

ORIGINAL ARTICLE

Increasing use of non-invasive ventilation in asthma: a long-term analysis of the Portuguese national hospitalization database

Daniela Alves, MD¹, Alberto S. Freitas, PhD², T. Jacinto, MSc^{2,3}, Manuel S. Vaz, MD⁴, Fernando O. Lopes, MD², and João A. Fonseca, PhD^{2,3}

¹Pulmonology Division, Hospital de Braga, Braga, Portugal, ²Department of Health Information and Decision Sciences, Faculty of Medicine, Center for Research in Health Technologies and Information Systems (CINTESIS), University of Porto, Porto, Portugal, ³Allergy and Clinical Immunology Division, CUF Porto Instituto and Hospital, Porto, Portugal, and ⁴Pulmonology Division, Centro Hospitalar S. João, Porto, Portugal

Abstract

Objectives: To describe the use and outcomes of non-invasive positive pressure ventilation (NPPV) and invasive ventilation (IV) in adults hospitalized for acute asthma exacerbations in Portugal. **Methods:** We analyzed the hospitalizations of adults with a principal diagnosis of asthma in mainland Portugal between 2000 and 2010. The data source was the national hospitalizations database, which includes administrative and clinical data produced by physicians trained in coding. **Results:** Ventilation support was used in 5.1% ($n = 747$) of the 14 515 hospitalizations with a principal diagnosis of asthma: NPPV in 1.7% ($n = 241$) and IV in 3.5% ($n = 506$); NPPV use increased from 1% in 2000 to 3.3% in 2010. In patients with asthma, the ratio of NPPV use to IV use increased from 0.27 to 1.06. This increase was observed even after exclusion of secondary diagnoses in which NPPV is frequently used. The mortality rate was 1.5% for all asthma hospitalizations: 2.5% when NPPV was used and 15.8% for those requiring IV. **Conclusions:** The use of ventilation support in asthma remained stable over time; however, the use of non-invasive ventilation has increased. Still, we do not have good data regarding the effectiveness of non-invasive ventilation when treating asthma exacerbations. Therefore, additional studies are much needed and should assess physiologic and clinical variables that might affect the effectiveness of non-invasive ventilation in patients with asthma exacerbations.

Keywords

Administrative data, asthma exacerbations, hospital admissions, invasive ventilation, non-invasive ventilation

History

Received 5 September 2013

Revised 6 June 2014

Accepted 23 June 2014

Published online 6 August 2014

Introduction

Non-invasive positive pressure ventilation (NPPV) is well established in the management of acute respiratory failure, particularly in acute exacerbations of chronic obstructive pulmonary disease (COPD) [1,2]. Improved outcomes with the avoidance of complications caused by endotracheal intubation and invasive ventilation (IV) have been demonstrated in acute exacerbations of COPD [2,3], acute cardiogenic pulmonary edema [4] and in immunocompromised patients [5].

Invasive ventilation is often required in patients who develop respiratory failure owing to severe asthma exacerbations that are refractory to standard treatment. However, the constraints and complications of this form of ventilation in asthma patients are well known [6–8]. Although NPPV may also be useful in severe asthma exacerbations, there is insufficient evidence for the use of this treatment in asthma [9]. In fact, the few studies that have reported on the use of NPPV for severe asthma exacerbations have included small

patient numbers, making it difficult to assess risks and benefits [7,10–14].

Recently, a large-scale retrospective study in USA revealed a substantial increase in the use of mechanical ventilation, accompanied by a shift from invasive mechanical ventilation to non-invasive ventilation in acute asthma exacerbations [15]. In fact, health administrative databases have the potential to contribute to the improvement of quality of healthcare, despite known problems including coding inaccuracy and limited clinical data [16–20]. They have been used to assess resource usage and quality in hospital systems [21–23], to produce quality indicators or benchmarks of hospital activity [24–26] and to model resource utilization [27–30]. Studies regarding asthma hospitalizations have also used administrative databases [31–34]. Recently, Tsai et al. [35] used a sample from hospital administrative databases to analyze the use of NPPV in patients with acute exacerbations of COPD. Health administrative databases are readily available, are relatively inexpensive, and contain large data sets of many healthcare facilities in the same format. In some situations, such as identifying long-term trends in hospital care, they can be the only source of information available to study a healthcare problem. The aim of this study was to describe the use and outcomes of NPPV and IV in patients hospitalized for acute asthma exacerbations in Portugal from 2000 to 2010.

Correspondence: João A. Fonseca, Department of Health Information and Decision Sciences, Faculty of Medicine, Center for Research in Health Technologies and Information Systems (CINTESIS), University of Porto, Al. Prof. Hernani Monteiro, 4200-319 Porto, Portugal. Tel: +351225513622. Fax: +351225513623. E-mail: jfonseca@med.up.pt

Methods

In this retrospective observational study, we used the national hospitalizations database (NHD) to analyze adult hospitalizations with a principal diagnosis of asthma in any of the 85 acute care hospitals of the national healthcare service in mainland Portugal between 2000 and 2010. In Portugal, all hospitals belonging to the National Health Service have a common database, the NHD. This database has been used since 1990 [29], and has had a positive impact on the productivity and technical efficiency of some diagnostic technologies [30].

