

NIV: past, present and future

Anita K. Simonds

The history of NIV is an intertwining chronicle of the development of negative and positive pressure modes, as at different times in history, each mode has dominated. For example, in the mid-1980s, all patients using respiratory support received NPV, whereas the vast majority of our patients now use positive-pressure NIV, and there are hundreds of thousands of individuals with sleep apnoea worldwide receiving CPAP and many thousands using NIV for respiratory failure.

Indeed, the history of NIV dates right back to the beginning:

“And the LORD God formed man of the dust of the ground, and breathed into his nostrils the breath of life; and man became a living soul”.

Genesis 2: 7

So NIV existed before invasive ventilation! More scientifically, from an invasive ventilation perspective, there are descriptions going back to antiquity of tracheostomy, and these are found in the medieval period and 1500s too. Vesalius, in the 16th century, was aware that positive pressure applied to the trachea would inflate the lungs and Hooke demonstrated that it was possible to keep a dog alive by applying bellows to the upper airway in 1667. For verifiable human accounts, we need to advance to the 18th century – and first deal with NPV.

Woolam (1976) credits John Dalziel, a Scot, as the first to describe a tank ventilator/iron lung type device and a fellow Scot, Alexander Graham Bell, developed the notion further. Bell is best known for inventing the forerunner of the telephone in 1876 but, in 1881, his first child Edward died of respiratory distress a few hours after birth. The story goes that shortly afterwards Bell was walking along a shingle beach in Ontario when the idea of a negative-pressure jacket to assist the breathing of infants came to him. He went on to patent this device. Figure 1 is an extract from his notebook, although it is quite difficult to decipher.

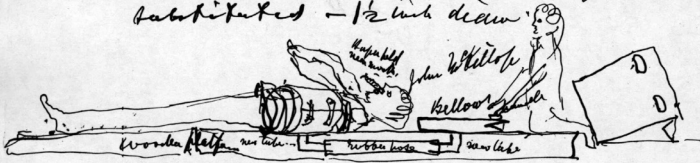
Key points

- The development of negative- and positive-pressure NIV is inextricably linked.
- NIV is one of the most evidence-based areas of respiratory medicine and indications for NIV continue to increase in number.

150

1892 Sept. 14 - Wed - at 186. Lub.

Exp. 1 Old ~~brass~~ vacuum jar made in England for me - many years ago - and returned by W. McCleary from Prof. Geo. of King's College - London - has been put in order for trial. Brass pipe attached seemed to have two small channels - so it has been removed and larger tube substituted - $\frac{1}{2}$ inch diam.



John McKillop submitted to experiment - seemed to succeed perfectly. W. Ellis worked bellows. John McKillop stated that he made no effort to breathe - yet a piece of paper was moved to and fro when held in front of

Figure 1. Drawing of a negative pressure device for children by Alexander Graham Bell. Image: US Library of Congress, Washington, DC, USA.

In fairness, similar ideas were flourishing elsewhere, in Europe, but it was not until the 1920s that an iron lung with a motorised pump was developed by Drinker in 1928 in the USA and demonstrated in London in 1931. This concept then entered the medical mainstream, disseminated by a brisk correspondence in the *Lancet*. That was fortuitous, as the coming scourge was epidemics of poliomyelitis, which had begun in the First World War and swept across Europe and the USA in the 1930s-1950s. Polio paralyses the respiratory muscles as well as limbs muscles, resulting in respiratory failure. Iron lungs were pressed into action, including the intimidating multitier versions in figure 2. There is no doubt that iron lungs saved thousands of lives but they were big, cumbersome and expensive (the original Drinker ventilator cost \$1500 - equivalent to the cost of a US new-build house at the time), and so were not going to be a practical way forward in respiratory care. In their observations on the use of negative-pressure respirators in polio, Plum and Wolff (1951) found that the tank ventilator was safest for managing respiratory insufficiency and that in the acute phase of polio, the cuirass was too inefficient. Upper airway obstruction provoked by the negative pressure was a common problem.

Practical limitations were compounded by the huge outbreak of polio in Denmark in 1952, which was associated with a very high prevalence of cases with bulbar weakness. Not only was an insufficient number of iron lungs available but these were also inadequate in caring for patients with bulbar problems - mortality rose to 90% and the only solution open to Ibsen (1954) and the Danish anaesthetic and medical teams was invasive positive-pressure ventilation *via* a tracheostomy Purchased by ,



Figure 2. Multitier iron lung used in poliomyelitis epidemics. Reproduced from Kacmarek (2011) *Respir Care*; 56: 1170–1180 with permission from the publisher.

or endotracheal tube. This switch to positive pressure continued and iron lungs began to disappear, heralding the arrival of the modern ICU. There was a brief resurgence of NPV in the 1970s and 1980s, but mainly to care for those with chronic ventilatory failure.

