

Review

Non-invasive ventilation for children with acute respiratory failure in the developing world: Literature review and an implementation example

R.E. Balfour-Lynn¹, G. Marsh², D. Gorayi³, E. Elahi⁴, J. LaRovere^{1,*}

¹ Division of Cardiovascular Critical Care, Boston Children's Hospital, Boston MA, USA

² Department of Physiotherapy, Royal Brompton Hospital, London UK

³ Tumu District Hospital, Tumu Ghana

⁴ Departments of Ophthalmic, Oculofacial Surgery and Global Health, Mount Sinai School of Medicine, New York NY, USA

ARTICLE INFO

Keywords:

Acute respiratory failure
Ventilation
Non-invasive
Developing world
Low income

SUMMARY

Over 2 million children die of acute respiratory infection every year, with around 98% of these deaths occurring in developing countries. Depending upon the clinical status of the patient, supplemental oxygen is usually the first line therapy. However this often proves inadequate for acute respiratory failure (ARF), in which case intubation and mechanical positive pressure ventilation are required. Adult intensive care successfully introduced non-invasive positive pressure ventilation (NIPPV) to treat ARF over a decade ago. This experience, coupled with the use of NIPPV in children with chronic respiratory insufficiency, has led to increasing use of NIPPV to treat ARF in paediatric populations. NIPPV can have similar or improved outcomes to IPPV, but with fewer complications. However there are no controlled trials of its use in children, and most data come from observational studies and retrospective reviews. In a developing world setting, where mortality from ARF is high and the risks of intubation are great and often not feasible, NIPPV can be a simple and cost-effective way to treat these patients. Its implementation in rural Northern Ghana shows NIPPV for ARF can be delivered safely with minimal training, and appears to impact significantly on mortality in those under 5 years.

INTRODUCTION

Acute respiratory failure (ARF) can be categorised into hypoxaemic ARF (type I) or the more common hypercapnic ARF (type II). The hypoxaemic type is usually defined by an arterial partial pressure of oxygen (P_{aO_2}) of <7.8 kPa (60 mmHg) with a normal or low P_{aCO_2} . These cut offs are to an extent arbitrary and the values must be put into the context of the child's pre-existing state and whether any supplemental oxygen is being given. In the

absence of supplemental oxygen, a hypercapnic patient is always hypoxaemic. The primary issue is often ventilation-perfusion mismatch due to intrapulmonary shunting. It can be associated with virtually all acute lung diseases, categorised into acute asthma, infection (bronchiolitis and pneumonia) and pulmonary oedema [1]. In addition to treating the underlying cause, supplemental oxygen must be administered to a hypoxic child. However if that is insufficient to produce a satisfactory rise in oxygen saturation, mechanical ventilation may be required. In the hypercapnic or ventilatory type, as well as hypoxaemia, there is an arterial partial pressure of carbon dioxide (P_{aCO_2}) of >6.5 kPa (50 mm Hg), usually accompanied by a fall in pH to <7.3 . Whilst this may be a chronic issue (for example in children with neuromuscular disease or chronic upper airways obstruction), it may follow on from type I ARF, when the child's respiratory muscles start to fatigue leading to hypoventilation. In this instance, oxygen alone is insufficient and ventilatory support is required.

Traditionally mechanical support has been delivered following intubation, i.e. with invasive positive pressure ventilation (IPPV).

* Corresponding author. Division of Cardiovascular Critical Care, Boston Children's Hospital, 300 Longwood Avenue, Boston, Massachusetts, 02116, USA.

E-mail address: Joan.LaRovere@cardio.chboston.org (J. LaRovere).

Abbreviations: ARDS, Acute respiratory distress syndrome; ARF, Acute respiratory failure; BiPAP, Biphase positive pressure ventilation; BiPAP, Bilevel positive pressure ventilation; CPAP, Continuous positive airway pressure; COPD, Chronic obstructive pulmonary disease; F_{iO_2} , Fraction of inspired oxygen; IPPV, Invasive positive pressure ventilation; NIPPV, Non-invasive positive pressure ventilation; NIV, Non-invasive ventilation; PICU, Paediatric intensive care unit; P_{aO_2} , Arterial partial pressure of oxygen; P_{aCO_2} , Arterial partial pressure of carbon dioxide; SpO_2 , Arterial oxygen saturation measured by pulse oximetry.

However the use of non-invasive positive pressure ventilation (NIPPV) to treat ARF is increasing as NIPPV can have a similar or improved outcome to IPPV with fewer complications [1]. NIPPV tends to refer to biphasic and bilevel (BiPAP) respiratory support not delivered via invasive endotracheal intubation. Interfaces used include nasal pillows, plugs or masks; facemasks – which can be total (mouth, nose, eyes) or full (mouth & nose); mouthpieces; or helmets [2]. Some authors use the term NIPPV to include Continuous Positive Airway Pressure (CPAP) which is not strictly 'ventilation' although could be included under the umbrella of non-invasive respiratory support. Nevertheless an International Consensus has defined NIPPV as 'any form of ventilatory support applied without the use of an endotracheal tube, and was considered to include continuous positive airway pressure (CPAP), with or without inspiratory pressure support' [3]. The use in ARF has generally been restricted to paediatric intensive care units or high dependency units in the technologically-rich developed world, but because of cost issues and its relative simplicity making it accessible to trained healthcare workers other than doctors, there is great potential for its use in the lower income setting of the developing world. This review will look at evidence for the benefit of NIV in ARF, and how it may be applied in the developing world. We will also describe our experience of setting it up in a rural hospital in Ghana.