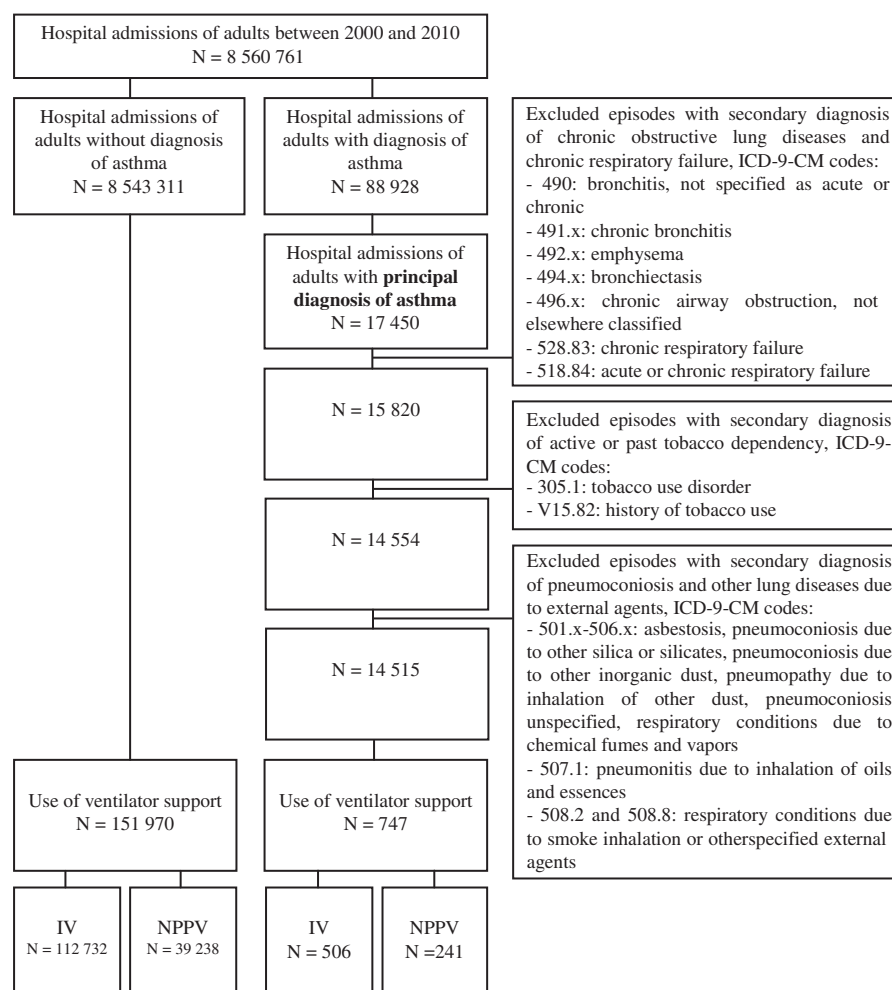
In this study, the source of data was the NHD provided by the ACSS (*Administração Central do Sistema de Saúde*), the Portuguese Ministry of Health's Authority for Health Services. This database contains inpatient hospitalization data, including clinical data that are coded by physicians trained in clinical coding who are regularly subjected to in-hospital and external audits. These coders are organized in a national network that provides online help and regular on-site training courses. When needed, the coder contacts the colleague who is responsible for the hospitalization to clarify any aspect that is being coded. The data include patient demographics, procedures and diagnostic codes according to the International Classification of Diseases – Ninth Revision – Clinical Modification (ICD-9-CM), as well as length of stay (LOS) and discharge destination from all of the public acute

care hospitals of the National Health Service. Data from private hospitals (representing ~15% of all inpatient stays in Portugal) were not included in this study.

Records for patients older than 17 years of age with a principal diagnosis of asthma (ICD-9-CM code 493.x) who were discharged between January 2000 and December 2010 were analyzed. We excluded episodes with a secondary diagnosis of COPD, chronic respiratory failure, active or past tobacco use, pneumoconiosis and other lung diseases due to external agents (Figure 1). To account for the use of NPPV in sleep-disordered breathing, acute cardiogenic pulmonary edema and pneumonia, we conducted a secondary analysis to study diseases that are formal indications for NPPV. Briefly, of the 88 928 hospitalizations with a diagnosis of asthma, we selected the 17 450 (19.6%) that had a principal diagnosis of asthma (meaning asthma was considered by the coder to be the main reason for hospitalization). From these, we excluded 16.8% that had an additional diagnosis or additional risk factors (mainly previous/current tobacco smoking) for other chronic respiratory diseases, as well as those with prior diagnosis of chronic respiratory failure.

Episodes requiring NPPV or IV were identified by searching for ICD-9-CM procedure codes 93.9x (non-invasive mechanical ventilation) or 96.7x (other continuous invasive mechanical ventilation). Patients who received both types of ventilation support ($n=38$) in the same episode were included in the IV group.

Figure 1. Patient dispensation during the study. Records for patients older than 17 years of age with a principal diagnosis of asthma (ICD-9-CM code 493.x) who were discharged between January 2000 and December 2010 were analyzed. We excluded episodes with a secondary diagnosis of COPD, chronic respiratory failure, active or past tobacco use, pneumoconiosis and other lung diseases due to external agents.



Comorbidities were defined using updated versions [36,37] of the Deyo modification of the Charlson comorbidity index and the Elixhauser index, which is a comorbidity risk adjustment measurement with higher values corresponding to higher in-hospital mortality. All of the secondary diagnoses in the records analyzed were listed. We identified 19 diagnoses that were considered clinically relevant in adults requiring ventilation support, and then tabulated those with significant between-group differences.

Three main analyses were performed: use of NPPV and IV over time, patient characteristics (sex, age, number of comorbidities and comorbidity index) and outcomes (in-hospital mortality, LOS and secondary diagnoses) for each group. We summarized patient characteristics and outcomes using percentages and medians with interquartile ranges. The chi-squared test was used to compare patients who used NPPV with those who did not use NPPV. The significance level was set at $p < 0.05$. The use of NPPV and IV and the mortality rate during the course of the study were plotted. We used linear regression to investigate NPPV trends among episodes with and without principal diagnoses of asthma. All analyses were performed using IBM SPSS Statistics Version 20.

