BMJ Open  Resource use, characteristics and outcomes of prolonged non-invasive ventilation: a single-centre observational study in China

Jun Duan, Linfu Bai, Lintong Zhou, Xiaoli Han, Lei Jiang, Shicong Huang

ABSTRACT

Objective To report the resource use, characteristics and outcomes of patients with prolonged non-invasive ventilation (NIV).

Design A single-centre observational study.

Setting An intensive care unit of a teaching hospital.

Participants Patients who only received NIV because of acute respiratory failure were enrolled. Prolonged NIV was defined as subjects who received NIV ≥14 days. A total of 1539 subjects were enrolled in this study; 69 (4.5%) underwent prolonged NIV.

Main outcome measures Predictors of prolonged NIV and hospital mortality.

Results The rate of do-not-intubate (DNI) orders was 9.1% (140/1539). At the beginning of NIV, a DNI order (OR 3.95, 95% CI 2.25 to 6.95) and pH ≥7.35 (2.20, 1.27 to 3.82) were independently associated with prolonged NIV. At days 1 and 7 of NIV, heart rate (1.01 (1.00 to 1.03) and 1.02 (1.00 to 1.03), respectively) and PaO2/FiO2 <150 (2.19 (1.25 to 3.85) and 2.05 (1.04 to 4.04), respectively) were other independent risk factors for prolonged NIV. When patients who died after starting NIV but prior to 14 days were excluded, the association was strengthened.

Regarding resource use, 77.1% of subjects received NIV<7 days and only accounted for 47.0% of NIV-days. However, 18.4% of subjects received NIV 7–13.9 days and accounted for 33.4% of NIV-days, 2.9% of subjects received NIV 14–20.9 days and accounted for 9.5% of NIV-days, and 1.6% of subjects received NIV≥21 days and accounted for 10.1% of NIV-days.

Conclusions Our results indicate the resource use, characteristics and outcomes of a prolonged NIV population with a relatively high proportion of DNI orders. Subjects with prolonged NIV make up a high proportion of NIV-days and are at high risk for in-hospital mortality.

INTRODUCTION

Non-invasive ventilation (NIV) improves oxygenation and reduces the work of breathing in subjects with hypoxaemia or hypercapnia, reduces intubation rates in subjects with acute respiratory failure, shortens the duration of invasive mechanical ventilation and reduces ventilator-associated pneumonia when used to facilitate early liberation from invasive mechanical ventilation. It also reduces postextubation respiratory failure in subjects at high risk for reintubation. A previous study reported that NIV significantly decreased pooled hospital mortality, based on data from 78 randomised controlled trials.

Given the benefits of NIV, its utilisation has dramatically increased in recent years in subjects with hypoxaemic or hypercapnic respiratory failure. This in turn has led to a sharp increase in admissions to intensive care units (ICUs) for NIV. This has taxed many ICUs, which have been unable to meet the higher demand for such treatment of critically ill patients. Of subjects who receive invasive mechanical ventilation, 4.4% of them spend more than 21 days on the ventilator but consume 29.1% of ICU beds. In addition, the rate of hospital mortality is high (20%–40%) in patients given long-term mechanical ventilation. The statistical data of prolonged invasive mechanical ventilation may help decision makers and clinicians improve management (eg, in developing prognostic modes and building regional weaning centres). However, recent studies have focused only on invasive mechanical ventilation. The resource
Duan J, et al. BMJ Open 2018;8:e019271. doi:10.1136/bmjopen-2017-019271

Open access

use, characteristics and outcomes of NIV are lacking. Therefore, we investigated these factors.

METHODS
Patient and public involvement
This was a single-centre observational study performed in a respiratory ICU (18 ICU beds, 600–800 admissions per year) of a teaching hospital from May 2011 to July 2017. All subjects who were admitted to our ICU for NIV because of respiratory failure were enrolled. To avoid confounders, we excluded subjects who received both NIV and invasive mechanical ventilation during hospitalisation. We referenced the cut-off value of prolonged mechanical ventilation and defined subjects who used NIV >14 days as prolonged NIV. A do-not-intubate (DNI) order can be made at ICU admission or at NIV as a first-line treatment failure. It was decided by patients themselves or their families.