THE BURDEN OF ARF

ARF develops in minutes to hours, and is more frequent in infants and children than in adults [4]. There are a multitude of causes, which can be reviewed in many text books [5]. However in the developing world, infection is paramount. Worldwide, a conservative estimate has suggested 2 million children die of acute respiratory infection every year, a figure that excludes sepsis and pneumonia in neonates [6]. Inevitably, around 98% of these deaths occur in developing countries [7]; estimates from 2000 suggest 70% were in Africa or SouthEast Asia [8]. From 2000–03, 19% of worldwide deaths in children under five were caused by pneumonia and 10% by neonatal sepsis and/or neonatal pneumonia [9]. Worryingly, in one of the few studies that were able to look at trends in mortality by cause, in Morocco between 1987 and 1997, despite a halving in overall infant and child mortality, there was little change in the rates of death due to pneumonia (report by Garenne M in French, quoted by Mulholland) [6]. Indeed, pneumonia kills more children every year than AIDS, tuberculosis, malaria and measles put together [10].

An important risk factor for respiratory deaths is malnutrition, which in itself is said to be an underlying cause in over half of all deaths in children under 5 years [9]. Poorly nourished children are more likely to develop respiratory fatigue and consequently ARF. Another factor is severe chronic anaemia which, by impeding oxygen transport, makes it more likely for hypoxaemia to develop during respiratory infections. Chronic anaemia is common in developing countries due to a variety of factors including malnutrition, helminthiasis, sickle cell anaemia, and chronic malaria [11].

There are many strategies to prevent deaths from childhood pneumonia in the developing world. These include use of vaccination (to *Haemophilus influenzae* type b, pneumococcus and measles), improvement in nutritional state, and possibly reduction of indoor air pollution [10]. If the child develops pneumonia, early recognition (of tachypnoea) and prompt treatment with antibiotics (often just oral amoxicillin for 3 days) can save lives [12]. If the pneumonia is severe, these children need to be managed in a district hospital. Use of oxygen saturation monitoring and oxygen concentrators to deliver supplemental oxygen when appropriate ($SpO_2 < 90\%$), led to a 35% reduction in

risk of death from pneumonia in a rural setting in New Guinea [13]. This is not surprising given hypoxaemia ($SpO_2 < 90\%$) has been shown to be associated with a 4.3-fold increase in mortality in Kenyan children under 3 years with pneumonia [14]. With the development of type II respiratory failure, oxygen alone will be insufficient, and only mechanical ventilation will save the child, hence our interest in non-invasive ventilation.

USE OF NIV FOR ARF IN THE DEVELOPED WORLD

Positive pressure ventilation is often used to provide respiratory support for children with ARF as it increases the tidal volume hence helps to recruit lung tissue and maximise lung volumes, reversing hypoxemia and hypercapnia. This is most frequently provided invasively via an endo- or nasotracheal tube, unless the child has a tracheostomy. However, following experience in patients with chronic respiratory insufficiency, the benefits of NIPPV for ARF are being increasingly recognised. Inevitably, experience in ARF has initially come from adult intensive care, where NIPPV has been successfully used for over a decade in a multitude of conditions, including exacerbations of chronic obstructive pulmonary disease [15], acute exacerbations of asthma [16] and cardiogenic pulmonary oedema [17].

One review over 15 years ago quoted 29 studies enrolling 748 patients successfully treated with NIPPV for hypoxaemic ARF [18]. Gas exchange can be maintained and there is a decrease in the necessity for endotracheal intubation, with the additional benefit of shorter length of stay and fewer serious complications [19]. In particular NIPPV is associated with a lower rate of ventilator-associated pneumonia and sinusitis than invasive ventilation [19,20]. The risk of secondary lung injury and barotrauma from positive pressure ventilation is lessened although not abolished with NIPPV. It also stops the risk of upper airway trauma including vocal cord damage and subglottic scarring with subsequent stenosis. Additionally it enhances the patient's comfort and aids eating and drinking, coughing and talking [21]. It also reduces the need for sedation although that can sometimes be needed for agitated or scared patients (assuming the agitation is not due to hypoxaemia) [21]. Contraindications to the use of NIPPV include congenital facial or airway abnormalities (precluding use of a tight fitting mask or prongs), severe cardiopulmonary instability, inability to protect the airway, and intractable apnoeic pauses [22]. Other problems include facial trauma or burns, and patients with recent gastrointestinal surgery (in case of gastric distension with air) [22].

Paediatric experience: Evidence for the paediatric use of NIPPV is limited because there are no consistent guidelines, and few prospective randomised controlled trials. The majority of published work is in the form of non-controlled trials and small case series yet its use is increasing [23]. Nevertheless, the results of available studies are encouraging. An excellent review from Najaf-Zadeh and Leclerc has summarised studies up until 2011, categorising the use of NIPPV (including CPAP) in children with acute airway obstruction (including asthma, bronchiolitis, malacia) and parenchymal lung disease (including pneumonia, acute respiratory distress syndrome (ARDS), acute chest syndrome) [1]; there were 13 studies in the first group and 7 in the second. They also categorised specific circumstances of its use, including in the post-operative period (6 studies), for facilitation of ventilation weaning and post-extubation management (2 studies), and in immunocompromised children (6 studies) [1]. A randomised controlled trial of NIPPV plus standard therapy versus standard therapy in 50 children with ARF (mostly due to bronchiolitis or pneumonia) carried out in Argentina and Chile, confirmed the improvement in cardiopulmonary parameters, and the intubation rate was 28% in the NIPPV group vs 60% in the other [24]. There has

also been recent prospective randomised controlled trial in 20 patients with status asthmaticus in the USA, which concluded that early initiation of NIPPV was safe, well tolerated and effective [25]. A recent large series from a PICU in Spain showed a 78% success rate in 149 children receiving NIV, the commonest reason for failure being apnoea and pneumonia [26]. Generally NIPPV is well tolerated with major complications occurring rarely, and it is associated with improved gas exchange, decreased work of breathing and a decreased need for endotracheal intubation [1].