Results

Between 2000 and 2010, 17 450 hospital admissions of adult patients with asthma as a principal diagnosis were recorded. After applying the strict exclusion criteria described in the ‘‘Methods’’ section, 14 515 inpatient episodes were analyzed (Figure 1).

The patient characteristics are shown in Table 1. The median age was 57 years, and most patients were female (73.7%). The median LOS was 6 days; overall mortality was 1.5% (Table 1). Ventilation support was used in 747 cases (5.1%): NPPV in 1.7% of cases ($n = 241$) and IV in 3.5% ($n = 506$). The use of NPPV and IV is detailed in Table 2. Most (52.3%) patients who received NPPV were older than 65 years old.

The most common comorbidities in the NPPV group were hypertension (34.9%), obesity (28.2%) and congestive heart failure (29%). In patients who received IV, the most common comorbidities were hypertension (20.4%), fluid and electrolyte disorders (16.8%) and congestive heart failure (11.1%). Secondary diagnoses are summarized in Table 3.

In the IV group, there was a high proportion of pneumonia and bacterial infections due to agents such as *Enterococcus*, methicillin-susceptible *Staphylococcus aureus*, *Escherichia coli* and pneumonia due to *Pseudomonas aeruginosa* ($p = 0.016$) (Table 3).

Figure 2 depicts the proportion of all hospitalizations and the proportion of those with a principal diagnosis of asthma in which NPPV was used between 2000 and 2010. The linear regression slopes (95% CI) were, respectively, 0.073 (0.057, 0.089) and 0.248 (0.153, 0.342). NPPV frequency clearly increased from 15 cases (1%) in 2000 to 58 (3.3%) in 2010 (Figure 3). This increase occurred mainly after 2007. IV use remained stable throughout the study period (3.7% in 2000 and 3.1% in 2010). The ratio between these two proportions of hospital admissions (i.e. the ratio between the use of NPPV

Table 1. Characteristics of adults hospitalized with asthma as a principal diagnosis in Portugal, 2000–2010.

	Principal diagnosis of asthma ($N = 14\,515$)
Sex (%)	
Male/female	26.3/73.7
Age, median (P25–75)	
Overall	57.0 (40–71)
Male/female	52.0 (35–69)/58 (43–72)
Comorbidities Elixhauser ^a	
Comorb. Index (avg.) ^b	1.19
Charlson/Deyo ^c	
Comorb. index (avg.)	0.37
LOS, median (P25–75)	6.0 (3–10)
Ventilation support, n (%)	747 (5.1)
In-hospital mortality, n (%)	212 (1.5)

Comorb., comorbidity; avg., average; LOS, length of stay.

^aElixhauser comorbidities updated by Quan et al. [36].

^bUsing points defined by van Walraven et al. [37].

^cCharlson/Deyo comorbidities [17], updated by Quan et al. [36].

Table 2. Characteristics of adults hospitalized for asthma who needed ventilation support.

	NPPV ($N = 241$)	IV ($N = 506$)
Sex (%)		
Male/female	21.4/38.0	78.6/62.0
Age, median (P25–75)	66.0 (57.5–76.0)	52.0 (36.0–68.0)
Comorbidities Elixhauser ^a		
Comorb. index (avg.) ^b	3.5	2.6
Charlson/Deyo ^c		
Comorb. index (avg.)	0.76	0.42
LOS, median (P25–75)	8.0 (5.0–13.0)	8.0 (4.0–15.0)
In-hospital mortality ($N = 86$, 11.5%)	6 (2.5%)	80 (15.8%)

^aElixhauser comorbidities updated by Quan et al. [36].

^bUsing points defined by van Walraven et al. [37].

^cCharlson/Deyo comorbidities [17], updated by Quan et al. [36].

NPPV, non-invasive positive pressure ventilation; IV, invasive ventilation; comorb., comorbidity; avg., average; LOS, length of stay.

and IV in patients with asthma) increased from 0.27 to 1.06. After exclusion of secondary diagnoses such as obstructive sleep apnea, obesity hypoventilation syndrome, pneumonia and acute cardiogenic pulmonary edema, the increase in NPPV use in patients with asthma continues to be observed, mainly after 2008 (Figure 4).

Overall, the median LOS for all asthma hospitalizations was 6 days and remained constant throughout the study period. For patients using ventilator support, the median LOS was 8 days for both the NPPV group and the IV group (Figure 5). The median LOS was 8 days among IV patients that died (Tables A1 and A2).

The annual mortality rate is plotted in Figure 6. The mortality rate was 2.5% ($n = 6$) among patients who received NPPV, and 15.8% ($n = 80$) among patients who received IV (Table 2). Thirty-eight patients in the IV group (4.5% of those requiring ventilator support) received both types of ventilation support during the same episode; 2 of these patients died (2.4% of deaths in the IV group).

Table 3. Relevant secondary diagnoses for the asthma hospitalizations in which ventilator support was used.

ICD 9 codes	NPPV N	IV N
482 Other bacterial pneumonia		
482.1 Pneumonia due to <i>Pseudomonas</i>	0	3
482.2 Pneumonia due to <i>Haemophilus influenzae</i> [<i>H. influenzae</i>]	0	5
482.41 Methicillin-susceptible pneumonia due to <i>Staphylococcus aureus</i>	0	6
486 Pneumonia, organism unspecified	5	38
041 Bacterial infections in conditions classified elsewhere and of unspecified site		
041.04 Group D [<i>Enterococcus</i>]	0	8
041.11 Methicillin-susceptible <i>Staphylococcus aureus</i>	0	4
041.4 <i>Escherichia coli</i> [<i>E. coli</i>]	4	12
416 Chronic pulmonary heart disease		
416.8 Other chronic pulmonary heart diseases	10	1
416.9 Chronic pulmonary heart disease, unspecified	9	7
428 Heart failure		
428.0 Congestive heart failure, unspecified	54	30
428.9 Heart failure, unspecified	1	4
278 Overweight, obesity and other hyperalimentation	71	46
348 Other conditions of brain		
348.1 Anoxic brain damage	0	28
780 General symptoms		
780.01 Alteration of consciousness: coma	0	9
780.39 Other convulsions	1	11
780.53 Hypersomnia with sleep apnea, unspecified	30	1
780.57 Unspecified sleep apnea	25	2
799 Other ill-defined and unknown causes of morbidity and mortality		
799.0 Asphyxia and hypoxemia	0	7
799.1 Respiratory arrest	1	23

NPPV, non-invasive positive pressure ventilation; IV, invasive ventilation.

