	+/- 10 bpm
Infrared thermography *(Al-Khalidi et al.,2011b)*	16 Children	Thoracic impedance	Correlation coefficient (r) = 0.994
Humidity detection *(Niesters et al.,2012)*	28 Adults	Capnography	95% limits: -1.1 - 1.3 bpm
Doppler radar *(Droitcour et al.,2009)*	24 Adults	Thoracic impedance	ICC: 0.885 95% limits: -4.5 - 1.8 bpm
Mobile application *(Karlen et al., 2014)*	10 Videos of adults	60 sec visual count	+/- 2.2 bpm
CPRM	50 Adults	Thoracic impedance	ICC: 0.619 95% limits: -6.8 - 6.1 bpm
CPRM	91 Children	Thoracic impedance	ICC: 0.437 95% limits: -19.1 - 13.6 bpm

The CPRM shows a level of accuracy lower than that of the other devices, both contact and non-contact. However, it is difficult to fully compare each of these devices with the CPRM. The testing and analysis of each device uses different methodological approaches and a variety of control methods to compare against. There are also differing population groups studied as well as varying methods of statistical analysis used. This makes a full comparison between each of the devices difficult and caution must be taken when doing so. Also, although appearing to show good

accuracy some of the devices are limited by either long set up times, the requirement for expensive equipment or full co-operation of the patient. Many devices also require equipment to be placed on the patient, which may not be well tolerated, or may even distort the RR measurements in some clinical settings and certain patient groups. As such these methods may not be appropriate for use in children and in clinical settings where a quick accurate RR measurement is required.

It is also useful to look at the accuracy of other medical devices that have been introduced into everyday clinical practice and are now accepted for routine use. The infrared tympanic membrane thermometer as compared with the axillary thermometry showed a mean difference of -0.09 with 95% limits of agreement -1.54 ^{0}C to 1.36 ^{0}C and a correlation coefficient (r) of 0.697 in 174 adult patients (Gasim et al., 2013). This thermometer could therefore read anything up to 1.36 ^{0}C above or 1.54 ^{0}C below the axillary thermometer. Van de Louw et al compared standard pulse oximeters with arterial blood gas analysis in 102 critically ill adult patients (Van de Louw et al., 2001). They reported a mean difference of -0.02 with a standard deviation of the differences of 2.1%, and suggested that a pulse oximetry reading of 94% or above was needed to ensure that the actual arterial blood saturation was above 90%. With both of these devices we see that there is a degree of error when compared to the standard measurement method. However despite this error the level of agreement has been deemed acceptable for the measurement of that particular parameter in clinical practice. Therefore when analysing the accuracy of the CPRM it is accepted that there will be a degree of error but we must establish the level of agreement that is acceptable.

As discussed in the separate pilot study sections, work by Lim et al (Lim et al., 2002) suggests that in adults the acceptable 95% limits of agreement for a respiratory rate measurement should be no greater than -4.86 to 4.94 breaths/min. In children, based upon our data collected in Chapter 3 of this thesis, the 95% limits of agreement should be no greater than -7.11 to 6.95 breaths/min. Therefore in the majority of cases in both adults and children the accuracy of the CPRM does not meet these acceptable limits of agreement. There are some occasions however, in certain settings where its accuracy has been shown to be superior to current methods of measurement. But in it's current format the CPRM does not possess the level of accuracy appropriate for use in a clinical setting, nor does it offer a viable alternative method of measuring respiratory rate.

5.10.2 The CPRM funnels

The pilot studies trialled a total of five different funnel attachments. The purpose of these funnels were to enhance the respiration signal from the subject. Four funnels were initially tested on healthy adults in Pilot study A, two of these were discarded and a further funnel developed for testing in Pilot study B.

The smaller funnels with a small air inlet area performed badly in testing (Funnel D and E). When measuring with these funnels it was difficult to obtain an adequate respiration signal as many of

the subject's breaths were not channeled into the CPRM and were missed and therefore not measured. The funnels that performed better, and showed a higher degree of accuracy, were those with larger air inlet areas. If held in a steady position these funnels (Funnel A, C and D) channeled the subject's breath more effectively and produced a better respiration signal that gave a more accurate RR measurement.

However, it was not just the measured accuracy of the funnels that was taken into account when assessing them. The usability of the device when the funnel was attached was also important. The larger the air inlet funnel the harder the CPRM was to hold and keep in position by the user. The device also became less portable, and was more intrusive when placed in front of the subject. These factors are essential to take into account when developing the CPRM. The device is designed to be portable and used in many different clinical areas and its appearance must not cause added stress and anxiety to the subject. It was with these factors in mind that led to Funnel A being used in the remaining Pilot studies and our recommendation that this funnel is used with further developments of the device.

5.10.3 Usability of the CPRM

For the CPRM to function well in a variety of clinical settings it needs to have a high degree of usability. It must be able to be operated by a number of different users with minimal prior training and show little or no variation between measurements taken by different users. The user of the CPRM should have little or no effect on the accuracy of measurements obtained. The usability of the CPRM can be evaluated by assessing the reproducibility of measurements and also the ease of obtaining a measurement in different subject groups.

5.10.3.1 Reproducibility of measurements

Only one of the pilot studies assessed the reproducibility of measurements taken by different users (Pilot study B). The agreement was substantial however only 24 paired measurements were assessed. In all of the other pilot studies only one user performed the CPRM measurement so no further analysis of variation between users could be made. In order for the CPRM to be a valuable tool in clinical settings the clinician must have confidence that measurements are not affected by the user that took them. Further larger scale analysis of reproducibility of measurements is needed once adjustments and improvements have been made to the CPRM.

5.10.3.2 Obtaining a CPRM measurement

The pilot studies assessed the CPRM in both adult and child subjects. There were some clear differences found in the positioning of the CPRM needed to obtain a respiratory rate measurement in both sets of subjects. In the studies with adult subjects we found that there were a variety of positions that the CPRM may be needed to be placed in front of the subject before an adequate signal was obtained (Figure 5.31a). This was due to the fact that there was a wide range of angles that breath could come off from the subject. This was influenced by many factors including facial shape, the angle of the subject's nose and nostrils and whether the subject

breathed through their nose or mouth. In practice this resulted in time spent optimising the CPRM position in front of the subject's face. In many cases this led to a delay in starting the recording, which if used in clinical practice may not be appropriate in time critical settings or in uncooperative subjects.

In child subjects the CPRM often only needed to be placed in one single position to pick up an adequate respiration signal (Figure 5.31b). This was likely due to the smaller size of a child's face, meaning that each child's breath came off at a similar angle. As a child grows older and their face shape changes the device would however need to be moved around the face to gain an adequate signal, as is seen in adult subjects.

These variations in positioning are important as they affect the overall usability of the device. The less experienced the user the longer it could take to find the optimum angle to gain an adequate signal. This could lead to user variation in measurements, delay in gaining a measurement and inaccuracies in the measurements obtained.

In its current form the CPRM does require a degree of training and practice before it can be used effectively. Users would need to be educated on the positioning of the CPRM and the best ways to obtain an adequate respiration signal. This is important to take into account when modifications are being made to the current device as steps to negate these issues would enhance the usability of the device and lend itself to being more widely used in a variety of clinical settings.

5.10.4 Advantages of the CPRM

The CPRM has many advantages that set it apart from some of the other devices that have been trialled to measure respiratory rate. These include:

1.Contactless

The CPRM is a non-contact device. There are no parts of the device that come into contact with the subject. This is particularly advantageous in children where a contact device may be less well tolerated by the child and could unintentionally alter their respiratory rate. Although some of the pilot studies indicated that the CPRM could cause an added amount of stress to the child by just being positioned near them, a contact device is likely to cause more stress and anxiety to the child and potentially alter their respiratory rate.

2.Infection Control

The contactless nature of the device also means it benefits from an infection control perspective. It does not require sterilisation as it is at no point in contact with the subject. Similar to other monitoring devices used in the general clinical setting, no specific cleansing is required other than the normal physical cleansing using soap and water or medical grade detergent wipes. The device's funnel is easily cleaned and the thermistor inside the device can be changed periodically if needed. This enables the device to be used on multiple patients with minimal or no cleaning required in between each patient.

3. Safety

During these pilot studies there were no safety concerns associated with the CPRM to either the subject or the user.

4. Set up time

There is minimal set up time required for the CPRM and no calibration of the device is needed prior to taking a measurement. Many other devices that have been proposed to measure respiratory rate have been limited by complex sensitive equipment and long set up times (Abbas et al., 2011, Arlotto et al., 2014). This feature of the CPRM lends itself to settings such as an emergency department triage where rapid measurements may be required.

5. Portability

The CPRM in its current form is somewhat limited by its portability, however it has the potential to become an extremely portable device. Unlike other devices that may have many component parts and heavy cumbersome equipment, the CPRM is relatively lightweight. The interface section itself is light and easy to carry. If the base unit is able to be incorporated into the interface section then the CPRM has the potential to be easily transported and used in a large variety of clinical settings, in and out of the hospital.

5. Cost

Many devices that have been used to measure respiratory rate require expensive equipment (Abbas et al., 2011, Al-Khalidi et al., 2011a, Arlotto et al., 2014). This equipment may not be practical to be brought into and used in many everyday clinical areas. The CPRM benefits from the fact that one device can be used to measure multiple patient's respiratory rates, although the lifespan of the device is not yet known. Also as the CPRM is manufactured from widely available commercial components, when produced on a larger scale the cost of a device will be significantly reduced. It is likely that the CPRM will be no more expensive than the devices currently used for measuring the other vital signs.

5.10.5 Limitations

5.10.5.1 Limitations of the CPRM

Through completing these pilot studies a number of limitations of the CPRM and its usability were identified. Limitations were either due to the subject, the user of the CPRM or the CPRM itself. All of these could directly or indirectly affect the signal received and as such the accuracy of measurements obtained. Table 5.9 describes and explains these limitations and offers recommendations for overcoming them.

Table 5.9: Limitations of the CPRM and its usability with recommendations

Factor	Description	Explanation	Recommendations
Subject	1. Movement of subject	Head movements of the subject can result in some respiration signals being missed or of inadequate strength.	-Gain attention of subject during recording. -Enhanced extraction of respiration signal. -Rejection of poor respiration signal. -Adjustment of the signal amplification. -Reduction in sampling time.
	2. Interference i.e. coughing, talking, yawning	Each of these create an artefact signal that is picked up by the CPRM and may be interpreted as a breath.	-Rejection of poor respiration signal. -Enhanced extraction of respiration signal.
	3. Size and shape of subjects face	These differences can alter the angle and strength of the subjects respiration signal leading to some breaths being missed or of inadequate strength.	-Enhanced extraction of respiration signal. -Rejection of poor respiration signal. -Adjustment of the signal amplification.
	4. Artificial altering of subject's respiratory rate	In children aged 5-8 years the CPRM caused an alteration in their RR.They often changed their RR, breathing into the device at a higher rate.	-Distract subject from CPRM measurement.

Table 5.9: Limitations of the CPRM and its usability with recommendations

Factor	Description	Explanation	Recommendations
User	1.Movement of the CPRM	The user moving the CPRM away from the respiration signal during the measurement period can cause some respiration signals to be missed and also vary the strength of the signal received.	-Reduction in sampling time. -Enhanced extraction of respiration signal. -Rejection of poor respiration signal. -Adjustment of the signal amplification. -Signal locking to start recording. -Develop user alerts and guidance.
	2. Initiation of measurement	The user may initiate the start of the measurement before the CPRM has found a respiration signal. This may lead to missed breaths at the start of the recording and an inaccurate measurement.	-Signal locking to start recording. -Develop user alerts and guidance.
	3. Variability in user practices	Different users may vary in how they use the CPRM to collect the respiration signal. This could cause inaccuracies in measurements between users.	-Develop user alerts and guidance. -Signal locking to start recording.
CPRM	1. Sampling time	The longer the sampling time the less cooperative the subject may be, and the more chance there is for movement and artefact to disrupt the measurement.	-Reduction in sampling time. -Enable sampling time to be adjusted based on the quality and consistency of the signal received.
	2. Appearance	If the CPRM is too obvious it can cause a child to alter their RR and breath into it. Also if a child is not attracted towards it then it is harder to pick up a respiration signal.	-Gain attention of subject and distract from CPRM measurement. -Improved appearance of CPRM.
	3. Portability	The CPRM has a battery life of 3-4 hours which limits its usage out of the hospital. It is also limited by its size and the relatively poor durability of the materials used in its manufacture.	-Improvements in battery life. -Integrate components into the hand held device to reduce CPRM size. -Firmer more durable casing to ensure the device is more robust.

5.10.5.2 Limitations of the pilot studies

The results and information obtained on the CPRM were also limited by the pilot studies themselves. Only small sample sizes were used in each of the different studies which can only give a crude indication of the accuracy and usability of the CPRM in each setting and on each cohort of participants. These results must therefore be used to help inform and develop the device further and give information to help develop larger scale more robust studies.

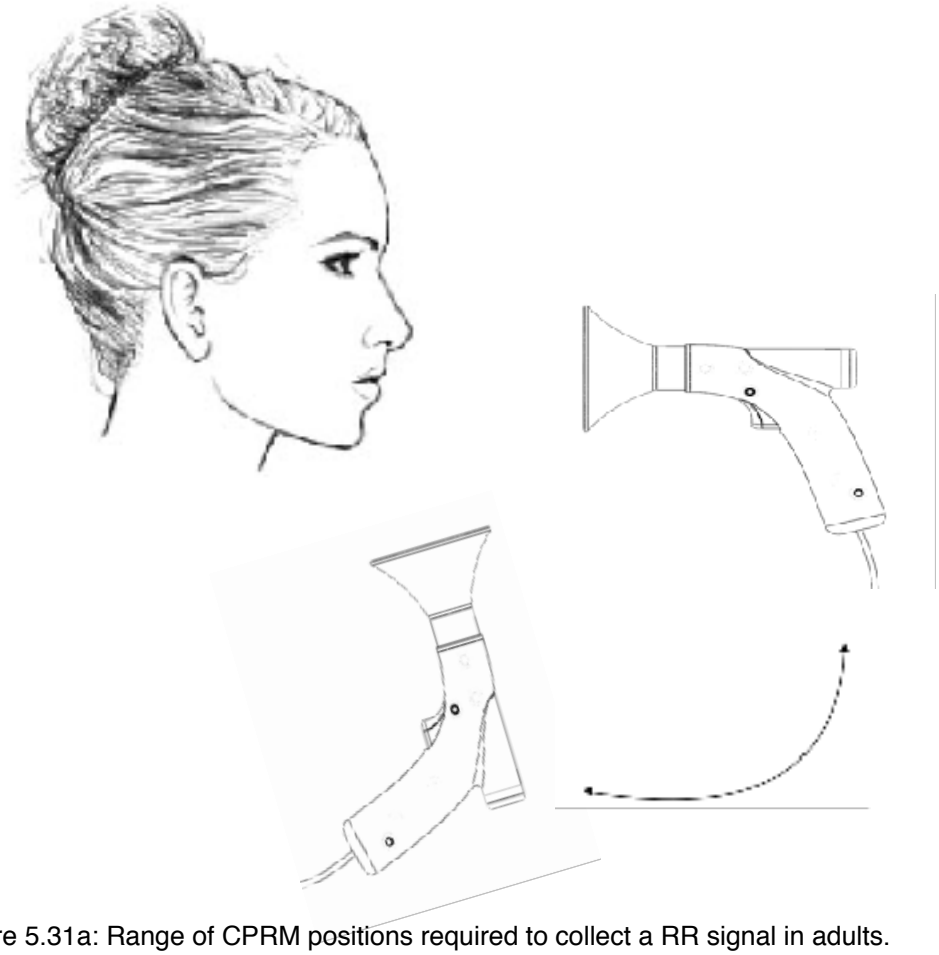


Figure 5.31a: Range of CPRM positions required to collect a RR signal in adults.