Complications such as tension pneumothorax and depressed cardiac output have been recorded so children still need careful monitoring; using NIPPV is not an excuse for having less supervision than invasive ventilation [23]. The interface is crucial, as problems encountered include discomfort and poor tolerance of the mask, nasal bridge skin breakdown (especially if needed 24 hours a day), eye irritation, and air leaks with a poor mask fit. It is important not to tighten the head straps too much and to use masks with soft silicone seals [2]. Ventilatory pressures above 15–20 cm H₂O may be problematic with facemasks. Nasal-oral [“full”] face masks are also a problem if the child is likely to vomit, in which case a nasal mask is preferred; gaseous distension of the stomach is also a potential issue which can result in vomiting and potentially in aspiration. Placement of a nasogastric tube may aid in managing this risk.

Of particular relevance to developing countries is its use in pneumonia which as outlined above is the leading cause of ARF. The role of NIPPV is to recruit alveoli, reduce the work of breathing, improve oxygenation and CO₂ clearance, and relieve symptoms of dyspnoea. However, in adults, results are generally disappointing with failure rates up to 66% in adults with severe community acquired pneumonia (although better in those with underlying COPD) [21]. In children with pneumonia, several case series have suggested NIPPV can improve ventilation whilst reducing the need for endotracheal intubation, without significant adverse events [27–32]. If the pneumonia progresses to ARDS then NIPPV is unlikely to succeed with a 78% failure rate [1].

Prediction of NIPPV failure, i.e. progressive hypercarbia, is important but difficult; selecting the right patients will avoid inappropriate delay of intubation with its associated risk of morbidity and mortality. It has been suggested that the best predictive factors of failure are the initial oxygen requirement (FiO₂ >0.6) and Paco₂ on admission or within a few hours of starting NIPPV [1,28]; blood pH <7.25 within 1–2 hours of starting was the only independent prognostic factor in another study [33]. Young age was often thought to be problematic but a recent review of 19 infants with median age 2 months showed NIPPV (given to all) prevented intubation in 64% cases; the majority had apnoeic episodes from bronchiolitis or pertussis [34]. In terms of underlying diseases, children with ARDS are the most likely to fail [28,32], but in one Swiss study of immunocompromised children with ARDS, just over half still avoided intubation [35].

USE OF NIV IN LOW INCOME COUNTRIES

There are clear benefits of the use of NIPPV in the developed world, but these may be even greater in developing countries with poor resources available for healthcare. Specifically, because of its relative simplicity to administer, healthcare workers other than doctors can be trained to use it, which makes it even more cost effective. Fully trained doctors are far less available, especially in rural communities, so with appropriate training, it can be more widely utilised than IPPV. Use of NIPPV was advocated back in 1994 for use in chronic respiratory failure in Jamaica as a means of overcoming a shortage of health personnel (including nurses), and a limited healthcare budget [36].

As well as an understanding of when to start it, it is critical to recognise when it is failing, leading to a need for IPPV if that is available. Careful monitoring by nurses and other healthcare workers in order to detect worsening respiratory distress is therefore still important. Although it has been advocated that NIPPV can be used in a non-intensive care setting, use on a general ward must not reduce the attention to detail that is so important for a successful outcome. Nevertheless use of anaesthetic and sedating agents is not required without the need for intubation, and sedation is not usually needed once NIPPV is established. Successful use of NIPPV follows a learning curve, so eventually success rates remain stable despite increasing severity of the ARF being treated [21]. Additionally, with experience, it is also not as time consuming as it was initially believed to be [21]. Reduction in intensive care and total hospital stay also contributes to the cost savings. The reduction in ventilator-associated pneumonia is another major advantage, especially in a setting of malnourished and immunocompromised children (many with AIDS), and less availability of sterile and single-use equipment.

Use of NIPPV in the developing world is still relatively new and it is certainly underutilised. As expected much of the existing literature concerns adult patients, but it is encouraging. In a review of the development of adult intensive care medicine in Bosnia & Herzegovina, they cite the introduction of NIV in 2007 as one of the crucial steps in their development of the specialty [37]. In a recent publication on sepsis management in resource-limited settings, from the Global Intensive Care working group of the European Society of Intensive Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies, it was suggested that “if available and medical staff is adequately trained, use non-invasive ventilation in patients with dyspnoea and/or persistent hypoxemia despite oxygen therapy” [38]. Furthermore it should be instituted early. Understandably they gave this recommendation a C for level of evidence, meaning it was supported only by observational studies. It was also suggested oxygen should be administered empirically to all patients with severe sepsis or septic shock if pulse oximeters are not available; and when available the aim is to keep the SpO₂ >90%. This is relevant to children also, as in a study of septic shock in children in Chennai, India, mortality was increased in the children who did not have access to mechanical ventilation of any sort [39].

A retrospective review of use of NIV in Karachi, Pakistan found 68 adult patients (aged 16–90, mean 60 years) were given BiPAP mostly on a high dependency unit between 1999 and 2000 [40]. Commonest diagnoses were pneumonia (29%) and COPD (21%). A successful outcome was achieved in 70% patients with type II ARF and 65% with type I. The authors suggested that NIV can be used successfully in developing countries and that with experience it could be used outside an intensive care setting with subsequent further cost savings. However they did point out the high initial cost of the equipment and accessories, and cost of training although these costs are much less than that required for invasive ventilation. In a prospective observational study in an intensive care unit in Vellore, south India, facemask BiPAP was used in 40 adults with type II ARF over a 2 year period [41]. They found an 85% success rate and stated this was comparable to developed countries.

