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Nationwide trends in inpatient admissions of pulmonary hypertension in the United States from 2000 to 2013

The authors declare no financial disclosure

Abstract

Introduction: Pulmonary Hypertension (PH) is a disorder of the pulmonary vasculature with high mortality and bears a large economic burden on the healthcare system. We conducted a review of the largest inpatient database in the United States and analyzed the trends in hospitalizations due to PH from the turn of the century (2000) to 2013 to evaluate the rate of hospitalizations and determine the cost and mortality associated with PH.

Material and methods: We analyzed the National Inpatient Sample Database (NIS) for all patients in which PH (Primary or Secondary) or cor pulmonale was the primary discharge diagnosis (ICD-9: 416.0, 416.8 and 416.9) from 2000 to 2013. The NIS is the largest all-payer inpatient database in the United States and contains data from approximately 8 million hospital stays each year. The statistical significance of the difference in the number of hospital discharges, lengths of stays and associated hospital costs over the study period was calculated.

Results: In 2000, there were 12,066 hospital admissions with the principal discharge diagnosis of pulmonary hypertension, which increased to 13,605 admissions in 2013 ($p < 0.001$). The mean length of stay for PH increased from 5.89 days to 6.67 days during this period ($p = 0.04$). During the same period, the hospital charges increase by 174.5% from US\$ 24,973 in 2000 to US\$ 68,545 in 2013 (Adjusted for inflation). The aggregate cost of hospital visits of a patient increased by 209.5% from US\$ 301,324,218 in 2000 to US\$ 932,554,725 in 2013.

Conclusion: The number of inpatient discharges related to PH has increased even though the number of inpatient discharges with PAH has been reported to be lower in literature. The mean length of stay has also shown a mild increase. This increase is associated with a significant increase in the mean and aggregate cost. These inpatient costs associated with PH contribute significantly to the total healthcare burden. Further research on cost-effective evaluation and management of PH is required.

Key words: pulmonary hypertension, epidemiology, length of stay, hospitalisations, mortality, healthcare burden

Adv. Respir. Med. 2017; 85: 77–86

Introduction

Pulmonary hypertension (PH) is a chronic and devastating disease characterized by progressive increases in pulmonary arterial pressure and pulmonary vascular resistance eventually leading to right ventricular failure and death [1, 2].

It is characterized by a mean pulmonary arterial pressure (mPAP) ≥ 25 mm Hg at rest and pulmonary arterial hypertension (PAH), a specific subgroup of PH, has the added criteria of a pulmonary capillary wedge pressure (PCWP) ≤ 15 mm Hg [3–5]. The World Health Organization (WHO) currently classifies PH into 5 groups (Table 1) [6].

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DOI: 10.5603/ARM.2017.0014

Received: 19.01.2017

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ISSN 2451–4934

Table 1. World Health Organization classification of pulmonary hypertension (PH)

| | |
|---------|---|
| Group 1 | Pulmonary arterial hypertension |
| Group 2 | PH due to left heart disease |
| Group 3 | PH due to lung disease and/or hypoxemia |
| Group 4 | Chronic thromboembolic PH and other pulmonary artery obstructions |
| Group 5 | PH due to unclear multifactorial mechanisms |

The exact prevalence of PH in the world is unknown, and its real burden may be largely underestimated [7]. A surveillance from the United States Centers for Disease Control and Prevention from 1980 to 2002, demonstrated an increased rates of hospitalization associated with PH with around 200,000 hospitalizations having PH as a primary or secondary diagnosis [8]. The severe symptoms of PH often present at an advanced stage of the disease process leading to a delay in diagnosis [9]. Hospitalizations related to PH also create a significant economic burden due to the costly nature of diagnostic procedures and medications. Most of the epidemiological information about PH is obtained from specialized disease registries [10, 11]. With the recently expanding research into the etiology, diagnosis and management of PH, it is important to provide updated epidemiological data regarding the disease to aid in the understanding of health utilization costs. Thus we conducted a review of the largest inpatient database in the United States and analyzed the trends in hospitalizations due to PH from the turn of the century (2000) to 2013.

Material and methods

The National Inpatient Sample (NIS) database was used to obtain a population-based estimate of national trends of PH. The NIS database is a tool developed as a part of the Healthcare Cost and Utilization Project (HCUP), and is sponsored by the Agency for Healthcare Research and Quality. The NIS database is the largest publicly available all-payer inpatient care database in the United States. The NIS database is designed to approximate a 20% sample of US community (nonfederal) hospitals, and is organized according to geographic region, hospital ownership, location, teaching status, and number of beds amongst others. The 2000 NIS database contains a total of approximately 7.5 million records. The

2013 NIS database contains a total of about 7.1 million records drawn from 44 states and includes information from 4363 hospitals. This database is drawn from all over the United States and represents a majority of the US population. The immense size of the NIS database provides an exceptional representative sample of the general US population. In order to identify cases of PH, the NIS database was queried for hospital data on all discharges with ICD-9-CM primary diagnosis codes of 416.0, 416.8 and 416.9 (Primary pulmonary hypertension, Secondary pulmonary hypertension & cor-pulmonale) from 2000 to 2013. In 2012, the NIS database was modified to draw data from all hospitals in the hospital frame to provide more efficient sampling while maintaining the same strata. The NIS database provides only administrative data for analysis and patient-specific clinical data are not available. It was assumed that the patients were formally diagnosed with PH by means of right heart catheterization.

Variables recorded

Recorded patient demographics include age and gender. Hospital characteristics included bed size (small, medium, and large) and owner (government, private non-profit or private for-profit) and the region of location (Northeast, Midwest, South & West). Hospital bed size varies depending on the hospital's location and teaching status. Small hospitals range from 1 to 299 beds, medium hospitals range from 50 to 499 beds, and large hospitals range from 100 to 500 or more beds. The payer status for all admissions was also considered and divided into categories of Medicare, Medicaid, private insurance, uninsured, and other. "Hospital Charges" are defined as the amount the hospital charged for the patient's entire hospital stay, but it does not include professional (physician) fees. As per NIS, "aggregate charges" or the national "bill" is defined as the sum of all charges for all hospital stays in the United States and "length of stay" as the number of nights the patient remained in the hospital per stay.