Discussion

This study shows that the use of NPPV markedly increased among Portuguese adults hospitalized for asthma exacerbations. The use of IV support in asthma remained stable from 2000 to 2010; however, a 3-fold increase in the use of NPPV was observed during the same period. This increase was apparent even after excluding patients with diseases that are formal indications for NPPV.

Our finding of a considerable increase in the use of NPPV is consistent with the results of previous single-center reports [7,10–14]. Very recently, a large-scale retrospective study was published [15]. This study with data from USA reported results that are very similar to ours: there was a substantial increase in the use of NPPV among adults hospitalized with acute asthma exacerbations, the increment was the same after excluding people with obstructive sleep apnea, and it was associated with a decrease in the use of invasive mechanical ventilation. Taken together, these large retrospective studies demonstrate an increase in the use of NPPV to treat asthma exacerbations, at least in Western countries.

The main limitations of our study are those inherent to the retrospective observational design: the use of hospital databases, the lack of physiologic data, time, duration and setting (ward or intensive care unit) of NPPV use. Large retrospective

observational studies are a first step in the assessment of a health technology. It is now clear that prospective, multicenter studies should be a research priority not only to assess NPPV effectiveness, but also to provide insight into the mechanisms that lead to the results observed. The real-life data analyzed from over 80 hospitals support the possible benefits of NPPV in some severe asthma exacerbations. Nevertheless, even in this large sample, the number of cases per year is too small for subgroup analysis (e.g. to compare mortality between NPPV and IV). Another limitation of this study is the potential misclassification of patients' diagnoses or even procedure codes, as the procedure codes for mechanical ventilation may be unrelated to the asthma exacerbation itself. We circumvented this problem by choosing only patients with a principal diagnosis of asthma and excluding secondary diagnoses of COPD, chronic respiratory failure, pneumoconiosis and other lung diseases due to external agents. Additionally, there are many conditions that can mimic asthma, and many authors recognize the overlapping phenotype of COPD-asthma in COPD [38]. In a case study that systematically assessed adult patients with difficult-to-treat asthma, 12% of patients were judged to have a diagnosis other than asthma [39]. We cannot rule out misclassification or biases in physician coding. Considerable variation in the sensitivity and specificity of the ICD-9-CM collected data has been demonstrated [40]. However, in Portugal, clinical coding is performed by skilled physicians who have practiced for 20 years. Moreover, those physicians that code the hospital admissions by reviewing the medical chart do not consider asthma as a principal motive of admission lightly, especially in individuals over 45 years old (the majority of the cases observed) and when an advanced procedure such as mechanical ventilation is used. In summary, the methods that we employed were an attempt to improve specificity at the expense of some decrease in sensitivity.

In 2010, the European Respiratory Society reviewed the available reports on the use of NPPV in asthma [9]. In spite of the lack of evidence, it recommended that selected patients with severe asthma exacerbations might benefit from a carefully and closely monitored trial of NPPV.

Within the currently available evidence, we observed an impressive increase in the use of NPPV in acute asthmatic exacerbations, which supports the need for studies assessing physiologic variables to define for what situations NPPV an effective treatment of asthma exacerbations. There may be several reasons for the increased use of NPPV observed in adults hospitalized for asthma, including greater availability of NPPV equipment, more experience of the teams, and increasing frequency of clinical conditions in which NPPV is showing benefits (e.g. obesity and sleep disorders). In our series, these conditions were significantly more common in the NPPV group than in the other asthma hospitalizations. In a study on clinical outcomes for acute asthma, Tsai et al. [32] briefly reported that the use of NPPV or IV was 3.9% among adults hospitalized for asthma in 2006–2008. This is lower than the 5.7% that we observed. We do not have adequate information to understand the reasons for these differences. However, the same authors reported an analysis using the same sample, and concluded that in COPD with acute respiratory failure, the adoption of NPPV was low and varied widely between hospitals [35].

Figure 2. Proportion of all hospitalizations and the proportion of those with a principal diagnosis of asthma in which non-invasive positive pressure ventilation (NPPV) was used between 2000 and 2010. The linear regression slopes (95% CI) were, respectively, 0.073 (0.057, 0.089) and 0.248 (0.153, 0.342).