Paediatric experience: There have been few publications relevant to children. One study in Ho Chi Minh City, Vietnam compared use of oxygen alone delivered by a facemask with nasal CPAP in 37 children under 15 years old with Dengue Shock Syndrome (grade 3–4 dengue haemorrhagic fever) [42]. In the syndrome, children may develop ARF after initial fluid resuscitation; alveolar oedema may be caused by increased vascular permeability, fluid overload, pleural and peritoneal effusions, ARDS or cardiac failure, and there is a high mortality rate [42]. In

this study, 92% had pleural effusions and 33% interstitial oedema. The authors initially did an open pilot study and found nasal CPAP decreased hypoxaemia and reduced the need for endotracheal intubation and ventilation. In the later study, they did exclude patients they felt had an immediate need for intubation. CPAP was delivered via nasal prongs at a pressure of 6 cms H₂O and was accompanied by oxygen with FiO₂ 0.6. Compared to oxygen alone, the CPAP group had a significantly decreased respiratory rate after 30 minutes of treatment. In both groups the SpO₂ and PaO₂ increased significantly. Over the subsequent 24 hours, 12/18 of the oxygen group were converted to CPAP. Those in the initial CPAP group had a higher rate of responsiveness to treatment, although 4/18 of them still went on to require intubation and ventilation and all four died with multiple organ failure; there were no deaths in the oxygen group. No complications of nasal CPAP were documented but it is unclear whether the 4 deaths that were all in the CPAP group were coincidental or if that should be a genuine concern. The authors concluded that nasal CPAP was a simple, cheap and safe way to provide respiratory support and was suitable for use in developing countries where facilities for PICU and ventilatory support are inadequate.

A randomised study of nasal CPAP took place in 4 district hospital emergency wards in rural Ghana using locally trained nurses [43]. Children aged 3 months to 5 years were included who had acute respiratory distress (tachypnoea, recession, nasal flaring), due to pneumonia, sepsis, malaria and severe anaemia. Nasal bubble CPAP was administered either immediately or 1 hour after presentation; this meant that children who might benefit were not denied CPAP, but could receive it after a relatively brief delay. Supplemental oxygen was given if SpO₂ was <92%. The study stopped early after the first 70 patients (due to predetermined criteria), with the respiratory rate falling in the first hour by a mean 16 breaths/min (95% CI 10–21) in the CPAP group, with no change in the delay group. Once the delay group were given CPAP in the 2nd hour, their respiratory rate fell by mean 13/min (95% CI 8–19). No major complications of CPAP were said to occur, but there were 3 deaths due to severe malaria, all in the immediate CPAP group. Just as with the Vietnamese study above this is a cause for concern and unexplained. The study's Data Safety & Monitoring Board felt the deaths were unrelated to CPAP.

There has also been a recent prospective observational study from a PICU in Kuala Lumpur, Malaysia, which is a middle-income country [44]. They state that in their unit, equipment and human resources are limited and demand for beds is high, so patients must be transferred out to the general ward as quickly as possible. NIV (BiPAP via nasal or naso-oral mask) was used for ARF (n=129), to facilitate extubation (n=98) or after a failed extubation to avoid reintubation (n=48) in children with a mean age of 9 months. Causes of ARF were pneumonia, asthma, bronchiolitis, cardiac failure, upper airway obstruction and a splinted diaphragm from ascites or tumour. Success was high with 79% avoiding intubation in the subsequent 5 days. Independent risk factors for NIV failure were a higher PRISM II score at admission, presence of sepsis, and higher FiO₂ at the start of NIV. Complications included pressure sores (6%); and healthcare-associated pneumonia (7%), although 80% of those had prior invasive ventilation. The authors felt that an education strategy for nurses and health caregivers in the "bedside titration of care" was the key factor in the success of the NIV program. The nurses were crucial for detecting airway obstruction by the mask, relieving pressure sores, positioning the child for postural drainage, suctioning secretions without stressing the child, and calming a lightly sedated but agitated child.

There has also been a recent published abstract reviewing use of NIV in a PICU in Bangkok, Thailand over a one year period [45]. There were 44 children (mean age 9.2 years) and BiPAP was successful in 82% cases (defined as avoiding intubation for

48 hours). Successful outcome was best predicted by a drop in heart rate at 30 mins and respiratory rate at 45 mins after initiation of the NIPPV. Complications were seen in 14% cases, with facial skin irritation the commonest adverse effect.

INTRODUCING NIV TO TUMU DISTRICT HOSPITAL, GHANA

The 2010 mortality rate for children under-5 was 74 per 1000 live births in Ghana (compared to 5 in the UK and 8 in the USA), albeit an improvement from the 1990 figure of 122 per 1000 live births [46]. Mortality figures in rural areas of Ghana are significantly worse than urban areas with a recognised shortage of health personnel and a general unwillingness of doctors to work in the rural areas [47]. Additionally although children make up 45% of the population, their health needs are still underrepresented [47].

Tumu District Hospital is the only referral hospital in the Sissala East District in the Upper West Region of Ghana (http://mofa.gov.gh/site/?page_id=1679). This region has an under-5 mortality figure of 142 per 1000 live births [48]. The hospital serves a district catchment population of over 56,000 people, the majority of whom are subsistent peasant farmers with 84% living below the poverty line and 92% having no formal education [49]. Tumu is the only part of the district with any degree of urbanization. Being a border town, the hospital's catchment area extends to Burkina Faso as well as surrounding villages of the Upper West and Upper East Regions of Ghana. The hospital has 82 beds divided between adult, paediatric and obstetric wards, with one operating theatre. There is one medical doctor, 29 nurses, including a nurse anaesthetist, and five midwives. The hospital has electricity but power cuts do occur. The 2011 Tumu District Hospital Annual Report lists malaria (48%), anaemia (16%), septicaemia (12%), and pneumonia (8%) as the primary causes of death for children under-5.

