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Coláiste na hOllscoile Corcaigh, Éire
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Improving the Care of Preterm Infants: Before, During, and After Stabilisation in the Delivery Room.

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Research conducted through the Department of Paediatrics and Child Health, University College Cork.

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Date of Submission: 3rd July 2015

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DECLARATION OF OWNERSHIP

This thesis submitted is my own work and has not been submitted for another degree, either at University College Cork or elsewhere.

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Gavin Hawkes

ACKNOWLEDGEMENTS

Firstly, I express my thanks to all the families who provided consent for their infants to be included in the investigations contained in this thesis. Without the generosity and kindness of these families, this thesis would not have been possible.

I also take this opportunity to thank all staff of the neonatal intensive care unit and labour ward at Cork University Maternity Hospital, who were involved with many of the investigations within this thesis. Similarly, I would like to thank the Department of Paediatrics and Child Health UCC as well as the INFANT centre for providing me with the opportunity to complete this thesis. In particular, I would like to thank Prof. Geraldine Boylan for her help and encouragement, as well as Dr. John O'Toole and Dr. Vicki Livingstone for their help with data analysis.

I thank my supervisors Prof. Gene Dempsey and Prof. Tony Ryan for giving me the opportunity to complete this thesis. I am extremely grateful for the amount of time that they have spent teaching and guiding me during the completion of this thesis. It has been a privilege to receive their mentorship as well as their constant encouragement, and generosity. Their enthusiasm for research and improving clinical care has been both inspirational and contagious.

Finally, I would like to thank my family, whose continued support and encouragement over the past three years has been essential in getting to, and over, the final hurdle that is submission.

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LIST OF ABBREVIATIONS (IN ALPHABETICAL ORDER)

AHA	American Heart Association
AUC	Area under the operating characteristic curve
BPM	Beats per minute
CI	Confidence interval
CO_2	Carbon dioxide
CPAP	Continuous positive airway pressure
CPR	Cardiopulmonary resuscitation
CREC	Clinical Research Ethics Committee Of The Cork Teaching Hospitals
CUMH	Cork university maternity hospital
ECG	Electrocardiography
$EtCO_2$	End tidal carbon dioxide
ETT	Endotracheal tube
FDA	Food and drug administration
FIB	Flow inflating bag
FRC	Functional residual capacity
Hb	Haemoglobin
HbO_2	Oxygenated haemoglobin
HDU	High dependency unit
HR	Heart rate
IQR	Interquartile range
IVH	Intraventricular haemorrhage
MPRG	Mobile phone resuscitation guide
NICU	Neonatal intensive care unit
NLS	Newborn life support
NRP	Neonatal resuscitation programme
PCO_2	Partial pressure of arterial CO2
$PvCO_2$	Partial pressure of venous CO2
PEEP	Positive end expiratory pressure
PI	Perfusion index
PICC	Peripherally inserted central catheters
PIP	Peak inspiratory pressure
PPV	Positive Pressure ventilation
PVL	Periventricular leukomalacia
PVR	Pulmonary vascular resistance
RCT	Randomised controlled trial
RFM	Respiratory function monitor
SFI	Science Foundation Ireland
SHO	Senior House Officer
SIB	Self inflating bag
SpO_2	Oxygen saturation
SVD	Spontaneous vaginal delivery
$TcPCO_2$	Transcutaneous carbon dioxide pressure
TPR	T-Piece resuscitator
VC	Vital capacity

PEER-REVIEWED PUBLICATIONS INCLUDED IN THIS THESIS

1. Efficacy and user preference of two CO2 detectors in an infant mannequin randomized crossover trial.
   Hawkes GA, O'Connell BJ, Livingstone V, Hawkes CP, Ryan CA, Dempsey EM. European Journal of Pediatrics. 2013. 172(10):1393-9. PMID= 23756915 (Appendix B)

2. The demand for an educational smartphone app.
   Hawkes GA, Hawkes CP. Ryan CA, Dempsey EM.Resuscitation. 2013. 84(10):e139. PMID= 23867648 (Appendix M)

3. Perceptions of Webcams in the Neonatal Intensive Care Unit: Here's Looking at you Kid!
   Hawkes GA, Livingstone V, Ryan CA, Dempsey EM. American Journal of Perinatology. 2014. 30(2):131-6. PMID=24896140 (Appendix J)

4. A review of carbon dioxide monitoring in preterm newborns in the delivery room.
   Hawkes GA, Kelleher J, Ryan CA, Dempsey EM. Resuscitation. 2014. 85(10):1315-1319. PMID= 25086296 (Appendix A)

5. Quantitative or Qualitative Carbon Dioxide Monitoring for Manual Ventilation: A Mannequin Study.
   Hawkes GA, Kenosi M, Ryan CA, Dempsey EM.
   Acta Paediatrica. 2014. 104(4):e148-51. PMID=25495353 (Appendix C)

6. Perfusion Index in the Preterm Infant Immediately after Birth.
   Hawkes GA, O'Toole JM, Kenosi M, Ryan CA, Dempsey EM
   Early Human Development, 2015. PMID=26025337 (Appendix G)

7. A randomized controlled trial of a mobile phone infant resuscitation guide.
   Hawkes GA, Murphy G, Dempsey EM, Ryan CA
   Journal of Paediatrics and Child Health. Accepted May 2015 (In Press).

8. Auscultate, palpate and tap: Time to re-evaluate.
   Hawkes GA, Hawkes CP, Kenosi M, Livingstone V, Ryan CA, Dempsey EM.
   Acta Paediatrica. Accepted June 2015 (In press)

9. Delivery room end tidal CO_2 monitoring in preterm infants less than 32 weeks.
Hawkes GA, Kenosi M, O'Toole JM, O'Halloran K, Boylan GB, Ryan CA, Dempsey EM
Archives of disease in childhood, Fetal and Neonatal edition. Accepted June 2015 (In press)

PRESENTATIONS ACHIEVED DURING THIS THESIS

Oral Presentations:

- *Webcams in the neonatal intensive care unit: Here's looking at you kid!*
  Hawkes GA, Ryan CA, Dempsey EM
  - European Society for Paediatric Research Annual Meeting, Porto, Portugal. October 2013

- *Outcomes of a feasibility study on CO_2 monitoring in the delivery suite.*
  Hawkes GA, Finn D, Kenosi M, Ryan CA, Dempsey EM
  - Irish Perinatal Society Annual Meeting, Dublin, Ireland. June 2014

- *Capnography improves neonatal facemask ventilation.*
  Hawkes GA, Kenosi M, Ryan CA, Dempsey EM
  - Irish Perinatal Society Annual Meeting, Dublin, Ireland. June 2014
  - European Academy of Paediatric Societies, Barcelona, Spain. October 2014

- *Resuscitation skills of Sudanese village midwives pre and post helping babies breathe program.*
  Araby A, **Hawkes GA,** Malik Y, Ryan CA, Ahmed S, Dempsey EM, Ibrahim S
  - Irish Perinatal Society Annual Meeting, Dublin, Ireland. June 2014

Poster Presentations:

- *Colorimeters in neonatal mask ventilation: An in vitro manikin based crossover comparison of two devices.*
  Hawkes GA, O'Connell B, Hawkes CP, Ryan CA, Dempsey EM.
  - Irish & American Paediatric Society Annual Meeting, Belfast, Northern Ireland. 2012
  - Pediatric Academic Society & Society for Pediatric Research Annual Meeting, Washington, USA. May 2013

- *The demand for an educational Smartphone App: A review of our experience*

  Hawkes GA, Hawkes CP, Ryan CA, Dempsey EM.

  - European Society for Paediatric Research Annual Meeting, Porto, Portugal. October 2013

- *Safe and unsafe practices in newborn resuscitation amongst village midwives in Sudan prior to the Helping Babies Breathe Programme.*

  Araby A, **Hawkes GA**, Malik Y, Ryan CA, Ahmed S, Dempsey EM, Ibrahim S

  - Pediatric Academic Society & Society for Pediatric Research Annual Meeting, Vancouver, Canada. May 2014

- *First Person Perspective Enhances Procedural Metrics.*

  Cunningham K, **Hawkes GA**, O'Connell L, Murphy B, Filan P, Ryan CA, Dempsey EM

  - Pediatric Academic Society & Society for Pediatric Research Annual Meeting, Vancouver, Canada. May 2014

- *Safe and unsafe practices in newborn resuscitation amongst village midwives in Sudan prior to the Helping Babies Breathe programme*

  Araby A, **Hawkes GA,** Malik Y, Ryan CA, Ahmed S, Dempsey EM, Ibrahim S

  - Irish Perinatal Society Annual Meeting, Dublin, Ireland. June 2014

- *Which infant mannequin do you prefer?: User preference and bag mask ability of different mannequin models.*

  Hawkes GA, Dempsey EM, Ryan CA

  - Irish Perinatal Society Annual Meeting, Dublin, Ireland. June 2014

  - European Academy of Paediatric Societies Annual Meeting, Barcelona, Spain. October 2014

- *Outcomes of a feasibility study on CO_2 monitoring in the delivery suite.*
  Hawkes GA, Finn D, Kenosi M, Ryan CA, Dempsey EM
  - European Academy of Paediatric Societies Annual Meeting, Barcelona, Spain. October 2014

- *Quantitative end tidal CO_2 monitoring of preterm infants in the delivery room.*
  Hawkes GA, Kenosi M, Finn D, O'Toole JM, O'Halloran KD, Boylan GB, Ryan CA, Dempsey EM
  - Pediatric American Societies Annual Meeting, San Diego, April 2015

- *Heart rate assessment in the delivery room: Not so APT.*
  Hawkes GA, Hawkes CP, Kenosi M, Demeulemeester J, Livingstone V, Ryan CA, Dempsey EM
  - Pediatric American Societies Annual Meeting, San Diego, April 2015

- *Perfusion index of the preterm infant in the delivery room.*
  Hawkes GA, Kenosi M, O'Toole JM, Ryan CA, Dempsey EM
  - Pediatric American Societies Annual Meeting, San Diego, April 2015

ABSTRACT

Introduction

Up to 10% of infants require stabilisation during transition to extrauterine life. Enhanced monitoring of cardiorespiratory parameters during this time may improve stabilisation outcomes. In addition, technology may facilitate improved preparation for delivery room stabilisation as well as NICU procedures, through educational techniques.

Aim

To improve infant care 1) **before** birth via improved training, 2) **during** stabilisation via enhanced physiological monitoring and improved practice, and 3) **after** delivery, in the neonatal intensive care unit (NICU), via improved procedural care.

Methods

A multifaceted approach was utilised including; a combination of questionnaire based surveys, mannequin-based investigations, prospective observational investigations, and a randomised controlled trial involving preterm infants less than 32 weeks in the delivery room. Forms of technology utilised included; different types of mannequins including a CO_2 producing mannequin, qualitative end tidal CO_2 ($EtCO_2$) detectors, a bespoke quantitative $EtCO_2$ detector, and annotated videos of infant stabilisation as well as NICU procedures

Results

Manual ventilation improved with the use of $EtCO_2$ detection, and was positively assessed by trainees. Quantitative $EtCO_2$ detection in the delivery room is feasible, $EtCO_2$ increased over the first 4 minutes of life in preterm infants, and $EtCO_2$ was higher in preterm infants who were intubated. Current methods of heart rate assessment were found to be unreliable. Electrocardiography (ECG) application warrants further evaluation. Perfusion index (PI) monitoring utilised in the delivery room was feasible. Video recording technology was utilised in

several ways. This technology has many potential benefits, including debriefing and coaching in procedural healthcare, and warrants further evaluation. Parents would welcome the introduction of webcams in the NICU.

Conclusions

I have evaluated new methods of improving infant care before, during, and after stabilisation in the DR. Specifically, I have developed novel educational tools to facilitate training, and evaluated $EtCO_2$, PI, and ECG during infant stabilisation. I have identified barriers in using webcams in the NICU, to now be addressed prior to webcam implementation.

OVERVIEW OF THIS THESIS

Aim of thesis

To; improve the training and education of trainees **before**; enhance physiological monitoring of infants and improve practice amongst medical staff **during**; and optimise the care that infants receive in the neonatal intensive care unit (NICU) **after** the stabilisation process.

Statistical analysis

Appropriate statistical and analytical methods for each chapter will be outlined in each relevant chapter. Advice regarding statistical analysis, when required, was kindly provided by Dr. Vicki Livingstone (Clinical Trial Biostatistician, Neonatal Brain Research Group, University College Cork). Dr. John OToole (Biomedical Engineer, Irish Centre for Fetal and Neonatal Translational Research, University College Cork) performed data analysis using MATLAB for various aspects within this thesis.

Structure

Chapter 1

This chapter will provide the reader with an overview of various aspects of current processes performed by the medical team during the stabilisation of an infant immediately after birth. As it is one of the most important aspects of the infant stabilisation process, the importance in achieving effective ventilation will be highlighted in this chapter, as well as throughout the entire thesis. While Chapter 1 will discuss this stabilisation process in a broad context, each subsequent chapter of this thesis will focus on particular aspects of the stabilisation process, in detail.

Chapter 2

Chapter 2 will have specific focus on the current methods of carbon dioxide (CO_2) monitoring that are utilised during the care of an infant in the delivery

room, as well as in the NICU. This chapter will examine the current literature on this topic and describe the current role of CO_2 detection during infant care.

Chapter 3

Chapter 3 will explain the formulation and completion of two *in vitro* investigations that assessed the use of three different methods of $EtCO_2$ detection during ventilation of a CO_2-producing mannequin. These investigations were extremely important prior to completion of any *in vivo* investigations as they highlighted several issues that may arise during the use of these methods.

Chapter 4

Chapter 4 will introduce the reader to the first of the *in vivo* investigations relating to the introduction of $EtCO_2$ monitoring in the delivery room as well as several issues that accompanied this. As this is a form of non-invasive technology for use on a high-risk population such as preterm infants, difficulties were experienced relating to enrolment of participants and logistics of monitoring equipment. This chapter will also highlight an important aspect of this entire thesis, the generosity and altruistic nature of the families who allowed my research to be completed on their preterm infants.

The *in vivo* data explored in Chapter 4 was extremely encouraging. Whilst initially commenced as a feasibility investigation, a more substantial investigation was soon developed to allow for the thesis to comprehensively assess the use of $EtCO_2$ detection during stabilisation of preterm infants as well as the $EtCO_2$ produced at this time.

Chapter 5

Progressing to Chapter 5, the reader will be introduced to an *in vivo* randomised controlled trial (RCT) involving two different $EtCO_2$ detecting methods. The results from the investigations described in Chapters 3 and 4 were required for the structure and focus of this RCT to be developed.

Chapter 6

Chapter 6 will provide the reader with a comprehensive understanding of the role of cardiovascular monitoring during stabilisation of preterm infants immediately after birth. There are many aspects investigated in this chapter including; the current methods of heart rate assessment, alternative methods of heart rate assessment in the form of electrocardiography (ECG), and perfusion index (PI) monitoring.

Chapter 7

In Chapter 7, I will describe several investigations assessing the role of video technology in improving infant care in the delivery room as well as the NICU.

Firstly an instructional video created for infant stabilisation will be described. This was seen as an opportunity for improving delivery room practice. Similarly, this chapter will then present the reader with an assessment of an instructional video and procedural metric used for peripherally inserted central catheter placement in the NICU. In particular, this assessment focused on the role of this video as an educational tool.

The final section in this chapter will explore opinions towards a webcam system within the NICU. The section will first describe a survey created to gather opinions towards the implementation of this webcam system. Parents, as well as medical staff completed this survey. The chapter will then conclude by describing the creation of a proposal for a webcam system within the NICU at CUMH.

Chapter 8

In this chapter, I will examine areas surrounding infant stabilisation training, albeit, in the context of three different approaches. The first section will assess the fidelity of different infant mannequins. These mannequins are typically used in the training of infant stabilisation and the assessment of these training tools was seen as a potential route to optimise the fidelity. Optimising training in this way may ultimately improve infant stabilisation in the delivery room.

The chapter will also focus on an educational smartphone app that was created 4 years ago to teach infant intubation. As well as providing a description of the app, the chapter will examine the uptake that this app has experienced during the last 4 years. Importantly, this chapter will also focus on issues relating to regulation during the creation of this category of smartphone applications.

To conclude, this chapter will describe the completion of a RCT on a mobile phone based infant resuscitation guide amongst CPR trained responders during the provision of CPR to an infant mannequin. Although not focused within the hospital setting, this investigation was seen as a potential route to optimising infant resuscitation in the out-of-hospital setting.

Chapter 9

In the final chapter I will summarise the journey of this PhD thesis, and how it has contributed to infant care locally and internationally. Encompassing a recollection of what was known on this research topic prior to this thesis, this chapter will highlight the impact that this thesis has made on various areas of the stabilisation process in the delivery room as well as the different areas of care within the NICU of CUMH. This chapter will also describe the role that this thesis may have on the future of the care that is provided to infants immediately after birth and in the NICU, as well as on future research opportunities. The final part of this chapter will attempt to provide the reader with an account of what this journey has meant to me.

CHAPTER 1: INTRODUCTION TO INFANT STABILISATION IN THE DELIVERY ROOM

1.1. INFANT STABILISATION

Was the baby born at term? Is the baby breathing or crying? Does the baby have good tone? The first important questions asked by medical staff at birth that may ultimately give an indication if an infant will require assistance in completing the transition from life inside the womb to life outside the womb. This evaluation, and subsequent preparation, of increased support for the infant are critical in helping to provide successful stabilisation.[1] The Neonatal Resuscitation Program (NRP) is the standard program provided to all healthcare workers working in a neonatal setting in Ireland. This evidence-based stabilisation program was developed by the American Academy of Pediatrics (AAP) and the American Heart Association (AHA) in 1987 and is currently on it's 6th edition.[2]

Ten percent of all infants may need some form of stabilisation at birth whilst one percent may require extensive interventional measures.[2] During the transition from intra- to extra-uterine life, an infant is required to complete a number of physiological adjustments during adaptation to a new environment. The NRP utilises a time-based flow diagram in order to highlight when interventions may be indicated throughout the stabilisation process (Figure 1.1).

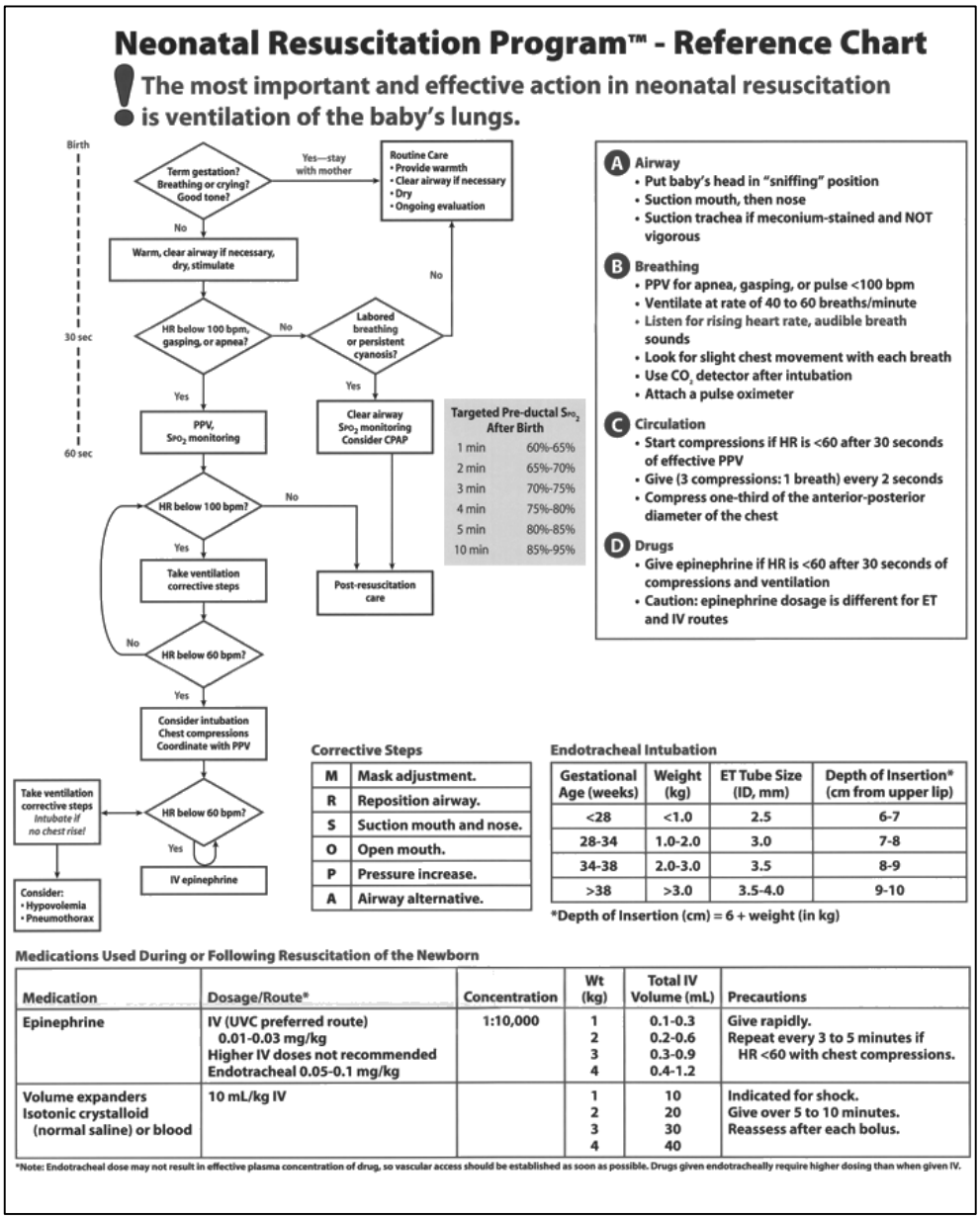


FIGURE 1.1 - NEONATAL RESUSCITATION PROGRAM REFERENCE CHART (WWW.AAP.ORG)

1.1.1. TEMPERATURE CONTROL

In the womb, maternal thermoregulation controls fetal temperature via the placental surface as well as the umbilical circulation.[3] At birth an infant has to transition from this stable environment, which is of a temperature similar to the core body temperature of a mother, to the colder temperature of the delivery room. The large body surface area in relation to body mass of an infant results in inevitable heat loss at this time.[4] An infant is unable to control heat loss via muscular activity in the form of a shivering response and instead relies upon a metabolic response in the form of non-shivering thermogenesis. This cold stress stimulates an increase in norepinephrine levels in the brown fat tissue, and a re-

esterification as well as oxidation of the free fatty acids resulting in the production of heat.[3,5,6] This metabolic response is a relatively slow process and an infant may often take several hours after birth to maintain a constant core body temperature.[4]

As a result of this, minimising heat loss is an important factor during the care of an infant, especially in the delivery room.[2,7] In most scenarios during an uncomplicated birth, this can be achieved by drying an infant, covering him/her with a towel, and subsequently placing him/her in skin-to-skin contact with his/her mother. However, in a scenario where an infant requires assistance during the transition, thermoregulation can be aided primarily by four methods including; a radiant warmer above the stabilisation unit; drying of the infant by the team; placement of a hat on the infant's head; and wrapping the infant in a blanket. The radiant warmer on the stabilisation unit should have been warmed prior to the delivery, warming the immediate surroundings that the infant will be introduced into as well as limiting heat loss due to radiation and conduction. Drying an infant is an important process that is carried out at the very start of the stabilisation process in order to limit evaporative heat loss. Placing a hat on an infant and wrapping the infant in a blanket reduces the skin surface exposed to the air, therefore limiting heat loss due to conduction. A preterm infant is at increased risk of hypothermia and this issue will be focused on later in this chapter.

1.1.2. THE ABCDS

Airway

An open, unobstructed, airway in an infant can often be difficult to maintain during stabilisation. One method of ensuring a patent airway is through correct positioning. The NRP advises placing an infant in a midline position on the stabilisation unit with the head in a slightly extended position, avoiding the head being over flexed or hyper extended. Due to the relatively large occiput on a newborn infant, it may be more likely to flex when an infant is supine on a flat surface. An infant's tongue is also large, relative to the rest of the mouth, and the epiglottis is long and thin. These factors may occlude the airway at any time and,

as a result, continuous assessment of airway patency is a vital component of the stabilisation process.

Breathing

One of the most important adjustments that an infant is required to make immediately after birth is the process of breathing. In utero, gas exchange between CO_2 and Oxygen (O_2) occurs across the placental membrane. At this time, the fetal lungs, in particular the alveoli, are collapsed and occupied by fetal lung fluid. At birth this fluid is normally absorbed through the alveoli into pulmonary lymphatics through negative inspiratory pressure being created in the intrapleural space as a result of an infant crying. This series of events typically allows for an increase in the functional residual capacity (FRC) of the lungs.[8] The alveoli then become responsible for gas exchange between O_2 and CO_2 as they fill with air.[2,4,9-13]

In parallel with these events, the peripheral capillary oxygen saturation level (SpO_2) should begin to increase when an infant is first exposed to the extrauterine environment. The NRP advises the stabilisation team to monitor this level at different time intervals within the first ten minutes, aiming to ultimately have a SpO_2 level greater than 90% after 10 minutes in an uncompromised infant (Figure 1.1). Studies have highlighted the dangers associated with providing 100% oxygen during infant stabilisation.[14,15] These risks have led infant stabilisation to be initiated with 21% oxygen (room air) allows for gradual increase in this level if an infant should require help to reach different SpO_2 levels within the first ten minutes of life (Figure 1.1). It is possible to deliver oxygen concentrations between 21% and 100% through the use of an air/oxygen blender. This device has a supply of 100% compressed oxygen and a separate supply of compressed air continually fed into it. The mixture then passes through a flow meter and is delivered to the ventilation device (Figure 1.2).

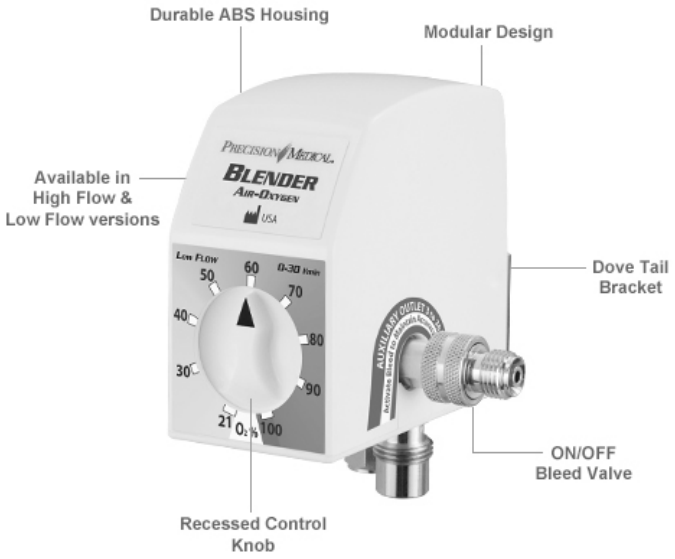


FIGURE 1.2 - PRECISION MEDICAL® PM5200 LOW FLOW AIR-OXYGEN BLENDER (PRECISION MEDICAL, PA,USA)(WWW.PRECISIONMEDICAL.COM)

Typically, an infant can achieve an increase in FRC of the lungs, and overall oxygenation, without any interventions. However, this process may often be compromised by certain factors such as anaesthetic received by the mother partially anaesthetizing the fetus prior to delivery, anatomical immaturity (typically associated with a preterm infant), fluid remaining in the airway and/or the lungs of the infant, prolonged delivery of the infant during a spontaneous vaginal delivery (SVD), and several other delivery related complications. If any of these complications should occur, then the medical team may be required to assist an infant to make an effective transition. This assistance may be in the form of positive pressure ventilation (PPV). There are 3 different devices that can be used to deliver PPV including; a T-Piece resuscitator (TPR) (Figure 1.3), a self inflating bag (SIB) (Figure 1.4), and a flow-inflating bag (FIB) (Figure 1.5). These devices can be used to deliver PPV via a facemask or via an endotracheal tube (ETT).[2,7,16]

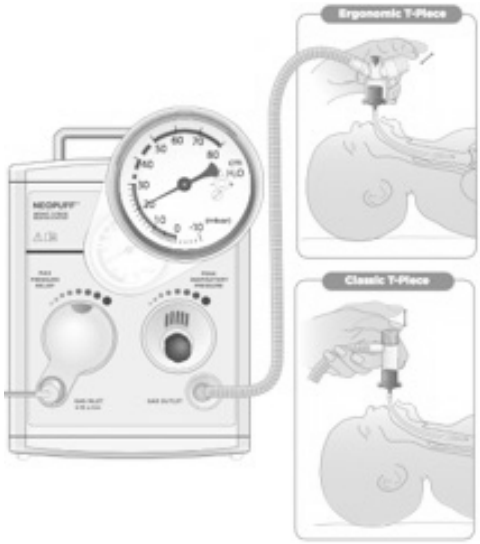


FIGURE 1.3 - NEOPUFF™ INFANT T-PIECE RESUSCITATOR (FISCHER AND PAYKEL HEALTHCARE, AUCKLAND, NEW ZEALAND)(WWW.FPHCARE.CO.NZ)

FIGURE 1.4 - AMBU® SPUR® II DISPOSABLE INFANT RESUSCITATOR (AMBU A/S, COPENHAGEN, DENMARK)(WWW.AMBU.COM)

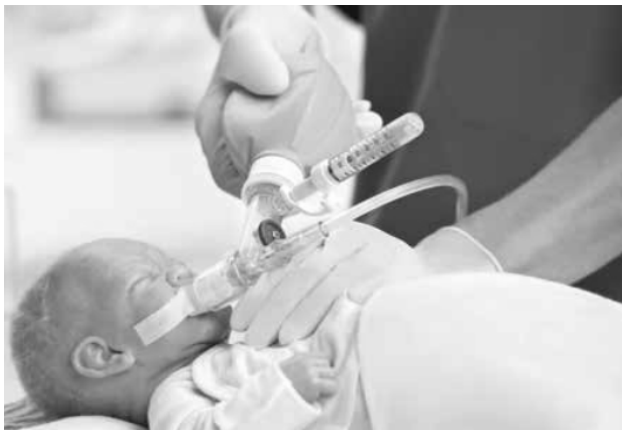


FIGURE 1.5 - AIRLIFE® FLOW INFLATING RESUSCITATION DEVICE (CAREFUSION, CA, USA)(WWW.CAREFUSION.COM)

PPV consists of peak inspiratory pressure (PIP), positive end expiratory pressure (PEEP), and continuous positive airway pressure (CPAP). PIP is the peak pressure applied during assisted inspiration, i.e. the pressure at the end of a

squeeze of a FIB or SIB, or at the end of ventilation delivered via the TPR. The provision of PIP simulates the inspiratory effort that an infant would make during an uncomplicated transition. PIP is suggested to be set at a starting pressure of 20 centimetres of water (cm H_2O), and to be slowly increased if required to do so during the stabilisation.[2]

PEEP is the pressure of gas remaining in the system between each completed ventilation; it is the pressure that is present before the next squeeze of a FIB or next ventilation provided by the TPR. PEEP provides end-expiratory pressure to prevent collapse of alveoli, and reduce the inspiratory pressures required for alveolar expansion in subsequent breaths. An un-well infant generates PEEP when they exhibit the clinical sign of grunting. PEEP is suggested to be a set at a level of 5 cm H_2O.[2]

CPAP is similar to PEEP, however, CPAP is used to describe PEEP when an infant is breathing spontaneously without PPV. It is used to provide background continuous pressure and prevent alveolar collapse in infants breathing spontaneously.[2]

PPV is recommended if an infant's heart rate (HR) is below 100 bpm, an infant is gasping, an infant is apnoeic, and the SpO_2 level remains below target values despite the use of supplemental oxygen (Figure 1.1).[2]

The NRP suggests that a SIB be made available in all stabilisations, either as a primary ventilating device for the stabilisation, or as a backup in case a primary device that is using a gas supply fails.[2] The SIB inflates automatically without requiring an oxygen source. As an operator squeezes the bag, PIP is produced in a uniform ratio with the strength at which he/she squeezes the bag. Due to this unregulated delivery of PIP with the SIB alone, the use of a pressure gauge attachment in order to prevent the provision of excess pressure is suggested. PEEP can only be delivered through the SIB if an additional valve is attached. CPAP cannot be delivered reliably with a SIB.[2]

A correctly functioning FIB has a continuous O_2 flow that inflates the main body of the device. As an operator squeezes this main body, PIP is produced and a

single ventilation is delivered to an infant. This device also has a flow control valve that allows the device to deliver PEEP and CPAP.[2]

A TPR is connected to a controllable supply of oxygen and pressure. PIP and PEEP pressures are pre set on the device prior to delivery of an infant; however, the operator may adjust them manually throughout the stabilisation if required to do so. Ventilations are delivered upon occlusion and opening of the device aperture with the operator's finger.[2]

Several studies have investigated the variation of pressures during the use of different devices.[17-23] Although further investigations are required to comprehensively determine the impact that each device has on the stabilisation process, previous studies have highlighted the consistent amount of pressure that can be achieved through the use of a TPR.[21,24-27] Use of PPV devices vary from unit to unit.[28] A 2008 study on 16 Irish Neonatal Units identified SIB use at 44%, TPR use at 31%, and FIB use at 25%.[29] In Cork University Maternity Hospital (CUMH), a NeoPuff (Fischer and Paykel Healthcare, Auckland, New Zealand) TPR is the primary device used during stabilisation in the delivery room.

Optimal use of the face mask should provide minimal mask leak whilst covering the tip of an infant's chin, mouth, and nose.[2] "Round" and "anatomical" are two shapes of facemask currently suggested by the NRP for use during infant stabilisation.[2]

Circulation

As the alveoli and the majority of vessels in the lungs are collapsed, high resistance to blood flow through the lungs results in a high level of pulmonary arterial pressure in a fetus. As the resistance to blood flow from the aorta through to the vessels of the placenta is low, the pressure in the aorta is also low allowing for most of the pulmonary arterial blood to travel through the ductus arteriosus, which connects the pulmonary artery to the aorta.[2,4]

At birth, resistance to blood flow through the pulmonary vascular vessels is alleviated significantly as an infant breathes and the alveoli fill with air. This results in a fall in pulmonary arterial pressure. As the placenta is separated from

an infant's circulatory system the aortic pressure rises as a result of the cessation of blood flow from the aorta to the placenta. The ductus arteriosus is no longer needed to pass blood from the artery to the pulmonary artery and therefore typically closes a few days after birth. Coinciding with the separation of the placenta from an infant through the process of cord clamping, systemic blood pressure also increases.[2,4,12]

In an infant without congenital cardiac anomalies, cardiac compromise is typically secondary to respiratory compromise i.e. after attempts at aiding the respiratory system are unsuccessful, cardiac interventions may be required. Chest compressions may be required to move the oxygenated blood and drugs to the coronary arteries in an attempt to stimulate cardiac recovery. Current NRP guidelines suggest providing chest compressions when the heart rate is lower than 60 bpm, after at least 30 seconds of effective PPV has been achieved.[2]

Two methods of chest compressions are currently recommended by the NRP. The "thumb technique" encompasses two thumbs being placed on an infant's sternum whilst the rest of the two hands support the spine; the two thumbs then compress the infant's sternum. This technique can be performed from the bottom of an infant's torso or the top. The "two finger technique" encompasses the middle finger and either the ring finger or the index finger of the same hand compressing the sternum, whilst the other hand supports the infant's back. This technique can be performed from the left or the right of an infant.[2]

Both techniques can be used to deliver compressions at the suggested depth of approximately one third of the anterior to posterior diameter of an infant's chest, at a ratio of three compressions for every single ventilation. A total of 90 compressions and 30 ventilations are required to be completed each minute.[2,30]

Drug

Approximately 1% of all stabilisations require more extensive forms of intervention, such as the use of medication. The three suggested routes for administration of medications in an infant are: intravenous access via the umbilical vein, via the ETT, and intraosseous access.

Epinephrine hydrochloride is suggested for use in severely compromised infants with a HR of less than 60 bpm after attempts of cardiac massage and PPV have been unsuccessful in improving the HR. The primary role of epinephrine is peripheral vasoconstriction allowing for an increase in blood flow to the coronary arteries, encouraging myocardial function, as well as an increase in cerebral blood flow. The suggested dose and concentration of epinephrine, administered intravenously, during infant stabilisation, is 0.1-0.3 mL/kg of 1:10,000 solution.[2]

In instances where a placenta previa has occurred and there has been fetal blood loss, then the blood volume of the infant may need to be increased through infusion of 0.9% sodium chloride (NaCL), at a suggested dose of 10 mL/kg.[2]

1.1.3. MR SOPA

If an infant has difficulty during this period of transition and the airway remains obstructed, then there are several corrective steps that the medical team can take to improve ventilation. In the teaching of these corrective steps, the NRP uses the acronym "MR SOPA", as a guide on the escalation of interventions (Figure 1.1).

*"**M**" - Mask Adjustment*

Many studies have highlighted the occurrence of mask leak during facemask ventilation[31-34] and demonstrated that it is a factor that may be resolved through proper technique.[33,34] Mask adjustment may relieve the problem of ineffective ventilation as it will attempt to reform the seal between the skin and the facemask. Instances of an operator incorrectly placing the facemask on an infant may also be alleviated as a result of the re placing of the mask.[2]

*"**R**" – Reposition Airway*

As previously described, airway obstruction may occur in an infant as a result of incorrect positioning when he/she is lying supine. By readjusting the head to the correct, slightly extended, position, then an obstructed airway may be alleviated.[2,33]

*"**S**" – Suctioning of Mouth and Nose*

Suctioning of an airway may be required to remove any fluid that is remaining in the airway as a result of an infant unsuccessfully clearing the airway via normal physiological mechanisms after birth. This suctioning can be completed with a bulb syringe or a suction catheter attached to a mechanical suction unit. An infant is primarily a nasal breather and in order to prevent the aspiration of fluid within the mouth during suctioning of the nose, the mouth should always be suctioned before the nose. Secondary to clearing the secretions from the airway, the process of suctioning may also stimulate an infant to begin spontaneous respirations.[2]

*"**O**" – Open Mouth*

Opening the mouth of an infant further, whilst also lifting the jaw forward may also alleviate airway obstruction. Due to the relatively small size of the nares of an infant, opening the airway further may allow for more effective PPV.[2]

*"**P**"- Pressure Increase*

As previously described, prior to delivery of an infant, the pressures that the PIP and PEEP are set to are 20 cm H_2O and 5 cm H_2O, respectively. If the ventilation is not improving during stabilisation then this step suggests for the gradual increase of PIP on a breath-to-breath basis to a level between 30 cm H_2O and 40 cm H_2O.[2,35-37]

*"**A**" – Airway Alternative*

If all previous steps have been completed correctly and there continues to be little or no improvement in the effectiveness of ventilation, then an airway alternative such as endotracheal (ET) intubation is suggested. ET intubation is used to insert an endotracheal tube (ETT) (Figure 1.6), via a laryngoscope. Allowing the tip of the ETT to rest just above the carina, intubation may allow for the lungs to be effectively ventilated, suctioned, and for the ET administration of medication. Several sizes of ETTs are available for use during infant stabilisation (Figure 1.1). The choosing of different sizes relies upon the

estimation of an infant's weight and through the correct estimation of the weight; the ETT should be correctly sized for the infant's trachea.

FIGURE 1.6 - PORTEX® ENDOTRACHEAL TUBE (SMITHS MEDICAL MD INC, SAINT PAUL, MN, U.S.A)(WWW.SMITHS-MEDICAL.COM)

In situations where ETT placement is proving to be difficult due to factors such as congenital anomalies of the upper airway, more effective ventilation may be achieved through the use of a laryngeal mask airway (LMA)(Figure 1.7).[2,38] An LMA is inserted to fit over the laryngeal inlet and allows for an infant to be ventilated.[2,39,40] Little evidence exists on the use of LMAs in preterm infants.[39,40] One size of LMA currently exists for use in infants with a weight of up to 5 kg.[2]

FIGURE 1.7 - LMA CLASSIC™ LARYNGEAL MASK AIRWAY (TELEFLEX INC, RESEARCH TRIANGLE PARK, NC, U.S.A)

1.1.4. STABILISATION OF A PRETERM INFANT

Heat loss

A preterm (gestational age of <32 weeks) infant may have several anatomically and physiologically immature features in comparison to a term infant. Being of a smaller size and weight compared to a term infant, a large surface area to body mass ratio exists. The skin of a preterm infant is also very thin. As a result of these factors, a preterm infant is far more likely to experience issues relating to heat loss.[41-43] Therefore, minimising this heat loss at this time is extremely

important and the use of a polyethylene bag is suggested in order to limit evaporative heat loss and attempt to keep an infant at the suggested axillary temperature of 36.5°C.[2]

Assessment of airway obstruction

Airway obstruction is a common occurrence in a preterm infant.[44] The small anatomical size of a preterm infant can make it especially difficult to obtain a patent airway during stabilisation. The small anatomical size of a preterm infant's face is a factor that impacts the effectiveness of over all facemask ventilation. Several studies have investigated the issue of mask leak during infant stabilisation, in particular, the large amount of facemask leak that may be witnessed during ventilation of preterm infants.[45,46]

One suggested method of determining a patent airway in an infant is through monitoring chest rise and fall,[2] however, the small size of a preterm infant can often make this difficult. This difficulty in assessing chest rise and fall may also be increased as a result of the use of a polyethylene bag that will have been placed around a preterm infant after delivery (resulting in occlusion of the view of the chest), the inexperience of resuscitation team members in stabilising a preterm infant, the assessor's positioning in relation to the infant (limiting the view of the assessor), and the difficulty that may be encountered in distinguishing between abdominal rise and stomach inflation.[47-49]

Achieving adequate ventilation

In the first few minutes of an uncomplicated transition, the FRC of the lungs should gradually increase as an infant cries.[8,13] However, due to the immaturity typically associated with a preterm infant's lungs, this transition may need to be assisted through interventions from the stabilisation team such as with the provision of CPAP, PEEP, and/or PPV. Immaturity of the lungs may also result in a deficiency of the surfactant typically present in the lungs, requiring surfactant to be administered by the stabilisation team.[2]

A preterm infant's underdeveloped chest muscles,[50,51] as well as immature nervous system,[2] may not allow for effective breathing. As a result, PPV may be

required. As mentioned, the small size of the preterm infant may cause difficulty in correctly assessing the rise and fall of the chest, however, in terms of providing PPV this creates an increased difficulty in relation to increasing the risk of over inflating the lungs.[47,48,52] Increased PIP has been shown to increase the occurrence of lung injury in preterm infants subsequently leading to issues such as: infection, surfactant dysfunction, and malnutrition.[53-55]

Circulation and Drug Infusion

The small volume of blood that exists in a preterm infant's circulatory system make issues such as hypovolaemia, as a result of any blood loss during delivery, more likely.[2] As previously discussed in this chapter, the use of sodium chloride may be used as a blood volume expander during infant stabilisation. However, due to the immaturity of capillaries within the germinal matrix of a preterm infant's brain, care is needed during infusion of volume expanding drugs as rapid infusion may increase the risk of intraventricular hemorrhage (IVH).[2]

1.2. Current Methods of Physiological Monitoring in the Delivery Room

1.2.1. Heart Rate

The primary method of HR assessment suggested by the NRP is through palpating the base of the umbilicus to measure the umbilical pulse. In some instances, the umbilical vessels may remain constricted and make it difficult to palpate the pulse. During these instances, it is suggested that the HR is auscultated via a stethoscope placed on the left hand side of an infant's chest. When the stabilisation team member completes either of these methods then they may communicate this to the rest of the team by making a tapping sound on a solid surface with their finger. This is completed in order to portray the real time HR to the rest of the team. If neither of these methods is successful then the NRP advises for the use of a pulse oximeter or electronic cardiac monitor to be used to obtain the HR.[2]

1.2.2. Oxygen Saturation

Although observing an infant's skin colour and determining whether it changes from blue to pink may be a rapid indication of oxygenation in the infant, the subjective nature of the assessment may cause inaccuracies.[2,56,57] Measuring the level of oxygen in the blood via a SpO_2 probe may be a more continuous and accurate method of assessment of the overall degree of oxygenation in an infant. SpO_2 levels have been indicated for use during infant stabilisation and pulse oximeters have been shown to provide reliable readings within 1-2 minutes of application.[58,59]

1.2.3. Monitoring Effective Ventilation

As mentioned previously, effective ventilation is an important factor throughout the entire stabilisation. The NRP currently suggests monitoring of the effectiveness of ventilation to include monitoring SpO_2 levels, and HR. When an infant is intubated and an ETT is inserted, an end tidal carbon dioxide ($EtCO_2$)

detector may be employed as an assessment tool of effective ventilation. The use of $EtCO_2$ detection will be examined in more detail in the next chapter.

1.3. CONCLUSION OF CHAPTER

This chapter commenced by outlining various aspects relating to the changes in physiology that occur as an infant adapts to the extra uterine environment. It then developed to outline the interventions that may be required to assist during this transition. The chapter closed by providing the reader with an outline of the current methods used to monitor an infant immediately after birth in the delivery room. The concepts summarised in this chapter are central to the investigations completed in this thesis.

CHAPTER 2: CARBON DIOXIDE DETECTION AND A REVIEW OF LITERATURE

Part published as:

A review of carbon dioxide monitoring in preterm newborns in the delivery room.

Hawkes GA, Kelleher J, Ryan CA, Dempsey EM.

Resuscitation. 2014. 85(10):1315-1319. PMID= 25086296

(Appendix A)

2.1. INTRODUCTION

As discussed in Chapter 1, the physiologic adaptation to extra uterine life immediately after birth requires the infant to increase pulmonary blood flow as well as expand fluid filled alveoli in order to facilitate gas exchange. Many infants require assistance in this adaptive process, with provision of PPV and oxygen therapy, also discussed in Chapter 1.[60,61] Alterations in CO_2 levels in a preterm infant are associated with adverse outcomes including chronic lung disease, brain injury, and long-term neurodevelopmental problems.[62,63] This chapter will aim to provide the reader with a comprehensive introduction to the specific methods of CO_2 detection before then progressing to review the available literature on the use of these methods.

In addition to arterial or venous blood gas sampling, two non-invasive methods of monitoring CO_2 levels are available including transcutaneous ($TcPCO_2$) monitoring and $EtCO_2$ detection. Transcutaneous assessment is a non-invasive method based upon locally heated electrochemical sensors applied to the skin surface that subsequently provide a continuous estimation of the partial pressure of arterial CO_2 ($PaCO_2$). $EtCO_2$ detection includes the use of qualitative methods including mainstream and sidestream capnography, as well as semi quantitative methods including colour detectors that change colour upon contact with CO_2. $TcPCO_2$ monitoring and $EtCO_2$ monitoring are often employed for the monitoring of ventilated infants in the NICU.

2.1.1. MAIN STREAM CAPNOGRAPHY

A mainstream capnography device utilises an infrared absorption technique to detect the presence of CO_2 in a sample of gas. Mainstream capnography performs all CO_2 analysis in line with the respiratory gas stream. Certain wavelengths emitted at the infrared source absorb CO_2 molecules within this respiratory gas stream and are subsequently detected on the infrared detector. The standard layout of a mainstream capnography device is provided in Figure 2.1.

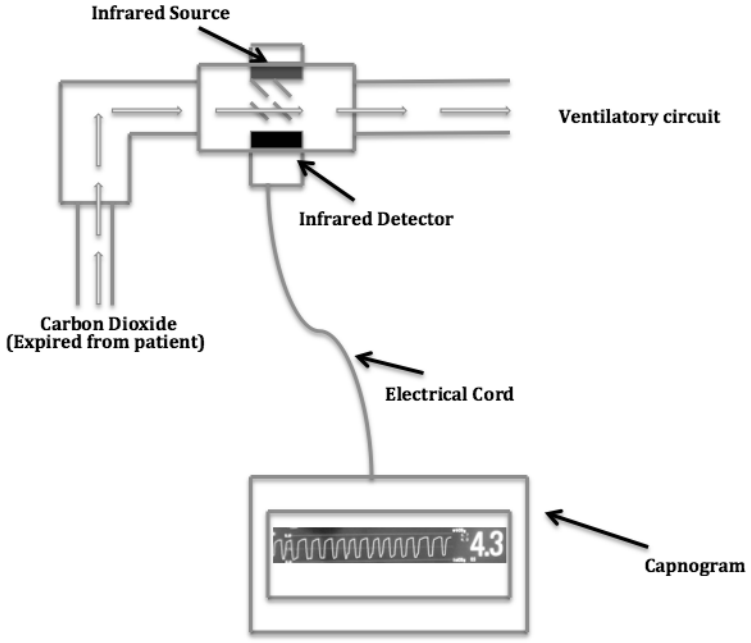


FIGURE 2.1 – MAINSTREAM CAPNOGRAPHY CIRCUIT

2.1.2. SIDE STREAM CAPNOGRAPHY

Although both mainstream and sidestream capnography employ infrared light detection in eventual CO_2 analysis; each method performs it through different processes and this is mainly in relation to the location that CO_2 analysis is performed. CO_2 is analysed at the gas flow source with mainstream capnography, whereas sidestream capnography uses a pumping function to export a sample of the gas flow to a separate site for analysis. The sample from the gas flow source passes through a sampling tube that is connected between an adapter in the breathing circuit and a sample cell within a monitor. As the gas flow source has to travel through this tube, the tube may become subject to condensation, ultimately distorting the CO_2 analysis performed at the sample cell. To reduce the amount of condensation that may build up within this tube, a water trap is typically fitted along the connection. The standard layout of a sidestream capnography device is provided in Figure 2.1. An external sidestream module attached to a Philips Intellivue MP70 (Philips Healthcare, MA, USA) is the routine method of sidestream capnography employed for use on infants receiving ventilatory support in the NICU of CUMH.

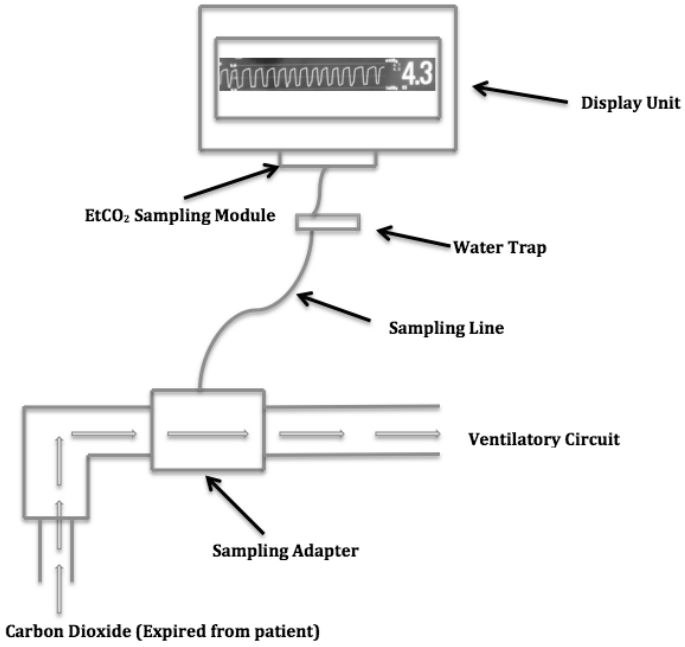


FIGURE 2.2 – SIDESTREAM CAPNOGRAPHY CIRCUIT

2.1.3. COLOURIMETRIC $ETCO_2$ DETECTION

Two different colourimetric $EtCO_2$ detectors that are available for use in CUMH are described below. Through a chemical detector integrated on to a strip of paper, both of these devices produce a colour change upon detection of CO_2. However, the physical configuration of each device differ slightly.

PediCap® $EtCO_2$ detector (Covidien, MA, USA)

This detector is a disposable colourimeter that has 3ml internal volume and weighs less than 5g (Figure 2.3). The colourimeter changes to a yellow colour upon detection of CO_2 (during expiration of an infant) and reverses to purple when the measured $EtCO_2$ level reduces to approximately 0.03% to <0.5% (4mmHg)(during inspiration of an infant). Although the manufacturer guidelines indicate an operating range within patients weighing 1-15kg; studies have shown that this colourimeter device will also work in ranges below the lower operating range i.e. body weight of less than 1000g.[64,65] The PediCap $EtCO_2$ detector is indicated for use at the connector of an ETT and breathing device however;

Leone et al found that the Pedi-Cap can also be used with a facemask, and positive pressure device, to determine airway patency.[49]

FIGURE 2.3 - PEDICAP $ETCO_2$ DETECTOR (WWW.MERCURYMED.COM)

NeoStatCO_2<kg™ (Mercury Medical, FL, USA)

The NeoStat $EtCO_2$ detector has an internal volume of 1ml, a weight of 3 grams, and changes from blue to yellow upon detection of CO_2 (Figure 2.4). The manufacturer guidelines have indicated the use of this device for infants with a weight between 0.25 and 6kg (www.mercurymed.com). Investigations into user preference and performance during use of the PediCap and NeoStat $EtCO_2$ detectors will be discussed in further detail in Chapter 3.

FIGURE 2.4 - NEOSTAT $ETCO_2$ DETECTOR (LEFT - COLOUR WHEN NO CO_2 DETECTED, RIGHT – COLOUR WHEN CO_2 DETECTED) (WWW.MERCURYMED.COM)

As discussed in Chapter 1, current NRP guidelines indicate the use of a disposable CO_2 detector as a method of confirming correct ETT placement during intubation of infants.[2] Correct identification of successful ETT placement is important as undetected misplacement can result in hypoxia as well as an increase in adverse outcomes.[66,67] The use of a disposable CO_2 detector has been shown to significantly reduce the time to confirm ETT placement.[64] However, there may be instances where a disposable CO_2 detector may give a false

negative reading. These may occur for several reasons including cardiopulmonary arrest and severe airway obstruction.[68]

2.2. LITERATURE REVIEW

2.2.1. AIM

To review available published studies relating to the use of CO_2 monitoring in preterm infants in the delivery room and to assess the available evidence on this type of enhanced monitoring based on clinically relevant outcomes.

2.2.2. METHODS

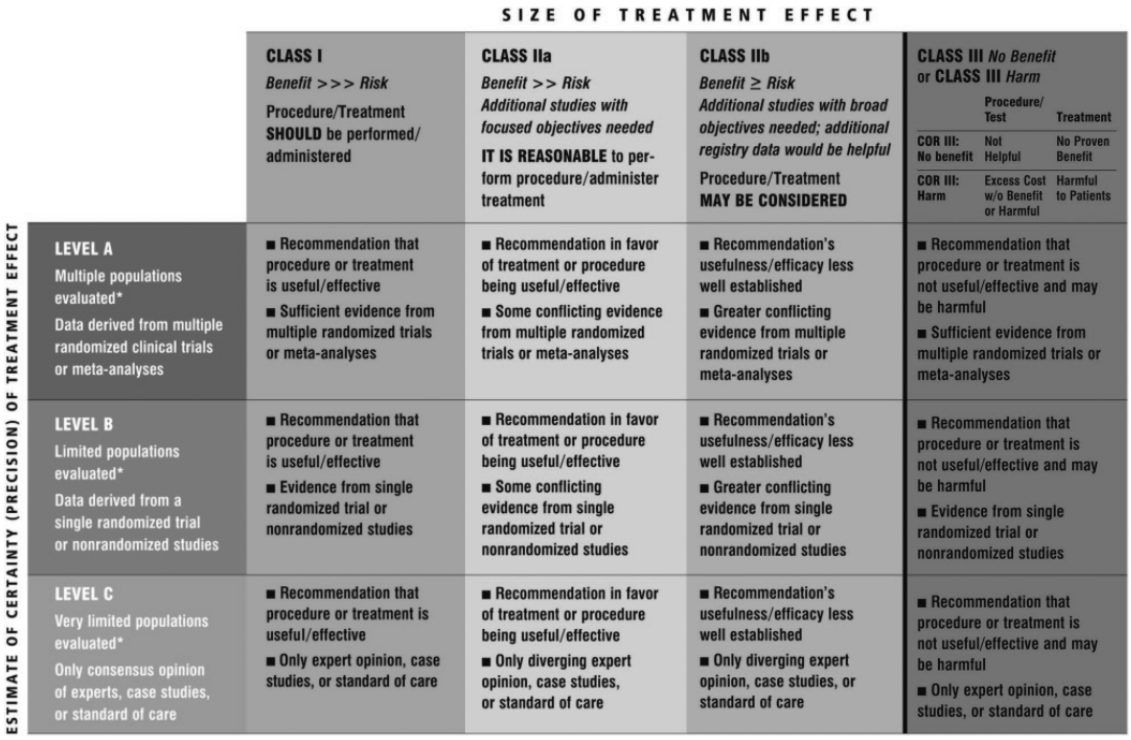
All studies were included if they; 1) addressed the use of, or application of, any form of CO_2 monitoring during ventilation of preterm infants in the delivery room, 2) included assessment of infants receiving respiratory support in the NICU and 3) had relevance to delivery room interventions such as PPV.

2.2.3. SEARCH STRATEGY

The search of literature for this chapter was completed in January 2015 using the Cochrane Central Register of Controlled Trials, MEDLINE (1966 - 2015) and PREMEDLINE, EMBASE (1980 -2015), CINAHL (1982 - 2015), Web of Science (1975- 2015) and the Oxford Database of Perinatal Trials. Ongoing trials were searched in the following databases: www.clinicaltrials.gov and www.controlled-trials.com. Abstract of conferences and proceedings of Pediatric Academic Societies were searched electronically from 2000 to 2015. Additional searches were made from the reference list of identified clinical trials.

Keywords used were; “carbon dioxide detector”, “capnography”, “end tidal carbon dioxide” and “resuscitation”. Articles were limited to being relevant to the infant population in the environment of the delivery room or the NICU.

All eligible studies were assessed via the American Heart Association (AHA) and American College of Cardiology Foundation (ACCF) classifications of recommendations and levels of evidence (Table 2.1) by thesis author (GAH) and thesis supervisor (ED). Each study was assigned a class of evidence in the form of Class I, Class IIa, Class IIb, or Class III as well as a level of evidence in the form of A, B, or C.



SIZE OF TREATMENT EFFECT

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT

	CLASS I *Benefit >>> Risk* Procedure/Treatment **SHOULD** be performed/ administered	CLASS IIa *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE** to perform procedure/administer treatment	CLASS IIb *Benefit ≥ Risk* *Additional studies with broad objectives needed; additional registry data would be helpful* Procedure/Treatment **MAY BE CONSIDERED**	CLASS III *No Benefit* or CLASS III *Harm* Procedure/ Test / Treatment COR III: No benefit / Not Helpful / No Proven Benefit COR III: Harm / Excess Cost w/o Benefit or Harmful / Harmful to Patients
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care

TABLE 2.1 - AHA AND ACCF CLASSIFICATION OF RECOMMENDATIONS AND LEVELS OF EVIDENCE (WWW.MY.AMERICANHEART.ORG)

2.2.4. RESULTS

Consensus of the thesis author (GAH) and supervisor of this thesis (EMD) resolved any disagreement in relation to study selection or data extraction from subsequent studies. The search revealed 148 articles for consideration and subsequently identified 34 articles relating to CO_2 detection in the delivery room.[44,49,64,65,67-97] Of these, there were six review articles.[82-87], one RCT[79], 20 *in vivo* observational studies[44,49,64,68,69,73,74,78,80,81,88-97], 4 questionnaire-based studies[70,72,76,77], two case reports[67,71], and two *in vitro* studies[65,75]. These studies are summarized below and categorized by the monitoring method and clinical utility of each study.

Use of quantitative CO_2 detection during ETT placement

Five studies relating to the use of quantitative capnography in confirming correct ETT placement were identified (Table 2.2).[68,69,71,73,75] Observing 100 intubation episodes in 55 neonates in a NICU, Roberts et al. highlighted the speed and accuracy in the use of capnography to confirm correct ETT placement compared to standard clinical indicators.[68] Repetto et al. described similar results on the use

of capnography to confirm correct ETT placement in 16 infants in the delivery room. This study also highlighted capnography as needing minimal training to use.[69] Through observation of 54 intubations during the stabilisation of 40 very low birth weight infants, Hosono et al. described the accuracy of capnography in confirming ETT placement.[73] In a case series of 4 infants Salthe et al. demonstrated that it was possible to determine correct ETT placement in neonates via midstream capnography. However, this study was limited by the use of an adult midstream capnography device that had a large internal volume and may have resulted in diluted as well as inaccurate values. The authors claim that their findings supported the use of capnography for all neonatal tracheal intubations.[71] In an *in vitro* based investigation utilizing an artificial lung model, Schmalisch et al. found that exhaled tidal volume as well as exhaled CO_2 was underestimated during periods where simulated ETT leak was produced. As a result of this, the authors concluded that it was not possible to give an upper limit of ETT leaks that may be tolerated for capnographic measurements, from a clinical point of view.[75] Based on these findings the overall level of evidence on the use of a quantitative CO_2 detection during confirmation of correct ETT placement in infants is level B.

One completed clinical trial that compared a disposable $EtCO_2$ detector against quantitative capnography to confirm correct ETT placement was identified (www.clinicaltrials.gov, NCT01870622). As of January 2015, no results from this trial had been published. An ongoing trial on quantitative capnography as a means of confirming correct ETT placement (www.clinicaltrials.gov, NCT01572272) was also identified.