Statistics

The trends for average length of stay, mean total charges, mortality and total number of discharges specifically for the diagnosis of PH were plotted and analyzed from 2000 to 2013. The frequency of discharges with PH was calculated by dividing the annual number of discharges with a primary discharge diagnosis of PH by the total number of all discharges listed in the NIS for each year. The Pearson Chi-Square test was used to

compare proportions between 2000 and 2013. All statistical calculations were computed using SAS (version 9.4, The SAS Institute, NC). HCUP provided consolidated data for all codes of PH (416.0, 416.8 and 416.9). The aggregate charges ("the national bill") were calculated by summing the individual ICD-9 codes (416.0, 416.8 and 416.9). Annual charges reported are the raw charges adjusted for the long-term average health-care annual inflation rate (Bureau of Labor Statistics: <http://data.bls.gov/>) such that all dollar values relate to 2013 dollars. The temporal trend in length of stay and hospital charges with PH observed from 2000 to 2013 was assessed via polynomial regression, in which the most appropriate functional form for the trend was assessed by examination of regression diagnostic plots. A linear shape plot was determined to be appropriate for discharge count, length of stay, and mortality. The statistical significance of the trend was determined via Spearman's correlation technique to obtain p-values. P-value < 0.05 was considered to be statistically significant.

In addition to the percentages available adjacent to the data in the tables, the frequency per 10,000 admissions for each variable was calculated. Thus the numbers are a representation of the density of patients admitted/discharged with PH compared with the total number of hospital discharges per category. Each frequency was calculated by dividing the number of patients with pulmonary hypertension by the total discharges in a specific categorical variable for each year and multiplying the number by 10,000. Rates that have been compared over time using Poisson regression, which yields relative rates (RRs) that express the ratio of rate per 10,000 in 2013 to that in 2000. P-value of < 0.05 was considered to be statistically significant.

Results

Results characterizing the trends in PH related hospitalizations, length of stay, cost, mortality and discharges have been outlined in Tables 2 and 3.

Number and cost of PH discharges

From 2000 to 2013, the total number of hospital discharges with the principal diagnosis of PH increased by 12.8% from 12,066 to 13,605 ($p < 0.001$). Thus the frequency of hospital discharges with PH as the principal diagnosis increased from 3.42 per 10,000 discharges to 3.82 per 10,000 discharges (RR = 1.12, 95% CI: 1.09–1.15;

$p < 0.001$). The linear trend of PH admissions and discharges also showed a statistically significant increase from 2000 to 2013 ($R^2 = p$) (Fig. 1).

The average length of stay of a PH admission showed an increase from 5.89 days in 2000 to 6.67 days in 2013 (Fig. 2). The aggregate cost of hospital visits of a patient with the principal diagnosis of PH increased 209.5% from US\$ 301,324,218 in 2000 to US\$ 932,554,725 in 2013. The mean hospital charges per patient increased 174.5% from US\$ 24,973 in 2000 to US\$ 68,545 in 2013 (Adjusted for inflation).

Patient characteristic by age

The highest number of patient discharges in both 2000 and 2013 was noted in the 65–84 age group. The frequency of discharges was noted to be higher in the 45–64 age group in 2000 (5.74 per 10,000 discharges) while it was highest in the 65–84 age group in 2013 (5.56 per 10,000 discharges). The increase in the frequency of discharge rates was most remarkable in age groups 65–84 and > 85 years. A drop in the rate of discharges was noted in the age groups 18–44 (RR = 0.85, 95% CI: 0.80–0.90; $p < 0.001$) and 45–64 (RR = 0.90, 95% CI: 0.86–0.94; $p < 0.001$).

Patient characteristics by sex

The number of PH admissions and discharges was noted to be greatest in females both in 2000 and 2013, increasing from 3.7 per 10,000 discharges in 2000 to 4.41 per 10,000 discharges in 2013. (RR = 1.19, 95% CI: 1.16–1.23; $p < 0.001$). The increase for males did not show a statistically significant rise and increased from 3 per 10,000 discharges in 2000 to 3.03 per 10,000 discharges in 2013 ($p = 0.74$).

Patient characteristics by payer group

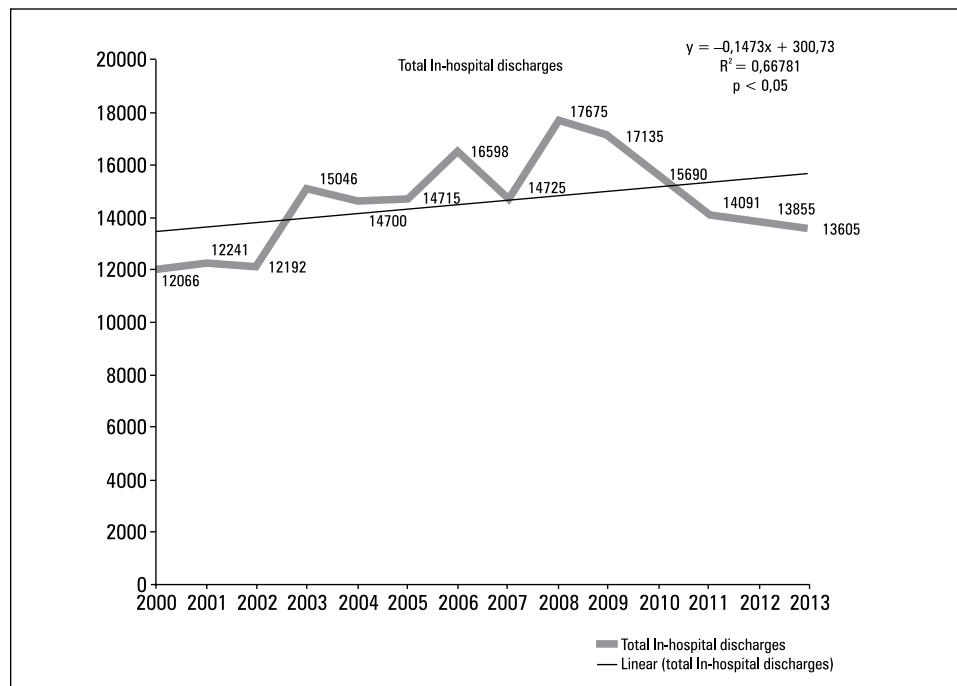
The relative frequency of PH discharges increased for all types of payer groups except Medicaid over this 13-year period. The highest absolute number of PH discharges was in the Medicare group in both 2000 and 2013, which increased from 4.93 per 10,000 discharges in 2000 to 5.71 per 10,000 discharges in 2013 (RR = 1.16, 95% CI: 1.12–1.20; $p < 0.001$). While in 2000, the frequency of discharges from the Medicare group was higher (2.87 per 10,000 discharges), the drop of discharges from Medicare group meant that the frequency of discharge of patients with Private insurance was higher in 2013 (2.66 per 10,000 discharges). There was a modest increase in the number of discharges in both the uninsured and other payer groups as noted in Table 1.