In January 2011, Tumu District Hospital made a commitment to reducing under-5 mortality, specifically in regard to malaria, with the introduction of a quality improvement initiative aimed at encouraging early presentation to medical services. Data from January to December 2012 revealed a median time from onset of symptoms to hospital admission at 2.7 days, a critical delay, as acute respiratory failure is often exacerbated by malnutrition and acute on chronic anaemia. Key interventions included local education on need for timely presentation for care, improving adherence to the malaria treatment protocol, strengthening the triage system on initial presentation, and fast tracking critically ill children. The introduction of Virtue Foundation's NIV Initiative was a timely and synergistic addition to Tumu District Hospital's key quality improvement initiatives.

In 2011 Virtue Foundation, a New York based non-profit with Ghanaian non-profit status and Special Consultative Status to the United Nations (www.virtuefoundation.org), donated two Nippy Junior paediatric pressure controlled portable ventilators (B&D Electromedical, Stratford-upon-Avon, UK) with facemasks and tubing to Tumu District Hospital (approximately £3000/\$5000 each). These ventilators were chosen for their ease of use, robustness, and few consumables. The ventilators run by electricity with an additional six-hour internal battery. Two filters (less than \$1 each) – one to be changed every six months and another to ideally be changed for each patient – are the only necessary consumables. A quantity of each was donated and contact details for obtaining the filters in Ghana provided. Virtue Foundation also donated two portable oxygen saturation monitors with finger probes so that heart rate and SpO₂ could be measured at least on an occasional basis; the hospital delivers oxygen from cylinders.

Table 1
Criteria for starting NIPPV in children under 5 years of age (score of 2 or more).

Score	0	1	2
Respiratory rate (% above baseline)	Baseline		$\geq 20\%$ or ≤ 20 bpm
SpO ₂ (% below baseline)	Baseline	$\geq 5\%$	
Intercostal recession	Absent	Marked	
Expiratory grunt	Absent	Audible	

Training was provided over one day in November 2011 and 2 days in April 2012 by two of the authors, a paediatric intensive care consultant (JLR) and specialist respiratory physiotherapist (GM). A series of interactive lectures and hands-on workshops were provided, followed by a competency assessment, with those passing provided with a certificate of training. Twenty-one health staff, including the hospital's medical officer and nurse anaesthetist were trained in the first session, followed by sixteen in the second training. Laminated guides were attached to each of the machines outlining criteria to commence non-invasive ventilator support; a guide to escalating between different modes of support; several case scenarios (bronchiolitis, respiratory distress, and respiratory fatigue), and a guide to sterilisation of equipment.

The criteria to start NIPPV were based on the respiratory rate, SpO₂, and presence of intercostal recession and expiratory grunting (Table 1). The ventilators are used to support patients with respiratory distress. One was initially allocated to the paediatric ward and one to the operating theatre to provide NIV in a more acute setting. The theatre machine has also been used in the adult ward since May 2012. Sedation is not used due to concern over lack of monitoring, level of nursing education and lack of back up support if the patient were to progress to respiratory failure as a result of over-sedation. This is a problem with some patients who are resistant to wearing the mask despite having a clinical need. The nurse anaesthetist (DG) is currently looking into developing a safe sedation protocol.

Figure 1 shows the under-5 mortality in the hospital from 2009 through 2012. January 2011 marked the initiation of the hospital's quality improvement initiatives. After a site visit in April 2011, Virtue Foundation commenced its NIV Initiative with a training programme in November 2011. In the first 4 months of NIPPV use

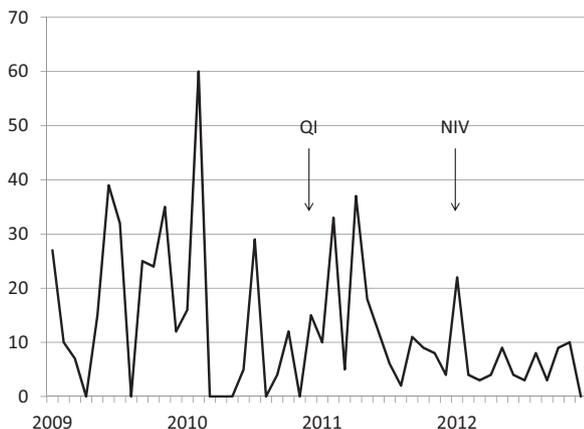


Figure 1. Number of deaths in children < 5 years old in Tumu Hospital, Ghana, from 2009 to 2012. Arrow with QI shows when Quality Improvement programme was started in Jan 2011, and arrow with NIV shows when Non-Invasive Ventilation was initiated in Dec 2011.

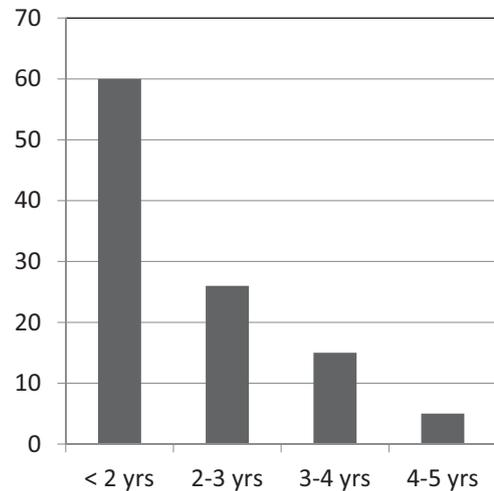


Figure 2. Age distribution of the 106 children ventilated during Jan to Dec 2012.