Use of qualitative CO_2 detection during ETT placement

Four studies relating to the use of a qualitative CO_2 detector in confirming correct ETT placement were identified (Table 2.2).[64,65,67,74] Roth et al. described a single patient case report on the success achieved in using an adult CO_2 detector (EasyCap) to determine correct ETT placement during resuscitation of a neonate in asystole.[67] Using a PediCap $EtCO_2$ detector, Aziz et al. highlighted the utility of the device in identifying correct ETT placement through observations of intubations in 24 infants in the NICU and 21 infants in the

delivery room. However, the authors highlight that use of the PediCap $EtCO_2$ detector during instances of cardiorespiratory compromise should be interpreted cautiously due to it's ability to give a false negative reading.[64] Utilizing an artificial lung model producing a tidal volume similar to that of a 400g infant, Garey et al. concluded that disposable CO_2 detectors were appropriate for use with infants above a birth weight of 400g to confirm ETT intubation.[65]

In a study investigating the accuracy of the PediCap detector in determining correct ETT position, Schmolzer et al. used the detector in conjunction with a respiratory function monitor on a sample of 35 intubations.[74] This study concluded that in some instances the PediCap device might not show colour change when there is correct ETT placement. Based on these findings the overall level of evidence for use of a qualitative CO_2 detector during confirmation of correct ETT placement in infants is level B.

Questionnaire based investigations on CO_2 detection during ETT placement

Four questionnaire-based studies relating to CO_2 detection in the delivery room were found (Table 2.2).[70,72,76,77] A survey on supplementary equipment used for neonatal resuscitation carried out on 25 tertiary perinatal centres in Australia and New Zealand by O'Donnell et al in 2005, determined that 3 centres (12%) used CO_2 detection to assess ETT position.[70] A year later, Leone et al. completed a survey on 797 neonatal directors across America. This survey had a response rate of 63% across 50 states and found 145 (32%) programs to be using $EtCO_2$ detection to confirm intubation. Of these 145 programs, 136 were using disposable $EtCO_2$ detectors and 9 were using capnography.[72] In 2012, El Naggar et al. distributed a survey to investigate the resuscitation practices on preterm infants after birth across 25 tertiary NICUs across Canada. With a response rate of 53% (78 respondents, 23 centres), this survey highlighted that 90% of respondents were using $EtCO_2$ detectors to confirm endotracheal intubation.[76] In 2014, Hosono et al. completed a survey on delivery room resuscitation practices in 287 neonatal departments across Japan. With a response rate of 66.6% (191 departments) it was found that 43.5% of respondents used CO_2 detectors and of these, 42.5% used CO_2 detectors routinely whilst 55.2% used them when confirming a difficult intubation.[77]

TABLE 2.2- LITERATURE RELATING TO THE USE OF $ETCO_2$ DETECTION DURING ENDOTRACHEAL INTUBATION

Author	Title	Study type	Key aspects of results	Author Conclusion	Strength of Evidence
Roberts WA. et al 1995[68]	The use of capnography for recognition of esophageal intubation in the neonatal intensive care unit	Observational	• 100 intubation episodes in 55 infants. • Capnograms obtained 15 and 120 seconds following tube placement. • 40 out of 100 intubation attempts resulted in esophageal intubation. • Capnography correctly identified esophageal intubation in 39 of these cases, within 1.6 seconds. • Clinical indicators required 97.1 sec to identify esophageal intubation and failed to identify successful ETT placement in 5 out of 60 cases.	Capnography is quicker and more successful in identifying incorrect ETT placement, compared to clinical indicators.	**Class IIb, LOE C**
Roth B. et al 1997[67]	Disposable CO_2 detector, a reliable tool for determination of correct tracheal tube position during resuscitation of a neonate	Case Report	• Infant weighing approximately 3kg experienced asystole soon after delivery via caesarean section. • Intubation performed and correct ETT placement confirmed via auscultation. • Uncertainty about correct ETT placement occurred, after period of chest compressions and catheterization of the umbilical cord, as a result of observing a change in pattern of chest and abdominal movements. • Adult disposable $EtCO_2$ detector (EasyCap) was attached to ETT and did not reveal a colour change. • After correction of ETT placement, colour change was observed on the $EtCO_2$ detector.	• Adult disposable CO_2 detector was successful in correctly identifying ETT placement in an infant.	**Class IIb, LOE C**

Aziz H. et al 1999[64]	The pediatric disposable end-tidal carbon dioxide detector role in endotracheal intubation in newborns	Observational	• 24 intubations in the delivery room and 21 intubations in the NICU correlated with and classified through radiography and clinical evaluation. • Colour change on $EtCO_2$ detector (PediCap) observed in 30 out of 33 successful intubations. • No colour change observed during esophageal intubation. • In 3 intubations without colour change, infants had significant cardiorespiratory compromise. • Determining correct ETT position was quicker with $EtCO_2$ detector compared to clinical evaluation (mean of 8.1sec versus 39.7sec).	The use of an $EtCO_2$ detector significantly reduces the time to verify correct ETT placement in term and preterm infants.	**Class IIa, LOE C**
Repetto JE. et al 2001[69]	Use of capnography in the delivery room for assessment of endotracheal tube placement	Observational	• 16 infants requiring intubation were included in the study. • ETT placement assessed via mainstream capnography that was only visible to an investigator who was not involved in the stabilisation. • Time taken for resuscitation team to determine correct ETT placement via clinical assessment (auscultation, chest wall movement, colour change, and heart rate) was noted. • Time for investigator to determine correct ETT placement was then compared to time taken for resuscitation team to determine correct ETT placement.	Determination of ETT placement was quicker with capnography than with clinical determination. The use of capnography required minimal training.	**Class IIb, LOE C**
O'Donnell C. et al 2005[70]	Use of supplementary equipment for resuscitation of newborn infants at tertiary perinatal centres in Australia and New Zealand	Questionnaire	• Questionnaire on the use of pulse oximetry, exhaled CO_2 detection, polyethylene wrapping, oxygen blenders, laryngeal masks, and oropharyngeal airways distributed to 25 tertiary perinatal centres with on site deliveries in Australia and New Zealand. • Response rate of 100%. • ETT position was assessed via $EtCO_2$ detection at 3 (12%) centres between 5% and 80% of all DR intubations.	Assessment of ETT placement via $EtCO_2$ detection was not routine practice at any centre.	**Class IIb, LOE C**

Salthe J. et al 2006[71]	Capnography rapidly confirmed correct endotracheal tube placement during resuscitation of extremely low birth weight babies (< 1000 g)	Case Report	• Case report on 4 infants (25.5-27 weeks gestation) (Birth weight 506-875g). • Limitation – Adult midstream capnography device used with a dead space of 8ml. As a result, values were diluted and could not be taken as exact.	Midstream capnography showed instant carbon dioxide exhalation when ETT placed correctly.	**Class IIb, LOE C**
Leone TA. et al 2006[72]	A survey of delivery room resuscitation practices in the United States	Questionnaire	• Questionnaire distributed to 797 neonatal directors in the US. • 63% response rate from programs across 50 states. • 70% of respondents from level III NICUs, 14% from level IV NICUs or ECMO centres. • $EtCO_2$ used to confirm intubation in 145 (32%) programs. • Of these, 136 programs were found to use disposable $EtCO_2$ detectors and 9 programs used capnography.	Results of survey useful in helping future revisions of neonatal resuscitation guidelines.	**Class IIb, LOE C**
Garey DM. et al 2008[65]	Tidal volume threshold for colormetric carbon dioxide detectors available for use in neonates.	Observational	• Lung model developed to replicate tidal volume of a 400g neonate. • Mini Stat CO_2 detector tidal volume threshold was 0.83ml and the PediCap tidal volume threshold was 1.08ml.	Threshold for detectors tested was less than tidal volume of 400g infant and therefore suitable for use in all infants to confirm intubation.	**Class IIb LOE C**
Hosono S. et al 2009[73]	A role of end-tidal CO_2 monitoring for assessment of tracheal intubations in very low birth weight infants during neonatal resuscitation at birth	Observational	• 54 intubations observed in 40 infants. • ETT placement assessed by investigator via $EtCO_2$ monitor. • Resuscitation team blinded to monitor. • Mean time taken to confirm correct ETT placement via monitor was quicker than clinical assessment (7.5 sec vs 17.0 sec) • $ETCO_2$ correctly identified all 40 tracheal and all 11 esophageal intubations. • Clinical assessment demonstrated discrepancies in 3 cases.	$EtCO_2$ is an accurate method of confirming ETT placement in very low birth weight infants.	**Class IIb, LOE B**

Schmolzer GM. et al 2011[74]	Assessment of flow waves and colorimetric CO_2 detector for endotracheal tube placement during neonatal resuscitation	Observational	• 35 intubations of 20 infants (<32 weeks gestation) had a video recording available. • A PediCap was used in these intubations and a flow sensor recording from a respiratory function monitor was also available. • In 21 intubations, both PediCap and the flow sensor identified correct ETT placement. • In 3 intubations both PediCap and the flow sensor identified incorrect ETT placement. • In remaining 11 intubations, PediCap showed no colour change however flow waves showed correct ETT placement.	Colourmetric CO_2 detectors may mislead clinicians during intubation of preterm infant by failing to change colour in spite of correct tube placement.	**Class IIb, LOE B**
Schmalisch G. et al 2012[75]	Effect of endotracheal tube leak on capnographic measurements in a ventilated neonatal lung model	Observational	• Lung model developed with two bellows, each with a volume of approximately 45mL. • Constant flow of 100% CO_2 was fed into these bellows. • Lung model ventilated with a neonatal ventilator and 3mm diameter ETT. • ETT leak was measured with the ventilator. • Both exhaled tidal volume and CO_2 were underestimated in the presence of ETT leaks. In contrast to tidal volumes, the effect of exhaled CO_2 airway leak is much more complex and more difficult to investigate *in vitro*.	It was not possible to give an upper limit of ETT leaks that may be tolerated for capnographic measurements from a clinical point of view.	**Class IIb, LOE C**
El Naggar W. et al 2012[76]	Delivery room resuscitation of preterm infants in Canada: current practice and views of neonatologists at level III centres	Questionnaire	• Questionnaire provided to 146 neonatologists across 25 tertiary NICUs across Canada. • 53% response rate (78 respondents from 23 centres) • 90% of respondents used a CO_2 detector to confirm endotracheal intubation. • 10% of respondents expressed opinion that use of a $EtCO_2$ detector is unnecessary in confirming correct ETT placement.	Resuscitation practice is highly variable across centres that completed the questionnaire.	**Class IIb, LOE C**

Hosono S. et al 2014[77]	Survey of delivery room resuscitation practices at tertiary perinatal centers in Japan	Questionnaire	• Questionnaire provided to 287 neonatal departments with 191 returned (66.6% response rate). • 45.3% of respondents used CO_2 detectors to confirm intubation. • Out of this, 42.5% used CO_2 detectors routinely and 55.2% used them when confirming a difficult intubation.	Equipment and techniques used during delivery room resuscitations across Japanese perinatal centres are highly varied.	**Class IIb, LOE C**

Use of qualitative CO_2 detection during facemask ventilation

Two studies relating to the use of qualitative $EtCO_2$ detection during facemask ventilation were identified (Table 2.3).[44,49] Leone et al. described the benefits of a PediCap $EtCO_2$ detector when used with a facemask during PPV in the NICU. It was found that during 21 instances of clear lack of colour change on the CO_2 detector, 20 displayed a colour change once the head/jaw position was adjusted. As a result of this finding, it was determined that using a CO_2 detector with a face mask may allow for an easier determination of airway patency on a near breath to breath basis.[49] In a study of 24 infants, the same research group found that a PediCap $EtCO_2$ detector allowed for the resuscitation team to recognize events of airway obstruction in the VLBW infant during PPV.[44] Based on these findings the overall level of evidence on the use of qualitative CO_2 detection during face-mask ventilation is level C.

Use of quantitative CO_2 detection during facemask ventilation

Four studies relating to the use of quantitative $EtCO_2$ detection during facemask ventilation were identified (Table 2.3).[78-81] Using a respiratory profile monitor (NM3, Philips, Respironics) with a combined pressure flow and CO_2 sensor on a cohort of 40 infants during resuscitation, Murthy et al. observed that CO_2 elimination improved during facemask PPV along with the onset of respiratory efforts.[78] In a randomised controlled trial carried out by Yee Kong et al. on a cohort of 48 infants, 7 infants were intubated and 41 received PPV via facemask. Thirty-seven capnography tracings were obtained from this group and it was found that although the capnography device provided useful physiological data, it did not reduce the occurrence of hypocapnia or hypercapnia, which was the trial hypothesis.[79] In a pilot study measuring the changes in $EtCO_2$, tidal volume, and rate of CO_2 elimination in preterm infants, Kang et al. highlighted the potential for $EtCO_2$ monitoring to guide respiratory support immediately after birth.[80] Using mainstream capnography with a convenience sample of 20 term infants immediately after birth, Schmolzer et al. described an increase in $EtCO_2$ levels as being associated with increasing tidal volumes in an infant. The authors suggested $EtCO_2$ monitoring to be suitable in the assessment of lung aeration immediately after birth.[81] Considering these studies, the overall level of evidence

on the use of quantitative CO_2 detection during facemask ventilation in infants is Level B.

TABLE 2.3- LITERATURE RELATING TO THE USE OF $ETCO_2$ DETECTION DURING FACEMASK VENTILATION					
Author	**Title**	**Study type**	**Key aspects of results**	**Author Conclusion**	**Strength of Evidence**
Leone TA. et al 2006[49]	Disposable colorimetric carbon dioxide detector use as an indicator of a patent airway during noninvasive mask ventilation	Observational	• 21 occurrences of clear lack of colour change in disposable $EtCO_2$ detector (Pedi-Cap) during stabilisation before intubation in 6 infants. • The manoeuvre that was used most frequently to achieve recovery of colour change was an adjustment in the head/jaw position (n = 20).	Disposable CO_2 detectors are a good method of determining airway patency during PPV with a face mask on a nearly breath to breath basis.	**Class IIa, LOE C**
Finer et al. 2009[44]	Airway obstruction during mask ventilation of very low birth weight infants during neonatal resuscitation	Observational	• Review of video recordings from resuscitations of 24 infants (<32week gestation). • $EtCO_2$ detectors used to assist bag mask ventilation and to confirm intubation. • 18 of the infants who required PPV had median of 14 obstructed breaths.	Airway obstruction occurs in majority of VLBW infants. CO_2 detectors allow for recognition of airway obstruction during mask ventilation.	**Class IIa, LOE C**
Murthy V. et al 2012[78]	End tidal carbon dioxide levels during the resuscitation of prematurely born infants	Observational	• Respiratory function monitor used on 40 infants during resuscitation. • During facemask ventilation, improved CO_2 elimination occurred with the onset of the infant's respiratory efforts.	Improved carbon dioxide elimination occurs with the onset of an infant's respiratory efforts.	**Class IIb, LOE C**

Yee Kong J. et al. 2013[79]	Quantitative end-tidal carbon dioxide monitoring in the delivery room: a randomized controlled trial	Randomised Controlled Trial	• Total of 48 infants. 7 intubated, 41 received facemask ventilation. • Control arm – adjusted PPV on standard clinical assessment. • Monitored arm – adjusted PPV based on $EtCO_2$ readings. • 37 $EtCO_2$ tracings available (19 control, 18 monitor), 11 incomplete tracings due to equipment malfunction. • Median $EtCO_2$ levels averaged from the last 5 breaths before leaving delivery room. • Median $EtCO_2$ levels were 44mmHg (16-66 mmHg) in control arm and 43 mmHg (29-59 mmHg) in the monitored arm. • On admission to the NICU, 33.3% of PCO_2 values from control arm were within levels of normocapnia (40-60mmHg) versus 37.5% of the PCO_2 levels from the monitored arm (p=0.763).	Capnography does not reduce hypercapnia or hypocapnia, however, does provide useful physiological information during PPV.	**Class IIb, LOE B**
Kang LJ. et al 2014[80]	Monitoring lung aeration during respiratory support in preterm infants after birth	Observational	• Pilot study to measure changes in $EtCO_2$, tidal volume, and rate of CO_2 elimination in preterm infants requiring respiratory support immediately after birth. • 51 infants (mean gestational age 29 weeks, Range 3weeks) receiving respiratory support in delivery room were included in study. • Delayed cord clamping of 60 seconds performed routinely on all infants. • 31 infants received CPAP. • 20 infants received PPV. • In the first 10 minutes after birth, infants in CPAP group had significantly higher $EtCO_2$ values compared to infants receiving PPV. • Tidal volume was significantly lower in the CPAP group. • Overall, infants who require PPV were shown to experience a different transitional period compared to infants who required CPAP. • Lower $EtCO_2$ values in PPV group may represent a delay in establishing functional residual capacity. • Data may suggest that infants establish FRC within 5 minutes after birth.	Measuring $EtCO_2$ has the potential to assess lung aeration and to guide respiratory support after birth.	**Class IIb, LOE C**

Schmolzer GM. et al. 2015[81]	Exhaled carbon dioxide in healthy term infants immediately after birth	Observational	• Convenience sample of 20 term infants included in the study (birth weight 2976g[697], gestational age 38 weeks [2]) • A respiratory function monitor with mainstream capnography was used to monitor $EtCO_2$ and tidal volume production by each infant for 120 seconds immediately after birth. • No infant required respiratory support. • It was found that infants took a median(range) of 3 (1-8) breaths before $EtCO_2$ was detected. • After 10 breaths this $EtCO_2$ increased to 27 (22-34) mm Hg in all infants. • Increase in $EtCO_2$ levels was associated with increasing tidal volumes.	Monitoring $EtCO_2$ levels can be used to assess lung aeration immediately after birth.	**Class IIb, LOE C**

Review articles on the use of $EtCO_2$ detection

Six review articles relating to $EtCO_2$ monitoring were identified (Table 2.4).[82-87] Molloy et al. reviewed literature relating to many forms of CO_2 monitoring including $TcPCO_2$, $PaCO_2$, and $EtCO_2$. This review suggested that colourimetric CO_2 detection is a valuable adjunct for airway management in infants, although the review did highlight the need for caution in relation to the potential ineffectiveness of $EtCO_2$ monitoring during instances of cardiopulmonary arrest.[82] Similarly, the potential ineffectiveness relating to colourimetric CO_2 detection during instances of cardiopulmonary arrest was highlighted in a literature review by Gowda.[83] A literature review by O'Reilly et al. identified that facemask leak and obstructions are generally unrecognized without the use of expired CO_2 detectors or respiratory function monitors. Although the authors acknowledge the benefits of qualitative CO_2 detectors, they highlight that such detectors are unable to differentiate between inadequate tidal volumes, airway obstruction, or circulatory failure.[84] This conclusion was reiterated in a literature review completed by the same group who suggested that exhaled CO_2 readings should always be interpreted with clinical signs, due to the potential of exhaled CO_2 to provide the user with misleading readings.[85]

Through a literature review, as well as an investigation utilizing a respiratory function monitor on preterm infants during stabilisation in the delivery room, the same group described issues relating to $EtCO_2$ detection when used during stabilisation in the delivery room. Analysing $EtCO_2$ readings obtained as well as reviewing literature, the authors highlighted the need for further studies in order to determine the utility of $EtCO_2$ monitoring during resuscitation.[86]

A systematic review by Schmolzer and Roehr was unsuccessful in identifying studies comparing radiographic determination of correct ETT tube placement to any commercially available form of $EtCO_2$ detection, as it had aimed to do.[87] A registered title for a review by Schmolzer is also available, entitled "The effect of respiratory support guided by exhaled CO_2 on morbidity and mortality in newborn infants requiring resuscitation"(www.cochrane.org).

TABLE 2.4- REVIEW ARTICLES ON THE USE OF $ETCO_2$ DETECTION

Author	Title	Key aspects of results	Author Conclusion
Molloy E. et al 2006[82]	Are carbon dioxide detectors useful in neonates?	• Analysis of literature relating to $TcPCO_2$, $PaCO_2$), and $EtCO_2$. • Authors highlight improvement in short term outcomes of infants receiving CO_2 whilst receiving respiratory support during transport. • Acquisition of $TcPCO_2$ readings may cause heat induced skin damage. • Inadequate tissue perfusion and acidosis may alter $TcPCO_2$ correlation with $PaCO_2$. • $EtCO_2$ detectors significantly decrease the time for assessment of correct ETT positioning during intubation. • Authors highlight ineffectiveness of $EtCO_2$ detector if exposed to acidic gastric contents or drugs such as epinephrine, and the ability of the detector to give a false negative result during times such as cardiopulmonary arrest.	Colourimetric CO_2 detectors are valuable adjuncts for airway management.
Gowda H. 2011[83]	Question 2. Should carbon dioxide detectors be used to check correct placement of endotracheal tubes in preterm and term neonates?	• Analysis of literature relating to $EtCO_2$ detection during intubation. • Highlights ability of $EtCO_2$ detection to confirm intubation in infants with a cardiac output quicker and more accurately than standard clinical assessment. • False negatives may occur during cardiac arrest.	The use of $EtCO_2$ detection in confirming intubation is important.
O'Reilly M. et al. 2013[84]	Short- and intermediate-term outcomes of preterm infants receiving positive pressure ventilation in the delivery room	• Analysis of literature relating to PPV in preterm infants in the delivery room. • Highlights the impact on clinical outcomes, and potential areas for further research. • Need for further RCTs to investigate the short and intermediate term outcomes, in relation to lung injury.	Disposable $EtCO_2$ detectors can be useful to assess effective PPV, however, they do not differentiate between inadequate tidal volume, airway obstruction, or circulatory failure

Schmolzer GM. et al. 2013[85]	Confirmation of correct tracheal tube placement in newborn infants.	• Review of literature on ETT placement in newborn infants. • Highlights the need for evaluation of new techniques for confirmation of ETT placement. • Radiography remains the accepted standard test to confirm ETT placement.	An increase in HR is the best indicator of effective ventilation. $EtCO_2$ may give misleading, false negative results and readings should be interpreted in conjunction with clinical signs.
van Os S. et al. 2014[86]	Exhaled carbon dioxide can be used to guide respiratory support in the delivery room	• Review of current literature on the use of $EtCO_2$ monitoring during respiratory support in infant stabilisation. • Using a respiratory function monitor, authors also provide gas flow, tidal volume, and $EtCO_2$ trends obtained from preterm infants during stabilisation in the delivery room.	$EtCO_2$ monitoring could help to assess lung aeration and improve lung recruitment immediately after birth.
Schmolzer GM. and Roehr CC. 2014[87]	Techniques to ascertain correct endotracheal tube placement in neonates	• Review aimed to access literature on the current techniques used for the identification of correct ETT placement in the delivery room or NICU, and compared with chest radiography. • Authors did not find any literature meeting the criteria for the review.	Evidence towards the use of $EtCO_2$ detection in confirming correct ETT placement is based only on evidence derived from observational studies and case reports.

Comparison of $EtCO_2$ with $PaCO_2$ and/or partial pressure of $PvCO_2$

A total of 11 studies comparing CO_2 levels to $PaCO_2$ and $PvCO_2$ were found (Table 2.5).[88-98] Four studies identified capnography as a useful means of screening infants for abnormal $PaCO_2$ levels.[90,92,93,96] In an investigation by Watkins et al. correlating 62 $EtCO_2/PaCO_2$ pairs in 19 infants with respiratory disease, it was concluded that $EtCO_2$ monitoring may be useful for management of preterm infants with normal lung function.[88] In a similar comparative study including 48 ventilated infants that produced 286 paired $EtCO_2/PaCO_2$ samples, Singh et al. demonstrated that correlations between $EtCO_2$ and PCO_2 readings were moderate, but the agreement was less than adequate. The authors concluded that capnography may be more reliable in conditions of less severe lung disease.[95] As a result of the correlation that Tai et al. discovered between $PaCO_2$ and $EtCO_2$ levels in non-intubated infants, it was suggested that $EtCO_2$ measurement by side stream capnography through nasal cannula, may also provide an accurate estimate of $PaCO_2$ levels.[94] The close correlation of $EtCO_2$ with $PaCO_2$ readings was also highlighted in 152 $EtCO_2/PaCO_2$ pairs by Nangia et al.[89], and in 130 $EtCO_2/PaCO_2$ pairs by Wu et al.[91]

Through a comparison of $EtCO_2$, $PvCO_2$, and $TcPCO_2$ readings amongst ventilated infants, Lopez et al. concluded that there was an insufficient correlation between $EtCO_2$ and $PvCO_2$. However, $EtCO_2$ was able to detect high and low levels of CO_2 with similar efficacy to that of $TcPCO_2$.[97] Tingay et al. identified $EtCO_2$ and $TcCO_2$ readings as having a clinically acceptable agreement with $PaCO_2$ readings in 50 mechanically ventilated postoperative infants.[98] Considering these studies, the overall level of evidence on the comparison of $EtCO_2$ readings with other forms of CO_2 monitoring in infants is Level B.

TABLE 2.5- LITERATURE ON THE COMPARISON OF $ETCO_2$ MONITORING WITH OTHER FORMS OF CO_2 MONITORING

Author	Title	Study type	Key aspects of results	Author Conclusion	Strength of Evidence
Watkins A et al. 1987[88]	Monitoring of end tidal CO_2 in neonatal intensive care	Observational	• 19 clinically stable infants with respiratory disease included. • Details presented from 62 measurements (15 intubated infants) acquired via capnometer attached to ETT via tube adapter. • In 11 infants with mild or moderate lung disease there was a useful correlation between $PaCO_2$ and $EtCO_2$. • A larger difference between $PaCO_2$ and $EtCO_2$ readings was noted amongst infants with short expiratory times, these infants tended to have a more severe degree of respiratory disease.	$EtCO_2$ may be a good approximation of $PaCO_2$ but it is not identical. $EtCO_2$ monitoring may be useful for management of premature infants with normal lung function.	**Class IIb, LOE C**
Nangia S. et al. 1997[89]	End tidal carbon dioxide monitoring--its reliability in neonates	Observational	• Arterial blood gases were obtained in ventilated babies with simultaneous $EtCO_2$ readings in the NICU. • 152 samples from in-dwelling radial artery catheters were analysed from babies with birth weight from 900 g to 3400 g and gestational age from 28 to 42 wks. • Infants ventilated for various indications such as severe birth asphyxia, meconium aspiration syndrome, recurrent apnoea, and hyaline membrane disease. • $ETCO_2$ correlates closely with $PaCO_2$ in most clinical situations in infants • Comparisons showed a high level of correlation in infants with a birth weight of >1.5kg and preterm infants (32-36weeks). • Correlation coefficient was lowest in babies with hyaline membrane disease.	$ETCO_2$ correlates closely with $PaCO_2$ in most clinical situations in infants. $EtCO_2$ detections should be used in ventilated infants in all level III NICUs.	**Class IIa, LOE C**

Rozycki HJ. et al 1998[90]	Mainstream end-tidal carbon dioxide monitoring in the neonatal intensive care unit	Observational	• Study of 411 $EtCO_2/PaCO_2$ pairs from 45 infants across 2 NICUs. • Capnometry identified 91% of instances of normocapnia, as indicated by $PaCO_2$ readings. • $EtCO_2$ readings outside the range of normocapnia had a 63% accuracy in indicating hypocarbia or hypercarbia. • $EtCO_2$ readings as accurate as capillary CO_2 and transcutaneous CO_2 levels, but not as precise. • Capnography a useful method of screening patients for abnormal levels of $PaCO_2$	$EtCO_2$ readings are as accurate as capillary CO_2 and transcutaneous CO_2 levels, but not as precise.	**Class IIa, LOE B**
Wu C. et al. 2003[91]	Good estimation of arterial carbon dioxide by end-tidal carbon dioxide monitoring in the neonatal intensive care unit	Observational	• $PaCO_2$ readings drawn from blood gas analysis, $EtCO_2$ readings obtained from mainstream capnography. • 130 $EtCO_2/PaCO_2$ comparisons were obtained from 61 infants (20 term and 41 preterm) receiving respiratory support in the NICU. • $EtCO_2$ was a valid and reliable method for monitoring $PaCO_2$ in infants due to the high level of correlation found between the readings.	As a result of method decreasing amount of blood loss, authors suggest the use of mainstream $EtCO_2$ monitoring instead of $PaCO_2$ in infants in the NICU.	**Class IIa, LOE C**
Amuchou Singh S. 2006[92]	Does End-tidal Carbon Dioxide Measurement Correlate with Arterial Carbon Dioxide in Extremely Low Birth Weight Infants in the First Week of Life?	Observational	• Retrospective chart review of 31 ELBW (<1000g) infants. • 754 $EtCO_2/PaCO_2$ pairs. • $PaCO_2$ readings obtained from blood gas and $EtCO_2$ readings obtained from mainstream capnography. • $EtCO_2$ successfully identified the range of normocapnia, as determined by $PaCO_2$ readings, in 84% of cases. • $EtCO_2$ successfully identified the range of hypocapnia or hypocapnia, as determined by $PaCO_2$ readings, in 57% of cases.	$EtCO_2$ monitoring can be helpful in trending or in screening for abnormal $PaCO_2$ levels in ELBW infants in the first week of life.	**Class IIb, LOE C**

Bhat YR. et al. 2008[93]	Mainstream end tidal carbon dioxide monitoring in ventilated neonates	Observational	• 133 $EtCO_2/PaCO_2$ obtained from 32 ventilated infants. • $PaCO_2$ readings obtained from indwelling arterial catheters and $EtCO_2$ readings obtained from mainstream capnography. • $EtCO_2$ value was lower than the corresponding $PaCO_2$ value in 86.5% of cases with a mean bias of -6.65mmHg. • Good correlation between mainstream $EtCO_2$ and $PaCO_2$ • Lower degree of correlation in infants with pulmonary disease.	Mainstream $EtCO_2$ monitoring is helpful in trending or screening for abnormal $PaCO_2$ values.	**Class IIb, LOE C**
Lopez E. et al 2009[97]	Detection of carbon dioxide thresholds using low flow sidestream capnography in ventilated preterm infants	Observational	• 99 simultaneous recordings of $EtCO_2$, $PvCO_2$, and $TcPCO_2$ in 37 ventilated preterm infants were included in the study. • $EtCO_2$ recordings where a leak of more than 30% was detected at the ETT, were excluded from the study. • Insufficient correlation found between $EtCO_2$ and $PvCO_2$. • Capnography was able to detect low and high CO_2 warning levels with a similar efficacy to that of $TcPCO_2$.	As a result of correlation with $TcPCO_2$ readings, capnography may be of clinical interest.	**Class IIb, LOE C**
Tai CC. et al 2010.[94]	Noninvasive capnometry for end tidal carbon dioxide monitoring via nasal cannula in nonintubated neonates	Observational	• Retrospective analysis of medical records from 34 non intubated infants admitted to the neonatal ward. • 54 $PaCO_2/EtCO_2$ pairs were available for analysis. • $EtCO_2$ measurement acquired through a nasal cannula via sidestream capnometry. • Significant difference between $EtCO_2$ and $PaCO_2$ levels in infants with respiratory disease. • No significant difference between $EtCO_2$ and $PaCO_2$ levels in infants without respiratory disease.	$EtCO_2$ measurement by sidestream capnometry through nasal cannula may provide an accurate and noninvasive estimate of $PaCO_2$ levels in non intubated neonates.	**Class IIa, LOE C**

Tingay DG. et al 2013[98]	End tidal carbon dioxide is as reliable as transcutaneous monitoring in ventilated postsurgical neonates	Observational	• Study paired transcutaneous CO_2 ($tcCO_2$) and $EtCO_2$ values with three consecutive $PaCO_2$ values in infants within 48hours of surgery. • $PaCO_2$ readings obtained from indwelling arterial catheters and $EtCO_2$ readings obtained from sidestream capnography. • 132 samples from 50 ventilated infants. • $EtCO_2$ underestimated $PaCO_2$, when compared to $tcCO_2$, however provided greater precision over repeated $PaCO_2$ readings. • Overall, $EtCO_2$, and $tcCO_2$ were found to have clinically acceptable agreement with $PaCO_2$ levels.	$EtCO_2$ and $TcCO_2$ monitoring are feasible methods of non-invasively monitoring CO_2 trends in postsurgical infants.	**Class IIb, LOE B**
Singh BS. et al 2013[95]	Sidestream microstream end tidal carbon dioxide measurements and blood gas correlations in neonatal intensive care unit	Observational	• 286 $EtCO_2/PaCO_2$ were collected from 48 ventilated infants admitted to the NICU. • $EtCO_2$ measurements acquired via sidestream microstream technology, $PaCO_2$ readings obtained from blood gas. • VLBW demonstrated that the correlation of $EtCO_2$ and $PaCO_2$ was moderate, but the agreement was less than adequate (bias > 5 mmHg in all groups). • The correlation improved with a lower ratio of physiological dead space to tidal volume.	The correlation between $EtCO_2$ and $PaCO_2$ in VLBW infants was moderate. Sidestream capnography may be more reliable in conditions of less severe lung disease.	**Class IIb, LOE C**

Mehta H. et al. 2014[96]	Correlation of end tidal and arterial carbon dioxide levels in critically ill neonates and children.	Observational	• $EtCO_2$ values obtained via mainstream capnography on 66 mechanically ventilated neonates (mean weight of 2.1 kg (SD ± 0.63). • 150 $EtCO_2/PaCO_2$ pairs available for analysis. • Overall, good correlation found between $EtCO_2$ values and $PaCO_2$ values. • Ventilation index did not have any conclusive effect on correlation. • Strong correlation found between variable in infants with mild to moderate lung disease.	$EtCO_2$ monitor provides validity in neonates, however, recommends that blood gas be measured in patients with increased severity of lung disease.	**Class IIb, LOE C**

2.2.5. CONCLUSION

These results highlight the paucity of convincing data on the role of CO_2 monitoring in the delivery room. In addition, studies were found to vary concerning the strength of correlation between $EtCO_2$ and $PaCO_2$ or $PvCO_2$.[88,90,92-95,97,98] The role of CO_2 monitoring in the delivery room is generally limited to the assessment of correct ETT placement. More often, this assessment is performed with a qualitative CO_2 detector than with capnography, both of which have been shown to be a more accurate as well as a quicker method of confirming correct ETT placement when compared to clinical assessment alone. As discussed in Chapter 1, the use of $EtCO_2$ detection for ETT placement is now advocated in the most recent NRP guidelines.[2]

$EtCO_2$ detection may be of particular benefit for preterm infants in assessment of effective PPV as using standard clinical methods can often be difficult due to various issues such as the difficulty encountered in visualizing chest rise and fall, as was described in Chapter 1. However, the use of a colourimetric CO_2 detector during the provision of PPV with a facemask has not been advocated in the recent AHA guidelines on neonatal resuscitation.[1] One concern may be that utilisation of a colourimeter will alter the ergonomics of manual ventilation devices, subsequently making manual ventilation more difficult, depending on the chosen device. However, users may already have experience in using and interpreting these qualitative devices in assessing ETT placement. Clinical observational research into the use of qualitative CO_2 detectors during PPV with a facemask has advocated their use[44,49,84], however, there are no randomised trials of colourimeters for provision of manual ventilation in the infant, and many studies have advised caution due to the ability of the device to give a false negative reading.[64,74,82,84,85]

There is only one completed randomised trial on the use of capnography with PPV during infant stabilisation. Yee Kong et al. did not find any significant difference between the incidences of hypercapnia and hypocapnia during infant stabilisation.[79] There may be a number of reasons for this finding. The introduction of a new technology into the stabilisation process may alter the

ergonomics of manual ventilation with the addition of increased dead space as well as altered hand positioning. It also requires visualization of a monitor not directly in the user's line of vision, and this may be a distracting phenomenon. However, this trial did highlight the benefits of having capnography available as a resource to provide physiological information during the provision of PPV. This outcome is encouraging and highlights the need for further investigations and RCTs.

There are other modalities available to the clinician to assess the adequacy of PPV in an infant. These include the use of a respiratory function monitor (RFM), either with or without incorporated CO_2 monitoring. These devices produce a continuous display of pressure and flow waves. Other readings can also be displayed in numerical form such as airway leak, PEEP, CPAP, and respiratory rate. A number of observational studies and one randomised controlled trial have assessed the role of RFMs during infant stabilisation.[74,99-102] Both van Os et al. and Schmolzer et al. have assessed the role of a RFM with incorporated $EtCO_2$ monitoring in the setting of the delivery room.[81,86]

Typically, capnography requires the user's attention to be briefly drawn away from an infant when interacting with quantitative CO_2 measurements. Whilst evidence from Yee Kong et al. may allude to the potential benefits of having a quantitative CO_2 reading visible to the provider of PPV[79], incorporation of this device into the delivery room setting warrants further education and training, and in-vitro simulation. It is important for these issues to be addressed before conducting randomised trials on the use of capnography in the delivery room.

2.3. CONCLUSION OF CHAPTER

In conclusion, this chapter has described several methods of $EtCO_2$ detection available for use during the care of an infant both in the NICU as well as in the delivery room. Although the role of $EtCO_2$ detection during intubation is now routine, a review of the available literature highlights the need for further research into $EtCO_2$ detection, in particular capnography, as a means of confirming effective facemask ventilation during infant stabilisation. More evidence, particularly in the form of randomised controlled trials, is needed in order to effectively warrant the use of such $EtCO_2$ detection. Over the next 3 chapters, this thesis will introduce three investigations that have focused on the utilisation $EtCO_2$ detection in the delivery room. As with most new therapies, the best way to demonstrate benefit and eliminate bias may be through *in vivo* simulations, that will be described in Chapter 3, as well as a RCT, that will be described in Chapter 5.

CHAPTER 3: IN VITRO ASSESSMENT OF $ETCO_2$ MONITORING

Part published as:

Efficacy and user preference of two CO_2 detectors in an infant mannequin randomized crossover trial.

Hawkes GA, O'Connell BJ, Livingstone V, Hawkes CP, Ryan CA, Dempsey EM.

European Journal of Pediatrics. 2013 PMID= 23756915 (Appendix B)

- AND -

Quantitative or qualitative carbon dioxide monitoring for manual ventilation: A mannequin study

Hawkes GA, Kenosi M, Ryan CA, Dempsey EM.

Acta Paediatrica. 2014 PMID= 25495353 (Appendix C)

3.1. INTRODUCTION

Effective PPV is a key component of infant stabilisation.[2,103] As discussed in Chapter 1, the indications for use of PPV during stabilisation include an infant being apneic or ineffectively breathing, having a HR of less than 100 bpm, or remaining cyanotic despite supplemental oxygen. Face mask leak can make the delivery of effective PPV difficult and a previous mannequin-based study has highlighted the occurrence of a leak of up to 33% of assumed tidal volume.[17] In order to confirm effective ventilation during stabilisation, the NRP recommends observing for an increase in HR, seeing or auscultating chest inflation, and observing for a rise in SpO_2 levels.[2]

As discussed in Chapter 2, $EtCO_2$ detectors have an established role in determining the correct placement of an ETT in a clinical setting, with several studies highlighting their benefit.[64,65,67,74] However, a limited number of studies relate to the role of $EtCO_2$ monitoring during the provision of PPV via a facemask. Studies have shown that a qualitative $EtCO_2$ detector will not change colour if insufficient tidal volume is produced[104], if there are obstructed ventilations[49], inadequate cardiac output[64], or device failure.[105]

In this chapter, two separate *in vitro* based investigations will be described. Through the utilisation of a CO_2 producing mannequin, these investigations aimed to examine different methods of $EtCO_2$ detection and the impact that these methods had on the effectiveness of PPV.

CO_2 Producing Mannequin

For both investigations discussed in this chapter, the same low fidelity CO_2 producing mannequin model was utilised. This bespoke system was created in conjunction with our biomedical engineer, Mr. Brian O'Connell (Department of Biomedical Engineering, Cork University Maternity Hospital). A graphical representation of this setup is presented in Figure 3.1.

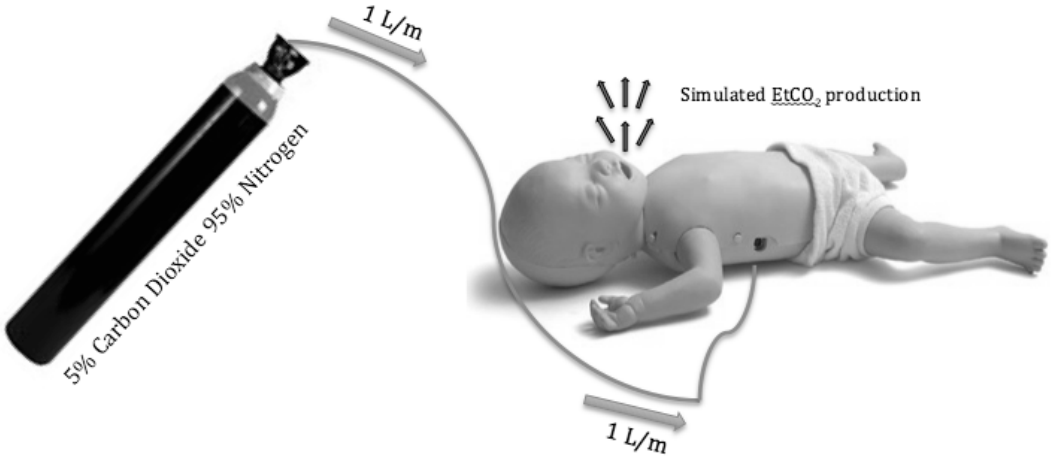


FIGURE 3.1 – CO_2 PRODUCING MANNEQUIN ARRANGEMENT

A standard "Resusci Baby" infant mannequin (Laerdal Medical AS, Stavanger, Norway) was modified to simulate CO_2 production of a newborn. This mannequin had an internal reservoir bag to simulate a lung. An internal rubber tube connected this reservoir bag to the mannequin's mouth, simulating a patient airway. A gas hose was inserted into this airway tube just above the reservoir bag using a 3-way adapter. The other end of the gas hose was connected to a compressed gas cylinder (5% Carbon Dioxide and 95% Nitrogen) via a gas regulator. The flow rate on this regulator was set to 1L/min. The TPR was fed by a 100% oxygen gas supply of approximately 8L/min. When the mannequin's lungs were filled successfully via effective PPV, the 100% oxygen gas mixed with the 5% CO_2 gas. On subsequent passive exhalation, the presence of CO_2 simulated the exhalation of a small infant. Using the TPR to initiate a new ventilation drove 100% oxygen back through the CO_2 detector and reset the colour to purple on each device. The mannequin design was such that if the head tilt angle was not correct it kinked the mannequin airway and simulated an obstructed airway and no colour change on either CO_2 detector occurred. In this event the infusing CO_2 supply would continue to inflate the mannequin lung reservoir. To prevent this reservoir from over expanding a blow-off valve was fitted to the reservoir. This valve opened to vent the gases at a pressure greater than 30 mBar. When the device was assessed with capnography it was found that the median CO_2 values were 5 kPa, consistent with expired $EtCO_2$ values of a healthy newborn infant.

3.2. EFFICACY AND USER PREFERENCE DURING THE USE OF QUALITATIVE METHODS OF $ETCO_2$ DETECTION

3.2.1. AIM

The primary aim of this investigation was to assess the efficacy of manual ventilation by paediatric trainees when utilising two different $EtCO_2$ detection methods during PPV in a mannequin model. The secondary aim of this investigation was to obtain feedback on these $EtCO_2$ detection methods from the participants.

3.2.2. METHODS

This was a randomised crossover trial instructing participants to provide three separate, three-minute, periods of manual ventilation with a TPR on the low fidelity CO_2 producing mannequin, in a randomly assigned order. The TPR was configured to provide 8 L of oxygen per minute, a PIP of 20 cm H_2O, and a PEEP of 5 cm H_2O throughout all participant interaction.

Participants were instructed to provide ventilation at an NRP standard of 40-60 ventilations per minute. There was approximately a one-minute period between each manual ventilation period to allow wash out of CO_2 within the mannequin. Block one of this investigation had no CO_2 detector attached to the TPR (ND), block two had a PediCap $EtCO_2$ detector attached to the TPR (HORIZ) and block three included a NeoStat $EtCO_2$ detector attached to the TPR (VERT)(Figure 3.2). All blocks were video recorded from the side and scored by two independent observers at a later date.

CO_2 detector

The way in which a user is required to hold the PediCap and NeoStat differ slightly. The PediCap is a device that requires manual ventilations to be delivered from a 90 degree angle with the TPR (Figure 3.2). The NeoStat is a device that requires manual ventilations to be delivered in parallel with the TPR (Figure 3.2).

Randomisation

The randomisation process was carried out with random sequence numbers in sealed opaque envelopes. If a participant drew the number "1" then that participant started with the ND method, then moved on to the HORIZ method, before finishing with the VERT method. If a participant drew the number "2" then that participant started with the HORIZ method, then moved on to the VERT method, before finishing with the ND method. Finally, if a participant drew the number "3" then that participant started with the VERT method, then moved on to the ND method, and finished with the HORIZ method.

Scoring of videos

The investigation was video recorded in order to determine the efficacy of the ventilations provided, retrospectively. The author (GAH) and supervisors (EMD and CAR) of this thesis independently assessed the videos and determined the number of ventilations provided, as well as the number of times there was sufficient chest rise and fall observed. As the videos were anonymous, showing only a participant's hands, each reviewer was unaware of the order in which the participant completed the different methods. Ventilation was deemed to be effective if chest rise and fall was observed during delivery of a ventilation. Where disagreement existed among the 3 reviewers, consensus was decided by majority decision. For the purpose of this investigation, percentage efficacy was defined as the number of ventilations that the reviewers deemed to be effective against the number of ventilations that were delivered overall. Results were reviewed for the first minute and for the entire three-minute period. All statistical analysis was performed using SPSS Statistics 22.0 (IBM, NY, USA). All tests were two-sided and a p-value <0.05 was considered to be statistically significant. Efficacy was described using medians and interquartile ranges. Non-parametric tests were used as the sample size, of 19, was small and the distribution of efficacy scores was non-normal.

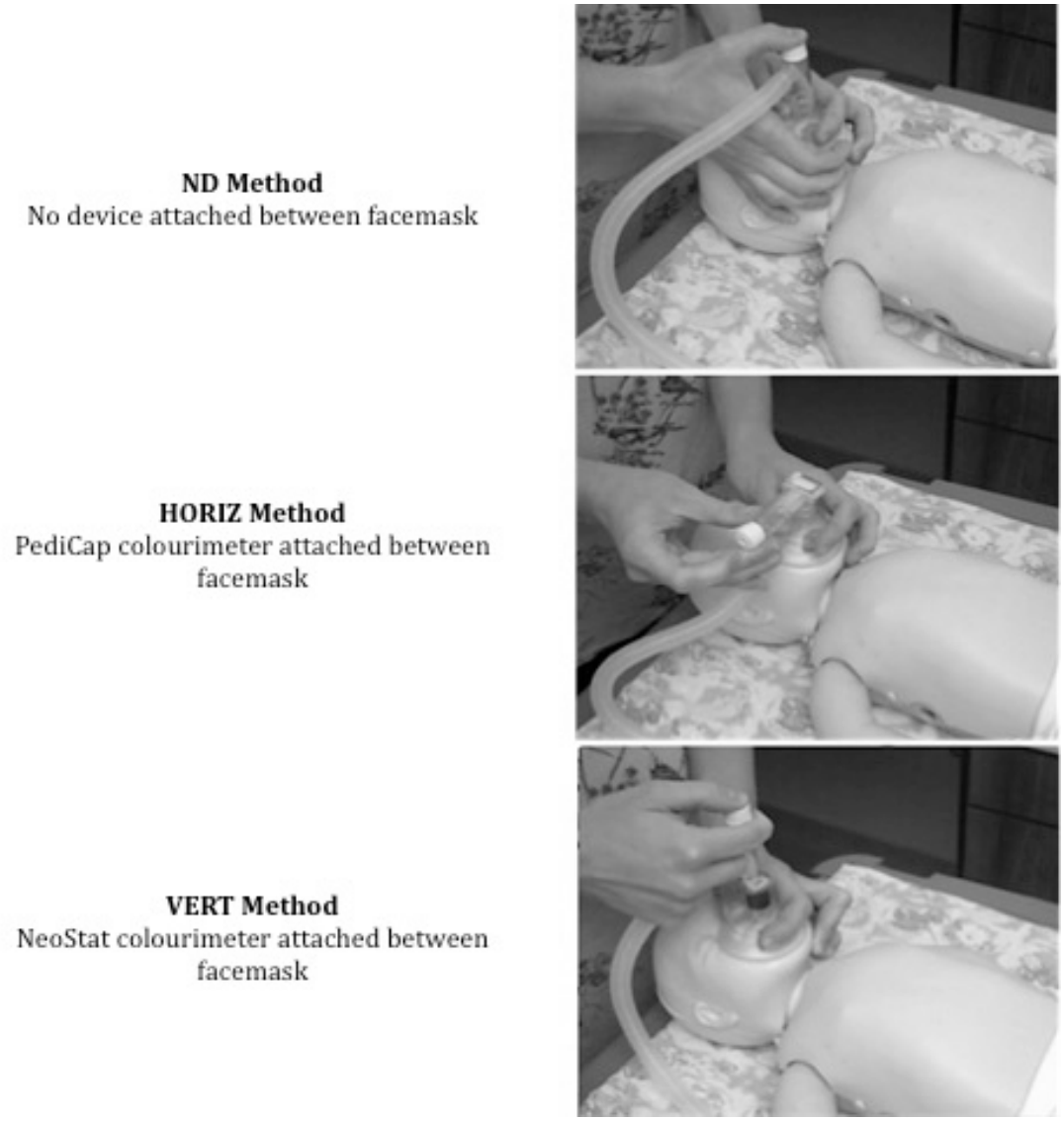


FIGURE 3.2 – CONFIGURATION OF THE 3 DIFFERENT METHODS

3.2.3. RESULTS

There were 19 participants overall, consisting of 10 senior house officers (SHOs) and 9 registrars. This was a convenience sample based on the number of trainees working in the NICU of CUMH at the time. All participants had completed NRP training within 2 years prior to commencement of this investigation.

A mean efficacy of ventilation of 88.9% in the first minute and 90.4% in the overall three-minute period, was observed in the ND method. The HORIZ method was found to have a mean efficacy of ventilation of 93.2% in the first minute and 91.7% in the overall three-minute period. The VERT method outperformed both other methods with a mean efficacy of ventilation 95.1% in the first minute and 96.0% in the overall three-minute period (p=0.004)(Table

3.1). This was also found over the one-minute period, apart from when the user began the trial with the ND method (Table 3.1).

TABLE 3.1 – COMPARISON OF THE PERFORMANCE ACCORDING TO ORDER AT WHICH COMPLETED

Order	Number of Participants	Mean % Efficacy ND	Mean % Efficacy HORIZ	Mean % Efficacy VERT	p-value
0-60 Seconds					
Order 1*	6	93.1	97.5	93.7	0.229
Order 2**	6	90.5	90.0	95.9	0.062
Order 3***	7	83.9	91.2	93.1	0.032
Overall	19	87.5	93.2	95.1	0.001
0-180 Seconds					
Order 1*	6	94.4	92.9	97.5	0.651
Order 2**	6	92.7	90.6	98.2	0.048
Order 3***	7	85.0	90.6	92.7	0.030
Overall	19	91.5	91.7	96.0	0.004

*** Order 1 = ND method followed by HORIZ method followed by VERT method.**

**** Order 2 = HORIZ method followed by VERT method followed by ND method.**

***** Order 3 = VERT method followed by ND method followed by HORIZ method.**

After each participant had completed the three-minute period of ventilation, with each different method, he/she received an informal debriefing to obtain feedback relating to each method used. 18 participants preferred the use of a CO_2 detector during ventilation of the mannequin. Of this, 12 participants had a preference for the VERT method and 6 participants had a preference for the HORIZ method. When asked to indicate why they choose the VERT method as being the preferred device, participant feedback related to ergonomics. Participants highlighted the similarity between the ergonomics of using the VERT method, in particular, the NeoStat connected to the TPR being similar to the TPR when used alone, the

latter being standard practice at the moment. Most participants disliked the HORIZ method due to the non-conventional angle at which the user is required to deliver PPV during use.

Positive feedback relating to the use of the PediCap device included the size of the colour indicator contained on the device as well as the direct visualization that participants were able to achieve as a result of no part of the hand being involved with their line of sight, in relation to viewing the colour indicator. Participants found any colour change that occurred was easier to see, in comparison to the NeoStat device. The one participant who preferred no CO_2 detecting device attached to the facemask felt that by having a CO_2 detector attached, a user may become reliant on a colour change and fail to take in any other indicator in determining effective ventilation, during an *in vivo* scenario.

3.2.4. DISCUSSION

This investigation has demonstrated that the use of a CO_2 detector during the provision of facemask ventilation in a mannequin model may improve the effectiveness of ventilation, and may allow for early identification of ineffective ventilations. Effective ventilation may be achieved with or without a CO_2 detector; however, this investigation has shown that the use of a CO_2 detector particularly increases effectiveness during the first 60 seconds, a time when effective ventilation is particularly important.[2,103]

It was found that the difference between the use of a CO_2 detector compared to the use of no CO_2 detector improved from the first minute to the last, suggesting that trainees may be able to identify problems with manual ventilation over time and make the necessary changes to enhance manual ventilation in a mannequin model.

The VERT method was shown to be the most effective method both for the first minute and for the three-minute period of manual ventilation, apart from when the participant began the trial with the ND method. Although the role of the PediCap device during PPV has been previously described[49,64,65,74,104],

comparisons with the NeoStat CO_2 detector, in relation to it's effectiveness and preference, have not been described.

There are a few potential confounders that could account for the differences between these two devices. A carryover effect is always a consideration with crossover studies. Although the order of methods used by participants was randomly assigned, the VERT method continued to show the greatest efficacy over the entire three-minute period, irrespective of which method a participant commenced with.

Through this mannequin based investigation it was found that participants preferred providing ventilations with a CO_2 detector attached to the TPR and, as well as having a higher efficacy, the VERT method was also the preferred method by the majority of participants. In order to standardize the manual ventilation device, the investigation elected to use only a TPR to provide ventilation pressures. Although it may be likely that the results can be extrapolated to the self-inflating and flow-inflating bags, this was not assessed.

One limitation of this investigation was that facemask leak was not assessed. Facemask leak may affect manual ventilation. The attachment of a flow meter to the TPR would have significantly altered the ergonomics of manual ventilation and if a flow meter was attached in series with either of the devices, the additional weight as well as the altered hand positioning may have impacted the results. The investigation attempted to replicate what happens in clinical practice in CUMH and so elected not to include a flow meter. The investigation video recorded each participant's ventilation of the mannequin. This subsequently allowed the reviewers of the video to look at adequacy of mask position and chest rise with each ventilation. While the exact concentration of CO_2 produced in this mannequin model may not be fully consistent with that produced by a small infant, the presence of an $EtCO_2$ detector did result in enhanced manual ventilation. The CO_2 produced by an infant is dependent on a number of factors including spontaneous breathing as well as the size of the tidal volumes expired. This can only be clarified by *in vivo* studies of infants.

The issue of ergonomics behind the use of each method is one that was highlighted by participants in this investigation. Although the PediCap CO_2 detector has a larger colour indicating area that is easier to view, its horizontal attachment requires manual ventilations to be delivered from the side, at a 90 degree angle. In contrast, the NeoStat CO_2 detector allows ventilations to be delivered from above, which is the traditional setup for manual ventilation in the absence of a CO_2 detector. It should also be noted, as discussed in Chapter 2, that the NeoStat CO_2 detector has only a third of the dead space that is contained in the PediCap CO_2 detector, potentially making it likely to detect changes more readily.

In conclusion, the $EtCO_2$ detectors investigated can improve manual ventilation of an infant mannequin amongst paediatric trainees. An $EtCO_2$ detector, when attached vertically in comparison to an $EtCO_2$ detector attached horizontally, appears to slightly improve efficacy and is the preferred device amongst paediatric trainees. To determine if these findings can be extrapolated to the clinical setting, further investigations are needed.

3.3. QUANTITATIVE OR QUALITATIVE $EtCO_2$ DETECTION FOR MANUAL VENTILATION: A MANNEQUIN INVESTIGATION

The results from the first investigation in this chapter demonstrated that the use of qualitative $EtCO_2$ detection during simulated PPV was preferred over standard methods of providing PPV and allowed for a greater degree of effective ventilation. Out of the two different $EtCO_2$ detectors assessed, the NeoStat $EtCO_2$ detector outperformed the PediCap $EtCO_2$ detector. With these results, as well as with the review of the $EtCO_2$ detection literature in Chapter 2, it was decided that the next step in exploring enhanced monitoring in the delivery room was the commencement of another *in vitro* investigation comparing the effectiveness of two different forms of $EtCO_2$ monitoring.

3.3.1. AIM

The aim of this investigation was to evaluate two different forms of $EtCO_2$ detection, qualitatively by means of an $EtCO_2$ detector, as well as quantitatively by means of capnography. The secondary aim was to obtain feedback on these devices from the participants in the investigation.

3.3.2. METHODS

This was a randomised crossover trial instructing participants to provide three separate two-minute periods of manual ventilation with a TPR on a low fidelity CO_2 producing mannequin, in a randomly assigned order. The TPR was configured to provide 8L of oxygen per minute, a PIP of 20 cm H_2O, and a PEEP of 5 cm H_2O throughout all participant interaction. Participants were asked to provide ventilation at an NRP standard of 40 to 60 ventilations per minute. There was approximately a one-minute period between each manual ventilation period to allow wash out of CO_2 from the mannequin.

Method one had no CO_2 detector attached to the TPR (ND), method two had a Neo-StatCO_2<Kg™ $EtCO_2$ detector attached to the TPR (DET) and method three had a Microstream® Vitastream™ CO_2 sampling line (Philips Medical Systems,

BG Eindhoven, The Netherlands) attached between the TPR and the facemask (CAP) (Figure 3.3).

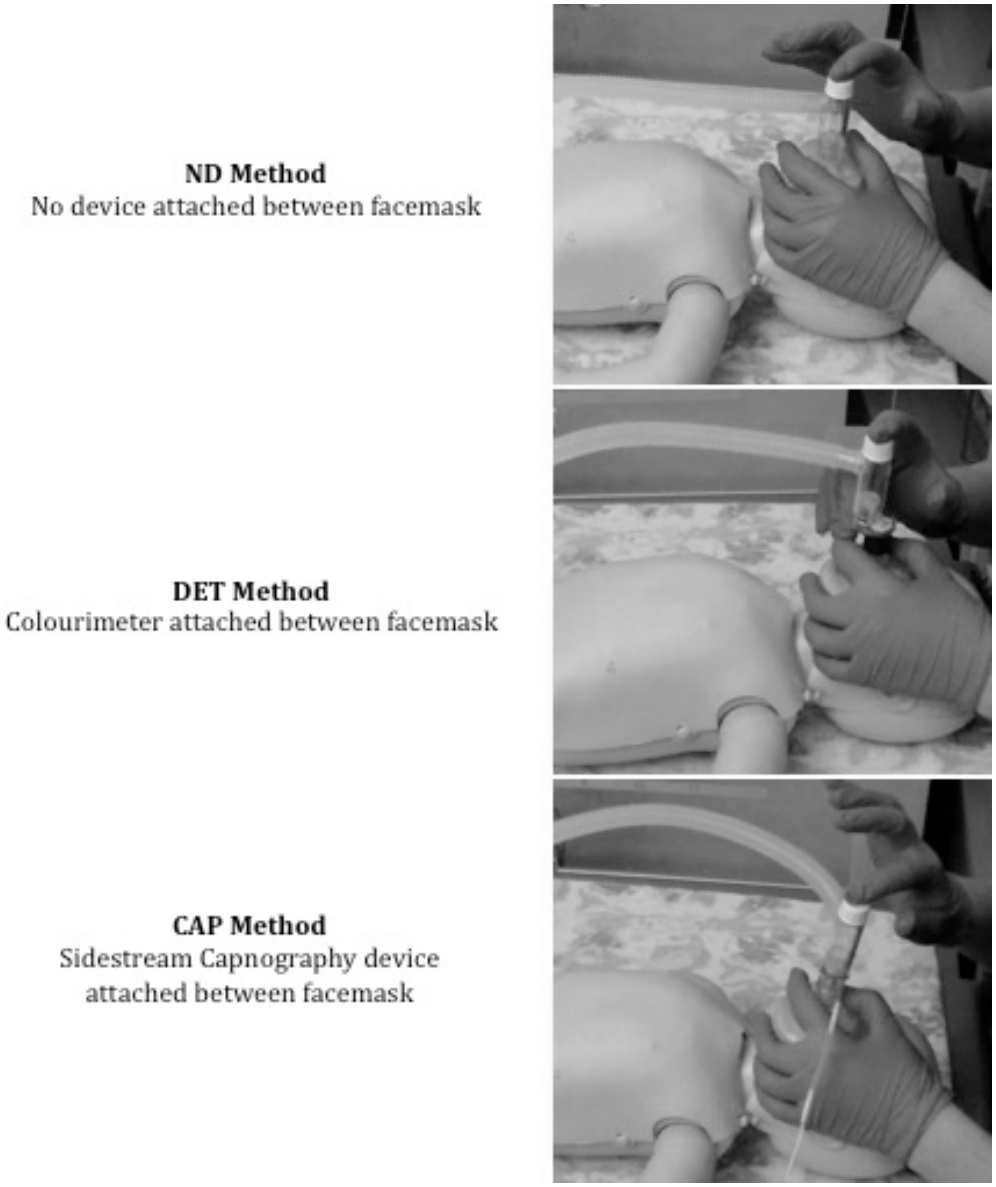


FIGURE 3.3 – THREE DIFFERENT FACEMASK CONFIGURATIONS USED DURING THE INVESTIGATION

All ventilations were video recorded from the side and retrospectively scored by two independent observers at a later date. All participants received an informal debriefing session after completion in order for the investigation to obtain feedback relating to the three different methods.