Table 2. Trends in characteristics of PH related hospitalizations from 2000 to 2013

| | Categorical Variable | 2000 PH (N,) | 2013 PH (N,) | 2000 Total (N,) | 2013 Total (N,) | PH per 10,000 admissions in 2000 | PH per 10,000 admissions in 2013 | RR (95% CI) | P-value |
|----------------------------|-------------------------|---------------|---------------|------------------|------------------|----------------------------------|----------------------------------|------------------|---------|
| All discharges | | 12,066 | 13,605 | 35,300,425 | 35,597,792 | 3.42 | 3.82 | 1.12 (1.09–1.15) | < 0.001 |
| Mean age (years) | | | | | | | | | |
| Age group (years) | < 1 | 146 | 175 | 4,541,823 | 4,232,808 | 0.32 | 0.41 | 1.29 (1.03–1.60) | 0.024 |
| | 1–17 | 234 | 415 | 1,626,291 | 1,393,028 | 1.44 | 2.98 | 2.07 (1.76–2.43) | < 0.001 |
| | 18–44 | 2,216 | 1,710 | 9,617,360 | 8,727,809 | 2.3 | 1.96 | 0.85 (0.80–0.90) | < 0.001 |
| | 45–64 | 4,110 | 4,520 | 7,159,251 | 8,753,270 | 5.74 | 5.16 | 0.90 (0.86–0.94) | < 0.001 |
| | 65–84 | 4,637 | 5,330 | 9,855,601 | 9,581,434 | 4.7 | 5.56 | 1.18 (1.14–1.22) | < 0.001 |
| | > 85 | 723 | 1,455 | 2,493,840 | 2,906,938 | 2.9 | 5.01 | 1.73 (1.58–1.89) | < 0.001 |
| Sex | Male | 4,318 | 4,585 | 14,372,338 | 15,154,195 | 3 | 3.03 | 1.01 (0.97–1.05) | 0.74 |
| | Female | 7,744 | 9,020 | 20,920,986 | 20,436,357 | 3.7 | 4.41 | 1.19 (1.16–1.23) | < 0.001 |
| Payer | Medicare | 6,294 | 7,990 | 12,763,012 | 13,986,550 | 4.93 | 5.71 | 1.16 (1.12–1.20) | < 0.001 |
| | Medicaid | 1,667 | 1,825 | 5,814,171 | 7,417,129 | 2.87 | 2.46 | 0.86 (0.80–0.92) | < 0.001 |
| | Private Insurance | 3,456 | 2,890 | 13,787,690 | 10,851,650 | 2.51 | 2.66 | 1.06 (1.01–1.12) | < 0.05 |
| | Uninsured | 324 | 505 | 1,724,382 | 2,070,848 | 1.88 | 2.44 | 1.30 (1.13–1.50) | < 0.001 |
| | Other | 306 | 390 | 1,070,236 | 1,216,485 | 2.86 | 3.20 | 1.12 (0.97–1.30) | 0.13 |
| Median income for zip code | Low (\$0–35,999) | * | 4,160 | * | 10,199,933 | * | 4.08 | | |
| | Not low (\$36,000+) | * | 9,120 | * | 24,599,165 | * | 3.71 | | |
| Owner | Government | 1,837 | 2,020 | 4,608,704 | 4,291,755 | 3.99 | 4.71 | 1.18 (1.11–1.26) | < 0.001 |
| | Private, not-for-profit | 9,050 | 9,920 | 26,471,999 | 26,111,822 | 3.42 | 3.80 | 1.11 (1.08–1.14) | < 0.001 |
| | Private, for-profit | 1,179 | 1,665 | 4,219,722 | 5,194,215 | 2.79 | 3.21 | 1.15 (1.06–1.24) | < 0.001 |
| Bed Size | Small | 1,148 | 1,495 | 4,049,244 | 4,884,892 | 2.84 | 3.06 | 1.08 (1.01–1.17) | 0.05 |
| | Medium | 2,955 | 3,205 | 9,621,509 | 9,512,936 | 3.07 | 3.37 | 1.10 (1.04–1.15) | < 0.001 |
| | Large | 7,945 | 8,905 | 2,1578,915 | 21,199,964 | 3.68 | 4.2 | 1.14 (1.11–1.18) | < 0.001 |
| Region | Northeast | 2,096 | 2,405 | 7,009,155 | 6,730,965 | 2.99 | 3.57 | 1.19 (1.13–1.27) | < 0.001 |
| | Midwest | 3,072 | 3,275 | 8,221,274 | 8,004,912 | 3.74 | 4.09 | 1.09 (1.04–1.15) | < 0.001 |
| | South | 4,566 | 4,900 | 13,340,212 | 13,818,031 | 3.42 | 3.55 | 1.04 (1.01–1.08) | 0.085 |
| | West | 2,332 | 3,025 | 6,729,784 | 7,043,884 | 3.47 | 4.30 | 1.24 (1.17–1.31) | < 0.001 |