(Dec 2011 to March 2012), there were 657 admissions of children under-5, with 11 deaths. NIPPV was used in 84 children, of which 70 were under the age of 5, with just 3 deaths. In the subsequent 9 months, NIPPV was used in 46 additional children and 11 adults, with no deaths. The decrease in the number of paediatric patients being ventilated is due to departmental rotation of nursing staff as well as staff turnover. JLR, GM and DG are modifying the previously administered training programme for DG to deliver local training to the current new cohort of nurses.

Further analysis was conducted on the patients ventilated from January through December 2012. Of 140 ventilated patients, 106 (76%) were under the age of five and 60 (43%) under the age of two (Figure 2). Twenty-three were aged 5 to 16 years and 11 were adults over the age of 16. Sex distribution showed more males amongst the children: under-5 year olds – 54% boys; 5-16 year olds – 57% boys; whilst all eleven adults were women. There were two deaths in January 2012, an 8 month old female infant with septicaemia, anaemia and malaria and a 12 month old infant with severe malaria and septicaemia. There were no other deaths with an overall mortality rate of 1.4% within the overall patient cohort and 1.9% in the under-5 cohort.

The primary indication for ventilation in the majority of children under-5 was malaria, septicaemia, pneumonia, gastroenteritis and anaemia. Children aged 5 to 16 years had a similar diagnostic profile whereas adults were ventilated predominantly for asthma and pneumonia. Diagnoses with percentage distributions by age are displayed in Figure 3. Despite setting out to record data, we do not have more complete details on the paediatric patients ventilated and can't be certain that all ventilated patients were captured, as it is not uncommon for data to be missing in the setting of critically ill children with low staff numbers. Additionally the concept of monitoring and recording vital signs (apart from temperature) is not part of their nursing culture, although training has now been provided on this. Nevertheless no complications were reported, although one issue identified is that patients are not always comfortable with the NIV and require frequent breaks. Generally speaking, they seem to ventilate patients for shorter periods than usual. This is probably because patients often come in acutely unwell from malaria with profound anaemia, and the NIV supports them until they receive a blood transfusion. Once oxygen carrying capacity has improved they are weaned from the ventilator. Those with respiratory tract infections and pneumonia tend to be ventilated longer and were

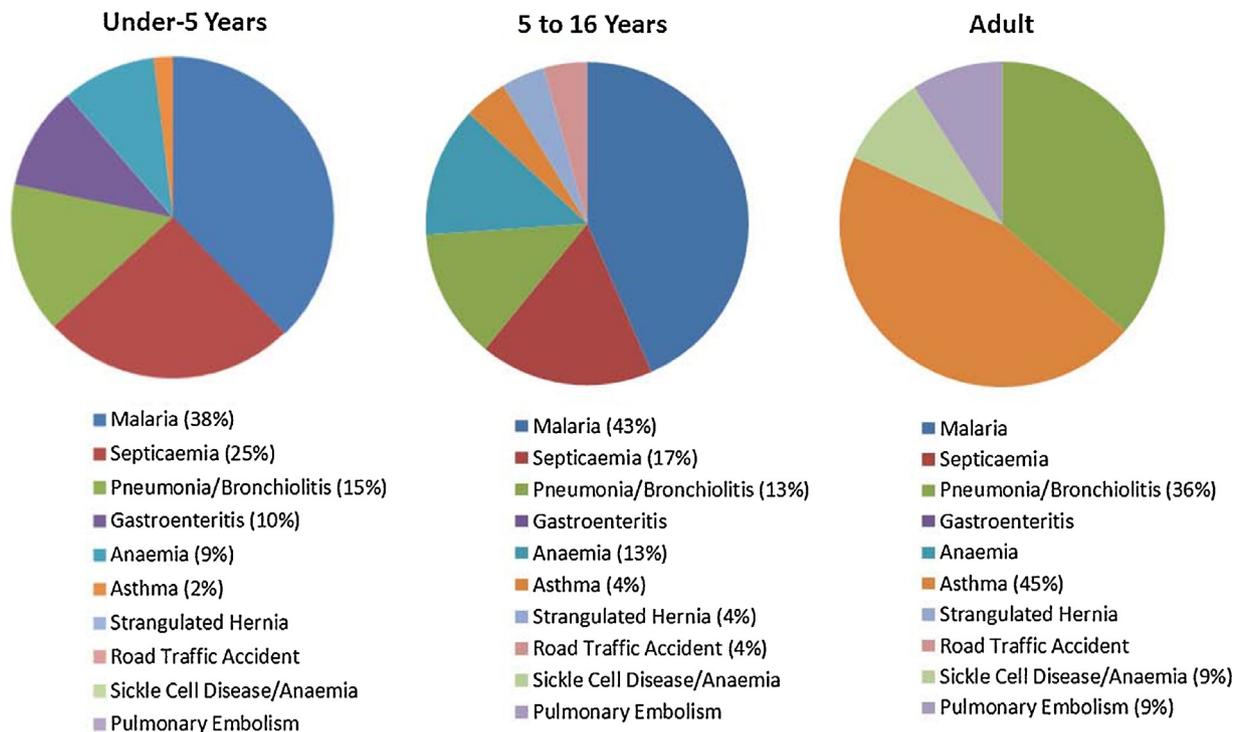


Figure 3. Diagnostic causes (by age) of patients admitted with acute respiratory failure in 2012.

often more comfortable with ventilation for longer periods at a time.

CONCLUSIONS

NIPPV has been used increasingly in adult intensive care and following this, has been its introduction into paediatric practice. There are no controlled trials of its use in children and most data comes from observational studies and retrospective reviews. Nevertheless outcomes are encouraging and there are a number of potential advantages, not least the reduction in ventilator-associated pneumonia. For additional reasons of cost effectiveness and ease of use by all types of trained healthcare workers, it is ideally suited for introduction into developing low-income countries.