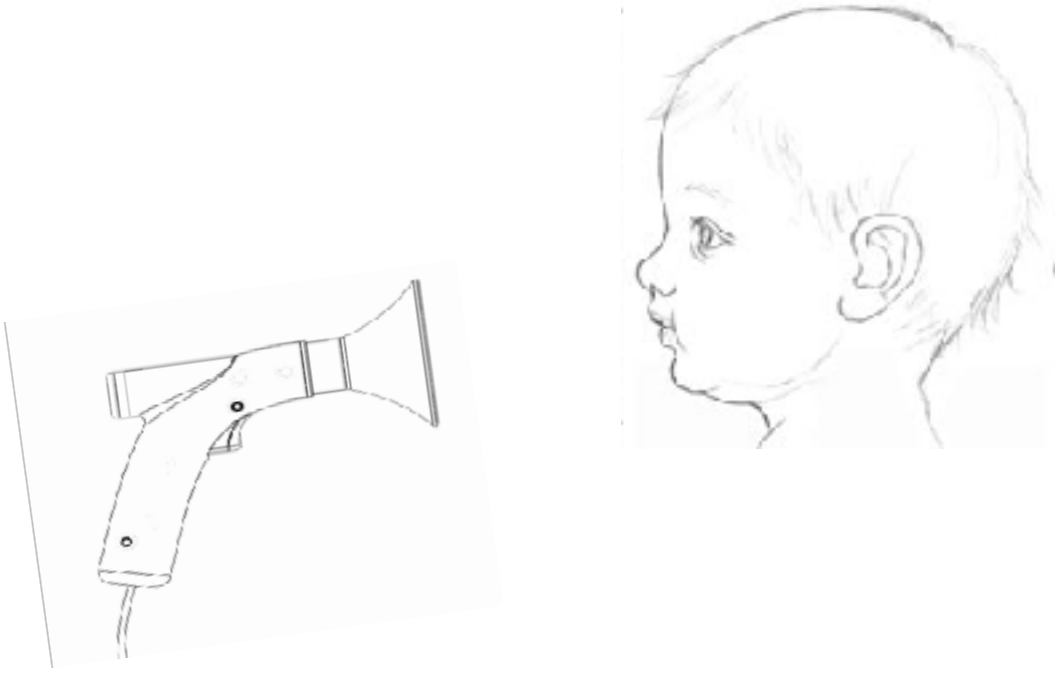


Figure 5.31b: CPRM position required for detecting a RR signal in a child.

The exclusion criteria of some of the pilot studies also limited the results obtained. In the pre-hospital setting those subjects who were deemed too unwell or required emergency treatment were not recruited. This meant that unwell patients who were potentially less cooperative and may have had altered respiratory rates were not tested. We were therefore unable to comment on the usability and accuracy of the CPRM in unwell children and adults. When designing future studies it will be important to include such patients. If the device is going to be implemented in an acute clinical setting where it is vital to get a quick and accurate respiratory rate measurement then it must be shown to have a sufficient level of accuracy and usability in these patients and settings.

5.10.6 Recommendations

Based upon the limitations described we have made recommendations to improve and enhance the overall accuracy, functionality and reliability of the CPRM. These include the following:

1. Reduction of sampling time

In its current design, the CPRM takes a total of 52 seconds to complete its measurement. Our studies have shown that this duration is too long for both users and subjects. The longer the measurement period the less cooperative the subject can become, moving their head away from the CPRM, and the more likely the user is to move the CPRM from the individuals face and lose the respiration signal. This becomes even more apparent in younger children below the age of 4 years whose attention span is shorter than older children and adults. By reducing the sampling time to between 15 - 20 seconds this will hopefully negate many of these difficulties encountered.

However in shortening the sampling time it will still be important to ensure that the accuracy of the measurement is maintained. New digital signal processing techniques and algorithms will need to be developed and applied to reduce the measurement time without compromising on accuracy. It may also be possible to develop variable sampling times which are adjusted based on the strength and consistency of the respiration signal received. Further testing and development of these new processing techniques and algorithms will then be needed to inform on the shortest acceptable measurement time that can be used to give a clinically accurate respiratory rate.

2. Improvement in extraction of respiration signal

Findings from the pilot studies have also indicated that the respiration signal received differs from subject to subject. There are many factors influencing this including the subjects age, facial profile, whether they are mouth or nasal breathers, the intensity of the exhaled breath, and the position that the CPRM is held by the user. All of these factors can cause the respiration signal to become distorted making the extraction of a signal complicated and prone to being misinterpreted.

Techniques such as multi-resolution analysis (MRA) could be used to help manage these distorted respiration signals (Saatchi et al., 1997). MRA is able to reconstruct decomposed signals to different levels of coarseness that can be associated with specific frequency bands, then adapt

them to the respiration signal. By adopting such a technique, distorted signals can then be processed by the CPRM thus greatly improving its accuracy and usability in various settings and on a variety of subjects.

3. Rejection of sections of respiratory signal

As well as receiving distorted signals, the CPRM's accuracy is also affected when it does not receive a signal for a prolonged period of time. This can occur when a subject has not cooperated and moved their head away from the device, or when the user does not lock on to the respiration signal from the subject. When this occurs during a recording the CPRM tries to interpret this signal which often results in a spurious measurement being produced. By developing the software of the CPRM these sections of recording can automatically be rejected and not included in the analysis. The measurement period can then be extended to ensure that an adequate signal is obtained for signal analysis.

4. Automatic adjustment of signal amplification

Within the subjects tested in these pilot studies there was a large variation in expired air strength, both in terms of volume and velocity. This affected how the respiration signal was processed and in turn the accuracy of the measurement. The CPRM does attempt to amplify these signals but currently it uses a fixed gain to do so. This gain is set to a level that best accommodates for the range of signals that are anticipated to be received. However, due to large variations in the age and size of subjects as well as the positioning of the CPRM this results in occasions where the fixed gain is not suitable for the signal received. In some instances the respiration signal may not be sufficiently amplified and in others it may be over amplified resulting in saturation of the signal, both of which cause a reduction in the accuracy of the measurement. Therefore by incorporating an improved automatic gain system into the CPRM, whereby the signal amplification is automatically increased for weaker signals and reduced for larger signals, the signal recording interpretation and overall accuracy can be improved.

5. Signal locking to start recording

Currently the CPRM operator views the device's signal display monitor to check for a recognisable respiration signal and then presses a trigger to start recording. There are a number of problems associated with doing this including difficulties in identifying the signal and loss of the signal during the recording period. By introducing a signal locking system into the CPRM the user can be sure when an adequate signal has been received and a recoding can be made. Also by including a signal strength indicator this will enable the user to find the respiration signal more quickly and efficiently, making the overall measurement period shorter.

6. User alerts and guidance

Even though many of the adaptations to the CPRM will aid its usability it is still important to ensure the CPRM is easy to use with little or no training, and that its accuracy is not affected by

the skill and experience of the user. This can be achieved by adding in user alerts to signify the start and end of the recording, signal strength indicator LEDs, as well as automatic recording when an adequate signal is obtained. It will also be useful to include with the CPRM a brief guidance document on how it should be operated, including the different operating positions needed for the different age groups as well as normal range values of RR for different aged children. All of these additions will help reduce any reliance on the user themselves in obtaining an accurate measurement.

7. Gain attention of subject and distract from CPRM measurement

During the recording period cooperation of the subject is needed to ensure that they face towards the CPRM. This is particularly challenging in younger children and unwell children, who can be more unsettled and resistant to the measurement being performed. Also, it is important to not focus some of the older children on breathing into the device as this can artificially alter their RR. Approaches to gain and maintain their attention during the recording will need to be developed so that the child can be distracted from the recording process without altering their respiration rate at the same time.

Approaches that could be explored include embedding the device in an object that the child is comfortable and familiar with such as a teddy bear, or by using audio and visual devices located near the CPRM to attract the child's attention. Feasibility studies will need to be completed to develop these methods and establish an effective approach that can both improve cooperation and distract the child from the measuring process.

8. Recording of measurements

Currently the CPRM displays the respiration signal in real time and indicates the numerical respiration rate at the completion of each recording. This measurement is then lost as soon as another recording is started. It would be beneficial if the CPRM was able to keep a record of measurements made and also interpret these in terms of the normal respiratory rate parameters for each patient. To achieve this the software and hardware of the CPRM would need to be extended to include either an SD Card or USB interfaces, or to be compatible with wireless facilities so that measurements can be stored and then downloaded for the user to access.

9. Improved appearance of CPRM

Feedback from subjects and subject's parents on the CPRM commented greatly on the device's appearance, stating that it was very clinical and not child friendly. Improving the appearance of the CPRM by making it more appealing to children may encourage cooperation. It may help the child to focus more on the device, reducing their head movements, and it could also reduce any anxiety during the measurement period. Both of which will help in improving the accuracy of measurements obtained in younger less cooperative children.

10. Improved portability of CPRM

The CPRM in its current form is limited by its portability. Its robustness, battery life and size all need adjusting to make this a viable device for the clinical setting. The casing of the CPRM needs improving to a tougher, lighter and more durable material that can withstand more external forces without being damaged. The battery life of the CPRM must also be extended. This is of particular importance in pre-hospital settings where charging facilities may not be easily accessible. Finally the device must be miniaturised. Integrating the electronic components and battery into the handset and eliminating the base unit will greatly enhance the usability and portability of the CPRM.

5.10.7 The participants

We tested the CPRM on a wide age range of participants (Table 5.10). A total of 134 participants were tested with an almost even split of males and females. 69% of the participants in the studies were children and the age ranges of these are shown in Figure 5.32. The CPRM was able to detect and measure a respiratory rate on all ages tested.

Table 5.10: Participant characteristics (n=134)

Age in years, mean, range	19 (1 - 97)
Male gender, n (%)	71 (53%)

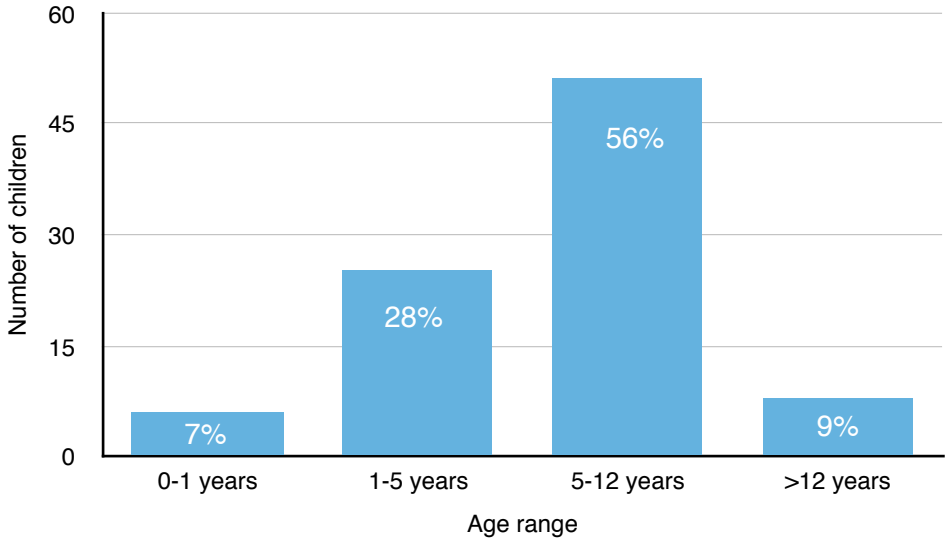


Figure 5.32: Age ranges of children tested in the pilot studies. Percentages also shown.

Within the cohort of children tested there was not an even distribution of ages. The majority of children tested were aged between 5-12 years and this is due to the fact that Pilot study C was completed at the primary school from only one school year. Most age ranges were captured within the studies, with the youngest child tested being only 8 months old. It would be useful to

test the CPRM in children younger than this to ascertain if it can accurately detect and measure RR from infants and neonates with lower volume breaths and if it is well tolerated in this age group.

5.10.8 Accuracy of the visual counting method

In all of the pilot studies the primary outcome measure was the agreement and correlation of the CPRM with both contact and visual methods of respiratory rate measurement. However these studies also gave interesting data on the accuracy of a visual count measurement of respiratory rate performed over 52 seconds. Table 1 shows the correlation between the visual counting method and the contact RIP method.

The results shown in Table 5.11 indicate that the visual counting method is highly accurate and shows excellent agreement and almost perfect correlation with the RIP contact method. Previous studies have evaluated the accuracy of a visual count completed over different time periods but never purely against a contact method of measurement (Simoes et al., 1991). The visual count of respiratory rate taken in these studies was over a period of 52 seconds and is most likely to be comparable to a count taken over a full minute.

Table 5.11: Visual counting method compared with contact method for each study

Study	Subjects (No. of measurements)	95% Limits of Agreement (Mean Difference)	Intraclass correlation coefficient (95% CI)
Pilot study A	Healthy Adults (159)	-1.459 - 1.736 (0.138)	0.971 (0.960 - 0.979)
Pilot study B	Healthy Children (60)	-3.338 - 5.185 (0.9237)	0.967 (0.945 - 0.980)
Pilot study C	Primary school - Children (38)	-5.450 - 1.898 (-1.776)	0.951 (0.907 - 0.974)
Pilot study D	Children undergoing sleep studies (61)	-7.551 - 7.728 (0.089)	0.674 (0.509 - 0.791)
Pilot study E	Emergency Department - Children (59)	-5.256 - 10.108 (2.426)	0.913 (0.858 - 0.947)
	General Practice - Adults (41)	-1.970 - 3.011 (0.521)	0.913 (0.858 - 0.947)
	Yorkshire Ambulance service - Adults (3) & Children (1)	-2.172 - 4.477 (1.153)	0.978 (0.708 - 0.999)
Overall	Adult subjects (203)	-1.877 - 1.882 (0.003)	0.962 (0.950 - 0.971)
	Child subjects (219)	-5.244 - 7.754 (1.2551)	0.900 (0.849 - 0.931)
	Total subjects (422)	-4.355 - 5.660 (0.6526)	0.941 (0.925 - 0.954)

The reduced accuracy of the visual count seen in Pilot study D, children undergoing sleep studies can possibly be attributed to two factors. Firstly in this setting it was harder to observe chest and abdominal movements due to the darkened conditions. This may have resulted in an inaccurate count and some breaths not being measured. Secondly, this was the only study in which the

same user took the CPRM measurement as well as the visual count measurement. In all other studies a separate observer was used. Therefore, it is possible that the observer could have been distracted by positioning the CPRM and missed counting some of the child's breaths.