CO_2 Detector

The NeoStat $EtCO_2$ detector was used for this investigation, as part of the DET method.

Capnography configuration

The Microstream® Vitastream™ CO_2 sampling line was connected between the TPR and face mask and this sampling line was then connected to a Philips IntelliVue MP70 monitor (Philips Medical Systems, BG Eindhoven, The Netherlands) that displayed the $EtCO_2$ values as well as a waveform (Figure 3.4). This was the CAP method.

FIGURE 3.4 – VIEW OF MONITOR (FROM PERSPECTIVE OF PARTICIPANT)

Randomisation

The randomisation process was carried out with random sequence numbers in sealed envelopes. Three different numbers determined whether participants carried out the investigation in the order of ND followed by DET, then CAP; DET followed by CAP, then ND; or CAP followed by ND, then DET.

Scoring of videos

The author (GAH) and supervisors (EMD and CAR) of this thesis independently reviewed the videos. The reviewers determined the number of ventilations

provided and the number of times there was sufficient chest rise observed. Similar to the first investigation in this chapter, these video recordings were anonymous, showing only the participants hands. As a result, the reviewers of the videos were unaware of the order in which participants completed the different methods.

Ventilation was deemed to be effective if chest rise was observed during delivery of PPV. Where disagreement existed among the 3 reviewers, consensus was decided by majority decision. Percentage efficacy was determined as the number of ventilations that the reviewers deemed to be effective against the number of ventilations that were delivered overall.

All statistical analysis was performed using SPSS Statistics 22.0 (IBM, NY, USA). All tests were two-sided and a p-value <0.05 was considered to be statistically significant.

3.3.3. RESULTS

A total of 23 paediatric trainees (12 Senior House Officers [SHOs] and 11 registrars) participated in this investigation. All participants had completed NRP training within 2 years of commencement of this investigation. Participants provided a total of 6035 ventilations, of which 91.2% were deemed to be effective. There were no statistical differences in the median percentage efficacy of ventilations delivered between the three methods (ND, the DET, and the CAP being 91.0%, 93.0% and 94.0%, respectively)($p=0.72$)(Table 3.2).

There were no differences in the median efficacy of ventilations between physician grade (SHO versus Registrar) across the ND method, DET method or CAP method, although there was a slightly higher median efficacy amongst registrars across all methods (Table 3.2). The order in which participants were randomised to start the investigation with (ND method, the DET method or the CAP method) did not impact efficacy ($p = 0.601$, 0.566 and 0.208 respectively).

TABLE 3.2 – MEDIAN AND INTERQUARTILE RANGE OF EFFICACY IN VENTILATION				
	% Efficacy of Ventilation			
	No Device	Neo-Stat	Capnography	
	Median (IQR)	Median (IQR)	Median (IQR)	p-value
SHO	90.0 (86.8, 91.8)	93.0 (86.8, 95.5)	93.5 (88.5,97.8)	0.74
Registrar	92.0 (91, 93)	93.0 (90, 98)	95.0 (93, 96)	0.93
Overall	91.0 (90, 92)	93.0 (89, 97)	94.0 (92, 97)	0.72

There was no difference in the overall efficacy of ventilation when occupational grades that participants held were considered (Figure 3.5).

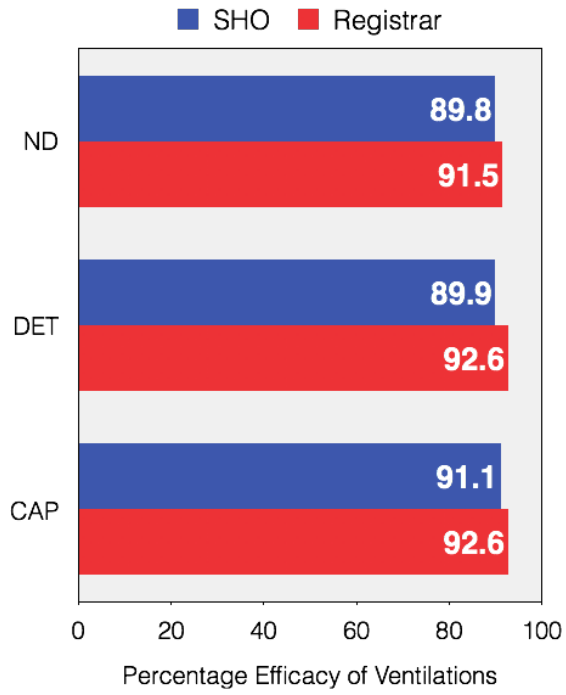


FIGURE 3.5 – PERCENTAGE EFFICACY OF VENTILATION OVER THE 2-MINUTE PERIOD

Fourteen (61%) of the trainees indicated a preference for the DET method, 8 (35%) for the CAP method and one (4%) for the ND method. However, when each individual's performance was assessed based on the method used, there was a non-significant difference between the groups whereby the CAP method

performed best in 45.4% of the cases, compared to the DET method (32% of cases) and the ND method (22.7% of cases)(p=0.42).

Participants highlighted the benefit of being able to assess the efficacy of the PPV that they were providing with an extra method as opposed to the standard method of assessing chest rise alone. Participants who favoured the DET method described the benefit of being able to maintain focus on the mannequin and colour indicator at the same time. In contrast, participants highlighted that they had to look away from the mannequin with the CAP method. However, participants who indicated a preference for the CAP method gave positive feedback to the quantitative aspect of this methodology, i.e. visualizing the ventilations provided through the waveforms on the monitor. The participant who indicated a preference for neither device highlighted the potential for complicating the stabilisation of a newborn through the addition of another indicator that had to be observed in ensuring effective PPV. Users were often uncomfortable with the change in hand positioning that was required when the $EtCO_2$ detecting devices were in place, leading to an increase in the distance between the TPR and the facemask.

3.3.4. DISCUSSION

This investigation has shown that although there was a preference for the use of $EtCO_2$ detection during PPV, in particular the use of the DET method, there was no statistical difference in efficacy of either method when used on a mannequin model. User performance is similar with or without the use of an $EtCO_2$ detecting device, confirming that $EtCO_2$ detecting methods are not associated with deterioration in performance in an *in vitro* setting. This was true for both grades of doctors included in this investigation. However, these findings may be very different from real life situations, where ventilation is dynamic and changes can occur on a breath-to-breath basis. There may be many scenarios requiring adjustment of facemask position and PPV, such as an obstructed airway.

The main preference for the DET method over the CAP method was accredited to the fact that a user's eyes were able to remain fixed on the mannequin during the DET method. This was in contrast to a user having to look away from the

mannequin during the CAP method. This is understandable as issues such as this may often accompany the implementation of disruptive technology in the medical setting. One potential way of alleviating this issue may be by the placing of a monitor close to the mannequin, perhaps next to the TPR pressure settings on the resuscitation unit, as this is an area that a user is already required to observe during the resuscitation process.

Participants highlighted having an extra indicator for a patent airway as being of particular benefit and reassurance during manual ventilation. They highlighted that this might be even more beneficial when applied to an *in vivo* setting, especially for preterm infants. Difficulty associated with observing chest rise in preterm infants during resuscitation has been described by Leone et al.[49] and Poulton et al.[52] $EtCO_2$ detection, through the use of capnography or the Neo-Stat device, may be of particular benefit for alleviating some of this difficulty.

This investigation has been the first to report on *in vitro* simulation of a capnography device during facemask ventilation of an infant mannequin model. This investigation has also highlighted many of the human factors that need to be addressed prior to any *in vivo* implementation of these devices. It is essential that healthcare personnel are appropriately trained in the use of these devices in a simulation setting prior to their introduction in the clinical care setting.

This investigation was limited by the fact that it did not assess mask leak, which is a method that may have gathered more accurate results in relation to efficacy of PPV. Similar to the first investigation in this chapter, a flow sensor was not attached due to the ergonomics of the resulting configuration that may have led to an altered indication of participants' performance. The use of a flow sensor during infant stabilisation training is currently not routine. The occurrence of chest rise and fall in the mannequin was used as an indicator of effective PPV as it was an indicator that is used in an in-vivo setting as well as being an indicator that was present across all three methods, keeping data collection consistent.

As with all mannequin-based studies, the results of this investigation may be significantly different to an *in vivo* investigation of the same nature. Participants were in a controlled simulation environment in which they were only asked to

focus on correct PPV technique. This is not the case *in vivo* as several other factors are required to be monitored by the resuscitation team. The investigation was also limited by the fact that some participants had no prior experience in the use of $EtCO_2$ detection with facemask ventilation prior to the investigation, as they would not have received this training in their NRP curriculum.

3.4. CONCLUSION OF CHAPTER

This chapter has highlighted the importance of *in vitro* investigations prior to the implementation of any new medical devices. Both investigations in this chapter identified several issues relating to disruptive technology and ergonomics. These issues may have the potential to also occur during *in vivo* use. Both the PediCap, NeoStat, and Microstream devices have been approved for use in Europe and the United States. As the NeoStat (510K number – K083056), the PediCap (K944400), and the Microstream (K121927) devices are classified as class II medical devices by the United States Food and Drug Administration (FDA)(www.fda.gov), no clinical trials were legally required to take place prior to each device's market approval. Due to the issues that this chapter has identified from end users, there may be a need to ensure mandatory simulation based *in vitro* trials, run externally from a manufacturer, prior to market approval of these devices.

Having an extra indicator for effective PPV is something that may be of benefit in clinical practice and this has also been highlighted elsewhere.[44,49,82,105-108] Coupled with a respiratory function monitor, capnography may be of benefit at highlighting airway leak and improving the effectiveness of facemask ventilation. However, comparisons between respiratory function monitors and capnographic monitors have not yet been investigated.

In summary, I have shown that trainees prefer carbon dioxide monitoring during manual ventilation. Either form of carbon dioxide detection, when compared to no carbon dioxide detection, has not shown a disimprovement in the efficacy of mask ventilation. The issues relating to disruptive technology may ultimately be resolved with increased training in the simulation setting. This chapter would suggest that these devices are unlikely to cause harm and may actually be beneficial. Consequently, future trials investigating the role of these $EtCO_2$ devices are warranted. In Chapter 4 the first *in vivo* investigation of carbon dioxide detection in this thesis will be discussed.

CHAPTER 4: INTRODUCTION OF ETCO_2 MONITORING TO THE DELIVERY ROOM

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Delivery room end tidal CO_2 monitoring in preterm infants less than 32 weeks.

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4.1. INTRODUCTION

This chapter will describe the progression made from *in vitro* investigations, completed in Chapter 3, to *in vivo* observational investigations into the use of $EtCO_2$ detection in the delivery room. Following a description of the basic respiratory terms used in these studies (Figure 4.1, Section 4.1.1), the chapter will progress through a description of the initial development of a feasibility investigation before moving on to the description of a larger observational investigation.

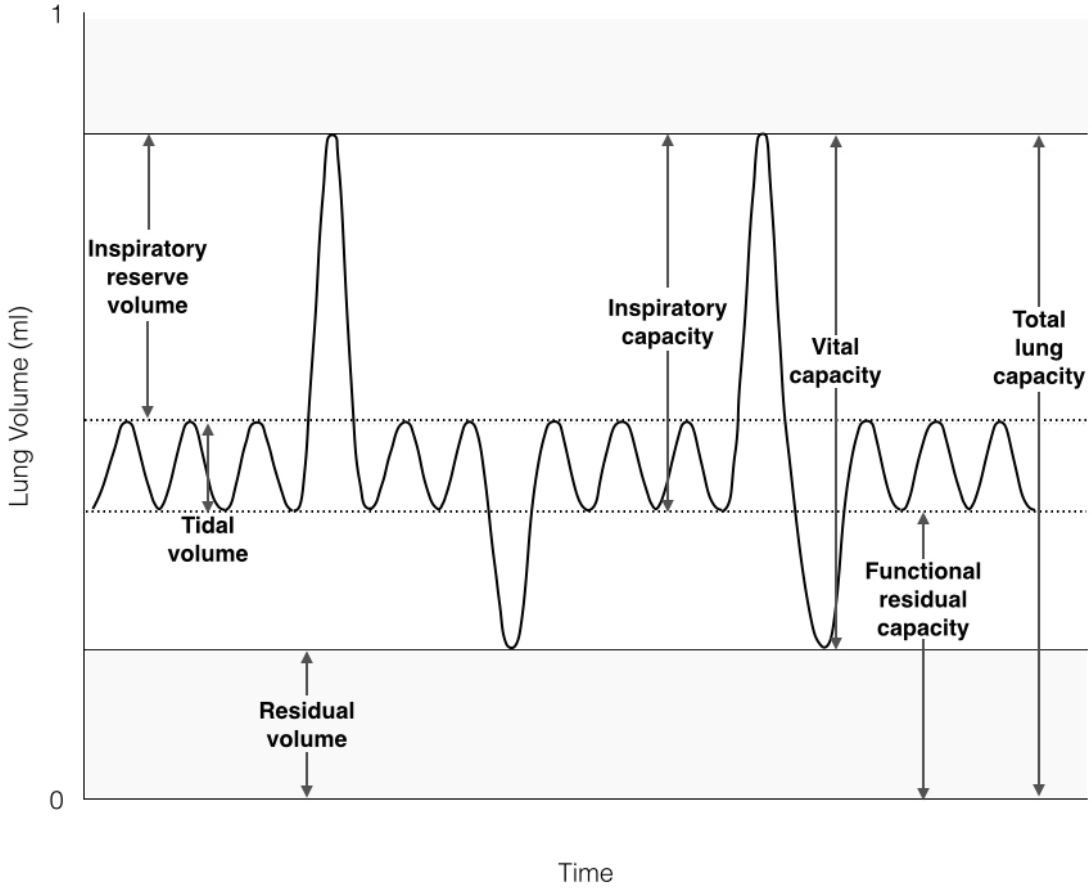

FIGURE 4.1 – REPRESENTATION OF LUNG VOLUME OVER TIME OF A HEALTHY INFANT DURING MAXIMAL INSPIRATION AND MAXIMAL EXPIRATION

4.1.1. LUNG VOLUME

The tidal volume of the lungs is the volume of air inspired or expired with each normal breath when there is no increased effort applied to the act of breathing.

The inspiratory reserve volume is the maximum volume of air that can be inhaled at the end inspiratory level. This volume is over and above the normal tidal volume and achieved through forceful inspiration. The expiratory reserve volume is the maximum volume of air that can be expired through forceful expiration after the end of a normal tidal expiration. The residual volume is the volume of air remaining in the lungs at the end of the most forceful expiration.[4]

4.1.2. LUNG CAPACITIES

The inspiratory capacity is equal to the tidal volume plus the inspiratory reserve volume. It is the amount of air inspired from the beginning of a normal expiration until the end of a maximum inhalation of the lungs. The total lung capacity is the maximum volume in which the lungs can be expanded, with the greatest possible effort. The functional residual capacity (FRC) is equal to the expiratory reserve volume plus the residual volume. It is the amount of air remaining in the lungs at the end of a normal expiration. The vital capacity (VC) is equal to the inspiratory reserve volume, plus the tidal volume, plus the expiratory reserve volume. It is the maximum amount of air that can be expelled from the lungs after first filling the lungs to their maximum extent, and then expiring to their maximum extent.[4] The VC and the FRC will be of particular importance in the assessment of $EtCO_2$ monitoring in this thesis and will be referred to several times in this chapter.

As highlighted in Chapter 1, the respiratory and cardiovascular systems are required to quickly adapt to life outside of the womb, immediately after birth.[109,110] Gas exchange in utero occurs via the placenta; after birth this occurs via an infant's lungs.[9,10] As an infant begins to breathe; lung aeration decreases pulmonary vascular resistance (PVR) and establishes a FRC within the infant's lungs.[12,13]

4.1.3. VENTILATION

Issues relating to the stabilisation of a preterm infant in the delivery room were briefly summarised in Chapter 1, with airway obstruction and subsequent effective ventilation being of particular concern. The small anatomical size of a

preterm infant can make it especially difficult to obtain a patent airway during stabilisation and large amounts of facemask leak have been described during ventilation of preterm infants.[45,46] The polyethylene bag, that will have been placed around the preterm infant immediately after delivery, often results in occlusion of the view of the preterm infant's chest. This has been shown to complicate the assessment of effective PPV during monitoring of chest rise and fall.[2,47-49]

In the first few minutes of an uncomplicated transition, the FRC of the lungs should gradually increase as an infant cries.[8,13] However, due to the immaturity typically associated with a preterm infant's lungs, this transition may need to be assisted through interventions from the stabilisation team. Some of these interventions may include; the provision of PEEP, and/or PPV[47,48,50-52], as discussed in Chapter 1.

$EtCO_2$ Detection

The *in vitro* studies discussed in Chapter 3 identified many issues relating to the use of $EtCO_2$ detection during PPV. One such issue was the potential impact of disruptive technology. All doctors involved in the *in vivo* based investigations described in this chapter were trained on, and were familiar with, the use of capnography during facemask ventilation, prior to commencement of both investigations. This was completed as a direct result of the investigations in Chapter 3.

CO_2 control by an infant is important as hypocapnia may contribute to lung injury[111] and periventricular leukomalacia (PVL)[112,113], whilst hypercapnia may contribute to an overall increase in cerebral blood flow leading to an increase in the risk of intraventricular haemorrhage (IVH).[114,115]

Although there is limited data available suggesting an improvement in short term outcomes from the use of $EtCO_2$ detection during facemask ventilation, the *in vitro* studies suggested that users tend to provide a higher degree of effective ventilation when using an $EtCO_2$ detector. The investigations also suggested that there was no dis-improvement in the degree of effective ventilation, a factor equally as important during commencement of any *in vivo* investigations. Similar

results were drawn by Yee Kong et al. who found that although there were no statistically significant improvements in short term outcomes from the use of $EtCO_2$ detection in the delivery room, there was no disimprovement.[79]

In the limited investigations available, $EtCO_2$ levels have been shown to initially rise before reaching a relative maintained level within the first few minutes of life, in a preterm infant.[79,116] Thus, $EtCO_2$ monitoring may be an early indication of lung expansion and may help to guide successful respiratory support in the delivery room.[80,86]

The investigations discussed in this chapter are observational in nature and focus on assessments of the overall utility of $EtCO_2$ monitoring of preterm infants in the delivery room. These investigations will also build on the limited knowledge of the physiological changes experienced by a preterm infant immediately after birth, in the context of $EtCO_2$ production and elimination within the lungs.

4.2. INVESTIGATION OF THE FEASIBILITY OF ENHANCED MONITORING IN THE DELIVERY ROOM

I have previously shown that that the use of $EtCO_2$ during PPV might lead to an improvement in efficacy as well as being an extra assessment tool, which participants favoured (Chapter 3). However, participants, primarily relating to the viewing of the capnography monitor, expressed some concerns. These concerns were relatively minor, such as viewing of the monitor display often being problematic. However, it was possible to readily develop solutions such as placing the monitor closer to the team member assisting an infant's airway. Also, no deterioration in performance was observed during PPV, therefore, it was felt that an *in vivo* based feasibility investigation into the use of capnography in the delivery room was now warranted. As well as briefly assessing the role of $EtCO_2$ detection during the stabilisation of preterm infants, via the feasibility nature of the investigation, it was hoped that any potential issues that may arise could be assessed prior to the completion of any further delivery room based $EtCO_2$ investigations.

4.2.1. AIM

This observational investigation aimed to assess the introduction of $EtCO_2$ monitoring for preterm infants immediately after birth, in the delivery room.

4.2.2. METHODS

This investigation was approved by the Clinical Research Ethics Committee of the Cork Teaching Hospitals (CREC) and subsequently commenced in CUMH in January 2013 (CREC reference number - ECM 4 [e] 05/02/13][Appendix D]).

Consenting Process

Any infant expected to be delivered preterm (less than 32 weeks gestation) was eligible for inclusion in this investigation. Informed written consent was obtained from parents during the antenatal period. Exclusion criteria included oligohydramnios (amniotic fluid index <5) and any expected congenital

anomalies of the infant, such as congenital diaphragmatic hernia, airway anomalies, and/or heart disease.

Investigation Awareness

This was the first delivery room based investigation assessing the use of new methods of monitoring of preterm infants to take place in CUMH. Through structured presentations to all medical staff working in the NICU, initial awareness of the investigation was developed. The time critical nature and importance of the investigation requiring consent to be obtained during the antenatal period was emphasised during these presentations.

The standard process for the neonatal team to be informed of any expectant mother, of a preterm infant, is through contact from staff of the high dependency unit (HDU). Staff of the HDU typically contacts the NICU nursing station and/or the neonatal registrar on-call phone. As a result of this process, neonatal staff in the NICU may often become aware of any mother expecting to deliver a preterm infant, a number of hours in advance. This was a time period in which awareness of the investigation was seen as being particularly important. To supplement the presentations that were initially given to all medical staff, and to also act as a reminder of the ongoing investigation, posters outlining the investigation criteria were placed close to the NICU phone. The on-call research phone number was placed on this poster as well as entered into the phone book of the neonatal registrar on-call phone. This was completed with the aim of making the process of the NICU staff contacting the research phone as simple as possible and to become part of normal procedure.

Monitoring Equipment Used

A Microstream® Vitastream™ CO_2 sampling line connected to an external sidestream module on a Philips Intellivue MP70 monitor was the sidestream capnography system employed for this investigation. The Microstream® CO_2 Filterline® device was attached between the TPR and the facemask, or ETT, in order to provide the user with $EtCO_2$ values as well as an $EtCO_2$ trace. This device adds an increased dead space volume of less than 0.5 mls to the system. All monitoring equipment was transported from the NICU by a member of the

research team and configured in the delivery room prior to delivery of the infant. This member was not a member of the medical team and had no direct interaction in the stabilisation of the infant. Where consent was obtained, the stabilisation process was video recorded. Recordings were placed on a secure hard drive within the neonatal research room in CUMH as well as on a secure server hosted by UCC.

TPR configuration

The default settings on the TPR, prior to delivery of the infant, were set at a gas flow of 8 L/min, a PIP of 20 cm H_2O, and a PEEP of 5 cm H_2O. The maximum attainable PIP pressure was limited to 30cm H_2O, as is routine practice for all preterm deliveries at CUMH. Once an infant was placed on the resuscitation unit, $EtCO_2$ monitoring commenced and was completed for the time that the infant remained in the delivery room.

4.2.3. RESULTS

10 infants were enrolled in this feasibility investigation. A number of issues were highlighted.

Investigation Awareness

Although NICU staff were aware of the investigation and contacted the on-call phone the majority of times, once made aware of a potential delivery, there were some instances where the on-call phone was not contacted. During preparation for delivery of a preterm infant, many resources may often be required within a short time period. At this time areas such as research, that aren't the priority in terms of clinical care, may be understandably overlooked.

It was also found that, in some instances, the NICU staff members were not made aware of the expectant mother by staff in the HDU until a very short amount of time prior to delivery. This resulted in the research phone then being contacted within a short time period of delivery. With the nature of the antenatal consenting process, it was not appropriate to discuss the investigation with

parents in such a short time period and therefore potential participants were not enrolled.

Consenting Process

No mother approached for participation in this investigation declined consent.

Logistics

In the NICU of CUMH, three portable Philips Intellivue MP70 monitors are available. The use of these monitors is typically required for infants that are in a location where the monitor that is closest to them is unable to perform certain parameters of physiological monitoring, such as ECG and capnography. At times, once an infant no longer requires extra physiological monitoring, he/she remains on the Philip Intellivue monitoring system whilst receiving the more standard parameters on this device such as SpO_2 monitoring. This process is typically completed in order to minimize disruption associated with moving monitoring equipment around the NICU environment.

As a result of this, there were times when no machine was readily available to be transported to the delivery room to perform $EtCO_2$ monitoring. If this situation did arise, then liaising with nursing staff within the NICU allowed the infant to be safely disconnected from the Philips Intellivue MP70 and connected to the monitor that he/she was on prior to any additional monitoring being required.

Video

Video recording during stabilisation in the delivery room was not routine practice in CUMH prior to commencement of this investigation. As a result of this, the introduction of video recording raised several issues, mainly relating to data protection as well as patient/staff anonymity. Some medical staff members initially raised concerns about visual and audio identifiers of staff members being available in video recordings. From a legal standpoint, staff were concerned as to how the video recordings would be used as well as who would have access to these videos. Parents of infants enrolled had similar concerns primarily relating

to identification of their infant, storage of the video recordings, and who would have access to the recordings.

Transfer of data

Although the primary aim of this investigation was to assess the feasibility of enhanced monitoring in the delivery room, physiological data was also obtained through the monitoring performed on participants. This data is included in the analysis performed in the MODS investigation that will be discussed later in this chapter.

Data Transfer

It was found that the only possible methods in transferring the data from the Philips Intellivue monitor were as follows:

1. The monitor was transferred out of the delivery room.
2. Using the review function within the monitor, a member of the research team scrolled through the physiological readings. These readings were displayed in 12-second by 12-second periods and the member simultaneously video recorded the data being displayed whilst scrolling through the readings.
3. These video recordings were then transferred to a laptop and the readings collected by the video were manually inputted into an excel spread sheet in preparation for future analysis

4.2.4. DISCUSSION

Overall it was found that providing this enhanced monitoring in the delivery room was feasible, however, it was evident that several issues needed to be resolved for more efficient completion of any further delivery room based investigations.

Investigation Awareness

The continued building of investigation awareness is an important factor during every research investigation. Due to the nature of this investigation and the time

frames required to obtain antenatal consent, early identification of eligibility for participant enrolment was of continuing importance. As it was evident that at times NICU staff were not made aware of an expectant mother until a short time period prior to delivery, it was felt that investigation awareness should also be targeted towards staff members within the HDU. It was hoped that these staff members could subsequently contact the investigation on-call phone soon after when an expectant mother arrived to the HDU. As well as this, frequent visits to the nursing station in the HDU were commenced to liaise with staff in order to 1) identify any expectant mothers of preterm infants and 2) continually promote investigation awareness amongst HDU staff.

Consenting Process

Although there were no incidences of refusal of consent during this investigation it was clear that there might be the potential for issues to arise, relating to consent, in future investigations.

During the time spent after initial admission to the HDU, a mother may be provided with a lot of information from several members of a multidisciplinary healthcare team, as is part of routine care. This information primarily relates to the care that her and her infant will receive and, unfortunately, this information may need to be delivered in a relatively short period of time. The initial stress of being admitted to a maternity hospital with the possibility of delivering a preterm infant, coupled with regular interaction with many disciplines of healthcare staff, may be intimidating and subsequently increase stress levels of the mother.

For this investigation, informed consent was also required during this time, potentially adding an extra factor of stress to a mother's experience. Although no parents approached for this investigation declined participation; it was felt that, if possible, obtaining consent prior to an expectant mother entering the HDU might help in decreasing the amount of stress that the consenting process would likely cause for the parents.

Similar to the resolution devised to increase investigation awareness, a resolution for beginning the consenting process as early as possible was also identified. Ward 2 south of CUMH is an antenatal ward that many expectant mothers may

be admitted to for observational reasons during their pregnancy. Completing frequent visits to this ward facilitated earlier consenting of potential participants. This allowed the research team to identify mothers that may have initially been admitted for observational reasons, however, were beginning to show clinical signs that may warrant being transferred to the HDU due to a risk of a preterm delivery.

In instances where a mother was admitted directly to the HDU, this consenting at an advanced stage was obviously not possible. In these instances another solution was devised. Upon arrival to the HDU a mother is typically introduced to a consultant neonatologist and he/she then informs the mother of the role that the neonatal team will have in the delivery room. It was felt that approaching the mother soon after this consultation may allow for a better understanding of the research investigation by the mother, as the process of delivery room care would have already been explained. This would also allow for the mother to be introduced to all neonatal aspects of her care within a more focused time frame as opposed to having healthcare personnel from different disciplines providing her with information in between the discussion with the consultant neonatologist and the discussion with neonatal research staff. It was hoped that this would therefore reduce some of the stress that may be experienced by the mother, as well as allowing for a greater understanding by the mother, during discussion of the research investigation.

Logistics

As discussed, there were times when the more routine functions on a Philips Intellivue MP70 were being employed for the monitoring of an infant in the NICU. In order to avoid the need of rotating monitoring devices in a short time period, it was found that visiting the NICU at a much earlier stage and identifying these monitors, to subsequently substitute them with a routine monitor that could provide the monitoring parameter required, generally resolved the issue. Through cooperation from the nursing staff in the NICU, it was then possible to make a Philips Intellivue MP70 monitor readily available for use in the delivery room. It was clear that this process would allow for a smoother acquisition of relevant monitoring equipment in future studies.

Video

Although none of the parents approached for this investigation declined participation, it was felt that parents, when being informed about the video recording aspect of this investigation, understandably displayed some anxiety. In recent years there have been several breaches of data protection in clinical research as well as routine clinical care, both nationally and internationally, and the media has generally reported on these breaches. As a result of this, it was felt that any future investigations should emphasise the aspect of video recording as an additional, and optional, component of the investigation. Therefore parents would be allowed to opt out of the video recording aspect of the investigation whilst still providing consent for the rest of the investigation.

Transfer of Data

Although programs exist to obtain the data from this monitor in one-second by one-second time periods, these programs are expensive (€1000-€3000 "per machine"). The purchase of these programs was not felt to be feasible as 1) lack of funding meant it was not possible to purchase a contract and 2) if the contract were to be purchased for any less than 4 machines (total amount of Philips Intellivue monitors available for use), it would limit the amount of monitors available for use during the investigation subsequently creating greater difficulty in transporting a suitable Philips Intellivue monitor from the NICU to the delivery room. This investigation also began a process for utilising of an existing Moberg CNS monitor (Moberg Research Inc, Ambler, PA, US), primarily used for electroencephalography (EEG) monitoring in the NICU, for compiling the delivery room data in real time. This monitor had the function of merging many parameters from different monitors into one single output, however, could not obtain $EtCO_2$ readings from the Philips Intellivue Monitor. This feasibility investigation highlighted a potential avenue for coordination with the manufacturer in order to provide a software adjustment that would allow for the acquirement of $EtCO_2$ readings.

4.2.5. CONCLUSION

This investigation has found that enhanced monitoring in the delivery room is feasible. The majority of the minor issues that were observed in this investigation were primarily related to the research aspect of the monitoring. However, a resolution for each of these issues was also of high priority in order to allow for a smoother completion of future research investigations. Any solutions relating to issues observed in this feasibility investigation were employed in all other delivery room based investigations discussed in this thesis.

4.3. ENHANCED MONITORING IN THE DELIVERY ROOM – THE MODS INVESTIGATION

Combining the results of the feasibility investigation (Section 4.2), with the results on improved PPV observed during *in vitro* capnography investigations (Chapter 3), allowed for a delivery room based investigation on the use of capnography to be designed. This investigation is a more in depth investigation on the introduction of $EtCO_2$ detection in the delivery room.

4.3.1. AIM

The aims of this investigation were to:

1. Examine the potential use of capnography as a means of measuring $EtCO_2$ levels during delivery room stabilisation in preterm infants.
2. Describe $EtCO_2$ levels in both intubated and non-intubated preterm infants during the first 10 minutes of life.
3. Examine the short-term outcomes, by means of incidences of hypocapnia and hypercapnia on admission to the NICU, among preterm infants who had $EtCO_2$ monitoring in the delivery room compared to infants who did not.

4.3.2. METHODS

This single centre observational investigation was approved by CREC, was commenced in the delivery room of CUMH in June 2013, and lasted until June 2014 (CREC reference number ECM 3 [o] 06/08/13 [Appendix E]). The same inclusion and exclusion criteria used in the feasibility investigation were also employed for this investigation. Delayed cord clamping was not routinely performed on infants in this investigation

Again, a Microstream® Vitastream™ CO_2 sampling line connected to an external sidestream module on a Philips Intellivue MP70 monitor was the sidestream capnography system employed for this investigation. The system was configured in the same way as in the feasibility investigation, i.e. the Microstream® Vitastream™ CO_2 sampling line was attached between the TPR and the

facemask, or ETT, in order to provide the user with $EtCO_2$ values as well as an $EtCO_2$ trace.

Users were instructed to obtain capnographic waveforms, but not to interact with the absolute values displayed. All users were familiar with the system and had undergone a training session in a simulation lab on the provision of PPV with the capnography system in place. This training session was designed as a direct result of the findings from the *in vitro* investigations discussed in Chapter 3.

The default settings on the TPR, prior to delivery of the infant, were set at a gas flow of 8 L/min, a PIP of 20 cm H_2O, and a PEEP of 5 cm. The maximum attainable PIP pressure was limited to 30cm H_2O, as is routine practice for all preterm deliveries at CUMH. Once an infant was placed on the resuscitation unit, $EtCO_2$ monitoring commenced and was completed for the time that this infant remained in the delivery room.

A member of the research team downloaded the $EtCO_2$ values from the Philips Intellivue monitor after an infant was transferred to the NICU, through the same methods of data transfer employed in the feasibility investigation. These data were then matched in time, by thesis author (GAH) and thesis supervisor (EMD), to video recordings of the infant that were obtained during the time spent in the delivery room. As the $EtCO_2$ data and video were synchronised in time, it was possible to exclude $EtCO_2$ readings that were inaccurate, as a result of loss of $EtCO_2$ signal, loss of seal, or gas leak around the facemask.

Median and interquartile range (IQR) was used to summarise $EtCO_2$ values determined over the first 10 minutes after birth. In addition, features relating to the linear increase of $EtCO_2$ were assessed using the linear least-squares method to fit a line to the first four minutes of $EtCO_2$ recordings. Due to the variability that existed in the first 4 minutes of data, the relative stabilisation of $EtCO_2$ production thereafter, and the explorative nature of this investigation, it was felt that a line fitted to the first 4 minutes of data was more appropriate in providing a representation of $EtCO_2$ production immediately after birth. From this line, the slope, intercept, and IQR about the line was calculated. These features were then used to summarise the time varying nature of $EtCO_2$. Thus, each infant's $EtCO_2$

was summarised by 5 features; median, IQR, and slope of the $EtCO_2$, as well as IQR and intercept of the line fitted to the $EtCO_2$ trends. All median values were reported in this investigation as "median (IQR)".

To compare features between the intubated and non-intubated groups, the area under the operating characteristic curve (AUC) was used as a measure of effect size.[117] AUC values are between 0–1, where 1 indicates complete separation between groups and 0.5 indicates no separation; values from 0–0.5 indicate separation but in a reverse direction. A 95% confidence interval for the AUC was generated using a bootstrap approach with 1000 iterations.[117] In addition to the effect size measure, the Mann–Whitney U-test was applied to the data with the value $p < 0.01$ indicating statistical significance, adjusted using a Bonferroni approach for the 5 comparisons. This analysis was performed using Matlab (version R2013a, The MathWorks, Inc., MA, USA), by Dr. John O'Toole.

The partial pressure of CO_2 in blood (PCO_2) was obtained from the infants who received $EtCO_2$ monitoring in the delivery room less than one hour from the time of birth. To compare to a group of infants with no $EtCO_2$ monitoring performed in the delivery room, PCO_2 data obtained from a previous cohort of infants was used. The latter cohort of infants was recruited for a blood sampling investigation on preterm infants that required PCO_2 analysis to be completed within one hour from time of birth (completed in CUMH from December 2012-April 2013). These infants did not have $EtCO_2$ monitoring in the delivery room. This investigation had the same inclusion and exclusion criteria as the MODS investigation and there was no change in overall resuscitation training or practice during the timeline of either of these investigations. Initial PCO_2 readings were deemed as being within the range of normocapnia if they fell between 5 kPa and 8 kPa.

Statistical analysis for the comparisons of PCO_2 values between these groups was performed using SPSS 21.0 (IBM, NY, USA). Comparative tests of medians were completed using Mann-Whitney U-tests and a $p < 0.05$ was deemed as being statistically significant. Comparative tests on the number of infants falling within the target range, the number of infants who were intubated, and the male/female distribution, were completed using Fisher's Exact tests and a p<

0.05 was deemed as being statistically significant. Cross-tabulation determining the effect of blood gas type on whether or not infants fell within the accepted range were completed using a Cramer's V test with a $p<0.05$ deemed as being statistically significant.

4.3.3. RESULTS

As the same data parameters were collected in both this investigation as well as the feasibility investigation, data analysis were performed on the data from both investigations together i.e. the data analysed for this investigation also includes data obtained from the feasibility investigation.

Feasibility

A total of 59 patients were consented in this convenience sample. Eleven patients subsequently delivered beyond 32 weeks' gestation and in 4 cases, a member of the research team was unavailable to attend the delivery, therefore 44 infants were included. All mothers of these infants received at least one dose of antenatal steroids prior to delivery. Of these 44 infants, 11 received PEEP and PPV, however, were subsequently intubated as a result of on-going respiratory distress in the delivery room. Of the 33 non-intubated infants, PEEP as well as PPV was provided to 11 infants. PEEP, alone, was provided to 22 separate infants. Of the total 44 infants, 39 (88.6%) infants had $EtCO_2$ readings suitable for analysis. Operator error in connecting the capnography sampling line to the Philips Intellivue monitor occurred in two instances; data retrieval from the Philips Intellivue monitor was unsuccessful in two separate instances, and a sampling error occurred on the capnography attachment for the monitor in another instance.

Trends

Thirty-nine recordings from infants who received $EtCO_2$ monitoring in the delivery room were available for trend analysis. $EtCO_2$, levels increased linearly initially, and subsequently levelled off (Figure 4.2). When analysed separately, similar characteristics were found in the trends of infants who were not intubated (n=29) as well as those who were intubated (n=10) (Figure 4.3 and Figure 4.4,

respectively). Of infants who were intubated, intubation occurred within 4 minutes of life and occurred as a result of clinical assessment by the stabilisation team in accordance with NRP guidelines for intubation.

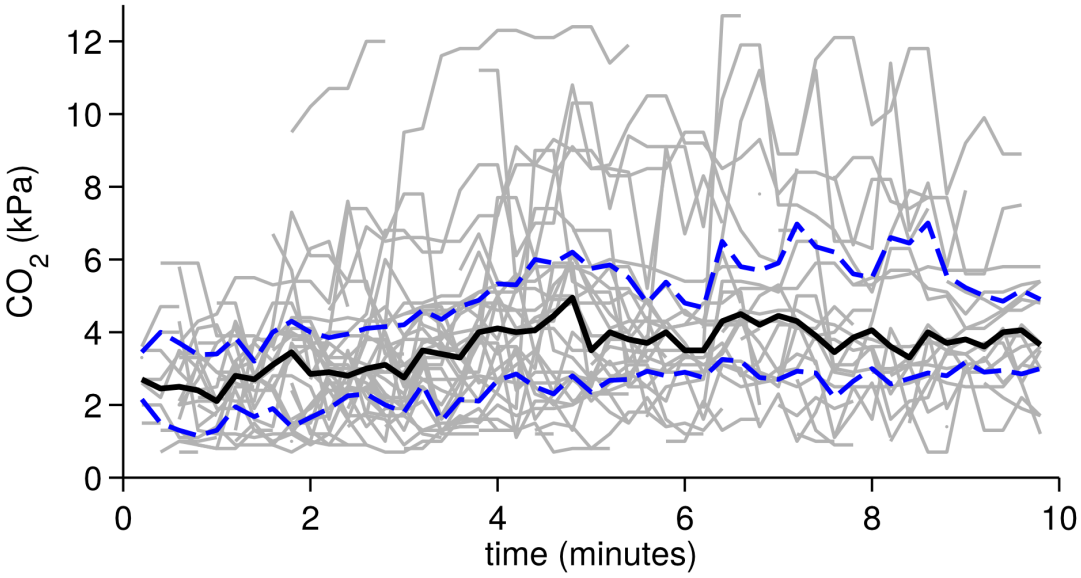

FIGURE 4.2 – $ETCO_2$ TRENDS FOR 39 PRETERM INFANTS. BLACK LINE: MEDIAN; BLUE LINES: INTERQUARTILE RANGE

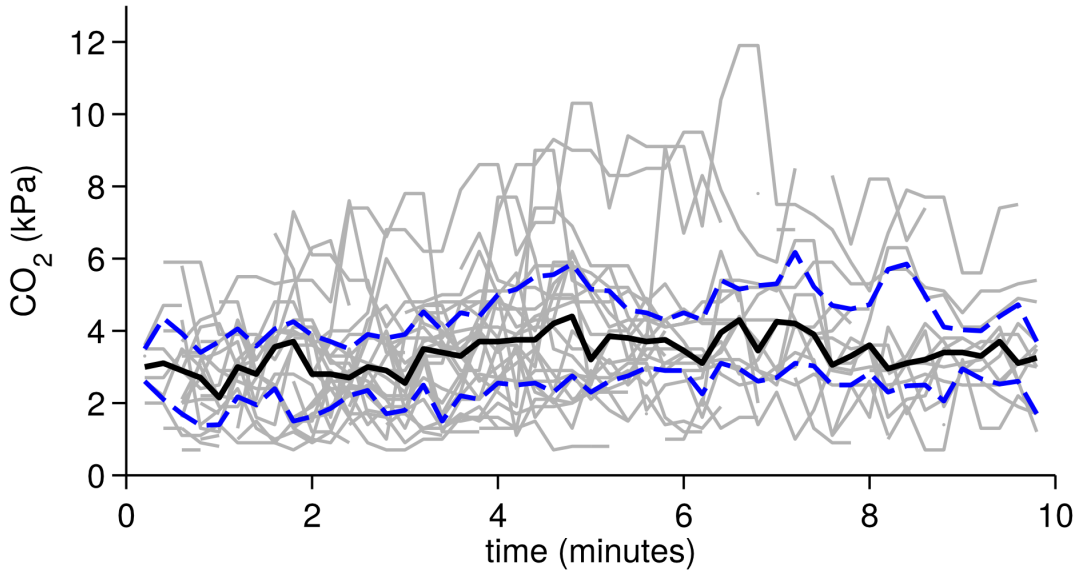

FIGURE 4.3 – $ETCO_2$ TRENDS FOR INFANTS THAT WERE NOT INTUBATED. BLACK LINE: MEDIAN; BLUE LINES: INTERQUARTILE RANGE.

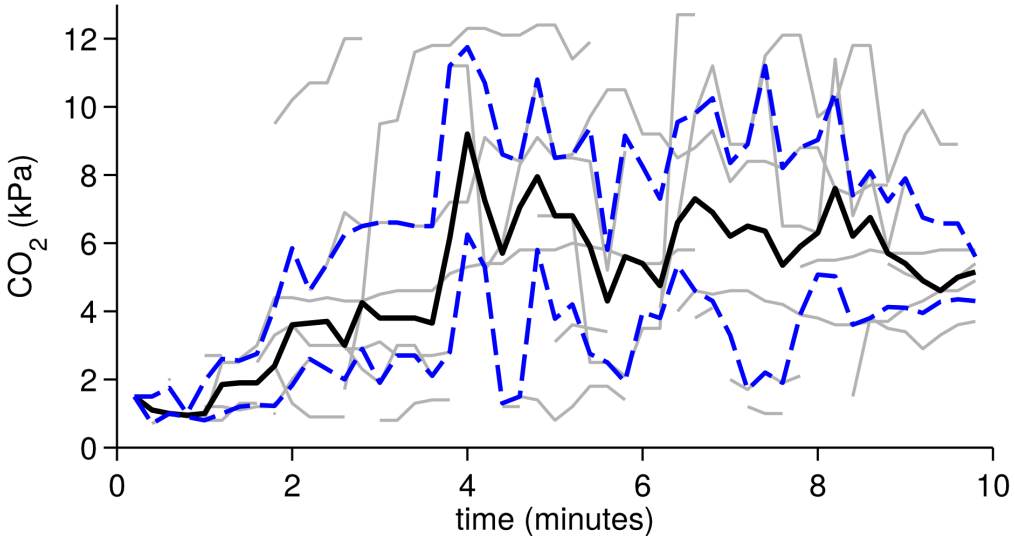

FIGURE 4.4- $ETCO_2$ TRENDS FOR INFANTS THAT WERE INTUBATED. BLACK LINE: MEDIAN; BLUE LINES: INTERQUARTILE RANGE.

When all five features from the $EtCO_2$ trends were compared between groups (intubated and non intubated), no difference was found in the level of the linear $EtCO_2$ increase (median line slope of 0.41 [0.85] versus 0.24 [0.52], p=0.05) (Figure 4.5). A significant difference was seen between groups for $EtCO_2$ IQR (2.3 [2.8] versus 1.2 [0.7] kPa, p=0.02) and $EtCO_2$ line IQR (0.58 [0.33] versus 0.93 [0.89] kPa, p=0.008) (Table 4.1). Non-intubated infants had an $EtCO_2$ median line intercept value of 2.3 (1.9) kPa that increased to between 3 and 4 kPa within the initial minutes after birth (Figure 4.3). In intubated infants, the $EtCO_2$ median line intercept value was 1.9 (2.7) kPa, which subsequently increased above 6 kPa (Figure 4.4). Overall, intubated infants had higher median $EtCO_2$ values compared to non-intubated infants (4.7 [5.1] kPa versus 3.2 [1.6] kPa, p=0.05) (Figure 4.5).

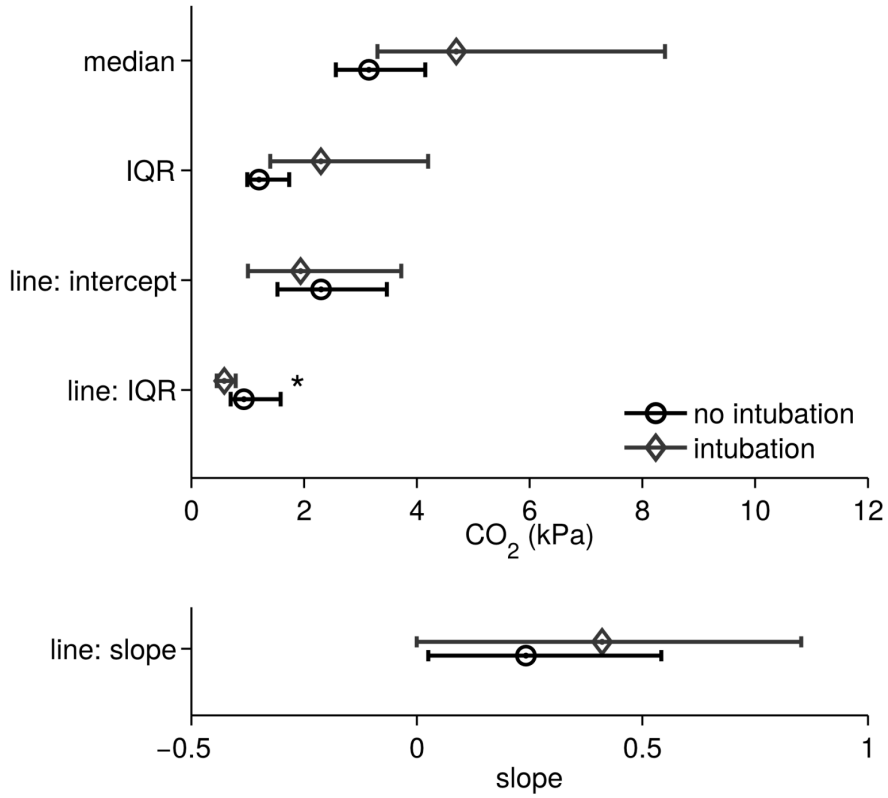

FIGURE 4.5 – FEATURES OF $ETCO_2$ COMPARING INFANTS IN NON INTUBATED GROUPS AND INTUBATED GROUPS. CIRCLES AND DIAMONDS REPRESENT MEDIAN VALUES AND LINES REPRESENT IQR. STARS INDICATE STATISTICAL SIGNIFICANCE AT P<0.01.

TABLE 4.1 COMPARISON OF $ETCO_2$ FEATURES IN INTUBATED AND NON INTUBATED PRETERM INFANTS

Feature	Non Intubated (n=29)	Intubated (n=10)	*p-value*	AUC (95% CI)
Median (kPa)	3.2 (1.6)	4.7(5.1)	0.050	0.71 (0.46-0.90)
IQR (kPa)	1.2 (0.7)	2.3 (2.8)	0.020	0.75 (0.55-0.92)
Line: Intercept (kPa)	2.3 (1.9)	1.9 (2.7)	0.728	0.54 (0.30-0.77)
Line: IQR (kPa)	0.93 (0.89)	0.58 (0.33)	0.008*	0.79 (0.61-0.94)
Line: Slope	0.24 (0.52)	0.41 (0.85)	0.417	0.60 (0.36-0.81)

*Statistical significance

Short-term outcome comparison

Forty-eight infants with a mean gestational age of 29 (+1/7) weeks did not have $EtCO_2$ monitoring in the delivery room (non-monitored group). The percentage of infants who required intubation in this group was similar to those who received continuous $EtCO_2$ monitoring in the delivery room (31.3% versus 22.7% p=0.150).

47.9% of infants in the non-monitored group had an acceptable PCO_2 reading within one hour of birth, compared with 56.8% in the monitored group (p=0.396) (Table 4.2). The distribution of blood gas sample methods in both groups did not impact whether the readings were within the acceptable range or not (Table 4.3).

TABLE 4.2 - COMPARISON OF FEATURES BETWEEN INFANTS THAT RECEIVED $ETCO_2$ MONITORING AND INFANTS THAT DID NOT

Feature	No $EtCO_2$ Monitoring (n=48)	With $EtCO_2$ Monitoring (n=44)	*p-value*
Median Birth weight (g)	1300 (IQR: 917, 1455)	1225 (IQR: 930, 1540)	0.713
Median Gestational age (weeks)	29+1 (IQR: 27, 31)	29+1 (IQR: 26+5, 30)	0.860
1st PCO_2 Value (Median) kPa	7.6	7.45	0.365
Within Target Range	47.9%	56.8%	0.396
Infants intubated	31.3%	22.7%	0.150
Sex M/F	68%/32%	60%/40%	0.440

TABLE 4.3 – DISTRIBUTION OF BLOOD SAMPLES OBTAINED FROM INFANTS WHO RECEIVED $ETCO_2$ MONITORING AND INFANTS THAT DID NOT.				
Group	**Arterial**	**Venous**	**Capillary**	***p-value***
No $EtCO_2$ Monitoring (n=48)	21	16	11	0.247
With $EtCO_2$ Monitoring (n=44)	13	18	13	0.324

4.3.4. DISCUSSION

This investigation has documented the evolution of $EtCO_2$ in a cohort of preterm infants over the first 10 minutes of life. The findings of a very low initial value, followed by an increase over the next few minutes are most likely consistent with increased alveolar gas exchange as lung recruitment and increasing gas exchange surface area occurs, in conjunction with increasing vital capacity of the lungs as the preterm infant adapts to extra uterine existence.

Two previous groups have reported on $EtCO_2$ values during adaptation in preterm infants. Hooper et al. highlighted the increase in $EtCO_2$ values over the first few minutes of adaptation in animal models and a cohort of 10 preterm infants.[116] The MODS investigation highlights a similar trend in $EtCO_2$ values, however, through analysis of a larger number of preterm infants. In a recent RCT in the delivery room, Kong et al. alluded to slowly increasing $EtCO_2$ values over the first 3.5 minutes of life in a cohort of 48 infants.[79] As the latter trial's primary aim was to focus on investigating the utility of $EtCO_2$ monitoring in the delivery room, analysis on $EtCO_2$ production was only completed through averaging the last 5 breaths at the end of the resuscitation. The MODS investigation has described the evolution of $EtCO_2$ in the first few minutes of life in greater detail through assessing a greater number of features for a longer period of time.

The MODS investigation has compared $EtCO_2$ values in infants who were intubated compared with those who were not. It was found that median $EtCO_2$ values were higher in infants who were intubated compared to those who were not (4.7 [5.1] kPa versus 3.2 [1.6] kPa). However, after adjusting for multiple comparisons, there was no statistical significance (p=0.05). As this investigation

did not measure the percentage mask leak, how leak might have affected the absolute $EtCO_2$ values cannot be accounted for. When the median line intercept value was calculated, no statistical difference was found between these extrapolated values in infants who were intubated compared to those who were not (1.9 [2.7] kPa versus 2.3 [1.9] kPa, p=0.728).

The slope of the line is likely to represent the subsequent rate of change in $EtCO_2$ values over the first 4 minutes of life and, again, no significant difference was found between those who were intubated compared to those who were not (line slope 0.41 [0.52] versus 0.24 [0.52], p=0.417). Whilst neither of these two comparisons were statistically significant, the initial lower intercept value and the subsequent higher slope of the line in the group who were intubated, as well as the difference in the line IQR between intubated and non intubated infants (p=0.008), does suggest a difference between these two groups clinically. It is unlikely that ineffective ventilation due to mask leak or airway obstruction was the cause as the $EtCO_2$ values were higher in those who were subsequently intubated; lower values would be expected if it was leak or obstruction related. It is likely that the values represent ineffective adaptation, secondary to underlying lung immaturity overall. Kang et al. have reported similar results in initially low $EtCO_2$ values produced in preterm infants receiving PPV possibly being an indication of ineffective adaptation immediately after birth.[80] Either way, the MODS investigation has shown that $EtCO_2$ monitoring in the delivery room may be a useful tool in confirming effective PPV. $EtCO_2$ detection may also act as an early indicator of impaired lung function and respiratory control in preterm infants, necessitating further respiratory intervention such as intubation.

Prior to commencement of this investigation, it was postulated that infants receiving $EtCO_2$ monitoring in the delivery room would more likely have PCO_2 values in the acceptable range compared to infants not receiving $EtCO_2$ monitoring. This did not prove to be the case, but neither did the introduction of $EtCO_2$ monitoring result in a worse outcome, as determined by an excess of abnormal CO_2 values. This is an important finding. The investigation has shown that the introduction of a new technology into the delivery room was not associated with a worse outcome when compared to the standard of care presently used in the delivery room. This finding should be seen as a positive

outcome of the investigation. Similar to this investigation, Kong et al. found no improvement in PCO_2 levels in preterm infants receiving $EtCO_2$ monitoring in the delivery room, however, this group did note the benefits of having an extra monitoring tool during resuscitation, namely the real time physiological parameter display provided.[79] PCO_2 levels are only a single endpoint in a complex physiological process during infant stabilisation. Improvements in short-term outcomes should be investigated in order to effectively determine the role that $EtCO_2$ monitoring may have in the delivery room. Examples of such outcomes may relate to the instances of delivery room interventions. The impact that the interpretation of $EtCO_2$ readings and waveforms may have on the interpretation of other physiological markers such as SpO_2, and heart rate, as well as on the continuous monitoring of face mask seal, should also be investigated.

Although users were not instructed to interpret the $EtCO_2$ during the stabilisation process and to only obtain capnographic waveforms, the importance of correct interpretation of $EtCO_2$ values during stabilisation is something that must be considered. As with all technology that may be introduced to a clinical setting such as the delivery room, it is important that all end users receive formal training in the use and interpretation of the technology prior to its introduction.[86] This factor has also been emphasised by the investigations in Chapter 3.

$EtCO_2$ detection is feasible in the delivery room setting. Although there were some issues with data retrieval, relating to the downloading of $EtCO_2$ data from the monitor, real-time $EtCO_2$ data was obtained in 90% of cases. Operator error in relation to preparation of the machine, that occurred in two of the stabilisations, highlights the need for on-going training in the use of any new technology during, as well as prior to, implementation.[86] User feedback regarding the use of $EtCO_2$ detection in the delivery room was positive in nature. Chapter 3 has also shown that user interaction with an $EtCO_2$ monitor during simulated infant stabilisation is mostly positive. The issue of regular training for staff members was also highlighted by Van Os et al. through their experience of the introduction of a respiratory function monitor (RFM) in the delivery room.[86]

RFMs may have an important role to play in the delivery room. As discussed in the previous chapter, these devices produce a continuous display of pressure and flow waves. Other readings can also be displayed in numerical form such as percentage airway leak, PEEP, CPAP, and respiratory rate. The findings of the *in vitro* studies (Chapter 3) would suggest that the use of an RFM in the delivery room may also require formal training as well as validation of this training in a simulation laboratory before use in the delivery room.

One limitation of this investigation was the lack of a RFM. This would have provided this investigation with a better indication of when $EtCO_2$ readings were impacted by face mask leak, however, the method of matching the capnography monitor data with video recordings allowed for the elimination of any inaccurate readings that may have occurred. However, it is acknowledged that this may not have been fully effective in all instances.

The aim of this investigation was to assess the role of capnography in the delivery room alone, and not capnography paired with other readings such as mask leak and tidal volumes. Although the NRP does not recommend the use of $EtCO_2$ detection during facemask ventilation, it does recommend $EtCO_2$ detection for intubation. Therefore, it is a form of technology that may be easier to introduce to a delivery room setting as many more neonatal centres may already have this system in place, for intubation reasons. No studies have investigated whether a RFM with $EtCO_2$ monitoring capability versus a device with $EtCO_2$ monitoring alone results in improved infant stabilisation. It is also important to note that although there is good correlation between both mainstream[88-91,93], and sidestream[94,98], $EtCO_2$ measurements and $PaCO_2$ measurements, the former may not be as accurate as the latter.

Another limitation of this investigation is that, apart from immediate stabilisation of infants in the delivery room, other clinical interventions in the NICU occurring within the first hour after birth will have also affected the initial PCO_2 values obtained from both groups of infants. This investigation was observational in nature; therefore, the PCO_2 readings were obtained as part of routine clinical care, albeit all were obtained within 1 hour of delivery. This value, whilst important in the clinical care of an infant, is only one factor in the overall

assessment of adaptation and, as a result, other end points should be considered during analysis performed during future studies.

4.3.5. CONCLUSION

The MODS investigation has progressed on findings from the feasibility investigation in this chapter by reaffirming that it is feasible to use capnography in the delivery room to monitor $EtCO_2$ levels of a preterm infant. The MODS investigation has demonstrated that $EtCO_2$ levels rise during the initial minutes after birth. Infants who are intubated are noted to have higher median $EtCO_2$ values. There is a need for further clinical trials to comprehensively investigate these higher $EtCO_2$ levels and whether this information can act as an additional indicator for the need for respiratory support, such as intubation, in the delivery room. Assessing respiratory support via $EtCO_2$ in the delivery room is possible, however, further research is needed to assess the most effective way to do this. In particular, further trials are needed to compare qualitative and quantitative means of $EtCO_2$ assessment of preterm infants in the delivery room.

4.4. CONCLUSION OF CHAPTER

This chapter has shown that it is feasible to use capnography to monitor $EtCO_2$ levels of preterm infants in the delivery room and its use appears to be safe. Although many minor issues became apparent, mainly during the feasibility investigation, they were relatively easy to resolve. Once these issues were resolved, it allowed for the MODS investigation to progress at a much smoother rate. However, issues still arose in the MODS investigation, such as operator error. This highlights the importance of initial, as well as continuous, staff training in the use of new technology in the delivery room.

Issues relating to obtaining consent were identified in the feasibility investigation and, as a result of the resolution to these issues, it was felt that the level of enrolment for participation in the MODS investigation was optimised.

Completion of the investigations in this chapter has shown that $EtCO_2$ levels rise during the initial minutes after birth, and that infants who are intubated are noted to have higher median $EtCO_2$ values. There is a need for further clinical trials to comprehensively investigate these higher $EtCO_2$ levels. Assessing the need for respiratory support via $EtCO_2$ in the delivery room is possible, however, further research is needed to assess the most effective way to complete this. In particular, further trials are needed to compare qualitative and quantitative means of $EtCO_2$ assessment of preterm infants in the delivery room. Chapter 5 of this thesis will describe a RCT comparing the use of qualitative and quantitative forms of $EtCO_2$ detection in preterm infants in the delivery room in an attempt to progress on the work completed in Chapter 3 as well as Chapter 4.

CHAPTER 5: QUANTITATIVE VERSUS QUALITATIVE $ETCO_2$ DETECTION IN THE DELIVERY ROOM

5.1. INTRODUCTION

Chapters 2-4 have described the use of different forms of $EtCO_2$ detection in monitoring respiratory function during infant stabilisation. During the *in vitro* investigation assessing PPV with the use of qualitative methods of $EtCO_2$ detection, I showed that they improved the provision of effective PPV. Participants also subjectively preferred using these devices. The next *in vitro* investigation assessed qualitative and quantitative methods of $EtCO_2$ detection. Although the overall efficacy of PPV was improved with the use of both the qualitative method as well as the quantitative method of $EtCO_2$ detection, this improvement was not statistically significant. Similarly in this investigation, participants indicated a preference for the use of $EtCO_2$ detection during PPV, in particular when using the qualitative method.