PROCEDURE
NIV (BiPAP Vision or V60; Philips Respironics, Carlsbad, California, USA) was initiated based on the following criteria, but it was decided by attending physicians at their discretion: PaO$_2$ <60 mm Hg at room air, PaCO$_2$ >45 mm Hg, pH <7.35 and clinical presentation of respiratory distress at rest (such as active contraction of the accessory inspiratory muscles or paradoxical abdominal motion).

NIV was managed as previously described. The use of an oronasal mask (ZS-MZA Face Mask; Shanghai Zhongshan Medical Technology, Shanghai, China) was the first choice for NIV treatment. Mask size was optimised to fit each subject’s face. In addition, to balance the trade-off between mask tightness (to minimise air leakage) and the propensity of the mask interface to cause skin lesions, we adjusted the straps to be as tight as comfortably possible while allowing air leaks at <30 L/min. The temperature of the sterile water in the humidifier was monitored and adjusted based on each subject’s comfort, tolerance and adherence. Intermittent drinking was administrated if the subject felt thirsty. If there were no contraindications, the head of the bed was elevated to 30–45° to limit aspiration risk. To prevent hospital-acquired infections, a

Table 1 continued

| Variable                                      | NIV duration<14 days | NIV duration≥14 days | P value |
|----------------------------------------------|----------------------|----------------------|---------|
| pH                                           | 7.42±0.06            | 7.44±0.06            | 0.09    |
| PaCO$_2$, mm Hg                              | 50±15                | 48±15                | 0.30    |
| PaO$_2$/FiO$_2$                               | 228±87               | 195±72               | <0.01   |

*At day 1 of NIV, only 1158 patients were left in the study. †At day 7 of NIV, only 343 patients were left in the study (9 patients were excluded because some data were unavailable).

AECOPD, acute exacerbation of chronic obstructive pulmonary disease; ARDS, acute respiratory distress syndrome; GCS, Glasgow Coma Scale; NIV, non-invasive ventilation.

Continued
Disposal bacterial filter was placed between the circuit and the ventilator. The bacterial filter was changed every day, and the ventilator circuit was changed every 7 days, in line with our hospital protocol.

The attending physicians or respiratory therapists selected the mode of the ventilator (continuous positive airway pressure (CPAP) or spontaneous/time [S/T]). CPAP is usually used in heart failure subjects or hypoxaemic subjects without laboured breathing. S/T, a bilevel positive airway pressure system used in assisted-control mode, is usually applied to hypercapnic subjects or hypoxaemic subjects whose accessory respiratory muscles show vigorous activity. FiO$_2$ was set to maintain SpO$_2$ >92%. During NIV intervention, if respiratory failure worsened and reached the criteria of intubation, then intubation for invasive mechanical ventilation was performed. Intubation was performed according to previously described criteria.$^{19}$ However, in subjects with DNI orders, NIV was continued. If the respiratory failure was reversed, liberation from NIV was performed according to hospital protocol.$^{20}$

Immediately before NIV, we collected data on age, sex, diagnosis, disease severity (assessed by APACHE II score), heart rate, respiratory rate, blood pressure, consciousness (assessed using the Glasgow Coma Scale (GCS)) and arterial blood gas tests. Data on these variables were also collected after 24 hours (day 1) and 7 days of NIV. We also collected information on variables reflecting outcomes such as duration of NIV, duration of ICU stay and hospital mortality.

**Statistical Analyses**

We analysed the data using statistical software (SPSS V.17.0). An unpaired Student’s t-test was used to analyse normally distributed continuous variables, and the $\chi^2$ test was used to analyse categorical variables. For abnormally distributed continuous variables, the Mann-Whitney U test was used. At the beginning of NIV, variables with a $p$ value $<$0.2 in univariate analyses were entered into multivariate analyses (forward stepwise multiple logistic regression analyses) to identify independent risk factors.