Table 3. Trends in characteristics of PH related hospitalizations & discharges from 2000 to 2013

| | 2000 PH | 2013 PH | RR(CI) | P-value |
|--|---------------|---------------|------------------|---------|
| Total number of discharges | 12,066 | 13605 | – | < 0.01 |
| Length of Stay | 5.89 days | 6.67 days | – | 0.04 |
| Charges (mean, adjusted for inflation) | \$24973 | \$68545 | – | – |
| Total charges (adjusted for inflation) | \$301,324,218 | \$932,554,725 | – | – |
| Mortality | 807 (6.69%) | 620 (4.56%) | 0.70 (0.63–0.77) | < 0.001 |
| Routine Discharges | 8232 (68.23%) | 7835 (57.59%) | 0.90 (0.88–0.92) | < 0.001 |
| Another short term hospital | 396 (3.28%) | 585 (4.30%) | 1.30 (1.14–1.47) | < 0.001 |
| Nursing Home or Rehabilitation | 1094 (9.07%) | 1760 (12.94%) | 1.38 (1.28–1.48) | < 0.001 |
| Home Health Care | 1490 (12.35%) | 2690 (19.77%) | 1.50 (1.42–1.60) | < 0.001 |
| Against medical advice | 46 (0.38%) | 105 (0.77%) | 2.02 (1.43–2.85) | < 0.001 |

**Figure 1.** Trends in in-hospital discharges

Pulmonary Hypertension discharges by hospital ownership, characteristics and region

There was a rise in the number of PH discharges from all 3, hospital owner categories from 2000 to 2013 (Government, Private (Not-for-profit) and Private (For-profit)). The overall highest number of discharges were seen from Private, not-for-profit hospitals. The highest increase in frequency was seen in discharges from Government hospitals (RR= 1.18, 95% CI: 1.11–1.26; $p < 0.001$). In 2000 a patient with PH was more likely

to be admitted and discharged from a hospital with a large number of beds (65.85%) as compared to hospital with medium or small number of beds, and this trend continued in 2013 (69.45%).

The South had the highest number of both PH discharges and total discharges in 2000 as well as 2013. Even then, the increase in the frequency of discharge in the South from 2000 to 2013 was not statistically significant ($p = 0.085$). On the contrary, the Midwest had the highest frequency of PH discharges in 2000 with 3.74 per 10,000 discharges while in 2013 it was highest in the

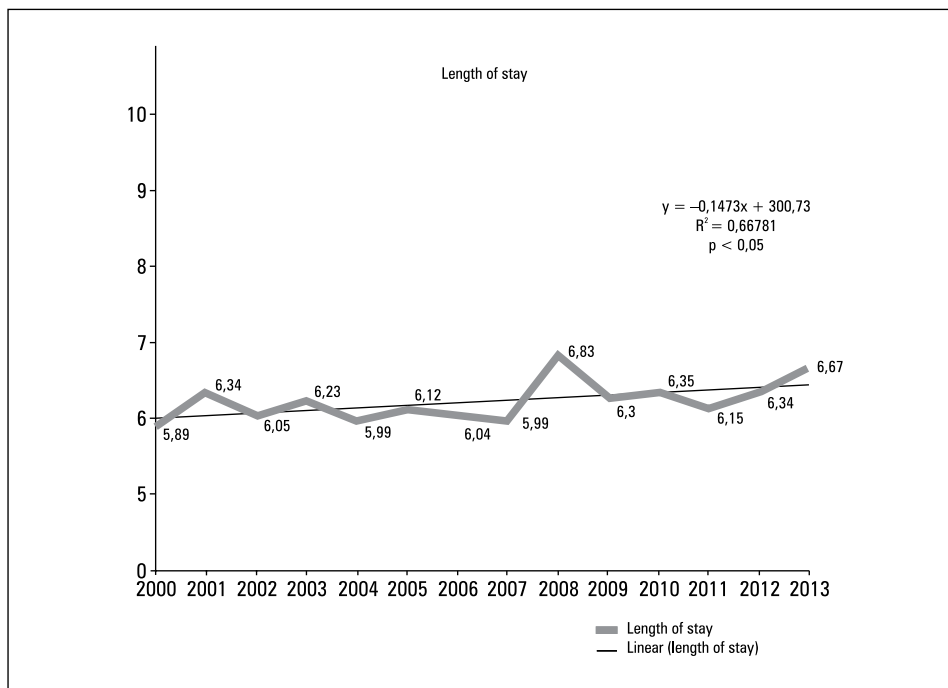


Figure 2. Trends in length of stay

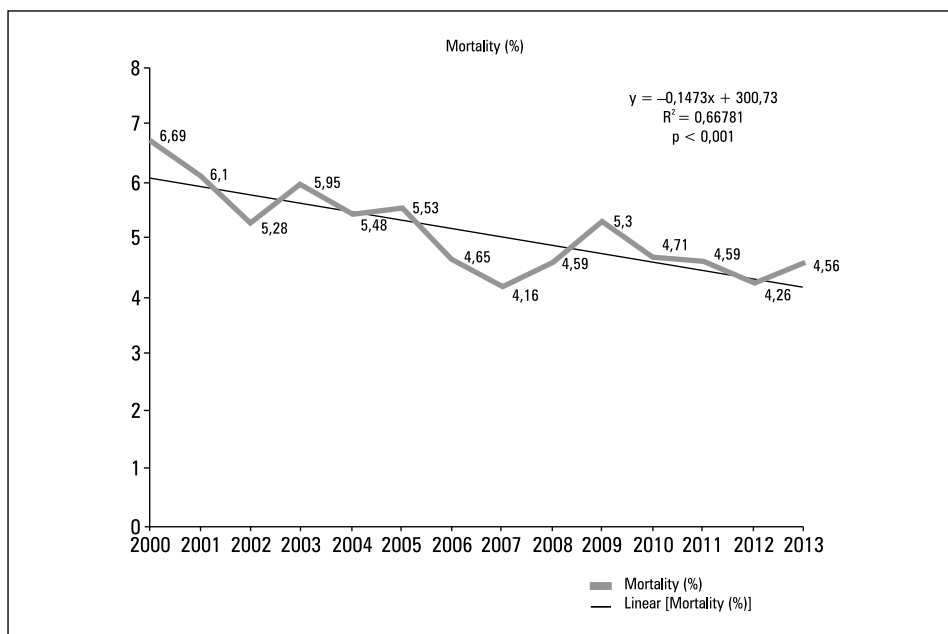


Figure 3. Trends in mortality

West with 4.3 per 10,000 discharges. The total number and frequency of discharges in all regions except the South showed a statistically significant increase (Table 1).