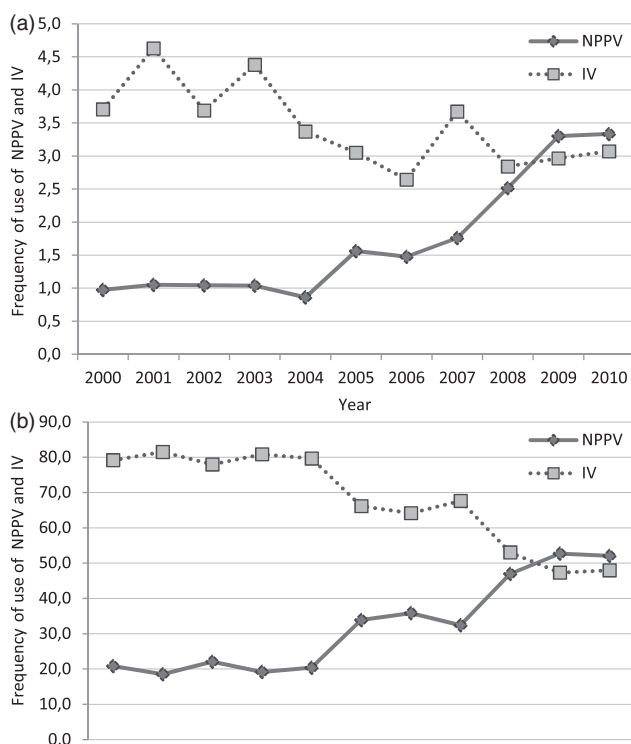
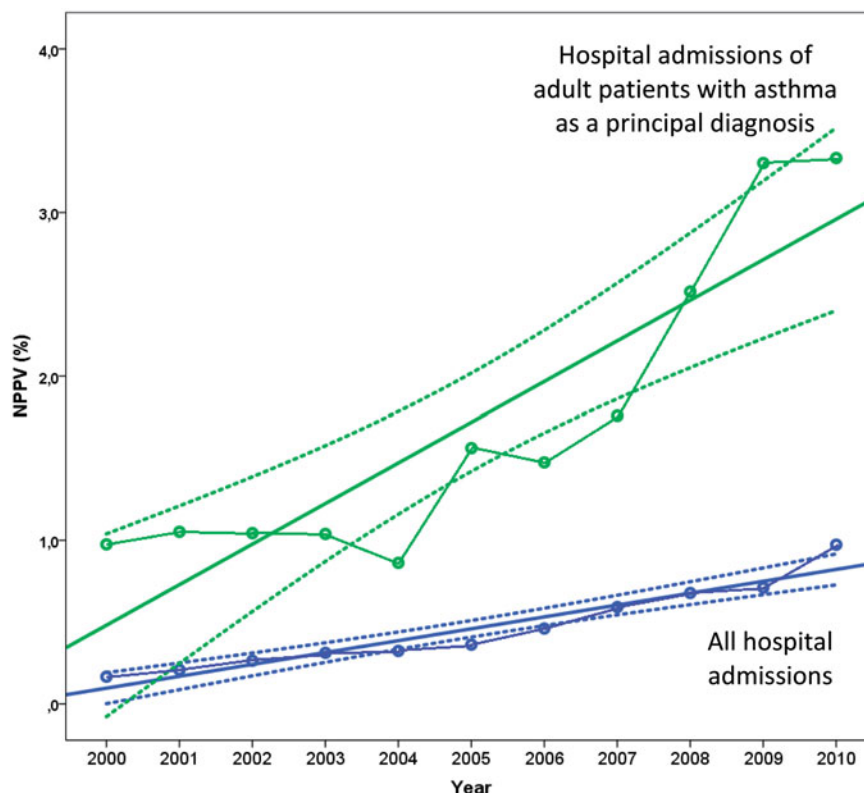


Figure 3. Frequency of non-invasive positive pressure ventilation (NPPV) use among specific patient populations, 2000–2010. (a) Among all hospitalizations with a principal diagnosis of asthma. (b) Solely among hospitalizations in which ventilation support was used: NPPV frequency clearly increased from 15 cases (1%) in 2000 to 58 (3.3%) in 2010.

A different type of explanation is that possible changes in admission criteria for asthma patients have reduced the admissions of patients with less severe exacerbations. We do not have data to directly test this hypothesis. Still, some

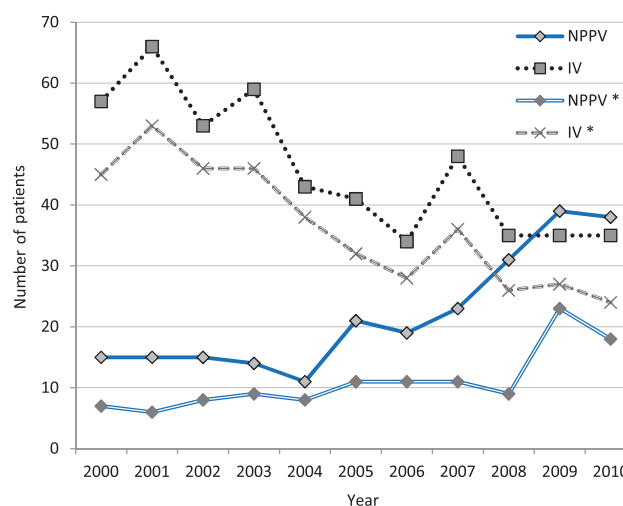


Figure 4. Non-invasive positive pressure ventilation (NPPV) use in adults with principal diagnosis of asthma after exclusion of secondary diagnoses such as obstructive sleep apnea, obesity hypoventilation syndrome, pneumonia and acute cardiogenic pulmonary edema (NPPV*); the increase in NPPV use continues to be observed, mainly after 2008.

indirect information is in line with this hypothesis: the overall median LOS exhibited a small but sustained increase during the second half of the study period; the increased use of ventilation support may be due, at least in part, to an increased proportion of more complex cases; and the mortality rate did not decrease over time.

In-hospital mortality was high, especially in the IV group. The high frequency of infections by nosocomial agents in the IV group may have contributed to the high mortality. Previous studies have shown that mechanically ventilated asthmatic patients have a high risk of complications, including

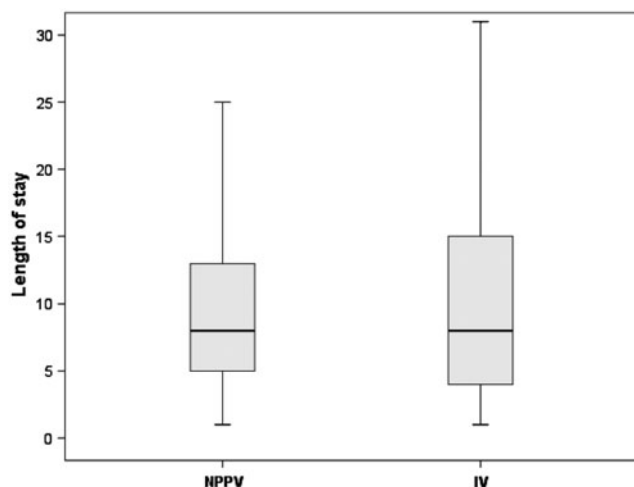


Figure 5. Length of hospital stay (LOS) (days) in adults with principal diagnosis of asthma, 2000–2010. The median LOS was 8 days for both the non-invasive positive pressure ventilation group (NPPV) and the invasive ventilation group (IV).