| Table 2 | Univariate and multivariate analyses of the risk factors associated with prolonged NIV |
|---------|----------------------------------------------------------------------------------|
|         | Univariate analyses | Multivariate analyses |
|         | OR (95% CI) | P value | OR (95% CI) | P value |
| Model 1 | Variables collected at the beginning of NIV | | | |
| Age, years | 1.02 (1.00 to 1.04) | 0.08 | – | – |
| Do-not-intubate order | 4.24 (2.42 to 7.42) | $<$0.01 | 3.95 (2.25 to 6.95) | $<$0.01 |
| Heart rate, beats/min | 1.01 (1.00 to 1.02) | 0.14 | – | – |
| PH≥7.35 | 2.36 (1.37 to 4.08) | $<$0.01 | 2.20 (1.27 to 3.82) | $<$0.01 |
| PaCO$_2$>45 mm Hg | 0.68 (0.42 to 1.09) | 0.11 | – | – |
| PaO$_2$/FiO$_2$<150 | 1.35 (0.83 to 2.19) | 0.22 | – | – |
| Diagnosis as AECOPD | 0.71 (0.44 to 1.16) | 0.17 | – | – |
| Diagnosis as pneumonia | 1.82 (1.09 to 3.03) | 0.02 | – | – |
| Diagnosis as pulmonary cancer | 2.70 (1.19 to 6.15) | 0.02 | – | – |
| Model 2 | Variables collected at day 1 of NIV | | | |
| Heart rate, beats/min | 1.02 (1.01 to 1.03) | $<$0.01 | 1.01 (1.00 to 1.03) | 0.02 |
| Respiratory rate, breaths/min | 1.04 (1.01 to 1.08) | 0.02 | – | – |
| PH≥7.35 | 1.02 (0.46 to 2.27) | 0.97 | – | – |
| PaO$_2$/FiO$_2$<150 | 2.39 (1.38 to 4.12) | $<$0.01 | 2.19 (1.25 to 3.85) | $<$0.01 |
| Model 3 | Variables collected at day 7 of NIV | | | |
| Heart rate, beats/min | 1.02 (1.00 to 1.03) | 0.01 | 1.02 (1.00 to 1.03) | 0.04 |
| PH≥7.35 | 1.41 (0.47 to 4.23) | 0.54 | – | – |
| PaO$_2$/FiO$_2$<150 | 2.19 (1.14 to 4.19) | 0.02 | 2.05 (1.04 to 4.04) | 0.04 |

Model 1, c-statistic=0.65 (95% CI 0.58 to 0.72).
Model 2, c-statistic=0.66 (95% CI 0.60 to 0.72).
Model 3, c-statistic=0.64 (95% CI 0.56 to 0.71).
AECOPD, acute exacerbation of chronic obstructive pulmonary disease; NIV, non-invasive ventilation.
The same method was used at days 1 and 7 to identify independent risk factors for prolonged NIV in subjects who were still on NIV. The c-statistic was used to analyse the predictive power. A p value <0.05 was considered significant.

RESULTS

We enrolled 1539 subjects in this study. The rate of DNI orders was 9.1% (140/1539), the rate of prolonged NIV was 4.5% (69/1539) and hospital mortality was 16.6% (256/1539). At days 1 and 7 of NIV, 1158 and 343 patients were left in the study, respectively. The demographics of patients are summarised in table 1.

Table 2 shows three models developed to identify independent risk factors associated with prolonged NIV. In model 1, a DNI order (OR 3.95, 95% CI 2.25 to 6.95) and pH ≥7.35 (2.20, 1.27 to 3.82) were independently associated with prolonged NIV. The c-statistic was 0.65 (95% CI 0.58 to 0.72) in model 1. At days 1 and 7 of NIV, heart rate (OR 1.01, 95% CI 1.00 to 1.03, and 1.02, 1.00 to 1.03, respectively) and PaO₂/FiO₂<150 (2.19, 1.25 to 3.85, and 2.05, 1.04 to 4.04, respectively) were other independent risk factors for prolonged NIV. The c-statistic was 0.66 (95% CI 0.60 to 0.71) and 0.64 (0.56 to 0.71) in models 2 and 3, respectively. Out of all patients given NIV for <14 days, 220 patients (14.5%) died. When these patients were excluded, the association for prolonged NIV. The same method was used at days 1 and 7 to identify independent risk factors for prolonged NIV in subjects who were still on NIV. The c-statistic was used to analyse the predictive power. A p value <0.05 was considered significant.
was strengthened (table 3). Furthermore, ICU and hospital stays increased with an increase in NIV days (table 4).

The proportion of subjects who used NIV <7 days was 77.1%, and they accounted for 47.0% of NIV-days (figure 1). In contrast, 18.4%, 2.9% and 1.6% of subjects used NIV 7–14 days, 14–21 days and >21 days but accounted for 33.4%, 9.5% and 10.1% of NIV-days, respectively.