Both these investigations demonstrated a preference for the use of $EtCO_2$ detection during PPV and, importantly, no adverse effect on performance was observed during their use. To begin the assessment of these methods of $EtCO_2$ detection in an *in vivo* environment, I investigated the role of quantitative $EtCO_2$ detection in the delivery room (Chapter 4). In this chapter, I described my investigation of the feasibility of using quantitative $EtCO_2$ monitoring during stabilisation of preterm infants in the delivery room. There was no statistically significant improvement in short term outcomes compared with a historical cohort, although patient selection and sample size may have contributed to this lack of demonstrable effect. Feedback received from medical staff during this investigation, relating to the use of quantitative $EtCO_2$ monitoring during stabilisation was positive.

Therefore, considering the findings from chapters 2-4, the next logical step was to perform a randomised controlled trial (RCT) to assess the use of different forms of $EtCO_2$ monitoring in the delivery room and address the limitations of my previous investigations.

5.2. A RANDOMISED CONTROLLED TRIAL OF QUANTITATIVE VERSUS QUALITATIVE $ETCO_2$ DETECTION IN THE DELIVERY ROOM (THE CAPNO TRIAL)

The results of the previously described *in vitro* (Chapter 3) and *in vivo* (Chapter 4) $EtCO_2$ detection investigations prompted this RCT. Prior to these investigations, clinicians were occasionally choosing to employ qualitative methods of $EtCO_2$ during manual ventilation in the delivery room of CUMH. Over a period of approximately 2 years, and largely as a result of the findings of my previous investigations, clinicans had begun regularly using a quantitative device for monitoring $EtCO_2$ during stabilisation of preterm infants. As this had become regular practice for many clinicians, it was important to consider this factor during the formation of a RCT in this area.

5.2.1. AIM

To determine

P: In preterm infants less than 32 weeks gestation

I: Does the use of quantitative $EtCO_2$ monitoring

C: Compared to qualitative $EtCO_2$ monitoring

O: Result in a reduction in the incidence of hypocapnia and hypercapnia within the first hour of life.

5.2.3. METHODS

Ethical approval

The CREC approved this RCT (CREC reference number ECM 4 [ss] 03/06/14)(Appendix F). The trial was commenced in the delivery room of CUMH in June 2014. Any infant delivered at less than 32 weeks' gestation was eligible for inclusion in this trial. Informed written consent was obtained from parents during the antenatal period. Exclusion criteria included oligohydramnios

(amniotic fluid index <5) and any known congenital anomalies such as congenital diaphragmatic hernia, congenital airway anomalies, chromosomal disorder and/or congenital heart disease. No change in overall stabilisation training or practice occurred during the timeline of this trial.

Registration of trial

This trial was registered on the ISRCTN registry with trial number ISRCTN10934870.

Outcome measures

Similar to the MODS investigation, PCO_2 from both groups of infants included in the trial was obtained from the blood gas analysis performed in the NICU less than one hour from the time of birth. The primary outcome was a combination of either hypocapnia was defined as an initial PCO_2 of less than 5 kPa, and hypercapnia was defined as an initial PCO_2 of greater than 8 kPa.

The secondary outcomes were the incidence of additional stabilisation interventions in the delivery room as well as the diagnosis of illness in the immediate neonatal period. These outcomes are shown in Table 5.1.

TABLE 5.1 –SECONDARY OUTCOME MEASURES TO BE COMPARED BETWEEN GROUPS

Secondary outcomes	
Delivery room interventions	**Illness diagnosed/requirements in the NICU (within 28 days of life)**
CPAP	Periventricular leukomalacia
PPV	Chorioamnionitis
Intubation	Ventilator support (duration)
Chest compressions	Bronchopulmonary dysplasia
Surfactant administration	Necrotizing enterocolitis
Epinephrine administration	Intraventricular haemorrhage
	Oxygen therapy (Duration)

Sample size calculation

At the time of trial design, an analysis of a historical cohort of preterm infants (less than 32 weeks) showed a combined incidence of hypercapnia and hypocapnia at approximately 60% with the use of a qualitative device. An a priori sample size calculation indicated that 27 babies would be required in each group (total n=54) to detect a reduction to 20% (60% in the qualitative group versus 20% in the quantitative group outside the range). This was completed using Fisher's exact test with 80% power, a 5% level of significance, and a two-tailed test. However, as twins were also eligible to be included in the trial, it may have reduced the overall statistical power. To account for this, the sample size was increased to n=30 per group (total n=60). This was based on a design effect of 1.0825 (assuming 25% of babies enrolled would be twins and ICC=0.33).

Using CUMH demographics for 2013, we estimated that if a similar birth rate were to continue into 2014-2015 then enrolment of 60 infants would be complete in approximately 9 months.

Groups

For the three years prior to this trial, some form of $EtCO_2$ detection had regularly been used in the delivery room of CUMH during the stabilisation of preterm infants. This was as a result of physician preference or through the completion of many $EtCO_2$ investigations in the delivery room, such as the CAPNO investigation (Chapter 4). As a result of this, it was considered that removing the option of having a form of $EtCO_2$ monitoring in the delivery room would be unethical and there was no equipoise to do this. Therefore, a randomisation group with no $EtCO_2$ detecting method was not included. This trial was designed with two arms, an arm utilising a qualitative method of $EtCO_2$ detection and an arm utilising a quantitative method.

The qualitative arm included infants being randomised to receive the use of a colourmetric $EtCO_2$ detecting device (PediCap® $EtCO_2$ detector, Covidien,

Dublin, Ireland) during respiratory support (PEDI). This device had a dead space of 3 ml, was attached between the facemask/ETT and T-Piece resuscitator (NeoPuff, Fisher & Paykel, Auckland, New Zealand), and the detector changed from purple to yellow upon detection of $EtCO_2$. When it returned to purple the measured $EtCO_2$ fell below approximately <0.5% (4mmHg).

The quantitative arm of this trial included infants being randomised to receive the use of a side stream capnography device (Microstream® CO_2 Filterline®, Covidien, Dublin, Ireland) during respiratory support (CAPNO). This device had a dead space of less than 0.5 ml, was attached between the facemask/ETT and T-Piece resuscitator, and ultimately provided the user with $EtCO_2$ values as well as an $EtCO_2$ trace during times in which $EtCO_2$ was detected.

Randomisation

Using a computer based randomisation program that assigned a number to each arm of the trial, randomisation envelopes were prepared by a physician who was not otherwise involved in the trial (Dr. Liam O'Connell, Consultant Neonatologist, CUMH). These envelopes were sealed and stratified to infants less than 28 weeks gestation and to infants greater than 28 weeks gestation.

All medical staff were familiar with both devices used in the trial and had undergone a training session in a simulation lab on the provision of PPV with these, prior to any interaction with participants of the trial. Similar to the MODS investigation, described in Chapter 4, continuous interaction with staff was identified as a key area to 1) continue awareness with the trial and 2) ensure staff familiarisation with all aspects of the trial.

Upon confirmation that an infant was to be delivered, a randomisation envelope was opened, group assignment determined, and a member of the research team transported the required equipment to the delivery room. The research team members were not part of the medical team responsible for the care of any participant. The default settings on the T-piece resuscitator, prior to delivery of the infant, were set at a gas flow of 8 L/min, a PIP of 20 cm H_2O, and a PEEP of 5 cm H_2O. The maximum attainable PIP pressure was limited to 30cm H_2O, as is

routine practice for all preterm deliveries at CUMH. Once an infant was placed on the resuscitation table, stabilisation commenced with the assigned randomisation group.

Where additional consent was provided, the stabilisation process was also video recorded. Recordings were placed on a secure hard drive within the neonatal research room in CUMH as well as on a secure server hosted by UCC.

Statistical analysis

Statistical analysis for the comparisons of PCO_2 values between the groups will be performed using SPSS 22.0 (IBM, NY, USA). Comparative tests of medians will be completed using Mann-Whitney U-tests and a $p < 0.05$ will be deemed as being statistically significant. Cross-tabulation determining the effect of blood gas type on whether or not infants fell within the accepted range will be completed using a Cramer's V test with a $p < 0.05$ considered statistically significant.

Data monitoring committee

The data monitoring committee for this trial consisted of Dr. Ali Khasan (Department of Epidemiology, University College Cork), and Dr Jan Miletan (Consultant Neonatologist, Coombe Women and Infants University Hospital).

5.2.4. RESULTS

At the completion of this thesis, the target recruitment was not achieved, and enrolment is continuing. The rate of preterm delivery during the trial period was less than previous years and this impacted upon enrolment rates. In order to determine the appropriate sample size for this trial, an interim analysis was performed by the data monitoring committee at 50% target enrolment. In order to protect the integrity of this trial, I have not been made aware of the results of this interim analysis. The target enrolment of n=60 was considered to be appropriate for the primary outcome, and recruitment is currently ongoing. The demographics of the enrolled participants prior to the completion of this thesis are shown in Table 5.2.

TABLE 5.2 – DEMOGRAPHIC DATA ENROLLED PARTICPANTS TO DATE (N=37)	
Factor	**Value**
Birth weight (g)(median [IQR])	1250 (920, 1640)
Gestational age (weeks+days)(median [IQR])	29+4 (28+2, 31+4)
Sex (M/F)	20(54%)/17 (46%)
TWIN GESTATION (INCIDENCE [%])	12 (32%)

5.2.5. RESEARCH RELATED ISSUES ENCOUNTERED

Birth rate of preterm infants

During the duration of this trial, the birth rate of preterm infants eligible for participation in the trial has been lower than expected. Although this is clearly a positive factor in terms of the overall health of infants, it has proven challenging for this component of my thesis. Prior to commencement of the trial, it was anticipated that 60 participants would be enrolled by March 2015. However, this has not been the case. In order to ensure that this RCT is completed, the enrolment period has been extended and the RCT is on-going and completion is estimated to be October 2015.

Trial awareness

Due to the lower than expected birth rate of infants eligible for participation in this trial, there was often a long period of time in which no participant was enrolled in the trial. In some cases, this period without a single eligible case has lasted up to 6 weeks. This ultimately meant that the research team wasn't visible in the delivery room for prolonged time periods. As a result of this, trial awareness amongst medical staff was difficult to maintain and medical staff subsequently failed to recognise eligible infants and inform the research team of mothers at risk of preterm deliveries.

To minimise this risk, the research team continued to complete daily checks in the HDU as well as the antenatal ward (2 south) of CUMH. Similar to the results from the delivery room investigations described in Chapter 4, the importance of

continued interactions with medical staff to increase trial awareness has, again, been highlighted throughout the duration of this RCT.

The time frame to obtain consent for delivery room investigations can represent a challenge, both for physicians and parents. There has been discussion in the neonatal literature on this important issue and the importance of research teams engaging with extensive discussion with ethics committees, as well as medical staff that will be involved with the deferred consent process, has been highlighted.[118-120] For future non-invasive delivery room based observational investigations, our experience during this RCT would advocate for discussion with our ethics committee for considering an adjusted consenting process.

Consideration of a deferred consenting process may optimise enrolment during future investigations. However, it is acknowledged that this deferred consent process may cause issues when applied to an RCT like this, where clinical care is affected. However, the impact of this may be somewhat alleviated in CUMH due to similar issues discussed during the creation of this trial. As a result of a substantial amount of preterm infants being included in $EtCO_2$ investigations, the medical team in CUMH have been regularly using different forms of $EtCO_2$ detection during stabilisation of preterm infants. Therefore, maintaining this and simply randomising as to which method of $EtCO_2$ monitoring an infant receives may be acceptable where equipoise exists regarding which device is optimal.

5.3. CONCLUSION OF CHAPTER

This chapter has described the design of a RCT to assess the relative efficacy of qualitative and quantitative $EtCO_2$ detection methods in the delivery room in reducing hypercapnia and hypocapnia in preterm infants. The overall assessment of these methods began in Chapter 3 through *in vitro* investigations on both qualitative and quantitative methods of $EtCO_2$ detection, and continued through to Chapter 4 where investigations of in vivo quantitative $EtCO_2$ in the delivery room were performed. The attempt to complete a RCT on $EtCO_2$ detection has added to this work and has been an important component of this thesis.

Although the RCT has not yet been completed, it still has a great degree of importance towards assessing the role of $EtCO_2$ monitoring in the delivery room. We have learned many lessons through the design and implementation of this trial, which will facilitate the completion of this trial, and facilitate future delivery room based RCTs at CUMH.

The interim review at participant enrolment level of 50% advised for the continuation of this trial. There have been no adverse events attributable to this trial and enrolment continues. It would also be unethical to abandon the trial at this time without reaching full enrolment. At the time of submission of this thesis, the trial has met 66% of participant enrolment.

CHAPTER 6: CIRCULATORY ASSESSMENT OF INFANTS IN THE DELIVERY ROOM

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Perfusion Index in the Preterm Infant Immediately after Birth

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(Appendix G)

6.1. INTRODUCTION

In this thesis, I have discussed several interventions that may improve stabilisation of an infant immediately after birth. The importance of decision-making during this time period has also been highlighted in several chapters. Knowing when to make these interventions inevitably adds to their importance.

Heart rate (HR) is a proxy indicator of oxygenation and is used as a guide for escalating the level of assistance required during stabilisation.[2,103] In Chapter 1 the importance of correctly acquiring the HR of an infant immediately after birth was highlighted. Many neonatal resuscitation curricula, such as the NRP and NLS, advise escalation of interventions when the heart rate falls below 100 beats per minute (bpm), and again when it falls below 60 bpm.[2,103] Implementation of these courses has been shown to improve infant stabilisation outcomes[121-124], and certification in one of these courses is a requirement for participation in infant stabilisation in many neonatal centres.[125] The importance of accurate HR assessment is a key component of this chapter.

As highlighted previously, another important factor during the stabilisation of an infant is the clinical assessment of the circulatory system. Observing for adequate oxygenation and continuous monitoring of overall tissue perfusion are important factors in assessing the circulation. This chapter will explore the utility of another continuous bedside assessment tool, namely the perfusion /pulsatility index (PI).

6.2. ASSESSMENT OF CURRENT METHODS OF HEART RATE DETECTION IN THE DELIVERY ROOM

The NRP and NLS guidelines recommend that HR is determined within ten seconds of delivery, using either palpation of the umbilical artery or cardiac auscultation.[2,103] The team member carrying out either of these methods is advised to communicate the HR to the other team members through tapping the rhythm in synchronisation with each beat.[2] However, there may be limitations to each of these methods. Examples include: the individual responsible for assessing and communicating the HR being unavailable for other tasks, the difficulty that may exist in correctly palpating the HR in a very low birth weight infant, and issues relating to communication of the HR to other team members.[126-128] Inaccuracies that can occur through auscultation of the HR as well as the palpation of the umbilicus suggest that these methods may be unreliable.[126,127,129]

The importance of accurate measurement and communication of HR is shown by the reliance of current guidelines on this parameter to guide in the escalation or de-escalation of stabilisation efforts. The NRP advises that PPV should be started if the HR falls below 100 bpm. Chest compressions are recommended if the HR falls below 60 bpm. If this HR remains less than 60 bpm then additional resuscitation steps, such as intubation and the administration of intravenous epinephrine, may be considered. Assessment of oxygenation and assessment of respiratory effort are equally as important to guide intervention. However, inaccurate HR measurement may result in failure by the team to take timely and appropriate resuscitation steps overall.

6.2.1. AIM

The aim of this investigation was to determine the relative accuracy and efficacy of the current methods of HR assessment.

6.2.2. METHODS

Nurses and physicians working at Cork University Maternity Hospital between January and July 2014 were eligible for inclusion in this investigation, and were

recruited as a convenience sample. This investigation was received ethics approval (CREC reference number – ECM 4 [k] 07/10/14)(Appendix H).

Three different methods of assessing HRs were simulated in this investigation and HRs of 54 bpm, 88 bpm, and 128 bpm were simulated across all methods. These rates were chosen as 1) each rate fell into a category that requires the need for different management approaches, as suggested by the NRP and NLS curricula and 2) a rate of 54 bpm is 10% below the threshold for commencing chest compressions, 88 bpm is greater than 10% from the threshold for commencing PPV, and the rate of 128 bpm is clearly in the normal range.

An investigator simulated a continuous pulsating umbilicus (UMB) using a Neonatalie infant mannequin (Laerdal Medical AS, Stavanger, Norway). The investigator was aware of the exact rate needed to be produced and was producing the pulsations in unison with a metronome that was audible only to the investigator. Auscultation was assessed by the participant listening to a continuous heart beat sound through headphones, simulating auscultation of an infant's chest (AUSC). In order to simulate a member of a resuscitation team tapping out the HR during a resuscitation scenario, participants observed an investigator who tapped a regular beat that they were listening to via headphones (TAP). All methods of assessment were performed in a simulated delivery room. Participants were not instructed to simulate any interventions relating to neonatal resuscitation and were only instructed to obtain a rate.

Each participant was required to indicate the exact rate when the three different rates (54 bpm, 88 bpm, and 128 bpm) were produced across each method. The order in which the participants completed each method, as well as the order in which each of the HRs were produced, were randomised. The randomisation process was completed via two groups of sealed envelopes. One group determined the sequence of heart rate assessment modalities, and the other determined the sequence of heart rates for each modality. This randomisation allowed for the sequence of the HR produced to vary, independent of the HR assessment modality randomisation. Each participant was required to pick an envelope from each group prior to starting the investigation and the investigator then opened these envelopes with the participant blinded to the starting order

chosen. The starting order resulted in each participant being subject to the investigator simulating the 3 different HRs across the three different methods. The exact rate chosen by the participant was never made visible to the participant and when the investigator was simulating a pulsating umbilicus in the mannequin, the squeezing of the balloon was not visible to the participant. There was a thirty-second break between each HR and method.

Analysis

The time taken for each candidate to verbally indicate a HR was noted and each participant also received an informal debriefing session on completion of the investigation in order to gather feedback on the preferred method of acquiring the HR by each participant. Analysis of the accuracy of each participant's indication, and whether or not this indication was in the correct category of less than 60 bpm, between 60 and 100 bpm, or greater than 100 bpm, was performed using SPSS Statistics 22.0 (IBM, NY, USA). P-values were derived from Cochran's Q-test with a p-value of <0.05 indicating statistical significance.

The exact heart rate given was not analysed as it was deemed that the accuracy of participants' determination of heart rate category was a more relevant portrayal of the level of each method's accuracy.

6.2.3. RESULTS

A total of 29 participants were included in this investigation (14 doctors and 15 nurse/midwives). 82.8% of participants had successfully completed NRP certification within the previous two years. All participants who agreed to participate completed assessment for all methods of HR measurement.

17.2% of participants indicated a HR of less than 60 bpm during the TAP method, and 17.2% when using the PALP method, when a HR of 54 bpm was simulated. This was compared with 31% of participants indicating a HR of less than 60 bpm when using the AUSC method (p=0.324)(Table 6.1, Figure 6.1).

TABLE 6.1 – PERCENTAGE OF PARTICIPANTS INDICATING THE CORRECT CATEGORY				
Rate <60bpm				
Method	**Palpating**	**Listening**	**Tapping**	**p-value**
Total (n=29)	17.2%	31.0%	17.2%	0.324
Rate between 60-100bpm				
Method	**Palpating**	**Listening**	**Tapping**	**p-value**
Total (n=29)	82.8%	79.3%	79.3%	0.846
Rate >100bpm				
Method	**Palpating**	**Listening**	**Tapping**	**p-value**
Total (n=29)	96.6%	93.1%	93.1%	0.607

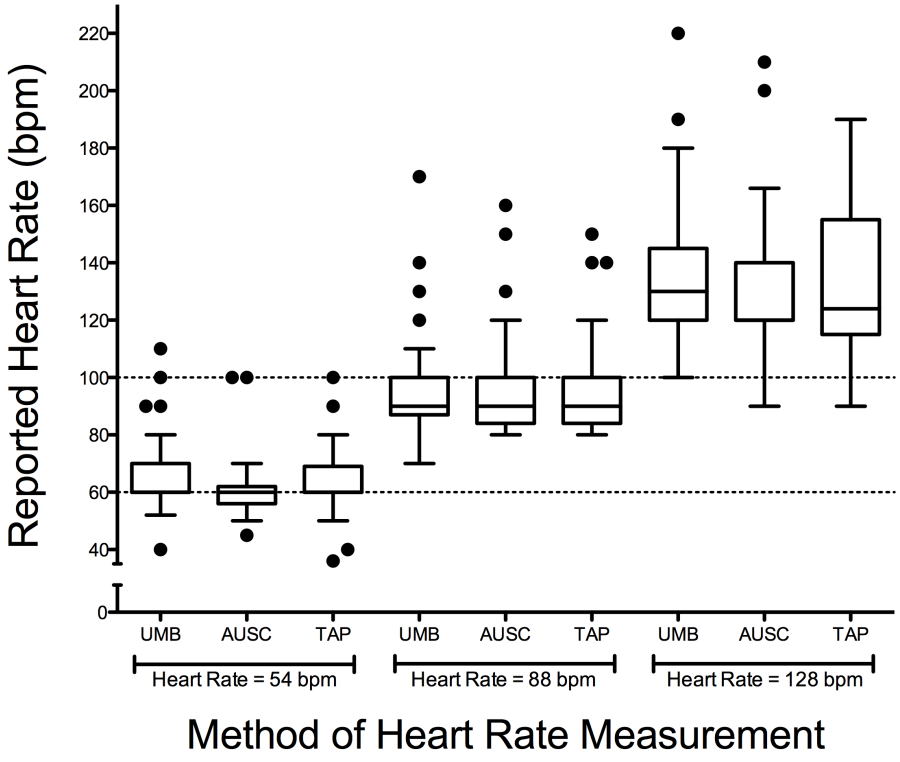

FIGURE 6.1 – REPORTED CATEGORY OF HEART RATES ACROSS ALL METHODS AND ACROSS ALL RATED PRODUCED

79.3% of participants indicated a HR of between 60 and 100 bpm during the TAP method, 82.8% during the PALP method, and 79.3% during the AUSC method, when a HR of 88 bpm was simulated (p=0.846)(Table 6.1, Figure 6.1).

93.1% of participants indicated a HR of greater than 100 bpm during the TAP method, 96.6% during the PALP method, and 93.1% during the AUSC method, when a HR of 128 bpm was simulated (p=0.846)(Table 6.1, Figure 6.1).

During the TAP method, the PALP method, and the AUSC method, and a HR of 54 bpm, a rate was obtained within ten seconds by 48.3%, 62.1%, and 65.5% of participants, respectively (p=0.097)(Table 6.2). During the TAP method, the PALP method, and the AUSC method, and a HR of 88 bpm, a rate was obtained within ten seconds by 55.2%, 55.2%, and 58.6% of participants, respectively (p=0.913)(Table 6.2). During the TAP method, the PALP method, and the AUSC method, and a HR of 128 bpm, a rate was obtained within ten seconds by 51.7%, 62.1%, and 55.2% of participants, respectively (p=0.497)(Table 6.2).

TABLE 6.2 – PERCENTAGE OF PARTICIPANTS INDICATING THE CORRECT CATEGORY WITHIN TEN SECONDS

54 bpm				
Method	**Palpating**	**Listening**	**Tapping**	**p-value**
Total (n=29)	48.3%	62.1%	65.5%	0.097
88 bpm				
Method	**Palpating**	**Listening**	**Tapping**	**p-value**
Total (n=29)	55.2%	55.2%	58.6%	0.913
128 bpm				
Method	**Palpating**	**Listening**	**Tapping**	**p-value**
Total (n=29)	51.7%	62.1%	55.2%	0.497

48.3% of participants indicated a preference for the AUSC method, 44.8% for the PALP method, and 6.9% for the TAP method.

6.2.4. DISCUSSION

This investigation assessed each method of acquiring HR, as currently recommended by the NRP and NLS. It was found that there is little accuracy when categorizing HR correctly, and that high degrees of inaccuracy occur when classifying a rate of less than 60 bpm in a simulation setting. A HR of less than 60 bpm is of particular importance, as recognising this HR would indicate that cardiac compressions should begin. The percentage of participants indicating a rate within 10 seconds was low across all of the different rates of as well as all of the different methods (Table 6.2).

Translating these findings into real life scenarios may result in a delay in interventions such as the provision of chest compressions, intubation, and/or administration of epinephrine to an infant. The findings of this investigation have led to these issues being highlighted to medical staff of CUMH, and to the exploration of other methods of heart rate determination during delivery room stabilisation.

Previous assessments of the accuracy of HR evaluation methods have been done in infants, but not at the simulated lower rates used in this investigation. Kamlin et al. investigated auscultation and palpation to acquire HR in infants, but did not include infants with a heart rate of less than 100 bpm. However, similar to this *in vitro* investigation, HR was underestimated when participants used palpation or auscultation to determine HR greater than 100 bpm.[126] Owen and Wyllie also highlighted the unreliability of palpation of the umbilical cord in healthy term infants that did not require resuscitation. Similar to this investigation, the authors also discussed the possibility of correct interventions not occurring during the resuscitation as a result of inaccuracy in determining HR by palpation.[130]

Participants indicated that they would most likely use auscultation as the primary method of acquiring HR. However, the AUSC method had a high degree of inaccuracy of being categorized when the HR was below 60 bpm (31%). The inaccuracy of HR assessment via auscultation has been highlighted by previous studies. Voogdt et al., through an *in vitro* trial investigating auscultation, found that 28% of participants incorrectly categorized HR and hypothesized that these

assessments would have prompted incorrect management. Similar to the results of this investigation, it was found that a large percentage (73%) of all HR assessments were estimated to be higher than they were.[131]

44.8% of participants indicated a preference for the PALP method and this method had a high degree of accuracy when determining a HR of greater than 100 bpm (96.6%). The results from this investigation, showing the inaccuracy of auscultation and palpation to determine HR, draw the same conclusions as previous studies in that neither of these methods is reliable in assessing HR.[126,129] Representation of the HR by means of the TAP method had a low degree of accuracy in determining the HR within the correct category across all simulated HRs and also had the lowest percentage of participants indicating a preference for acquiring HR with this method (6.9%).

One limitation of this investigation was that a structured questionnaire was not employed for the debriefing session, as there was a primary focus on the method indicated as being preferred by each participant. Another limitation of this investigation was that not all participants were NRP trained 2 years prior to completion of this investigation. This was an observational investigation that did not require participants to partake in any training outside of their formal training schedule. The limitation of applying data from an *in vitro* investigation to infant stabilisation is important. While it was not possible to simulate a real life, high-pressure resuscitation scenario, such an environment is unlikely to improve the accuracy in using any of these methods. There is likely to be little difference, particularly in the tapping and auscultating modalities used in this investigation, in a real life scenario.

The current methods of HR assessment are not reliable and therefore more objective forms of assessment should be available to the team during stabilisation. While the NRP alludes to objective assessment of HR in situations where it is not possible to obtain HR through palpating and auscultating, and the results of this investigation suggests that the objective measurement of HR is likely to improve accuracy, particularly in high-risk deliveries where extensive resuscitation measures may be required.

There are two readily available methods of objectively acquiring HR: electrocardiogram (ECG) or pulse oximetry. These methods have been previously evaluated and compared *in vivo*. ECG is quicker in terms of application of the electrodes, compared with the application of the SpO_2 probe. ECG is also quicker in acquiring a signal.[127] The use of ECG during infant stabilisation is also safe and reliable.[132] Although a pulse oximeter does provide the user with an assessment of the pulse rate, the device may take some time (1 to 2 minutes) to apply and display a correct value, and correct function of the monitor is not guaranteed in the setting of poor cardiac output or poor peripheral perfusion.[1,133]

ECG monitoring via cardiac leads may be the most accurate method of obtaining HR and, if utilised, the medical team members should be trained in the timely placement of ECG electrodes in scenarios where it is deemed necessary. This method takes less than 5 seconds to provide the user with a HR and in the majority of instances a continuous objective assessment of HR is visually displayed to the resuscitation team.[132] As with any new technology correct in-vitro training is important before it's use is implemented into an in-vivo setting.

6.2.5. CONCLUSION

This investigation has shown that current methods of HR measurement in the delivery room are inaccurate. The inaccuracies associated with these methods (AUSC, PALP, TAP), as well as the time taken to acquire them, suggests that alternative methods should be considered and studied.

6.3. ECG MONITORING IN THE DELIVERY ROOM

Section 6.2 demonstrated inaccuracies that existed in current methods of HR assessment employed in the delivery room. In each of the delivery room based investigations discussed in Chapter 4 and Chapter 5, a Philips Intellivue MP70 monitor was utilised to facilitate $EtCO_2$ monitoring. This monitor also had the ability to acquire a HR, via ECG monitoring (HR_{ECG}) as well as via pulse oximetry (HR_{OXI}).

6.3.1. AIMS

The primary aim of this investigation was to assess the feasibility of using ECG monitoring to obtain HR during the stabilisation of preterm infants in the delivery room. The secondary aim of this investigation was to assess the level of variability between HR_{ECG} and HR_{OXI} values.

6.3.2. METHODS

All infant's included in this investigation had been included in the MODS investigation and CAPNO trial discussed in Chapter 4 and Chapter 5, respectively. Parents were informed of the HR aspect of each investigation during the consenting process. Therefore, informed written consent was obtained for all infants included.

When possible, a 3 lead ECG module was attached to the Philips Intellivue MP70 monitor during configuration of the monitor in the delivery room. A 3M™ Red Dot™ (3M, St Paul, MN, USA) prewired 3 lead device was then attached to this ECG module.

Once each infant was placed on the resuscitaire with the stabilisation team, a pre assigned team member attached the three electrodes to the infant's chest. This subsequently displayed an ECG trace and a numerical HR_{ECG} value. Users were instructed to focus only on the numerical HR_{ECG} and not to interpret the ECG trace. The SpO_2 value as well as the HR_{OXI} value (a "pulse" value) was also displayed at this time.

After an infant left the delivery room, a member of the research team obtained the HR_{ECG} data and the HR_{OXI} data, when available, by using the review function within the Philips Intellivue monitor. As video recordings were also available for each infant's time in the delivery room, 2 reviewers (thesis author GAH and thesis supervisor EMD) synchronised the video in time with any data obtained from the monitor.

Statistical analysis

This statistical analysis for this investigation was performed using Matlab (version R2013a, The MathWorks, Inc., MA, USA), by Dr. John O'Toole. A mixed-effects model was fitted to the ECG data using the lme4 package (version 1.1-7) in the statistical software program R (version 3.1.2).[96,134] Models were defined by including fixed and random effects that provided the best fit to the data, by comparing models with increasing levels of complexity.

In context, the random effects represent each infant's HR data and fixed effects represent the group average. Starting from a simple model (with linear-time and random intercepts), time-squared, random-time, and random-time-squared effects were sequentially added. Each model was compared to the proceeding model, and the extra terms were added only if model fit significantly improved. The log-likelihood ratio test using Chi-squared distribution determined model fit, with $p < 0.05$ representing a significant improvement.

6.3.3. RESULTS

Demographic data

A convenience sample size of 81 infants was available for this. This sample size was acquired from January 2013 until June 2015 and stabilisation practice did not change over this time period. A total of 37 infants (46%) had both HR_{ECG} data as well as HR_{OXI} data available for analysis. Issues with configuration of the Philips Intellivue monitor resulted in incomplete data for the other 44 participants, as it wasn't possible to extract HR_{ECG} and HR_{OXI} data for analysis in these infants. Obtaining HR_{ECG} wasn't the primary aim of the MODS

investigation or CAPNO trial, and it was not always successfully completed during the stabilisation process in the delivery room for this reason.

Data analysis

Heart rate tended to increase immediately after birth before levelling off after approximately 4 minutes. This was evident in both HR_{ECG} data as well as HR_{OXI} data (Figure 6.2 and Figure 6.3, respectively).

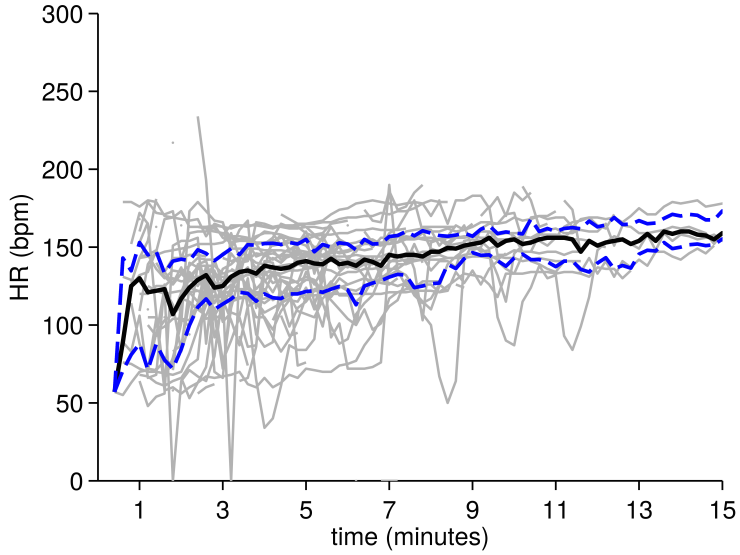

FIGURE 6.2 – HEART RATE DATA FROM 37 PRETERM INFANTS, AQUIRED VIA ECG MONITORING. GREY LINES REPRESENT EACH INFANT'S DATA, BLACK LINE REPRESENT THE MEDIAN ACROSS INFANTS, AND THE BLUE LINES REPRESENT THE IQR

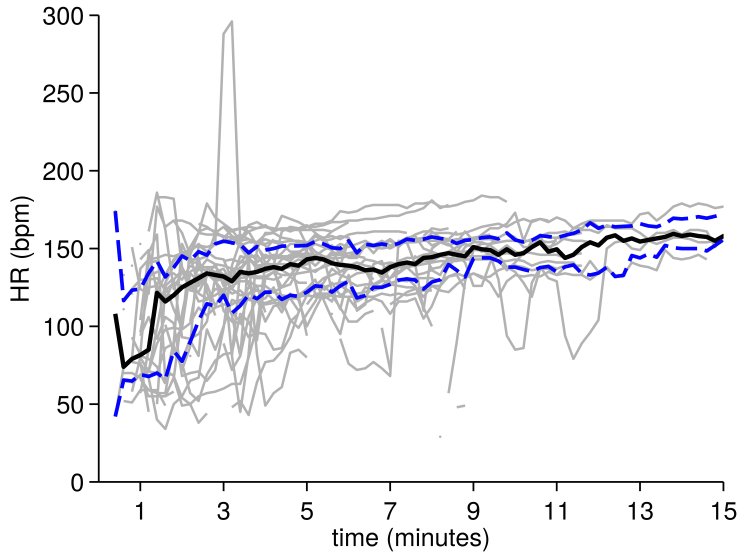

FIGURE 6.3 – HEART RATE DATA FROM 37 PRETERM INFANTS, AQUIRED VIA PULSE OXIMETRY GREY LINES REPRESENT EACH INFANT'S DATA, BLACK LINE REPRESENT THE MEDIAN ACROSS INFANTS, AND THE BLUE LINES REPRESENT THE IQR

Error occurred between the HR when acquired by ECG and HR when acquired through pulse oximetry (Figure 6.4).

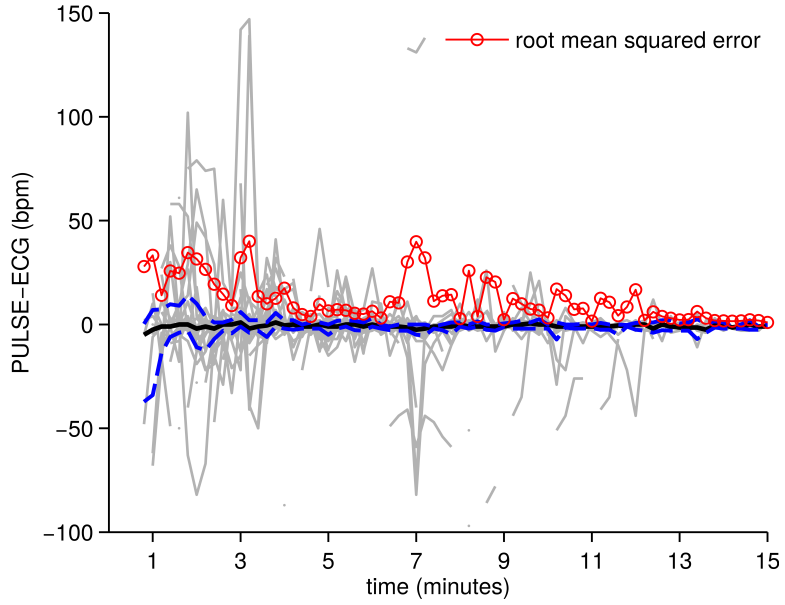

FIGURE 6.4 – ERROR BETWEEN ECG MONITORING AND PULSE OXIMETRY. GREY LINES REPRESENT EACH INFANT'S DATA, BLACK LINES REPRESENT THE MEDIAN ACROSS INFANTS, AND THE BLUE LINES REPRESENT THE IQR

It was found that a linear mixed-effects model with random intercept and random slope best fit the HR data (Appendix I). The fixed and random effects for the model are contained in Figure 6.5. Table 6.3 shows the coefficients of the model. On average, a linear increase of approximately 4 bpm per minute, starting from an initial value of approximately 110 bpm, was found over the 15-minute period.

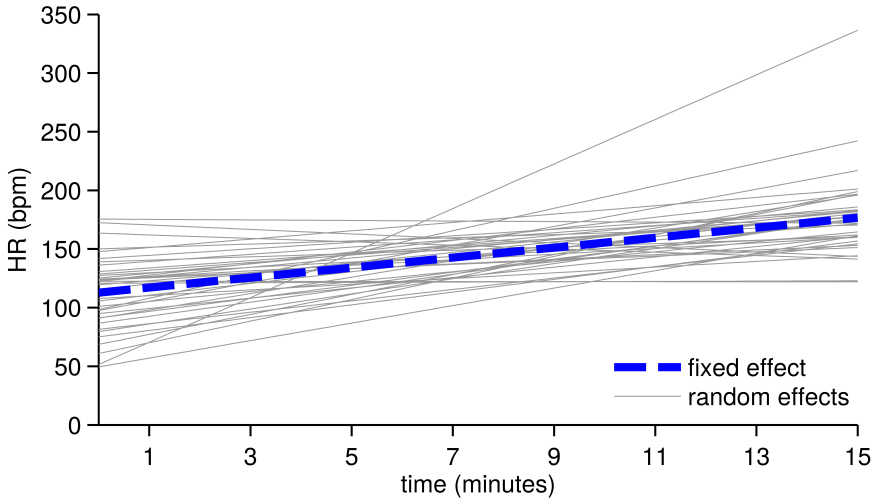

FIGURE 6.5 – MIXED EFFECTS MODEL FOR THE HR_{ECG} DATA SET. THE MODEL INCLUDES FIXED AND RANDOM INTERCEPTS AND SLOPES (TIME)

TABLE 6.3 – FIXED EFFECTS ESTIMATES		
Coefficient	**Estimate (95% CI)**	**p-value**
Intercept (bpm)	112.8 (102.2 to 123.5)	<0.001
Slope (bpm per second)	0.0709 (0.0469 to 0.949)	<0.001

6.3.4. DISCUSSION

The utilisation of ECG monitoring to obtain the HR of a preterm infant in the delivery room is feasible. Once this HR_{ECG} was obtained, the team had a continuous reading available to help in guiding the stabilisation process. The availability of a continuous, objective, HR reading during stabilisation is beneficial as this method of HR acquisition allows a team member, who would typically be required to continuously check the HR, to perform other tasks during the stabilisation process. During this time the team also has access to continuous and more accurate HR values.

Informal feedback relating to this method of obtaining HR was positive. The continuous HR availablity during stabilisation (after the ECG electrodes were applied) were reported as the most significant advantage of this method.

Descriptive analysis indicated an increasing HR across all infants immediately after birth. Previous research has suggested that HR values acquired via ECG monitoring may be more accurate than HR values acquired via pulse oximetry[127,132,134] and the unreliability of HR measurement though a pulse oximeter has also been highlighted by the NRP[1]. The results from acquiring HR_{ECG} and HR_{OXI} in the delivery room during this investigation confirm this. We found that the greatest degree of inaccuracy was in the first 2 mins of life, when acquiring an objective assessment of heart rate may be the most important time.

Although the analysis in this investigation was primarily descriptive, future investigations should incorporate short term outcomes to evaluate the potential clinical benefit of ECG monitoring during stabilisation.

It is important to mention the method in which an ECG monitor typically calculates HR. HR is measured by assessing the frequency of recorded R waves in the ECG tracing. However, at times this ECG tracing may be distorted during initial application of the ECG electrodes and therefore may incorrectly identify R waves. This incorrect identification of R waves may subsequently result in the ECG monitor momentarily displaying an incorrect HR. This occurrence may have been limited in the data analysis as a result of the assessment of video recordings (performed by thesis author GAH and thesis supervisor EMD). During assessment of these video recordings, HR_{ECG} that were deemed to be inaccurate during the initial application of the electrodes were eliminated from the data. This may be one of the potential shortcomings of ECG electrode application in preterm infants in the DR.

It is important to review manufacturer guidelines relating to ECG electrodes prior to their utilisation in the delivery room. Many of these guidelines describe the risk of skin irritation to an infant as a result of the adhesive gel contained on ECG electrodes, however, this primarily relates to prolonged use rather than the short-term application during stabilisation. Although we were aware of these potential complications, and monitored for them, we did not note any adverse effects of using ECG electrodes in this population during this investigation.

6.3.5. CONCLUSION

We have demonstrated that HR assessment using recommended methods can be inaccurate. We have also shown that the utilisation of ECG in the delivery room is possible, and that this monitoring may provide a more objective HR to guide the stabilisation team.

6.4. ASSESSMENT OF AN ENHANCED FORM OF CARDIOVASCULAR MONITORING IN THE DELIVERY ROOM

The NRP and NLS recommend that target oxygen saturation (SpO_2) levels are reached within the first few minutes of life.[2,103] Current methods of non invasive monitoring of peripheral perfusion, and overall oxygenation, are predominantly subjective and include observing skin colour, capillary refill time and temperature of the periphery.[2,103]

PI is a non-invasive method of assessing real-time peripheral perfusion. Although determined at the same time as SpO_2, PI is calculated independently of a patient's SpO_2. PI is derived from the photoelectric plethysmographic signal of transcutaneous oximetry. Pulse oximetry uses two light sources with different wavelengths (red light at 660 nm and near infrared light at 940 nm). Oxygenated haemoglobin (HbO_2) absorbs more light at 940 nm and deoxygenated haemoglobin (Hb) absorbs more light at 660 nm.[135] SpO_2 is then calculated by obtaining the ratio between the amount of red light and infrared light absorbed. By using a third wavelength (800 nm), the overall haemoglobin concentration can be determined, allowing the pulsatile component of arterial blood to be distinguished from the non pulsatile component. The PI is then calculated as the ratio between the pulsatile component and the non pulsatile component.[136]

Several studies investigating PI in the adult population have highlighted the potential of PI in monitoring the circulation in patients admitted to the emergency department, and in monitoring the effect of therapies and interventions on peripheral perfusion.[136,137] Studies in the infant population have highlighted the potential for postnatal PI to be used as an assessment tool in various aspects of an infant's health.[138] In particular, postnatal PI in the newborn may identify subclinical chorioamnionitis[139], or be used as a possible screening tool for congenital heart malformations.[140,141] It may also be an indicator of low superior vena cava flow[142], or a sign of improved tissue oxygenation following blood transfusion in preterm infants.[143] PI is highly reproducible in preterm infants[144], and it increases over the first 3 days of life[142,145]before stabilising by day 5.[146] Normative PI values have been described for preterm infants in the first

day of life.[146,147] However, PI values immediately after birth have not previously been described.

6.4.1. AIM

The aim of this investigation was to evaluate the PI of preterm infants in the delivery room and to determine if this continuous measurement was related to other markers of cardiovascular assessment.

6.4.2. METHODS

This was a single centre prospective observational investigation conducted in the delivery room of Cork University Maternity Hospital, Ireland, and was a sub investigation of infants involved in the delivery room CO_2 investigation discussed in Chapter 4. Any infant delivered at less than 32 weeks' gestation was eligible for inclusion in this investigation. Exclusion criteria included oligohydramnios (amniotic fluid index <5) and known congenital anomalies of the infant such as congenital diaphragmatic hernia, congenital airway anomalies, and/or congenital heart disease. As the MODS investigation and CAPNO trial had CREC approval to gather other parameters, such as PI, in the delivery room, this investigation did not need separate CREC approval. Parents were made aware of this aspect when being informed about the MODS investigation or the CAPNO trial. The medical staff members were informed of the infant's participation in the investigation and all monitoring equipment was prepared, prior to delivery.

A SpO_2 monitoring probe (Nellcor OxiMax, Covidien, Mass, USA) connected to a Philips IntelliVue MD70 (Philips Healthcare, Andover, USA) was placed on the right forearm of each infant to monitor SpO_2 levels during the initial adaptation phase in the delivery rom. This monitor obtained the PI as well as the heart rate of each infant with an averaging rate of 5 seconds. A member of the research team downloaded this information after the infant left the delivery room. All physiological data downloaded from the delivery room was exported as 12-second intervals. Authors GAH and EMD subsequently correlated this information with a video recording of the infant, that was also obtained during

the time spent in the delivery room. This allowed for clarification, and subsequent elimination, for potentially incorrect PI readings due to inappropriate placement of the SpO_2 probe or at times of poor signal quality.

Lactate was measured on the first blood gas within an hour of birth. Similarly, non-invasive blood pressure values were obtained after admission to the NICU, within an hour from birth. Instances of intraventricular haemorrhage (IVH) were determined by means of cerebral ultrasound, within 7 days after birth.

The following analysis was performed on the PI values for 10 minutes after birth. The median and IQR of each infant was assessed and compared between the first and last 5 minutes. Using the Mann-Whitney *U*-test, median values over the 0-5 minute period were compared to median values over the 5-10 minute period, and similarly for the IQR values. Statistical significance was determined as $p < 0.05$.

Median values of PI over the 10 minutes were correlated with gestational age, lactate concentrations, and blood pressure. Pearson's correlation coefficient was used and significant correlation ($p<0.05$) was determined if the 95% CI excluded 0. CIs were computed using the bootstrap approach with 1,000 iterations. For each infant, PI values were correlated with heart rate over the 10-minute period. The Fisher-z transform was used in calculating the average correlation coefficient over all infants.[148] This average correlation was deemed statistically significant if the 95% CI excluded 0. Again, the bootstrap procedure, with 1,000 iterations, was used to compute the CI. Unless stated otherwise, median values and IQR are reported as "median (IQR)".

6.4.3. RESULTS

33 infants with a median gestational age of 29 (IQR 26, 30) weeks and a median birth weight of 1205 (IQR 925, 1520) g were included for analysis. The overall median PI value for the first 10 minutes was 1.3 (IQR 0.86, 1.68)(Figure 6.6). There was no significant correlation between delivery room PI and gestational age of the infant (r=0.28 CI: -0.087, 0.585), lactate concentrations within one hour of birth (r=-0.251 CI:-0.618, 0.177), or blood pressure within an hour of birth (r=-0.175 CI:-0.456, 0.200)(Table 6.4). There was an average correlation

value of r=-0.417 (95% CI: -0.531, -0.253) between simultaneous heart rate / PI values.

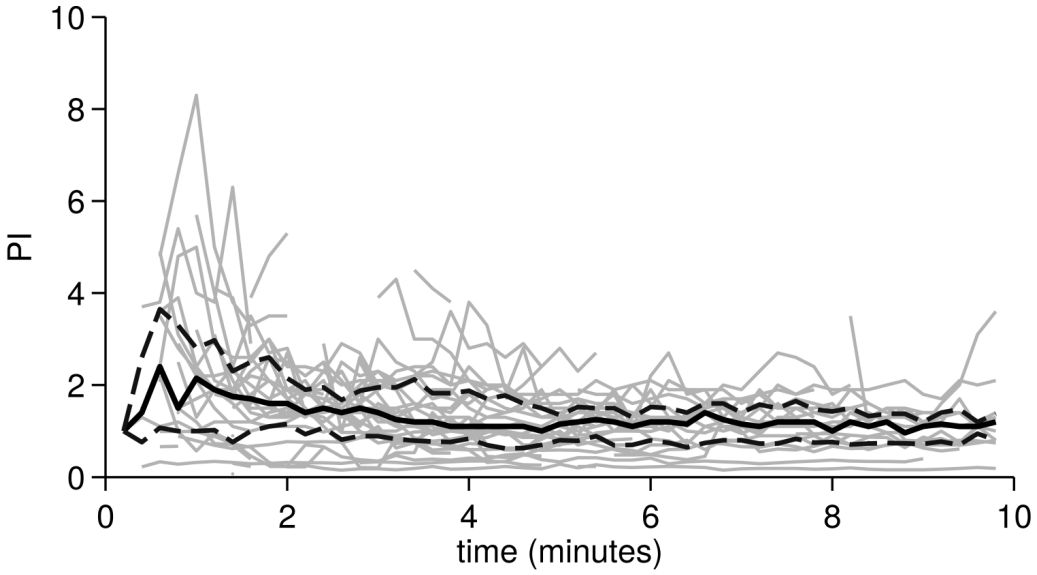

FIGURE 6.6 – PI FOR 33 INFANTS DURING THE FIRST 10 MINUTES AFTER BIRTH

TABLE 6.4 – CORRELATION COEFFICIENT R OF MEDIAN PI VALUE WITH DIFFERENT MEASURES

	r-value	95% CI
Gestational Age	0.288	(-0.087, 0.585)
Lactate	-0.251	(-0.618, 0.177)
Blood Pressure	-0.175	(-0.456, 0.200)

The median PI value over the first 5 minutes of life was slightly, although not significantly, greater compared to the median PI values in the second 5 minutes (1.5 [IQR 0.97, 1.96] vs 1.2 [IQR 0.80, 1.50], p=0.22)(Figure 6.7). The PI values were significantly greater for the first 5 minutes compared to the second 5 minutes (0.5 [IQR 0.27, 0.92] vs 0.2 [IQR 0.10, 0.30], p<0.00)(Figure 6.8). There was no relationship between delivery room median PI values and instances of IVH within one week of birth (p=0.822).

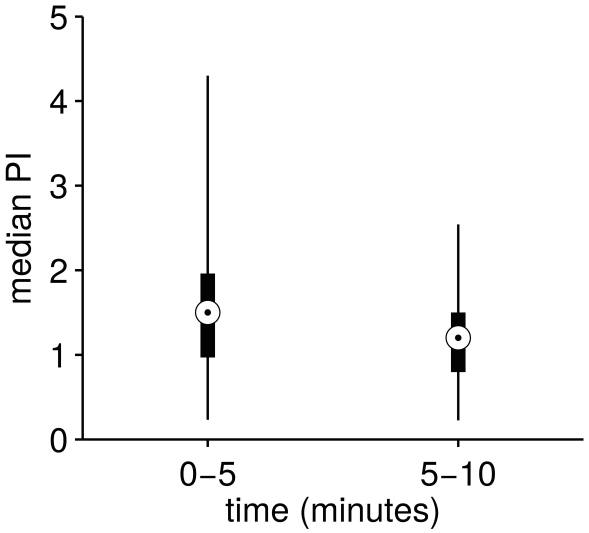

FIGURE 6.7 – MEDIAN PI VALUE FOR THE FIRST AND LAST 5 MINUTE SEGMENTS (P=0.216).

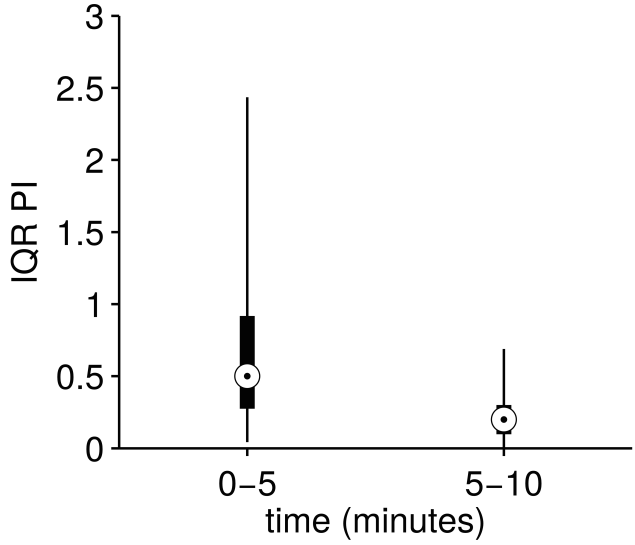

FIGURE 6.8 – IQR VALUES FOR THE FIRST AND LAST 5 MINUTE SEGMENTS (P<0.001).

6.4.4. DISCUSSION

This investigation has assessed the PI of preterm infants immediately after birth. PI has been shown to have significant variability over the first 5 minutes of life. One explanation for this variability may be related to the location and method of application of the monitoring probe. However, the reliability and reproducibility of probe placement with this method is high.[144] Therefore, the observed variability in the PI may reflect normal circulatory adaptation to extra uterine existence and reflect the complex neonatal haemodynamic changes that are taking place over the first few minutes of life. These changes in PI may be similar to circulatory changes described in by Van Vonderson et al.[149] In a study

on the use of echocardiography immediately after birth in 24 infants, fluctuations in ductal flow were suggested to reflect changes from right-to-left shunting to left-to-right shunting; ultimately reflecting overall changes in pulmonary and vascular resistance.[149]

Two previous studies have reported on PI values in the first few days of life. Hakan et al. reported a median PI value of 0.88 (IQR 0.6, 1.26) in a cohort of 45 preterm infants[146] and Vidal et al. showed a median PI of 0.70 (IQR 0.50, 1.05) in a similar number of preterm infants.[147] In this investigation, we found slightly higher median values in preterm infants immediately after birth (1.3 [IQR 0.86, 1.68]). Again, these higher values may reflect the dynamic changes that are occurring over this time period.

Although the PI values most likely reflect circulatory adaptation, they do not correlate with the other markers of cardiovascular status that were investigated, including blood pressure on admission to the NICU. The lack of correlation between blood pressure and PI values may be due to the time period between acquisitions of these parameters, but also may reflect the fact that a single blood pressure measurements is a suboptimal indicator of cardiovascular wellbeing in this population. Similarly, there was a lag period of approximately one hour between acquisitions of lactate values. As this was an observational investigation, blood pressure and blood gas analysis were acquired as part of routine clinical care, usually within one hour of birth. Therefore, any clinical interventions performed during that time may have affected the correlation analysis between the PI values, and also the time lag itself may account for the lack of any correlation. The absence of correlation between PI values and cardiovascular markers during the first 3 days of life has previously been described.[144]

Circulatory assessment at birth, or indeed at anytime in the first few days of life, can be subjective. In evaluating peripheral perfusion of an infant, the current method of assessing skin colour has been suggested as a potential indicator of the severity of illness[150]. However, this method varies amongst care givers as a result of the subjective nature of the assessment.[151] Therefore, a readily available, potentially more objective, bedside measurement was chosen for this

investigation. The application of the probe to obtain the PI of a preterm infant during stabilisation in the delivery room is possible. Oxygen saturation monitoring is now a standard of care and, as a result of the application of an oxygen saturation probe; PI values are now often available. In this investigation the medical staff was not instructed to interact with the PI value. Although measurement of PI does not deviate from routine care during resuscitation, other than a visual display of a value on a bedside monitor, the clinical utility of this measure is currently undefined in this population. Thus, interpretation and interaction with PI values cannot be advocated at present.

There are a number of limitations to this investigation. Various users applied the saturation probe and this may be a source of variability in the results. The gestational age of the infants was wide and it is possible that PI varies across gestational ages within the timeframe of this investigation. As discussed, blood pressure values were not obtained simultaneously. Maternal cord blood gas values were not included in analysis, and this may have allowed for an assessment of lactate values at the time of birth.

6.4.5. CONCLUSION

This investigation has shown that the monitoring of PI in preterm infants in the delivery room is feasible, and values become readily available to the resuscitation team. However, as this investigation has failed to find a correlation between PI and other markers of cardiovascular wellbeing, their role as an early biomarker of circulatory status has yet to be fully elucidated. Monitoring of PI in the delivery room may yet have a role to play in the overall assessment of a preterm infant immediately after birth. Further delivery room-based trials of PI are worthwhile, in particular, trials correlating PI with other objective assessments of cardiovascular function immediately after birth.

6.5. CONCLUSION OF CHAPTER

This chapter commenced by describing an investigation into the current methods of HR assessment currently advised for use in the delivery room. These methods were found to be inaccurate and, alarmingly, this was more evident at lower HRs. The chapter then progressed to describe experiences of using ECG monitoring in the delivery room, where ECG monitoring was shown to be feasible in this setting. The combination of the results from these investigations has suggested that the current methods of acquiring HR may not be sufficient and it may be beneficial to introduce routine ECG monitoring in the delivery room. However, ECG monitoring potentially requires an additional person present at the stabilisation in order to apply the electrodes. In the next chapter, we will describe a stabilisation video outlining methods that attempted to alleviate this concern.

Chapter 6 also described an investigation of PI monitoring in the delivery room. Although the investigation did not find any correlation between PI and other markers of circulatory adaptation, the investigation did show it was feasible and safe to carry out this modality of cardiovascular monitoring. SpO_2 monitoring is already the standard of care during stabilisation of preterm infants, and PI evaluation does not require additional equipment. However, the potential role of PI interpretation in this context remains unknown and further studies are required to evaluate this.

As with all new forms of monitoring equipment introduced to clinical care, training and familiarity with devices are essential. This is particularly true in the delivery room setting, where insufficient training has the potential to disrupt infant stabilisation. Prior to each of the investigations discussed in this chapter and throughout this thesis, appropriate training of staff in a simulation lab was provided. This training is essential and has regularly highlighted minor issues that can be subsequently resolved prior to the commencement of any *in vivo* investigation

CHAPTER 7: THE ROLE OF VIDEO IN IMPROVING INFANT CARE

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Perceptions of Webcams in the Neonatal Intensive Care Unit: Here's Looking at you Kid!

Hawkes GA, Livingstone V, Ryan CA, Dempsey EM.

American Journal of Perinatology. 2014. PMID=24896140

(Appendix J)

7.1 INTRODUCTION

The enhanced monitoring methods described in this thesis have included many forms of technology. This includes the use of qualitative $EtCO_2$ detection, quantitative $EtCO_2$ detection, ECG, and perfusion index monitoring, in the delivery room. Video recording was also employed in the delivery room. The experience gained in using these new technologies has prompted me to consider how these technologies can be optimised in the delivery room, as well as the NICU.

Many issues were identified in the implementation of new technology, particularly video recording, in the delivery room. Video recording in this setting has the potential to provide feedback on the stabilisation team's performance, but the use of this technology had ethical and medico-legal concerns that were addressed before implementation. In this chapter, I will describe a metric that was created using these videos to evaluate performance of the stabilisation team, as well as an educational video that was designed to improve this performance.

Similarly, a metric and instructional video was also created for procedural care in the NICU, namely for the placement of peripherally inserted central catheters (PICCs). The ability to examine and learn from video recordings of delivery room stabilisations, obtained from the investigations described in Chapters 4 and 5, were essential in influencing the formation and structure of this investigation.

Having successfully integrated video recording to neonatal care, we considered alternative uses of this technology to enhance postnatal care. The stress that parents of a preterm infant experience, both in the antenatal period as well as the time period in which an infant spends in the NICU, is a factor that has been continually observed during completion of this thesis. I explored the barriers to adapting a novel webcam system in the NICU to facilitating parent observation of their infant when the parent is not physically in the NICU, through an investigation into the attitudes from healthcare staff and from parents towards this intervention.

7.2. DEVELOPMENT OF A TEACHING VIDEO FOR ENHANCED DELIVERY ROOM STABILISATION OF PRETERM INFANTS

7.2.1. BACKGROUND

Thomas et al. have highlighted the importance of effective teamwork during infant stabilisation, particularly in workload management during the stabilisation process.[152,153] The importance of teamwork is continually highlighted throughout the NRP curriculum especially during the *in vitro* scenario training aspect of the curriculum.[2]

Video recording in the delivery room was a component of many of the investigations described in this thesis. Using these videos, it was possible to observe teamwork during infant stabilisation. This information was then used to develop an educational tool, described in this investigation.

7.2.2. AIM

The aims of this investigation were to 1) develop an annotated educational video on delivery room practice and 2) assess if implementation of this video resulted in an improvement in practice.

7.2.3. METHODS

This was an ethically approved observational investigation (CREC reference number – ECM 6 [yy] 14/04/15)(Appendix K).

Creation of video

An annotated instructional video was created utilising a 7-step process (Figure 7.1). The first part of this process was an assessment of current delivery room practice and was completed via the review of 39 delivery room video recordings. This review highlighted areas of improper practice relating to; drying technique, hat application, head positioning of the infant, role assignment, application of a SpO_2 probe, and placement of the polyethylene bag. Following this review, the physicians working in the NICU of CUMH were invited to the simulation lab to demonstrate stabilisation technique during a simulated stabilisation scenario.