Overall it could be argued that a visual measurement of respiratory rate is accurate enough and that this method of measurement does not need to be superseded by a medical device. However as shown in chapter 3 of this thesis there is still a significant degree of variation between different observers performing a visual measurement. Also, as described in Section A and throughout this thesis we know that in everyday clinical practice visual counts are often counted over a shorter period of time, which can lead to inaccuracies. A medical device that not only acts as a prompt to measure but can also give an accurate measurement in a shorter period of time and on patients who are agitated, upset, or uncooperative could still be of benefit.

5.11 Conclusions

Whilst medical devices should not replace a clinician's assessment, a device that accurately measures and reminds clinicians to take a respiratory rate will be of great significance. Results obtained from our contactless respiratory rate monitor are varied. The CPRM can measure the respiratory rate in both adults and children, and when a good respiration signal is received the measurement is highly accurate. The CPRM is safe and the portable and contactless nature of the device makes it ideal for measuring respiratory rate in children. However, the CPRM is limited by a number of factors which directly and indirectly impact upon its accuracy. As such, in its current form, the CPRM does not appear accurate enough to be used in clinical practice or to supersede current methods of measuring respiratory rate.

Through these pilot studies we have been able to complete a thorough evaluation of the CPRM and make comprehensive suggestions for its modification and development. Should these improvements be undertaken then further more extensive testing would be required, on larger sample sizes and in a variety of clinical settings in order to establish whether the CPRM can then be introduced as a clinically deployable device.

CHAPTER 6

OVERALL THESIS DISCUSSION LIMITATIONS AND CONCLUSIONS

6.1 Introduction

This thesis has explored in depth many aspects of measuring respiratory rate in children. Firstly it has comprehensively analysed current paediatric healthcare professionals methods and approaches to measuring respiratory rate. It has then explored the variability in measurements obtained, the agreement between individuals and the consequences of using different measurement methods. It has also assessed the value of a respiratory rate measurement in detecting and identifying children at risk of clinical deterioration, comparing and contrasting it with the other vital signs. Finally this thesis has given an in depth appraisal and analysis of an alternative method of respiratory rate measurement, using a novel contactless handheld device. In the sections below we will seek to summarise our overall findings, outline the strengths and limitations of this thesis and suggest areas for future further research and development.

6.2 Overall thesis findings

This thesis has addressed and answered all of the research questions that were set out in the first chapter. The main findings can be divided into three main areas and are each outlined below.

6.2.1 Respiratory rate measurement practices and variability

Chapters 2 and 3 began this thesis by assessing current practices in measuring respiratory rate in children and examined for any variation that may exist in measurements. We found wide ranging differences in the methods used by many different healthcare professionals across the paediatric speciality. Many of which differed greatly from recommended practice and guidance, and are well known to be inaccurate. We also showed an inherent variability in measurements between observers when even the most accurate of measurement methods was used.

The importance of these findings cannot be under estimated. Respiratory rate measurements are used daily in clinical practice and relied upon greatly by clinicians and other healthcare professionals (Cooper et al., 2005). With such large potential inaccuracies in measurements, unwell children may be being missed and others unnecessarily treated. Not only this, but the very foundation of what we base a normal respiratory rate on could be flawed. Respiratory rate reference range values have been developed from data obtained from measurements by healthcare professionals in clinical practice (O'Leary et al., 2015). With inaccuracies in certain measurement methods and variation between measurers we may still not truly know what constitutes a child’s normal range of respiratory rate. These findings formed the basis of the remainder of this thesis and it is through the lens of these findings that subsequent chapters and studies should be interpreted.

6.2.2 The importance and relevance of a respiratory rate measurement

If our measurements of respiratory rate are inherently inaccurate then attempting to assess the usefulness of them through evaluating clinical data will be flawed from the outset. However, until

more accurate, less subjective measurement techniques and methods are introduced, it is through these data sets that we had to work to answer the questions set out in chapter 4.

We were able to firmly establish that respiratory rate was a powerful predictor of clinical deterioration in children, and was superior to both heart rate and blood pressure. Respiratory rate can not only help us in identifying and detecting children at risk of deterioration but we showed that a raised respiratory rate occurred well in advance of the deterioration occurring. Through our analysis we were also able to suggest particular threshold values that could be used to identify these children. This could then lead to the targeting of resources, the implementation of more aggressive management plans and hopefully ultimately lead to improved patient outcomes.

This was the first time such findings had been described in the paediatric population. Although the identification of respiratory rate as a significant marker of deterioration is clearly important, it is crucial we do not get drawn into solely relying on a single one off respiratory rate measurement or discount other vital signs. In serious illnesses a single pathophysiological disturbance is unlikely, and vital signs form just one component of the full clinical assessment of a child. This work does however inform us that greater weighting and importance should be placed on our respiratory rate measurements in children.

6.2.3 A novel device to measure respiratory rate

Both the inherent inaccuracies in current methods and the importance of a respiratory rate measurement in clinical practice support the need for the introduction of more objective methods of measurement. In chapter 5 of this thesis we developed and tested a novel contactless device to measure respiratory rate. It was designed to increase the accuracy of RR measurements, alleviate the subjective nature of its measurement and also act as a prompt to clinicians.

The CPRM was able to measure respiratory rates in both children and adults. When a good respiration signal was received the measurement was highly accurate. The CPRM was a safe device that was portable and easily used in a number of different settings. However on numerous occasions it was difficult to establish a good respiration signal especially in an uncooperative child and therefore the measurement obtained was highly inaccurate.

The CPRM does offer a promising alternative to current measurement methods but in its present form it does not appear accurate enough to be used in clinical practice, or to supersede current measurement methods. The studies completed here do however give a clear insight into how such a device could be integrated into everyday clinical practice and also the potential improvement in the accuracy of measurements that could be gained.

6.3 Thesis strengths and dissemination achievements

This thesis has added considerably to the overall body of evidence regarding respiratory rate measurements in children, including its measurement, its accuracy, its variability, and its usefulness as a vital sign. It has also provided comprehensive data and evidence for an alternative method of respiratory rate measurement in children. It has bridged existing knowledge gaps and opened up areas of further future research potential.

The thesis has walked through the process of evaluating respiratory rate measurements in children in a thorough and systematic way. From the outset clear and attainable research questions were set. These have all been addressed and answered, adding new understanding and directing future work. The research methods and statistical analysis used in each of the studies were robust, rigorous and had good external validity. This enabled pertinent conclusions to be drawn and clear comparisons to be made with other studies within the field. Studies were all completed in a timely fashion. Data collection spanned an appropriate time frame and results were analysed soon after. All of these practices strengthened the quality of this research, allowing firm and well grounded conclusions to be drawn adding to and enhancing the overall body of evidence.

Many components of this thesis have been disseminated to date. The literature review in chapter 1 has been published in a peer reviewed journal (Daw et al., 2016). The questionnaire in Chapter 2 has been presented in poster form at the King's John Price Paediatric Respiratory conference. The study described in chapter 3, assessing the variability in respiratory rate measurements, has been presented orally at the RCPCH national conference and has been published in BMJ Paediatrics Open (Daw et al, 2017). Two of the CPRM pilot studies described in chapter 5 have been presented in poster form at the international European Respiratory Society congress in both Amsterdam and London and one of the studies has been presented orally at the RCPCH national conference. Finally, at the time of writing, further enhancement and development of the CPRM by a commercial company has been agreed in principle. The aim being to make the necessary alterations and modifications based on the findings and recommendations from this thesis to produce a clinically deployable device.

6.4 Key limitations

This thesis had a number of limitations which are important to mention. Many of these come from a limitation in the time and funding available to complete each of the studies and are outlined below.

6.4.1 Single centre studies

The majority of the studies completed within this thesis were conducted at a single tertiary children's hospital. The questionnaire study completed in chapter 2 extended outside of this

centre but was restricted to the Yorkshire region. As such results could have been biased by local practices that were particular to the region and may not be generalisable to other hospitals and centres. Realistically though, it is likely that practices do not differ that much nationwide and results are likely to represent overall practice. Ideally other centres from across the country could have been used to gather data and recruit patients from, however this was outside the scope of the thesis and the funding available.

6.4.2 Methodology

Although many of the methodologies used for each of the different studies were appropriately robust, there were some cases where the methodology limited the results obtained. Firstly there were specific methodological limitations associated with the questionnaire surveys that were used in chapter 2 and chapter 3. Respondents were unable to freely express their opinions and were forced to choose their answers based upon pre-defined options. This may have led to answers being selected even if they did not reflect the respondent's true response. Ideally to get a better understanding of respondents views and answers interviews could have been conducted giving HCPs a chance to share their views outside the constraints of a questionnaire.

Secondly some studies were limited as true blinding was unable to be achieved. In chapter 3 healthcare professionals were sometimes aware of the ongoing study and as such may have altered their practice, being more thorough in their assessment of a child's respiratory rate. Also with the questionnaire studies some respondents may have chosen answers which they believed reflected best practice rather than their usual practice. When questionnaires were completed in a group setting HCP may have been influenced by the group as a whole and altered their responses accordingly.

6.4.3 Sample sizes

The study in chapter 3 was the only study where a power calculation could be completed and the appropriate number of participants recruited. For each of the other studies a convenience sample was selected as there are no established criteria for sample sizes for these types of studies. Also for the retrospective case note analysis in chapter 4 we were limited by the number of cases that fulfilled the inclusion criteria and as such the number of cases analysed was lower than what was hoped for. Therefore it is difficult to say whether the samples used in each of these studies was representative of the population as a whole and also to what extent these results can be applied to the general population.

6.4.4 Exclusion criteria

For many of the studies we applied certain exclusion criteria to the participants that could be recruited. Although this was done to ensure the correct individuals were selected and analysed it could also have hindered the results obtained. In both the studies in chapters 3 and 5 children who were deemed too unwell were not recruited. Applying this exclusion criteria meant that we

were unable to gain an insight into these children's respiratory rate, both in terms of the variation in measurements and the accuracy of the medical device. Future studies would have to look at including such patients as results may be considerably different when compared to those children who were less unwell.

6.5 Areas of future research beyond this thesis

The work in this thesis has not only added to the overall body of evidence it has also opened up a number of new areas of potential future research.

Firstly the studies in chapter 3 which showed a significant difference in the agreement in respiratory rate measurements needs further exploration. Now that the degree of variation has been established it would be pertinent to assess the effect to which this variation has upon the clinical assessment, management and outcome of children in hospital. This would take our initial findings and put them into a clear clinical context which would be of importance for clinicians in day to day practice.

Secondly, based on our findings outlined in chapter 4, further studies could be completed to assess certain respiratory rate threshold values in identifying children at risk of deterioration. Prospective studies could be undertaken where these respiratory rate thresholds are either used alone or in conjunction with other early warning scoring systems to target resources earlier and in turn potentially prevent children from deteriorating and requiring admission to high dependency areas.

Finally, there are further studies that need to be conducted with the CPRM. Ultimately these would be completed on a device modified from the findings from this thesis. It would then be appropriate to complete more extensive testing on larger sample sizes in a variety of clinical settings. Not only could the accuracy of the device be assessed but it may also be possible to assess the effect the device could have on the child's management during their hospital admission. It may also be possible to assess for any health economic benefits that the CPRM could have by potentially reducing the time it took for of a respiratory rate measurement to be made or by reducing the need for extra repeat measurements to be taken.

6.6 Overall conclusions

These collection of studies, have enlightened and enriched our knowledge of the assessment and measurement of respiratory rate in children. We have provided clear evidence that there are wide ranging practices used by paediatric healthcare professionals to measure respiratory rate in children, and it is clear from the literature that these different practices will have an impact on the accuracy of measurements obtained. We have also shown an inherent variability in respiratory

rate measurements between observers. These findings have highlighted the need for a robust review of what may constitute a normal respiratory rate and the clinical impact of these inconsistencies in measurements.

Through this thesis we have also firmly established that respiratory rate is a powerful predictor of clinical deterioration in children, superior to both heart rate and blood pressure. A raised respiratory rate occurs well in advance of a child's subsequent deterioration and if targeted early this could be prevented. Future prospective studies are needed to further validate particular threshold values, however it is clear a greater weighting and importance should be placed on respiratory rate measurements in unwell children.

Finally we have successfully measured respiratory rates in both adults and children using a novel contactless device, the CPRM. Our device offers a promising alternative to current measurement methods but in its present form does not appear accurate enough to be used in clinical practice, or to supersede current methods. However, if the device was to be modified sufficiently, providing accurate and prompt respiratory rate measurements then it could be an important tool in the assessment of unwell children.

Measuring respiratory rate in children remains a subjective assessment and until changes are implemented this vital sign will still be liable to variability and a large degree of measurement error. Given the clinical importance of respiratory rate measurements in children, this body of work should make us intent on gaining accurate and reproducible measurements through improving and perfecting our current practices and striving to optimise devices that can ultimately supersede our current methods.

CHAPTER 7

BIBLIOGRAPHY

AARTS, L. A., JEANNE, V., CLEARY, J. P., LIEBER, C., NELSON, J. S., BAMBANG OETOMO, S. & VERKRUYSSE, W. 2013. Non-contact heart rate monitoring utilizing camera photoplethysmography in the neonatal intensive care unit - a pilot study. *Early Hum Dev,* 89**,** 943-8.

ABBAS, A. K., HEIMANN, K., JERGUS, K., ORLIKOWSKY, T. & LEONHARDT, S. 2011. Neonatal non-contact respiratory monitoring based on real-time infrared thermography. *Biomed Eng Online,* 10**,** 93.

ADVANCED LIFE SUPPORT GROUP 2016. Advanced Paediatric Life Support: The Practical Approach. 6*th ed. WileyBlackwell.*

ADVANCED LIFE SUPPORT GROUP 2004. ATLS: Advanced Trauma Life Support for Doctors. 7th ed.

AL-KHALIDI, F. Q., SAATCHI, R., BURKE, D., ELPHICK, H. & TAN, S. 2011a. Respiration rate monitoring methods: a review. *Pediatr Pulmonol,* 46**,** 523-9.

AL-KHALIDI, F. Q., SAATCHI, R., ELPHICK, H. & BURKE, D. 2011b. An Evaluation of Thermal Imaging Based Respiration Rate Monitoring in Children. *Invited paper for the special issue of the American Journal of Engineering and Applied Sciences.,* 4**,** 586-597.