Pulmonary hypertension discharges with mortality rates and discharge disposition

The percent mortality of patients admitted and discharged with a principal diagnosis of PH

decreased from 6.69% in 2000 to 4.56% in 2013 with a statistically significant decrease in the linear trend ($R^2 =$; $p < 0.01$) (Fig. 3). The number of routine discharges decreased from 68.23% to 57.59% of the total discharges. On the other hand, discharges from the hospital to nursing home and rehabilitation increased from 9.07% to 12.94% ($RR = 1.38$, 95 CI: 1.28–1.48; $p < 0.001$). Also notable was the fact patients discharged with

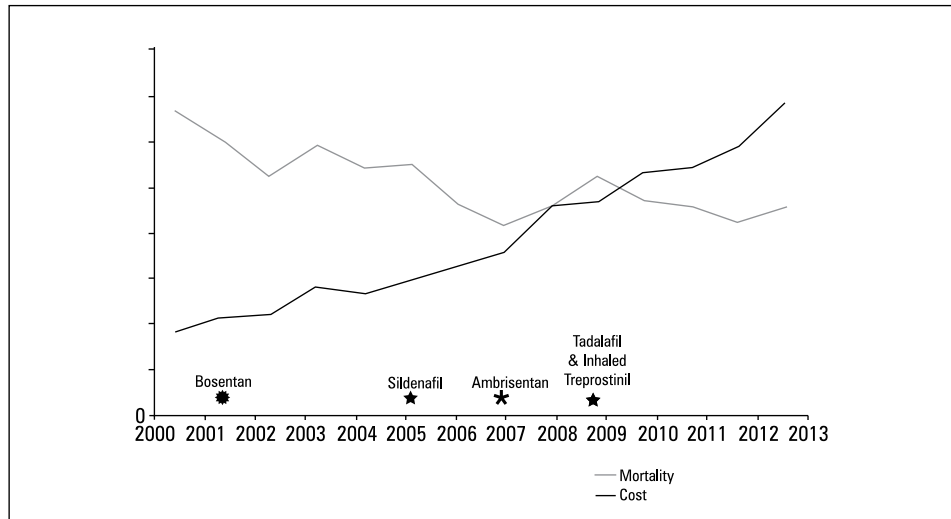


Figure 4. Trends graph in mortality of pulmonary hypertension and cost along with sentinel events in management of pulmonary arterial hypertension

home health care increased from 12.35% of total discharges in 2000 to 19.77% of total PH discharges in 2013 (RR= 1.50, 95% CI: 1.42–1.60; $p < 0.001$).

Discussion

Pulmonary hypertension continues to be a challenging disease to diagnose and manage due to its heterogeneous etiology and complex pathogenesis. There appears to be a growing number of diagnoses of PH, possibly due to the greater awareness of this once considered, rare disease or due to better screening and diagnostic availability i.e. right heart catheterizations and echocardiography. However determining the exact epidemiology has proven challenging due to a lack of global consensus on prevalence. In the United Kingdom, a prevalence of 97 cases per million with a female: male ratio of 1.8 has been reported and in the United States the age-standardized death rate ranges between 4.5 and 12.3 per 100,000 population [12]. The United States' national inpatient database provides valuable information, exploring aspects of patient characteristics, epidemiology as well as providing a snapshot of economic burden of this disease.

Discharges and length of stay

Our study demonstrated that in the national trend of the United States; there was a statistically significant increase in the overall number of hospitalizations for PH from 2000 through to 2013. This was in spite of the fact that a recent study reported a decline in the number of hospitalizations associated with PAH (Group 1) alone from 2001 through 2012 [13]. This would indicate

that the rise in the number of hospitalizations due to PH can actually be attributed to an increase in admissions due to secondary causes of PH i.e. WHO Group 2–5 PH. A review of literature did not yield any comparative data in terms of hospital admissions for all WHO groups of PH. Most available data in literature focuses of WHO Group I PAH, possibly due to the fact that there is available pharmacological treatment.

This overall increase in hospitalizations may be attributed to a number of causes. One explanation may be the increased awareness about PH in the modern management era. While PH was once known as an orphan disease [8], new effective therapies to treat PAH are now available. Primary or idiopathic PH was once considered a rare disease that affected young women at the time of the initial National Institutes of Health (NIH) registry [14]. Thus older patients might have often been not considered candidates for diagnosis of PH at that time. This fact has likely changed thus leading to an increase in the diagnosis of PH especially in that subgroup (Group I PH). This is reinforced by the fact that the number of admissions in the age group > 85 years has shown a significant rise from 2000 to 2013. Thus increased awareness has likely played a major role in increasing the total number of patients diagnosed with PH.

Another contributing factor is the wide spread use of doppler echocardiography and other imaging modalities in the community leading to increase in the diagnosis of PH. Papolos et al. recently showed that between 2001 and 2011, the absolute volume and incidence of echo increased at an average annual rate of 3.41% and 3.04%

respectively [15]. A study in 2009 concluded that the use of computed tomography (CT) had doubled and the use of magnetic resonance imaging (MRI) had tripled in the 10 years preceding the study [16]. Both these tests demonstrate an enlarged pulmonary arterial size or other radiographical features of PH, which may lead to the diagnosis of PH. The rise of hospitalizations could also be attributed to the fact that previously diagnosed PH patients might be readmitted due to an overall decrease in mortality as discussed later.