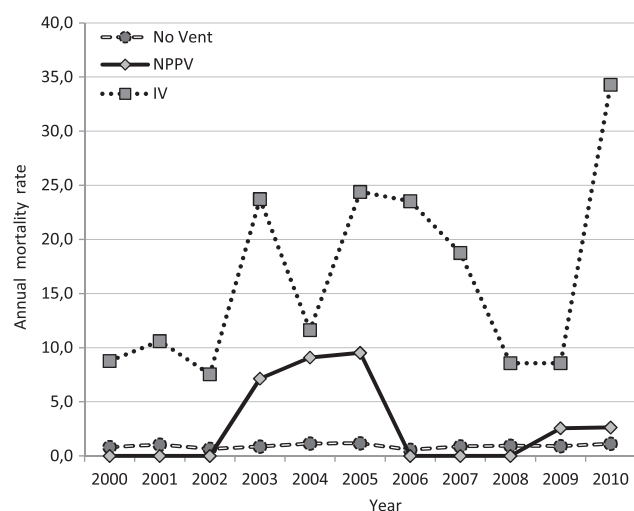


Figure 6. Annual mortality rate in adults with principal diagnosis of asthma: 1.5% ($n=212$) for all asthma hospitalizations, 2.5% ($n=6$) among patients who received non-invasive positive pressure ventilation (NPPV) and 15.8% ($n=80$) among patients who received Invasive ventilation (IV). No Vent, no ventilation.

nosocomial infections [6–8]. In fact, intubated patients have a 1% risk per day of developing pneumonia [2,41,42]. The data now presented confirms this observation in a large, real-life data set.

A high frequency of obesity and overweight (40.3%) was observed in the NPPV group. Obesity is associated with adverse changes in pulmonary physiology in patients with chronic respiratory illnesses, including asthma [43].

Although the mechanism by which NPPV may improve clinical outcome of acute asthma exacerbations is not well understood, a combination of factors might explain some of the benefits: positive pressure can dilate small to moderately sized bronchi and improve alveolar recruitment [44]; it may disperse bronchodilators to more peripheral airways, improving the maximum forced expiratory volume in 1 s (FEV1) and peak expiratory flow [45,46]; it may prevent bronchospasm [47,48] and it enhances ventilation by unloading fatigued

ventilator muscles. Improvements in gas exchange and FEV1 and fewer complications have been observed with NPPV versus IV [7].

Conclusion

Although the use of ventilation support in asthma remained stable during the study, the use of non-invasive ventilation has increased. Still, we do not have good data regarding the effectiveness of NPPV in the treatment of asthma exacerbations. Therefore, additional studies are much needed and should assess physiologic and clinical variables that might affect the effectiveness of NPPV in the treatment of asthma exacerbations.

Acknowledgements

The authors wish to thank ACSS (*Administração Central do Sistema de Saúde*), the Portuguese Ministry of Health's Authority for Health Services, for providing access to the data.

Declaration of interest

The authors of this manuscript report no conflicts of interest.

References

1. Carrera M, Marín JM, Antón A, Chiner E, Alonso ML, Masa JF, Marrades R. A controlled trial of noninvasive ventilation for chronic obstructive pulmonary disease exacerbations. *J Crit Care* 2009;24:e7–473.e14.
2. Brochard L, Mancebo J, Wysocki M, Lofaso F, Conti G, Rauss A, Simonneau G. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. *N Engl J Med* 1995;333:817–822.
3. Ram FS, 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 Syst Rev* 2004;(1):CD004104.
4. Gray A, Goodacre S, Newby DE, Masson M, Sampson F, Nicholl J. Noninvasive ventilation in acute cardiogenic pulmonary edema. *N Engl J Med* 2008;359:142–151.
5. Rocco M, Dell'Utri D, Morelli A, Spadetta G, Conti G, Antonelli M, Pietropaoli P. Noninvasive ventilation by helmet face mask in immunocompromised patients: a case-control study. *Chest* 2004;126:1508–1515.
6. Afessa B, Morales I, Cury JD. Clinical course and outcome of patients admitted to an ICU for status asthmaticus. *Chest* 2001;120:1616–1621.
7. Gehlbach B, Kress JP, Kahn J, DeRuiter C, Pohlman A, Hall J. Correlates of prolonged hospitalization in inner-city ICU patients receiving noninvasive and invasive positive pressure ventilation for status asthmaticus. *Chest* 2002;122:1709–1714.
8. Kao CC, Jain S, Guntupalli KK, Bandi V. Mechanical ventilation for asthma: a 10-year experience. *J Asthma* 2008;45:552–556.
9. Soroksky A, Klinowski E, Ilgyev E, Mizrahi A, Miller A, Ben Yehuda TM, Shpirer I. Noninvasive positive pressure ventilation in acute asthmatic attack. *Eur Respir Rev* 2010;19:39–45.
10. Meduri GU, Cook TR, Turner RE, Cohen M, Leeper KV. Noninvasive positive pressure ventilation in status asthmaticus. *Chest* 1966;110:767–774.
11. Fernández MM, Villagrà A, Blanch L, Fernández R. Non-invasive mechanical ventilation in status asthmaticus. *Intensive Care Med* 2001;27:486–492.
12. Soroksky A, Stav D, Shpirer I. A pilot prospective, randomized, placebo-controlled trial of bilevel positive airway pressure in acute asthmatic attack. *Chest* 2003;123:1018–1025.