ANDERSEN, L. W., KIM, W. Y., CHASE, M., BERG, K. M., MORTENSEN, S. J., MOSKOWITZ, A., NOVACK, V., COCCHI, M. N. & DONNINO, M. W. 2016. The prevalence and significance of abnormal vital signs prior to in-hospital cardiac arrest. *Resuscitation,* 98**,** 112-7.

AOKI H, TAKEMURA Y, MIMURA K & M., N. 2001. Development of non-restrictive sensing system for sleeping person using fibre grating vision sensor. *Proceedings of 2001 International Symposium on Micromechatronics and Human Science, Nagoya, Japan:.* 155:160.

ARLOTTO, P., GRIMALDI, M., NAECK, R. & GINOUX, J. M. 2014. An ultrasonic contactless sensor for breathing monitoring. *Sensors (Basel),* 14**,** 15371-86.

BABAEIZADEH, S., ZHOU, S. H., PITTMAN, S. D. & WHITE, D. P. 2011. Electrocardiogram-derived respiration in screening of sleep-disordered breathing. *J Electrocardiol,* 44**,** 700-6.

BERMAN, S., SIMOES, E. A. & LANATA, C. 1991. Respiratory rate and pneumonia in infancy. *Arch Dis Child,* 66**,** 81-4.

BIANCHI, W., DUGAS, A. F., HSIEH, Y. H., SAHEED, M., HILL, P., LINDAUER, C., TERZIS, A. & ROTHMAN, R. E. 2013. Revitalizing a vital sign: improving detection of tachypnea at primary triage. *Ann Emerg Med,* 61**,** 37-43.

BLAND, J. M. & ALTMAN, D. G. 1986. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet,* 1**,** 307-10.

BONAFIDE, C. P., BRADY, P. W., KEREN, R., CONWAY, P. H., MARSOLO, K. & DAYMONT, C. 2013. Development of heart and respiratory rate percentile curves for hospitalized children. *Pediatrics,* 131**,** e1150-7.

BUIST, M. & STEVENS, S. 2013. Patient bedside observations: what could be simpler? *BMJ Qual Saf,* 22**,** 699-701.

BURKE, D. 2007. Audit of feverish children against the NICE standard. Emergency Department, Sheffield Childrens Hospital. Data On File – Available upon request.

CASTAGNA, J., WEIL, M. H. & SHUBIN, H. 1974. Factors determining survival in patients with cardiac arrest. *Chest,* 65**,** 527-9.

CHAN, A., LANGLEY, J. & LEBLANC, J. 2001. Interobserver variability of croup scoring in clinical practice. *Paediatr Child Health,* 6**,** 347-51.

CHAN, A. M., FERDOSI, N. & NARASIMHAN, R. 2013a. Ambulatory respiratory rate detection using ECG and a triaxial accelerometer. *Conf Proc IEEE Eng Med Biol Soc,* 2013**,** 4058-61.

CHAN, A. M., SELVARAJ, N., FERDOSI, N. & NARASIMHAN, R. 2013b. Wireless patch sensor for remote monitoring of heart rate, respiration, activity, and falls. *Conf Proc IEEE Eng Med Biol Soc,* 2013**,** 6115-8.

CHAPMAN, S. M., GROCOTT, M. P. & FRANCK, L. S. 2010. Systematic review of paediatric alert criteria for identifying hospitalised children at risk of critical deterioration. *Intensive Care Med,* 36**,** 600-11.

CHEN, J., HILLMAN, K., BELLOMO, R., FLABOURIS, A., FINFER, S. & CRETIKOS, M. 2009. The impact of introducing medical emergency team system on the documentations of vital signs. *Resuscitation,* 80**,** 35-43.

CLINICAL practice guideline: diagnosis and management of childhood obstructive sleep apnea syndrome. 2002. *Pediatrics,* 109**,** 704-12.

COOPER, R. J., SCHRIGER, D. L., FLAHERTY, H. L., LIN, E. J. & HUBBELL, K. A. 2002. Effect of vital signs on triage decisions. *Ann Emerg Med,* 39**,** 223-32.

CRETIKOS, M., CHEN, J., HILLMAN, K., BELLOMO, R., FINFER, S. & FLABOURIS, A. 2007. The objective medical emergency team activation criteria: a case-control study. *Resuscitation,* 73**,** 62-72.

CRETIKOS, M. A., BELLOMO, R., HILLMAN, K., CHEN, J., FINFER, S. & FLABOURIS, A. 2008. Respiratory rate: the neglected vital sign. *Med J Aust,* 188**,** 657-9.

DHAND, N. K., and KHATKAR, M. S. 2014. Statulator: An online statistical calculator. Sample Size Calculator for Comparing Two Independent Means. Accessed at http://statulator.com/SampleSize/ss2M.html.

DAW W. 2015. Pilot study of the inter-observer agreement in the measurement of respiratory rates in children. Data on file – Available on request.

DAW, W. J., KINGSHOTT, R., SAATCHI, R., BURKE, D., HOLLOWAY, A., TRAVIS, J., EVANS, R., JONES, A., HUGHES, B. & ELPHICK, H. 2016. Medical Devices for Measuring Respiratory Rate in Children: a Review. *Journal of advances in biomedical engineering and technology,* 3**,** 21-27.

DAW W., KINGSHOTT, R., ELPHICK H. 2017. Poor inter-observer agreement in the measurement of respiratory rate in children: a prospective observational study. BMJ Paediatrics Open; 0:e000173. doi:10.1136/ bmjpo-2017-000173.

DROITCOUR, A. D., SETO, T. B., PARK, B. K., YAMADA, S., VERGARA, A., EL HOURANI, C., SHING, T., YUEN, A., LUBECKE, V. M. & BORIC-LUBECKE, O. 2009. Non-contact respiratory rate measurement validation for hospitalized patients. *Conf Proc IEEE Eng Med Biol Soc,* 2009**,** 4812-5.

EDMONDS, Z. V., MOWER, W. R., LOVATO, L. M. & LOMELI, R. 2002. The reliability of vital sign measurements. *Ann Emerg Med,* 39**,** 233-7.

EDWARDS, M., MCKAY, H., VAN LEUVAN, C. & MITCHELL, I. 2010. Modified Early Warning Scores: inaccurate summation or inaccurate assignment of score? *Critical Care,* 14**,** P257-P257.

EDWARDS, S. M. & MURDIN, L. 2001. Respiratory rate--an under-documented clinical assessment. *Clin Med,* 1**,** 85.

EUROPEAN RESUSCITATION COUNCIL. 2006. European paediatric life support course. *2nd ed. Resuscitation Council (UK)*.

FIESELMANN, J. F., HENDRYX, M. S., HELMS, C. M. & WAKEFIELD, D. S. 1993. Respiratory rate predicts cardiopulmonary arrest for internal medicine inpatients. *J Gen Intern Med,* 8**,** 354-60.

FLEMING, S., THOMPSON, M., STEVENS, R., HENEGHAN, C., PLÜDDEMANN, A., MACONOCHIE, I., TARASSENKO, L. & MANT, D. 2011. Normal ranges of heart rate and respiratory rate in children from birth to 18 years: a systematic review of observational studies. *Lancet,* 377**,** 1011-1018.

FOLKE, M., GRANSTEDT, F., HOK, B. & SCHEER, H. 2002. Comparative provocation test of respiratory monitoring methods. *J Clin Monit Comput,* 17**,** 97-103.

FRASCA, D., GERAUD, L., CHARRIERE, J. M., DEBAENE, B. & MIMOZ, O. 2015. Comparison of acoustic and impedance methods with mask capnometry to assess respiration rate in obese patients recovering from general anaesthesia. *Anaesthesia,* 70**,** 26-31.

FREUNDLICH, J. J. & ERICKSON, J. C. 1974. Electrical impedance pneumography for simple nonrestrictive continuous monitoring of respiratory rate, rhythm and tidal volume for surgical patients. *Chest,* 65**,** 181-4.

GAJDOS, V., BEYDON, N., BOMMENEL, L., PELLEGRINO, B., DE PONTUAL, L., BAILLEUX, S., LABRUNE, P. & BOUYER, J. 2009. Inter-observer agreement between physicians, nurses, and respiratory therapists for respiratory clinical evaluation in bronchiolitis. *Pediatr Pulmonol,* 44**,** 754-62.

GANDEVIA, S. C. & MCKENZIE, D. K. 2008. Respiratory rate: the neglected vital sign. *Med J Aust,* 189**,** 532.

GASIM, G. I., MUSA, I. R., ABDIEN, M. T. & ADAM, I. 2013. Accuracy of tympanic temperature measurement using an infrared tympanic membrane thermometer. *BMC Res Notes,* 6**,** 194.

GIAVARINA, D. 2015. Understanding Bland Altman analysis. *Biochemia Medica,* 25**,** 141-151.

GOLDHILL, D. R., MCNARRY, A. F., MANDERSLOOT, G. & MCGINLEY, A. 2005. A physiologically-based early warning score for ward patients: the association between score and outcome. *Anaesthesia,* 60**,** 547-53.

GRENEKER, E. F. 1997. Radar sensing of heartbeat and respiration at a distance with applications of the technology. *Radar,* 97**,** 150-154.

HAFNER, N., MOSTAFANEZHAD, I., LUBECKE, V. M., BORIC-LUBECKE, O. & HOST-MADSEN, A. 2007. Non-contact cardiopulmonary sensing with a baby monitor. *Conf Proc IEEE Eng Med Biol Soc,* 2007**,** 2300-2.

HELFENBEIN, E., FIROOZABADI, R., CHIEN, S., CARLSON, E. & BABAEIZADEH, S. 2014. Development of three methods for extracting respiration from the surface ECG: a review. *J Electrocardiol,* 47**,** 819-25.

HOGAN, J. 2006. Why don't nurses monitor the respiratory rates of patients? *Br J Nurs,* 15**,** 489-92.

HSU C.H., CHOW. C J. 2005. Design and clinic monitoring of monitoring of a newly developed non-attached infant apnea monitor. *Centre for Biomedical Engineering, Taiwan, Province De Chine,* 17**,** 126-133.

HUTCHINSON, J. (ed.) 1849. Cyclopedia of Anatomy and Physiology, London, united Kingdom: Todd RB, ed.

JOHANSSON, A., OBERG, P. A. & SEDIN, G. 1999. Monitoring of heart and respiratory rates in newborn infants using a new photoplethysmographic technique. *J Clin Monit Comput,* 15**,** 461-7.

KARLEN, W., BROUSE, C. J., COOKE, E., ANSERMINO, J. M. & DUMONT, G. A. 2011. Respiratory rate estimation using respiratory sinus arrhythmia from photoplethysmography. *Conf Proc IEEE Eng Med Biol Soc,* 2011**,** 1201-4.

KARLEN, W., GAN, H., CHIU, M., DUNSMUIR, D., ZHOU, G., DUMONT, G. A. & ANSERMINO, J. M. 2014. Improving the accuracy and efficiency of respiratory rate measurements in children using mobile devices. *PLoS One,* 9**,** e99266.

KAUSE, J., SMITH, G., PRYTHERCH, D., PARR, M., FLABOURIS, A. & HILLMAN, K. 2004. A comparison of antecedents to cardiac arrests, deaths and emergency intensive care admissions in Australia and New Zealand, and the United Kingdom--the ACADEMIA study. *Resuscitation,* 62**,** 275-82.

KOOLEN, N., DECROUPET, O., DEREYMAEKER, A., JANSEN, K. & VERVISCH, J. 2015. Automated Respiration Detection from Neonatal Video Data. *International Conference on Pattern Recognition Applications and Methods*.

LANASPA, M., VALIM, C., ACACIO, S., ALMENDINGER, K., AHMAD, R., WIEGAND, R. & BASSAT, Q. 2014. High reliability in respiratory rate assessment in children with respiratory symptomatology in a rural area in Mozambique. *J Trop Pediatr,* 60**,** 93-8.

LEONARD, P., BEATTIE, T. F., ADDISON, P. S. & WATSON, J. N. 2003. Standard pulse oximeters can be used to monitor respiratory rate. *Emerg Med J,* 20**,** 524-5.

LEUVAN, C. H. & MITCHELL, I. 2008. Missed opportunities? An observational study of vital sign measurements. *Crit Care Resusc,* 10**,** 111-15.

LIM, W. S., CARTY, S. M., MACFARLANE, J. T., ANTHONY, R. E., CHRISTIAN, J., DAKIN, K. S. & DENNIS, P. M. 2002. Respiratory rate measurement in adults--how reliable is it? *Respir Med,* 96**,** 31-3.

LIU, L. L., GALLAHER, M. M., DAVIS, R. L., RUTTER, C. M., LEWIS, T. C. & MARCUSE, E. K. 2004. Use of a respiratory clinical score among different providers. *Pediatr Pulmonol,* 37**,** 243-8.

LOVETT, P. B., BUCHWALD, J. M., STURMANN, K. & BIJUR, P. 2005. The vexatious vital: neither clinical measurements by nurses nor an electronic monitor provides accurate measurements of respiratory rate in triage. *Ann Emerg Med,* 45**,** 68-76.

LYNCH, T., PLATT, R., GOUIN, S., LARSON, C. & PATENAUDE, Y. 2004. Can we predict which children with clinically suspected pneumonia will have the presence of focal infiltrates on chest radiographs? *Pediatrics,* 113**,** e186-9.

MARGOLIS, P. & GADOMSKI, A. 1998. The rational clinical examination. Does this infant have pneumonia? *Jama,* 279**,** 308-13.

MIMOZ, O., BENARD, T., GAUCHER, A., FRASCA, D. & DEBAENE, B. 2012. Accuracy of respiratory rate monitoring using a non-invasive acoustic method after general anaesthesia. *Br J Anaesth,* 108**,** 872-5.

MIN, S. D., YOON, D. J., YOON, S. W., YUN, Y. H. & LEE, M. 2007. A study on a non-contacting respiration signal monitoring system using Doppler ultrasound. *Med Biol Eng Comput,* 45**,** 1113-9.

MOODY, G., BUMP, M., WEINSTEIN, J., BERMAN, A., MIETUS, J., GOLDBERGER, A. 1986. Clinical validation of ECG-derived respiration (EDR) technique. *Comput Cardiol,* 13**,** 507-510.

NCEPOD 2005. An Acute Problem? National Confidential Enquiry into Patient Outcome and Death (NCEPOD); Report. Section 5 Key Findings; Patient observations and review criteria.

NICE 2007a. Feverish illness in children-assessment and initial management in children younger than 5 years. *NICE*.

NICE 2007b. NICE Clinical Guideline 50 - Full Guidance - Acutely ill patients in hospital.

NIELSEN, L. G., FOLKESTAD, L., BRODERSEN, J. B. & BRABRAND, M. 2015. Inter-Observer Agreement in Measuring Respiratory Rate. *PLoS One,* 10**,** e0129493.