After completion of this scenario, informal debriefing occurred with particular emphasis placed on the roles of the medical team during stabilisation and how these roles could be optimised.

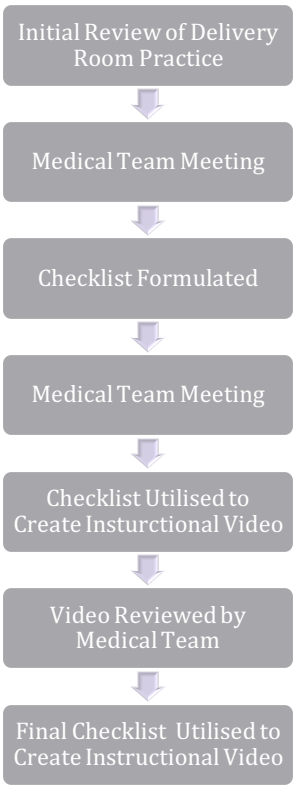

FIGURE 7.1 – 7-STEP PROCESS USED FOR THE CREATION OF THE INSTRUCTIONAL VIDEO

A checklist was subsequently formulated to display what was felt to be the optimised locations and roles for each team member during stabilisation of an infant. Again, physicians working in the NICU of CUMH were invited to the simulation lab to complete a stabilisation scenario, however, the checklist was utilised in this instance. The team were then were then asked to provide informal feedback relating to the use of the checklist during the scenario. This suggested minor critiques to the checklist and the checklist was subsequently adjusted.

Utilising the adjusted version of the checklist, an instructional video was created to demonstrate instructors utilising the checklist during a simulated scenario. Three people were involved in the creation of the video including a consultant and two neonatal registrars. Staff were then invited to view the video and to provide informal feedback. Considering this feedback, the final version of the instructional video was then created.

Finalised video content

As many of the delivery room investigations have incorporated extra monitoring tools, this annotated video aimed to incorporate these extra monitoring tools, as well as to address the current methods utilised during the stabilisation process for preterm infants

The finalised instructional video focused on three main areas; pre delivery preparation, the roles and positioning of team members during the stabilisation process, and the roles and positioning of team members during an intubation procedure.

The pre delivery preparation aspect of this video began by providing a checklist of equipment that would need to be prepared prior to delivery of an infant (Figure 7.2). Once this checklist was displayed on the video the layout was then demonstrated.

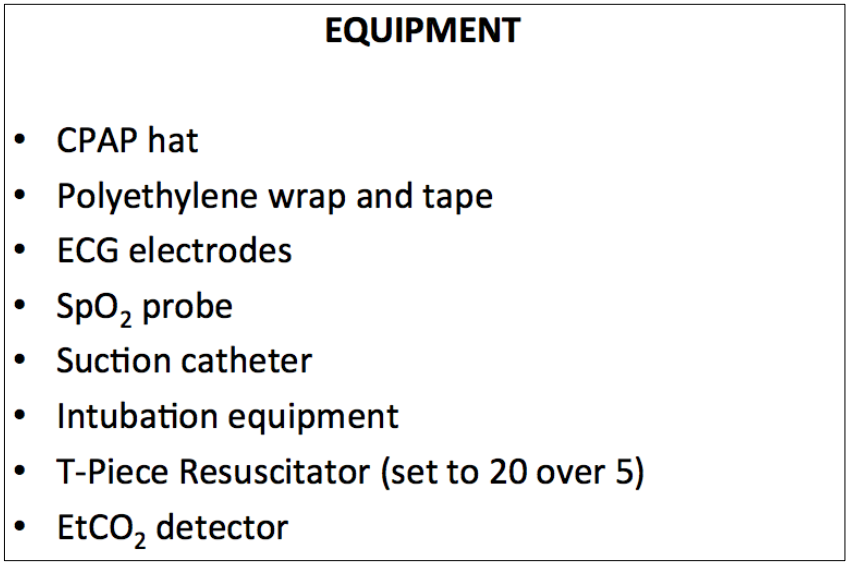

FIGURE 7.2 – SCREENSHOT CHECKLIST PROVIDED DURING THE VIDEO

The instructional video then progressed to describe optimised roles for each member of the team during the stabilisation of a preterm infant. This aspect of the video had particular focus on what the member in a certain position (e.g. at the head, to the left of the infant, or to the right of the infant) would be responsible for during the stabilisation process (Figure 7.3). The instructional

video then demonstrated 3 team members performing the initial steps of stabilisation whilst each member performed tasks previously outlined for their respective location (Figure 7.4).

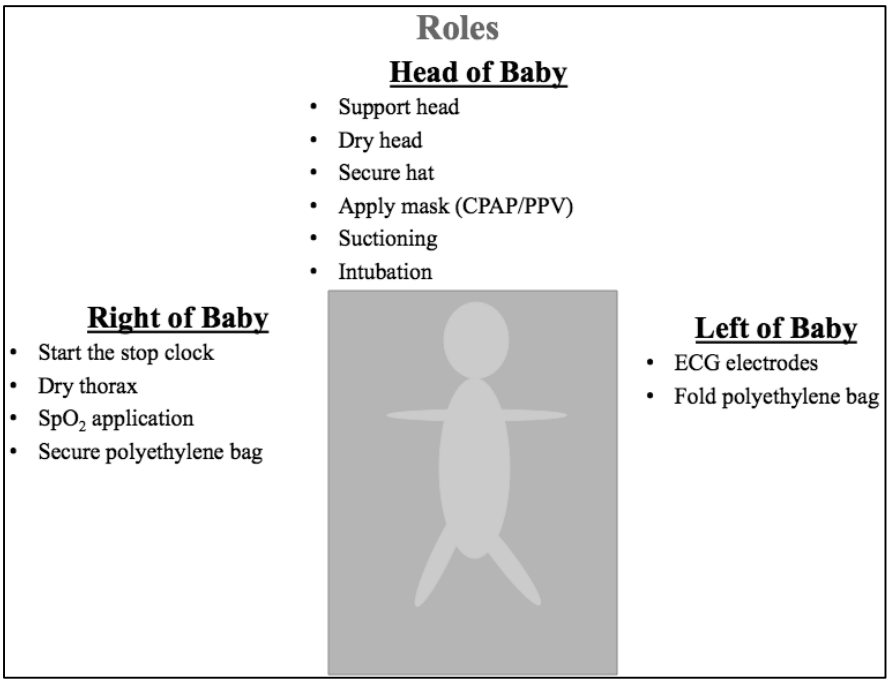

FIGURE 7.3 – ROLE ASSIGNMENT FOR STANDARD STABILISATION PROCEDURE

FIGURE 7.4 – SCREENSHOT OF DEMONSTRATION OF THE INITIAL STEPS OF THE STABILISATION PROCEDURE

The instructional video took a similar approach in describing intubation, a procedure that is often required during stabilisation of preterm infants. Firstly, the position and role of each team member was highlighted before a demonstration was then provided with team members in these subsequent roles and position (Figure 7.5 and Figure 7.6 respectively).

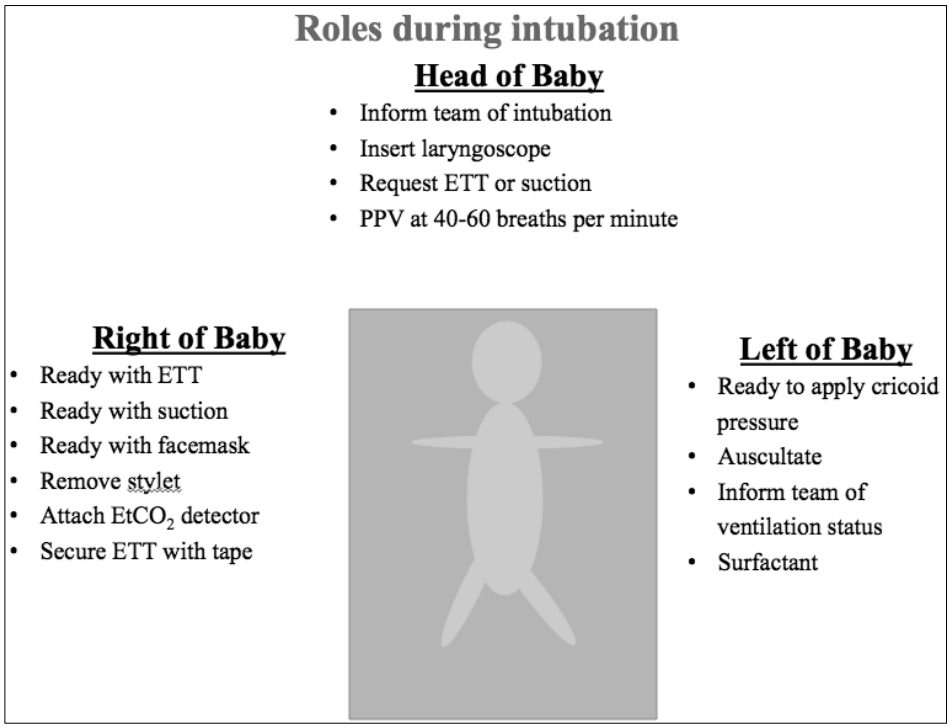

FIGURE 7.5 – ROLE ASSIGNMENT FOR INTUBATION PROCEDURE AS PROVIDED IN VIDEO

FIGURE 7.6 – SCREENSHOT OF VIDEO RECORDING SHOWING INTUBATION PROCEDURE

All neonatal trainees were then required to view the finalised instructional video as part of their weekly training schedule. Post implementation of this instructional video, stabilisation practice was assessed. This assessment paid particular attention to how well the team utilised the checklist that would have been displayed during the instructional video.

7.2.4. FINDINGS TO DATE

Four preterm deliveries occurred post implementation of this video. Delivery room practice was notably improved in the areas of role assignment, and temperature control (hat placement and placing the infant onto the polyethylene bag). The stabilisation team were observed to perform these tasks more effectively. Tasks such as securing the polyethylene bag, applying ECG electrodes, applying an SpO_2 probe, and achieving correct facemask seal, were achieved within one minute of the infant being placed with the stabilisation team.

One infant required intubation in the delivery room. The process was not clearly followed as per the instructional video. In particular, improper role assignment was found during an intubation procedure. This was evident by the team member at the left of the infant handing the ETT to the team member performing the intubation, as opposed to the person at the right of the infant being responsible for handing the ETT.

We continue to enrol in respect of assessing the role that this video may have in delivery room practice. Recruitment issues with the CAPNO trial, as well as refusal of consent from parents for the video recording aspect has meant that, to date, reviewing of delivery room practice has been impacted by video recording availability.

7.2.5. DISCUSSION

This investigation has described the creation of an instructional video and the assessment of this video on delivery room practice. Through a 7-step process, various issues were highlighted. This highlights the importance of peer review when creating an educational platform such as this instructional video.

Delivery room practice was observed to be improved post implementation of the instructional video, although it is acknowledged that only 4 delivery room stabilisation procedures occurred in this time. Improper role assignment occurred during one intubation procedure. This highlights the continued importance of maintaining skills in complicated and infrequent procedures such as intubation. Frequent viewing of the instructional video may alleviate this.

This investigation has demonstrated the utility of video recordings in retrospectively assessing delivery room performance. These video recording can act as an important resource during efforts to enhance delivery room practice. Use of video recording has the potential to supplement training by providing a trainee with continued feedback on performance as he/she completes his/her neonatology rotation. Currently, it may be difficult for a mentor to provide an individualised performance review to each trainee due to that mentor typically being employed for other tasks during the stabilisation.

As it is often difficult to have a team member assigned to the role of note taking during the stabilisation process, completing the notes for an infant relating to the first few minutes of life is typically completed soon after leaving the delivery room. Other than pharmacological interventions, it may be difficult to have access to the exact time of interventions performed when completing these notes. The availability of a video recording could alleviate this issue and allow for exact times of interventions to be obtained during completion of the notes.

In order to precisely identify the roles completed by each team member, a recording system that utilised first person perspectives was developed through collaboration with a company called OTTERA (www.ottera.com). This was a wearable system that utilised a frame, similar to the frame contained on a pair of eyeglasses, which had a high definition video camera located on the bridge of the nosepiece (Figure 7.7). This allowed for a video recording to be created from the direct view of the wearer. A first person perspective video recording obtained via this system may have the ability to provide more personalised feedback for a trainee as well as a more focused review of role assignment during assessment of the instructional video.

FIGURE 7.7 – VIDEO RECORDING SYSTEM TO PROVIDE FIRST PERSON PERSPECTIVES

The role of video recordings during neonatal resuscitation debriefing has been assessed by Nadler et al.[154] In a study assessing teamwork and procedure during neonatal resuscitation over the timeframe that a video de briefing system was implemented, it was found that areas of teamwork improved. As a result of having gained substantial experience in the use of video recording during infant stabilisation as well as having highlighted the need for on going evaluation of delivery room procedure, trainees will now receive video review sessions bi weekly as part of their formal training schedule in CUMH.

7.2.6. CONCLUSION

The utility of an instructional video for use in the teaching of infant stabilisation has been suggested by this investigation. Positive feedback was received from viewers of the video and an improvement was seen in delivery room practice, after implementation of this video. The experience gained from the creation and assessment of this video has been important in utilising this video in an attempt to improve future delivery room practice in CUMH.

7.3. TEACHING VIDEO AND VIDEO COACHING IN THE NEONATAL UNIT

Learning to complete a procedure has two distinct components. Basic theoretical knowledge of the components of the procedure is acquired through information, and technique in the practical completion of the procedure is learned through repetition. Tertiary neonatal units must provide the environment in which trainees have the opportunity to achieve the necessary procedural skills. However, a recent national survey of practice highlighted a lack of opportunity to perform certain procedures.[155] There may be limited opportunities for practice in many NICU procedures. This may be as a result of many factors such as reduced working hours for trainees in order to comply with the European Working Time Directive (2003/88/EC). Securing vascular access can be a life-saving and challenging skill to obtain. The successful placement of a PICC requires theoretical knowledge and experience. In this chapter, I will describe the development and use of a novel educational tool to facilitate acquisition of this skill.

PICCs are often used in the care of preterm and critically ill full-term infants soon after birth and are an important component of infant care.[157] This form of central venous access allows for the provision of fluids, medications, concentrated nutritional solutions[156], and also avoids the need for repeated peripheral intravenous cannula insertion. PICC insertion can be a technically challenging skill to acquire, especially in extremely preterm infants. PICC insertion has a wide array of potential complications (e.g. infections).[158] Insertion success rates vary and enhancing PICC insertion skills may be an important factor in reducing complications from unsuccessful insertions.

In order to maximize the success rates of neonatal trainees, and subsequently limit the exposure of neonates to increasing risk of complications, there has been a move away from the 'see one, do one, teach one' approach to teaching medical procedures. Where possible, teaching has been supplemented by simulation. However, it is difficult to create a high fidelity simulation model for PICC insertion. With similar principles to the stabilisation video discussed in the

previous section, an annotated video outlining the PICC procedure was created. Mayer's cognitive theory of multimedia learning asserts that individuals assimilate information at their peak when images are combined with words in an electronic learning environment.[159] This is being increasingly utilised in medical education to provide knowledge and to facilitate the acquisition of clinical skills.

Video recording assisted feedback in conjunction to oral feedback is hypothetically a superior method of information acquisition and skills retention. It allows for the appropriate consideration of positive and negative aspects of performance of a trainee. It may also allow for trainee self-improvement via self assessment and reflection.[160] Visual communication in association with verbal communication could potentially allow for a greater understanding of areas for future improvement, in addition to reinforcing a trainee's progress.

7.3.2. AIM

The aim of this investigation was to assess the effectiveness of video coaching in enhancing PICC insertion skills in trainees in neonatology.

7.3.3. METHODS

Investigation Design

This was a prospective observational investigation performed in the NICU of CUMH. Trainees in neonatal medicine, at registrar level, who were working at CUMH between February and July 2013 were eligible for inclusion in this investigation. A convenience sample of four registrars participated. All registrars had similar training in PICC insertion prior to participation in this investigation. All had previously observed a PICC procedure being performed and had prior intravenous catheter insertion experience. All participants reviewed the PICC insertion educational video. The trainees then performed PICC insertion on neonatal patients in the NICU between February and July 2013. Whilst efforts were made to reduce the time interval between individual participants and the subsequent order of participants, clinical necessity and registrar availability were the determining factors in the initiation of PICC procedures. Written consent for

participation was obtained from both the neonatal trainees and infants' parents (Appendix L).

Investigation measures

- *Annotated Video and Procedural metric*

Consultant neonatologists at CUMH created an annotated instructional video demonstrating PICC insertion technique. This video was an annotated example of a PICC insertion performed by a senior consultant neonatal physician and comprised of visual enactment of PICC insertion accompanied by text describing each procedural step. Three senior neonatal physicians independently prepared a procedural checklist with an assigned metric for PICC line insertion (Appendix L). The PICC video was then reviewed before a final metric was agreed. The checklist comprised of points scoring for completion of pre, intra, and post-PICC line insertion components. Pre-procedural points included: choosing a suitable insertion site, measuring insertion distance, positioning the infant appropriately, procedural tray preparation, and aseptic technique. Intra-procedural points for completion included: step-by-step techniques for catheter insertion. Post-procedural points related to ensuring correct catheter positioning. Four additional critical points were included, ensuring correct measurements, maintaining intra procedural sterility, procedural pause during insertion, and securing the line position.

- *Post-procedural video feedback and coaching*

A senior physician reviewed the video recording with the trainee after the insertion attempt, as a form of video coaching. This review process aimed to relay a trainee's strengths, weaknesses, and any areas of improvement that could then be worked upon by the trainee for future PICC procedures. Each subsequent PICC insertion performed by the trainee was video recorded and used for video coaching. All video recording was performed with a fixed camera. At a later date, these video recordings were reviewed and scored using the procedural based checklist with an assigned metric. An independent assessor then scored the recordings, unaware of the participant's identity and status.

Recordings were scored using binary measures i.e. 1= completed procedural point, 0= procedural point not completed, n/a= unclear whether procedural point completed. The maximum attainable pre procedural score was 9, inter procedural score was 12, and post procedural score was 6.

Ethical approval

This investigation received ethical approval from CREC (CREC reference number – ECM 4 [w] 09/01/13)(Appendix L). The data collected was anonymised and was stored securely on a password controlled hard drive in the neonatal brain research room of CUMH. The video recordings did not involve any identifying features of an infant. The only area recorded was the PICC line insertion site. No identifying features of the investigation participants were included in the video recordings. Once created, these recordings received a unique identifier number.

Data analysis

Data were analysed using SPSS version 22. After data were collected and scored, information was manually entered into the SPSS package. The denominator included only those values where a decision could be clearly determined and an overall percentage score was derived for pre, intra, and post procedure. Repeated measures ANOVA analysis was performed to examine the average score change within participants during the investigation. A Mauchlys test for sphericity was performed to determine the relationship between trainee performance with increasing number of procedures. A paired t-test between the first and third procedure was also performed.

7.3.4. RESULTS

Procedure

Four neonatal trainees performed seventeen neonatal PICC line insertion procedures over a 4-month period (February to June 2013), all of which were video recorded. The PICC insertion procedure was performed on infants with a median and interquartile range (IQR) gestational age of 28 weeks (27-31 weeks),

and birth weight of 1140g (800-1370g). Procedures were performed at 3 days (2-6 days) of life.

Two trainees attempted five insertions, one trainee attempted four insertions, and one trainee attempted three insertions. Trainees achieved an overall success rate of insertion of 53% (9/17). The success rate per person ranged from 40-100%. A wide variation in successful completion time was noted, with a range of 10-37 minutes. Trainee's favoured upper limb insertion sites for catheterisation, with 10 attempts initially performed on an upper limb. Inter-procedure time for individual trainees ranged from one day to six weeks.

Video-analysis

The ability to visualise all components of the pre-procedural component was 66% (50%-77%) and the ability to visualise the inter-procedural component was 68% (58%-83%%). The minimum number of procedures performed was three per participant. Therefore analysis on the first 3 procedures for each trainee was performed.

Repeated measures ANOVA identified a statistically significant increase in trainees' pre-procedural percentage score from procedure 1 to procedure 3 (sphericity assumed p= 0.021, partial Eta squared=72%). The mean score increased from 78.5 to 95.7% (p=0.039), from procedure 1 to procedure 3. Figure 7.8. shows the linear increase in mean performance scores within subjects over the time period between the first and third procedures.

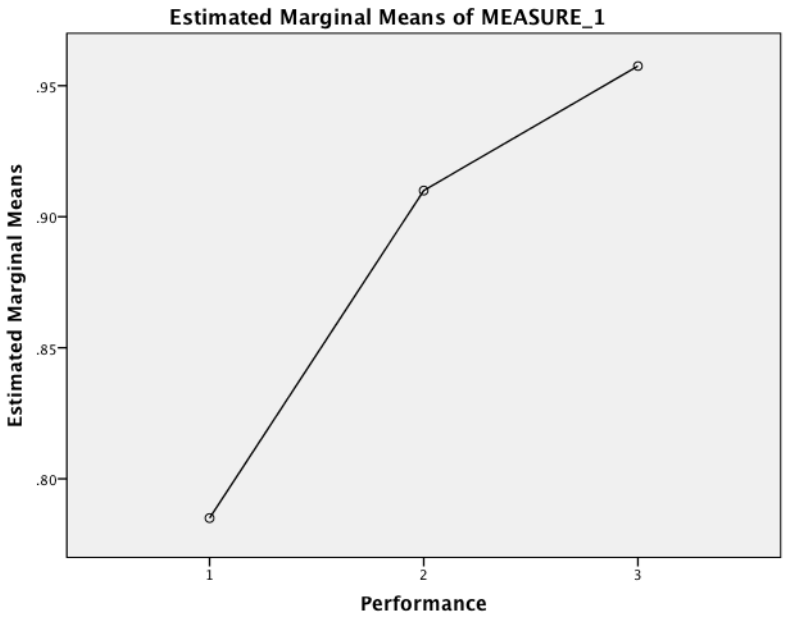

FIGURE 7.8. - MARGINAL MEANS BETWEEN FIRST AND THIRD PROCEDURES

There was no statistically significant increase in the intra-procedural scores from procedure 1 to 3 (p=0.25, partial Eta squared=37). The inter-procedural score of correctly performed visible components of the procedure increased from 92.5% to 100% between procedure 1 and procedure 3 (p=0.187).

The overall success of trainees was as follows: 50% for procedure 1, 50% for procedure 2 and 75% for procedure 3 (p=0.77). On a paired test comparison between the first and third procedure, there was no significant difference (r value=0.57, p=0.43).

Additional video Findings

Each trainee, throughout the investigation period, maintained sterility in PICC insertion. Common difficulties associated with PICC insertion were identified through examination of the video recordings. Excessive cleaning with alcohol wipes at cannula insertion point occurred, and in one case this resulted in skin desquamation and excoriation. Incorrect positioning of the infant, pre-procedure, was also observed. The head was positioned to the contralateral side in two instances, which could potentially lead to misplacement into a neck vein. If a trainee attempted to advance the PICC line before tourniquet removal,

predictable line “bounce-back” and an increase in procedural completion time was observed.

7.3.5. DISCUSSION

This investigation showed that a teaching video, the video recording of procedures, and video assisted feedback demonstrated little improvement in trainees’ overall performance in PICC insertion. There was no notable improvement in overall time for insertion or successful completion of the PICC insertion procedure. There was also no improvement in overall procedural metric from the first insertion to the last insertion per trainee. This is similar to previous work utilising video coaching in other disciplines. Backstein et al. evaluated 29 surgical residents while performing three technical skills. Participants were randomly assigned to receive no feedback, video feedback alone, or video feedback with the help of an expert (orthopaedic surgeon). This investigation failed to demonstrate an improvement in technical skills based on the utilisation of video feedback.[160] In a separate study, the same author evaluated the role of repeated video feedback on surgical trainees performing a vascular anastomosis bench model. Again, no improvement in technique with the use of video feedback was observed.[161] In a time series study, Srivastava et al. evaluated emergency medicine trainees performing lumbar punctures (LP). The study investigators then provided a second cohort of trainees with an instructional video prior to this cohort performing the lumbar puncture. Although the video increased participants' self reported comfort level with the performance of LPs and adherence to evidence-based best practices overall, it was not associated with an increase in the LP success rate in the second time period compared to the first.[162]

A number of recent trials have highlighted the efficacy of video feedback for enhancing acquisition of procedural skills. Farquharson et al. evaluated video recording as an effective modality for enhancing feedback, when compared to standard verbal feedback alone.[163] Trainees performed a surgical procedure, returned on the following day, and then performed the procedure again following video and standard verbal feedback (group 1) or standard verbal feedback alone

(group 2). Group 1 performed better as evidenced by an improvement in the overall procedural score. The authors concluded that video feedback should be incorporated into surgical curricula. Helland et al. investigated the efficacy of a new video-based training model in spinal surgery amongst neurosurgical trainees. They concluded that video-based training can improve microsurgical skills and help to promote a higher acquisition of surgical skills.[164]

There are several factors that may have contributed to the lack of trainee's improvement in PICC line insertion in this investigation. A wide variation in inter-procedural time may impact upon a trainee's retention of skills. This is consistent with performance in infant stabilisation where the retention of skills has been found to be reduced the longer the time between follow up assessments.[165] A shorter period between PICC insertions may result in a greater recall of the original annotated video. Secondly, video coaching by senior staff members may not be recalled the longer the duration of time between procedures and hence any possible advice gained may not be recalled. The lack of situated learning could be a factor. In this investigation, trainees did not review the procedure prior to each attempt at the bedside. Making this video available at the bedside, just before the procedure takes place, may be worth exploring in future studies.

The overall success rate was low at 53%. This figure is for first year senior trainees attempting PICC insertion and serves as a baseline to gauge future performance, and also highlights the importance of developing techniques to improve education in this area. There may be many reasons to explain this relatively low success rate. The individual variability in each infant's anatomy may be a factor, especially when procedures are performed early, during the first few days of life. The small number of procedures overall may have emphasised this issue and may also have contributed for this lack of improvement. The impact that the presence of a video recording device may have on a trainee's performance must also be considered. Anxiety relating to this may have accounted for increased procedural time, including tentative mistaken insertion technique. This anxiety may have also contributed to over-caution regarding

sterile procedure e.g. excessive cleaning with alcohol swabs as evidenced in a number of the videos.

This investigation has highlighted a number of other technological aspects. An alternative method of obtaining video recordings should be considered. A stationary mounted camera was used for recording procedures during this investigation. Although overall this medium made for clear, easy to score videos, there were negatives associated with this method also. The tripod mount made it difficult to manoeuvre the camera to gain the optimal angle of the trainee's procedure, often as a result of the distance of the camera from the infant. A handheld camera would additionally prove troublesome and could potentially interrupt what is an already intricate procedure. Overall, approximately two thirds of all procedures were visualised completely with the mounted camera, which is an important factor to consider when it is being used to provide feedback to the trainees. Future consideration should be given to a head-mounted miniature camera for completion of procedures. This would provide first person perspective of the procedure, and allow a greater recognition of the problems encountered during attempted insertion.

7.3.6. CONCLUSION

This investigation has highlighted several important outcomes. Firstly, video-analysis confirmed that sterile field compliance was well maintained by all trainees during completion of the procedure. This is relevant as many PICC insertions may be complicated by avoidable infection, potentially resulting in mortality. These findings are consistent with those of Xiao et al. who used video-based training to demonstrate increased sterile-technique compliance during central venous catheter insertion in adults in the intensive care unit setting.[166] Secondly, the development and utilisation of instructional video, as well as video coaching, resulted in trainees' increased adherence to preparedness for the PICC procedure, as is evidenced by an increase in trainees' pre-procedural percentage scores. This increase in trainees' preparedness and compliance with video instruction is promising.

7.4. ASSESSMENT OF THE POTENTIAL INTRODUCTION OF A WEBCAM SYSTEM IN THE NICU

The role of video technology use by medical staff in improving infant care was discussed in the first investigations in this chapter. Following these studies, we considered the potential role of video technology in other areas of perinatal care. We considered the problem of parental anxiety when separated from their infant in the NICU, and developed a study to determine if webcam use would be accepted in this setting by staff and parents.

7.4.1. INTRODUCTION

CUMH and many other tertiary neonatal units have a strict NICU visiting policy allowing for parental visitation only. This is used to reduce movement within the NICU and to reduce nosocomial infection risk. This means that siblings, grandparents, and extended family are generally not allowed to visit the NICU.

Admission of an infant to the NICU is a stressful period for the entire family, often with many important decisions having to be made during the inpatient stay.[167-169] The physical environment of the NICU often adds to the stress experienced by the family.[170,171] Preterm birth and an infant's unstable condition can impact on the mother-infant attachment.[171] This difficulty in establishing a mother-infant attachment can add another stressor to the overall NICU experience.

There are several support programs available in the neonatal setting to support families during this stressful time.[172] The degree of separation experienced by a mother from her infant is associated with an increased level of anxiety for the mother.[173] This may have significant implications for maternal bonding.

Through the implementation of a Baby CareLink system in 4 hospital NICUs, that allowed parents to view pictures of their baby, Safran et al. suggested that the digital pictures provided by the Baby CareLink system were of a substantial benefit to parents who were geographically distant from their baby.[174]

Webcams have previously been implemented in the neonatal intensive care unit setting in a number of countries including the Netherlands, Australia and the USA. The NICVIEW (Kentucky, USA) webcam service is one example of such a service. While they have presented many technological, administrative, operational and clinical challenges, they may have a worthwhile positive impact on parent experience.

7.4.2. AIM

The primary aim of this questionnaire-based survey was to evaluate the views of eventual end users of a webcam system namely; parents, physicians, and neonatal nursing staff. The secondary aim of this survey was to help in building a platform for a webcam system to be implemented in the NICU of CUMH.

7.4.3. METHODS

This investigation received ethical approval by CREC (CREC reference number – ECM 4 (f) 04/09/12)(Appendix J).

An anonymous 8-item questionnaire was developed specifically to assess parental views on the use of a webcam monitoring system within the NICU (Appendix J). This questionnaire used a Likert scale and also contained a feedback section where the participant was free to write additional comments. Parents were informed that participation was voluntary and completion of the questionnaire was considered to be consent to participate in the investigation. All questionnaires were anonymous and the information collected from the parents was analysed using frequency tests.

A second questionnaire relating to the potential implementation of a webcam monitoring system within the NICU was created for medical and nursing staff (Appendix J). This questionnaire consisted of 6 questions, again utilizing a Likert scale as well as a free text section that allowed medical staff to provide written feedback. The questionnaires were answered anonymously, but respondents indicated their clinical role in the NICU (i.e. physician, neonatal nurse). Again

the voluntary completion of the questionnaire was considered consent to participate in the investigation.

Statistical analysis was performed using SPSS version 22.0 (IBM, NY, USA). All tests performed were two sided and a p-value <0.05 was considered to be statistically significant. Differences between the two groups (medical and nursing staff) were investigated using the Mann Whitney U test.

7.4.4. RESULTS

There were 99 responses in total (50 nurses, 26 physicians and 23 parents). Two sets of parents declined to participate.

82.6% of parents used a computer regularly. 73.9% indicated that they would use a webcam system in the NICU regularly, if it were implemented. Parents also thought that a webcam system would reduce the amount of phone calls they would make to the NICU, but felt it would not reduce the amount of times that they would physically visit the NICU. Overall, parents expressed a view that a webcam system would reduce the levels of stress that they might experience when they are away from the NICU (Table 7.1).

In the feedback section, parents highlighted issues such as guilt when they are away from the NICU, however, these parents felt that a webcam system might alleviate some of this guilt. Mothers also indicated that being unwell in the immediate newborn period and unable to visit the NICU was a source of stress. Again, the utilisation of webcams was suggested by them as a potential way of alleviating the impact of this.

TABLE 7.1- LIKERT SCALE RESPONSES TO PARENTAL QUESTIONNAIRE (% FREQUENCY)(N=23)			
	Likert Score (1=Not at all, 5=Very much so)		
Question	**1/2**	**3**	**4/5**
How often do you use a computer?	4.3	13.0	82.6
How often do you use a webcam?	52.2	17.4	30.4
How often do you think you would use this service if it were to be implemented?	8.6	0.0	91.3
Do you feel confident in the security behind webcam use to view your baby?	4.3	4.3	91.3
Would you share your password with another person e.g family member or friend?	47.8	8.7	43.5
Do you think you would experience less stress when you were away from the hospital if this service was available?	8.7	17.4	73.9
Do you think it would reduce the number of phone calls you would make to the unit?	34.7	8.7	56.5
Do you think it would reduce the number of times you would visit the NICU?	86.9	4.3	8.6

The majority of the nursing staff indicated feeling the opinion that the frequency of calls would not be reduced following the introduction of a webcam system to the NICU. Over three quarters of nurses felt that the webcam system would have no impact on the amount of times parents would visit the NICU. There was a statistically significant difference between responses from nurses and doctors to the question relating to the stress levels experienced by staff with a webcam system in place (p-value< 0.001). 72% of nurse indicated that a webcam system would increase the stress levels of staff, compared to less than 20% of physicians who had this opinion (Table 7.2).

TABLE 7.2 - LIKERT SCALE RESPONSES TO MEDICAL STAFF QUESTIONNAIRE (% FREQUENCY)(N=49)								
Question	**1=Not at all, 5=Very much so**							
	Nurses (n=50)				**Doctors (n=26)**			
Answers	**1/2**	**3**	**4/5**		**1/2**	**3**	**4/5**	***p-value***
Do you feel confident in the security behind webcam use to view babies in the NICU?	68	20	10		19.2	30.8	50	<0.001
Are you familiar with any webcam use, similar to this, elsewhere?	84	8	8		57.7	15.4	26.9	0.020
Do you think this would reduce the amount of time parents spend in the NICU?	76	22	2		65.3	11.5	23.1	<0.001
Do you think this will reduce the amount of calls made to the NICU by parents?	92	4	4		46.1	11.5	42.3	<0.001
Although the webcam will not be assessing performance of staff, do you think that the presence of a webcam will add to stress levels experienced by staff?	6	12	82		26.9	15.4	57.7	<0.001
Are you in favour of a system such as this being implemented?	76	12	12		60.6	13.2	26.3	<0.001

Feedback from the health care staff highlighted a number of issues. The nursing staff appeared to have far more concerns about the security behind the use of webcams in the NICU than the physicians. Members of the nursing staff were concerned about data protection and in general concerned about security risks. These differed significantly from physicians' views (p-value <0.001). However there was no difference between both groups in relation to familiarity with similar webcam systems being implemented in hospitals elsewhere.

Overall, there was a negative sentiment expressed from nursing staff in the free text section of the questionnaire. Many of the negative comments on the feedback section highlighted issues such as funding for the implementation, and subsequent maintenance, of a webcam system. This expense was felt to be

inappropriate at a time when they are experiencing salary reductions due to budget restrictions. Many nurses also felt uncomfortable about the possibility of being seen on the webcam as they leaned over the cot of the baby.

7.4.5. DISCUSSION

This questionnaire-based investigation has shown that the majority of parents who completed the questionnaire had a positive attitude towards the implementation of a webcam system in the NICU and, as a result, were in favour of such a system being introduced. The positive feedback received from parents would suggest that the implementation of a webcam system in the NICU of CUMH is something that warrants consideration. While parents are encouraged to spend as much time as possible with their infant in the NICU, the introduction of webcams to the NICU may provide a link for them during the times that it is not possible for them to be with their infant. This continuity of access to their infant may promote bonding, and allow other family members, who are restricted in visiting the NICU, to see the infant. The opinion that it would reduce stress levels for the parents is encouraging, but this can only be answered prospectively with objective assessments of parental stress levels when a webcam system would be in place.

However, this investigation has shown that there is an overall negative attitude towards a webcam system from health care providers. This is more noticeable amongst the nursing staff, but is also the case with physicians. There may be many reasons for this negative feedback. There may be a lack of understanding as to what a webcam system and what it entails for the end users, both parents and physicians. Concerns over potential workload, such as having to deal with malfunctioning equipment and additional phone calls from parents about the use of the system as well as about their infant, may have negatively influenced responses. The timing of the questionnaire may have also influenced responses, considering current resource and personnel reductions.

The feedback received from parents as well as medical staff has raised some interesting issues and may allow for better implementation of any future webcam

systems in the NICU setting, once concerns expressed by respondents are addressed.

Family centered care involves parents primarily, however, involvement of siblings, grandparents and the extended family cannot be overstated. Currently, the extended family's role is limited when the infant is admitted to the NICU. Family centered care revolves around the theory that the family has the greatest influence in the health and well being of an infant. Health care professionals should strive to involve the family in the care giving roles as much as realistically possible.[175] Whilst the NICU is not conducive to these, their importance should not be underestimated. With advances in technology, webcam infrastructure, smartphones, and overall access to the internet; many people now have access to the internet 24/7 via broadband in a home or internet network on a smartphone.

Another potential area in which webcams may influence care is for consultant neonatologists, who are on-call from home overnight. They are often called for advice from nursing staff and medical trainees. Although not explored in this investigation, high definition webcams would allow the consultant to see the infant being discussed. Visual inspection combined with medical history and vital signs described over the phone and remotely accessible laboratory/radiographic results, may improve the consultant's assessment of the situation and impact upon the advice provided. This could represent another area of future research.

7.4.6. CONCLUSION

The results of this investigation provide a basis for the implementation of such a webcam system in the NICU of CUMH. Specifically, we have identified a number of concerns that need to be addressed prior to progressing with introducing webcams to the NICU.

This is the first step towards the introduction of a webcam system in the NICU of CUMH. The investigation has identified parental demand as well as perceived advantages and disadvantages of a webcam system. The introduction of webcams

to the NICU at CUMH has recently been funded by Science Foundation Ireland (SFI), and future studies will evaluate and address the concerns identified in this thesis.

7.5. CONCLUSION OF CHAPTER

This chapter has demonstrated the utility of different forms of technology when applied to various aspects of infant care. The potential role of a teaching video on improving the stabilisation procedure of infants in the delivery room was discussed. Many inconsistencies were found in stabilisation procedures performed prior to the implementation of this instructional video and, although a small number of videos were analysed following implementation of this video, minimal inconsistencies were observed in these videos.

The next step was to develop an educational video for PICC insertion that integrated direct video-mediated feedback in an effort to improve teaching of this skill. Unfortunately, the results from the assessment of this video were disappointing. Although the assessment demonstrated that visual educational tools might be helpful, frequent practice of technical skills is clearly more important.

Another potential use of video technology in infant care is the use of webcams to improve the family's experience when their infant is admitted to the NICU. This assessment was essential in creating a proposal for a webcam system in the NICU of CUMH. SFI has now funded this project. As well as providing a means for parents to view their infant when away from the NICU, this system will include an interactive monitor at the cot side that will allow parents to view information about their infant's treatment in the NICU. This will supplement the regular interaction that parents receive from medical staff about the infant's treatment in the NICU. This system will also provide a remote viewing platform to consultants. An educational component of this system will also exist. Prior to completing a procedure, a physician will be able to log in to the cot side monitor to access a library of annotated procedural videos.

Despite the potential of technology to advance infant care, potential users can meet the introduction of new aspects, such as webcams, with scepticism. These opinions require close consideration during implementation of this technology in the clinical setting.

CHAPTER 8: ENHANCING STABILISATION TRAINING

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The Demand for an Educational Smartphone App.

Hawkes GA, Hawkes CP. Ryan CA, Dempsey EM.

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(Appendix M)

-AND-

A Randomized Controlled Trial of a Mobile Phone Infant Resuscitation Guide.

Hawkes GA, Murphy G, Dempsey EM, Ryan CA

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8.1. INTRODUCTION

In the first section of this chapter, I describe an investigation designed to optimise a commonly used tool during infant stabilisation training.

One of the most challenging procedures for trainees in neonatology to perform is the insertion of an endotracheal tube to secure the neonatal airway. Intubation is a procedure that may be required both in the delivery room as well as in the NICU and can be life sustaining in the emergency setting of respiratory arrest. There are many forms of medical orientated technology that are increasing in usage amongst all healthcare staff, such as smartphone technology. A neonatal research group in CUMH, through collaboration with the UCC Department of Business Information Systems, created an educational smartphone application ("Neotube") designed to facilitate trainees learning this technique. The demand for these educational approaches to teaching procedures in neonatology had not previously been described. Prior to developing our own educational materials, we assessed this demand using Neotube use in the 2 years following release in 2011.

The final investigation in this chapter will assess the use of a mobile phone infant resuscitation guide amongst a group of teenagers in an *in vitro* setting. This was developed to provide guidance in infant resuscitation to the larger out-of-hospital community. The aim of this application was to improve the performance of out-of-hospital infant resuscitation, which could be applicable to inadvertent home deliveries, or cardiorespiratory arrest in an infant.

8.2. ASSESSMENT OF DIFFERENT MANNEQUIN MODELS

8.2.1. BACKGROUND

Practicing stabilisation scenarios are central in learning skills required during infant stabilisation. There are a number of infant mannequins available for teaching infant bag mask ventilation (BMV) skills.[2,103] These mannequins are designed to demonstrate chest wall rise and fall during effective BMV, and absence of chest wall excursions if there is incorrect positioning of the mannequin airway during BMV. Popular training mannequins include the collapsible "NeoNatalie" newborn mannequin (Figure 8.1) and the rigid "Resusci Baby" infant mannequin (Figure 8.2) (both Laerdal Medical Foundation, Stavanger, Norway).

FIGURE 8.1 - NEONATALIE NEWBORN MANNEQUIN (WWW.LAERDAL.COM)

FIGURE 8.2 – RESUSCI BABY INFANT MANNEQUIN (WWW.LAERDAL.COM)

In an investigation of four different infant mannequins used for resuscitation training, the rigid Resusci Baby infant mannequin was determined to have the highest level of fidelity out of all of the different mannequins investigated.[176] This mannequin has also been employed in many *in vitro* studies investigating various aspects of PPV that may be required during infant stabilisation.[17,25,31,34,177-179]

While the Resusci Baby mannequin is a fixed model requiring no additional assembly to operate, the NeoNatalie newborn mannequin is a collapsible plastic mannequin, designed to be filled with air or water prior to use. Manufacturer guidelines recommend that the NeoNatalie is filled with two litres of water or, alternatively, filled with air.[180] Filling this mannequin with a mixture of air and water has not previously been explored as an option to optimise fidelity. The NeoNatalie, is used worldwide as the standard teaching mannequin for the Helping Babies Breathe (HBB) program.[180]

8.2.2. AIM

To examine user preference and user ability in performing effective BMV with a Resusci Baby infant mannequin as well as a NeoNatalie neonatal mannequin configured with different air/water arrangements.

8.2.3. METHODS

All medical staff working in the neonatal unit of CUMH were eligible for inclusion. Each participant was required to provide 30 seconds of BMV to one of four mannequin configurations: 1) A Resusci Baby infant mannequin (RB), 2) a NeoNatalie mannequin fully filled with air (NNA), 3) a NeoNatalie mannequin fully filled with water (2 litres) (NNW), and 4) a NeoNatalie mannequin filled with a mixture of 50% air and 50% water (approximately 1 litre) (NNAW). Participants were allowed to familiarize themselves with each mannequin and, once comfortable, the order in which they were to perform BMV on each different mannequin was randomised. This randomisation was completed by means of sealed envelopes containing the name of each configuration and each participant was instructed to pick 4 of these envelopes at random. The order in

which these envelopes were picked subsequently determined the order in which participants were assigned to use each mannequin.

After participants completed the 30 seconds of BMV in each configuration of mannequin they were asked to complete a questionnaire. Utilising a 5-point Likert scale, participants were asked to assess the level of fidelity of the mannequins to a "real infant" and a Likert score of 4 or 5 was deemed to indicate a high level of fidelity. The categories assessed with each mannequin configuration included; the feel, the tone, the weight, the realism of ventilation, and how the mannequin felt to hold. A short debriefing took place with each participant upon completion of BMV in the 4 different mannequins to obtain further, informal, feedback.

Each 30-second period of BMV was video recorded. The camera was placed to the side of the mannequin at a position that allowed any chest rise to be visible. Two reviewers (thesis author GAH and thesis supervisor ED) independently analysed the recordings in order to assess the amount of effective breaths delivered within each of the mannequin configurations, by each participant. A ventilation was deemed to be effective if chest rise and fall was observed during the squeeze of the bag mask device. The video recordings were anonymised and the observers were unaware of the order in which the participants completed the investigation. Where disagreement existed, relating to effective ventilation, among the 3 observers consensus was decided by a majority decision.

Statistical analysis for this investigation was performed using IBM SPSS Statistics 22.0. For each category, fidelity was described using percentages and comparisons of the four configurations with regard to their likert score. Comparisons were performed using a Cochran's Q Test. If statistically significant differences were found, pairwise comparisons were performed using McNemar's test, with Bonferroni correction for multiple testing. The number of effective ventilations for each configuration was summarised using median and interquartile range (IQR). Friedman's test was used to compare the distributions of effective ventilations between the four configurations. If a statistically significant difference was found, pairwise comparisons were performed using the

Wilcoxon Signed Rank test, with Bonferroni correction. All tests were two-sided and a p-value <0.05 was considered to be statistically significant.

8.2.4. RESULTS

20 participants completed this observational investigation, consisting of 10 doctors and 10 nurses. All participants had completed NRP training within 2 years prior to commencement of the investigation. Participants' perceptions of the level of fidelity of each mannequin configuration, in terms of hold, tone, appearance, touch, weight and providing positive pressure ventilation compared to a "real baby" are as follows.

To hold

There was a statistically significant difference in fidelity of the "to hold" variable among the four configurations (p<0.001). 65% of participants indicated that the NNW configuration had a high level of fidelity to hold. This was compared to 50% for the NNAW configuration and 10% for the RB configuration. No participant indicated the NNA configuration as having a high level of fidelity to hold (Table 8.1). Pairwise comparisons revealed that the significant differences were between the NNA configuration and both the NNW (adjusted p<0.001) and NNAW (adjusted p=0.004) configurations and between the RB configuration and both NNW (adjusted p=0.001) and NNAW (adjusted p=0.036) configurations.

TABLE 8.1 – PERCENTAGE OF PARTICIPANTS WHO INDICATED A HIGH LEVEL OF FIDELITY (N=20)

Category	RB	NNW	NNA	NNAW	p-value
Appearance	45	15	20	45	0.035*
Touch	15	30	10	35	0.183
To Hold	10	65	0	50	<0.001*
Weight	40	45	0	50	0.003*
Tone	20	40	5	50	0.008*
Realism of Ventilation	25	60	20	55	0.007*

*Statistically significant

Tone

There was a difference in the participants' perception of fidelity of mannequin "tone" among the four configurations (p=0.008). 50% of participants indicated that the NNAW configuration had a high fidelity relating to tone. This was compared with 40% for the NNW configuration, 20% for the RB configuration, and 5% for the NNA configuration (Table 8.1). Pairwise comparisons revealed that the only significant difference was between the NNA configuration and the NNAW configuration (adjusted p=0.010).

Appearance

There was a statistically significant difference in participant's perceptions of fidelity in terms of mannequin appearance among the four configurations (p=0.035). 45% of participants indicated the RB configuration, and 45% of participants indicated the NNAW configuration as having a high level of fidelity in terms of appearance. This contrasted with 20% of participants indicating a high level of fidelity of appearance in the NNA method, and 15% in the NNW method (Table 8.1). None of the pairwise comparisons were statistically significant after controlling for multiple comparisons.

Touch

35% of participants indicated the NNAW configuration as having a high level of fidelity to how it felt to touch. This was compared to 30% for the NNW configuration, 15% for the RB configuration, and 10% for the NNA configuration (p=0.183)(Table 8.1).

Weight

There was a statistically significant difference in fidelity in relation to weight among the four configurations (p=0.003). 50% of participants indicated that the weight of the NNAW configuration had a high level of fidelity. This was compared with 45% for the NNW configuration and 40% for the RB configuration. No participant indicated that the NNA had a high level of fidelity in relation to weight (Table 8.1). Pairwise comparisons revealed that the

significant differences were between the NNA configuration and the three other configurations (adjusted p=0.005 for NNA vs NNAW, adjusted *p*=0.015 for NNA vs NNW, and adjusted *p*=0.043 for NNA vs RB).

Providing ventilation

There was a statistically significant difference in fidelity of providing BMV among the four configurations (*p*=0.007). In relation to the level of fidelity of providing BMV to each configuration, 60% of participants indicated a high level of fidelity in the NNW configuration compared to 55% in the NNAW configuration, 25% in the RB configuration, and 20% in the NNA configuration (Table 8.1). Pairwise comparisons revealed that the only significant difference was between the NNA configuration and the NNW configuration (adjusted *p*=0.034)

There was a statistically significant difference in the distributions of effective ventilations among the four configurations (*p*=0.001). Over the 30-second period of BMV, participants delivered a median of 18 (IQR 13, 26) effective ventilations to the NNW configuration, 17 (IQR 6, 20) to the NNAW configuration, 14 (IQR 7, 16) to the NNA configuration, and 14 (IQR 1, 20) to the RB configuration (Table 8.2). Pairwise comparisons revealed that the significant differences were between the NNW configuration and both the NNA (adjusted *p*=0.005) and RB (adjusted *p*=0.016) configurations.

TABLE 8.2 – MEDIAN (IQR) NUMBER OF EFFECTIVE VENTILATIONS (PER PARTICIPANT) AND TOTAL NUMBER OF EFFECTIVE VENTILATIONS (PER TOTAL NUMBER OF PARTICIPANTS)

	RB	NNW	NNA	NNAW	p-value
Median	14(1,20)	18(13, 26)	14 (7, 16)	17(6,20)	0.001*
Total number of ventilations	250	247	378	297	0.001*

*Statistically significant

Through the informal debriefings undertaken after each participant had completed the interactions with all mannequins, it was found that the majority of participants disliked the RB configuration. They reported that the required head positioning, in order for the RB mannequin to have an unobstructed airway, was

of a low level of fidelity and difficulty in comparison to their experience with an actual infant. Participants also reported that the lack of fidelity in the airway of the "bloated" NNA mannequin caused them unrealistic difficulties in the provision of the effective ventilation.

8.2.5. DISCUSSION

This investigation has assessed 2 mannequins (in a total of 4 different configurations) that are currently available for use in neonatal resuscitation training. The configurations of the collapsible NeoNatalie infant mannequin when fully filled with water, as well as filled with a mixture of 50% air and 50% water, were both shown to have the highest number of effective ventilations delivered. Participants, when comparing to a "real baby", also rated these configurations to have the highest level of fidelity in most categories. Since there is no apparent advantage to completely filling the NeoNatalie with water, this investigation highlights that a mixture of water and air may be more suitable for the NeoNatalie mannequin.

During the use of the earlier model of the NeoNatalie mannequin in the teaching of neonatal resuscitation in CUMH, the mannequin experienced a number of leaks and punctures in the neck and shoulder areas. While the cause of this design flaw is unclear, the manufacturers have subsequently strengthened these areas in the newer models. While this investigation does not suggest that overfilling with water was a contributory factor in this problem, the results of this investigation do indicate that fully filling the mannequin with water is not necessary to achieve good fidelity to a "real baby" and to achieve optimum user ventilations during BMV. However, it is important to note that optimum ventilations in a mannequin may indicate that the mannequin format is not necessarily challenging for the user. This may be unrealistic; when compared to the difficulty often encountered when ventilating an asphyxiated newborn infant or a premature infant with surfactant deficient lungs.

This investigation also investigated the configuration of the NeoNatalie fully filled with air, as it is one of the possible configurations recommended by the manufacturers. This configuration was given the lowest overall fidelity score by

participants, across all categories. This configuration was also shown to have the lowest number of effective ventilations delivered by participants. When inflated with air, the NeoNatalie tends to become bloated and rigid, similar to a baby with extensive subcutaneous emphysema. Such babies can be more difficult to ventilate, as was the air-filled configuration of the mannequin. The low fidelity of this configuration indicated by participants is understandable. When filled with air, the NeoNatalie is extremely light and tense, and is not realistic in terms of holding, weight, touch and tone. This investigation would therefore recommend, for fidelity and user ability reasons, that the configuration of using the NeoNatalie filled exclusively with air is not suitable for training purposes.

From the feedback highlighting the lack of fidelity in terms of touch, tone and realism of ventilation, the results of this investigation would suggest that the rigid Resusci Baby mannequin is not desirable in newborn resuscitation training. Although participants were not asked to comment on size, the mannequin is unrealistically larger than the average term newborn. The findings of this investigation are similar to previous studies assessing the use of low fidelity rigid mannequins that also found how they might not be appropriate for neonatal resuscitation training.[176,181] Howells et al. highlighted a low level of fidelity in the rigid Resusci Baby with a investigation encompassing views expressed by 4 participants.[176] However, the investigation in this chapter has encompassed views from 20 participants. Although Curran et al. found similar issues relating to fidelity in a rigid low fidelity mannequin, similar to the Resusci Baby, investigation participants included medical students who may not have had much physical experience in providing care for newborn infants.[181] The participants of the investigation in this chapter were either neonatal nurses or doctors, all of whom had extensive, regular, experience with infants in the delivery room as well as the NICU.

High fidelity neonatal simulators are also available for teaching newborn resuscitation. The SimNewB® is an interactive simulator designed by Laerdal in collaboration with the American Academy of Pediatrics to meet the training requirements of the NRP. The SimNewB simulator accurately represents a full-term, 50th percentile newborn female measuring 21 inches and weighing 7

pounds. A wide variety of patient conditions can be simulated, ranging from a cyanotic newborn with no vital signs to a moving, crying, and vigorous newborn infant. Previous studies have found that the use of high fidelity mannequins compared to low fidelity mannequins in neonatal resuscitation training does not necessarily result in improved learning outcomes.[181,182] Norman et al. have highlighted the issue of the substantial cost that is often associated with high fidelity mannequins versus their subsequent impact on learning outcomes.[183]

The NeoNatalie mannequin is employed for use in the HBB curriculum in the developing world partly due to the low cost associated with the mannequin. The guidelines for the use of these mannequins during neonatal training currently do not suggest the mannequin to be used with a configuration of 50% air and 50% water. However, this investigation has shown that this configuration may have the same level of simulation as the mannequin filled with 100% water, which is currently one of the configurations recommended.

A limitation of this investigation is that the observers of the video recordings were not blinded to the type of mannequin being used by the participant. This could not be avoided; however, the observers were blinded to the order in which each participant completed the investigation.

8.2.6. CONCLUSION

In this investigation, I have shown that the NeoNatalie mannequin configurations that contain water have the highest level of user preference. NeoNatalie configurations filled with 100% water have been shown to offer no advantages over a 50% water/50% air mix. The NeoNatalie filled with air should no longer be used for training purposes in view of poor fidelity and user difficulty in providing effective ventilations. Similarly, due to the low level of fidelity found, consideration should be given to avoid the rigid Resusci Baby in the teaching of newborn resuscitation, if more effective alternatives are available.

The majority of candidates ventilated these configurations with little difficulty which would be unlikely in a real life setting. Therefore, these mannequins may not be the most effective and challenging simulation tools. By completing this

investigation, I have highlighted areas in which future infant mannequin design may improve in order to optimise the teaching of neonatal resuscitation. Perhaps mannequins with airways of adjustable and graded resistance could be developed. Further investigations into learning outcomes with the use of different mannequins will determine the importance of these recommendations.

8.3. UPTAKE OF A NEONATAL INTUBATION SMARTPHONE APP

8.3.1. Introduction

Smartphone use amongst the medical profession is becoming more popular with most medical textbooks, medical calculators and drug formularies now being available on smartphone platforms. The Department of Health (DoH), in the United Kingdom, is one of many organizations that have already acknowledged this advance in technology. The DoH highlighted that the use of innovative educational technologies such as e-learning, simulation, and smartphones may enhance patient care by providing opportunities for students, as well as health care providers, to accumulate essential knowledge and skills that they can then use in the treatment of patients.[184] The uses of smartphone applications for trainees in specialties such as surgery and pain management have been recently reviewed.[185,186] After a review of 10 smartphone applications available for paediatric anaesthesia, Bhansali and Armstrong drew attention to the accessibility of most of the applications for trainees and in particular, their use in paediatric drug calculations for anesthesia.[185] In an assessment of various orthopaedic smartphone applications, Al-Hadithy et al. highlighted the wide range of uses that smartphone applications may have for surgical trainees.[186]

Infant intubation is a potentially life-saving skill. Opportunities for trainees to intubate infants have reduced in recent years[187], as a result of reducing indications for this procedure[188,189] and reduced working hours, as per the European Union's Working Time Directive (2003/88/EC)[190]. In 2011, a smartphone application entitled "Neotube" was developed to assist paediatric trainees in learning infant intubation. This application sought to maximize the benefit of each intubation opportunity for paediatric trainees, to overcome the impact that reduced opportunities to perform intubations may have on skill acquisition.

This application was based on "just in time" training and "situated learning" and the application development procedure has been described in more detail by the team that developed the educational tool.[191] The development of this application included five components including; planning, content compilation, layout

design, implementation, and evaluation. Development incorporated user feedback at each stage, with independent external peer review occurring before release. This review process was considered by the application project team to be essential for effective development of an evidence-based application. This process of external peer review, that was undertaken for this application, and which is mandatory for most medical publications, is not required for smartphone applications. The application was released in February 2011.

The application consists of 29 pages, 7 videos, 19 images and a calculations section. All information and calculations provided within the application were based on NRP guidelines. The application provides a detailed description of the anatomy of an infant, relevant to the intubation procedure (Figure 8.3), the relevant equipment needed for intubation (Figure 8.4), and complications that may occur during intubation (Figure 8.5). The application also provides a section to allow the user to input an infant's weight before then providing the user with the correct endotracheal tube size, laryngoscope blade size, and depth of endotracheal tube insertion for that infant (Figure 8.6). Use of this application has been shown to improve intubation knowledge and technique technique, as well as reducing the time taken to intubate a mannequin model.[192]

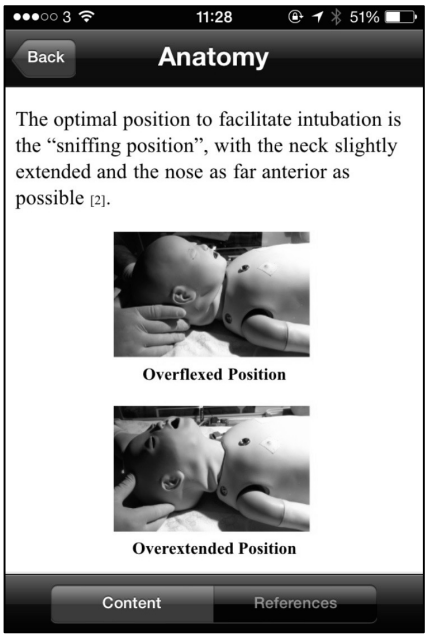

FIGURE 8.3 – SCREENSHOT OF THE ANATOMY SECTION

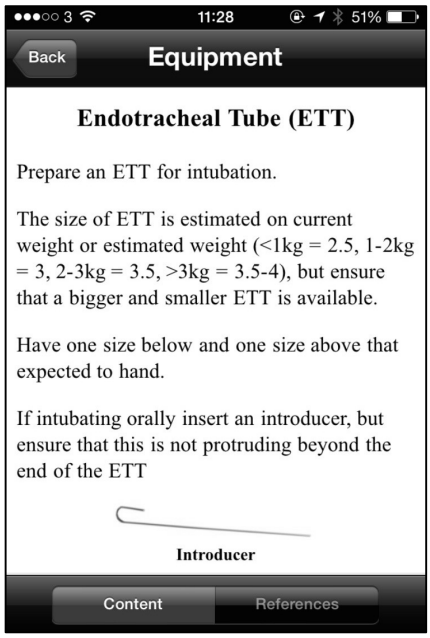

FIGURE 8.4 – SCREENSHOT OF THE EQUIPMENT SECTION

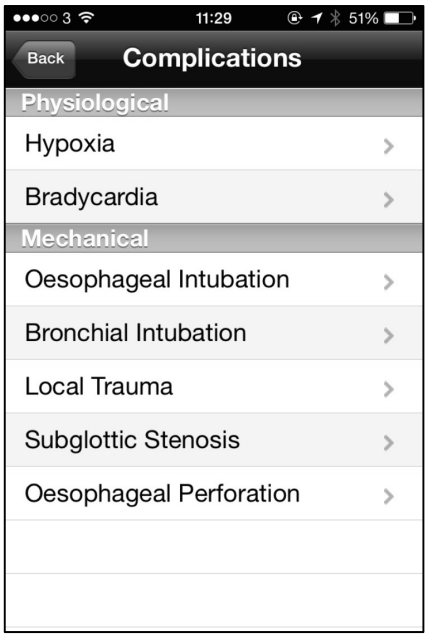

FIGURE 8.5 – SCREENSHOT OF THE COMPLICATIONS SECTION

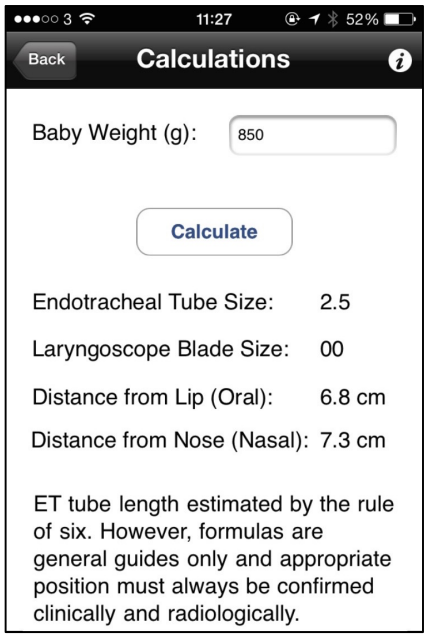

FIGURE 8.6 – SCREENSHOT OF THE CALCULATIONS SECTION FOR A 850G INFANT

8.3.2. AIM

The aim of this investigation was to examine the distribution of this application, and subsequent uptake by users over the last 4 years since its release. This investigation will examine the issue of regulation, in particular the regulation of medical applications.