Turning to the development of noninvasive positive pressure, this started at a slightly earlier time. Possibly the first well documented use of mask ventilation, in the 1760s, was in “resuscitation boxes”, which contained bellows to insufflate the lungs, tubing and glass nasal masks, and were placed by the Royal Humane Society (London, UK) to be used in the rescue of “drowned persons”. The first was located by the Serpentine Lake in Hyde Park, London. Ice skating was much in vogue at that time and the Serpentine froze in the winter. It seems children frequently fell through the ice and had to be rescued; there is even a protocol for the resuscitation of children rescued from a frozen lake. In retrospect, it is difficult to think of a better prognostic group to resuscitate – young, fit and cooled, providing they were retrieved quickly enough.

But this was all manually applied positive-pressure ventilation and the first true motorised ventilator did not appear until the turn of the 20th century. In May 1908, under the headline “Smother small dog to see it revived”, *The New York Times* described a demonstration to the King County Medical Society, in Brooklyn, NY, USA, of a mechanised ventilator developed by Prof. George Poe (spookily related to mystery writer Edgar Allan Poe). A young boy was given a quarter to find a stray dog on the streets and this “cur” was smothered till apparently lifeless and then successfully resuscitated with the ventilator, to the acclaim of the audience! So, a good day for ventilators, but a bad day for stray dogs in Brooklyn.

The best description of use in real clinical practice comes from Germany with the Dräger Pulmotor (Drägerwerk AG, Lubeck, Germany). This was patented by Heinrich Dräger in 1907 and was an innovative time-cycled device that delivered positive pressure during inspiration and negative pressure during expiration. However, it had a flaw in that the mask was connected to the ventilator by a

single limb of tubing, meaning that the carbon dioxide in the exhaled breath was rebreathed, which could eventually result in asphyxiation. Fortunately, Heinrich's son Bernard redesigned the circuitry with two sets of tubing, one for inhalation, the other for exhalation, which solved that problem; this modification went into production and 30 years later, the 12000th Pulmotor rolled off the production line in Lubeck. The Pulmotors were supplied to mines for poisoning accidents, to deal with victims of fires and for other acute uses. This is crucial, as the stimulus for ventilator use had been entirely for ARF up to this point.

It was not until the 1970s and 1980s that long-term chronic use began to be the spur to ventilatory progress. This was partly related to better understanding of the physiology of breathing during sleep, the rediscovery of sleep apnoea and CPAP therapy, and underlying global trends in the switch from acute to chronic healthcare. OSA is associated with recurrent episodes of upper airway obstruction, which can lead to a number of vascular complications if not addressed, but which Sullivan showed in 1981 could be effectively treated with CPAP, as the air-flow splints the airway open. In addition, developments in masks and technology extended NIV to respiratory failure in patients with neuromuscular disease.

The original CPAP machines were very large – about the size of a vacuum cleaner – but have improved, and become smaller and portable over time. Importantly, mask design and comfort have improved too. To complete the timeline, the developments from the end of the 1980s to the present are shown in figure 3.

A great deal of progress has occurred such that NIV is now one of the most evidence-based areas of respiratory medicine, as this handbook will describe. Really significant interventions are the discovery and confirmation by RCT that NIV halves mortality and morbidity in acute exacerbations of COPD, and this

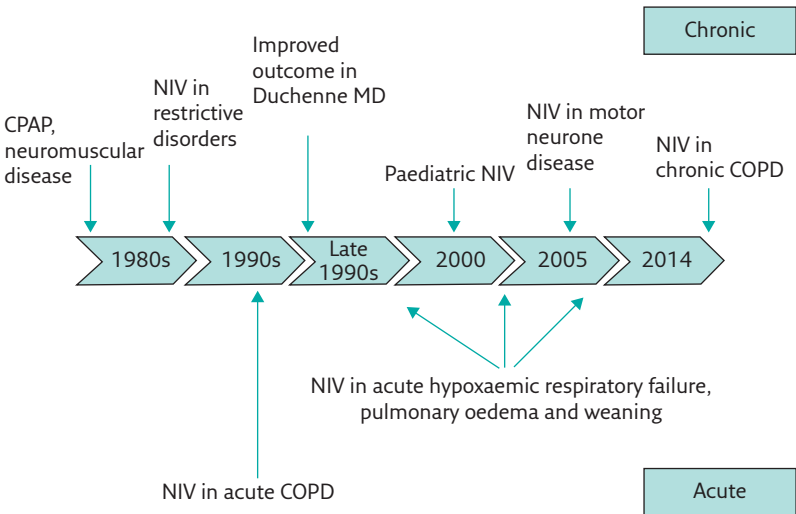


Figure 3. Timeline of developments in NIV from the 1980s to the present day. MD: muscular dystrophy.