NIESTERS, M., MAHAJAN, R., OLOFSEN, E., BOOM, M., GARCIA DEL VALLE, S., AARTS, L. & DAHAN, A. 2012. Validation of a novel respiratory rate monitor based on exhaled humidity. *Br J Anaesth,* 109**,** 981-9.

NIJMAN, R. G., VERGOUWE, Y., THOMPSON, M., VAN VEEN, M., VAN MEURS, A. H., VAN DER LEI, J., STEYERBERG, E. W., MOLL, H. A. & OOSTENBRINK, R. 2013. Clinical prediction model to aid emergency doctors managing febrile children at risk of serious bacterial infections: diagnostic study. *Bmj,* 346**,** f1706.

NOONAN, P. J., HOWARD, J., TOUT, D., ARMSTRONG, I. & WILLIAMS, H. 2012. Accurate markerless respiratory tracking for gated whole body PET using the Microsoft Kinect. *EEE Nuclear Science Symposium Conference RecordIIEEE Nucl. Sci. Symp. Conf. Rec.***,** 3973-3974.

O'LEARY, F., HAYEN, A., LOCKIE, F. & PEAT, J. 2015. Defining normal ranges and centiles for heart and respiratory rates in infants and children: a cross-sectional study of patients attending an Australian tertiary hospital paediatric emergency department. *Arch Dis Child,* 100**,** 733-7.

OLSSON, E., UGNELL, H., OBERG, P. A. & SEDIN, G. 2000. Photoplethysmography for simultaneous recording of heart and respiratory rates in newborn infants. *Acta Paediatr,* 89**,** 853-61.

OPIYO, N. & ENGLISH, M. 2011. What clinical signs best identify severe illness in young infants aged 0-59 days in developing countries? A systematic review. *Arch Dis Child,* 96**,** 1052-9.

PALS 2015. Paediatric advanced life support. *Paediatric advanced life support*.

PATINO, M., REDFORD, D. T., QUIGLEY, T. W., MAHMOUD, M., KURTH, C. D. & SZMUK, P. 2013. Accuracy of acoustic respiration rate monitoring in pediatric patients. *Paediatr Anaesth,* 23**,** 1166-73.

PHILIPS. 2015. www.vitalsignscamera.com [Online]. [Accessed].

PREECE, M. H., HILL, A., HORSWILL, M. S. & WATSON, M. O. 2012. Supporting the detection of patient deterioration: observation chart design affects the recognition of abnormal vital signs. *Resuscitation,* 83**,** 1111-8.

RAMBAUD-ALTHAUS, C., ALTHAUS, F., GENTON, B. & D'ACREMONT, V. 2015. Clinical features for diagnosis of pneumonia in children younger than 5 years: a systematic review and meta-analysis. *Lancet Infect Dis,* 15**,** 439-50.

RCGP 2013. The 2022 GP Compendium of evidence. The Royal College of General Practioners Compendium of Evidence.

RCPCH 2002. Clinical practice guideline: diagnosis and management of childhood obstructive sleep apnea syndrome. *Pediatrics,* 109**,** 704-12.

ROLAND, D., OLIVER, A., EDWARDS, E. D., MASON, B. W. & POWELL, C. V. 2014. Use of paediatric early warning systems in Great Britain: has there been a change of practice in the last 7 years? *Arch Dis Child,* 99**,** 26-9.

RUSCONI, F., CASTAGNETO, M., GAGLIARDI, L., LEO, G., PELLEGATTA, A., PORTA, N., RAZON, S. & BRAGA, M. 1994. Reference values for respiratory rate in the first 3 years of life. *Pediatrics,* 94**,** 350-5.

S. DING, X. Z., W. CHEN, D. WEI 2004. Derivation of respiratory signal from single- channel ECGs based on source statistics. *Int. J. Bioelectromagnetism,* 6**,** 43-49.

SAATCHI, R., GIBSON, J., ROWE, W. K. & ALLEN, E. M. 1997. Adaptive multiresolution analysis based evoked potential filtering,. *IEE Proceedings - Science, Measurement and Technology,* 144**,** 149-155.

SCHEIN, R. M., HAZDAY, N., PENA, M., RUBEN, B. H. & SPRUNG, C. L. 1990. Clinical antecedents to in-hospital cardiopulmonary arrest. *Chest,* 98**,** 1388-92.

SCHMIDT, P. E., MEREDITH, P., PRYTHERCH, D. R., WATSON, D., WATSON, V., KILLEN, R. M., GREENGROSS, P., MOHAMMED, M. A. & SMITH, G. B. 2015. Impact of introducing an electronic physiological surveillance system on hospital mortality. *BMJ Qual Saf,* 24**,** 176-7.

SHAH, S., BACHUR, R., KIM, D. & NEUMAN, M. I. 2010. Lack of predictive value of tachypnea in the diagnosis of pneumonia in children. *Pediatr Infect Dis J,* 29**,** 406-9.

SIMOES, E. A., ROARK, R., BERMAN, S., ESLER, L. L. & MURPHY, J. 1991. Respiratory rate: measurement of variability over time and accuracy at different counting periods. *Arch Dis Child,* 66**,** 1199-203.

SINGHI, S., BHALLA, A. K., BHANDARI, A. & NARANG, A. 2003. Counting respiratory rate in infants under 2 months: comparison between observation and auscultation. *Ann Trop Paediatr,* 23**,** 135-8.

STORCK, K., KARLSSON, M., ASK, P. & LOYD, D. 1996. Heat transfer evaluation of the nasal thermistor technique. *IEEE Trans Biomed Eng,* 43**,** 1187-91.

SUBBE, C. P., DAVIES, R. G., WILLIAMS, E., RUTHERFORD, P. & GEMMELL, L. 2003. Effect of introducing the Modified Early Warning score on clinical outcomes, cardio-pulmonary arrests and intensive care utilisation in acute medical admissions. *Anaesthesia,* 58**,** 797-802.

THOMPSON, M., COAD, N., HARNDEN, A., MAYON-WHITE, R., PERERA, R. & MANT, D. 2009. How well do vital signs identify children with serious infections in paediatric emergency care? *Arch Dis Child,* 94**,** 888-93.

USEN, S. & WEBERT, M. 2001. Clinical signs of hypoxaemia in children with acute lower respiratory infection: indicators of oxygen therapy. *Int J Tuberc Lung Dis,* 5**,** 505-10.

VAN DE LOUW, A., CRACCO, C., CERF, C., HARF, A., DUVALDESTIN, P., LEMAIRE, F. & BROCHARD, L. 2001. Accuracy of pulse oximetry in the intensive care unit. *Intensive Care Med,* 27**,** 1606-13.

VAN DEN BRUEL, A., HAJ-HASSAN, T., THOMPSON, M., BUNTINX, F. & MANT, D. 2010. Diagnostic value of clinical features at presentation to identify serious infection in children in developed countries: a systematic review. *Lancet,* 375**,** 834-45.

WANG, E. E., LAW, B. J., STEPHENS, D., LANGLEY, J. M., MACDONALD, N. E., ROBINSON, J. L., DOBSON, S., MCDONALD, J., BOUCHER, F. D., DE CARVALHO, V. & MITCHELL, I. 1996. Study of interobserver reliability in clinical assessment of RSV lower respiratory illness: a Pediatric Investigators Collaborative Network for Infections in Canada (PICNIC) study. *Pediatr Pulmonol,* 22**,** 23-7.

WANG, E. E., MILNER, R. A., NAVAS, L. & MAJ, H. 1992. Observer agreement for respiratory signs and oximetry in infants hospitalized with lower respiratory infections. *Am Rev Respir Dis,* 145**,** 106-9.

WARDLAW TM, J. E., HODGE M, WORLD HEALTH ORGANIZATION, UNICEF 2006. Pneumonia: the forgotten killer of children. *World Health Organization*.

WERTHAMMER, J., KRASNER, J., DIBENEDETTO, J. & STARK, A. R. 1983. Apnea monitoring by acoustic detection of airflow. *Pediatrics,* 71**,** 53-5.

WERTHEIM, D., OLDEN, C., SAVAGE, E. & SEDDON, P. 2009. Extracting respiratory data from pulse oximeter plethysmogram traces in newborn infants. *Arch Dis Child Fetal Neonatal Ed,* 94**,** F301-3.

WERTHEIM, D., OLDEN, C., SYMES, L., RABE, H. & SEDDON, P. 2013. Monitoring respiration in wheezy preschool children by pulse oximetry plethysmogram analysis. *Med Biol Eng Comput,* 51**,** 965-70.

WERTHEIM, D., SOBOWIEC-KOUMAN, S., CASTRONOVO, G. & SEDDON, P. 2014. Respiratory analysis of pulse oximetry plethysmogram recordings in preterm infants. *European Respiratory Journal,* 44.
WEST, J. 1990. Respiratory Physiology: the essentials.

WHO 2002. Integrated management of childhood illness: caring for newborns and children in the community. *Manual for the community health worker. Geneva: World Health Organization*.

WINBERG, H., NILSSON, K. & ANEMAN, A. 2008. Paediatric Rapid Response Systems: a literature review. *Acta Anaesthesiol Scand,* 52**,** 890-6.

WORSTER, A., ELLIOTT, L., BOSE, T. J. & CHEMERIS, E. 2003. Reliability of vital signs measured at triage. *Eur J Emerg Med,* 10**,** 108-10.

CHAPTER 8

APPENDIX

8.1 Respiratory rate measurement questionnaire

Your role:

Nurse : Band 5 ☐ Band 6 ☐ Band 7 ☐ Band 8 ☐

Doctor : F1/2 ☐ ST1-3 ☐ ST4-8 ☐ Consultant ☐

Healthcare worker: ☐

How long do you measure respiratory rate for?

<15 seconds ☐

15 seconds ☐

30 seconds ☐

60 seconds ☐

Other - Please state ☐

What method of timing do you use?

Wrist/fob watch ☐

Wall Clock ☐

Phone Timer ☐

Other - Please state ☐

How do you measure respiratory rate?

	0-1 Month	1-12 months	1-5 years	5 + years
Ausculatation				
Palpation of chest				
Observation				
Palpation for breaths				
Other (Please state)				

8.2 REC, HRA and local approval: Inter-observer variation in the measurement of respiratory rate in children

8.2.1 REC approval letter 1: 16/YH/0262

NHS
Health Research Authority

Yorkshire & The Humber - South Yorkshire Research Ethics Committee
Unit 001
Jarrow Business Centre
Rolling Mill Road
Jarrow
Tyne and Wear
NE32 3DT

Telephone: 0207 1048091

Please note: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval

12 July 2016

Professor Heather Elphick
Paediatric Consultant in Respiratory Medicine
Sheffield Children's Hospital
Western Bank
Sheffield
South Yorkshire
S10 2TH

Dear Professor Elphick

Study title:	**Inter-observer variation in the measurement of respiratory rate in children**
REC reference:	**16/YH/0262**
IRAS project ID:	**205102**

The Research Ethics Committee reviewed the above application at the meeting held on 30 June 2016. Thank you and Dr William Daw for attending to discuss the application.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point, wish to make a request to defer, or require further information, please contact the REC Manager Mrs Helen Wilson, nrescommittee.yorkandhumber-southyorks@nhs.net . Under very limited circumstances (e.g. for student research which has received an unfavourable opinion), it may be possible to grant an exemption to the publication of the study.

A Research Ethics Committee established by the Health Research Authority

Ethical opinion

The members of the Committee present gave a **favourable ethical opinion** of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below. .

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

1 The Committee confirm that an email must be sent around the Trust informing staff that the research study would be taking place.

2 The Participant Consent Form to be changed from 'I' to 'I/my' to allow for 13-15 year olds to consent.

You should notify the REC once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. Revised documents should be submitted to the REC electronically from IRAS. The REC will acknowledge receipt and provide a final list of the approved documentation for the study, which you can make available to host organisations to facilitate their permission for the study. Failure to provide the final versions to the REC may cause delay in obtaining permissions.

Management permission must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for HRA Approval (England)/ NHS permission for research is available in the Integrated Research Application System, at www.hra.nhs.uk or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations.

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database. This should be before the first participant is recruited but no later than 6 weeks after recruitment of the first participant.

feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Training

We are pleased to welcome researchers and R&D staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

16/YH/0262	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

pp

Dr Rhona Bratt
Chair

E-mail: nrescommittee.yorkandhumber-southyorks@nhs.net

Enclosures: *List of names and professions of members who were present at the meeting and those who submitted written comments*

"After ethical review – guidance for researchers"

Copy to: Mrs Wendy Swann, Sheffield Children's NHS Foundation Trust

8.2.2 REC approval letter 2: 16/YH/0262

NHS
Health Research Authority

Yorkshire & The Humber - South Yorkshire Research Ethics Committee
Unit D01
Jarrow Business Centre
Rolling Mill Road
Jarrow
Tyne and Wear
NE32 3DT

Telephone: 0207 1048091

21 July 2016

Professor Heather Elphick
Paediatric Consultant in Respiratory Medicine
Sheffield Children's Hospital
Western bank
Sheffield
South Yorkshire
S10 2TH

Dear Professor Elphick

Study title: **Inter-observer variation in the measurement of respiratory rate in children**
REC reference: **16/YH/0262**
IRAS project ID: **205102**

Thank you for your letter of 20 July 2016. I can confirm the REC has received the documents listed below and that these comply with the approval conditions detailed in our letter dated 12 July 2016.