**DISCUSSION**

In this study, we enrolled a large number of NIV patients, and a small proportion of these patients required prolonged NIV. However, patients with prolonged NIV accounted for a large proportion of NIV-days. At the beginning of NIV, a DNI order and pH ≥7.35 were independent risk factors for prolonged NIV. Tachycardia and low oxygenation were other independent risk factors for prolonged NIV at days 1 and 7 in subjects who were still on NIV.

The use of NIV has sharply increased in recent years.10 23 However, ICU beds are scarce resources. Refusal of or delayed ICU admission due to a full unit is associated with increased cardiac arrest and mortality.24–27 Therefore, it is important to reserve ICU beds for patients who require them the most. In the management of patients receiving invasive mechanical ventilation, it is cost-effective to transfer them from the ICU to a regional weaning centre when they reach prolonged ventilation status. In this study, we investigated the resource use, characteristics and outcomes of subjects who required prolonged NIV. Generally speaking, patients receiving prolonged NIV are in a less severe state than those who require prolonged mechanical ventilation. Thus, it may be possible to transfer such patients to a regional weaning centre. However, the benefits and risks of doing this require further exploration.

A multicentre observational study reported that one-fifth of ICU subjects who received NIV in France and Belgium had DNI orders.30 The hospital mortality of such patients ranged from 44% to 74%, much higher than subjects without a DNI order.30–32 In our study, a DNI order was an independent risk factor for prolonged NIV. As ICU beds are a scarce resource, it may benefit more patients if NIV is used in subjects without a DNI order. However, cultural norms and ethics differ among different countries. In some countries, NIV may be terminated in palliative care patients with a DNI order when they require intubation; this would lead to a shorter NIV duration. However, in other countries, NIV may be used in palliative care.33 In the present study, we enrolled patients who received NIV as palliative care with a DNI order. We believe this is valuable to patients and clinical practitioners who use NIV in this situation.

An interesting result of our study is that pH >7.35 at initiation of NIV was an independent risk factor for prolonged NIV; a pH <7.35 indicated acidosis. We speculate that patients with a pH <7.35 are more likely to receive intubation and to die within 14 days of NIV. Other independent risk factors for prolonged NIV were tachycardia and low oxygenation at days 1 and 7 of NIV. It is not surprising that such patients require ventilation support and thus NIV was prolonged.

We also found that the proportion of subjects who required NIV for >14 days was small. However, they accounted for many more NIV-days than other subjects. As ICU space is limited, it is important to appropriately identify which subjects require admission to an ICU. In fact, many studies have reported that use of NIV in the general ward is safe and feasible.34–36 Thus, it may be a good idea to assign subjects who require prolonged NIV while they are in the general ward. In addition, high-flow nasal oxygen benefits patients with acute respiratory failure in the same as does NIV.37 38 Hence, it is another

| Duration of NIV, days | <7 days n=1187 | 7–13.9 days n=283 | 14–20.9 days n=45 | ≥21 days n=24 | P value |
|-----------------------|----------------|------------------|------------------|--------------|---------|
| Duration of NIV, days | 3.0 (1.7–4.0) | 9.0 (7.8–10.8) | 16.7 (15.1–18.6) | 30.0 (23.3–35.2) | <0.01 |
| ICU stay, days        | 4.7 (2.8–6.6) | 10.2 (8.9–13.2) | 18.0 (16.1–19.8) | 32.7 (25.2–47.3) | <0.01 |
| Hospital stay, days   | 10.6 (5.9–16.1) | 16.8 (12.5–25.9) | 21.0 (18.5–28.7) | 43.8 (30.8–61.9) | <0.01 |
| Hospital mortality    | 15.3% | 13.4% | 51.1% | 54.2% | <0.01 |

As the duration of NIV, ICU stay and hospital stay were not normally distributed variables, they are reported as medians and IQRs.

ICU, intensive care unit; NIV, non-invasive ventilation.

**Figure 1** Distribution of resource use classified by duration of non-invasive ventilation (NIV). ICU, intensive care unit.
choice for subjects with respiratory failure if NIV is unavailable.

Our study had several limitations. First, we enrolled subjects who used NIV only. As patients who use both NIV and invasive mechanical ventilation may have longer ICU/hospital stays, our study may underestimate the resource use of patients who received NIV. In addition, our selection method may have led to an artificially high number of DNI orders relative to the general population. Thus, whether DNI orders are an independent risk factor for prolonged NIV should be confirmed across all patient groups. Second, this was a single-centre observational study. NIV was managed in the context of the local culture and our hospital protocol. As different centres may have different protocols, extrapolating our results to other centres should be done cautiously. Third, patients who received prolonged NIV had higher rates of pneumonia and pulmonary cancer. When we considered this in multivariate analyses, these patients did not remain in the final model. This indicates that these variables contribute little to the final model.