8.3.3. METHODS

Application use was analysed with Google Analytics (Google Inc, California, USA). This software package allowed for detailed performance data to be generated on this application from any time frame selected (in this instance, February 2011-February 2015). Representations of application usage were generated with graphics as well as absolute numbers of visits to the application. An option was also provided to the user of the application to provide feedback through a section of the application. Google Analytics then provided this feedback for analysis via email responses.

8.3.4. RESULTS

Between February 2011 and June 2015, the application has been downloaded over 9500 times. These downloads have resulted in the application being used for 38,545 sessions. Of these, 75% (28,924) of sessions were by returning users. The application was used most frequently in the United States (14,509 sessions), followed by the United Kingdom and then Ireland (4,964 sessions and 2,307 sessions, respectively) (Figure 8.7). There were over 179,715 page views with the most popular pages being “anatomy of the airway”, “calculations” and “videos and images”. The average duration of each session was 3 minutes and 33 seconds.

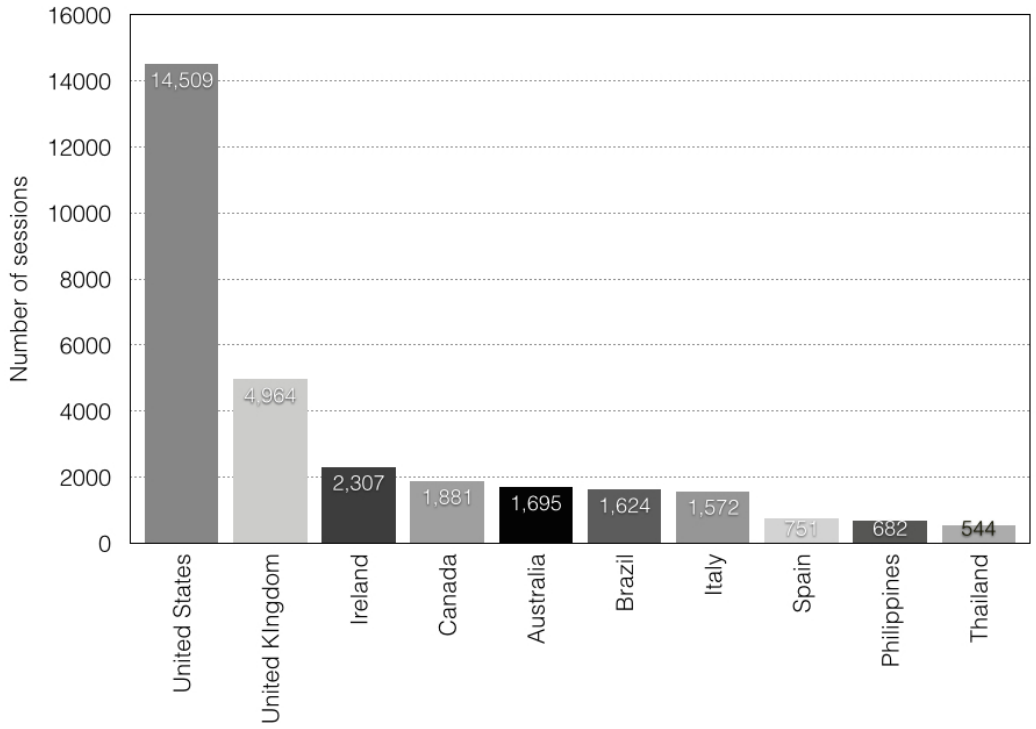

FIGURE 8.7 –TOP TEN COUNTRIES, BY NUMBER OF SESSIONS

8.3.5. DISCUSSION

Smartphones are increasingly used worldwide. The Neotube application has been downloaded in over 100 countries internationally, with a high number of users returning to the application following initial download. This application does not require wireless internet or 3G/4G access after initial download, so full access to all the features of the application is possible in remote areas. This widespread uptake of this educational tool occurred without any conventional dissemination through media outlets. While greater marketing of the application may have promoted downloads, this would have limited the ability to keep the application free of charge, which may have subsequently affected download frequency.

Whilst its direct role in infant care has not been assessed, this application has been shown to improve users acquisition of knowledge in neonatal intubation as well as effectiveness in improving various aspects of skills during neonatal intubation in a simulated model of intubation.[192] Whether this translates into improved performance at the bedside and results in improved patient safety remains to be evaluated. The application's impact on the stress levels of trainees

in performing this technically difficult procedure has also not been explored. The application interface does allow for feedback to be provided from users, via an email link. Whilst the overall percentage feedback was very low at less than 2%, the comments were generally positive, with some suggestions for the next version of the application, such as inclusion of a section on performing nasal intubation.

Use of medical applications in clinical care is now standard. In 2012 Franko and Tirrell found that 56% of doctors surveyed used smartphone applications in their clinical practice.[193] As a result of the increasing sales of smartphones worldwide, it is reasonable to assume that this value has increased over the past 3 years. However, regulation and guidance in this area is lacking. Currently, it is possible for an individual from any discipline to create and publish a smartphone application. In the absence of regulation, users need to be aware that application content is not regulated and may be factually incorrect. Visvanathan *et al.* have highlighted the low level of medical involvement (34%) in the creation of medical applications.[194] The potential for smartphone educational tools to cause harm is real. This is evidenced recently in an instance where a pharmaceutical company had to withdraw a smartphone application that miscalculated scores for rheumatoid arthritis patients.[195] This highlights the need for stricter guidelines and regulation to be in place, especially for applications that may affect patient care either through guiding clinical practice as well as providing patients with information for self-care.

The FDA has recently developed a guidance document for developers of smartphone applications in the United States entitled "Mobile Medical Applications: Guidance for Industry and Food and Drug Administration Staff (9th February 2015)".[196] Although this document does indicate that there will be future regulatory documents developed, the content of the current document is highlighted as being "nonbinding recommendations". Therefore, it does not establish legally enforceable responsibilities but describes the FDA's current opinion on this area. This document defines "mobile medical applications" as being those that can 1) be used as an accessory to a regulated medical device, 2) transform a mobile platform into a regulated medical device, or 3) become a

regulated medical device by providing patient specific analysis (e.g. apps that use patient specific parameters and calculate dosages for medication). However, this document also highlights that the FDA does not distinguish apps that provide medical educational resources, such as procedural based guidance applications, as being medical devices. Therefore, it is likely that the FDA does not intend to regulate the content and structure of information that these applications may provide.

There are several websites that are dedicated to reviewing smartphone applications that are available to healthcare professionals including: www.imedicalapps.com, and www.medicalappjournal.com. However, this is not a process that the medical smartphone application has to legally go through before it can be made available to smartphone users.

Smartphones are capable of holding vast amounts of material and data, and are increasingly available and affordable. The App Store (Apple Inc., California, USA) has recently dedicated a specific section of the store as "Apps for healthcare professionals". This emphasizes the growing market for applications aimed at healthcare professionals. It is for these reasons that the use of smartphones, especially in the procedural teaching role, should be carefully evaluated.

8.3.6. CONCLUSION

This section has highlighted many issues, such as medical content, that should be consider during the creation of smartphone based educational apps. Feedback from end-users is key to the ongoing improvement of educational tools, and therefore a secure email feedback mechanism should be included, either as an option or mandatory following use. Whilst this will require significant coordination at the application creation process, and ultimately a longer time to creation, it may address some of the current shortcomings of the process and potentially enhance patient safety.

Although the use of this application has been shown to improve outcomes in the intubation of a mannequin[197], it remains to be determined if this is applicable to

infants. The uptake of this application makes it clear that there is a demand for these procedural educational tools in neonatology. Therefore, similarly structured apps for various other infant procedures have potential to reach a worldwide audience and, if properly designed and tested, may improve many aspects of infant care.

8.4. A RANDOMISED CONTROLLED TRIAL OF A MOBILE PHONE INFANT RESUSCITATION GUIDE

8.4.1. BACKGROUND

The incidence of out-of-hospital cardiac arrest (OHCA) is lower in infants than in adults (72.71 versus 126.52 per 100 000 people).[198] Survival rates are also low overall for OHCA, but particularly so for infants (3.3% versus 4.5% adults).[198] It is known that, in the paediatric population, respiratory arrest commonly occurs prior to cardiac arrest. Survival rates may be improved if there is early activation and availability of the emergency services.[199]

Studies analysing the effectiveness of visual aids in cardiopulmonary resuscitation (CPR) performance in adults have conflicting results. One of the first mobile phone first aid applications to be tested was *M-AID*®. Zanner et al. performed a randomised controlled trial in a mannequin model that described a marginal improvement in overall adult resuscitation techniques with individuals equipped with the *M-AID*® application compared to those without.[200]

Another adult mannequin based trial found an improvement in first aid technique in laypeople supplied with a mobile phone application[201]. However, while these studies showed improvements in ventilation**,** they also highlighted potential drawbacks to a cognitive aid. There was a significant delay in time to first chest compression among volunteers using a mobile phone application[202]. Studies analysing mobile phone first aid guides have highlighted both advantages and disadvantages to their use. Nevertheless, no trial has evaluated the role of these guides in improving paediatric resuscitation skills.

There has been an on-going debate over the benefits of video CPR self-instruction and other innovative media compared to instructor led classroom CPR instruction.[203] However, recent studies have convincingly demonstrated the efficacy of self-training kits in adult CPR providers.[204-206] One such self-training kit is Infant CPR Anytime®, produced by the American Heart Association in accordance with their BLS resuscitation guidelines.

8.4.2. AIM

To assess a mobile phone resuscitation guide (MPRG) for infant CPR that could be used through all forms of mobile phone platforms.

8.4.3. METHODS

Mobile-phone guide development

A MPRG was developed, under direction from the University College Cork (UCC) Business Information Systems (BIS) department, using a mobile phone data analyser. The guide consisted of a series of questions to ascertain the situation. These questions were followed by written prompts guiding the BLS provider through infant CPR if required. The resuscitation guide was designed using the exact sequence and language of the American Heart Association (AHA) 2010 infant resuscitation guidelines.[1] These guidelines were used for this trial, as they were the guidelines suggested by the Irish Heart Foundation.[207] The guide was designed to be compatible with any mobile phone platform. Six individuals without previous medical or first aid training read the guide questions and instructions, to assure they were understandable. Examples of two of these instructions from this MPRG are demonstrated in Figure 8.8.

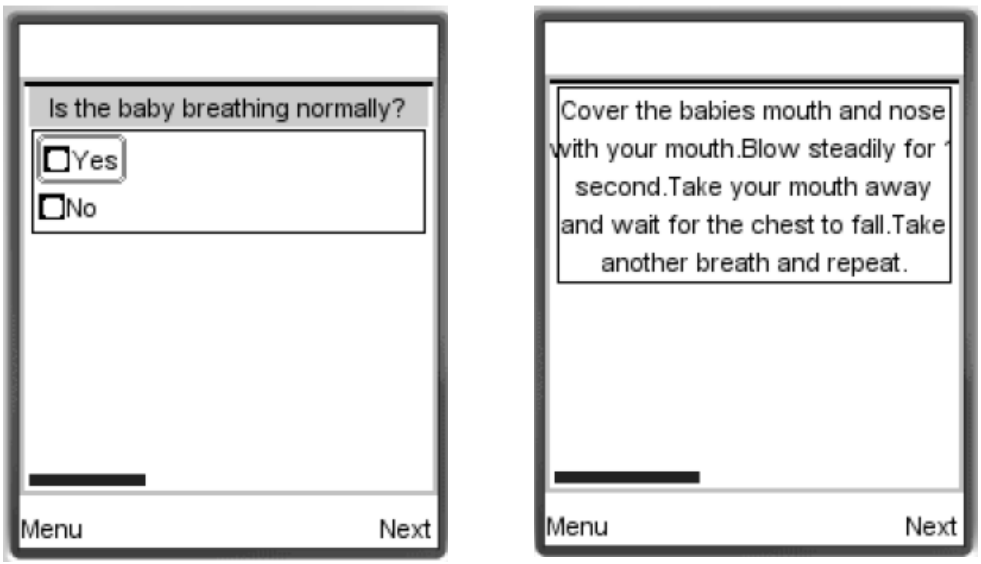

FIGURE 8.8 – EXAMPLE OF TWO DIFFERENT PROMPTS DISPLAYED TO MPRG USER.

Training

The trial was conducted in secondary level schools in the Cork suburbs during school time. Each school was visited twice by the research team (investigator Geraldine Murphy and thesis author GAH). During the first visit, all candidates received training in infant CPR. Instruction began with a 20-minute instructional movie, Infant CPR Anytime®. In conjunction with the movie, a trained CPR instructor demonstrated the skills (GAH). Participants were then divided into groups of three individuals and received personal instruction and practice time with trial investigators (GM and GAH). A Resusci Baby infant mannequin was used during the demonstration and practice time. Parental consent was provided prior to enrolment in the trial (Appendix N). This trial received CREC approval (CREC reference number – ECM 4 [ss] [06/11/12])(Appendix N).

Randomisation process

At the second visit, two weeks later, candidates who had provided written consent to participate were randomised using a Microsoft Excel (Redmond, WA, USA) worksheet to enter assessment with or without the MPRG.

Scenario

The assessment consisted of a scenario involving an infant who was not breathing and was performed using the same Resusci Baby infant mannequin that was used in the initial demonstration two weeks prior. Trial performance was assessed using an original checklist based on those of similar studies and the American Heart Association BLS guidelines.[208-211] The checklist consisted of 17 variables examining the areas of assessment technique, calling for help, compression technique, timing technique, and ventilation technique (Appendix N).

The participants allocated to use the MPRG were given a tutorial demonstrating how to use it and were instructed to use it if necessary, prior to the evaluation. No time limit was enforced during the assessment. Two observers (trial investigators GM and GAH) independently evaluated each participant via the

checklist. Discrepancies were resolved with discussion and mutual agreement. The maximum obtainable score in this checklist was 26.

Data Analysis

Statistical analysis was performed using SPSS software version 20.0 (SPSS Inc, Chicago, IL, USA). The data was analysed using bivariate analysis. All of the variables were assessed using chi-squared analysis to investigate the relationship between the use of the mobile phone resuscitation guide and each variable.

The overall resuscitation performance was also assessed using a system scoring each parameter. The maximum score attainable was 26 points. The results were recoded to include three ranks in scoring and interpreted using logistic analysis. The results were also coded into acceptable and unacceptable levels and assessed using Pearson chi squared analysis.

Logistic regression analyses were conducted on two variables, to examine the relationship between the use of a mobile phone guide and an acceptable "Hands off Time" and an adequate overall resuscitation standard. Both variables were recoded to allow for logistic regression. Ten seconds of Hands off Time per cycle of CPR was acknowledged to be within acceptable limits, as per current European Resuscitation Council (ERC) guidelines.[212]

8.4.4. RESULTS

36 students were trained initially, 21 consented to participate in the follow-up, all of whom owned a mobile phone. These subjects included twelve boys and nine girls aged between 15-16 years old. Of these 21 volunteers, ten were randomised to use the MPRG during the assessment and 11 were randomised to use no MPRG during assessment.

There was no significant difference between the MPRG and control group in terms of checking infant responsiveness ($p=0.757$).

Although there was no difference between the control group and the MPRG group in the area of calling for help (p=0.593), the MPRG group was more likely to call the emergency services (80% versus 36.4% p= 0.044)(Table 8.3).

TABLE 8.3 – ANALYSIS OF THE "CALLING FOR HELP" VARIABLES

Variable	Action	MPRG Group	Control Group	p-value
Shout for Help	Yes	90% (n=9)	81.8% (n=9)	
	No	10% (n=1)	18.2% (n=2)	0.593
Call 112	Yes	80% (n=8)	36.4% (n=4)	
	No	20% (n=2)	63.6% (n=7)	0.044*

*Statistical significance

There was a significant difference in the relationship between the mobile phone guide use and the number of cycles performed within a two-minute period (#Cycles) (x^2 (1) = 6.109, p = 0.047). A participant was determined to have performed the correct sequence of CPR if they completed the CPR algorithm in the correct order (order numbered 1-5, Appendix N). Analysis of the association between mobile phone guide use and the appropriate sequence of CPR, using Pearson Chi-Squared test demonstrated a significant difference (x^2 (1) = 6.109, p = 0.013). The control group was 2.273 (95% CI 1.040-4.967) times more likely to conduct the resuscitation through the incorrect sequence.

There was no significant difference in the completion of 5 cycles per 2 minutes and an acceptable Hands Off Time (x^2 (1) = 0.531, p = 0.466 and x^2 (1) = 0.403, p = 0.525 respectively). The predicted odds for the controls to obtain an acceptable "Hands off Time" were 1.169 (95% CI 0.714-1.912) in comparison with the test group (Table 8.4).

TABLE 8.4 – ANALYSIS OF THE "COMPRESSIONS" VARIABLES				
Variable	**Action**	**MPRG Group**	**Control Group**	**p-value**
Hand Position	Yes	70% (n=7)	90.9% (n=10)	0.223
	No	30% (n=3)	9.1% (n=1)	
Compression Depth	Always Sufficient	30% (n=3)	54.5% (n=6)	0.249
	Sometimes Sufficient	70% (n=7)	36.4% (n=4)	
	Insufficient	0	9.1% (n=1)	
Compression Rate	100-120	60% (n=6)	45.5% (n=5)	0.593
	80-100/120-140	30% (n=3)	27.3% (n=3)	
	< 80/> 120	10% (n=1)	27.3% (n=3)	

There was no significant difference in the relationship between the use of a mobile phone guide and Hand Position (p=0.023), Compression Depth (p=0.249) or Compression Rate (p = 0.592)(Table 8.5). In addition, there was no statistically significant difference between the use of the MPRG and the ventilation techniques (Table 8.6)

TABLE 8.5 – ANALYSIS OF THE "COMPRESSIONS" VARIABLES				
Variable	**Action**	**MPRG Group**	**Control Group**	**p-value**
Hand Position	Yes	70% (n=7)	90.9% (n=10)	0.223
	No	30% (n=3)	9.1% (n=1)	
Compression Depth	Always Sufficient	30% (n=3)	54.5% (n=6)	0.249
	Sometimes Sufficient	70% (n=7)	36.4% (n=4)	
	Insufficient	0	9.1% (n=1)	
Compression Rate	100-120	60% (n=6)	45.5% (n=5)	0.593
	80-100/120-140	30% (n=3)	27.3% (n=3)	
	< 80/> 120	10% (n=1)	27.3% (n=3)	

TABLE 8.6 – ANALYSIS OF THE "VENTILATION TECHNIQUE" VARIABLES				
Variable	**Action**	**MPRG Group**	**Control Group**	**p-value**
Position	Yes	40% (n=4)	72.7% (n=8)	0.130
	No	60% (n=6)	27.3% (n=3)	
First Breaths	Two	50% (n=5)	54.4% (n=6)	0.280
	One	20% (n=2)	0	
	None	30% (n=3)	45.5% (n=5)	
Observing for chest rise	Yes	30% (n=3)	36.4% (n=4)	0.757
	No	70% (n=7)	63.6% (n=7)	
Breathing Time	Good	60% (n=6)	54.4% (n=6)	0.620
	Satisfactory	20% (n=2)	36.4% (n=4)	
	None	20% (n=2)	9.1% (n=1)	
Breathing Volume	Always	40% (n=4)	54.5% (n=6)	0.780
	Mostly	20% (n=2)	18.2% (n=2)	
	Never	40% (n=4)	27.3% (n=3)	

There was no difference between the MPRG group and the control group in the incidences of an acceptable total score (80% versus 72.7%)(p=0.153)(Table 8.7)

TABLE 8.7 - ANALYSIS OF THE INCIDENCE OF "ACCEPTABLE SCORES"

Variable	Action	MPRG Group	Control Group	p-value
Acceptable Total Score	Yes	80% (n=8)	72.7% (n=8)	0.153

8.4.5. DISCUSSION

Individuals equipped with a mobile phone resuscitation guide were more likely to call the emergency services when faced with a simulated resuscitation. This is imperative as it ensures the victim will get professional help without delay. This is in keeping with the findings of Zanner *et al.*, where the test group more frequently placed emergency calls.[200] This is intuitive as a person with a mobile phone "in hand" is more likely to remember to call the emergency services. As stated in this trial's introduction, early calling of the emergency services has the potential to increase survival rates.

The MPRG group was also more likely to complete the optimal number of cycles of rescue breaths and compressions before pausing to call emergency services. This is important during CPR as it may maximise perfusion, increase the chances of the return in spontaneous circulation, and improve upon survival rate if continuity is maintained. This finding has not been demonstrated in previous studies and it may be as a result of the MPRG acting as a visual checklist that the user can work through, step by step, during the resuscitation.

The MPRG group executed the correct sequence of resuscitation more often in comparison to the control group. This has many advantages, including minimal time wasting and possibly optimized compression:ventilation ratio. Resuscitation should be fluent, guaranteeing a constant circulation, thus improving the chances of survival. Executing the standard sequence of resuscitation may optimize the chance of a more positive outcome. In this trial, subjects supplied with the mobile phone guide did not display superior overall CPR skills in comparison

with the control group. This is not surprising since the MPRG did not contain any advice or visual aids (such as videos) demonstrating resuscitation skills. This is supported by Zanner et al., examining M-AID®, in which the test group only achieved a marginally higher average score.[200]

In contrast to other studies, this trial was unable to find a statistically significant difference between the control and test groups in the assessment of ventilation technique and airway management. Artificial ventilation was the most improved area identified by both Zanner et al and Ertl et al.[200,201] This may be attributable to the sample size of this current MPRG trial. The assessment variables, including breathing check and the check for responsiveness, were performed at a comparable level amongst our groups. This is in contrast to Zanner et al. and Ertl et al. who revealed variations in execution of both skills between their test and control groups.[200,201]

The quality of compressions was similar between the groups in this trial. There was a trend towards superior technique in the control group: however, this was not shown to be significant. Comparable results have been found by similar studies.[200,213,214] Studies have shown that survival rates of adult cardiac arrest victims who receive chest compressions alone are better than those who receive compressions and ventilation.[215] Provision of chest compressions may be difficult to improve upon through written instruction by means of the MPRG. The trial may have seen a difference between the two groups if the MPRG had visual picture based aids or videos that instructed the user on how to perform CPR.

The ERC 2010 Resuscitation Guidelines recommend that Hands Off Time should be minimal and this is a current area of focus for improvement by medical professionals.[212] Although there was no difference in Hands off Time between the MPRG group and non MPRG group, observation of the latter revealed that the use of the mobile phone during the actual resuscitation by the user varied. Some students were more likely to read the instructions and then leave the mobile phone aside to perform CPR. Others held the mobile phone continuously, reading as they went along. Either method may be a hindrance during CPR,

through time delay or physical obstruction. It may be that through the implementation of voice prompts and/or visual guides within the guide, Hands off Time may be reduced even further.

The controlled environment in which it took place, as well as the mannequin based design, limited this trial. The outcomes may be very different in real life emergency situations, during which fear, stress and other factors may influence behaviour. The trial population was also limited by the narrow index of teenagers, aged 15-16 years. This is not an accurate reflection of the general population and represents a select group that may be more familiar and comfortable with mobile phone technology. However, it is an age group in which the Red Cross recommends to learn CPR in order to safely and responsibly care for infants during babysitting.[216] Finally, although this trial was randomised, it was not possible to conduct a blind trial and therefore the trial may have been subject to observer bias.

A mobile phone guide may not prevent skills decay, however, having a mobile phone guide "to hand" will continue to make the responder more likely to call the emergency services. It is not possible to guarantee that the responder will have the composure to open the guide and follow the sequence thus completing the optimal amount of cycles and the correct sequence, however, if they do open the guide then this trial suggests that these components of resuscitation will improve and not regress.

8.4.6. CONCLUSION

The use of this MPRG has been shown to improve the calling of emergency services, the completion of the recommended CPR cycles, and the correct CPR sequence by teenagers in a mannequin based trial. If responders remember to use a guide in a real infant resuscitation scenario, they may get emergency services to the scene earlier, which in itself has been shown to improve survival in the adult population. This trial has demonstrated the potential improvement that the use of a mobile phone guide may have on infant resuscitation outside of the hospital setting. Further studies are needed to determine if mobile phone guides can sustain overall CPR performance during a real life situation.

8.5. CONCLUSION OF CHAPTER

This chapter has suggested potential ways of improving care during infant stabilisation with particular attention to the role of physician education and training. If the level of fidelity can be optimised in the in vitro setting during training, improvement may subsequently be observed in the vivo environment.

The feedback received from participants in the mannequin investigation highlights a lack of fidelity that manufacturers should consider during the development of new mannequin models. Although many high fidelity mannequins may already account for these fidelity issues, the cost associated with these mannequins may not be feasible for many centres; therefore, the improvement of these more affordable low cost mannequins remains essential.

Through analysing use of an educational smartphone application, I have demonstrated a significant worldwide demand for tools to improve learning of procedures in neonatology. Smartphone applications have a worldwide audience, and may subsequently have a huge impact on medical care.

Similarly, the use of a mobile phone based educational guide for resuscitation in an out of hospital setting was developed and assessed in this chapter. I highlighted the benefit of having an extra tool, in the form of an infant resuscitation guide, during resuscitation in mannequin model. The development of more of these guides, and subsequent encouragement of their uptake, may now be warranted.

CHAPTER 9: CONCLUSION OF THESIS

9.1. INTRODUCTION

In this thesis, I have performed investigations focused before, during and after stabilisation in the delivery room. These investigations have been designed to improve the care of infants. I have advanced our understanding of many aspects, including the integration of technology and devices to physiological monitoring, and education. Despite this, there are still many unresolved issues. In this conclusion, I will highlight the specific advances made. I will also highlight the unresolved existing issues and potential approaches that future investigations may take towards resolving these.

The completion of this thesis has been a challenging but equally rewarding experience. This chapter will conclude by outlining my personal experience over the past three years.

9.2. MAIN FINDINGS OF THIS RESEARCH

9.2.1. DELIVERY ROOM CARE

$EtCO_2$ Detection

In Chapter 1 I summarised the current approach to infant care in the delivery room. Emphasis is placed on the importance of ensuring effective ventilation immediately after birth yet the current methods for monitoring effectiveness of ventilation are primarily based on clinical observation, and may not be comprehensive. Similarly, the importance of cardiovascular assessment of an infant immediately after birth is emphasised yet the methods for doing so may be inaccurate. An improvement in delivery room management in these areas of monitoring needed to be evaluated.

As a result, I focused on enhanced forms of physiological monitoring technology, such as $EtCO_2$ detection, in the delivery room. During Chapter 3 and Chapter 4 many *in vitro* and *in vivo* investigations were discussed. From these investigations it was found that:

1) $EtCO_2$ detectors improved PPV in a mannequin model.
2) Users indicated a preference in using $EtCO_2$ detection during PPV.
3) It was possible to implement $EtCO_2$ monitoring in the delivery room.
4) Medical staff members were comfortable with $EtCO_2$ monitoring in the delivery room.
5) The use of $EtCO_2$ monitoring in the delivery room did not cause any harm or disimprovement in the short term outcomes of preterm infants.

The combination of these investigations also led to the acquisition of data relating to $EtCO_2$ production of preterm infants during the first minutes of life. These data suggest that the increase in $EtCO_2$ levels over the first few minutes of life might be an important indicator of how effectively the lungs are performing as the infant transitions to extra uterine life. Potentially more important, failure to observe an increase in these $EtCO_2$ levels may be an early marker of complications in the respiratory adjustment to extra uterine life.

In Chapter 5, I described a unique randomised controlled trial, which aimed to compare qualitative and quantitative $EtCO_2$ detection of preterm infants in the delivery room. This was seen as a progression from Chapter 3 and Chapter 4 and the results of this trial will help towards the overall assessment of $EtCO_2$ detection in the delivery room.

Through these investigations, I have demonstrated that $EtCO_2$ monitoring in the delivery room is possible, requires little extra training by end users, and obtains a parameter that may act as an extra tool in assessing the effectiveness of respiratory support immediately after birth. For these reasons, $EtCO_2$ monitoring should be considered for use during the stabilisation of preterm infants in the delivery room.

Cardiovascular assessment

Chapter 6 focused on cardiovascular assessment in the delivery room. I have investigated the accuracy of the current methods of HR assessment, and shown that these are largely inaccurate. This was particularly evident when the HR was below 60 bpm. The HR falling below 60 bpm is a critical time point during the stabilisation of an infant in the delivery room and, alarmingly, this investigation demonstrated that this was the rate in which the highest degree of inaccuracy existed. This is a HR in which a high level of intervention may be required. It is possible that failure or delay in acknowledging this HR as well as the subsequent delay in providing the indicated intervention, may negatively impact upon the stabilisation process.

Chapter 6 also investigated the use of ECG monitoring to acquire HR in preterm infants in the delivery room. This method of cardiovascular monitoring was shown to be feasible, required little training, and successfully measured HR in all infants in the study. This demonstrated the utility of a monitoring method that is available in most neonatal centres, and provides a solution to the inaccuracies in current methods of HR assessment described previously.

Perfusion index is another modality of assessing cardiovascular function in infants. Although no correlation was found between perfusion index and other

markers of cardiovascular status, it was found that the monitoring was feasible (Chapter 6). Continued investigations in this area may demonstrate a role for this assessment in infant care. Ideally, an appropriately powered study should be designed to determine if correlations exist between perfusion index and different physiological measures during the stabilisation process in the delivery room.

I have described the inaccuracies associated with current methods of cardiovascular assessment in the delivery room and I have provided evidence for the use of alternative methods of assessment. As a result of these findings, we believe ECG monitoring should be used, or be readily available for use, during the stabilisation of preterm infants in the delivery room.

Stabilisation procedure

Building upon many of the inconsistencies highlighted in delivery room video recordings, the creation and implementation of an annotated instructional video on delivery room procedure was described in Chapter 7. This video placed particular emphasis on the role and positioning of each team member, and ultimately aimed to allow for more effective delivery room practice to be implemented in the delivery room of CUMH. Although it was only possible to assess the impact of this video through assessment of 4 delivery room recordings, acquired post implementation, it was clear that many of the inconsistencies observed prior to implementation of the video, were reduced. I feel that this thesis now encourages further research in this area on order to comprehensively assess if video teaching tools have a role in improving the care that an infant receives in the delivery room. We plan to review the videos on an ongoing basis as a method of improving delivery room practice.

9.2.3. NICU CARE

The utilisation of new technology in the delivery room identified many important factors to be considered when introducing new technologies to a challenging environment. The lessons learned from this implementation were transferrable towards their introduction to the NICU.

The role of a procedural training video for complex interventions that take place in the NICU, such as a PICC placement, was also explored (Chapter 7). An improvement in the preparation of equipment prior to completing a PICC procedure was demonstrated through the use of this video, however, no improvement was found in the procedural aspect of the PICC procedures. Results of this investigation were influenced by the relatively low number of physicians completing the investigation as well as the intermittent nature in the indication for this procedure. However, this investigation provided the background for the development of more videos in this area and the development of structured training for neonatal trainees.

My survey regarding NICU-based webcam system was essential in determining the attitudes of parents, as well as staff, towards such a system. These questionnaires gathered important information that allowed us to prepare a proposal for a webcam system to be implemented in the NICU, which has recently been funded by SFI. For parents, we plan to prospectively study the introduction of this system to assess whether it reduces parental stress levels whilst away from the NICU. This system will also allow for parents to have continuous access to information relating to the care of their infant via the cot side monitor that will be included in this system. For physicians, this system may allow for remote visual assessment of patients in their care during times that they are away from the NICU. As a result of identifying the acceptance of visual educational tools by staff, the cot side monitor will also include a library of procedural videos that a physician can view prior to completing a procedure.

The uptake of the neonatal intubation app (Chapter 8) was extensive, demonstrating an acceptance of medical staff for educational tools. However, a lack of regulation creates the possibility of unsafe medical applications to be distributed widely.

9.2.4. TRAINING

Optimising the level of fidelity during infant stabilisation training may ultimately result in enhanced care for an infant in the delivery room. Considering this, I evaluated two mannequins that are frequently utilised during infant stabilisation

training. In certain configurations, these mannequins were found to be inadequate in simulating a newborn infant, particularly in relation to the airway anatomy. This particular lack of fidelity caused concern as airway management is an important factor during infant stabilisation. Although when the Neonatalie mannequin is utilised in water-based configurations it does allow for a higher degree of fidelity, a high degree of fidelity is still not achieved. The need for increasing the level of fidelity during the creation of low cost mannequins in the future has now been highlighted.

The utility of a mobile phone based infant resuscitation guide was also highlighted during this thesis. This guide may act to supplement a recently CPR-trained responder's knowledge whilst performing infant resuscitation. The investigation highlighted the positive impact that a guide could have on the CPR sequence performed by the responder as well as an increase in the likelihood of that responder calling the emergency services. If this were to be similar in a real life situation, the results would be extremely important as 1) the responder may ensure optimum ventilation and perfusion of the patient as they are reminded of the correct ratio and sequence through the guide and 2) the responder may be more likely to progress the "chain of survival" sequence via the calling of emergency services. With the possibility of an infant resuscitation guide improving real life out-of-hospital resuscitation, further development and evaluation of these tools is encouraged.

9.2. DEVELOPMENTS AND FUTURE DIRECTIONS AS A RESULT OF THIS THESIS

- ***The enhancement of delivery room practice in CUMH***

The investigations described in this thesis have resulted in substantial changes in delivery room care at CUMH. These changes pertain specifically to the monitoring of effective ventilation and cardiovascular status of infants.

Prior to commencing this thesis, $EtCO_2$ detection was available in the delivery room primarily for confirming correct placement of the endotracheal tube following infant intubation. As a result of my investigations of $EtCO_2$ detection during infant stabilisation, neonatal staff have now become familiar with the benefits of both quantitative and qualitative forms of $EtCO_2$ monitoring during the provision of manual ventilation. $EtCO_2$ detecting devices are now readily available for manual ventilation during all deliveries of preterm infants in CUMH. The use of this device during manual ventilation remains subject to the physician's preference. Similarly, ECG monitoring is also now readily available during stabilisation of preterm infants in the delivery room of CUMH and its use is also subject to the medical team's preference.

A process of video recording during delivery room stabilisations has been a challenge, but an extremely important achievement for the department. This system has provided opportunities for staff to receive feedback on their performance. Subject to research enrolment, the use of first person perspective video recording glasses on each team member is now employed in the delivery room of CUMH (Chapter 7). Although additional ethical approval will be required to use these glasses during delivery room stabilisations outside of the approved research context, this system has the potential to provide the entire stabilisation team with a novel debriefing and learning tool. This could also be essential in retrospectively pinpointing delivery room interventions, something that is often difficult due to staff unavailability to transcribe during the stabilisation process.

Through completing many of the investigations described in this thesis, we created a procedural metric on optimised delivery room practice, as well as an instructional video. Although the assessment of this instructional video has been brief, the improvements in stabilisation practice in CUMH have been clearly visible. Therefore, trainees are now required to view this instructional video regularly during their neonatal training curriculum during the neonatology rotation at CUMH. Informal feedback from neonatal trainees towards the use of this video has been positive.

- ***Framework for future delivery room studies***

There were many hurdles related to performing investigations in the delivery room to overcome during this thesis. The solutions created have left a framework for future studies. These issues related to consent, introducing new technology and video recording in the NICU.

Opportunities to obtain informed consent for participation in clinical studies prior to preterm delivery are limited. This was a significant challenge to recruitment initially, but I developed procedures that optimised the necessary time period for parents to consider the research as well as allowing the research team to prepare for the delivery.

Although this approach may help to optimise the level of enrolment, another approach that could be taken to improve upon the level of enrolment may be through the development of a deferred consenting process, as discussed in Chapter 5. The combination of deferred consent and a primary system of an early consenting process can greatly optimise the level of enrolment. This will need to be presented to the ethics committee and will need to be evaluated on an individual investigation basis.

Staff awareness of investigations required regular reminders and presentations. This is typically an issue with clinical investigations in large centres. However, assessing whether an expected infant meets relevant research criteria, and subsequently contacting the research team, has now become the common procedure upon admission of an expectant mother to the HDU of CUMH. This

has been assisted by the positive attitudes of staff towards research, and the identification of key personnel in these areas to communicate with directly. It is assumed that this attitude towards research will continue for future investigations and will hopefully lead to an easier commencement of investigations requiring consent to be obtained during the antenatal period.

The delivery room environment of CUMH is now more accessible for research. The ethos is one of collaboration. During the commencement of the delivery room based investigations, theatre staff and neonatal staff were generally unfamiliar with such unique delivery room based research. However, the staff remained accommodating and enthusiastic towards this research throughout the entire duration. As a result of the familiarity that now exists with this type of research, as well as the continuing level of enthusiasm and accommodation, future investigations within the delivery room will no doubt benefit from the ease in which they can be completed. This has already been seen in the recent commencement of a delivery room based investigation, not associated with this thesis, assessing $EtCO_2$ production of term infants immediately after birth in CUMH.

- ***New device implementation practice***

Many of the investigations described in this thesis were carried out in an *in vitro* setting, and were used to identify technical issues prior to enrolling infants in clinical investigations. These issues were then addressed through interaction with staff as well as providing staff members with time to familiarise themselves with new devices. If these issues were not identified through the use of exploratory *in vitro* investigations then it is reasonable to assume that the same issues would have arisen during *in vivo* investigations, with the inherent risk of impacting on patient safety.

Prior to this thesis commencement, the non-interventional nature of these devices as well as their established use in other areas of infant care, may have suggested that their use could easily be translated to the delivery room environment. However, I have now described the potential consequences of such a suggestion. As a result, extensive *in vitro* training takes place with all new devices prior to

any implementation in a clinical setting at CUMH. This is completed in order for the relevant staff members to fully familiarise themselves with all aspects of the device, as well as to highlight any issues that may exist with the device.

- ***Data synchronisation systems***

Combining large amounts of different parameters from different monitoring devices into a single time synchronised output is both a technical challenge and an expensive endeavour. However, through optimisation of current features offered by clinical monitors, as well as collaboration with different manufacturers, a manageable, cost effective, method of data collection has been achieved in CUMH.

Collaboration with Moberg (Moberg Research Inc, PA, USA) has allowed us to optimise an existing Moberg CNS electroencephalogram (EEG) monitor, used by the Neonatal Brain Research Group in CUMH. Initially, this monitor was able to compile parameters such as heart rate and SpO_2 from the Philips Intellivue monitor via "second by second" sampling rates. However, the ability for the EEG monitor to extract $EtCO_2$ from the Philips Intellivue monitor was not coded into the software. After discussion with Moberg, through several emails and phone calls, an update was created to allow the software to also compile $EtCO_2$ data. Unfortunately, due to the time associated with recoding medical based software, this system wasn't fully configured to obtain $EtCO_2$ values until the latter part of this thesis. Therefore, I could not utilise this advance during the delivery room investigations. However, this monitoring system has now been made available for future delivery room investigations in CUMH and will be utilised during the completion of the CAPNO trial.

During the completion of this thesis, new monitoring equipment was implemented in the NICU of CUMH in the form of Mindray iPM10 patient monitors (Mindray Medical International Limited, Shenzhen, P.R. China). Along with this implementation of fixed monitoring equipment in the NICU, there was also a portable monitor made available for research purposes. This portable monitor had functionality to obtain $EtCO_2$ parameters along with standard parameters such as HR and SpO_2. It also had the ability to retrospectively

transfer the data to a computer for analysis, however, in one-minute intervals. Optimising this function on the monitor through collaboration with the company representative in Ireland, eventually allowed for a software package to be developed that allowed for data transfer to be completed in real-time 5-second intervals. Unfortunately, due to similar issues associated with development of medical based software, this optimised method of obtaining $EtCO_2$ values also only became available in latter part of this thesis. Similarly, this enhanced method of data collection is now available for future investigations at CUMH. This method can now be used as a secondary method of data collection in the CAPNO trial, if the Moberg system should be unavailable.

- ***Enhanced education***

The implementation of annotated instructional videos as learning tools has been described in this thesis. The methods employed in the creation of these videos can now be extended to allow for effective creation of future instructional videos in many areas of neonatal care. This will allow for the development of enhanced training programs for junior physicians as they complete their neonatology rotation at CUMH.

Additionally, the experience gained by the wider research team involved with this thesis will facilitate future collaboration during the development of learning modules by training centres in UCC, such as the "Application of Science to Simulation, Education and Research on Training" (ASSERT) centre. A potential collaboration may be through the development of a platform to allow junior doctors to create a procedural portfolio throughout their neonatology rotation. This project is currently being discussed between the Department of Neonatology and the ASSERT centre.

Prior to commencement of this thesis, neonatal stabilisation training at CUMH typically incorporated the use of a Neonatalie newborn mannequin filled with air, and a Resusci Baby infant mannequin. However, as a result of the issues that I have highlighted in relation to these models (Chapter 8), training at CUMH now solely incorporates the use of the Neonatalie mannequin with water

configurations. It is anticipated that this change in training practice would help to improve the overall effectiveness of this training.

- ***A novel NICU webcam system***

The results from the webcam survey, from the investigations utilising annotated video tools for PICC procedures and delivery room procedures, and the assessment of smartphone medical app regulation, has allowed for the proposal for an integrated and novel system within the NICU of CUMH.

As discussed in Chapter 7, this proposal has been successfully funded by SFI. The implementation of this system will be on a small scale in the NICU, however, it will allow parents improved access to their infants whilst away from the NICU. Similarly, this system will offer a remote viewing platform for consultant physicians in order to view their patients when away from the NICU. The stress levels of parents will be assessed after the implementation of this system and feedback will be gathered from physicians. Resolving any issues that may be highlighted during this process will be essential in optimising the system, as well assessing the role of expansion of this system on a wider scale in the NICU of CUMH.

As a result of seeing how medical information contained in medical smartphone apps can be unregulated, the information displayed on these monitors will be subject to a comprehensive review process by a panel of senior physicians in CUMH. This will be essential in ensuring correct and appropriate information is available to parents. Prior to any procedures taking place within the NICU, a physician will be able to log on to the system and access a library of annotated procedural videos. There would also be a checklist for each part of the procedure that would be worked through as a physician was performing a procedure. Again, this aspect would be subject to a comprehensive review process by a panel of senior physicians.

9.3. FUTURE AREAS OF RESEARCH

9.3.1. PROSPECTIVE CLINICAL TRIALS

Many of the investigations contained in this thesis revealed several important results. However, due to the exploratory and observational nature of these investigations, it is difficult to accurately assess if these findings would be achieved during more robust, appropriately powered, investigations. The time frame in order for large, possibly multicentre, investigations to commence would be unrealistic to achieve within the timeframe of a PhD thesis; however, the groundwork has been completed for these investigations to now take place.

The results of these investigations have now allowed for CUMH and UCC to have the opportunity to lead further investigations as a result of the familiarity in delivery room based research. Through various enhanced monitoring methods being of regular use within these centres, they now have the potential to become global leaders in enhancing the monitoring that a preterm infant receives immediately after birth as well as during an infant's time in the NICU.

Through completion of larger trials, partly encouraged by the findings within this thesis, the utility of enhanced monitoring methods may be reflected in future neonatal stabilisation guidelines. This would hopefully help in improving the care that an infant receives immediately after birth, achieving one my primary aims.

9.3.2. DEVELOPMENT OF A NEW DISPLAY SYSTEM

I have highlighted the role of additional information in improving infant stabilisation. Issues relating to how the team interacts with this information have been highlighted at various stages, particularly relating to the act of visually identifying these parameters. Many of the participants in these investigations identified the issue of removing the direct field of vision from an infant, in order to look at the monitor displaying the parameters, as being potentially problematic.

During all delivery room investigations, care was given by the research team in placing the Philips Intellivue monitor at locations as close as realistically possible to the stabilisation team. This allowed for the member of the team to only remove his/her eyes from the infant for a very short amount of time.

Although no negative feedback relating to this issue was received from medical staff during the clinical investigations, the development of a stabilisation support platform that would allow for a visual display of physiological parameters to be displayed close to where an infant's head is placed may be beneficial. This may allow for a member of staff to provide respiratory support whilst simultaneously being able to keep his/her eyes fixed on the parameter display. For similar reasons, it may be beneficial to move the PIP and PEEP gauge to a similar area of the infant stabilisation unit, as opposed to the wall area of the stabilisation unit where it is typically located. Care should be taken to ensure that moving parameter displays such as $EtCO_2$ readings, SpO_2 readings, and heart rate, allows for these parameters to still be visible for the entire medical team. This may be achieved through the addition of a second, separate, visual display of these parameters in an area where other members of the team can easily visualise it.

As a result of integrating this form of enhanced monitoring into the infant stabilisation unit, less physiological monitoring equipment would subsequently be required to be transported to, and configured in, the delivery room. Although this was not a major issue for investigations included in this thesis, it may be an issue for other centres due to staffing levels as well as monitoring equipment availability. Having such a system integrated into the infant stabilisation unit would also ensure that $EtCO_2$ detection as well as electrocardiography for heart rate acquirement would be available to the team for all deliveries. This may be particularly beneficial during delivery of term infants that unexpectedly deteriorate and require further assistance during the stabilisation process.

9.4. PERSONAL REFLECTION

The completion of this thesis has been a challenging and exciting learning experience for me. The generous and altruistic nature of all the parents who consented to many of the investigations involved in this thesis was one of the most important experiences for me. I was always aware that I was meeting these parents at times in which they would have been experiencing an extreme amount of stress. Often this was a time when, 2 or 3 hours beforehand parents were at home with the natural feeling of excitement in expecting a new baby; yet, within the space of a few hours they were now in a high dependency unit of a maternity hospital in the unfortunate circumstance of expecting to deliver an infant preterm gestation. As part of clinical practice, parents would meet with physicians from many different specialties providing information on how they were now anticipating delivery of a preterm baby. Yet, throughout this entire time, parents remained more than accommodating in allowing a member of the research team come to speak with them about a delivery room investigation. This really reminded me of the generosity of human nature.

All staff members at CUMH, throughout the entire duration of the thesis, also facilitated my journey through their continued enthusiasm and support. As a result of the enthusiasm for research exhibited by these staff members, regular contact was made with me regarding expectant mothers, ultimately allowing me a greater opportunity to enrol a participant. This really displayed the importance of multidisciplinary teamwork in the context of a research team. I learned a lot from this aspect and it is something that I know will benefit my career.

Developing many of the investigations of this thesis was a challenge to me at first. However, I feel that I have developed many research skills throughout completing my research. I can now develop a research hypothesis, review and assess medical literature relevant to this hypothesis, and I can formulate a relevant investigation to engage with my hypothesis. Like most clinical research, this thesis was subject to many hurdles along the way. The skills I developed whilst dealing with these hurdles will be extremely beneficial in completing future research.

I now understand the continued importance of contributing to the medical research community and the relevant skills necessary for doing so. Having the opportunity to engage in discussion whilst presenting my research at international conferences has been an extremely exciting experience for me. I have now had first hand engagement with the beneficence that exists within the medical research community and I feel that this has developed me as a person.

The aim of this thesis was to improve upon the already excellent level of care that preterm infants receive immediately after birth as well as during the time spent within the NICU of CUMH. It is difficult to assess whether or not this aim has been achieved during the short time period of this thesis. However, I would hope that this aim would eventually be achieved through the enhancement of delivery room practice in CUMH.

Having the opportunity to be part of a research team that has contributed towards improving the clinical care provided to preterm infants in CUMH has been a tremendous honour for me. It would be an unexplainable sense of personal achievement to be part of a team that, through publications achieved by this thesis, would also be successful in encouraging national and international centres to adopt similar enhancements in clinical care; ultimately leading to an improvement in care amongst a larger number of infants.

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APPENDICES

Appendix A

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Review article

A review of carbon dioxide monitoring in preterm newborns in the delivery room☆

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ABSTRACT

Introduction: The physiologic adaptation to extra uterine life during the immediate neonatal period is unique. Many newborns require assistance in this adaptive process. Recent evidence now supports titrating oxygen to guide resuscitation but no guidance is provided on utilizing exhaled CO_2 measurements.
Aim: To review the current evidence relating to the use of CO_2 monitoring in preterm newborns in the delivery room.
Methods: Search was performed using the Cochrane Central Register of Controlled Trials, MEDLINE (1966–2014) and PREMEDLINE, EMBASE (1980–2014), CINAHL (1982–2014), Web of Science (1975–2014) and the Oxford Database of Perinatal Trials.
Results: The search revealed 21 articles relating to CO_2 detection, either quantitative or qualitative, in the newborn infant. The majority of these were observational studies, eight relating to CO_2 detection as a means of confirming correct endotracheal tube placement in the newborn infant. The other indication is for mask ventilation, and there is one randomized control trial and four observational studies of CO_2 detection during mask ventilation. The overall recommendation for CO_2 detection for both clinical uses in the delivery suite is level B.
Discussion: CO_2 detection may be of particular benefit for preterm infants in the delivery suite. However there is a need for further research into CO_2 detection, in particular capnography, as a means of confirming effective PPV in neonatal resuscitation.

1. Introduction

The physiologic adaptation to extra uterine life during the immediate neonatal period is unique as the neonate is required to increase pulmonary blood flow as well as expand fluid filled alveoli in order to facilitate gas exchange. Many newborns require assistance in this adaptive process, with provision of positive pressure ventilation and oxygen therapy. Recent evidence now supports titrating oxygen to guide resuscitation of the preterm infant.[1,2] However, there is limited information on the role of carbon dioxide (CO_2) monitoring during this adaptive process. Alterations in carbon dioxide levels in the preterm are associated with adverse outcomes including chronic lung disease, brain injury and/or long-term neurodevelopmental problems.[3,4]

In addition to arterial or venous blood gas sampling, two non-invasive methods of monitoring carbon dioxide levels are available, either transcutaneous ($TcPCO_2$) monitoring or exhaled carbon dioxide ($EtCO_2$) detection. Transcutaneous assessment is based upon locally heated electrochemical sensors applied to the skin surface and provides a continuous noninvasive estimation of the partial pressure of arterial CO_2 ($PaCO_2$). Exhaled CO_2 detection includes the use of a qualitative or semi quantitative disposable colormetric CO_2 detectors that change color upon contact with CO_2, and quantitative capnography, via either mainstream or sidestream end tidal capnography. A mainstream capnography device utilizes an infrared absorption techniques that is located in line with the respiratory gas stream and a sidestream capnography device utilizes a sampling line that continuously transports a sample of gas through a sampling line tube to a sampling cell within a monitor. Both capnography methods provide a continuous visual display of carbon dioxide values. Transcutaneous and exhaled monitoring are

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commonly used in the neonatal intensive care unit, but their use in the delivery suite remains uncertain.

Current Neonatal Resuscitation Program guidelines indicate the use of a disposable CO_2 detector as a primary method of confirming correct endotracheal tube (ETT) placement during intubation of neonates.[5] Correct identification of successful ETT placement is extremely important as undetected misplacement can result in hypoxia and an increase in adverse outcomes.[6,7] The use of a disposable CO_2 detector has been shown to significantly reduce the time to confirm ETT placement.[8] However, there may be instances where a disposable CO_2 detector may give a false negative reading. These may occur for several reasons including cardiopulmonary arrest and severe airway obstruction.[9]

Many studies have compared $EtCO_2$ readings to other invasive methods. Both Rozycki and Bhat identified capnography as a useful means of screening patients for abnormal $PaCO_2$ levels.[10,11] In a comparison of $EtCO_2$, mixed venous ($PvCO_2$), and $TcPCO_2$ readings; Lopez et al.[12] found that $EtCO_2$ was able to detect high and low levels of CO_2 with similar efficacy to $TcPCO_2$. Overall, the evidence suggests that $EtCO_2$, although not as accurate as blood gas sampling, is a reliable tool in measuring CO_2 levels in newborns.

The use of quantitative or qualitative assessment of CO_2 in manual ventilation has been suggested by some groups who have highlighted some of the potential benefits of exhaled CO_2 monitoring in the delivery room. Our aim was to review the current evidence relating to the use of CO_2 monitoring in preterm newborns in the delivery room and to assess the efficacy of this type of enhanced monitoring on clinically relevant outcomes.

2. Methods

2.1. Criteria for inclusion

All literature was included if it addressed the use of, or application of, any form of CO_2 monitoring of preterm neonates in the delivery room or related to delivery room interventions, including facemask positive pressure ventilation (PPV) and intubation.

2.2. Search strategy

The search was performed using the Cochrane Central Register of Controlled Trials, MEDLINE (1966–2014) and PREMEDLINE, EMBASE (1980–2014), CINAHL (1982–2014), Web of Science (1975–2014) and the Oxford Database of Perinatal Trials. Ongoing trials were searched in the following databases at the following websites: www.clinicaltrials.gov and www.controlled-trials.com. Abstract of conferences and proceedings of Pediatric Academic Societies were searched electronically from 2000 to present. Additional searches were made from the reference list of identified clinical trials.

Keywords used were; "carbon dioxide detector", "capnography", "end tidal carbon dioxide", "resuscitation" and limited to "newborn". Each article was assessed according to it's suitability and was assessed for quality as per 2010 American Heart Association levels of evidence and recommendations (available online at www.heart.org). Each of our studies were assigned a class of evidence in the form of Class I, Class IIa, Class IIb, or Class III as well as a quality of evidence in the form of A, B, or C.

3. Results

Authors GAH and EMD independently searched the databases described. Any disagreement in relation to study selection or data extraction was resolved by consensus of all authors. The search revealed 128 articles for consideration and subsequently identified 22 studies relating to CO_2 detection in the delivery room.[7–9,12–30] Of these, there were four review articles.[9,13,15,16] One registered systematic review protocol,[29] one registered systematic review title, no published systematic reviews, one randomized controlled trial (RCT),[17] eight in vivo based observational studies,[8,14,24–28,30] two questionnaire-based studies,[18,19] two case reports,[7,20] three in vitro based observational studies[21–23] and two ongoing trials. There were no studies investigating the role of transcutaneous CO_2 detection in the delivery room. We have summarized these studies as determined below, by the monitoring method and its clinical utility. We assessed these studies according to the American Heart Association levels of evidence and grades of recommendation.

3.1. Use of qualitative CO_2 detector in confirming correct ETT placement

Four studies described the use of a qualitative CO_2 detector in confirming correct ETT placement.[7,8,16,28] Roth et al.[7] describe a single patient case report on the success achieved in using an adult CO_2 detector to determine correct ETT placement during resuscitation of a neonate in asystole (Table 1). Aziz et al.[8] showed that the Pedi-Cap® (Covidien, MA, USA) disposable CO_2 detector was useful in identifying correct ETT placement as demonstrated in 24 infants in the NICU and 21 infants in the delivery room. However, the authors highlight that its use during cardiorespiratory compromise should be interpreted cautiously due to its ability to give a false negative reading (Table 1). A review by Molloy et al.[14] on disposable CO_2 detectors drew a similar conclusion.

In a study investigating the Pedi-Cap's accuracy in determining correct ETT position, Schmolzer et al. used the Pedi Cap in conjunction with a respiratory function monitor on a sample of 35 intubations (Table 1).[28] This study concluded that in some instances the Pedi-Cap device might not show color change when there is correct ETT placement. This was reiterated in a literature review completed by the same group who suggested that exhaled CO_2 readings should always be interpreted with clinical signs, due to exhaled CO_2 often giving misleading readings.[16] Based on these findings the overall recommendation for use of a qualitative CO_2 detector in confirming ETT placement in neonates is level B.

3.2. Use of quantitative capnography in confirming correct ETT placement

We identified four studies describing the use of quantitative capnography in confirming correct ETT placement.[14,20,24,27] In a case series of four infants Salthe et al.[20] showed that it was possible to determine correct ETT placement in neonates via midstream capnography (Table 1). However, this study was limited by the use of an adult midstream capnography device. This has a large internal volume that resulted in diluted and inaccurate values. However, the authors claim that their findings supported the use of capnography for all neonatal tracheal intubations.

Quantitative capnography was shown to be quicker and more accurate in confirming correct ETT placement compared to clinical assessment in the delivery room,[24,27] while research by Roberts et al.[9] showed it to be quicker and more accurate in 100 intubations carried out on 55 neonates in the NICU (Table 1). We identified two ongoing clinical trials, one of which compares a CO_2 detector against quantitative capnography to confirm correct ETT placement (www.clinicaltrials.gov, NCT01870622) and another investigating quantitative capnography as a means of confirming correct ETT placement (www.clinicaltrials.gov, NCT01572272). We also identified one registered review protocol for a systematic review by Schmolzer and Roehr[29] which proposed to investigate the role of exhaled CO_2, to identify correct ET tube placement. A registered

Table 1
Use of CO_2 detection in confirming correct ETT placement.

Author	Title	Article type	Outcome	Strength of recommendation made
Roberts et al.[14]	The use of capnography for recognition of esophageal intubation in the neonatal intensive care unit	Observational study	Capnography is quicker and more successful in identifying esophageal intubation compared to clinical indicators	Class IIb, LOE C
Roth et al.[7]	Disposable CO_2-detector, a reliable tool for determination of correct tracheal tube position during resuscitation of a neonate	Case study	Adult CO_2 detector was successful in identifying correct ETT placement	Class IIb, LOE C
Aziz et al.[8]	The pediatric disposable end-tidal carbon dioxide detector role in endotracheal intubation in newborns	Observational study	Color change using Pedicap during intubation, however results on infants with apgars <3 should be interpreted cautiously	Class IIa, LOE C
Repetto[27]	Use of capnography in the delivery room for assessment of endotracheal tube placement	Observational study	Determination of ETT placement was quicker with capnography than with clinical determination	Class IIb, LOE C
Salthe et al.[20]	Capnography rapidly confirmed correct endotracheal tube placement during resuscitation of extremely low birthweight babies (<1000 g)	Case study	Midstream capnography showed instant carbon dioxide exhalation when ETT placed in trachea	Class IIb, LOE C
Schmolzer et al.[28]	Assessment of flow waves and colorimetric CO_2 detector for endotracheal tube placement during neonatal resuscitation	Observational study	Colormetric CO_2 detectors may mislead clinicians during intubation of preterm infant by failing to change color in spite of correct tube placement	Class IIb, LOE B

title for a review is also available, entitled "The effect of respiratory support guided by exhaled CO_2 on morbidity and mortality in newborn infants requiring resuscitation". Based on these findings the overall recommendation for use of quantitative capnography in confirming ETT placement in neonates is level B.

3.3. Use of qualitative CO_2 detector during facemask ventilation

We identified two video based studies and one review article describing the use of CO_2 detectors during facemask ventilation.[15,25,30] Leone et al.[25] described the benefits of a CO_2 detector when used with a facemask during positive pressure ventilation (PPV) in the NICU (Table 2). This study found that during 21 instances of clear lack of color change on the CO_2 detector, 20 displayed a color change once the head/jaw position was adjusted. As a result of this finding, it was determined that using a CO_2 detector with a facemask allows for an easier determination of airway patency on a near breath to breath basis. Although this study focused on NICU as opposed to delivery room facemask ventilation, we have nevertheless included it in our review. In a study of 24 infants, the same group showed that a colormetric CO_2 detector allows the resuscitation team to recognize events of airway obstruction in the very low birth weight infant during PPV provided during delivery room resuscitation (Table 2).[30] A literature review by O'Reilly et al.[15] identified that facemask leak and obstructions are generally unrecognized without the use of expired CO_2 detectors or respiratory function monitors. Although the authors acknowledge the benefits of qualitative CO_2 detectors, they highlight that such detectors are unable to differentiate between inadequate tidal volumes, airway obstruction and circulatory failure. Based on these findings the overall recommendation for use of qualitative CO_2 detectors during facemask PPV is level C.

3.4. Use of quantitative capnography during facemask ventilation

One RCT and two observational studies describe the use of quantitative capnography during facemask ventilation.[17,26,30] In an RCT carried out by Kong et al.[17] on a cohort of 48 infants, 7 infants were intubated and 41 received PPV via facemask (Table 2). Thirty-seven capnography tracings were obtained from this group and it was found that although the capnography device provided useful physiological data, it did not reduce the occurrence of hypocapnia or hypercapnia, which was the trial hypothesis. Using a respiratory profile monitor (NM3, Philips, Respironics) with a combined pressure, flow and CO_2 sensor on a cohort of 40 infants during resuscitation, Murthy et al.[26] observed that CO_2 elimination improved during facemask PPV with the onset of the infant's respiratory efforts. Van Os et al.[30] described their experience of using exhaled carbon dioxide, in combination with a respiratory function monitor, to guide PPV in the delivery room. They analyzed $EtCO_2$ readings from infants receiving PPV in the delivery room and concluded that further studies are needed to determine if $EtCO_2$ monitoring can be used during resuscitation (Table 2). Considering these studies, the overall recommendation for the use of quantitative capnography during facemask PPV in neonates is level B.