Documents received

The documents received were as follows:

Document	*Version*	*Date*
Covering letter on headed paper [REC covering letter]	1	19 July 2016
IRAS Checklist XML [Checklist_21072016]		21 July 2016
Participant consent form [205102 Participant Consent Form - observer study]	1.3	19 July 2016
Participant consent form [205102 Parent Consent form- video recording]	1.4	19 July 2016

Approved documents

The final list of approved documentation for the study is therefore as follows:

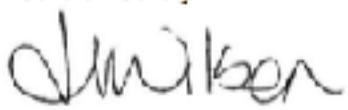
Document	*Version*	*Date*
Copies of advertisement materials for research participants [Email Advert]	1	14 July 2016
Costing template (commercial projects) [205102 costings]	1	23 November 2015
Covering letter on headed paper [REC covering letter]	1	08 June 2016
Covering letter on headed paper [REC covering letter]	1	15 July 2016
Covering letter on headed paper [REC covering letter]	1	19 July 2016
IRAS Application Form [IRAS_Form_08062016]		08 June 2016
IRAS Checklist XML [Checklist_21072016]		21 July 2016
Letter from funder [Funding letter]	1	22 March 2016
Other [205102 Response to unfavourable opinion]	1	22 May 2016
Other [205102 Unfavourable opinion]	1	18 May 2016
Participant consent form [205102 Assent form]	1	05 April 2016
Participant consent form [205102 Healthcare professionals Consent Form]	1.1	03 June 2016
Participant consent form [205102 Parent Consent Form - observer study]	1.1	03 June 2016
Participant consent form [205102 Parent Consent form- video recording]	1.2	03 June 2016
Participant consent form [205102 Participant consent form ages 13-15 inter-observer study]	1.1	14 July 2016
Participant consent form [205102 Participant consent form ages 13-15 - video recording study]	1.1	14 July 2016
Participant consent form [205102 Participant Consent Form - observer study]	1.3	19 July 2016
Participant consent form [205102 Parent Consent form- video recording]	1.4	19 July 2016
Participant information sheet (PIS) [205102 Healthcare professionals information sheet]	1.1	03 June 2016
Participant information sheet (PIS) [205102 Participant Information Sheet ages 0-5 years]	1	05 April 2016
Participant information sheet (PIS) [205102 Parent Information Sheet]	1.1	03 June 2016
Participant information sheet (PIS) [205102 Parent information sheet- video recording]	1.1	03 June 2016
Participant information sheet (PIS) [205102 Participant Information sheet ages 13-15 years]	1.1	03 June 2016
Participant information sheet (PIS) [205102 Participant Information Sheet ages 13-15 years - video recording]	1.1	03 June 2016
Participant information sheet (PIS) [205102 Participant information sheet ages 6-12 years]	1	05 April 2016
Participant information sheet (PIS) [205102 Participant information sheet ages 6-12 years -video recording]	1	05 April 2016
Referee's report or other scientific critique report [Internal review]	1	27 November 2015
Referee's report or other scientific critique report [External Review]	1	07 December 2015

Research protocol or project proposal [Protocol]	1.1	03 June 2016
Summary CV for Chief Investigator (CI) [Heather Elphick signed CV]	1	03 December 2015

You should ensure that the sponsor has a copy of the final documentation for the study. It is the sponsor's responsibility to ensure that the documentation is made available to R&D offices at all participating sites.

16/YH/0262	**Please quote this number on all correspondence**

Yours sincerely



Mrs Helen Wilson
REC Manager

E-mail: nrescommittee.yorkandhumber-southyorks@nhs.net

Copy to: Mrs Wendy Swann, Sheffield Children's NHS Foundation Trust

8.2.3 HRA approval letter: 16/YH/0262

NHS
Health Research Authority

Professor Heather Elphick
Paediatric consultant in respiratory medicine
Sheffield Children's Hospital
Western bank
Sheffield
South Yorkshire
S10 2TH

Email: hra.approval@nhs.net

27 July 2016

Dear Professor Elphick

Letter of HRA Approval

Study title:	**Inter-observer variation in the measurement of respiratory rate in children**
IRAS project ID:	**205102**
REC reference:	**16/YH/0262**
Sponsor	**Sheffield Children's NHS Foundation Trust**

I am pleased to confirm that **HRA Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications noted in this letter.

Participation of NHS Organisations in England

The sponsor should now provide a copy of this letter to all participating NHS organisations in England.

Appendix B provides important information for sponsors and participating NHS organisations in England for arranging and confirming capacity and capability. **Please read *Appendix B* carefully**, in particular the following sections:

- *Participating NHS organisations in England* – this clarifies the types of participating organisations in the study and whether or not all organisations will be undertaking the same activities
- *Confirmation of capacity and capability* - this confirms whether or not each type of participating NHS organisation in England is expected to give formal confirmation of capacity and capability. Where formal confirmation is not expected, the section also provides details on the time limit given to participating organisations to opt out of the study, or request additional time, before their participation is assumed.
- *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* - this provides detail on the form of agreement to be used in the study to confirm capacity and capability, where applicable.

Further information on funding, HR processes, and compliance with HRA criteria and standards is also provided.

It is critical that you involve both the research management function (e.g. R&D office) supporting each organisation and the local research team (where there is one) in setting up your study. Contact details and further information about working with the research management function for each organisation can be accessed from www.hra.nhs.uk/hra-approval.

Appendices

The HRA Approval letter contains the following appendices:

- A – List of documents reviewed during HRA assessment
- B – Summary of HRA assessment

After HRA Approval

The document "*After Ethical Review – guidance for sponsors and investigators*", issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

In addition to the guidance in the above, please note the following:

- HRA Approval applies for the duration of your REC favourable opinion, unless otherwise notified in writing by the HRA.
- Substantial amendments should be submitted directly to the Research Ethics Committee, as detailed in the *After Ethical Review* document. Non-substantial amendments should be submitted for review by the HRA using the form provided on the HRA website, and emailed to hra.amendments@nhs.net.
- The HRA will categorise amendments (substantial and non-substantial) and issue confirmation of continued HRA Approval. Further details can be found on the HRA website.

Scope

HRA Approval provides an approval for research involving patients or staff in NHS organisations in England.

If your study involves NHS organisations in other countries in the UK, please contact the relevant national coordinating functions for support and advice. Further information can be found at http://www.hra.nhs.uk/resources/applying-for-reviews/nhs-hsc-rd-review/.

If there are participating non-NHS organisations, local agreement should be obtained in accordance with the procedures of the local participating non-NHS organisation.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application

procedure. If you wish to make your views known please email the HRA at hra.approval@nhs.net. Additionally, one of our staff would be happy to call and discuss your experience of HRA Approval.

HRA Training

We are pleased to welcome researchers and research management staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

Your IRAS project ID is **205102**. Please quote this on all correspondence.

Yours sincerely

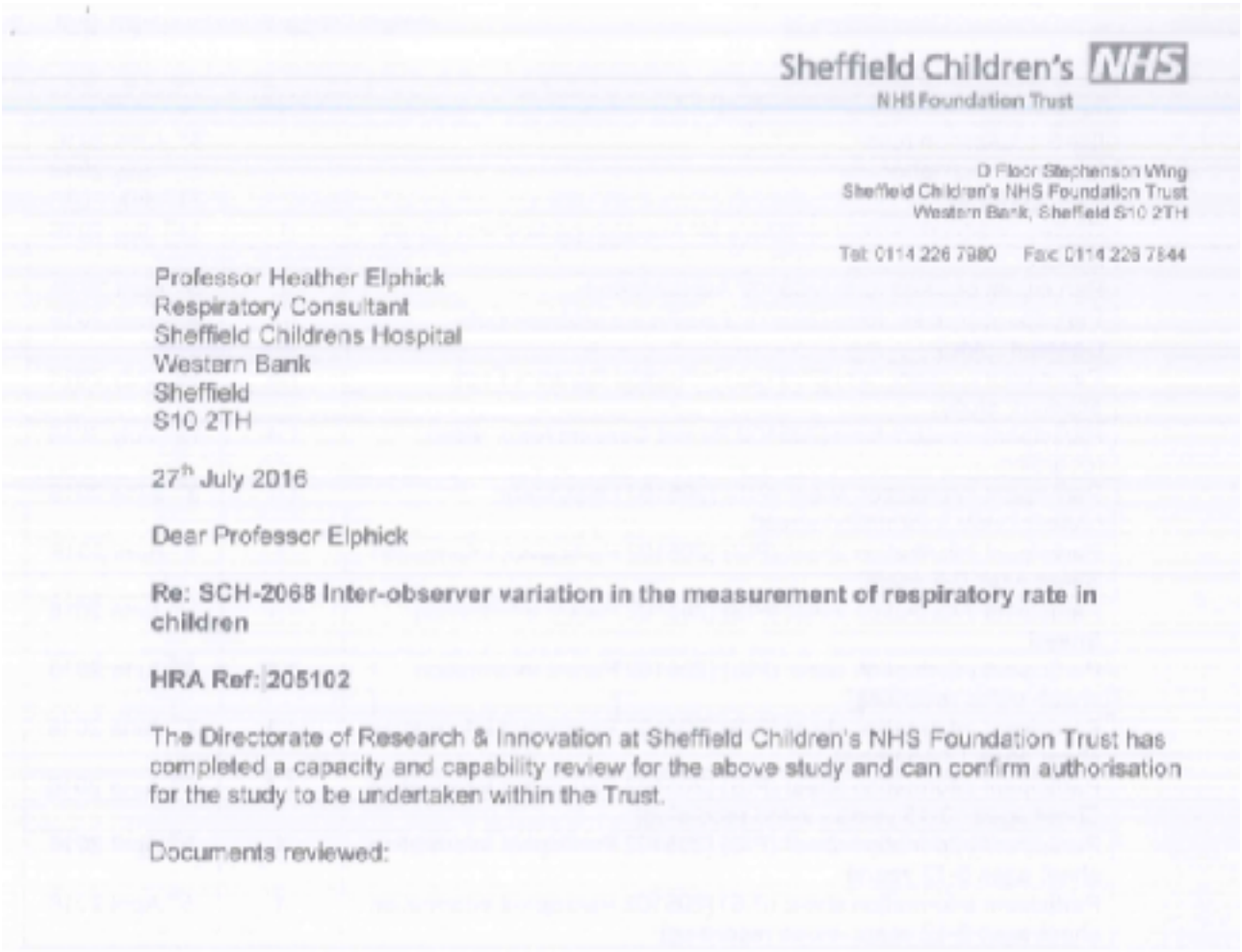
Thomas Fairman
HRA Assessor

Email: hra.approval@nhs.net

Copy to: *Mrs Wendy Swann, Sheffield Children's NHS Foundation Trust (Lead NHS R&D Contact and Sponsor Contact)*

NIHR CRN Portfolio Applications Team

8.2.4 Sheffield Children's Hospital R&D approval letter



Sheffield Children's NHS
NHS Foundation Trust

D Floor Stephenson Wing
Sheffield Children's NHS Foundation Trust
Western Bank, Sheffield S10 2TH

Tel: 0114 226 7980 Fax: 0114 226 7844

Professor Heather Elphick
Respiratory Consultant
Sheffield Childrens Hospital
Western Bank
Sheffield
S10 2TH

27th July 2016

Dear Professor Elphick

Re: SCH-2068 Inter-observer variation in the measurement of respiratory rate in children

HRA Ref: 205102

The Directorate of Research & Innovation at Sheffield Children's NHS Foundation Trust has completed a capacity and capability review for the above study and can confirm authorisation for the study to be undertaken within the Trust.

Documents reviewed:

Document	Version	Date
IRAS application form		6th June 2016
HRA Approval letter		27th July 2016
REC approval		21st July 2016
Copies of advertisement materials for research participants [Email Advert]	1	14th July 2016
Participant consent form [205102 Assent form]	1	5th April 2016
Participant consent form [205102 Healthcare professionals Consent Form]	1.1	3rd June 2016
Participant consent form [205102 Participant Consent Form - observer study]	1.3	19th July 2016
Participant consent form [205102 Parent Consent form- video recording	1.4	19th July 2016
Participant information sheet (PIS) [205102 Healthcare professionals information sheet]	1.1	3rd June 2016
Participant information sheet (PIS) [205102 Participant Information Sheet ages 0-5 years]	1	5th April 2016
Participant information sheet (PIS) [205102 Parent Information Sheet]	1.1	3rd June 2016
Participant information sheet (PIS) [205102 Parent information sheet- video recording]	1.1	3rd June 2016
Participant information sheet (PIS) [205102 Participant Information sheet ages 13-15 years]	1.1	3rd June 2016
Participant information sheet (PIS) [205102 Participant Information Sheet ages 13-15 years - video recording]	1.1	3rd June 2016
Participant information sheet (PIS) [205102 Participant information sheet ages 6-12 years]	1	5th April 2016
Participant information sheet (PIS) [205102 Participant information sheet ages 6-12 years -video recording]	1	5th April 2016
Research protocol	1.1	3rd June 2016

The Trust authorisation for this research study is on the understanding and provision that you will adhere to the following conditions:-

That the research should:

Be conducted in accordance with, ICH GCP, the Declaration of Helsinki and the NHS Research Governance Framework (Second Edition, 2005).

- Comply with regulatory requirements and legislation including The Medicines for Human Use (Clinical Trials) Regulations 2004 and subsequent amendments, Data Protection, Health & Safety, Trust Caldicott Guidelines and the use of Human Tissue for research purposes.

You must also:

- Ensure you and your team are familiar with issues of informed consent within research having completed the Good Clinical Practice (GCP) training in accordance with the Sponsor's requirements.
- Request written approval for any change to the approved protocol/study documents that you or the Chief Investigator wish to implement.

- Ensure that all study personnel, not employed by Sheffield Children's NHS Foundation Trust hold either an honorary contract with the Trust or a letter of access issued by the Trust, before they have access to any facilities, patients, staff, their data, tissue or organs.

- Complete and return progress report requests and notify the Directorate of Research & Innovation when your research is completed. At the point of completion, please submit your findings and any publication or presentations of your findings.

- Inform the Directorate of Research & Innovation if you decide to terminate this research prematurely, by sending a report and indicating the reason for the early termination.

- Advise the Directorate of Research & Innovation of any unusual or unexpected results that raise questions about the safety of the research.

In line with our continued commitment to the above mentioned laws, guidance and statutes, it will be necessary for the Directorate of Research & Innovation to be involved in the conduct of your study as it progresses. Therefore, please ensure that your documentation, including this letter is maintained in the Investigator Site File the appropriate manner and up-to-date.

The target date for recruitment of the first participant is 26th August 2016. If you are unlikely to meet this target date, please let us know as soon as possible.

I would like to take this opportunity to wish you every success with your project. If you have any questions or we can be of any further assistance to you, do not hesitate to contact the Directorate of Research & Innovation.

Yours sincerely

Professor Paul Dimitri
Director of Research & Innovation

8.3 REC and local approval: Development of the 'BreathEasy': a non-contact, hand-held device for measurement of respiratory rate (CPRM)

8.3.1 REC approval letter 1: 14/YH/1137

NHS
Health Research Authority

National Research Ethics Service

NRES Committee Yorkshire & The Humber - Sheffield
HRA NRES Centre Manchester
Barlow House
3rd Floor
4 Minshull Street
Manchester
M1 3DZ

Telephone: 0161 625 7832
Fax: 0161 625 7299

15 September 2014

Dr Heather Elphick
Consultant in Paediatric Respiratory Medicine
Sheffield Children's NHS Foundation Trust
Western Bank
Sheffield
South Yorks
S10 2TH

Dear Dr Elphick

Study title:	**Development of the "BreathEasy": a non-contact, hand-held device for measurement of respiratory rate (CPRM)**
REC reference:	**14/YH/1137**
Protocol number:	**SCH/13/018**
IRAS project ID:	**149145**

The Research Ethics Committee reviewed the above application at the meeting held on 01 September 2014. Thank you for attending to discuss the application.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details, unless you expressly withhold permission to do so. Publication will be no earlier than three months from the date of this favourable opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to withhold permission to publish, please contact the REC Manager Miss Helen Penistone, nrescommittee.yorkandhumber-sheffield@nhs.net.

Ethical opinion

The members of the Committee present gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

The following points relate to the Participant Information Sheets:

- The Committee asked if an extra sentence on the general benefits of research could be added to the information sheets. In the opinion of the Committee, this would help to introduce children to the idea.
- Please add information about where the results of the study can be obtained from.
- Please add a picture of the device and explain how big the device is.
- Please state that this is a pilot study.