provides the rationale for NIV to be available in every acute unit that admits respiratory patients, and for NIV to be used post-operatively in high-risk patients and for weaning. An additional major change in the past 30–40 years has been the increasing indications for long-term, chronic NIV and, of course, long-term application of CPAP in OSA.

For patients with a range of causes of ventilatory failure, the natural history progresses from normal breathing, to a gradual loss in lung volumes and then, initially, changes in blood gases are seen at night due to hypoventilation, and if that is not addressed, ultimately, progression to daytime respiratory failure, cardiac decompensation and premature death. The interval between the onset of respiratory failure and death may be as short as a few years. In Duchenne muscular dystrophy, once a patient has developed a raised carbon dioxide level during the day, there is a 90% chance that they will be dead within a year.

Figure 4 shows the long-term outcome of different groups of patients treated with NIV having developed severe ventilatory failure or progressed to cor pulmonale pretreatment. In post-polio patients, 5-year survival with NIV is 100% and it appears that these individuals will live to their normal life expectancy. 5-year survival is ~80% in the other restrictive conditions. Results are less good in COPD and bronchiectasis for two reasons: these are intrinsic lung disease conditions rather than being restrictive disorders with normal lungs, and the patients were severely end-stage when treated – with some being on the transplant waiting list. In COPD, recent trials have shown NIV may be of benefit in stable hypercapnic patients, as discussed further in the section entitled “Chronic NIV in COPD”. In Duchenne patients, median survival is now nearly 30 years, and around a third of our Duchenne patients are living into their late thirties and early forties.

NIV has been extended to the paediatric age range, with the feasibility of using NIV to control nocturnal hypoventilation in children initially being demonstrated

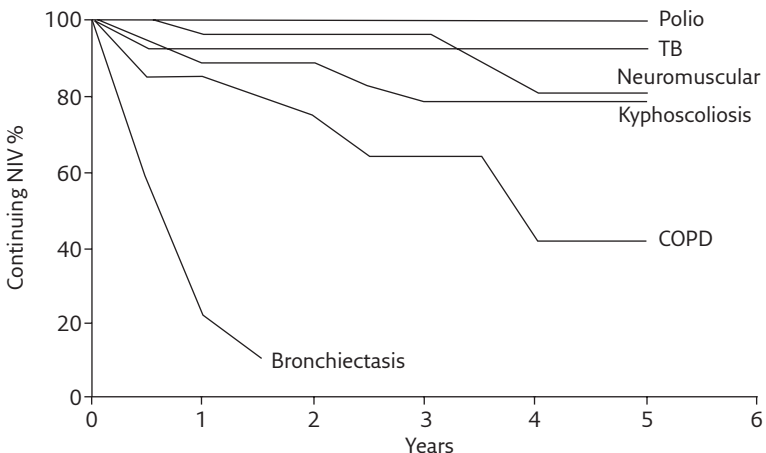


Figure 4. Probability of continuing NIV long term, which is equivalent to survival in most cases. Reproduced from Simonds et al. (1995) with permission from the publisher. Purchased by,

predominantly in neuromuscular conditions. Many of these children now survive to adolescence or adulthood, as shown in the section entitled “Chronic NIV in hereditary neuromuscular disorders”. Furthermore, characterisation of the genotypes and phenotypes of some congenital disorders (*e.g.* congenital myasthenia and congenital muscular dystrophies) has clarified the natural history of these conditions, thereby facilitating anticipatory care plans and enabling personalised ventilatory care.