13. Soma T, Hino M, Kida K, Kudoh S. A prospective and randomized study for improvement of acute asthma by non-invasive positive pressure ventilation (NPPV). *Intern Med* 2008;47:493–501.
14. Ram FS, Wellington S, Rowe BH, Wedzicha JA. Non-invasive positive pressure ventilation for treatment of respiratory failure due to severe acute exacerbations of asthma. Review. Update in: *Cochrane Database Syst Rev* 2005;(3):CD004360.
15. Nanchal R, Kumar G, Majumdar T, Taneja A, Patel J, Dagar G, Jacobs ER, Whittle J. Utilization of mechanical ventilation for asthma exacerbations: analysis of a national database. *Respir Care* 2014;59:644–653.
16. Calle JE, Saturno PJ, Parra P, Rodenas J, Pérez MJ, Eustaquio FS, Aguinaga E. Quality of the information contained in the minimum basic data set: results from an evaluation in eight hospitals. *Eur J Epidemiol* 2000;16:1073–1080.
17. Powell AE, Davies HTO, Thomson RG. Using routine comparative data to assess the quality of health care: understanding and avoiding common pitfalls. *Qual Saf Health Care* 2003;12:122–128.
18. Sutherland JM, Botz CK. The effect of misclassification errors on case mix measurement. *Health Policy* 2006;79:195–202.
19. Williams J, Mann R. Hospital episode statistics: time for clinicians to get involved? *Clin Med* 2002;2:34–37.
20. Freitas JA, Silva-Costa T, Marques B, Costa-Pereira A. Implications of data quality problems within hospital administrative databases. In: Bamidis PD, Pallikarakis N, eds. *IFMBE proceedings*, Vol 29. Springer: Berlin Heidelberg; 2010:823–826.
21. Lezzoni LI. Assessing quality using administrative data. *Ann Intern Med* 1997;127:666–674.
22. Torchiana D, Meyer G. Use of administrative data for clinical quality measurement. *J Thorac Cardiovasc Surg* 2005;129:1222–1224.
23. Scott I, Youlden D, Coory M. Are diagnosis specific outcome indicators based on administrative data useful in assessing quality of hospital care? *Qual Saf Health Care* 2004;13:32–39.
24. Jarman B, Gault S, Alves B, Hider A, Dolan S, Cook A, Hurwitz B. Explaining differences in English hospital death rates using routinely collected data. *BMJ* 1999;318:1515–1520.
25. Zhan C, Miller MR. Administrative data based patient safety research: a critical review. *Qual Saf Health Care* 2003;12:58.
26. Freitas A, Costa T, Marques B, Gaspar J, Gomes J, Lopes F, Lema I. A framework for the production and analysis of hospital quality indicators. In: Böhm C, Khuri S, Lhotská L, Pisanti N, eds. *Information Technology in Bio- and Medical Informatics, Lecture Notes in Computer Science*. Volume 6865. Springer: Berlin Heidelberg; 2011:96–105.
27. Evans E, Imanaka Y, Sekimoto M, Ishizaki T, Hayashida K, Fukuda H, Oh EH. Risk adjusted resource utilization for AMI patients treated in Japanese hospitals. *Health Econ* 2007;16:347–359.
28. Freitas A, Silva-Costa T, Lopes F, Garcia-Lema I, Teixeira-Pinto A, Brazdil P, Costa-Pereira A. Factors influencing hospital high length of stay outliers. *BMC Health Serv Res* 2012;12:265.
29. Bentes ME, Urbano JA, Carvalho MDC, Tranquada MS. Using DRGs to Fund Hospitals in Portugal: an Evaluation of the Experience. In: Casas, M. M, Wiley M, eds. *Diagnosis Related Groups in Europe: uses and perspectives*. Springer-Verlag Berlin Heidelberg; 1993:173–192.
30. Dismuke CE, Sena V. Has DRG payment influenced the technical efficiency and productivity of diagnostic technologies in Portuguese public hospitals? An Empirical analysis using parametric and non-parametric methods. *Health Care Manag Sci* 1999;2:107–116.
31. Bugalho de Almeida A, Covas A, Prates L, Fragoso E. Asthma hospital admission and mortality in mainland Portugal 2000–2007. *Rev Port Pneumol* 2009;15:367–383.
32. Tsai CL, Lee WY, Hanania NA, Camargo Jr CA. Age-related differences in clinical outcomes for acute asthma in the United States, 2006–2008. *J Allergy Clin Immunol* 2012;129:1252–1258.e1.
33. Pascal L, Fuhrman C, Durif L, Nicolau J, Charpin D, Dujols P, Delmas MC. Trends in hospital admissions for asthma in France, 1998–2002. *Rev Mal Respir* 2007;24:581–590.
34. Krishnan V, Diette GB, Rand CS, Bilderback AL, Merriman B, Hansel NN, Krishnan JA. Mortality in patients hospitalized for asthma exacerbations in the United States. *Am J Respir Crit Care Med* 2006;174:633–638.
35. Tsai CL, Lee WY, Delclos GL, Hanania NA, Camargo Jr CA. Comparative effectiveness of noninvasive ventilation vs. invasive mechanical ventilation in chronic obstructive pulmonary disease patients with acute respiratory failure. *J Hosp Med* 2013;8:165–172.
36. Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi JC, Saunders LD. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care* 2005;43:1130–1139.
37. van Walraven C, Austin PC, Jennings A, Quan H, Forster AJ. A modification of the Elixhauser comorbidity measures into a point system for hospital death using administrative data. *Med Care* 2009;47:626–633.
38. Soler-Cataluña JJ, Cosío B, Izquierdo JL, López-Campos JL, Marín JM, Agüero R, Balboa A. Documento de consenso sobre el fenotipo mixto EPOC-asma en la EPOC. *Arch Bronconeumol* 2012;48:331–337.
39. Robinson DS, Campbell DA, Durham SR, Pfeffer J, Barnes PJ, Chungz KF. Systematic assessment of difficult-to-treat asthma. *Eur Respir J* 2003;22:478–483.
40. Quan H, Li B, Saunders D, Parsons GA, Nilsson CI, Alibhai A, Ghali WA. Assessing validity of ICD-9-CM and ICD-10 administrative data in recording clinical conditions in a unique dually coded database. *Health Serv Res* 2008;43:1424–1441.
41. Antonelli M, Conti G, Rocco M, Bufi M, De Blasi RA, Vivino G, Gasparetto A. A comparison of noninvasive positive-pressure ventilation and conventional mechanical ventilation in patients with acute respiratory failure. *N Engl J Med* 1998;339:429–435.
42. Girou E, Schortgen F, Delclaux C, Brun-Buisson C, Blot F, Lefort Y, Lemaire F. Association of noninvasive ventilation with nosocomial infections and survival in critically ill patients. *JAMA* 2000;284:2361–2367.
43. Mandal S, Hart N. Respiratory complications of obesity. *Clin Med* 2012;12:75–78.
44. Barach AL, Sweson P. Effect of gases under positive pressure on lumens of small and medium sized bronchi. *Arch Intern Med* 1939;63:946–948.
45. Pollack CV, Fleish KB, Dowsey K. Treatment of acute bronchospasm with beta-adrenergic agonist aerosols delivered by a nasal BiPAP circuit. *Ann Emerg Med* 1995;26:552–557.
46. Brandao DC, Lima VM, Filho VG, Silva TS, Campos TF, Dean E, de Andrade AD. Reversal of bronchial obstruction with bi-level positive airway pressure and nebulization in patients with acute asthma. *J Asthma* 2009;46:356–361.
47. Wang CH, Lin HC, Huang TJ, Yang CT, Yu CT, Kuo HP. Differential effects of nasal continuous positive airway pressure on reversible or fixed upper and lower airway obstruction. *Eur Respir J* 1996;9:952–959.
48. Martin JG, Shore S, Engel LA. Effect of continuous positive airway pressure on respiratory mechanics and pattern of breathing in induced asthma. *Am Rev Respir Dis* 1982;126:812–817.