3.5. In Vitro based studies on CO_2 detection

Three in vitro based studies relating to CO_2 detection were identified.[21–23] Garey et al.,[21] using lung models with expected tidal volume as low as that of a 400 g neonate, concluded that disposable CO_2 detectors were appropriate for use with neonates above that birth weight to confirm ETT intubation. Schmalisch et al.,[23] in an investigation of air leak during ETT ventilation, in terms of volume and capnographic shape on a neonatal lung model, showed that, in contrast to tidal volumes, the effect of exhaled CO_2 leak is much more difficult to measure in vitro. We have shown that the use of a CO_2 detector improves the efficacy of PPV through a facemask on a mannequin model.[22] These studies' level of recommendation is level C.

3.6. Questionnaire based studies

Two questionnaire based studies relating to CO_2 detection in the delivery room were found.[18,19] In a survey of the resuscitation practices of preterm infants at birth from 78 respondents from 23 tertiary NICUs, El Naggar et al.[18] highlighted that the majority of respondents were using qualitative CO_2 detectors to confirm endotracheal intubation. This is in contrast to a survey on supplementary equipment used for neonatal resuscitation carried out on 25 tertiary perinatal centers in Australia and New Zealand 5 years previously by O'Donnell et al. This survey determined that only 3

Table 2
Use of CO_2 detection during facemask ventilation.

Author	Title	Article type	Outcome	Strength of recommendation made
Leone et al.[25]	Disposable colorimetric carbon dioxide detector use as an indicator of a patent airway during noninvasive mask ventilation	Observational study	Disposable CO_2 detectors are a good method of determining airway patency during PPV with a facemask	Class IIa, LOE C
Finer et al.[31]	Airway obstruction during mask ventilation of very low birth weight infants during neonatal resuscitation	Observational study	CO_2 detectors allow for recognition of airway obstruction during mask ventilation	Class IIa, LOE C
Hosono et al.[24]	A role of end-tidal CO_2 monitoring for assessment of tracheal intubations in very low birth weight infants during neonatal resuscitation at birth	Observational study	$EtCO_2$ is an accurate method of confirming ETT placement in very low birth weight infants during resuscitation	Class IIb, LOE B
Murthy et al.[26]	End tidal carbon dioxide levels during the resuscitation of prematurely born infants	Observational study	Improved carbon dioxide elimination occurs with the onset of infants' respiratory efforts	Class IIb, LOE B
Kong et al.[17]	Quantitative end-tidal carbon dioxide monitoring in the delivery room: a randomized controlled trial	Randomized controlled trial	Capnography does not reduce hypercapnia or hypocapnia, however does provide useful physiological information during PPV	Class IIb, LOE B
Van Os et al.[30]	Exhaled carbon dioxide can be used to guide respiratory support in the delivery room	Observational study	$EtCO_2$ monitoring could help to assess lung aeration and improve lung recruitment immediately after birth	Class IIb, LOE B

centers (12%) used CO_2 detection to assess ETT position.[19] There was no mention of its use in manual ventilation.

4. Discussion

These results highlight the paucity of good quality data on the role of CO_2 monitoring in the delivery room. In addition, studies vary concerning the strength of correlation between $EtCO_2$ and $PaCO_2$ or $PvCO_2$.[10–12,32–36] The role of carbon dioxide monitoring in the delivery room is generally limited to the use of end tidal CO_2 detection following intubation to confirm correct ETT placement, more often with a qualitative CO_2 detector than with capnography, both of which have been shown to be a more accurate as well as a quicker method of confirming correct ETT placement, compared to clinical assessment alone. The use of end tidal CO_2 detection for ETT placement is now advocated in the most recent NRP guidelines.[5]

CO_2 detection may be of particular benefit for preterm infants as assessment of effective PPV as using standard clinical methods can often be difficult due to various issues such as the difficulty encountered in visualizing chest rise and fall.[25,37] However, the use of a colorimetric CO_2 detector during the provision of PPV with a facemask has not been advocated in the recent International Liaison Committee on Resuscitation guidelines as there is limited data to support their use. One concern may be that utilization of a colorimeter will alter the ergonomics of manual ventilation devices and this may make manual ventilation more difficult, depending on the chosen device. However, users may already have experience in using and interpreting these qualitative devices in assessing endotracheal tube placement. We have shown that physicians have no difficulty in using CO_2 detectors during facemask ventilation, in particular the Neo-StatCO_2<Kg^{TM} CO_2 detector (Mercury Medical, Florida, USA), and it was the preferred method of confirming effective facemask ventilation with a mannequin model.[22] Clinical observational research into the use of qualitative CO_2 detectors during PPV with a facemask has advocated their use,[15,25,31] but currently there are no randomized trials of colorimeters for provision of PPV in the newborn, and many studies have advised caution due to the ability of the device to give a false negative reading.[8,9,15,16,28]

The only randomized trial of CO_2 detection in newborn resuscitation investigated the role of capnography during the provision of PPV via a facemask. Kong et al.[17] did not find any significant difference between the incidences of hypercapnia and hypocapnia during newborn resuscitation. There may be a number of reasons for this finding. The introduction of a new technology into resuscitation may alter the ergonomics of the manual ventilation with increased dead space and alteration of hand positioning. It also requires visualization of a monitor not directly in the user's line of vision, and this may be a distracting phenomenon. However, this trial did highlight the benefits of having capnography as a method of providing physiological information during the provision of PPV. This outcome is encouraging and warrants further investigations via randomized controlled trials. Nevertheless, we believe the introduction of such new technology into the delivery room should require additional training prior to its routine introduction.

There are other modalities available to the clinician to assess the adequacy of positive pressure ventilation in the newborn infant. These include the use of respiratory function monitors (RFM), either with or without incorporated CO_2 monitoring. These devices produce a continuous display of pressure and flow waves. Other readings can also be displayed in numerical form such as airway leak, positive end expiratory pressure (PEEP), continuous positive airway pressure (CPAP) and respiratory rate. A number of observational studies and one randomized controlled trial have assessed the role of RFMs in neonatal resuscitation[28,38–41] and van Os et al.[30] have assessed the role of RFM with incorporated $EtCO_2$ monitoring in the setting of the delivery room.

In a mannequin based study we have found that physicians tend to perform more efficient ventilation when visualizing the capnography display. However, drawing the user's attention away from the mannequin to look at the capnography readings remains a concern. Similar concerns apply when interacting with a RFM. While we consider that the potential benefits of having a quantitative CO_2 reading visible to the provider of PPV is desirable, incorporation of this device into the delivery room setting warrants further education and training, and in vitro simulation. The same applies to the RFM and also with the incorporation of $EtCO_2$ and RFM simultaneously. These issues should be addressed before conducting randomized trials of the use of capnography.

A trial is currently ongoing comparing qualitative CO_2 detectors with quantitative capnography to confirm correct ETT placement (www.clinicaltrials.gov, NCT01870622). Further randomized controlled trials are needed to compare the two methods of exhaled CO_2 detection during facemask ventilation.

5. Conclusion

In conclusion, this review of available literature highlights the need for further research into CO_2 detection, in particular capnography, as a means of confirming effective facemask PPV in neonatal resuscitation. The only way that this method can be shown to be beneficial is through randomized controlled trials, which we encourage.

Conflict of interest

The authors of this study do not have any conflicts of interest to disclose.

Authors' contribution

Mr. Gavin Anthony Hawkes had primary responsibility for overall content and manuscript preparation. He was also involved with study design, research collection and research interpretation.

Dr. John Kelleher was involved with manuscript design and preparation.

Prof. C. Anthony Ryan was involved with manuscript design and preparation.

Prof. Eugene Michael Dempsey was the supervisor for this study. He was involved with overall content, manuscript design, manuscript preparation, research collection and research interpretation.

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Appendix B

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ORIGINAL ARTICLE

Efficacy and user preference of two CO_2 detectors in an infant mannequin randomized crossover trial

G. A. Hawkes · B. J. O'Connell · V. Livingstone · C. P. Hawkes · C. A. Ryan · E. M. Dempsey

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Abstract Assessment of effective ventilation in neonatal mask ventilation can be difficult. This study aims to determine whether manual ventilation with a T-piece resuscitator containing an inline CO_2 detector (either a Pedi-Cap® CO_2 detector or a Neo-StatCO_2<Kg® CO_2 detector connected to a facemask) facilitates effective positive pressure ventilation compared to no device in a mannequin study. Paediatric and neonatal trainees were randomly assigned to determine which method they began with (no device, Pedi-Cap or a Neo-Stat). The participants used each method for a period of 3 min. They were video-recorded to determine the amount of effective ventilations delivered and the overall percentage efficiency of each method. Efficacy of ventilation was determined by comparing the number of manual ventilations delivered with the number of times chest rise was observed in the video recording. There were 19 paediatric trainees who provided a total of 7,790 ventilations, and 93% were deemed effective. The percentage of effective ventilations with the T-piece resuscitator alone, the PediCap and the NeoStat were 90, 94 and 96%, respectively. The difference was greatest in the first minute (T-piece resuscitator alone 87.5%, PediCap 94%, NeoStat 96%). Two thirds preferred the Neo-Stat. The use of a CO_2 detector improves positive pressure ventilation in a mannequin model, especially in the first minute of positive pressure ventilation. The Neo-Stat CO_2 detector was the preferred device by the majority of the participants.

Keywords Colorimeter · CO_2 detector · Mask ventilation · Neonates · Pedicap · Neostat

Abbreviations

NRP	Neonatal Resuscitation Program
IPPV	Intermittent positive pressure ventilation
ETT	Endotracheal tube
CUMH	Cork University Maternity Hospital
HORIZ	Horizontally attached CO_2 detector
VERT	Vertically attached CO_2 detector
TPR	T-piece resuscitator
SHO	Senior House Officer

Background

The Neonatal Resuscitation Programme (NRP) provides guidelines for neonatal resuscitation procedures [7] and has been shown to be effective in improving neonatal and infant outcomes [2, 3, 12, 15]. Effective positive pressure ventilation is a key component of neonatal resuscitation. Intermittent positive pressure ventilation (IPPV) is indicated when the infant is apneic or ineffectively breathing, has a heart rate of less than 100 beats per minute or remains cyanotic despite supplemental oxygen [7]. It can be difficult to assess the level of chest wall movement during PPV in a clinical setting, particularly in small infants [9]. When delivering IPPV via a facemask, leak of 33% of assumed tidal volume that is provided can occur in a mannequin model [11]. In order to confirm effective ventilation during resuscitation, the NRP currently recommends observing for an increase in heart rate, seeing or auscultating chest inflation and observing for a rise in oxygen saturation level (SpO_2) [7].

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CO_2 detectors have an established role in determining the correct placement of an endotracheal tube in a clinical setting [1] but have recently been used to assess the effectiveness of neonatal mask ventilation through clinical investigations [4]. Despite this possible advantage, their use is not indicated in current neonatal guidelines [8]. Even with the application of a good seal, the CO_2 detector will not change colour if insufficient tidal volume is produced [6] and if there are obstructed ventilations [9], inadequate cardiac output or device failure [10].

To the best of our knowledge, two methods of reliably connecting inline disposable CO_2 detectors to a Neopuff (Fisher and Paykal, Auckland, New Zealand) T-piece resuscitator (TPR) exist. They can be connected horizontally to the facemask, requiring the CO_2 detector to be connected from the side (Fig. 1) or they can be connected vertically, requiring the CO_2 detector to be connected from above (Fig. 2). It is not known which of these methods is preferred amongst physicians or which is more effective.

The aims of this study were to (1) assess the efficacy of manual ventilation by paediatric trainees with each method in a mannequin study and (2) to determine if there was a user preference for either of these methods.

Methods

A total of 19 NRP certified trainees in paediatrics and neonatology participated in this randomized crossover trial. The trainees provided three separate 3-min periods of manual ventilation with a TPR on a CO_2-producing mannequin in a randomly assigned order. The TPR was configured to a peak inspiratory pressure of 20 cmH_2O and a positive end expiratory pressure of 5 cmH_2O throughout all participant interactions. The participants were instructed to provide

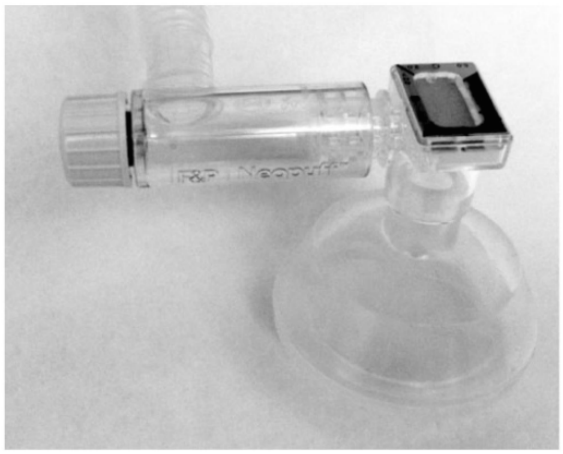

Fig. 1 CO_2 detector connected to the TPR horizontally (from the side)

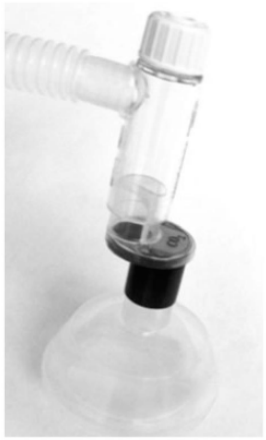

Fig. 2 CO_2 detector connected to the TPR vertically (from above)

ventilation at an NRP standard of 40 ventilations per minute. There was approximately a 1-min period between each manual ventilation period to allow washout of CO_2. Block one had no CO_2 detector attached to the TPR (ND), block two had a Pedi-Cap® (Covidien, MA, USA) CO_2 detector attached horizontally to the TPR (HORIZ) and block three included a Neo-StatCO_2<Kg ™ (Mercury Medical, FL, USA) CO2 detector attached vertically to the TPR (VERT). The same mannequin model was used for all blocks. All blocks were video-recorded from the side and scored by two observers afterwards. This trial was approved by the Cork Research Ethics Committee, and informed consent was received from all participants.

CO_2 detector

The Pedi-Cap is a device that requires ventilations to be delivered from the side (Fig. 1). The manufacturer indicates the use of this device for intubation in patients weighing 1–15 kg; however, Garey et al. have shown that the Pedi-Cap CO_2 detector is appropriate for use with any neonate weight to confirm intubation [5]. This CO_2 detector is currently the standard CO_2 detector used in Cork University Maternity Hospital for neonatal intubation.

The Neo-StatCO_2<Kg is a device that requires ventilation to be delivered from above (Fig. 2). The manufacturer indicates the use of this device for intubation up to a maximum of 24 h in patients weighing 0.25–6 kg.

CO_2-producing mannequin

During ventilation provided through a facemask, unrecognized airway obstruction as well as gas leak around the facemask is a common cause of ineffective IPPV [13]. To simulate these issues, we used a CO_2-producing mannequin model with an

airway simulating the airway of a newborn. The mannequin model was found to have a tidal volume of approximately 15 ml.

The mannequin (Laerdal Medical AS) had an internal reservoir bag to simulate a lung. An internal rubber tube connected this reservoir bag to the mannequin's mouth, simulating a patient airway. A gas hose was inserted into this airway tube just above the reservoir bag using a three-way adapter. The other end of the gas hose was connected to the gas cylinder (5% carbon dioxide and 95% nitrogen) via a gas regulator. The flow rate on this regulator was set to 1 L/min. The TPR was fed by a 100% oxygen gas supply of approximately 8 L/min. When the mannequin's lungs were filled by PPV, the 100% oxygen gas mixed with 5% CO_2 gas and on passive exhalation the presence of CO_2 simulated the exhalation of a small infant. Using the TPR to initiate new ventilation drove 100% oxygen back through the CO_2 detector and, at the chosen pressures, reset the colour to purple on each device. We subsequently assessed the quantity of CO_2 with a side-stream CO_2 detector and found the CO_2 value to be consistently 5 kPa when no leak was present. The absence of an appropriate seal resulted in no CO_2 being detected, over-extending or deflexing the head excessively resulted in no CO_2 being detected and, finally, holding the mask at approximately 2 mm from the mannequin's mouth resulted in no CO_2 being detected. The mannequin's design was such that if the head tilt angle was not correct, it kinked the patient airway and simulated obstructed ventilation. In this event, the infusing CO_2 supply would continue to inflate the mannequin lung reservoir, and to prevent this reservoir from over-expanding, a blow-off valve was fitted to the reservoir. This valve opened to vent the gases at a pressure greater than 30 mbar.

Randomization

The randomization process was carried out with random sequence numbers in sealed opaque envelopes. If the participants drew the number “1”, then they started with the ND method and then moved on to the HORIZ method followed by the VERT method. If the participants drew the number “2”, then they started with the HORIZ method and then moved on to the VERT method followed by the ND method. Finally, if the participants drew the number “3”, then they started with the VERT method and then moved on to the ND method followed by the HORIZ method.

Scoring of videos

The study was video-recorded in order to determine the most effective device. Two reviewers (authors GAH and EMD) assessed the videos and counted the number of ventilations provided and the number of times when there was sufficient chest rise. Author GAH is an NRP-trained emergency medical technician and author EMD is a consultant neonatologist and a certified NRP trainer. As the videos were anonymized, showing only the participants' hands, these reviewers were unaware of the order in which the participants completed the different methods. Ventilation was deemed to be effective if chest rise was observed during delivery. Prior to the study, we investigated if it was possible to see a colour change in the CO_2 detector when ventilation was not being provided correctly. We found out that if the mannequin's airway was incorrectly positioned and/or the facemask did not make a correct seal, then no colour change occurred on the CO_2 detector as described previously. All video recordings were taken from the side of the mannequin in a consistent order for chest rise to be easily visible. The recordings were allocated a study number and placed on a secure server. Where disagreement existed, the average of both counts was used. Inter- and intra-rater variability was assessed in a randomly selected 10% of recordings. Percentage efficacy was determined as the number of ventilations that the reviewers deemed to be effective against the number of ventilations that were delivered overall. We used chest lift primarily to equate effective ventilation as we were comparing two individual devices to no device and as such required an endpoint that was applicable to all. We ensured consistency of assessment by using the same mannequin and had the video camera placed in the same position throughout so as to optimize visualization of chest lift.

Results were reviewed for the first minute and for the entire 3-min period. All statistical analyses were performed using PASW Statistics 18.0 (IBM, NY, USA). All tests were two-sided, and a p-value <0.05 was considered to be statistically significant. Efficacy was described using medians and interquartile ranges. Non-parametric tests were used as the sample size of 19 was small and the distribution of efficacy scores was non-normal.

Results

There were 19 participants overall, which consisted of ten senior house officers (SHOs) and nine registrars. This was a convenience sample based on the number of trainees working in our unit at the time. All participants had completed the NRP, with the most junior doctors having completed the NRP within the preceding 3 months.

The participants provided more ventilations in the first minute as well as the entire 3-min period when no CO_2 detector was in situ (Table 1), with a mean efficacy of ventilation of 88.9% in the first minute and 90.4% in the overall 3-min period. We found the HORIZ method to have a mean efficacy of ventilation of 92.8% in the first minute and 91.3% in the overall 3-min period. The VERT method outperformed both other methods with a mean efficacy of ventilation of 94.2% in the first minute and 96.0% in the

Table 1 Comparison of performance of the different methods within 1 and 3 min, respectively

	Mean number of ventilations delivered					
Position	1-min ND	1-min HORIZ	1-min VERT	3-min ND	3-min HORIZ	3-min VERT
SHO	47.9	40.2	44.1	147.1	122.8	132.8
Registrar	48.1	48.1	44.0	131.2	143.2	135.8
Overall	48	44.0	44.1	145.5	132.5	134.2

overall 3-min period. The VERT method was always superior to the other methods, and the ND method surpasses the HORIZ method once, but this was not found to be statistically significant (Tables 2 and 3).

The occupational grade that the participants held was considered in order to determine whether experience had a factor in the use of the methods (Table 1; Figure 3). This test showed that both SHOs and registrars performed better ventilation with a CO_2 detector attached. For the SHOs, the VERT method outperformed the HORIZ method; however, for the registrars, there was no notable statistical difference between the HORIZ method and the VERT method, suggesting that the level of experience of the trainee also had an influence.

After each participant had completed 3 min of ventilation with each method, he/she received an individual debriefing in order to provide feedback relating to each one. A total of 18 participants preferred a CO_2 detector during ventilation of the mannequin. There were 12 participants who had a preference for the VERT method, while six had a preference for the HORIZ method. This outlines the VERT method as being the preferred method amongst participants.

When asked why they choose the VERT method as their preferred device, recurrent participant feedback related to ergonomics. This preference was due to the similarity between the ergonomics of using the Neo-StatCO_2<Kg CO_2 detector connected to the TPR being similar to TPR when used alone, which is standard practice at the moment. Most participants disliked the HORIZ method due to the non-conventional angle at which the user has to deliver PPV during use.

To assess video rater reliability, a random sample of 10% of recordings was evaluated. The intra-rater variability was very high at r^2=0.9, and the inter-rater variability was very high at r^2=0.92. Feedback relating to the use of the PediCap CO_2 detector showed positivity towards the size of the colour indicator contained on the device as well as the direct visualization that participants were able to achieve due to the fact that no part of the hand was being involved with their line of sight of the colour indicator. They found that any colour change that occurred was easier to see compared to the Neo-StatCO_2<Kg CO_2 detector, which they felt had a smaller colour indicator, and this indicator had a tendency to become occluded by the user's hand. The one participant who preferred no CO_2 detecting device attached to the facemask felt that by having a CO_2 detector attached, the user tended to become reliant on the colour change and failed to take in any other aspect in determining effective ventilation.

Discussion

This study has shown that the use of a CO_2 detector during the provision of IPPV with a facemask in a mannequin model improves the effectiveness of ventilation, as assessed by video recordings, and allows for early identification of ineffective ventilations. Effective ventilation can be achieved with or without a CO_2 detector; however, we have shown that the use of a CO_2 detector particularly increases the effectiveness during the first 60 s, a time when effective ventilation is particularly important. Although more ventilations were delivered by the participants without a CO_2 detector attached, these ventilations were not as efficient.

The VERT method was shown, statistically, to be the most effective method both for the first minute and for the 3-min period of manual ventilation, apart from when the participant

Table 2 Comparison of the performance of different orders at 0–60 s

	0–60 s				
	Number of participants	Mean % efficacy ND	Mean % efficacy HORIZ	Mean % efficacy VERT	*p*-value
Order 1	6	93.1	97.5	93.7	p=0.229
Order 2	6	90.5	90.0	95.9	p=0.062
Order 3	7	83.9	91.2	93.1	p=0.032
Overall	19	87.5	93.2	95.1	p=0.001

Order 1 ND followed by HORIZ method followed by NSTAT, *Order 2* HORIZ method followed by NSTAT followed by ND, *Order 3* NSTAT followed by ND followed by HORIZ method

Table 3 Comparison of the performance of different orders at 0–180 s

	0–180 s				
	Number of participants	Mean % efficacy ND	Mean % efficacy HORIZ	Mean % efficacy VERT	*p*-value
Order 1	6	94.4	92.9	97.5	$p=0.651$
Order 2	6	92.7	90.6	98.2	$p=0.048$
Order 3	7	85.0	90.6	92.7	$p=0.030$
Overall	19	91.5	91.7	96.0	$p=0.004$

Order 1 ND followed by HORIZ method followed by NSTAT, *Order 2* HORIZ method followed by NSTAT followed by ND, *Order 3* NSTAT followed by ND followed by HORIZ method

began the trial with the ND method. Although the role of PediCap CO_2 detectors in facemask ventilation has been previously described [5, 6, 14], comparison with the NeoStatCO_2<Kg CO_2 detector in effectiveness and preference has not previously been studied. There are a few potential confounders that could account for these differences. As a carryover effect is always a consideration with crossover studies, the order of methods used by the participants was randomly assigned, and regardless of which method a participant started with, the VERT method always showed the greatest efficacy over the entire 3-min period. The second relates to the experience of the trainee, and again the order was randomized. There was no effect of years of training. However, we did note that the difference between the use of a CO_2 detector compared to the use of no CO_2 detector improved from the first minute to the last, suggesting that trainees are able to identify problems with manual ventilation over time and make the necessary changes to enhance manual ventilation in a mannequin model.

Through our mannequin-based study, we have found that participants preferred providing ventilations with a CO_2 detector attached to the TPR and that such was the most effective method; the VERT method was also the preferred method by participants. In order to standardize the manual ventilation device, we elected to use only the TPR in this study, and whilst it is likely that the results can be extrapolated to the self- and flow-inflating bags, this was not assessed.

Through analysis of the mean number of ventilations delivered, we have shown that SHOs delivered more ventilations in the first minute as well as the entire 3-min period when there was no CO_2 detector attached. However, this

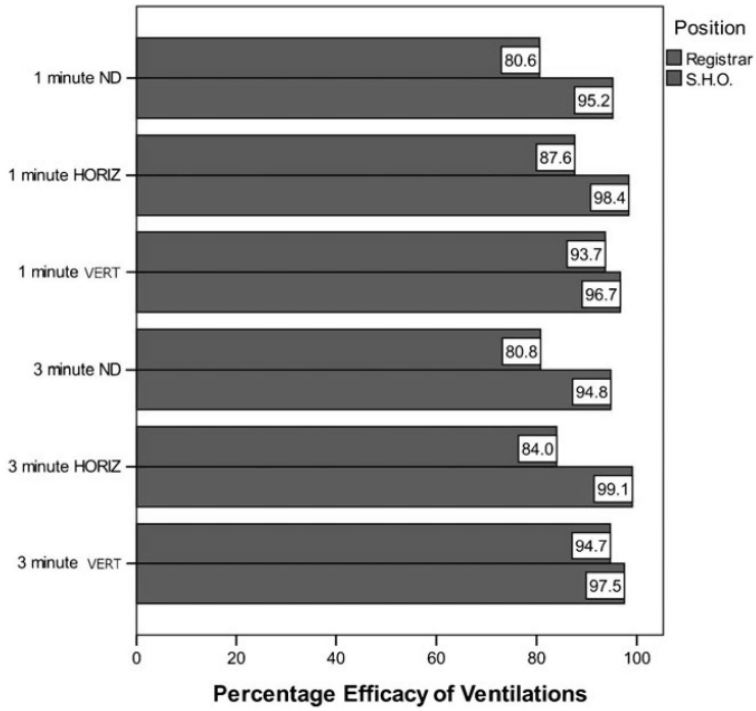

Fig. 3 Percentage efficacy of ventilations

analysis showed that this was not the case with the registrars who participated (Table 1). This may suggest that by having an extra item attached to the TPR, a user with less experience may have increased difficulty providing manual ventilation or the contrary may be the case, such that the time taken to observe the colour changes on a CO_2 detector results in slower provision of manual ventilation by the user with less experience.

One limitation of this study is that the effect of different methods on facemask leak was not assessed. The attachment of a flow meter to the TPR would have significantly altered the ergonomics of manual ventilation and if a flow meter was attached in series with either of the devices, the additional weight as well as the altered hand positioning may have affected results. We attempted to replicate what happens clinically and so elected not to include a flow meter. We recorded each participant's ventilations of the mannequin, which permitted us to look at adequacy of mask position and chest lift for each ventilation. While it is not known if the concentration of CO_2 produced in this mannequin model is consistent with that produced by a small infant, the presence of the colorimeter resulted in enhanced manual ventilation. The CO_2 produced by an infant is dependent on a number of factors including spontaneous breathing and size of the tidal volumes expired. This can only be clarified by in vivo studies of infants.

Another limitation to this study is the use of a low-fidelity mannequin model. This was an issue of cost, and although a high-fidelity mannequin model may have provided precise assessments of tidal volume, it was deemed to be not feasible for this study. The in vitro nature of this study made it difficult to replicate a clinical care setting where variables such as different anatomy of patients and stress levels experienced by staff are always present.

The issue of ergonomics behind the use of each method is one that was highlighted by the participants in this trial. Although the PediCap CO_2 detector has a larger colour-indicating area that is easier to view, its horizontal attachment requires manual ventilations to be delivered from the side. In contrast, the Neo-StatCO_2<Kg CO_2 detector allows ventilations to be delivered from above, which is the traditional setup for manual ventilation in the absence of a CO_2 detector. It should also be noted that the Neo-StatCO_2<Kg CO_2 detector has only a third of the dead space that is contained in the PediCap CO_2 detector, making it likely to detect changes more readily.

Whilst there are times when there are false-negatives with these detectors, it is important to note also that false-positive readings on CO_2 detectors can occur in a clinical setting. These include intubation of the hypopharynx and/or in cases where a significant amount of bag and mask ventilation was administered pre-intubation, resulting in large amounts of air being present in the stomach. These false-negative and false-positive scenarios are not applicable to our in vitro mannequin model.

In conclusion, inline CO_2 detectors can improve the manual ventilation of an infant mannequin amongst paediatric trainees. A CO_2 detector when attached vertically in comparison to a CO_2 detector attached horizontally appears to slightly improve efficacy and is preferred. While it is likely that these findings can be extrapolated to the clinical setting, further studies are warranted.

Contributorship Gavin Anthony Hawkes had primary responsibility for overall content and manuscript preparation. He was also involved with study design, data collection and data interpretation. Brian O'Connell was involved with mannequin design and maintenance of all devices used in the study. Vicki Livingstone was involved with the statistical analysis carried out in the study. Colin Hawkes was involved with study design and manuscript preparation. C. Anthony Ryan was involved with study design, data analysis and manuscript preparation. Eugene Michael Dempsey was the supervisor for this study. He was involved with overall content, study design, manuscript preparation, data collection and data interpretation.

Conflicts of interest The authors of this study do not have any conflicts of interest to disclose.

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CREC Approval letter

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Our ref: ECM 4 (f) 06/08/13

10th July 2013

Dr Gene Dempsey
Consultant Neonatologist
Department of Paediatrics and Child Health
Cork University Hospital
Wilton
Cork

Re: During *in-vitro* usage of two different CO2 detectors and one capnography device, which is the most efficient and which is the most preferred?

Dear Dr Dempsey

Expedited approval is granted to carry out the above study at:

- Cork University Maternity Hospital.

The following documents have been approved:

- Signed Application Form
- Information leaflet/Consent Form Version 1 dated 2nd July 2013
- Study Protocol Version 1 dated 2nd July 2013
- CV for Chief Investigator.

We note that the co-investigator involved in this study will be:

- Gavin Hawkes.

29.7.13

Yours sincerely

Professor Michael G Molloy
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

The Clinical Research Ethics Committee of the Cork Teaching Hospitals, UCC, is a recognised Ethics Committee under Regulation 7 of the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004, and is authorised by the Department of Health and Children to carry out the ethical review of clinical trials of investigational medicinal products. The Committee is fully compliant with the Regulations as they relate to Ethics Committees and the conditions and principles of Good Clinical Practice.

Participant information and consent form

Version 1 14/6/2012

Ospideal Maithreachais na h'Ollscoile Corcaigh
Cork University Maternity Hospital

ucc
Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

Research Study:

During in-vitro usage of the Pedi-Cap® (Nellcor) CO2 detector and the Neo-StatCO2<Kg® (Mercury Medical), which is the most efficient and which is the most preferred?

Hawkes GA, O'Connell B, Olu Oyedeji, Hawkes CP, Ryan CA, Dempsey EM

Information

Aim of the Study

This research aims to determine which device is the most preferred, the Pedi- Cap® (Nellcor) CO2 detector or the Neo-StatCO2<Kg® (Mercury Medical) CO2 detector and out of each of these devices, which is statistically the most effective.

What does this study involve?

During this *in-vitro* study, physicians' hands will be video recorded performing facemask ventilation to a mannequin model. Two different devices, the Pedi- Cap® (Nellcor) CO2 detector and the Neo-StatCO2<Kg® (Mercury Medical) CO2 detector will be attached to a T-piece. You will be asked to perform manual ventilation in a mannequin model for three one-minute periods, alternating between no device, the Neo-Stat and the Pedi-cap.

Eligibility:

All NCHDs and consultants are eligible for this *in-vitro* study.

Consent:

By agreeing to this research you agree to your hands being video recorded during the *in-vitro* study. Performance will not be investigated in this study; the study will solely focus on the preferred colorimeter, determined through feedback, as well as the most effective, determined through analysis of video recordings.

Ospideal Maithreachais na h'Ollscoile Corcaigh
Cork University Maternity Hospital

ucc
Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

Research Study:

During in-vitro usage of the Pedi-Cap® (Nellcor) CO2 detector and the Neo-StatCO2<Kg® (Mercury Medical), which is the most efficient and which is the most preferred?

Hawkes GA, O'Connell B, Olu Oyedeji, Hawkes CP, Ryan CA, Dempsey EM

Consent form

- I have read the information leaflet about this research, the information has been fully explained to me and I have been able to ask questions if I wished. I understand why the research is being completed. ☐
- I agree to allow myself to be video recorded during the *in-vitro* study ☐
- I give permission for the recording and information collected during the recording to be stored for possible future research unrelated to this study without my further consent being required and subject to approval by a research ethics committee. ☐

Name (Print): _____

Position held: _____

Signature: _____

Date: _____

Appendix C

ACTA PÆDIATRICA
NURTURING THE CHILD

Acta Pædiatrica ISSN 0803-5253

REGULAR ARTICLE

Quantitative or qualitative carbon dioxide monitoring for manual ventilation: a mannequin study

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Keywords
capnography, carbon dioxide, CO_2 detector, mask ventilation, neonates

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ABSTRACT

Aim: To compare the effectiveness of an in-line $EtCO_2$ detector (DET) and a quantitative $EtCO_2$ detector (CAP), both attached to a t-piece resuscitator, during PPV via a face mask.

Methods: Paediatric trainees were randomly assigned to determine the method of PPV they commenced with (No device (ND), DET or CAP). Participants used each method for 2 min. Participants were video-recorded to determine the amount of effective ventilations delivered with each method.

Results: Twenty-three paediatric trainees provided a total of 6035 ventilations, and 91.2% were deemed effective. The percentages of median effective ventilations with the ND, the DET and the CAP were 91.0%, 93.0% and 94.0%, respectively. Fourteen (61%) of the trainees indicated a preference for the DET method, 8 (35%) for the CAP method, and 1 (4%) of the trainees indicated a preference for the ND method. Capnography was the most effective method per patient.

Conclusion: There was no adverse effect with the addition of $EtCO_2$ detectors. Trainees favoured methods of $EtCO_2$ monitoring during ventilation. The NeoStat device was the preferred device by the majority. The greatest efficacy was achieved with the capnography device. Capnography may enhance face mask ventilation.

BACKGROUND

Effective positive pressure ventilation (PPV) is a key component of neonatal resuscitation. The Neonatal Resuscitation Program (NRP) currently suggests the use of PPV for many reasons including the infant experiencing apnoea, having a heart rate of <100 beats per minute, or remaining cyanotic despite supplemental oxygen (1).

Research on the role of end tidal carbon dioxide ($EtCO_2$) monitoring during the provision of PPV via a face mask during the stabilisation process after birth remains limited (2–4). Alterations in carbon dioxide levels in the preterm are associated with adverse outcomes including chronic lung disease, brain injury and/or long-term neurodevelopmental problems (5,6).

Exhaled carbon dioxide detection includes (1) the use of a qualitative or semiquantitative disposable colorimetric $EtCO_2$ detectors that change colour upon contact with CO_2 and (2) quantitative capnography which displays an $EtCO_2$ value to the user along with a capnographic waveform.

Qualitative and quantitative $EtCO_2$ detectors have been shown to have a role in determining the correct placement of an endotracheal tube (ETT) in a clinical setting (7–9) but have recently been used to assess the effectiveness of PPV through clinical investigations (2,10). Studies have shown that a qualitative $EtCO_2$ detector will not change colour if insufficient tidal volume is produced (11), if there are obstructed ventilations (3), inadequate cardiac output, and/or device failure (12). We have shown that the use of a qualitative $EtCO_2$ detector improves the efficacy of PPV in a mannequin model and was the preferred method of face mask ventilation (13).

The addition of carbon dioxide detectors to face mask ventilation in newborn infants is a recent addition to the provision of manual ventilation. The primary aim of our study was to compare the effectiveness of two different methods of $EtCO_2$ monitoring during the provision of PPV in a mannequin model, qualitatively by means of an $EtCO_2$ detector and quantitatively by means of capnography, and to investigate how this efficacy compares to the current standard of PPV. The secondary aim of our study was to

Key notes

- The role of $EtCO_2$ detection in the confirmation of intubation is well established; however, the role of $EtCO_2$ detection during positive pressure ventilation via a face mask in newborn infants is not clear.
- This study found no adverse effect on performance with the addition of $EtCO_2$ detection during PPV.
- Users preferred providing PPV with $EtCO_2$ detection available.

obtain feedback on these devices from the trainee physicians that participated in the study.

METHODS

All trainees had completed an NRP course within 6 months of participating in this study. Trainees were instructed to provide three separate 2-min periods of manual ventilation with a T-piece resuscitator (TPR) on a low-fidelity CO_2-producing mannequin, in a randomly assigned order. The TPR was configured to a peak inspiratory pressure (PIP) of 20 cm H_2O and a positive end-expiratory pressure (PEEP) of 5 cm H_2O throughout all participant interaction. Participants were asked to provide ventilation at an NRP standard of 40 to 60 ventilations per minute. There was approximately a 1-min period between each manual ventilation period to allow washout of CO_2 from the mannequin. Method one had no CO_2 detector attached to the TPR (ND), method two had a Neo-StatCO_2<kg™ (Mercury Medical, Clearwater, FL, USA) EtCO_2 detector attached to the TPR (DET), and block three had a Microstream® Vitastream™ CO_2 sampling line (Philips Medical Systems, BG Eindhoven, the Netherlands) attached between the TPR and the face mask (CAP).

All ventilations were video-recorded from the side and retrospectively scored by three observers. This trial was approved by the Cork Hospitals Research Ethics Committee, and informed consent was received from all participants. All participants received an individual debriefing session after their participation in order to obtain feedback and user preference relating to the three methods.

CO_2-producing mannequin

The mannequin (Laerdal Medical AS) had an internal reservoir bag to simulate a lung. An internal rubber tube connected this reservoir bag to the mannequin's mouth simulating a patient airway. A gas hose was inserted into this airway tube just above the reservoir bag using a 3-way adapter. The other end of the gas hose was connected to the gas cylinder (5% carbon dioxide and 95% nitrogen) via a gas regulator. The flow rate on this regulator was set to 1 L/min.

The face mask was fed by a 100% oxygen gas supply of approximately 8 L/min. When the mannequin's lungs were filled by PPV, the 100% oxygen gas mixed with the 5% CO_2 gas, and on passive exhalation, the presence of CO_2 attempted to simulate the exhalation of a small infant. Using the t-piece and face mask to initiate a new ventilation forced 100% oxygen back through the EtCO_2 detector.

The mannequin's design was such that if the head tilt angle was not correct, it kinked the mannequin airway and simulated an obstructed ventilation, thereby no colour change of the EtCO_2 detector occurred and no EtCO_2 values were displayed on the capnography machine. In this event, the infusing CO_2 supply would continue to inflate the mannequin lung reservoir and to prevent this reservoir from overexpanding a blow off valve was fitted to it. This valve opened to vent the gases at a pressure >30 m bar.

CO_2Detector

We used the Neo-StatCO_2<kg™ for this study. This colorimetric EtCO_2 detector requires manual ventilations to be delivered in parallel with the TPR and face mask. The manufacturer indicates the use of this device for intubation up to a maximum of 24 h in patients weighing 0.25 kg–6 kg.

Capnography

We connected the Microstream® Vitastream™ CO_2 sampling line between the TPR and face mask, and this sampling line was connected to a Philips IntelliVue MP70 monitor (Philips Medical Systems, BG Eindhoven, the Netherlands) that displayed the EtCO_2 values.

Randomisation

The randomisation process was carried out with random sequence numbers in sealed envelopes. Three different numbers determined whether participants carried out the study in the order of ND followed by DET then CAP, DET followed by CAP then ND, or DET followed by CAP then ND.

Scoring of videos

The study was video-recorded to determine the most effective device. Three reviewers (authors GAH, MK and EMD) assessed the videos and counted the number of ventilations provided by each participant and the number of times there was sufficient mannequin chest rise. As the videos were anonymised, showing only the participants' hands, these reviewers were unaware of the order in which the participants completed the different methods.

Ventilation was deemed to be effective if chest rise was observed during the delivery of PPV. Where disagreement existed amongst the three observers, consensus was decided by the majority decision. Percentage efficacy was determined as the number of ventilations that the reviewers deemed to be effective against the number of ventilations that were delivered overall.

All statistical analysis was performed using SPSS Statistics 21.0 (IBM, Armonk, NY, USA). All tests were two-sided and a p-value <0.05 was considered to be statistically significant.

RESULTS

A total of 23 paediatric trainees consisting of 12 senior house officers (SHOs) and 11 registrars provided a total of 6035 ventilations, of which 91.2% were deemed to be effective. There was no statistical difference in the median efficacy of ventilations across the three different methods ($p = 0.72$)(Table 1).

There were no differences in the median efficacy of ventilations between physician grade (SHO versus registrar) across the ND method, DET method or CAP method, although there was a slightly higher median efficacy amongst registrars across all methods (Table 1). The order with which participants were randomised to start the

Table 1 Median and interquartile range (IQR) of efficacy in ventilation

	% Efficacy No Device		% Efficacy NeoStat		% Efficacy Capnography		
	Median	IQR	Median	IQR	Median	IQR	p-value
SHO	90.0	(86.8, 91.8)	93.0	(86.8, 95.5)	93.5	(88.5,97.8)	0.74
Registrar	92.0	(91, 93)	93.0	(90, 98)	95.0	(93, 96)	0.93
Overall	91.0	(90, 92)	93.0	(89, 97)	94.0	(92, 97)	0.72

experiment with (ND method, the DET method or the CAP method) did not affect efficacy (p = 0.601, 0.566 and 0.208, respectively).

Fourteen (61%) of the trainees indicated a preference for the DET method, 8 (35%) for the CAP method and 1 (4%) for the ND method. However, when each individual's performance was assessed according to the method used, there was no difference between the groups whereby the CAP method performed best (45.4%) compared to DET method (32%) and the ND method (22.7%)(p value = 0.42).

Users highlighted that they liked being able to assess the efficacy of the PPV that they are providing with an extra method as opposed to the standard method of assessing chest rise alone. The DET method was favoured by some participants as they were able to maintain focus on the mannequin and colour indicator at the same time. In contrast, they had to look away from the mannequin with the CAP method. However, users who indicated a preference for the CAP method gave positive feedback to the quantitative aspect of this methodology, visualising the ventilations provided through the waveforms on the monitor. The participant who indicated a preference for neither device highlighted the potential for complicating the resuscitation of a newborn by adding another indicator that the resuscitator had to observe in order to ensure effective PPV. Users were often uncomfortable with the change in hand positioning that was required when the $EtCO_2$ detecting devices were in place, leading to an increase in the distance between the TPR and the face mask.

DISCUSSION

The findings of this study show that although there is a preference for the use of $EtCO_2$ detection during PPV, in particular the use of the DET method, there is no statistical difference in efficacy of either method when using it in a mannequin model. User preference is similar with or without the use of an $EtCO_2$ detecting device, confirming that $EtCO_2$ detecting methods are not associated with a deterioration in performance, *in vitro*. This was true for both grades of doctors studied. However, these findings may be very different from real-life situations, where ventilation is dynamic and changes occur from breath to breath. There may be many scenarios requiring adjustment of face mask position and positive pressure ventilation, such as an obstructed airway (10).

The results were similar to the previous work performed on mannequin models (13). The main preference for the DET method over the CAP method was accredited to the fact that users' eyes were fixed on the mannequin during the DET method compared to users having to look away from the mannequin during the CAP method. This is understandable as issues such as this often accompany the implementation of disruptive technology in the medical setting. This may be alleviated if a monitor was to be placed closer to the mannequin, perhaps next to the TPR pressure settings on the resuscitation unit, as this is an area that the user is already required to look at during the resuscitation process.

Participants highlighted having an extra indicator for a patent airway as being of great benefit and reassurance during manual ventilation. They highlighted that this might be even more beneficial when applied to an *in vivo* setting, especially for preterm infants. Difficulty associated with observing chest rise in preterm infants during resuscitation has been described by Leone (3) and Poulton (14), and as a result, $EtCO_2$ detection may be of particular benefit for alleviating some of this difficulty.

This study has been the first study to report on *in vitro* simulation of a capnography device during face mask ventilation of an infant mannequin model. This study has highlighted many of the human factors that need to be addressed prior to *in vivo* implementation of these devices. It is essential that healthcare personnel are appropriately trained in the use of these devices in a simulation setting prior to their introduction in the clinical care setting.

This study was limited by the fact that we did not investigate mask leak, which is a method that may have gathered more accurate results in relation to efficacy of PPV. We choose not to include this in our study as we feel the ergonomics of the added flow sensor, that would be required to measure mask leak, may have impacted negatively on the participants' performance. We do not currently use a respiratory function monitor in newborn resuscitation training. We choose chest rise of the mannequin as our indicator of efficient PPV as it is an indicator that is used in an *in vivo* setting as well as being an indicator that was present across all three methods, keeping our data collection consistent. As with all mannequin-based studies, the results of our study may be significantly different to an *in vivo* study of the same nature as we had a controlled environment in which participants were only asked to focus on correct PPV technique. This is not the case *in vivo* as several other factors are required to be monitored by the

resuscitator. The study was also limited by the fact that some participants had no prior experience in the use of $EtCO_2$ detection with face mask ventilation prior to the study, as they would not have received this training in their NRP course.

CONCLUSIONS

The study has highlighted the importance of *in vitro* studies during the implementation of any new medical devices, identifying the problems relating to disruptive technology and ergonomics arising during *in vivo* usage. Both the NeoStat and Microstream devices are approved to be marketed in Europe and the United States (15). As both the NeoStat and Microstream devices are classified as class II medical devices by the FDA, no clinical trials were required to take place prior to their market approval. Due to the issues that we have identified from end-users in our trial, there may be a greater need to ensure simulation-based *in vitro* trials, run externally from the manufacturer, prior to market approval of these devices for different indications. Having an extra indicator for effective PPV is something that may be of benefit in clinical practice, and this has been described elsewhere (10). Coupled with a respiratory function monitor, capnography may be of even greater benefit at highlighting airway leak and improving the effectiveness of face mask ventilation.

In summary, we have shown that trainees prefer carbon dioxide monitoring during mask ventilation, and whilst the qualitative device was the preferred method, greatest efficacy was achieved with the quantitative method. We have highlighted issues relating to the introduction of disruptive technology into the delivery suite and some of the potential concerns relating to this. These issues can be resolved with increased training in the simulation setting. The study has highlighted that these devices are not likely to cause harm in an *in vivo* setting, and as a result, future trials investigating the role of these $EtCO_2$ devices are now warranted.

CONTRIBUTORSHIP STATEMENT

Mr. Gavin Anthony Hawkes had primary responsibility for overall content, study design, data collection, data interpretation and manuscript preparation. Dr. Mmoloki Kenosi was involved with data collection and data interpretation. Prof. C. Anthony Ryan was involved with manuscript design and preparation. Prof. Eugene Michael Dempsey was the supervisor for this study. He was involved with overall content, study design, data collection, data interpretation and manuscript preparation.

FUNDING

This study was supported by a Science Foundation Ireland Research Centre Award (INFANT-12/RC/2272).

CONFLICT OF INTERESTS STATEMENT

The authors of this study do not have any conflict of interests to disclose.

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CREC approval letter

COISTE EITICE UM THAIGHDE CLINICIÚIL
Clinical Research Ethics Committee

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Fax: + 353-21-490 1919

Lancaster Hall,
6 Little Hanover Street,
Cork,
Ireland.

Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

Our ref: ECM 4 (f) 06/08/13

10th July 2013

Dr Gene Dempsey
Consultant Neonatologist
Department of Paediatrics and Child Health
Cork University Hospital
Wilton
Cork

Re: During *in-vitro* usage of two different CO2 detectors and one capnography device, which is the most efficient and which is the most preferred?

Dear Dr Dempsey

Expedited approval is granted to carry out the above study at:

- Cork University Maternity Hospital.

The following documents have been approved:

- Signed Application Form
- Information leaflet/Consent Form Version 1 dated 2nd July 2013
- Study Protocol Version 1 dated 2nd July 2013
- CV for Chief Investigator.

We note that the co-investigator involved in this study will be:

- Gavin Hawkes.

29.7.13

Yours sincerely

Professor Michael G Molloy
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

The Clinical Research Ethics Committee of the Cork Teaching Hospitals, UCC, is a recognised Ethics Committee under Regulation 7 of the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004, and is authorised by the Department of Health and Children to carry out the ethical review of clinical trials of investigational medicinal products. The Committee is fully compliant with the Regulations as they relate to Ethics Committees and the conditions and principles of Good Clinical Practice.

Participant information leaflet and consent form

Version 1 4th Jan 2013

Ospideal Maithreachais na h'Ollscoile Corcaigh
Cork University Maternity Hospital

UCC
Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

Research Study:

A study in to the level of skills retention by pediatric trainees after a six month period.

Hawkes GA, O'Connell B, Hawkes CP, Ryan CA, Dempsey EM

Information

Aim of the Study

This research follows on from previous research, in which you may have participated in, entitled "During *in-vitro* usage of the Pedi-Cap® (Nellcor) CO2 detector and the Neo-StatCO2<Kg® (Mercury Medical), which is the most efficient and which is the most preferred?". This study will only focus on manual ventilation provided without a CO_2 detecting device.

What does this study involve?

During this *in-vitro* study, physicians' hands will be video recorded performing facemask ventilation to a mannequin model. You will be asked to perform manual ventilation in a mannequin model for a period of three minutes with three different forms of manual ventilation technique utilizing $EtCO_2$ detection.

Eligibility:

All NCHDs and consultants are eligible for this *in-vitro* study.

Consent:

By agreeing to this research you agree to your hands being video recorded during the *in-vitro* study.

Ospideal Maithreachais na h'Ollscoile Corcaigh
Cork University Maternity Hospital

UCC
Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

Research Study:

A study in to the level of skills retention by pediatric trainees after a six month period.
Hawkes GA, O'Connell B, Hawkes CP, Ryan CA, Dempsey EM

Consent form

- I have read the information leaflet about this research, the information has been fully explained to me and I have been able to ask questions if I wished. I understand why the research is being completed. ☐
- I agree to allow myself to be video recorded during the *in-vitro* study ☐
- I give permission for the recording and information collected during the recording to be stored for possible future research unrelated to this study without my further consent being required and subject to approval by a research ethics committee. ☐

Name (Print): _____

Position held: _____

Signature: _____

Date: _____

Appendix D

CREC approval letter

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Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

COISTE EITICE UM THAIGHDE CLINICIÚIL
Clinical Research Ethics Committee

Lancaster Hall,
6 Little Hanover Street,
Cork,
Ireland.

Our ref: ECM 4 (e) 05/02/13

10th January 2013

Dr Eugene Dempsey
Consultant Neonatologist
Cork University Maternity Hospital
Wilton
Cork

Re: Enhanced monitoring in the delivery suite – a feasibility study.

Dear Dr Dempsey

Expedited approval is granted to carry out the above study in:

- Cork University Maternity Hospital.

The following documents have been approved.

- Signed Application Form
- Study Protocol Version 1 dated 9th January 2013
- Parent Information Leaflet Version 1 dated 9th January 2013
- Consent Form Version 1 dated 9th January 2013.

The co-investigators involved in this study will be:

- Gavin Hawkes, Niamh Lagan, Daragh Finn, Tony Ryan, Brendan Murphy, Liam O'Connell and Peter Filan.

Yours sincerely

Dr Michael Hyland
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

Research Study:

Enhanced monitoring in the delivery suite - a feasibility study.

Your baby is invited to participate in a study that is explained below.
Thank you for taking the time to read this Information Statement.

What is the study about?
Approximately 10% of babies born require assistance at their delivery. The majority of these are premature babies. Though many babies around the world are given help at birth each year, the ways in which they are evaluated and treated have not been studied well.

The delivery of premature babies less than 32 weeks are attended by the neonatal team, to assist the baby with their breathing and circulation. We currently follow guidelines according to the Neonatal Resuscitation Programme which advises listening to the heart to assess heart beat and using a monitor to measure oxygen saturations. This study hopes to assess the feasibility of using more sophisticated monitoring in the delivery suite. We hope to monitor the heart rate, respiration rate, oxygen saturations and carbon dioxide levels with each breath. This form of monitoring happens routinely in the neonatal intensive care unit following admission. We wish to begin this monitoring in the delivery room. We hope to video the resuscitation of your baby post delivery in the delivery suite to assess whether it is possible to measure these outcomes.

Why am I and my baby being asked to participate in this study?
You are being asked because your baby has a high likelihood to be born less than 32 weeks and the neonatal team will be present to assist your baby at delivery. This study may help improve the care of babies who need help at birth. It can only be done by carefully studying the effects of the treatments given to babies who get are given help at birth.

Is there likely to be a benefit to my baby or will there be potential benefits to improve future medical care?

Your baby will receive the best possible care that we can give. Your baby's treatment will not be affected if he/she participates in the study The results of this study will be important in helping improve the care of babies in the future. We will continue to adhere to the Neonatal Resuscitation Programme guidelines.

What will my baby's role be in this study?

If your baby participates in the study, the care that he or she is given at birth will be recorded with a video camera. ECG leads which measure heart rate and a carbon dioxide monitor will be placed on your baby in the delivery suite during the initial resuscitation. These leads are normally placed on your baby when they are admitted to the neonatal unit. Your baby will not have extra investigations or treatments compared with babies who do not participate in the study. The recording will be examined by the investigators to assess the feasibility of this enhanced monitoring.

What are the possible risks, discomforts, side effects or inconveniences?

There will be no risks for your baby in this study above those for any baby who needs help with their breathing or circulation at birth. Babies who participate in this study will not experience discomfort, side effects or inconvenience other than that encountered in the normal course of their treatment.

Who are the Researchers?
Dr Eugene Dempsey, Dr Daragh Finn, Dr Niamh Lagan and Mr G Hawkes

What measures will be taken to ensure confidentiality?

Individual babies are not identifiable from the video recordings. Other people in the delivery room (mothers, partners, midwives, doctors) are not visible in the recordings. The recordings will not have a date or time stamp. The recordings will be stored on a password–protected computer which will be locked securely in a private office. The recordings will be stored without names or other identifiers. No copies of the recording will be made for other staff or family members, as we cannot guarantee the confidentiality of copies which are not in our possession. Unless the recording is of particular educational value and we have your permission to keep it for that purpose, the recordings will be erased after 3 years.

If you require non-English versions of the Information Statement and Permission Form, please ask for it to be provided in your language.

You are free to decide whether or not to give permission for your child to take part in this study, or to withdraw him/her at any time without explanation.

More Information?

You may wish to discuss participation in this research project with your family and with your doctor. Please feel free to ask for further information before deciding if your baby will take part. If more information is required please contact one of the neonatal consultants at 021 4920525.

Ospideal Maithreachais
na h'Ollscoile Corcaigh
Cork University
Maternity Hospital

ucc
Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

Research Study:

Enhanced monitoring in the delivery suite - a feasibility study.

Consent form

- I have read the information leaflet about this research, the information has been fully explained to me and I have been able to ask questions if I wished. I understand why the research is being completed. ☐

- I understand that the recording of my baby has had no effect on the outcome of the resuscitation procedure performed. ☐

- Although these anonymous recordings will be placed on a secure server with strict accessibility restrictions, as with all video recordings, there is always the potential of a breach in clinical confidentiality. I am aware of this potential hazard. ☐

- I agree to allow my baby's video recording to be used in this research study. ☐

Mother's Name (Print): _____

Mother's Signature: _____

Father's Name (Print): _____

Father's Signature: _____

Date: _____

Appendix E

CREC approval letter

UCC

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Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

COISTE EITICE UM THAIGHDE CLINICIÚIL
Clinical Research Ethics Committee

Lancaster Hall,
6 Little Hanover Street,
Cork,
Ireland.

Our ref: ECM 3 (o) 06/08/13

10th July 2013

Dr Eugene Dempsey
Consultant Neonatologist
Cork University Maternity Hospital
Wilton
Cork

Re: Enhanced monitoring in the delivery suite.

Dear Dr Dempsey

The Chairman approved the following:

- Amendment Application Form
- Change in Study Title
- Change in Study Population from 10-50
- Revised Consent Form.

Yours sincerely

29.7.13
for

Professor Michael G Molloy
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

The Clinical Research Ethics Committee of the Cork Teaching Hospitals, UCC, is a recognised Ethics Committee under Regulation 7 of the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004, and is authorised by the Department of Health and Children to carry out the ethical review of clinical trials of investigational medicinal products. The Committee is fully compliant with the Regulations as they relate to Ethics Committees and the conditions and principles of Good Clinical Practice.

Ospideal Maithreachais na h'Ollscoile Corcaigh
Cork University Maternity Hospital

ucc
Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

The MODS trial

Enhanced Monitoring in the Delivery Suite

What is this trial about?
Approximately 10% of babies born require assistance at their delivery. The majority of these are premature babies. Though many babies around the world are given help at birth each year, the ways in which they are evaluated and treated have not been studied well.

The delivery of premature babies less than 32 weeks are attended by the neonatal team, to assist the baby with their breathing and circulation. We currently follow guidelines according to the Neonatal Resuscitation Programme which advises listening to the heart to assess heart beat and using a monitor to measure oxygen saturations. This study hopes to assess the feasibility of using more sophisticated monitoring in the delivery suite. We hope to monitor the heart rate, respiration rate, oxygen saturations and carbon dioxide levels with each breath. This form of monitoring happens routinely in the neonatal intensive care unit following admission. We wish to begin this monitoring in the delivery room. We hope to video the resuscitation of your baby post delivery in the delivery suite to assess whether it is possible to measure these outcomes.

Why is my baby being chosen to participate in this study?
You are being asked because your baby has a high likelihood to be born less than 32 weeks and the neonatal team will be present to assist your baby at delivery. This study may help improve the care of babies who need help at birth. It can only be done by carefully studying the effects of the treatments given to babies who get are given help at birth.

Is there likely to be a benefit to my baby?
Your baby will receive the best possible care that we can give. Your baby's treatment will not be affected if he/she participates in the study The results of this study will be important in helping improve the care of babies in the

future. We will continue to adhere to the Neonatal Resuscitation Programme guidelines.

What will my baby's role be in this study?
If your baby participates in the study, the care that he or she is given at birth will be recorded with a video camera. ECG leads which measure heart rate and a carbon dioxide monitor will be placed on your baby in the delivery suite during the initial resuscitation. These leads are normally placed on your baby when they are admitted to the neonatal unit. Your baby will not have extra investigations or treatments compared with babies who do not participate in the study. The recording will be examined by the investigators to assess the feasibility of this enhanced monitoring.

What are the possible risks, discomforts, side effects or inconveniences?
There will be no risks for your baby in this study above those for any baby who needs help with their breathing or circulation at birth. Babies who participate in this study will not experience discomfort, side effects or inconvenience other than that encountered in the normal course of their treatment.

What measures will be taken to ensure confidentiality?
Individual babies are not identifiable from the video recordings. Other people in the delivery room (mothers, partners, midwives, doctors) are not visible in the recordings. The recordings will not have a date or time stamp. The recordings will be stored on a password–protected computer which will be locked securely in a private office. The recordings will be stored without names or other identifiers. No copies of the recording will be made for other staff or family members, as we cannot guarantee the confidentiality of copies which are not in our possession. Unless the recording is of particular educational value and we have your permission to keep it for that purpose, the recordings will be erased after 3 years.

If you require non-English versions of the Information Statement and Permission Form, please ask for it to be provided in your language.

You are free to decide whether or not to give permission for your child to take part in this study, or to withdraw him/her at any time without explanation.

More Information?

You may wish to discuss participation in this research project with your family and with your doctor. Please feel free to ask for further information before deciding if your baby will take part. If more information is required please contact one of the neonatal consultants at 021 4920525.

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The MODS trial

Enhanced Monitoring in the Delivery Suite

Consent form

- I have read the information leaflet about this research, the information has been fully explained to me and I have been able to ask questions if I wished. I understand why the research is being completed. ☐
- I understand that the recording of my baby has had no effect on the outcome of the resuscitation procedure performed. ☐
- Although these anonymous recordings will be placed on a secure server with strict accessibility restrictions, as with all video recordings, there is always the potential of a breach in clinical confidentiality. I am aware of this potential hazard. ☐
- I agree to allow my baby's video recording to be used in this study. ☐
- I agree to allow my baby's recording to be used for future educational and research purposes ☐

Mother's Name (Print): _____

Mother's Signature: _____

Father's Name (Print): _____

Father's Signature: _____

Date: _____

Appendix F

CREC approval letter

UCC
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University College Cork, Ireland

COISTE EITICE UM THAIGHDE CLINICIÚIL
Clinical Research Ethics Committee
Lancaster Hall,
6 Little Hanover Street,
Cork,
Ireland.