Present trends

There is also growing interest in NIV in cardiology. There is no doubt that patients with heart disease and OSA benefit from treatment of the OSA. By contrast, Cheyne-Stokes respiration is a form of central sleep apnoea that has been recognised for centuries in chronic heart failure. It was previously thought to be simply a marker of severe disease and an epiphenomenon, but recently, the link to the progression of disease has been explored and it has been found to be more prevalent in milder cases. This is important, as heart failure is common and the majority of those affected have mild cardiac impairment. Recent work shows that around half of patients with mild heart failure have sleep disordered breathing too. CPAP can be used to treat OSA but does not work in central sleep apnoea or Cheyne-Stokes respiration. The new ventilatory concept of ASV aims to smooth out the Cheyne-Stokes pattern and, in doing so, may reduce associated sympathetic stimulation and arousals from sleep (see the section entitled “Chronic NIV in heart failure patients: ASV, NIV and CPAP”). Several large international multicentre trials of ASV in heart failure patients with predominant central sleep apnoea are now in progress, with cardiac and all-cause mortality or unplanned admissions as major outcome measures. However early results suggest ASV may not improve outcome contrary to expectations, and may cause harm in severe heart failure patients with central sleep apnoea.

Palliative care

NIV is now being used in some situations to palliate symptoms without the aim of prolonging survival or substantially modifying arterial blood gas tensions. Here, goals such as reduction in dyspnoea and control of symptoms of nocturnal hypoventilation should be set pre-emptively so that if these are not met, NIV can be discontinued and palliative efforts directed elsewhere. Nava *et al.* (2013) have shown that in oncology patients with solid tumours complicated by ARF and an expected life expectancy of <6 months, NIV reduced dyspnoea more rapidly than oxygen therapy alone and patients required less morphine. The benefit was most marked in hypercapnic patients and within the first hour of therapy, suggesting that responses can be rapidly gauged. NIV combined with cough-assist devices can also be used to manage severely ill type 1 spinal muscular atrophy infants with the aim of discharging the patient to their home and managing breathlessness.

However, these approaches have been used in units familiar with NIV, and wide translation to oncology units and other palliative care centres needs to be carefully considered and managed. The use of NIV to palliate symptoms is discussed further in the section entitled “NIV in palliative care and at the end of life”.

Implementation of NIV in clinical practice

The newer applications discussed above underscore a problem of implementation of “good practice” in NIV, which affects all units to a greater or lesser extent. There is evidence that patients who would benefit from NIV are not receiving it even for gold standard indications, such as acute hypercapnic exacerbation of COPD, for a number of reasons, but mainly because the medical team does not feel skilled enough to deliver it. Of course, the answer to this problem is to provide knowledge and skills to remedy these deficiencies, which is the purpose of this handbook, many NIV courses and the ERS Skills-based Simulator Training in Non-Invasive Ventilation.

Intelligent ventilators

The question arises, if medical teams are inexperienced, can you make the ventilator intelligent? A variety of approaches have been adopted in the past few years to try to combine bilevel pressure support with the delivery of an assured minute ventilation or V_t . The underlying aim of these modes is to better adapt to the patient’s own ventilatory requirements, which will vary during different stages of sleep and with different activities during the day. Some devices also have an “intelligent” backup rate and a “learn” mode in which the ventilator adapts to patient’s respiratory effort and pattern.

AVAPS was one of the first of these new modes. An initial randomised cross-over trial of AVAPS *versus* standard pressure support in obesity hypoventilation patients showed a small improvement on nocturnal carbon dioxide tension but no long-term quality of life improvement. Murphy *et al.* (2012) confirmed there was no long-term advantage of using AVAPS over optimally titrated bilevel pressure support in very obese patients, and results in COPD patients are equivocal. The IVAPS ventilator targets V_t rather than minute ventilation and has been shown to produce equivalent control of nocturnal hypoventilation to a group of patients expertly set-up on NIV. In addition, in a group with predominantly restrictive disorders starting NIV for the first time, IVAPS resulted in improved adherence overnight and a reduction in stage 1 sleep, suggesting sleep initiation when starting NIV was improved. These results suggest that intelligent modes of ventilation may have a role in certain subgroups but they have not been demonstrated to be superior to conventional pressure support NIV in all patient groups.

Other developments

Interface development has also advanced very significantly, with better choice and design particularly the use of softer contoured material, rather than rigid plastic or vinyl. However, problems with pressure sores and midfacial hypoplasia have not yet been solved and tactics to overcome these issues are discussed in the section entitled “Choosing the interface”.

Organisation and delivery of ventilatory care is likely to evolve too. In acute NIV, there has been a trend to manage sicker patients successfully in high-dependency units. For homecare, greater information from ventilator software enables problems to be solved remotely, and telemonitoring approaches are increasing but need to be validated. There is every hope that the future of NIV will be as exciting as its past!