Appendix

Table A1. Median length of stay, per ventilation group, of adults hospitalized with asthma as a principal diagnosis: no ventilation support, non-invasive positive pressure ventilation (NPPV) and invasive ventilation (IV).

Year	No ventilator support		NPPV		IV		Total	
	<i>N</i> (%)	Median LOS	<i>N</i> (%)	Median LOS	<i>N</i> (%)	Median LOS	<i>N</i>	Median LOS
2000	1466 (95.3)	6	15 (1.0)	5	57 (3.7)	8	1538	6
2001	1345 (94.3)	6	15 (1.1)	11	66 (4.6)	8	1426	6
2002	1369 (95.3)	6	15 (1.0)	9	53 (3.7)	8	1437	6
2003	1274 (94.6)	6	14 (1.0)	7.5	59 (4.4)	9	1347	6
2004	1222 (95.8)	6	11 (0.9)	9	43 (3.4)	7	1276	6
2005	1282 (95.4)	7	21 (1.6)	7	41 (3.1)	7	1344	7
2006	1234 (95.9)	6	19 (1.5)	13	34 (2.6)	6	1287	6
2007	1236 (94.6)	6	23 (1.8)	7	48 (3.7)	8.5	1307	7
2008	1166 (94.6)	6.5	31 (2.5)	8	35 (2.8)	10	1232	7
2009	1107 (93.7)	6	39 (3.3)	8	35 (3.0)	9	1181	7
2010	1067 (93.6)	6	38 (3.3)	8	35 (3.1)	8	1140	7
Total	13 768 (94.9)	6	241 (1.7)	8	506 (3.5)	8	14 515	6

Table A2. Median length of stay, per ventilation group, of adults hospitalized with asthma as a principal diagnosis who died: no ventilation support, non-invasive positive pressure ventilation (NPPV) and invasive ventilation (IV).

Year	No ventilator support		NPPV		IV		Total	
	<i>N</i> (%)	Median LOS	<i>N</i> (%)	Median LOS	<i>N</i> (%)	Median LOS	<i>N</i>	Median LOS
2000	12 (70.6)	6	0 (0)	–	5 (29.4)	8	17	8
2001	14 (66.7)	2.5	0 (0)	–	7 (33.3)	7	21	3
2002	9 (69.2)	7	0 (0)	–	4 (30.8)	30.5	13	8
2003	11 (42.3)	3	1 (3.8)	4	14 (53.8)	17	26	5
2004	14 (70.0)	8.5	1 (5.0)	1	5 (25.0)	31	20	9.5
2005	15 (55.6)	3	2 (7.4)	11	10 (37.0)	5.5	27	4
2006	7 (46.7)	3	0 (0)	–	8 (53.3)	5.5	15	5
2007	11 (55.0)	3	0 (0)	–	9 (45.0)	7	20	5
2008	11 (78.6)	5	0 (0)	–	3 (21.4)	42	14	7.5
2009	10 (71.4)	5	1 (7.1)	1	3 (21.4)	5	14	4.5
2010	12 (48.0)	6	1 (4.0)	38	12 (48.0)	10.5	25	10
Total	126 (59.4)	5	8 (3.8)	2.5	80 (37.7)	8	212	6