CONCLUSION

Our data indicate the resource use, characteristics and outcomes of a prolonged NIV population with a relatively high rate of DNI orders. Subjects with prolonged NIV form a small NIV population but account for a high proportion of NIV-days.

Contributors JQ designed this study, joined in data collection, analysed the data and prepared the manuscript. LB, LZ and XH joined in data collection, data analysis and manuscript preparation. LJ joined in data analysis, data interpretation and manuscript preparation. SH joined in data interpretation and manuscript revision.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Not required.

Ethics approval The ethics committee and the institutional review board of the First Affiliated Hospital of Chongqing Medical University.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Data can be accessed upon reasonable request. Please contact Dr Jun Duan.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is

REFERENCES

1. L’Her E, Deye N, Lellouche F, et al. Physiologic effects of noninvasive ventilation during acute lung injury. Am J Respir Crit Care Med 2005;172:1271–9.

2. Giraud C, Richard JC, Chevreron V, et al. Comparative physiologic effects of noninvasive assist-control and pressure support ventilation in acute hypercapnic respiratory failure. Chest 1997;111:1639–48.

3. Ferrer M, Esquinas A, Leon M, et al. Noninvasive ventilation in severe hypoaxemic respiratory failure: a randomised clinical trial. Am J Respir Crit Care Med 2003;168:1438–44.

4. Ram FS, Picot J, Lightowler J, et al. Non-invasive positive pressure ventilation treatment of respiratory failure due to exacerbations of chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2004;CD004104.

5. Burns KE, Meade MO, Premji A, et al. Noninvasive ventilation as a weaning strategy for mechanical ventilation in adults with respiratory failure: a cochrane systematic review. CMAJ 2014;186:E112–22.

6. Zhu F, Liu ZL, Long X, et al. Effect of noninvasive positive pressure ventilation on weaning success in patients receiving invasive mechanical ventilation: a meta-analysis. Chin Med J 2013;126:1337–43.

7. Ferrer M, Valencia M, Nicolas JM, et al. Early noninvasive ventilation averts extubation failure in patients at risk: a randomized trial. Am J Respir Crit Care Med 2006;173:164–70.

8. Natall S, Gregoretti C, Fanfalla F, et al. Noninvasive ventilation to prevent respiratory failure after extubation in high-risk patients. Crit Care Med 2005;33:2465–70.

9. Cabrini L, Landoni G, Oriani A, et al. Noninvasive ventilation and survival in acute care settings: a comprehensive systematic review and metaanalysis of randomized controlled trials. Crit Care Med 2015;43:880–8.

10. Demoule A, Chevet S, Carlucci A, et al. Changing use of noninvasive ventilation in critically ill patients: trends over 15 years in francophone countries. Intensive Care Med 2016;42:82–92.

11. Schnell D, Timst JT, Darmon M, et al. Noninvasive mechanical ventilation in acute respiratory failure: trends in use and outcomes. Intensive Care Med 2014;40:582–91.

12. Stefan MS, Shieh MS, Pekow PS, et al. Trends in mechanical ventilation among patients hospitalized with acute exacerbations of COPD in the United States, 2001 to 2011. Chest 2015;147:959–68.

13. Sasabuchi Y, Yasunaga H, Matsui H, et al. The volume-outcome relationship in critically Ill patients in relation to the ICU-to-Hospital Bed Ratio. Crit Care Med 2015;43:1239–45.

14. Lone Ni, Walsh TS. Prolonged mechanical ventilation in critically ill patients: epidemiology, outcomes and modeling the potential cost consequences of establishing a regional weaning unit. Crit Care 2011;15:R102.

15. Cox CE, Carson SS. Medical and economic implications of prolonged mechanical ventilation and expedited post-acute care. Semin Respir Crit Care Med 2012;33:357–61.

16. Udeh CI, Hadder B, Udeh BL. Validation and extension of the prolonged mechanical ventilation prognostic model (ProVent) Score for predicting 1-year mortality after prolonged mechanical ventilation. Ann Am Thorac Soc 2015;12:1845–51.