Further reading

- Bradley TD, *et al.* (2003). Sleep apnea and heart failure. Part I: obstructive sleep apnea. *Circulation*; 107: 1671–1678.
- Bradley TD, *et al.* (2005). Continuous positive airway pressure for central sleep apnea and heart failure. *N Engl J Med*; 353: 2025–2033.
- Carlucci A, *et al.* (2003). Changes in the practice of non-invasive ventilation in treating COPD patients over 8 years. *Intensive Care Med*; 29: 419–425.
- Chatwin M, *et al.* (2011). Outcome of goal-directed non-invasive ventilation and mechanical insufflation/exsufflation in spinal muscular atrophy type I. *Arch Dis Child*; 96: 426–432.
- Fauroux B, *et al.* (1995). Home treatment for chronic respiratory failure in children: a prospective study. *Eur Respir J*; 8: 2062–2066.
- Ibsen B (1954). The anaesthetist's viewpoint of the treatment of respiratory complications in poliomyelitis during the epidemic in Copenhagen, 1952. *Proc R Soc Med*; 47: 72–74.
- Jaye J, *et al.* (2009). Autotitrating *versus* standard noninvasive ventilation: a randomised crossover trial. *Eur Respir J*; 33: 566–571.
- Jenkinson C, *et al.* (1999). Comparison of therapeutic and subtherapeutic nasal continuous positive pressure airway pressure for obstructive sleep apnoea: a randomised prospective parallel trial. *Lancet*; 353: 2100–2105.
- Köhnlein T, *et al.* (2014). Non-invasive positive pressure ventilation for the treatment of severe stable chronic obstructive pulmonary disease: a prospective multi-centre, randomised, controlled clinical trial. *Lancet Respir Med*; 2: 698–705.
- Lloyd-Owen SJ, *et al.* (2005). Patterns of home mechanical use in Europe: results from the Eurovent survey. *Eur Respir J*; 25: 1025–1031.
- Maheshwari V, *et al.* (2006). Utilization of noninvasive ventilation in acute care hospitals: a regional survey. *Chest*; 129: 1226–1233.
- Murphy PB, *et al.* (2012). Volume targeted *versus* pressure support non-invasive ventilation in patients with super obesity and chronic respiratory failure: a randomised controlled trial. *Thorax*; 67: 727–734.
- Nava S, *et al.* (1998). Noninvasive mechanical ventilation in the weaning of patients with respiratory failure due to chronic obstructive pulmonary disease. A randomized controlled trial. *Ann Intern Med*; 128: 721–728.
- Nava S, *et al.* (2013). Palliative use of non-invasive ventilation in end-of-life patients with solid tumours: a randomised feasibility trial. *Lancet Oncol*; 14: 219–227.
- Plant PK, *et al.* (2000). Early use of noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease on general respiratory wards: a multi-centre randomised controlled trial. *Lancet*; 355: 1931–1935.
- Plum F, *et al.* (1951). Observations on acute poliomyelitis with respiratory insufficiency. *JAMA*; 146: 442–446.

Purchased by ,

- Shaw LA, *et al.* (1929). An apparatus for the prolonged administration of artificial ventilation. *J Clin Invest*; 8: 33–46.
- Simonds AK, *et al.* (1995). Outcome of domiciliary nasal intermittent positive pressure ventilation in restrictive and obstructive disorders. *Thorax*; 50: 604–609.
- Simonds AK, *et al.* (2000). Outcome of paediatric domiciliary mask ventilation in neuromuscular and skeletal disease. *Eur Respir J*; 16: 476–481.
- Storre JH, *et al.* (2006). Average volume-assured pressure support ventilation in obesity hypoventilation. A randomised crossover trial. *Chest*; 130: 815–821.
- Sullivan CE, *et al.* (1981). Reversal of obstructive sleep apnoea by continuous positive pressure applied through the nares. *Lancet*; 1: 862–865.
- Vazir A, *et al.* (2007). A high prevalence of sleep disordered breathing in men with mild symptomatic chronic heart failure due to left ventricular systolic dysfunction. *Eur J Heart Fail*; 9: 243–250.
- Vianello A, *et al.* (1994). Long-term nasal intermittent positive pressure ventilation in advanced Duchenne’s muscular dystrophy. *Chest*; 105: 445–448.
- Woollam CHM (1976). The development of apparatus for intermittent negative pressure respiration (1) 1832–1918. *Anaesthesia*; 31: 537–547.
- Woollam CHM (1976). The development of apparatus for intermittent negative pressure respiration (2) 1919–1976. *Anaesthesia*; 31: 666–685.

Online resources

- Hare A, *et al.* Skills-based Simulator Training in Non-Invasive Ventilation. www.ers-education.org/Media/Media.aspx?idMedia=234264