You should notify the REC in writing once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. The REC will acknowledge receipt and provide a final list of the approved documentation for the study, which can be made available to host organisations to facilitate their permission for the study. Failure to provide the final versions to the REC may cause delay in obtaining permissions.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations.

Registration of Clinical Trials

All clinical trials (defined as the first four categories on question 2 of the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to contest the need for registration they should contact Catherine Blewett (catherineblewett@nhs.net), the HRA does not, however, expect exceptions to be made. Guidance on where to register is provided within IRAS.

Notice of no objection must be obtained from the Medicines and Healthcare products Regulatory Agency (MHRA).

The sponsor is asked to provide the Committee with a copy of the notice from the MHRA, either confirming no objection or giving grounds for objection, as soon as this is available.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

NHS Sites

The favourable opinion applies to all NHS sites taking part in the study taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Non NHS sites

The Committee has not yet completed any site-specific assessment(s) (SSA) for the non-NHS research site(s) taking part in this study. The favourable opinion does not therefore apply to any non-NHS site at present. I will write to you again as soon as an SSA application(s) has been reviewed. In the meantime no study procedures should be initiated at non-NHS sites.

Summary of discussion at the meeting

Social or scientific value; scientific design and conduct of the study

The Committee noted that this is a pilot, feasibility study with much potential value.

The Committee asked for further information about the contactless design. You used some pictures of the device to explain the design and how it is used. In future the device will be wireless and the electronics would be incorporated into the body of the device.

The Committee asked if the device had been tested on children for acceptability. You explained that you had carried out a focus group with children aged 6-10 years of age. There had been no problems with this age group but they need to test the device with toddlers.

The Committee asked for further information about any public or patient involvement in the design of the study. You advised that originally you had carried out a focus group which involved parents. Subsequent focus groups had involved professionals as they wanted to seek their views. A group of children had also 'played' with the device.

The Committee asked for more information about how it would be decided whether the device works. You advised that a comparison would be made between the device and the gold standard. The correlation co efficient would be obtained in order to do simple statistical tests.

The Committee recommended a paper (Statistical methods for assessing agreement between two methods of clinical measurement, Bland & Altman) to you which clarified the differences between testing agreement and testing correlation. The Committee had brought a copy of the paper for further information. You agreed that you could consider this.

Recruitment arrangements and access to health information, and fair participant selection

The Committee noted that potential participants and or their parents would have 3 to 4 weeks to consider participating in the study.

The Committee asked for further information about the adult volunteer group. You explained that the adults would be colleagues from the University and Children's Hospital. They would have a band with sensors around their chest. The results of this would be compared with the results from the hand held device.

Favourable risk benefit ratio; anticipated benefit/risks for research participants (present and future)

The Committee agreed that the study is very low risk.

The Committee asked if there was risk that the child would be frightened by the device. You explained that you had tested the device on adults and found that it was acceptable to have the device at a distance of 30 cm from their face. In practice they would distract the child so they would not really notice the device.

The Committee asked whether children might be frightened if they wake up during the study and see the device. You explained that they would only be taking the measurements for 1 minute so this is unlikely.

The Committee suggested showing the child the device before they went to sleep. You agreed.

Suitability of the applicant and supporting staff

The Committee asked for more information about the PhD student who would set the device up. You explained that the PhD student who had previous experience with the device and who was going to be involved in the set-up had now left. A physiologist who works on the sleep unit would now be involved in this aspect of the study.

Other ethical issues were raised and resolved in preliminary discussion before your attendance at the meeting.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Covering letter on headed paper [Cover Letter]		05 August 2014
Letter from funder [Funding Letter - NIHR i4i]		26 November 2012
Other [MHRA Advice Regarding No Objection Requirements]		02 May 2014
Participant consent form [Assent Form]	1.1	17 June 2014
Participant consent form [Adult Consent Form]	1.1	17 June 2014
Participant consent form [Consent Form]	1.1	17 June 2014
Participant information sheet (PIS) [Information Sheet 0-5yrs]	1.1	17 June 2014
Participant information sheet (PIS) [Information Sheet 13-15yrs]	1.1	17 June 2014
Participant information sheet (PIS) [Information Sheet - Adult Volunteer]	1.1	17 June 2014
Participant information sheet (PIS) [Information Sheet - Parent/Legal Guardian]	1.1	17 June 2014
Participant information sheet (PIS) [Information Sheet 6-12yrs]	1.1	17 June 2014
REC Application Form [REC_Form_05082014]		05 August 2014
Research protocol or project proposal [Protocol]	3.0	01 June 2014
Summary CV for Chief Investigator (CI) [CV Dr Heather Elphick]	1	12 June 2014

Membership of the Committee

The members of the Ethics Committee who were present at the meeting are listed on the attached sheet.

After ethical review

Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Training

We are pleased to welcome researchers and R&D staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

14/YH/1137	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

On behalf of
Professor Basil Sharrack
Chair

E-mail: nrescommittee.yorkandhumber-sheffield@nhs.net

Enclosures: List of names and professions of members who were present at the meeting and those who submitted written comments

"After ethical review – guidance for researchers"

8.3.2 REC approval letter 2: 14/YH/1137

NHS
Health Research Authority

National Research Ethics Service

NRES Committee Yorkshire & The Humber - Sheffield
HRA NRES Centre Manchester
Barlow House
3rd Floor
4 Minshull Street
Manchester
M1 3DZ

Telephone: 0161 625 7832
Fax: 0161 625 7299

10 December 2014

Dr Heather Elphick
Consultant in Paediatric Respiratory Medicine
Sheffield Children's NHS Foundation Trust
Western Bank
Sheffield
South Yorks
S10 2TH

Dear Dr Elphick

Study title:	**Development of the "BreathEasy": a non-contact, hand-held device for measurement of respiratory rate (CPRM)**
REC reference:	**14/YH/1137**
Protocol number:	**SCH/13/018**
IRAS project ID:	**149145**

Thank you for your email of 03 December 2014. I can confirm the REC has received the documents listed below and that these comply with the approval conditions detailed in our letter dated 15 September 2014.

Documents received

The documents received were as follows:

Document	*Version*	*Date*
Participant information sheet (PIS) [Adults]	4	03 December 2014
Participant information sheet (PIS) [Parent/ Carer]	4	03 December 2014
Participant information sheet (PIS) [13-15]	4	03 December 2014

Approved documents

The final list of approved documentation for the study is therefore as follows:

Document	*Version*	*Date*
Covering letter on headed paper [Cover Letter]		05 August 2014
Letter from funder [Funding Letter - NIHR HI]		26 November

		2012
Other [MHRA Advice Regarding No Objection Requirements]		02 May 2014
Participant consent form [Adult Consent Form]	1.1	17 June 2014
Participant consent form [Assent Form]	1.1	17 June 2014
Participant consent form [Consent Form]	1.1	17 June 2014
Participant information sheet (PIS) [Information Sheet 0-5yrs]	1.1	17 June 2014
Participant information sheet (PIS) [Information Sheet 6-12yrs]	1.1	17 June 2014
Participant information sheet (PIS) [Adults]	4	03 December 2014
Participant information sheet (PIS) [Parent/ Carer]	4	03 December 2014
Participant information sheet (PIS) [13-15]	4	03 December 2014
REC Application Form [REC_Form_05082014]		05 August 2014
Research protocol or project proposal [Protocol]	3.0	01 June 2014
Summary CV for Chief Investigator (CI) [CV Dr Heather Elphick]	1	12 June 2014

You should ensure that the sponsor has a copy of the final documentation for the study. It is the sponsor's responsibility to ensure that the documentation is made available to R&D offices at all participating sites.

14/YH/1137 **Please quote this number on all correspondence**

Yours sincerely

H Penistone

Miss Helen Penistone
REC Manager

E-mail: nrescommittee.yorkandhumber-sheffield@nhs.net

Copy to: Dr Gillian Gatenby

Wendy Swann,
Sheffield Children's NHS Foundation Trust

8.3.3 Sheffield Children's Hospital R&D approval letter: SCH/13/018

Sheffield Children's NHS
NHS Foundation Trust

D Floor Stephenson Wing
Sheffield Children's NHS Foundation Trust
Western Bank, Sheffield S10 2TH

Tel: 0114 226 7980 Fax: 0114 226 7844

27th January 2015

Dr Heather Elphick
Consultant in Paediatric Respiratory Medicine
Sheffield Children's NHS Foundation Trust
Western Bank
Sheffield
S10 2TH

Dear Dr Elphick

SCH/13/018 – Development of the "BeathEasy": a non-contract, hand-held device for measurement of respiratory rate (CPRM)

CSP Ref: 149145

I am pleased to confirm Trust Management Approval for you to proceed with your project in accordance with The Medicines for Human Use (Clinical Trials) Regulations 2004, ICH GCP, the Declaration of Helsinki and the NHS Research Governance Framework (Second Edition).

Your project will be indemnified by Sheffield Children's NHS Foundation Trust subject to strict adherence to the research protocol and the status of your contract remaining unchanged. Non-compliance will lead to nullification of indemnity.

It is essential that all research has a sponsor who is willing to take on ultimate responsibility for the initiation, management (or arranging the initiation and management) of and/or financing (or arranging the financing) for that research. The sponsor takes primary responsibility for ensuring that the design of the study meets appropriate standards and that arrangements are in place to ensure appropriate conduct and reporting. This is confirmation that Sheffield Children's NHS Foundation Trust have agreed to take on this responsibility for the above research project subject to all other relevant approvals remaining in place.

In line with our continued commitment to the above mentioned laws, guidance and statutes, it will be necessary for the R&D Department to be involved in the conduct of your study as it progresses. Therefore, please ensure that your documentation is maintained in the appropriate manner and up-to-date.

Please supply the R&D Department with the following documents on request:

1. Notification of any adverse events.
2. Changes to the protocol (this includes Ethics and MHRA amendments).
3. Notification of study suspension or termination.
4. Copies of regulatory progress reports with site recruitment summary.
5. Copies of monitoring reports.
6. Copies of regulatory annual reports.

Please note that approval for this study is dependent on full compliance with all of the above conditions. This letter must be stored securely with the documentation relating to this study.

If you require further information or have any queries please do not hesitate to contact the R&D team on 0114 2267980 or email crf@sch.nhs.uk.

I would like to take this opportunity to wish you every success with the study.

Yours sincerely

Prof Paul Dimitri
Director of Research & Innovation

These are the documents which have been approved for SCH/13/018 (Inc. Minor Am 1):

Document	*Version*	*Date*
Covering letter on headed paper [Cover Letter]		05 August 2014
Letter from funder [Funding Letter - NIHR I4i]		26 November 2012
Other [MHRA Advice Regarding No Objection Requirements]		02 May 2014
Participant consent form [Adult Consent Form]	1.2	03 December 2014
Participant consent form [Parent/Legal Guardian Consent Form]	1.2	03 December 2014
Participant consent form [Assent Form]	1.1	17 June 2014
Participant information sheet (PIS) [Information Sheet 0-5yrs]	1.1	17 June 2014
Participant information sheet (PIS) [Information Sheet 6-12yrs]	1.1	17 June 2014
Participant information sheet (PIS) [Adults]	4	03 December 2014
Participant information sheet (PIS) [Parent/ Carer]	4	03 December 2014
Participant information sheet (PIS) [13-15]	4	03 December 2014
REC Application Form [REC_Form_05082014]		05 August 2014
Research protocol or project proposal [Protocol]	3.0	01 June 2014
Summary CV for Chief Investigator (CI) [CV Dr Heather Elphick]	1	12 June 2014

8.4 REC and local approval: Evaluation and validation of the 'Breatheasy' Respiratory Rate Monitor in pre-hospital care

8.4.1 REC approval letter 1: 15/YH/0297

NHS
Health Research Authority
NRES Committee Yorkshire & The Humber - South Yorkshire
Unit 001
Jarrow Business Centre
Rolling Mill Road
Jarrow
Tyne and Wear
NE32 3DT

Telephone: 0191 428 3565

5 October 2015

Professor Heather Elphick
Consultant in Paediatric Respiratory Medicine
Sheffield Children's NHS Foundation Trust
Western Bank
Sheffield
South Yorkshire
S10 2TH

Dear Professor Elphick

Study title:	**Evaluation and validation of the "Breatheasy" Respiratory Rate Monitor in pre-hospital care**
REC reference:	15/YH/0297
IRAS project ID:	182744

Thank you for your letter of , responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair].

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to make a request to postpone publication, please contact the REC Manager, Ms Gillian Mayer, nrescommittee.yorkandhumber-scuthyorks@nhs.net.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a **Favourable** ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Additional conditions specified by the REC:

The participant information sheets need to note the correct name of the REC in the section 'Who has reviewed the study?' – NRES Committee Yorkshire and the Humber – South Yorkshire.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Covering letter on headed paper [REC covering letter]	1	07 July 2015
Letter from funder [Funding letter]	1	06 March 2015
Non-validated questionnaire [Breathing Monitor Questionnaire]	1.1	11 August 2015
Other [Infection control]	1	27 February 2014
Other [MHRA no objection]	1	02 May 2014
Participant consent form [Assent form]	1.1	26 May 2015
Participant consent form [Adult consent form]	1.2	12 August 2015
Participant consent form [Parent/guardian consent form]	1.1	12 August 2015
Participant information sheet (PIS) [Participant information sheet 0-5 years]	1	15 May 2015
Participant information sheet (PIS) [Participant information sheet ages 6-12 years]	1.1	12 August 2015
Participant information sheet (PIS) [Participant information sheet ages 13-15 years]	1.1	12 August 2015
Participant information sheet (PIS) [Participant information sheet adults]	1.1	12 August 2015
Participant information sheet (PIS) [Parent information sheet]	1.1	12 August 2015
REC Application Form [REC_Form_10062015]		10 June 2015
Referee's report or other scientific critique report [review 1]	1	15 November 2014
Referee's report or other scientific critique report [review 2]	1	15 November 2014
Research protocol or project proposal [Respiratory rate protocol]	1	23 October 2014
Summary CV for Chief Investigator (CI) [Heather Elphick CV]	1	12 June 2014

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the

feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Training

We are pleased to welcome researchers and R&D staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

15/YH/0297	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely
pp

Dr Ian Woollands
Chair

Email:nrescommittee.yorkandhumber-southyorks@nhs.net

Enclosures: 'After ethical review – guidance for researchers'

Copy to: *Dr Gillian Gatenby – R&D Dept, Sheffield Children's NHS Foundation Trust*

8.4.2 REC approval letter 2: 15/YH/0297

NHS
Health Research Authority

Yorkshire & The Humber - South Yorkshire Research Ethics Committee
Unit 001
Jarrow Business Centre
Rolling Mill Road
Jarrow
Tyne and Wear
NE32 3DT

Telephone: 0191 428 3467

07 October 2015

Professor Heather Elphick
Consultant in Paediatric Respiratory Medicine
Sheffield Children's NHS Foundation Trust
Western Bank
Sheffield
South Yorkshire
S10 2TH

Dear Professor Elphick

Study title: **Evaluation and validation of the "Breatheasy" Respiratory Rate Monitor in pre-hospital care.**
REC reference: **15/YH/0297**
IRAS project ID: **182744**

Thank you for your notification of 6 October 2015. I can confirm the REC has received the documents listed below and that these comply with the approval conditions detailed in our letter dated 05 October 2015.