Our study also demonstrated a significant, 13% increase of length of hospital stay from 2000 to 2013. This may seem counterintuitive as our diagnostic and treatment modalities have advanced over the analyzed time period. The exact reason for the increase in length of stay is unknown however it may be attributed to possible complications associated with advanced stages of PH disease. A German study by Wilkens et al. demonstrated that the average length of stay of PAH a patient was 11.8 ± 28.2 days [17]. As the availability of advanced diagnostics i.e. right heart catheterization become available in all healthcare centers the increase in the number of inpatient diagnostic tests could also contribute to the increased length of stay in these patients. Another recent study noted an increased frequency of cardiogenic shock, cardiac dysrhythmias, acute respiratory failure and renal failure in patients with PH [13], which in turn may lead to an increased length of stay.

Age characteristics and payer status

There was a trend towards admission of patients greater than 65 years of age that is in line with all recent studies that found a shift in diagnosis of PH to an older age [13, 18–20]. Most patients continued to be women in both 2000 and 2013. There was no statistically significant increase in the frequency of men with hospitalizations due to PH in 2013 compared to 2000. In terms of payer status, we found that the highest absolute number of PH discharges was in the Medicare group in both 2000 and 2013. This is likely due to the fact that 44.4% of the patients in 2000 and 49.80% of the patients in 2013 were above the age of 65. Although there was a decrease in the number of PH patients with private insurance, this was likely a reflection of the national trend in 2013 where lesser patients had private insurance as compared to patients in 2000. The relative frequency of PH with private insurance actually showed a small increase. We noted that patients with PH were more likely to be admitted to private, not-for-pro-

fit hospitals. We also observed that patients with PH were more likely to be admitted to hospitals with a large number of beds as compared to hospitals with a medium or small number of beds. This might be due to the fact that tertiary care hospitals, which usually have large number of beds, are better equipped to deal with the complex course of a pulmonary hypertension patient. In terms of regional distribution, the southern part of United States had the highest number of absolute discharges of PH patients in both 2000 and 2013. On the other hand, the Midwestern United States had the highest frequency.

Health utilization costs

We found that the aggregate hospital charges adjusted for inflation for patients with PH increased 2.1 fold from 2000 to 2013. There are several possible explanations for this rise. As noted earlier, there is an increased frequency of complications in patients with PH. Increased complications leads to an increased length of stay and an associated increased cost of hospitalization. There has also been a tremendous rise in the usage of diagnostic modalities amongst patients admitted to the hospitals in United States in the last decade [15, 16]. This increased use of diagnostic modalities is associated with an increased healthcare expenditure.

The approval of new, expensive drugs targeted against WHO Group I PAH such as Epoprostenol, Bosentan, Sildenafil, Ambrisentan, Tadalafil and Riociguat have likely also contributed to the increased healthcare burden while the patients are admitted to the hospital (Fig. 4). The European Society of Cardiology's practice guideline on PAH released in 2004 redefined PAH as per the new clinical classification and described an algorithm of various investigative tests, procedures and evidence-based treatment. This likely contributed to an accurate diagnosis and management of PAH at the expense of increasing healthcare costs [21]. A study by Kirson et al. that analyzed a private insurance database from 2002–2007 demonstrated as compared to the general population patients with PAH had substantially higher costs and comorbidity resulting in 40% of excess costs associated with management and treatment of PAH patients [22]. On the contrary, management of PH WHO Group II & III is focused on treatment of the underlying disease. Newer therapies for these diseases such as heart failure, chronic lung disease and other connective tissue disorders also contribute to an increased cost of hospitalization. This includes the use of invasive modalities and

implantable cardiac devices for cardiac condition in patients with Group II PH and the use of novel drugs in the treatment of patients with Group III PH. Our results are consistent with previous studies that have found an increased length of hospitalization and an increased inpatient cost for PH related hospitalizations [13].

As our analysis focuses on data from the United States, the perspective provided is that of a multi-payer health system that is semi privatized. It is important to understand the dynamics of PH admission and the health utilization costs in single payer health systems. In a study by Vaid *et al.* [23] on Ontario in Canada, it was noted that there were higher hospitalization costs, nearly fivefold, in the cohort of PAH patients who died due to their disease as compared those who survived. Though this is a small sample size we are able to see that costs are high, and that patients with more severe disease have greater health utilization costs regardless of whether they were hospital or pharmaceutical related. There is yet to be comprehensive data on PH as a whole in a single payer system. From the data put forth, emphasis of PH should be placed on early diagnosis and management. In a study by Sikirica [24], it was found that subjects with evidence of PAH had substantively high health care costs. Medical costs appeared to decrease following medication use for PAH, but with a concomitant increase in pharmacy costs. Cost of PH diagnosis and management is detrimental as there is a correlation between socioeconomic status of patients with clinical outcomes and disease severity at presentation in PH [25, 26].

Mortality

Our analysis showed that there was a 23% reduction in mortality in 2013 as compared to 2000 amongst patients hospitalized with diagnosis of PH. The mortality rate reduced from 6.69% in 2000 to 4.56% in 2013 (Fig. 4). The progressive decrease in mortality has been heralded by newer therapies for Group 1 and Group 4 PH and improvement in treatment options for chronic lung and chronic heart disease. An early diagnosis due to the increased use of imaging modalities, follow up at dedicated PH centers and close outpatient follow up have all likely contributed to this reduced mortality. A review of the discharge disposition revealed that there was a significant increase of the number of discharges with home health care from 2000 to 2013. This possibly reflects the multiple co-morbidities as well as the complex nature of the patient's illness. This also

contributes significantly to the increased burden on healthcare expenditure. A significant increase was also seen in the number of patients discharged to a nursing home or rehabilitation facility. The increases in discharges to a nursing home is consistent with the fact that more patients admitted for PH are above the age of 85 and thus are more likely to be nursing home residents. Patients with increased length of stay and associated physical debilitation are also more likely to require rehabilitation facilities before discharge back to home or nursing home.