17. Scheinhorn DJ, Chao DC, Stearn-Hassennpflug M, et al. Post-ICU mechanical ventilation: treatment of 1,123 patients at a regional weaning center. Chest 1997;111:1654–9.

18. Damuth E, Mitchell JA, Bartock JL, et al. Long-term survival of critically ill patients treated for prolonged mechanical ventilation: a systematic review and meta-analysis. Lancet Respir Med 2015;3:544–53.

19. Zhang Z, Duan J. Nosocomial pneumonia in non-invasive ventilation patients: incidence, characteristics, and outcomes. J Hosp Infect 2015;91:163–7.

20. Duan J, Tang X, Huang S, et al. Protocol-directed versus physician-directed weaning from noninvasive ventilation: the impact in chronic obstructive pulmonary disease patients. J Trauma Acute Care Surg 2012;72:1271–5.

21. Leimane V, Riekstina V, Holtz TH, et al. Clinical outcome of individualised treatment of multidrug-resistant tuberculosis in Latvia: a retrospective cohort study. Lancet 2005;365:318–26.

22. Wartenberg KE, Schmidt MJ, Claassen J, et al. Impact of medical complications on outcome after subarachnoid hemorrhage. Crit Care Med 2006;34:617–23.

23. Stefan MS, Shieh MS, Pekow PS, et al. Epidemiology and outcomes of acute respiratory failure in the United States, 2001 to 2009: a national survey. J Hosp Infect 2013;83:76–82.

24. Restrepo MI, Mortensen EM, Reijo J, et al. Late admission to the ICU in patients with community-acquired pneumonia is associated with higher mortality. Chest 2010;137:552–7.

25. Champunot R, Thawitsri T, Kamsawang N, et al. Cost effectiveness analysis of an initial ICU admission as compared to a delayed ICU admission in patients with severe sepsis or in septic shock. J Med Assoc Thai 2014;97:S102–7.

26. Town JA, Churpek MM, Yuen TC, et al. Relationship between ICU bed availability, ICU readmission, and cardiac arrest in the general wards. Crit Care Med 2014;42:2037–41.

27. Hrubetz R, Reiniger J, Tournoux-Facon C, et al. Refusal of intensive care unit admission due to a full unit: impact on mortality. Am J Respir Crit Care Med 2012;185:1081–7.
28. Carpenè N, Vagheggini G, Panait E, et al. A proposal of a new model for long-term weaning: respiratory intensive care unit and weaning center. *Respir Med* 2010;104:1505–11.

29. Pilcher DV, Bailey MJ, Treacher DF, et al. Outcomes, cost and long term survival of patients referred to a regional weaning centre. *Thorax* 2005;60:187–92.

30. Azoulay E, Kouatchet A, Jaber S, et al. Noninvasive mechanical ventilation in patients having declined tracheal intubation. *Intensive Care Med* 2013;39:292–301.

31. Bülow HH, Thorsager B. Non-invasive ventilation in do-not-intubate patients: five-year follow-up on a two-year prospective, consecutive cohort study. *Acta Anaesthesiol Scand* 2009;53:1153–7.

32. Fernandez R, Baigorri F, Artigas A. Noninvasive ventilation in patients with "do-not-intubate" orders: medium-term efficacy depends critically on patient selection. *Intensive Care Med* 2007;33:350–4.

33. Nava S, Ferrer M, Esquinas A, et al. Palliative use of non-invasive ventilation in end-of-life patients with solid tumours: a randomised feasibility trial. *Lancet Oncol* 2013;14:219–27.

34. Plant PK, Owen JL, Elliott MW. Early use of non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease on general respiratory wards: a multicentre randomised controlled trial. *Lancet* 2000;355:1931–5.

35. Olper L, Cabrini L, Landoni G, et al. Non-invasive ventilation after cardiac surgery outside the Intensive Care Unit. *Minerva Anestesiol* 2011;77:40–5.

36. Olivieri C, Carenzo L, Vignazia GL, et al. Does noninvasive ventilation delivery in the ward provide early effective ventilation? *Respir Care* 2015;60:6–11.

37. Frat JP, Thille AW, Mercat A, et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *N Engl J Med* 2015;372:2185–96.

38. Stéphan F, Barrucand B, Petit P, et al. High-Flow Nasal Oxygen vs Noninvasive positive airway pressure in hypoxemic patients after cardiothoracic surgery: a randomized clinical trial. *JAMA* 2015;313:2331–9.