Documents received

The documents received were as follows:

Document	*Version*	*Date*
Participant consent form [Adult consent form]	1.2	06 October 2015
Participant consent form [Parent/guardian consent form]	1.3	06 October 2015
Participant information sheet (PIS) [Participant information sheet ages 13-15 years]	1.2	06 October 2015
Participant information sheet (PIS) [Participant information sheet adults]	1.2	06 October 2015
Participant information sheet (PIS) [Parent information sheet]	1.2	06 October 2015

Approved documents

The final list of approved documentation for the study is therefore as follows:

Document	*Version*	*Date*
Covering letter on headed paper [REC covering letter]	1	07 July 2015
IRAS Checklist XML [Checklist_06102015]		06 October 2015
Letter from funder [Funding letter]	1	06 March 2015
Non-validated questionnaire [Breathing Monitor Questionnaire]	1.1	11 August 2015
Other [Infection control]	1	27 February 2014
Other [MHRA no objection]	1	02 May 2014
Participant consent form [Assent form]	1.1	26 May 2015
Participant consent form [Adult consent form]	1.2	06 October 2015
Participant consent form [Parent/guardian consent form]	1.3	06 October 2015
Participant information sheet (PIS) [Participant information sheet 0-5 years]	1	15 May 2015
Participant information sheet (PIS) [Parent information sheet]	1.1	12 August 2015
Participant information sheet (PIS) [Participant information sheet ages 13-15 years]	1.2	06 October 2015
Participant information sheet (PIS) [Participant information sheet adults]	1.2	06 October 2015
Participant information sheet (PIS) [Parent information sheet]	1.2	06 October 2015
REC Application Form [REC_Form_10062015]		10 June 2015
Referee's report or other scientific critique report [review 1]	1	15 November 2014
Referee's report or other scientific critique report [review 2]	1	15 November 2014
Research protocol or project proposal [Respiratory rate protocol]	1	23 October 2014
Summary CV for Chief Investigator (CI) [Heather Elphick CV]	1	12 June 2014

You should ensure that the sponsor has a copy of the final documentation for the study. It is the sponsor's responsibility to ensure that the documentation is made available to R&D offices at all participating sites.

15/YH/0297 **Please quote this number on all correspondence**

Yours sincerely

Jade Robinson
Amendment Coordinator

E-mail: nrescommittee.yorkandhumber-southyorks@nhs.net

Copy to: *Dr. Gillian Gatenby, R&D Sheffield Children's NHS Foundation Trust*

Ms Wendy Swann, Sheffield Children's NHS Foundation Trust

A Research Ethics Committee established by the Health Research Authority

8.4.3 Sheffield Children's Hospital R&D approval letter: SCH/15/048

Sheffield Children's NHS
NHS Foundation Trust

D Floor Stephenson Wing
Sheffield Children's NHS Foundation Trust
Western Bank, Sheffield S10 2TH

Tel: 0114 226 7980 Fax: 0114 226 7844

Professor Heather Elphick
E Floor Stephenson Wing
Sheffield Childrens Hospital
Western Bank
Sheffield
S10 2TH

15th October 2015

Dear Professor Elphick

SCH/15/048 – Evaluation and validation of the "Breatheasy" Respiratory Rate Monitor in prehospital care.

I am pleased to confirm Trust Management Approval for you to proceed with your project in accordance with The Medicines for Human Use (Clinical Trials) Regulations 2004, ICH GCP, the Declaration of Helsinki and the NHS Research Governance Framework (Second Edition).

Your project will be indemnified by Sheffield Children's NHS Foundation Trust subject to strict adherence to the research protocol and the status of your contract remaining unchanged. Non-compliance will lead to nullification of indemnity.

It is essential that all research has a sponsor who is willing to take on ultimate responsibility for the initiation, management (or arranging the initiation and management) of and/or financing (or arranging the financing) for that research. The sponsor takes primary responsibility for ensuring that the design of the study meets appropriate standards and that arrangements are in place to ensure appropriate conduct and reporting. This is confirmation that Sheffield Children's NHS Foundation Trust have agreed to take on this responsibility for the above research project subject to all other relevant approvals remaining in place.

In line with our continued commitment to the above mentioned laws, guidance and statutes, it will be necessary for the R&D Department to be involved in the conduct of your study as it progresses. Therefore, please ensure that your documentation is maintained in the appropriate manner and up-to-date.

Please supply the R&D Department with the following documents on request:

1. Notification of any adverse events.
2. Changes to the protocol (this includes Ethics and MHRA amendments).
3. Notification of study suspension or termination.
4. Copies of regulatory progress reports with site recruitment summary.
5. Copies of monitoring reports.
6. Copies of regulatory annual reports.

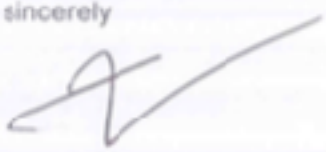
The target date for recruitment of the first participant is **15th November 2015**. If you are unlikely to meet this target date, please let us know as soon as possible.

Please note that approval for this study is dependent on full compliance with all of the above conditions. This letter must be stored securely with the documentation relating to this study.

If you require further information or have any queries please do not hesitate to contact the R&D team on 0114 2267560 or email crf@sch.nhs.uk.

I would like to take this opportunity to wish you every success with the study.

Yours sincerely



Prof Paul Dimitri
Director of Research & Innovation

These are the documents which have been approved for <SCH/15/048>

Document	Version	Date
REC approval		7.10.2015
SSI form		09.10.2015
Protocol	1	23.10.2014
Non-Validated questionnaire (Breathing Monitor Questionnaire)	1.1	11.08.2015
Assent Form	1.1	26.05.2015
Adult Consent Form	1.2	06.10.2015
Parent/Guardian Consent form	1.3	06.10.2015
Participant information sheet 0-5 years	1	15.05.2015
Participant information sheet 6-12 years	1.1	12.08.2015
Participant information sheet 13-15 years	1.2	06.10.2015
Adult information sheet	1.2	06.10.2015
Parent information sheet	1.2	06.10.2015

8.4.4 Doncaster Clinical Commissioning Group approval

NHS
Doncaster
Clinical Commissioning Group

Doncaster Clinical Research
Joint Research Office with Doncaster & Bassetlaw Hospitals
NHS Foundation Trust and NHS Bassetlaw
Tel: 01302 366666
Email: doncasterclinicalresearch@dbh.nhs.uk

Doncaster Royal Infirmary
Armthorpe Road, Doncaster
South Yorkshire DN2 5LT

Tel: 01302 366666
Fax: 01302 320098

Minicom: 01302 553140
(only for people who are deaf)

www.dbh.nhs.uk

26 January 2016

CONFIDENTIAL

Dr Mark Boon
GP Partner
Conisbrough Group Practice
Gardens Lane
Conisbrough
DN12 3JW

Dear Dr Boon,

Study Title:	**Evaluation and validation of the "Breatheasy" Respiratory Rate Monitor in pre-hospital care**
Chief Investigator:	**Professor Heather Elphick**
Sponsor:	**Sheffield Childrens NHS Foundation Trust**
DCCG Reference:	**0059/2015/CTN**
REC Reference:	15/YH/0297
IRAS ID:	182744

The above mentioned project has been reviewed by Doncaster Clinical Research, on behalf of NHS Doncaster Clinical Commissioning Group, to ensure that the research proposal meets the statutory regulatory governance requirements. For your information, the project reference is 0059/2015/CTN. I would be grateful if you could quote this number in any further correspondence with this department.

This letter confirms that the above project has satisfied the requirements of an appropriate research governance review.

Please note that this letter is confirmation of assurance only, and permission from each individual primary care practice (including GPs, Pharmacists, Dentists and Opticians) must be sought. A copy of this letter should be presented to each practice you wish to conduct your study in, in order to aid the approval process.

Please note that the finances have not been assessed as part of this assurance, as these need to be confirmed and appropriate systems put in place at an individual practice level.

Documentation
This assurance has been granted based on submission of the following documentation:

- Study Protocol (Version 2, dated 11 December 2012)
- IRAS R&D Form (Submission code: 182744/858777/14/936 signed by Professor Heather Elphick on 09 October 2015)
- IRAS SSI Form (Submission code: 182744/908984/8/15/309321/339726 signed by Dr Mark Boon on 26 January 2016)
- CV of Professor Heather Elphick
- CV of Dr Mark Boon
- Parent/Legal Guardian Information Sheet (Version 1.2, dated 06 October 2015)
- Adult Volunteer Information Sheet (Version 1.2, dated 06 October 2015)

- Participant Information Sheet for Young Children Aged 0-5 years (Version 1, dated 15 May 2015)
- Participant Information Sheet for Children Aged 6-12 years (Version 1.1, dated 12 August 2015)
- Participant Information Sheet for Young People Aged 13-15 years (Version 1.2, dated 06 October 2015)
- Adult Participant Consent Form (Version 1.2, dated 06 October 2015)
- Assent Form for Children and Young People (Version 1.1, dated 26 May 2015)
- Parent/Legal Guardian Consent Form (Version 1.3, dated 06 October 2015)
- Breathing Monitor Questionnaire - Parent (Version 1.1, dated 11 August 2015)
- Infection Control document (dated 27 February 2014)
- Letter stating 'favourable ethical opinion, with conditions' from Yorkshire & The Humber – South Yorkshire Research Ethics Committee, dated 05 October 2015 and subsequent letter confirmation approval of conditions, dated 07 October 2015.
- Letter from Sponsor confirming minor amendment dated 08 January 2016

Assurance has only been given for the activities for with a favourable opinion has been given by the Research Ethics Committee and that have been authorised by the MHRA, where applicable.

Please note that it is the responsibility of the Chief Investigator or appropriate Sponsor's represent to ensure that each participating practice is fully informed of any protocol deviations requiring notifications to a regulatory body. You are also obliged to inform Doncaster Clinical Research if your project deviates in any way from the original proposal / documentation you have submitted.

The Research Sponsor, or the Chief Investigator, or the local Principal Investigator, may take appropriate urgent safety measures in order to protect research participants against any immediate hazard to their health or safety. Each individual primary care practice and Doncaster Clinical Research must be notified that such measures have been taken in the same timeframe as notifying the Research Ethics Committee and any other regulatory bodies. The notification must include the reasons why the measures were taken and the plan for further action.

Amendments
This assurance covers the document versions stated above; any revised documents must be submitted for approval by the Research Ethics Committee and other regulatory bodies, where applicable, in accordance with guidance in the Integrated Research Application System (IRAS). If the study has been adopted onto the NIHR Portfolio, any amendments to the study must be reported to the Lead CLRN. In addition, all amendments must receive separate assurance from Doncaster Clinical Research.

Permissions
This letter gives assurance in relation to the aforementioned study, however, it is your responsibility to ensure that individual practices are informed about the study and issue individual practice permission. This department accepts no liability for non-co-operation of practices or patients.

Contracts
It is your responsibility to ensure you have sufficient indemnity to undertake this project. In addition, it is also your responsibility to ensure that letters of access / honorary contracts are in place where necessary.

Good Clinical Practice training
In accordance with ICH GCP guidelines and the UK Statutory Instruments, all key personnel involved in a Clinical Trial as part of the research team, must have completed GCP training within the last three years. It is your responsibility to ensure the research team have received this training. For information regarding upcoming GCP training courses, please contact Doncaster Clinical Research.

Auditing
I would strongly urge you to maintain an accurate and up to date site file for your documentation, as research in the NHS may be subject to periodic, random audits. In addition, where monitoring and auditing procedures are carried out by the Sponsor, you will be required to cooperate, where appropriate.

Monitoring
In order to ensure adequate monitoring of ongoing studies, Doncaster Clinical Research will send through periodic monitoring forms which require completion by the Principal Investigator or delegated individual. These forms need to be completed and sent through to Doncaster Clinical Research as a condition of the assurance of this study.

I would like to take this opportunity to wish you well with your project. If you have any questions or if I can be of any further assistance to you, please do not hesitate to contact me.

Yours sincerely

Emma Hannaford
Research Management & Governance Manager

cc Samya Armoush
Research Support Assistant
Sheffield Children's NHS Foundation Trust
Email: samya.armoush@sch.nhs.uk

cc Dr William Daw
Clinical Research Fellow
Sheffield Children's Hospital
Email: w.caw@nhs.net

cc Dr Gillian Gatenby
Sheffield Children's NHS Foundation Trust
Email: gillian.gatenby@sch.nhs.uk

cc Professor Heather Elphick
Consultant in Paediatric Respiratory Medicine
Sheffield Children's NHS Foundation Trust
Email: heather.elphick@sch.nhs.uk

8.4.5 Yorkshire Ambulance Service approval

Yorkshire Ambulance Service NHS
NHS Trust

Springhill 1
Brindley Way
Wakefield 41 Business Park
Wakefield
WF2 0XQ

Research & Development

Tel: 07795 646475
Email: jane.shewan@yas.nhs.uk

21st January 2016

Prof Heather Elphick
Sheffield Children's NHS Foundation Trust
Western Bank
Sheffield. S10 2TH
Heather.Elphick@sch.nhs.uk

Dear Prof Elphick,

Re: Evaluation of the "Breatheasy" in prehospital care; YASRD80; IRAS Ref 182744

I am happy to confirm that this study has R&D approval from the Yorkshire Ambulance Service NHS Trust. This relates to study documents listed below, and as approved by NRES Yorkshire & The Humber – South Yorkshire (their ref 15/YH/0297) in their letter dated 5th October 2015.

There are some conditions to this approval:

- If the project receives approval of any amendment from NRES Yorkshire & The Humber – South Yorkshire, the amendment must be submitted for our review.
- The study must be conducted in compliance with the terms and conditions of this letter, the NRES Yorkshire & The Humber – South Yorkshire approval, and the Research Governance Framework for Health & Social Care (Department of Health, 2005) and the YAS placement experience policy.
- A copy of the final report is provided to Yorkshire Ambulance Service NHS Trust.
- The support of the Yorkshire Ambulance Service NHS Trust is acknowledged on presentations or publications of this project.

Yorkshire Ambulance Service NHS
NHS Trust

If you agree with these terms, please will you sign and return a copy of this letter to myself.

I would like to take this opportunity to wish you every success with your research.

Yours sincerely

Jane Shewan
Head of Research and Development

pp. Dr Julian Mark
Associate Medical Director

I agree with the terms of approval stipulated by the Yorkshire Ambulance Service.

Signature of Investigator..... Date..21/01/2016