Limitations

The design of this study and the nature of the NIS database set leads to some important limitations. As this is an administrative data set, it reflects the coding practices of each institution. Thus it is likely that these results underestimate the actual number of patients admitted and discharged with the diagnosis of PH. It is likely that patient's discharges may have been coded with an alternative primary diagnosis such as heart failure, hypoxemia, chronic lung diseases or other underlying connective tissue disorders with PH as a secondary diagnosis. For our study these patients were excluded as they might have been admitted for a non-cardiopulmonary manifestation and carried a secondary diagnosis of PH. With the use of the NIS database it would also be hard to calculate or determine if patients were admitted from the emergency room or transferred from community hospitals to expert PH centers. While it is plausible to think that hospitals were not able to manage these patients and thus transferred the patient to a tertiary center, it reflects real world practice. In addition, this data set does not control for errors during the entry of the data. Also, patient specific clinical information was not obtainable which thereby limited the demographic data presented in the research. Results of right heart catheterization were not available for these patients and thus adherence to the diagnostic criteria for PH could not be confirmed. Further studies analyzing hospital coding practices may clarify these concerns. In addition, the NIS data set does not provide details regarding the patient or the hospital, which could help us, explain the rise or decline in the hospital discharges and associated costs.

Conclusion

In conclusion, PH is an escalating concern in the United States healthcare system. This is

demonstrated by the significant increase in the hospital cost associated with PH admissions from 2000 to 2013. Future studies analyzing the diagnostic modalities, algorithms and treatment practices of physician's treating PH are necessary to reduce the burden it has on the healthcare system.

Conflict of interest

The authors declare no conflict of interest.

References:

- Badesch DB, Champion HC, Sanchez MA, et al. Diagnosis and assessment of pulmonary arterial hypertension. *J Am Coll Cardiol.* 2009; 54(1 Suppl): S55–S66, doi: [10.1016/j.jacc.2009.04.011](https://doi.org/10.1016/j.jacc.2009.04.011), indexed in Pubmed: [19555859](https://pubmed.ncbi.nlm.nih.gov/19555859/).
- Farber HW, Loscalzo J. Pulmonary arterial hypertension. *N Engl J Med.* 2004; 351(16): 1655–1665, doi: [10.1056/NEJMra035488](https://doi.org/10.1056/NEJMra035488), indexed in Pubmed: [15483284](https://pubmed.ncbi.nlm.nih.gov/15483284/).
- Hoepfer MM, Bogaard HJ, Condliffe R, et al. Definitions and diagnosis of pulmonary hypertension. *J Am Coll Cardiol.* 2013; 62(25 Suppl): D42–D50, doi: [10.1016/j.jacc.2013.10.032](https://doi.org/10.1016/j.jacc.2013.10.032), indexed in Pubmed: [24355641](https://pubmed.ncbi.nlm.nih.gov/24355641/).
- Palkar AV, Agrawal A, Verma S, et al. Post splenectomy related pulmonary hypertension. *World J Respirol.* 2015; 5(2): 69–77, doi: [10.5320/wjr.v5.i2.69](https://doi.org/10.5320/wjr.v5.i2.69), indexed in Pubmed: [26949600](https://pubmed.ncbi.nlm.nih.gov/26949600/).
- Sahni S, Ojrzanowski M, Majewski S, et al. Pulmonary arterial hypertension: a current review of pharmacological management. *Pneumonol Alergol Pol.* 2016; 84(1): 47–61, doi: [10.5603/PiA.Pa.2015.0084](https://doi.org/10.5603/PiA.Pa.2015.0084), indexed in Pubmed: [26693827](https://pubmed.ncbi.nlm.nih.gov/26693827/).
- Simonneau G, Gatzoulis MA, Adatia I, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll Cardiol.* 2013; 62(25 Suppl): D34–D41, doi: [10.1016/j.jacc.2013.10.029](https://doi.org/10.1016/j.jacc.2013.10.029), indexed in Pubmed: [24355639](https://pubmed.ncbi.nlm.nih.gov/24355639/).
- Humbert M, Khaltaev N, Bousquet J, et al. Pulmonary hypertension: from an orphan disease to a public health problem. *Chest.* 2007; 132(2): 365–367, doi: [10.1378/chest.07-0903](https://doi.org/10.1378/chest.07-0903), indexed in Pubmed: [17699126](https://pubmed.ncbi.nlm.nih.gov/17699126/).
- Hyduk A, Croft JB, Ayala C, et al. Pulmonary hypertension surveillance--United States, 1980-2002. *MMWR Surveill Summ.* 2005; 54(5): 1–28, indexed in Pubmed: [16280974](https://pubmed.ncbi.nlm.nih.gov/16280974/).
- Deaño RC, Glassner-Kolmin C, Rubenfire M, et al. Referral of patients with pulmonary hypertension diagnoses to tertiary pulmonary hypertension centers: the multicenter RePHerral study. *JAMA Intern Med.* 2013; 173(10): 887–893, doi: [10.1001/jamainternmed.2013.319](https://doi.org/10.1001/jamainternmed.2013.319), indexed in Pubmed: [23568223](https://pubmed.ncbi.nlm.nih.gov/23568223/).
- McGoon MD, Krichman A, Farber HW, et al. Design of the REVEAL registry for US patients with pulmonary arterial hypertension. *Mayo Clin Proc.* 2008; 83(8): 923–931, doi: [10.4065/83.8.923](https://doi.org/10.4065/83.8.923), indexed in Pubmed: [18674477](https://pubmed.ncbi.nlm.nih.gov/18674477/).
- Humbert M, Simonneau G, Rubin LJ. A decade of achievement in pulmonary hypertension. *Eur Respir Rev.* 2011; 20(122): 215–217, doi: [10.1183/09059180.00007311](https://doi.org/10.1183/09059180.00007311), indexed in Pubmed: [22130812](https://pubmed.ncbi.nlm.nih.gov/22130812/).
- Galiè N, Humbert M, Vachiery JL, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS); Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). *Eur Respir J.* 2015; 46(4): 903–975, doi: [10.1183/13993003.01032-2015](https://doi.org/10.1183/13993003.01032-2015), indexed in Pubmed: [26318161](https://pubmed.ncbi.nlm.nih.gov/26318161/).
- Anand V, Roy SS, Archer SL, et al. Trends and Outcomes of Pulmonary Arterial Hypertension-Related Hospitalizations in the United States: Analysis of the Nationwide Inpatient Sample Database From 2001 Through 2012. *JAMA Cardiol.* 2016; 1(9): 1021–1029, doi: [10.1001/jamacardio.2016.3591](https://doi.org/10.1001/jamacardio.2016.3591), indexed in Pubmed: [27851838](https://pubmed.ncbi.nlm.nih.gov/27851838/).
- Rich S, Dantzker DR, Ayres SM, et al. Primary pulmonary hypertension. A national prospective study. *Ann Intern Med.* 1987; 107(2): 216–223, indexed in Pubmed: [3605900](https://pubmed.ncbi.nlm.nih.gov/3605900/).
- Papoulos A, Narula J, Bavishi C, et al. U.S. Hospital Use of Echocardiography: Insights From the Nationwide Inpatient Sample. *J Am Coll Cardiol.* 2016; 67(5): 502–511, doi: [10.1016/j.jacc.2015.10.090](https://doi.org/10.1016/j.jacc.2015.10.090), indexed in Pubmed: [26846948](https://pubmed.ncbi.nlm.nih.gov/26846948/).
- Smith-Bindman R, Miglioretti DL, Larson EB. Rising use of diagnostic medical imaging in a large integrated health system. *Health Aff (Millwood).* 2008; 27(6): 1491–1502, doi: [10.1377/hlthaff.27.6.1491](https://doi.org/10.1377/hlthaff.27.6.1491), indexed in Pubmed: [18997204](https://pubmed.ncbi.nlm.nih.gov/18997204/).
- Wilkins H, Grimminger F, Hoepfer M, et al. Burden of pulmonary arterial hypertension in Germany. *Respir Med.* 2010; 104(6): 902–910, doi: [10.1016/j.rmed.2010.01.002](https://doi.org/10.1016/j.rmed.2010.01.002), indexed in Pubmed: [20149617](https://pubmed.ncbi.nlm.nih.gov/20149617/).
- Burke JP, Hunsche E, Régulier E, et al. Characterizing pulmonary hypertension-related hospitalization costs among Medicare Advantage or commercially insured patients with pulmonary arterial hypertension: a retrospective database study. *Am J Manag Care.* 2015; 21(3 Suppl): s47–s58, indexed in Pubmed: [25734573](https://pubmed.ncbi.nlm.nih.gov/25734573/).
- Jinjuvadia C, Jinjuvadia R, Mandapakala C, et al. Trends in Outcomes, Financial Burden, and Mortality for Acute Exacerbation of Chronic Obstructive Pulmonary Disease (COPD) in the United States from 2002 to 2010. *COPD.* 2017; 14(1): 72–79, doi: [10.1080/15412555.2016.1199669](https://doi.org/10.1080/15412555.2016.1199669), indexed in Pubmed: [27419254](https://pubmed.ncbi.nlm.nih.gov/27419254/).
- Gjesing A, Gislason GH, Køber L, et al. Nationwide trends in development of heart failure and mortality after first-time myocardial infarction 1997-2010: A Danish cohort study. *Eur J Intern Med.* 2014; 25(8): 731–738, doi: [10.1016/j.ejim.2014.08.009](https://doi.org/10.1016/j.ejim.2014.08.009), indexed in Pubmed: [25225051](https://pubmed.ncbi.nlm.nih.gov/25225051/).
- Galiè N, Humbert M, Vachiery JL, et al. Task Force. Guidelines on diagnosis and treatment of pulmonary arterial hypertension. The Task Force on Diagnosis and Treatment of Pulmonary Arterial Hypertension of the European Society of Cardiology. *Eur Heart J.* 2004; 25(24): 2243–2278, doi: [10.1016/j.ehj.2004.09.014](https://doi.org/10.1016/j.ehj.2004.09.014), indexed in Pubmed: [15589643](https://pubmed.ncbi.nlm.nih.gov/15589643/).
- Kirson NY, Birnbaum HG, Ivanova JI, et al. Excess costs associated with patients with pulmonary arterial hypertension in a US privately insured population. *Appl Health Econ Health Policy.* 2011; 9(5): 293–303, doi: [10.2165/11592430-000000000-00000](https://doi.org/10.2165/11592430-000000000-00000), indexed in Pubmed: [21875160](https://pubmed.ncbi.nlm.nih.gov/21875160/).
- Vaid HM, Camacho X, Granton JT, et al. The Characteristics of Treated Pulmonary Arterial Hypertension Patients in Ontario. *Can Respir J.* 2016; 2016: 6279250, doi: [10.1155/2016/6279250](https://doi.org/10.1155/2016/6279250), indexed in Pubmed: [27445555](https://pubmed.ncbi.nlm.nih.gov/27445555/).
- Sikirica M, Iorga SR, Bancroft T, et al. The economic burden of pulmonary arterial hypertension (PAH) in the US on payers and patients. *BMC Health Serv Res.* 2014; 14: 676, doi: [10.1186/s12913-014-0676-0](https://doi.org/10.1186/s12913-014-0676-0), indexed in Pubmed: [25539602](https://pubmed.ncbi.nlm.nih.gov/25539602/).
- Wu WH, Yang Lu, Peng FH, et al. Lower socioeconomic status is associated with worse outcomes in pulmonary arterial hypertension. *Am J Respir Crit Care Med.* 2013; 187(3): 303–310, doi: [10.1164/rccm.201207-1290OC](https://doi.org/10.1164/rccm.201207-1290OC), indexed in Pubmed: [23220911](https://pubmed.ncbi.nlm.nih.gov/23220911/).
- Talwar A, Sahni S, Talwar A, et al. Socioeconomic status affects pulmonary hypertension disease severity at time of first evaluation. *Pulm Circ.* 2016; 6(2): 191–195, doi: [10.1086/686489](https://doi.org/10.1086/686489), indexed in Pubmed: [27252845](https://pubmed.ncbi.nlm.nih.gov/27252845/).