Our ref: ECM 4 (ss) 03/06/14

18th May 2014

Professor Gene Dempsey
Consultant Neonatologist
Cork University Maternity Hospital
Wilton
Cork

Re: Capnography in the delivery suite: a randomised controlled trial of exhaled carbon dioxide monitoring in the preterm infant: the CAPNO Trial.

Dear Professor Demspey

Expedited approval is granted to carry out the above study at:

- Cork University Maternity Hospital
- Limerick University Maternity Hospital.

The following documents have been approved:

- Application Form
- Study Proposal Version 1 dated 12th May 2014
- Parent Information Leaflet Version 1 dated 12th May 2014
- Consent Form Version 1 dated 12th May 2014.

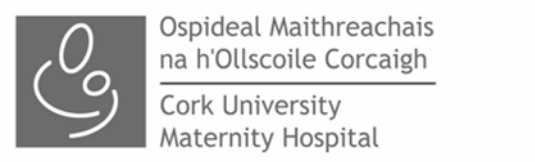
The co-investigators involved in this study will be:

- Mr Gavin Hawkes, Dr John Kelleher, Dr Mmaloki Kenosi and Professor Anthony Ryan.

Yours sincerely

Professor Michael G Molloy
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

The Clinical Research Ethics Committee of the Cork Teaching Hospitals, UCC, is a recognised Ethics Committee under Regulation 7 of the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004, and is authorised by the Department of Health and Children to carry out the ethical review of clinical trials of investigational medicinal products. The Committee is fully compliant with the Regulations as they relate to Ethics Committees and the conditions and principles of Good Clinical Practice.



The CAPNO trial

Capnography in the Delivery Suite: A randomized controlled trial of exhaled carbon dioxide monitoring in the preterm infant

What is this trial about?

Approximately 10% of babies born require assistance at their delivery. The majority of these are premature babies. Though many babies around the world are given help at birth each year, the ways in which they are evaluated and treated have not been studied well.

The neonatal team, to assist the baby with their breathing and circulation, attends all deliveries of premature babies less than 32 weeks. We currently follow guidelines according to the Neonatal Resuscitation Programme which advises listening to the heart to assess heart beat and using a monitor to measure oxygen saturations. This study hopes to assess the outcomes of using more sophisticated monitoring in the delivery suite in the form of electrocardiography (ECG), respiratory monitoring and carbon dioxide monitoring.

Two forms of carbon dioxide monitoring currently exist, a colourimetric device that changes colour upon detection of carbon dioxide and a capnography machine that measures the exact levels of carbon dioxide exhaled by the baby. All the monitoring that we will do will be non invasive and is carried out routinely in the neonatal intensive care unit following admission. We wish to begin this monitoring in the delivery room with the

primary aim of determining the effectiveness of each form of carbon dioxide monitoring. All babies will receive ECG and respiratory monitoring and the type of carbon dioxide monitoring that each baby will receive will be randomly assigned prior to delivery.

We hope to video the resuscitation of your baby post delivery in the delivery suite to assess whether it is possible to measure these outcomes.

Why is my baby being chosen to participate in this study?

You are being asked because your baby has a high likelihood to be born less than 32 weeks and the neonatal team will be present to assist your baby at delivery. This study may help improve the care of babies who need help at birth. It can only be done by carefully studying the effects of the treatments given to babies who are given help at birth.

Is there likely to be a benefit to my baby?

Your baby will receive the best possible care that we can give. Your baby's treatment will not be affected if he/she participates in the study The results of this study will be important in helping improve the care of babies in the future.

What will my baby's role be in this study?

If your baby participates in the study, the care that he or she is given at birth will be recorded with a video camera. ECG leads which measure heart rate and a carbon dioxide monitor will be placed on your baby in the delivery suite during the initial resuscitation. These leads are normally placed on your baby when they are admitted to the neonatal unit. Your baby will not have extra investigations or treatments compared with babies who do not participate in the study.

What treatment will my baby receive?

When an infant is given assistance with ventilation in the NICU, exhaled carbon dioxide is constantly monitored. Two ways that exist to do this is by a device that changes colour when in contact with carbon dioxide or a device that displays a reading of the level of carbon dioxide that is being produced. We are hoping to investigate which of these devices may be more effective for infants in the delivery suite. To properly assess this we need to randomize which device each infant uses during the short time spent in the delivery suite. This means that before the delivery we will randomize your baby as to which device he/she receives. This is the most effective way of assessing these devices.

What are the possible risks, discomforts, side effects or inconveniences?

There will be no risks for your baby in this study above those for any baby who needs help with their breathing or circulation at birth. Babies who participate in this study will not experience discomfort, side effects or inconvenience other than that encountered in the normal course of their treatment.

What measures will be taken to ensure confidentiality?

Individual babies are not identifiable from the video recordings. The recordings will not have a date or time stamp. The recordings will be stored on a password–protected computer that will be locked securely in a private office. The recordings will be stored without names or other identifiers. No copies of the recording will be made for other staff or family members, as we cannot guarantee the confidentiality of copies which are not in our possession. Unless the recording is of particular educational value and we have your permission to keep it for that purpose, the recordings will be erased after 3 years.

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You are free to decide whether or not to give permission for your child to take part in this study, or to withdraw him/her at any time without explanation.

More Information?

You may wish to discuss participation in this research project with your family and with your doctor. Please feel free to ask for further information before deciding if your baby will take part. If more information is required please contact one of the neonatal consultants at 021 4920525.

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The CAPNO trial

Capnography in the Delivery Suite: A randomized controlled trial of exhaled carbon dioxide monitoring in the preterm infant

Consent form

- I agree to take part in this randomized controlled trial ☐
- I have read the information leaflet about this research, the information has been fully explained to me and I have been able to ask questions if I wished. I understand why the research is being completed. ☐
- I understand that the recording of my baby has had no effect on the outcome of the resuscitation procedure performed. ☐
- I agree to allow my baby's video recording to be used in this study. ☐
- I agree to allow my baby's recording to be used for future educational and research purposes ☐

Mother's Name (Print): _____

Mother's Signature: _____

Father's Name (Print): _____

Father's Signature: _____

Researcher Present: _____

Date: _____

Appendix G

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Perfusion index in the preterm infant immediately after birth☆,☆☆,★,★★

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ABSTRACT

Aim: To evaluate PI in preterm infants during the first 10 min of life.
Design/methods: An observational study was conducted in the delivery room on preterm infants (less than 32 week gestation). PI values were obtained from a pre ductal saturation probe placed on the right wrist. Analysis was performed on the first 10 min of data to investigate the correlation of PI with gestational age, heart rate, blood pressure, and lactate values.
Results: 33 infants with a median gestational age of 29 wks (IQR, 26–30 wks) and median birth weight of 1205 g (IQR, 925–1520 g) were included for analysis. The overall median PI value for the first 10 min was 1.3 (IQR, 0.86–1.68). There was no significant correlation found between delivery room PI and gestational age($r = 0.28$, 95% CI: −0.09, 0.59), lactate levels ($r = -0.25$, 95% CI: −0.62, 0.18) and blood pressure values ($r = -0.18$, 95% CI: −0.46, 0.20). An average correlation value of $r = -0.417$ (95% CI: − 0.531, −0.253) was found between PI and heart rate values. There was no statistical difference between the median of the median PI value over the first 5 min of life compared to the second 5 min ($p = 0.22$). Variability, as quantified by the IQR, was higher in the first 5 min compared to the second 5 min: median of 0.5(IQR, 0.27, 0.92) vs 0.2(IQR, 0.10, 0.30) ($p < 0.00$).
Conclusions: Delivery room PI values are easily obtained, however, have significant variability over the first 5 min of life and may add little to delivery room assessment.

1. Introduction

Adequate oxygenation and continuous monitoring of overall tissue perfusion are important factors in the care of an infant immediately after birth. The Neonatal Resuscitation Programme (NRP) [1] and Neonatal Life Support (NLS) [2] currently recommends assessing heart rate and targeting specific oxygen saturation (SpO_2) levels within the first few minutes of life. Current methods of non invasive monitoring of peripheral perfusion are predominantly subjective and include observing skin colour, capillary refill time and temperature of the periphery [1, 2].

Perfusion index (PI) is a non-invasive method of assessing real-time peripheral perfusion. Although determined at the same time as SpO_2, PI is calculated independently of the patients SpO_2 level. PI is derived from the photoelectric plethysmographic signal of transcutaneous oximetry. Pulse oximetry uses two light sources with different wavelengths (red light at 660 nm and near infrared light at 940 nm). Oxygenated hemoglobin (HbO_2) absorbs more light at 940 nm and deoxygenated hemoglobin (Hb) absorbs more light at 660 nm [3]. SpO_2 is then calculated by obtaining the ratio between the amount of red light and infrared light absorbed. By using a third wavelength (800 nm), the overall hemoglobin concentration can be determined, allowing the pulsatile component of arterial blood to be distinguished from the non pulsatile component. The PI is then calculated as the ratio between the pulsatile component and the non pulsatile component [4].

Several studies investigating PI in the adult population have highlighted the potential for PI monitoring to be used to monitor the circulatory condition of patients admitted to the emergency department, and as an appropriate method of assessment to monitor the effect that therapeutic interventions have on peripheral perfusion [4, 5]. Studies in the neonatal population have highlighted the potential for PI to be used as an assessment tool in various aspects of an infant's health [6]. In particular, studies have associated PI in the newborn period with subclinical chorioamnionitis [7], as a possible screening tool for the presence of congenital heart malformations [8, 9], as a predictor of low superior vena cava flow [10], and as a sign of improved tissue

Abbreviations: NRP, Neonatal Resuscitation Programme; NLS, Neonatal Life Support; SpO_2, Oxygen saturation; PI, Perfusion index; HbO_2, Oxygenated hemoglobin; Hb, Deoxygenated hemoglobin; IQR, Interquartile range.

☆ Funding source: This study was supported by a Science Foundation Ireland Research Centre Award (INFANT-12/RC/2272).
☆☆ Dr. John M O'Toole received financial support from the Irish Research Council (Government of Ireland Postdoctoral Fellowship Scheme GOIPD/2014/396).
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★★ Financial disclosure: The authors have no financial relationships related to this article to disclose.

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0378-3782/

oxygenation following blood transfusion in preterm infants [11]. It has also been shown that PI is highly reproducible in preterm infants [12], that this value increases over the first 3 days of life [10, 13], and that PI may stabilise within 5 days of life [14]. Normative PI values have been described for preterm infants in the first day of life [14, 15]. However, to our knowledge, PI values immediately after birth have not previously been determined. The aim of our study was to evaluate the PI in preterm infants in the delivery room and determine if this continuous measurement has any relationship with other markers of cardiovascular assessment.

2. Methods

This was a single centre prospective observational study conducted in the delivery room of Cork University Maternity Hospital, Ireland, and was a sub study of infants involved in a study assessing enhanced methods of monitoring in the delivery room. Any infant expected to be delivered at less than 32 weeks' gestation was eligible for inclusion in this study. Exclusion criteria included oligohydramnios (amniotic fluid index <5) and any expected congenital anomalies of the infant such as congenital diaphragmatic hernia, congenital airway anomalies, or congenital heart disease. The study was approved by the Cork Research Ethics Committee. Informed written consent was obtained from parents antenatally. The medical staff was informed of the infant's participation in the study and all monitoring equipment was prepared, prior to delivery.

A SpO_2 monitoring probe (Nellcor OxiMax, Covidien, Mass, USA) connected to a Philips IntelliVue MD70 (Philips Healthcare, Andover, USA) was placed on the right forearm of each infant to monitor SpO_2 levels during the initial adaptation phase in the delivery rom. This monitor obtained the PI as well as the heart rate of each infant with an averaging rate of 5 s. A member of the research team downloaded this information after the infant left the delivery room. All physiological data downloaded from the delivery room was exported as 12-second intervals. Authors GAH and EMD subsequently correlated this information with a video recording of the infant, that was also obtained during the time spent in the delivery room. This allowed for clarification, and subsequent elimination, of potentially incorrect PI readings due to inappropriate placement of the SpO_2 probe or at times poor signal quality from the probe.

Lactate values were obtained from the first blood gas analysis that was performed within an hour after birth. Similarly, non-invasive blood pressure values were obtained after admission to the NICU, within an hour from birth. Instances of intraventricular haemorrhage (IVH) were determined by means of cerebral ultrasound, within 7 days after birth.

The following analysis was performed on the PI values for 10 min after birth. The median and IQR of each infant was assessed and compared between the first and last 5 min. Using the Mann–Whitney *U*-test, median values over the 0–5 minute period were compared to median values over the 5–10 minute period, and similarly for the IQR values. Statistical significance was determined by $p < 0.05$.

Median values of PI over the 10 min were correlated with gestational age, lactate levels, and blood pressure. Pearson's correlation coefficient was used and significant correlation ($p < 0.05$) was determined if the 95% CIs excluded 0. CIs were computed using the bootstrap approach with 1000 iterations. For each infant, PI values were correlated with heart rate over the 10-minute period. The Fisher-z transform was used in calculating the average correlation coefficient over all infants [16]. This average correlation was deemed statistically significance if the 95% CI excluded 0. Again, the bootstrap procedure, with 1000 iterations, was used to compute the CI. Unless stated otherwise, median values and IQR are reported as "median (IQR)".

3. Results

33 infants with a median gestational age of 29 weeks (26, 30 weeks) and a median birth weight of 1205 g (925, 1520 g) were included for analysis. The overall median PI value for the first 10 min was 1.3 (0.86–1.68)(Fig. 1). There was no significant correlation found between delivery room PI and gestational age of the infant ($r = 0.28$ CI: −0.087, 0.585), lactate levels within an hour of birth ($r = -0.251$ CI: −0.618, 0.177), or blood pressure readings within an hour of birth ($r = -0.175$ CI: −0.456, 0.200) (Table 1). An average correlation value of $r = -0.417$ (95% CI: −0.531, 0.253) was found between simultaneous heart rate and PI values.

The median PI value over the first 5 min of life was slightly, although not significantly, greater compared to the median PI values in the second 5 min (1.5 [0.97, 1.96] vs 1.2[0.80, 1.50], $p = 0.22$). The IQR PI values were significantly greater for the first 5 min compared to the second 5 min (0.5[0.27, 0.92] vs 0.2[0.10, 0.30], $p < 0.00$). There was no relationship between delivery room median PI values and instances of IVH within one week of birth ($p = 0.822$).

4. Discussion

This study has investigated the PI of preterm infants immediately after birth. We have found that these PI values, which have not previously been described, have significant variability over the first 5 min of life. One explanation for this variability may be related to the location and method of application of the monitoring probe. However, we have previously assessed reliability and reproducibility of probe placement and found this to be high [12]. Therefore we believe that the observed PI variability reflect normal circulatory adaptation to extrauterine existence and reflect the complex neonatal haemodynamic changes that are taking place over the first few minutes of life. These changes in PI may be similar to circulatory changes described by Van Vonderson et al. [17] In a study on the use of echocardiography immediately after birth in 24 infants, fluctuations in ductal flow were suggested to reflect changes from right-to-left shunting to left-to-right shunting; ultimately reflecting overall changes in pulmonary and vascular resistance [17].

Two previous studies have reported on PI values in the first few days of life. Hakan et al. reported a median PI value of 0.88(0.6, 1.26) in a cohort of 45 preterm infants [14] and Vidal et al found a median PI of 0.70 (0.50, 1.05) in a similar number of preterm infants [15]. We describe slightly higher values in preterm infants immediately after birth, 1.3 (0.86, 1.68). Again, we postulate that these higher values may reflect the dynamic changes that are occurring over this time period.

Although the PI values most likely reflect circulatory adaptation, they do not correlate with the other markers of cardiovascular status investigated in this study, including blood pressure on admission to the NICU, and simultaneous heart rate and PI values. We did not find any correlation between simultaneous heart rate and PI values. This may be as a result of the complex nature of cardiovascular transition that an infant is required to make immediately after birth. The lack of correlation between blood pressure and PI values may be as a result of the time period between acquisitions of both parameters, but also

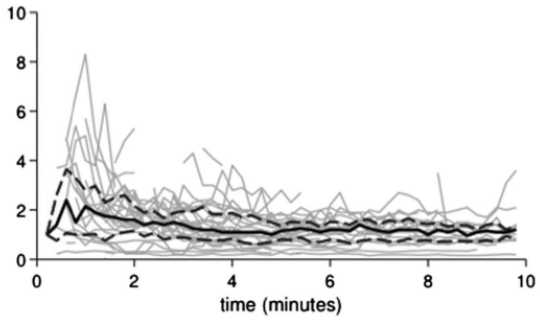

Fig 1. PI values across all 33 infants over the first 10 mins of life, Black line: Median; Blue lines: interquartile range.

Table 1
Correlation coefficient *r* of median perfusion index with gestational age, lactate, and mean blood pressure. No significant correlations found.

	r-value	95% CI
Gestational age	0.288	(−0.087, 0.585)
Lactate	−0.251	(−0.618, 0.177)
Blood pressure	−0.175	(−0.456, 0.200)

may reflect the fact that a single blood pressure measurement may not reflect cardiovascular well being. Similarly, there was a lag period of approximately an hour between acquisitions of lactate values. As this was an observational study, blood pressure and blood gas analysis was acquired as part of routine clinical care, usually within one hour after birth. Therefore, any clinical interventions performed during that time may have impacted on the correlation analysis between the PI values, and also the time lag itself may account for the lack of any correlation. We have previously reported on the lack of correlation between PI values and cardiovascular markers during the first 3 days of life [12].

Circulatory assessment at birth, or indeed at anytime in the first few days of life is often very subjective. During the monitoring of peripheral perfusion of an infant assessment of skin colour has been suggested to be a potential indicator of the severity of illness [18]. However, this has been shown to vary amongst care givers as a result of the subjective nature of the assessment [19]. We chose to evaluate a readily available, potentially more objective, bedside measurement. We have found that it is easy to apply the probe and to obtain the PI of a preterm infant during stabilisation in the delivery room. Oxygen saturation monitoring is now a standard of care and as a result of the application of an oxygen saturation probe PI values are now often available. In our study, the medical staff was not instructed to interact with the PI value. Although its acquisition does not deviate from the routine care during resuscitation other than a visual display of a value on a bedside monitor, any interpretation and interaction with PI values cannot be advocated at present.

There are a number of limitations to this study. Various users applied the saturation probe. The gestational age of the infants was wide. As discussed, blood pressure values were not obtained simultaneously, and we did not have maternal cord blood gas values available to assess lactate values at the time of birth. The number of babies enrolled is also relatively small. Despite these limitations we have shown that monitoring of PI in preterm infants in the delivery room is feasible, values are readily available to the resuscitation team and whilst they do not correlate with other markers of cardiovascular wellbeing their role as an early biomarker of circulatory status has yet to be fully elucidated. Monitoring of PI in the delivery room may yet have a role to play in the overall assessment of a preterm infant immediately after birth and we believe that further delivery room trials of PI are worthwhile, in particular, trials correlating PI with other objective assessments of cardiovascular function immediately after birth.

Conflicts of interest statement

The authors of this study do not have any conflicts of interest to disclose.

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Appendix H

CREC approval letter

UCC

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Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

COISTE EITICE UM THAIGHDE CLINICIÚIL
Clinical Research Ethics Committee

Lancaster Hall,
6 Little Hanover Street,
Cork,
Ireland.

Our ref: ECM 4 (kk) 07/10/14

26th September 2014

Professor Eugene Dempsey
Consultant Neonatologist
Department of Paediatrics and Child Health
Cork University Maternity Hospital
Wilton
Cork

Re: Methods of accuracy of different modalities used in determining heart rate in a mannequin model.

Dear Professor Dempsey

Expedited approval will be granted to carry out the above study at:

- Cork University Maternity Hospital

subject to receipt of the following:

- Original Signed (wet ink) Application Form

The following documents have been approved:

- Study Protocol Version 1 dated 18th September 2014
- CV for Chief Investigator
- Information Leaflet/Consent Form Version 1 dated 18th September 2014.

The co-investigators involved in this study will be:

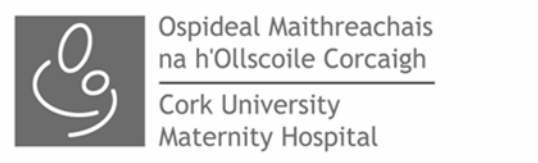
- Mr Gavin Hawkes, Dr Colin Hawkes, Dr Mmoloki Kenosi and Professor Anthony Ryan.

Yours sincerely

Professor Michael G Molloy
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

The Clinical Research Ethics Committee of the Cork Teaching Hospitals, UCC, is a recognised Ethics Committee under Regulation 7 of the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004, and is authorised by the Department of Health and Children to carry out the ethical review of clinical trials of investigational medicinal products. The Committee is fully compliant with the Regulations as they relate to Ethics Committees and the conditions and principles of Good Clinical Practice.

Participant information and consent form for the assessment of current methods of heart rate detection in the delivery room



Methods and accuracy of different modalities used in determining heart rate in a mannequin model

Hawkes GA, Hawkes CP, Kenosi M, Ryan CA, Dempsey EM

What is this trial about?

This trial aims to investigate the different methods of obtaining a heart rate of an infant through methods currently suggested by the Neonatal Resuscitation Program (NRP).

What will my role be in this study?

This in vitro study will have three different parts. You will be asked to palpate 3 different simulated umbilical pulses of a mannequin, listen to 3 audio recording of a heart rate, and listen to an investigator tapping out 3 different heart rates. You will be asked to describe each of these heart rates.

Name of Participant: _____

Signature: _____

Date: _____

Position Held: _____

Last NRP Completed: _____

Appendix I

A Fitting the Mixed-Effects Model

The full quadratic model, with fixed effects $\{\beta_0, \beta_1, \beta_2\}$ and random effects $\{b_1, b_2, b_3\}$, is defined for time t as

$$\hat{y} = \beta_0 + \beta_1 t + \beta_2 t^2 + b_1 + b_2 t + b_3 t^2.$$

The procedure for model selection was as follows:

- Comparing the basic linear model ($\beta_0 + \beta_1 t + b_1$) to a quadratic model ($\beta_0 + \beta_1 t + \beta_2 t^2 + b_1$), we find no significant improvement ($p = 0.934$, Table 2) and thus do not include the time-squared factor.
- Next, we compare the linear model with only a random intercept ($\beta_0 + \beta_1 t + b_1$) to the model with both random intercept and random slope ($\beta_0 + \beta_1 t + b_1 + b_2 t$) and find a significant improvement ($p < 0.001$, Table 3) and thus incorporate the random slope into the model.

Thus the final model is a linear–time model with both random intercept and random slope; we do not test with random time-squared factor there was no improvement for the fixed-effect time-squared.

Tab. 2: Comparing linear and quadratic models. Abbreviations: AIC: Alaike information criteria; BIC: Bayes information criteria.

model	AIC	BIC	log-likelihood	p-value
$\beta_0 + \beta_1 t + b_1$	12178.1	12199.0	-6085.0	
$\beta_0 + \beta_1 t + \beta_2 t^2 + b_1$	12180.1	12206.2	-6085.0	0.9343

Tab. 3: Comparing models with random-intercept and random-intercept and random-slope.

model	AIC	BIC	log-likelihood	p-value
$\beta_0 + \beta_1 t + b_1$	12178.1	12199.0	-6085.0	
$\beta_0 + \beta_1 t + b_1 + b_2 t$	11991.9	12023.2	-5990.0	<0.0001

Appendix J

Perceptions of Webcams in the Neonatal Intensive Care Unit: Here's Looking at you Kid!

Gavin A. Hawkes, BSocSc[1] Vicki Livingstone, PhD[2] C Anthony Ryan, MD, FRCPI[1,2] Eugene Michael Dempsey, MD, FRCPI[1,2]

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Address for correspondence Eugene Michael Dempsey, MD, FRCPI, Department of Neonatology, Cork University Maternity Hospital, Ireland (e-mail: gene.dempsey@hse.ie).

Am J Perinatol

Abstract

Introduction Many tertiary neonatal units employ a restricted visiting policy. Webcams have previously been implemented in the neonatal unit setting in several countries.

Objectives This study aims to determine the views from parents, physicians, and nursing staff before implementation of a webcam system.

Methods A questionnaire-based study.

Results There were 101 responses. Parental computer usage was 83%. The majority of parents indicated that they would use the webcam system. Parents felt that a webcam system would reduce stress. Members of the nursing staff were most concerned about privacy risks (68%), compared with parents who were confident in the security of these systems (92%, p-value < 0.001). Seventy two percent of nurses felt that a webcam system would increase the stress levels of staff as compared with less than 20% of the physicians (p-value < 0.001).

Discussion The majority of parents who completed the questionnaire have positive attitudes toward implementation of a webcam system in the NICU. Education of health care staff is required before implementation.

Keywords
- webcam
- NICU
- neonatology

Approximately 10% of newborns require admission to the neonatal intensive care unit (NICU). For many reasons, but primarily to reduce movement within the NICU and to reduce nosocomial infection risk, many tertiary neonatal units employ a strict visiting policy of parental visitation only. This means that siblings, grandparents, and extended family are generally not allowed, or have limited access, to the NICU.

Admission of a baby to the NICU is a stressful period for the entire family, often with many important decisions having to be made during the inpatient stay.[1–3] The physical environment of the NICU often adds to the stress experienced by the family.[4,5] Premature birth and the infant's unstable condition can impact on the mother–infant attachment.[5] This difficulty in establishing a mother–infant attachment can add another stressor to the overall NICU experience.

Increased maternal levels of anxiety are known to be associated with the degree of separation between the mother and her newborn.[6] Mothers are often unwell in the immediate newborn period and are unable to visit the NICU. This may have significant implications for maternal bonding. While there are several support programs available in many neonatal settings to support families at this stressful time,[7] there may be other potential modalities available to enhance parental bonding and reduce stress levels.

One such modality was highlighted following hurricane Katrina. Through the implementation of a Baby CareLink system in four hospital NICUs that allowed parents to view pictures of their baby in the aftermath of hurricane Katrina, Safran et al noted that the digital pictures provided by the Baby CareLink system were a substantial benefit to parents who were geographically distant from their baby.[8]

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Webcam use has already been shown to be useful in various areas of medicine. Bradford et al have described utilizing internet video to carry out medication checks with patients away from the hospital.[9] Hori et al also noted the benefit of videophone communication between elderly patients with dementia and their caregivers.[10]

Webcams have previously been implemented in the NICU setting in countries such as the Netherlands, Australia, and the United States. The NICVIEW (Louisville, KY) webcam service is one such system available. While they have presented many challenges (technologically, administratively, operationally, and clinically) overall they would seem to have a positive impact. However, there is very limited data available to support webcam use or the concerns of the staff, on webcam use, before the implementation of such a service.

The aim of this questionnaire-based survey was to evaluate the views of potential end users, namely, parents, physicians, and neonatal nursing staff before the possible implementation of a webcam system in the NICU of a large tertiary level NICU.

Methods

An anonymous eight-item questionnaire was developed specifically to address parental views on the use of a webcam monitoring system within the NICU (Appendix A). This used a Likert-scale answering system. This questionnaire also contained a feedback section where the participant was free to write any comments that they may have had. Parents were informed that participation was voluntary and completion of the questionnaire was considered to be consent to participate in the study.

A second questionnaire was created for medical and nursing staff (Appendix B). This questionnaire consisted of six questions, again utilizing a Likert scale as described above and again a free text section that allowed medical staff to provide a written feedback. The questionnaires were answered anonymously, other than identification as to whether a doctor or a nurse had participated. Again completion of the questionnaire was deemed as consent to participate.

Questionnaires were administered over a 1-month period (January 2013). Differences between the two groups (medical and nursing staff) were investigated using the Mann–Whitney U test. Statistical analysis was performed using IBM Statistics 20.0 (Armonk, NY). All tests were two sided and a p-value < 0.05 was considered to be statistically significant. The study was approved by the Cork Research Ethics Committee.

Results

There were 101 responses in total (50 nurses, 25 parents, and 26 physicians). The response rate overall was high (total 82%; nurses 83%, parents 83%, and physicians 79%). Parental computer usage was high overall, with 83% using a computer regularly. While many respondents currently do not use a webcam, 91% indicated that they would use the webcam system in our NICU regularly if it were implemented. A total of 57% of parents also indicated that they were of the opinion that a webcam system would reduce the amount of phone calls they would make to our NICU but 87% felt that it would not reduce the amount of times that they would physically visit the NICU. Overall, 74% of parents expressed a view that a webcam system would reduce the levels of stress that they might experience when they are away from the NICU (►**Table 1**). Parents highlighted issues such as guilt when they are away from the NICU and felt that a webcam system might alleviate some of this guilt.

Feedback from the health care professionals highlighted several issues. The nursing staff had more concerns about the security issues relating to webcam use in the NICU compared with physicians (68 and 19%, respectively). Feedback from members of the nursing staff raised concerns about privacy risks. These differed significantly from physicians' views (p-value < 0.001) (►**Table 2**). However, there was no difference between both groups in relation to familiarity with

Table 1 Percentage frequencies of answers to parental questionnaire

Questions	Parents ($n = 23$)		
	Answers		
	1/2	3	4/5
How often do you use a computer?	4.4	13.0	82.6
How often do you use a webcam?	52.2	17.4	30.4
How often do you think you would use this service if it were to be implemented?	8.7	0.0	91.3
Do you feel confident in the security behind webcam use to view your baby?	4.3	4.3	91.3
Would you share your password with another person, for example, family member or friend?	47.8	8.7	43.5
Do you think you would experience less stress when you were away from the hospital if this service was available?	8.7	17.4	73.9
Do you think it would reduce the number of phone calls you would make to the unit?	34.8	8.7	56.5
Do you think it would reduce the number of times you would visit the NICU?	86.9	4.3	8.7

Abbreviation: NICU, neonatal intensive care unit.
Note: 1 = not at all; 5 = very much so.

Table 2 Percentage frequencies of answers to medical staff questionnaire

	Nurses ($n = 50$)			Doctors ($n = 26$)			p-Value[a]
	Answers			Answers			
Questions	1/2	3	4/5	1/2	3	4/5	
Do you feel confident in the security behind webcam use to view babies in the NICU? ($n = 49$)	68	20	12	19.2	30.8	50	< 0.001
Are you familiar with any webcam use, similar to this, elsewhere?	84	8	8	57.7	15.4	26.9	0.020
Do you think this would reduce the amount of time parents spend in the NICU?	76	22	2	65.4	11.5	23.1	< 0.001
Do you think this will reduce the amount of calls made to the NICU by parents?	92	4	4	46.2	11.5	42.3	< 0.001
Although the webcam will not be assessing performance of staff, do you think that the presence of a webcam will add to stress levels experienced by staff?	6	12	82	26.9	15.4	57.7	< 0.001
Are you in favor of a system such as this being implemented?	76	12	12	60.6	13.2	26.2	< 0.001

Abbreviation: NICU, neonatal intensive care unit.
Note: 1 = not at all; 5 = very much so.
[a]p-Value is gathered from a Kruskal-Wallis test. Responses were kept in five categories for this test.

similar webcam systems being implemented in hospitals elsewhere. These findings were in contrast to the parents views on security, whereby 92% had confidence in the security behind such a system.

Nurses had fewer concerns about parental visitation to the NICU but felt the frequency of calls would be increased following the introduction of a webcam system. Total 76% of nurses felt that the webcam system would have no impact on the amount of times parents would visit the NICU but 82% felt that it may increase the amount of phone calls made to the NICU by parents. There was a statistically significant difference between the stress levels that nurses and doctors felt that they would experience with a webcam system in place (p-value < 0.001). Approximately 72% of nurses felt strongly that a webcam system would increase the stress levels of staff compared with less than 20% of physicians.

The response to the question regarding implementation of a webcam system in our NICU differed in that 76% of the nursing staff and 61% of physicians were not in favor which is in contrast to the parents, who seemed overall to be positive about the idea.

Overall, there was a negative sentiment expressed from nursing staff in the free text section of the questionnaire. Many of the negative comments on the feedback section highlighted issues such as funding for the implementation, and subsequent maintenance, of a webcam system. This expense was felt to be inappropriate at a time when the health service, as a whole, is facing financial constraints and the staff is facing salary reductions. Many nurses also felt uncomfortable about the possibility of coming into view of the webcam as they leaned over the cot of the baby.

Physicians' main concern was the increase in stress levels with the presence of a webcam system in place. Many of the free text comments referred to the issue of performing procedures while being in view of the webcam and severe increase in stress levels that they feel it would cause.

Discussion

This study has shown that the majority of parents who completed the questionnaire had a positive attitude toward the implementation of a webcam system in our NICU and, as a result, was in favor of such a system being introduced. The positive feedback received from parents would suggest that the implementation of a webcam system is warranted.

While parents are encouraged to spend as much time as possible with their baby in the neonatal unit, the introduction of webcams to the neonatal unit may provide a link for parents during the times that it is not possible for them to be with their infant in the unit. Often parents may be geographically distant from the NICU and/or may have several other important commitments such as other members of the family to care for. Although, the parents may want to be in the NICU as often as they can, they may not physically be able to do so. This continuity of access to their child through viewing a video link may promote bonding, and allow other family members, who are not allowed into the neonatal unit, to see the infant.

These findings were interesting considering the significant advancement of smartphone technology, which permits parents to obtain high quality video and images of their newborn. The sentiment that it would reduce stress levels for the parents is encouraging, but this can only be answered prospectively with objective assessments of parental stress levels when webcams are in use.

There was a negative attitude toward a webcam system from health care providers. This is more noticeable among nurses, but is also the case with physicians. There may be many reasons for this negative feedback. There may be a lack of understanding as many respondents are not users of such systems. The majority of the nursing staff is not familiar with how such a system would function in their work environment. Staff members highlighted areas such as privacy risks

and potential personal stress that they may feel from having a webcam system present in the NICU. It is noteworthy that parents were confident in the security behind such a system, and that no issues were documented in the free text section of the responses in relation to privacy matters. However, as most of the health care concerns related to times when procedures were being performed, better awareness through education would highlight the fact that the webcams would be switched off during these times. During the time that the webcam was switched off it would be arranged for a message, selected by the medical staff, to appear explaining the reason for the pause in transmission of the video feed. This awareness could change medical staff's attitudes.

With a live stream being sent away from the hospital, there is the obvious concern about privacy risks and how secure this stream would be. The implementation of previous webcam systems have highlighted the need for close collaboration with a hospital's information and technology (IT) department as well as the staff of the NICU.[11] The introduction of such a system would require this close collaboration and security. As the web cameras will be solely focused on the baby in the cot, it will not be possible for any staff identifiers to become visible to anybody who is watching the stream. These concerns need to be addressed through information sessions with staff before any implementation of a webcam system.

There may be a lack of understanding of what a webcam system entails for the end users, both parents and physicians. Concerns over potential work load issues such as having to deal with malfunctioning equipment and additional phone calls from parents about the use of the system and about their baby may have negatively influenced responses. The timing of the questionnaire may have also influenced responses, considering current resource and personnel implications.

We expected the NICU staff to have a more positive response of the idea of a webcam system. Again some of these concerns may represent a misunderstanding of how the system would operate. The majority of our medical trainees utilize technology at the bedside including the use of many applications on mobile devices and so are not technologically naive.[12,13] Our intensive care unit has ongoing clinical studies that utilize video in the delivery suite at newborn resuscitation, in the neonatal unit to document proficiency in procedural training and also in 24 hour video electroencephalogram for the first few days of life. The feedback received from parents as well as medical staff has raised some interesting issues that have highlighted the need for a collaborative project team to liaise with all staff members before any implementation to address concerns and to provide education on the system. Through an evaluation of their hospitals webcam system, Rhoads et al have highlighted the importance of nursing staff having an active part in any webcam system before and during implementation.[14] We feel that a project team would allow for this.

Family centered care primarily involves parents but involvement of siblings, grandparents, and the extended family cannot be overstated. At present, the extended family role is limited when the infant is admitted to the NICU. Health care professionals should strive to involve the family in the caregiving roles as much as realistically possible.[15] While the neonatal unit is not conducive to these, their importance should not be underestimated. With advances in technology, webcam infrastructure, smartphones, and access to the Internet is becoming easier, as well as more affordable. Many people now have access to the Internet via broadband in their home or the internet network on their smartphone.

Our results warrant further research in attitudes toward a webcam system and/or a pilot study on the development and implementation of a webcam system in our NICU. It would be important to address the concerns raised by staff before implementation, as it would allow for an easier implementation process. This is the first step toward the introduction of a webcam system in our NICU. We have identified parental demand, the perceived advantages and disadvantages of a webcam system, and nursing and medical concerns. The introduction of a phased system with ongoing user feedback, will help to determine if these concerns are validated and can be addressed, and allow us to evaluate the role of webcams in helping parents cope with the stress of having a critically ill baby in the NICU.

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Appendix A: Parental Questionnaire

The following questions relate to the possible implementation of a webcam system for the NICU. This would involve a webcam being focused on your baby in the NICU, following your permission, in order for you to be able to view your baby when you are away from the NICU. The webcam access would be password protected and you would be the only person with access to the webcam. The webcams would not be focused on staff or other babies. We would welcome your participation in this questionnaire as your views will help us make this project a success.

This questionnaire is anonymous and by completion of this questionnaire you are consenting for this questionnaire to be used in the study.

Please circle one number in each question.

1 = Not at all, 5 = Very much so.

1. How often would you use a computer?

1 2 3 4 5

2. How often would you use a webcam?

1 2 3 4 5

3. How often do you think you would use this service if it were to be implemented?

1 2 3 4 5

4. Do you feel confident in the security behind webcam use to view your baby?

1 2 3 4 5

5. Would you share your password with another person, for example, family member or friend?

1 2 3 4 5

6. Do you think you would experience less stress when you were away from the hospital if this service was available?

1 2 3 4 5

7. Do you think it would reduce the number of phone calls you would make to the unit?

1 2 3 4 5

8. Do you think it would reduce the number of times you would visit the NICU?

1 2 3 4 5

9. Do you have any comments relating to webcam use to view your baby?

_____

_____

_____

_____

_____

_____

_____

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_____

_____

_____

Appendix B: Medical staff Questionnaire

The following questions relate to the possible implementation of a webcam system for the NICU. This would involve webcam's being focused on babies in the NICU in order for parents of these babies to view their baby when the parents are away from the NICU. The webcam access would be password protected and the parents would be the only people with access to the webcam. The webcams would not be focused on staff and not on other newborns. The webcams would be able to be turned off manually by staff at any time. We would welcome your participation in this questionnaire prior to the possible implementation.

This questionnaire is anonymous and by completion of this questionnaire you are consenting for this questionnaire to be used in the study.

Please circle one number in each question. 1=Not at all, 5=Very much so

1. Do you feel confident in the security behind webcam use to view babies in the NICU?

1 2 3 4 5

2. Are you familiar with any webcam use, similar to this, elsewhere?

1 2 3 4 5

3. Do you think this would reduce the amount of time parents spend in the NICU?

1 2 3 4 5

4. Do you think this will reduce the amount of calls made to the NICU by parents requesting information about their baby?

1 2 3 4 5

5. Although the webcam will not be assessing performance of staff, do you think that the presence of a webcam will add to stress levels experienced by staff?

1 2 3 4 5

6. Are you in favor of a system such as this being implemented?

1 2 3 4 5

7. Do you have any comments relating to webcam use to view babies in the NICU?

CREC approval letter

UCC

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Fax: + 353-21-490 1919

Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

COISTE EITICE UM THAIGHDE CLINICIÚIL
Clinical Research Ethics Committee

Lancaster Hall,
6 Little Hanover Street,
Cork,
Ireland.

Our ref: ECM 4 (r) 04/09/12

24th August 2012

Dr Gene Dempsey
Consultant Neonatologist
Department of Pediatrics & Child Health
Cork University Maternity Hospital
Wilton
Cork

Re: A questionnaire based assessment of webcams in the NICU.

Dear Dr Dempsey

Expedited approval is granted to carry out the above study at:

- Cork University Maternity Hospital.

The following documents have been approved:

- Application Form
- Study Protocol Version 1 dated 22nd August 2012
- Nursing Staff/Medical Staff Questionnaire Version 1 dated 22nd August 2012
- Parent's Questionnaire Version 1 dated 22nd August 2012.
-

The following co-investigators will be involved in this study:

- Gavin Hawkes and Professor Anthony Ryan.

Yours sincerely

Dr Michael Hyland
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

The Clinical Research Ethics Committee of the Cork Teaching Hospitals, UCC, is a recognised Ethics Committee under Regulation 7 of the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004, and is authorised by the Department of Health and Children to carry out the ethical review of clinical trials of investigational medicinal products. The Committee is fully compliant with the Regulations as they relate to Ethics Committees and the conditions and principles of Good Clinical Practice.

Parental questionnaire

The following questions relate to the **possible** implementation of a webcam system for the NICU. This would involve a webcam being focused on your baby in the NICU, following your permission, in order for you to be able to view your baby when you are away from the NICU. The webcam access would be password protected and you would be the only person with access to the webcam. The webcams would not be focused on staff or other babies. We would welcome your participation in this questionnaire as your views will help us make this project a success.

This questionnaire is anonymous and by completion of this questionnaire you are consenting for this questionnaire to be used in the study.

Please circle one number in each question.

1=Not at all, 5=Very much so

1. How often would you use a computer?
   1 2 3 4 5

2. How often would you use a webcam?
   1 2 3 4 5

3. How often do you think you would use this service if it were to be implemented?
   1 2 3 4 5

4. Do you feel confident in the security behind webcam use to view your baby?
   1 2 3 4 5

5. Would you share your password with another person e.g. family member or friend?
   1 2 3 4 5

6. Do you think you would experience less stress when you were away from the hospital if this service was available?
   1 2 3 4 5

7. Do you think it would reduce the number of phone-calls you would make to the unit?
   1 2 3 4 5

8. Do you think it would reduce the number of times you would visit the NICU?
   1 2 3 4 5
   2
9. Do you have any comments relating to webcam use to view your baby?

   _____

   _____

   _____

Medical staff questionnaire

The following questions relate to the possible implementation of a webcam system for the NICU. This would involve webcam's being focused on babies in the NICU in order for parents of these babies to view their baby when the parents are away from the NICU. The webcam access would be password protected and the parents would be the only people with access to the webcam. The webcams would not be focused on staff and not on other newborns. The webcams would be able to be turned off manually by staff at any time. We would welcome your participation in this questionnaire prior to the possible implementation.

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   1 2 3 4 5

4. Do you think this will reduce the amount of calls made to the NICU by parents requesting information about their baby?
   1 2 3 4 5

5. Although the webcam will not be assessing performance of staff, do you think that the presence of a webcam will add to stress levels experienced by staff?
   1 2 3 4 5

6. Are you in favour of a system such as this being implemented?
   1 2 3 4 5

7. Do you have any comments relating to webcam use to view babies in the NICU?

Appendix K

CREC approval letter

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COISTE EITICE UM THAIGHDE CLINICIÚIL
Clinical Research Ethics Committee
Lancaster Hall,
6 Little Hanover Street,
Cork,
Ireland.

Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

ECM 6 (yy) 14/04/15

20th March 2015

Professor Eugene Dempsey
Department of Neonatology
Cork University Maternity Hospital
Wilton
Cork

Re: Establishment of a validated procedural metric and training results in improved outcomes in stabilization of the preterm baby.

Dear Professor Dempsey

The Chairman has approved the above project.

The study will take place at the Cork University Maternity Hospital.

The Medical Student involved in the research will be:

- Kieran Denis Brosnan.

Yours sincerely

Professor Michael G Molloy
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

Appendix L

CREC approval letter

UCC

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Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

COISTE EITICE UM THAIGHDE CLINICIÚIL
Clinical Research Ethics Committee

Lancaster Hall,
6 Little Hanover Street,
Cork,
Ireland.

Our ref: ECM 4 (w) 09/01/13

12th December 2012

Dr Eugene Dempsey
Consultant Neonatologist
Department of Paediatrics
Cork University Maternity Hospital
Wilton
Cork

Re: Technology enhanced learning in neonatal peripherally inserted central catheter placement.

Dear Dr Dempsey

Expedited approval is granted to carry out the above study in:

- Cork University Maternity Hospital.

The following documents have been approved:

- Application Form
- Questionnaire
- Information Sheets and Consent Form.

We note that the co-investigator involved in this study will be:

- Treasa Murphy, Medical Student.

Yours sincerely

Dr Michael Hyland
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

The Clinical Research Ethics Committee of the Cork Teaching Hospitals, UCC, is a recognised Ethics Committee under Regulation 7 of the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004, and is authorised by the Department of Health and Children to carry out the ethical review of clinical trials of investigational medicinal products. The Committee is fully compliant with the Regulations as they relate to Ethics Committees and the conditions and principles of Good Clinical Practice.

Doctor Consent form

Title of Research:

Technology Enhanced Learning in Neonatal Peripherally Inserted Central Catheter Placement

Project Supervisor: Dr. Eugene Dempsey, Consultant Neonatologist, CUMH

Student Co-Investigator: Treasa Murphy

Purpose and Background

If you agree to participate in this research study, the PICC insertion procedure you will perform will be video recorded, and used to assess your performance order to enchance future skill of this procedure. The video recording will not involve any identifying features of baby or of you, but will be assigned a unique identifier number. The only area being recorded is the insertion site of the PICC line.

Confidentiality:

The information gathered from this study will be kept as confidential as possible. Your s name will not be used in the report and all files, transcripts and data will be stored confidentially. No one, with the exception of the study researchers, will have access to this information. No identifying personal information will be included in the research report.

Potential Risks and Benefits

There are no further associated risks other than those associated directly with the procedure itself. We hope that this process will lead to improved performance in this area.

Alternatives

You may choose not to participate. Your participation in this study is entirely voluntary. You may opt to leave at any time.

Consent

The research project and the treatment procedures associated with it have been fully explained to me. All experimental procedures have been identified and no guarantee has been given about the possible results. I have had the opportunity to ask questions concerning any and all aspects of the project and any procedures involved. I am aware that participation is voluntary and that I may withdraw my consent at any time. Confidentiality of records concerning my involvement in this project will be maintained in an appropriate manner. When required by law, the records of this research may be reviewed by government agencies and sponsors of the research.

I, the undersigned, hereby consent to participate as a subject in the above described project conducted at the Cork Teaching Hospitals. I have received a copy of this consent form for my records.

Doctor: _____

Witness: Date: _____

Time: _____AM/PM(Circle)

Parental consent form

Department of Paediatrics and Child Health,

University College Cork

Title of Research:

Technology Enhanced Learning in Neonatal Peripherally Inserted Central Catheter Placement

Project Supervisor: Dr. Eugene Dempsey, Consultant Neonatologist, CUMH **Student Co-Investigator:** Treasa Murphy **A. Purpose and Background**

Your baby has been admitted to the Neonatal intensive care unit. A decision has been made to insert a PICC line. This is standard of care for a baby born at this gestation and birth weight. Under the supervision of Dr. Dempsey, Consultant Neonatologist at Cork University Maternity Hospital, Treasa Murphy, a UCC medical student in research of neonatology, is conducting research about the effects of technology enhanced learning on neonatal peripherally inserted central catheter placement (PICC). The purpose of this research is to improve patient care concerning this procedure and to provide a basis for competency based training in medical education.

Procedures

If you agree for your child to participate in this research study, the PICC insertion procedure your child is scheduled to receive will be video recorded, and used to critique the doctor preforming the task in order to enhance their future performance. The video recording will not involve any identifying features of your baby. The only area being recorded is the insertion site of the PICC line.

Confidentiality:

The information gathered from this study will be kept as confidential as possible. Your child's name will not be used in the report and all files, transcripts and data will be stored confidentially. No one, with the exception of the study researchers, will have access to this information. No identifying personal information will be included in the research report.

Potential Risks and Benefits

There are no further associated risks to your baby other than those associated directly with the procedure itself. There are no guaranteed benefits to your child.

Alternatives

You may choose not to participate, and the procedure will not take place. Your participation in this study is entirely voluntary. You may opt to leave at any time. If you decide not to participate, or if you decide to leave the study, you will not be penalised and will not give up any benefits, which you had before entering the study.

Costs

There will be no costs to your child or you as a result of your child taking part in this research study.

Consent

The research project and the treatment procedures associated with it have been fully explained to me. All experimental procedures have been identified and no guarantee has been given about the possible results. I have had the opportunity to ask questions concerning any and all aspects of the project and any procedures involved. I am aware that participation is voluntary and that I may withdraw my consent at any time. I am aware that my decision not to participate or to withdraw will not restrict my access to health care services normally available to me. Confidentiality of records concerning my involvement in this project will be maintained in an appropriate manner. When required by law, the records of this research may be reviewed by government agencies and sponsors of the research.

I understand that the sponsors and investigators have such insurance as is required by law in the event of injury resulting from this research.

I, the undersigned, hereby consent for my baby to participate as a subject in the above described project conducted at the Cork Teaching Hospitals. I have received a copy of this consent form for my records. I understand that if I have any questions concerning this research, I can contact the doctor(s) listed above. If I have further queries concerning my rights in connection with the research, I can contact the Clinical Research Ethics Committee of the Cork Teaching Hospitals, Lancaster Hall, 6 Little Hanover Street, Cork.

After reading the entire consent form, if you have no further questions about giving consent, please sign where indicated.

Doctor/Student:_____

Signature of Parent or Guardian _____

Witness: Time: _____AM/PM(Circle)

Procedural Checklist Score for PICC Insertion

Pre procedure

1. Carefully chose your site of insertion. Recommended sites include antecubital fossa (basilic or cephalic vein) or saphenous vein. Measure the anticipated distance e.g. for basilic from insertion site to shoulder and then from shoulder to sternoclavicular jt.
2. Document anticipated distance. Cephalic is sometimes more difficult to thread to a central position due to narrowing of vessel prior to entering subclavian vein.
3. Maximal Barrier precautions: Wear hat, mask, scrub to elbows, gown and double glove.
4. Ask assistant to open pic line pack and deposit contents onto sterile tray. PIC size will depend on size of baby, generally <1.5KG size 28F, >1.5kg size 24 F.
5. Ask assistant to deposit chlorhexidine wipes, steristrips, draw up saline flush
6. Flush line with 5ml syringe
7. Ensure introducer is patent
8. Prepare equipment, arrange steristrips, tegaderm
9. Ensure equipment is to right hand side

Procedure

1. Ask assistant to administer sucrose
2. Turn babys head to face the chosen arm (to prevent line tip from traveling cephalad through jugular vein)
3. Ask assistant to raise arm and place green sterile dressing under this Apply further green dressings and make a large sterile field. Place equipment on field.
4. Clean with 2% chlorhexidine, starting from the centre and working outwards. Allow to dry, 30 secs

5. Apply tourniquet (elastic band or cord tie) to upper part of arm
6. Stabilise arm with left hand and then enter chosen vein with introducer.
7. Go slowly (sometimes you may enter and no blood will return, it may take a number of secs for blood return). Often one will feel a “pop” on entering the vein.
8. Remove tourniquet.
9. When blood returns carefully place PIC line through introducer with mosquito forceps (held in right hand) and insert to chosen distance.
10. Remove needle introducer and peel away introducer.
11. Put pressure on insertion site (diameter of introducer is larger than PIC line and hence will bleed initially).
12. Call for Xray.

Post procedure

1. Secure with steristrips and leave area sterile for now.
2. Stay with baby when xray is being placed.
3. Inject Contrast 0.7mls with 5 ml syringe
4. Confirm position of tip. If in good position then secure in place. apply tegaderm dressing and remove linens.
5. If not in position;
    a. too far : pull back to correct position
    b. Not far enough: Never try to advance if not far enough, this may be used as a peripheral iv if the case dictates such although preferably not.
    c. Incorrect vessel (internal mammary vein or jugular vein, pull back and may use as a peripheral iv if very difficult access)
    d. Rexray

6. Please fill in PIC line sheet documenting insertion.

Appendix M

Resuscitation 84 (2013) e139

Contents lists available at ScienceDirect

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Letter to the Editor

The demand for an educational smartphone app

Sir,

Smartphones are popular; they are capable of holding vast amounts of material and are increasingly becoming more available and more affordable. The App Store available for iPhone (Apple Inc, California, USA) users has recently dedicated a specific section of the store as "Apps for healthcare professionals", emphasizing the growing market for applications aimed at healthcare professionals. The Department of Health, UK, has stated that '. . . smartphones can enhance patient care by providing opportunities for students, trainees and staff to accumulate essential knowledge skills, values and behaviours' [1]. Reviews on the use of smartphone applications for various medical fields including surgery, pediatric pain management, and infectious disease have already been published. In a recent survey, Franko identified that 56% of physicians used smartphone apps in their clinical practice [2]. However, regulation and guidance in this area of medicine is currently lacking.

In 2011, we developed a smartphone application to assist neonatal trainees in learning neonatal intubation. We sought to maximize the benefit of each intubation opportunity for our trainees so as to overcome the reduced opportunities available to trainees to acquire this live saving skill. This application was based on "just in time" training and "situated learning". The application development included five steps: planning, content compilation, layout design, implementation and evaluation. It incorporated user feedback at each stage of development, with independent external peer review prior to final release. We subsequently demonstrated that use of the application prior to intubation improved intubation knowledge, technique and reduced the time taken to intubate a mannequin model [3]. Two years following release, the application has over 6000 unique downloads, over 20,000 returns and 120,000 page views in over 100 different countries, highlighting the ability for widespread dissemination and use.

Notwithstanding the many benefits, there is real potential for smartphone educational tools to cause harm. This is important as often there is a low level of medical involvement (34%) in the creation of medical apps [4]. Recently a pharmaceutical company withdrew a smartphone application that miscalculated scores for rheumatoid arthritis patients [5]. In the absence of any regulation, users need to be aware that the application content is not regulated and may not be factually correct. Stricter guidelines and regulation needs to be in place, especially for apps that may affect patient care either through guiding clinical practice and/or providing patients with information for self care.

We have described a process we believe addresses some important aspects in medical app creation. This includes careful internal review at institutional level, with subsequent external review by experts in the field. Greater physician involvement should be encouraged and national training authorities/specialties could endorse applications prior to their general release. Feedback from end-users is extremely important, and a secure email feedback mechanism should be included, either mandatory or optional. Whilst entire process will require significant coordination at the app creation stage, and ultimately a longer time to creation, it would address some of the shortcomings of the current process and potentially enhance patient safety.

http://dx.doi.org/10.1016/j.resuscitation.2013.07.005

Contributors

Mr. Gavin Anthony Hawkes contributed to study design, data acquisition and data interpretation. He had primary responsibility for initial manuscript preparation as well as the final manuscript that was submitted.

Dr Colin Patrick Hawkes and Dr Eugene Michael Dempsey had primary responsibility for application content, supervised manuscript preparation and reviewed the final manuscript that was submitted.

Prof C. Anthony Ryan contributed to application development, study design, initial manuscript preparation and revision of the final version of the manuscript.

Conflict of interest statement

The authors of this letter have no conflicts of interest to disclose.

References

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3. Hawkes CP, Walsh BH, Ryan CA, Dempsey EM. Smartphone technology enhances newborn intubation knowledge and performance amongst paediatric trainees. Resuscitation 2013;84:223–6.
4. Visvanathan A, Hamilton AD, Brady RRW. Smartphone apps in microbiology – is better regulation required. Epidemiology 2012;18:E218–20.
5. Philips B. 'Pfizer Rheumatology Calculator' iPhone/Android Application-important information. http://mhra.gov.uk/home/groups/fsn/documents/fieldsafetynotice/con137658.pdf

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Colin Patrick Hawkes [a,b]
C. Anthony Ryan [a,b]
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4 July 2013

Appendix N

CREC approval letter

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Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

COISTE EITICE UM THAIGHDE CLINICIÚIL
Clinical Research Ethics Committee

Lancaster Hall,
6 Little Hanover Street,
Cork,
Ireland.

Our ref: ECM 4 (ss) 06/11/12

22nd October 2012

Professor Anthony Ryan
Department of Paediatrics & Child Health
Cork University Maternity Hospital
Wilton
Cork

Re: The development and evaluation of a mobile phone resuscitation guide.

Dear Professor Ryan

The Chairman approved the following:

- Amendment Application Form
- Addition of Gavin Hawkes as co-investigator in the above study.

Yours sincerely

Dr Michael Hyland
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

The Clinical Research Ethics Committee of the Cork Teaching Hospitals, UCC, is a recognised Ethics Committee under Regulation 7 of the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004, and is authorised by the Department of Health and Children to carry out the ethical review of clinical trials of investigational medicinal products. The Committee is fully compliant with the Regulations as they relate to Ethics Committees and the conditions and principles of Good Clinical Practice.

Guardian/participant information and consent form

Guardian Permission Form

Title of the Project: The Development and Evaluation of a Mobile Phone Resuscitation Guide.

Researcher: Professor Anthony Ryan, Geraldine Murphy and Gavin Hawkes.

My name is Geraldine Murphy and I am a final year medical student at the University College Cork. Your permission is being sought to have your child participate in this study. Please read the following information carefully before you decide whether or not to give your permission.

Purpose of the Research: The purpose of this study is to determine if the use of a simple mobile phone application could be beneficial to a member of the public when performing cardiopulmonary resuscitation (CPR).

Procedure Involved: During testing your child will be thought basic life-saving skills using "Infant CPR Anytime", a self-teaching kit by the American Heart Association. The teaching will include a 20 minute instructional DVD and the use of a plastic manikin to practise chest compressions and rescue breaths. Your child's skills will then be evaluated using a fictional scenario (e.g. a baby that has stopped breathing or showing signs of life.). They will be expected to demonstrate infant resuscitation on a plastic manikin and may use the mobile phone application to prompt them. Their recall of the life-saving skills will be evaluated using a previously validated checklist.

Discomforts/Risks: There are no foreseeable discomforts or risks to you or child in this study.

Benefits for Participants: Your child will become familiar with the skills required to resuscitate an infant. The results of the study will increase our knowledge on the usefulness of mobile phone applications in basic life support.

Time Duration of Participation: Participation will not exceed 2 hours.

Voluntary participation: Your child's participation is voluntary. If you feel your child has in any way been coerced into participation, please inform the researcher. We also ask that you read this letter to your child and inform your child that participation is voluntary. At the time of the study, the researcher will once again remind your child of this.

Termination of participation: If at any point during the study you or your child wishes to terminate their participation, we will do so.

Questions or concerns regarding the research or participation in this research should be directed to:

Geraldine Murphy at geraldineamurphy@gmail.com

This research has been reviewed and approved by The Clinical Research Ethics Committee of the Cork Teaching Hospitals. If at any time before, during or after the study your child experiences any physical or emotional discomfort that is a result of his/her participation, or if you have any questions about the study or its outcomes, please feel free to contact us.

SIGNING THE FORM BELOW WILL ALLOW YOUR CHILD TO PARTICIPATE IN THE STUDY DURING SCHOOL HOURS WITHOUT YOUR PRESENCE. Please return by 20/11/12. If you do not sign and return this form, the researchers will understand that you do not wish to allow your child to participate.

Parent Signature Box

I, the parent or guardian of _____, a minor _____ years of age, ***permit*** *his/her participation in a program of research named above and being conducted by Geraldine Murphy, Gavin Hawkes and Prof. Anthony Ryan.*

_____ _____

Signature of Parent or Guardian Date

_____

Please print your name here.

Student Signature Box

I, _____, agree to participate in the program of research named above and understand that my participation is voluntary.

_____ _____

Signature of Student Date

_____

Please print your name here.

Signature of Investigator _____ Date_____

Resuscitation Assessment Checklist

Participant Number:

Mobile Phone: Yes ☐ No ☐

CPR Order	CPR Factor	Scoring Factor (Each scoring factor = 1 point, unless stated otherwise)	Score obtained
1	**Checking responsiveness**	• Stimulate Foot • Call infant	
	Shouting for help	• Yes	
2	**Opening airway**	• Head tilt • Chin lift	
	Assessment of breathing	• Observe for chest rise and fall • Listen for breathing • Feel for breathing on ear	
3	**Correct head positioning**	• Yes	
	First rescue breaths	• one effective ventilation • Two effective ventilations (2 points)	
	Observing for chest rise during ventilations	• Yes	
4	**Proper hand positioning during compressions**	• Yes	
	Compression depth	• Mostly sufficient • Always sufficient (2 points)	
	Compression Rate		
5	**Breathing time**	• Satisfactory • Good (2 points)	
	Chest rise	• Most of the time • Every time (2 points)	
	Number of cycles of CPR performed	• ≤3 (1 point) • 4 (2 points) • 5 (3 points)	
	Would perform 5 cycles in 2 minutes	• Yes	
	Dial 112	• Yes	
	Correct sequence of CPR	• Yes	
	Total hands of time <10 Seconds	• Yes	
			Total =