LEARNING OBJECTIVES

- To understand the burden of acute respiratory failure (ARF) in children, particularly in the developing world.
- To understand the evidence for the use of non-invasive ventilation (NIV) in children with ARF.
- To discuss the potential for its use, including an implementation example, in a developing world setting.

FUTURE DIRECTIONS/RESEARCH DIRECTIONS

- To construct reliable methodology in order to enable more robust patient data collection in resource-poor hospitals. This would allow us to use larger patient cohorts in order to assess outcomes in the use of NIV for ARF in the developing world.
- To consider ethical means of conducting randomised controlled trials of NIV for ARF.
- To further define and better understand the different clinical scenarios and clinical course when NIV is used, thus enabling selection of the right patients who will likely benefit from NIV.

- To create scalable training and competency assessment programs for NIV use in the developing world.

References

- [1] Najaf-Zadeh A, Leclerc F. Noninvasive positive pressure ventilation for acute respiratory failure in children: a concise review. *Annals of Int Care* 2011;**1**:15.
- [2] Nava S, Hill N. Non-invasive ventilation in acute respiratory failure. *Lancet* 2009;**374**:250–9.
- [3] American Thoracic Society. International Consensus Conferences in Intensive Care Medicine: Noninvasive Positive Pressure Ventilation in Acute Respiratory Failure. *Am J Resp Crit Care Med* 2001;**163**:283–91.
- [4] Rotta AT, Wiryawan B. Respiratory emergencies in children. *Respir Care* 2003;**48**:248–58.
- [5] Gutierrez JA, Duke T, Henning R, South M. Respiratory failure and acute respiratory distress syndrome. In: Taussig LM, Landau LI, editors. *Pediatric Respiratory Medicine*. 2nd ed., Philadelphia: Mosby Elsevier; 2008. p. 253–74.
- [6] Mulholland K. Childhood pneumonia - a permanent global emergency. *Lancet* 2007;**370**:285–9.
- [7] Murray CJL, Lopez AD. Mortality by cause for eight regions of the world: global burden of disease study. *Lancet* 1997;**349**:1269–76.
- [8] Williams BG, Gouws E, Boschi-Pinto C, Bryce J, Dye C. Estimates of world-wide distribution of child deaths from acute respiratory infections. *Lancet Infect Dis* 2002;**2**:25–32.
- [9] Bryce J, Boschi-Pinto C, Shibuya K, Black RE, the WHO Child Health Epidemiology Reference Group. WHO estimates of the causes of death in children. *Lancet* 2005;**365**:1147–52.
- [10] Wardlaw T, Salama P, Johansson EW, Mason E. Pneumonia: the leading killer of children. *Lancet* 2006;**368**:1048–50.
- [11] Menendez C, Fleming AF, Alonso PL. Malaria-related anaemia. *Parasitol Today* 2000;**16**:469–76.
- [12] Steinhoff M, Black R. Childhood pneumonia: we must move forward. *Lancet* 2007;**369**:1409–10.
- [13] Duke T, Wandt F, Jonathan M, et al. Improved oxygen systems for childhood pneumonia: a multihospital effectiveness study in Papua New Guinea. *Lancet* 2008;**372**:1328–33.
- [14] Onyango FE, Steinhoff MC, Wafula EM, Wariua S, Musia J, Kitonyi J. Hypoxaemia in young Kenyan children with acute lower respiratory infection. *BMJ* 1993;**306**:612–5.
- [15] Ram FSF, Wellington SR, Rowe BH, Wedzicha JA. Non-invasive positive pressure ventilation for treatment of respiratory failure due to severe acute exacerbations of asthma. *Cochrane Database of Systematic Reviews* 2005, Issue 3. Art. No.: CD004360. <http://dx.doi.org/10.1002/14651858.CD004360.pub3>.
- [16] Ram FSF, Picot J, Lightowler J, Wedzicha JA. Non-invasive positive pressure ventilation for treatment of respiratory failure due to exacerbations of chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews* 2004,

- Issue 3. Art. No.: CD004104. <http://dx.doi.org/10.1002/14651858.CD004104.pub3>.
- [17] Vital FMR, Saconato H, Ladeira MT, et al. Non-invasive positive pressure ventilation (CPAP or bilevel NPPV) for cardiogenic pulmonary edema. Cochrane Database of Systematic Reviews 2008, Issue 3. Art. No.: CD005351. <http://dx.doi.org/10.1002/14651858.CD005351.pub2>.
- [18] Meduri GU. Noninvasive positive-pressure ventilation in patients with acute respiratory failure. *Clin Chest Med* 1996;**17**:513–53.
- [19] Antonelli M, Conti G, Rocco M, et al. A comparison of noninvasive positive-pressure ventilation and conventional mechanical ventilation in patients with acute respiratory failure. *N Engl J Med* 1998;**339**:429–35.
- [20] Girou E, Brun-Boisson C, Taille S, Lemaire F, Brochard L. Secular trends in nosocomial infections and mortality associated with noninvasive ventilation in patients with exacerbation of COPD and pulmonary edema. *JAMA* 2003;**290**:2985–91.
- [21] Ambrosino N, Vagheggin G. Noninvasive positive pressure ventilation in the acute care setting: where are we? *Eur Respir J* 2008;**31**:874–86.
- [22] Loh LE, Chan YH, Chan I. Noninvasive ventilation in children: a review. *J Pediatr (Rio J)* 2007;**83**(2 suppl):S91–9.
- [23] Teague WG. Non-invasive positive pressure ventilation: current status in paediatric patients. *Paediatr Respir Rev* 2005;**6**:52–60.
- [24] Yañez LJ, Yunge M, Emilfork M, et al. A prospective, randomized, controlled trial of noninvasive ventilation in pediatric acute respiratory failure. *Pediatr Crit Care Med* 2008;**9**:484–9.
- [25] Basnet S, Mander G, Andoh J, Klaska H, Verhulst S, Koirala J. Safety, efficacy, and tolerability of early initiation of noninvasive positive pressure ventilation in pediatric patients admitted with status asthmaticus: a pilot study. *Pediatr Crit Care Med* 2012;**13**:393–8.
- [26] Abadeso C, Nunes P, Silvestre C, Matias E, Loureiro H, Almeida H. Non-invasive ventilation in acute respiratory failure in children. *Pediatr Rep* 2012;**4**:e16.
- [27] Padman R, Lawless ST, Kettrick RG. Noninvasive ventilation via bilevel positive airway pressure support in pediatric practice. *Crit Care Med* 1998;**26**:169–73.
- [28] Munoz-Bonet JI, Flor-Macian EM, Rosello PM, et al. Noninvasive ventilation in pediatric acute respiratory failure by means of a conventional volumetric ventilator. *World J Pediatr* 2010;**6**:323–30.
- [29] Bernet V, Hug MI, Frey B. Predictive factors for the success of noninvasive mask ventilation in infants and children with acute respiratory failure. *Pediatr Crit Care Med* 2005;**6**:660–4.
- [30] Fortenberry JD, Del Toro J, Jefferson LS, Evey L, Haase D. Management of pediatric acute hypoxemic respiratory insufficiency with bilevel positive pressure (BiPAP) nasal mask ventilation. *Chest* 1995;**108**:1059–64.
- [31] Joshi G, Tobias JD. A five-year experience with the use of BiPAP in a pediatric intensive care unit population. *J Intensive Care Med* 2007;**22**:38–43.
- [32] Essouri S, Chevret L, Durand P, Haas V, Fauroux B, Devictor D. Noninvasive positive pressure ventilation: five years of experience in a pediatric intensive care unit. *Pediatr Crit Care Med* 2006;**7**:329–34.
- [33] Dohna-Schwake C, Stehling F, Tschiedel E, Wallot M, Mellies U. Non-invasive ventilation on a pediatric intensive care unit: feasibility, efficacy, and predictors of success. *Pediatr Pulmonol* 2011;**46**:1114–20.
- [34] Cavari Y, Sofer S, Rozovski U, Lazar I. Non invasive positive pressure ventilation in infants with respiratory failure. *Pediatr Pulmonol* 2012;**47**:1019–25.
- [35] Piastra M, De Luca D, Pietrini D, et al. Noninvasive pressure-support ventilation in immunocompromised children with ARDS: a feasibility study. *Intensive Care Med* 2009;**35**:1420–7.
- [36] Scarlett MD, Hanna WJ. Nasal non-invasive positive pressure ventilation. A new method of ventilatory support for patients with chronic respiratory failure. *West Indian Med J* 1994;**43**:143–5.
- [37] Thiéry G, Kovacević P, Straus S, et al. From mechanical ventilation to intensive care medicine: a challenge for Bosnia & Herzegovina. *Bosn J Basic Med Sci* 2009;**9**:S69–76.
- [38] Dunser MW, Festic E, Dondorp A, et al. Recommendations for sepsis management in resource-limited settings. *Intensive Care Med* 2012;**8**:3557–74.
- [39] Santhanam I, Sangareddi S, Venkataraman S, Kissoon N, Thiruvengadamudayan V, Kasthuri RK. A prospective randomized controlled study of two fluid regimens in the initial management of septic shock in the emergency department. *Pediatr Emerg Care* 2008;**24**:647–55.
- [40] Hussain SF, Haqqee R, Iqbal J. Non-invasive ventilation in the management of acute respiratory failure in Pakistan. *Trop Doct* 2004;**34**:238–9.
- [41] George IA, John G, John P, Peter JV, Christopher S. An evaluation of the role of noninvasive positive pressure ventilation in the management of acute respiratory failure in a developing country. *Indian J Med Sci* 2007;**61**:495–504.
- [42] Cam BV, Tuan DT, Fonsmark L, et al. Randomized comparison of oxygen mask treatment vs. nasal continuous positive airway pressure in dengue shock syndrome with acute respiratory failure. *J Trop Paediatr* 2002;**48**:335–9.
- [43] Wilson PT, Morris MC, Biagas KV, Otupiri E, Moresky RT. A randomized clinical trial evaluating nasal continuous positive airway pressure for acute respiratory distress in a developing country. *J Pediatr* 2013;**162**:988–92.
- [44] Lum LCS, Abdel-Latif ME, de Bruyne JA, Nathan Am, Gan CS. Noninvasive ventilation in a tertiary paediatric intensive care unit in a middle-income country. *Pediatr Crit Care Med* 2011;**12**:e7–13.
- [45] Marukatat C, Kuptanon T, Preuthipan A. Parameters of noninvasive ventilation (NIV) success in pediatric impending respiratory failure. *Paediatr Resp Rev* 2012;**13**(suppl1):S48.
- [46] Inter-agency Group for Child Mortality Estimation. Levels and trends in child mortality. Report 2011 http://childmortality.org/files_v10/download/Levels%20and%20Trends%20in%20Child%20Mortality%20Report%202011.pdf (accessed 14.12.12).
- [47] Asirifi Y. Child health: past, present and future challenges. *Ghana Med J* 2009;**43**:82–4.
- [48] Ghana Statistical Service; Ghana Health Service. *Ghana demographic and Health Survey 2008*. 2009.
- [49] United Nations development Programme Ghana Office, Accra. Sissala East District. Human Development Report 2010. www.undp-gha.org/design/docs/Sissala%20ACCOMPLISHED%20R%203.pdf (accessed 5.8.13).