Characteristics of Patients Treated for Pulmonary Arterial Hypertension in a Real-World Database Representing a Large US Health Plan

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Background

- Pulmonary arterial hypertension (PAH) is a chronic, progressive disease characterized by high blood pressure in the pulmonary arterioles, which can result in right heart failure and premature mortality.
- The estimated annual incidence of PAH in the US is 2.3 per million, with an estimated prevalence of 12.4 per million.[1]
- In a US registry (REVEAL), PAH was found to be associated with common comorbidities including systemic hypertension, sleep apnea, diabetes, and renal insufficiency.[2]
- With several new PAH therapies becoming available since 2013, more information is needed to characterize the patients treated with these medications.

Objective

- This study was conducted to describe demographic and clinical characteristics, healthcare resource utilization, and healthcare costs among patients with PAH in a large representative US health plan.

Methods

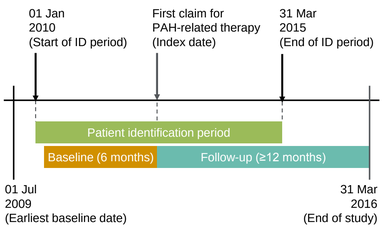
Study design

- This was a retrospective administrative claims study using the Optum Research Database, which contains medical and pharmacy data from individuals enrolled in US commercial and Medicare Advantage with Part D (MAPD) health plans.
- Identification period: 1 January 2010 – 31 March 2015 (Figure 1)
- Index date: date of the first claim for a PAH-related medication, including endothelin receptor antagonists (ambrisentan, bosentan, macitentan); phosphodiesterase type 5 inhibitors (sildenafil, tadalafil); prostacyclins and selective prostaglandin IP receptor agonists (epoprostenol, iloprost, treprostinil, and selexipag); and soluble guanylate cyclase stimulators (riociguat)
- Inclusion criteria:
  - At least 1 pharmacy claim for a PAH-related medication during the identification period
  - At least 1 claim with a diagnosis code for pulmonary hypertension (ICD-9-CM codes 416.0, 416.8, or 416.9) in any position during the 6 months prior to and including the index date
  - No pharmacy claims for PAH-related medications during the 6 months prior to the index date
  - Continuous enrollment with medical and pharmacy benefits during the 6 months prior to and 12 months after and including the index date
  - Age ≥ 18 as of the index date
- Patients were assigned to a study cohort based on the number of different PAH-related medication classes filled within 30 days, starting with the index date:
  - Monotherapy: patients with pharmacy claims for only 1 class of PAH-related medication
  - Combination therapy: patients with pharmacy claims for > 1 class of PAH-related medication

Study measures

- Baseline patient characteristics were assessed during the 6 months prior to the index date (baseline period; Figure 1).
- Between-cohort differences in patient characteristics were analyzed using Student's *t* test, a chi-square test, and/or Fisher's exact test, as appropriate.
- Outcomes (follow-up healthcare resource utilization and healthcare costs) were assessed during a variable follow-up period of at least 12 months after the index date (Figure 1).

Figure 1. Study design schematic



Results

Patient selection and attrition

- Of 6,925 patients with at least 1 pharmacy claim for a PAH-related therapy during the identification period, 1,637 met all study criteria.
- The monotherapy cohort and combination therapy cohort contained 1,535 patients and 102 patients, respectively.

Results (continued)

Patient characteristics and comorbidities

- Baseline patient characteristics are given in Table 1:
  - The study population was majority female (63.7%); mean (SD) age was 65.3 (13.8) years.
  - Slightly more patients were enrolled in Medicare Advantage (54.4%) than in commercial insurance plans (45.6%).
  - Mean (SD) follow-up duration was 2.5 (1.2) years, with 53.8% of patients followed for more than 2 years and 12.7% followed for more than 4 years.
  - Mean Charlson comorbidity score was 3.3, with 67.7% of patients scoring ≥ 3.
  - Over 90% of patients had lower respiratory disease. Other common comorbidities included systemic hypertension (80.5%), lipid metabolism disorders (55.2%), connective tissue diseases (42.6%), type 2 diabetes (39.2%), and sleep apnea (37.2%).
  - More than 70% of patients were using diuretics during the baseline period, and nearly half were using anticoagulants.
- Patients in the monotherapy cohort were older, more likely to be male, and more often enrolled in Medicare Advantage plans compared with those in the combination therapy cohort ($p \leq 0.001$; Table 1).
- Comorbidity profiles were mostly similar between the monotherapy and combination therapy cohorts, although sleep apnea was more common in the monotherapy cohort ($p = 0.04$; Table 1).

Table 1. Baseline patient characteristics

Characteristic	Total (n = 1,637)	Mono-therapy (n = 1,535)	Comb. therapy (n = 102)	P-value
Age, mean (SD)	65.3 (13.8)	**65.7 (13.7)**	**59.1 (14.2)**	**< 0.001**
Female, n (%)	1,043 (63.7)	**963 (62.7)**	**80 (78.4)**	**0.001**
Insurance type, n (%)				
Commercial	746 (45.6)	**684 (44.6)**	**62 (60.8)**	**0.001**
Medicare	891 (54.4)	**851 (55.4)**	**40 (39.2)**	**0.001**
Years of follow-up, mean (SD)	2.5 (1.2)	2.5 (1.2)	2.4 (1.2)	0.429
Years of follow-up, n (%)				
1 to ≤ 2	757 (46.2)	707 (46.1)	50 (49.0)	0.561
> 2 to ≤ 3	440 (26.9)	412 (26.8)	28 (27.5)	0.893
> 3 to ≤ 4	232 (14.2)	219 (14.3)	13 (12.8)	0.670
> 4 to ≤ 5	122 (7.5)	116 (7.6)	6 (5.9)	0.533
> 5	86 (5.3)	81 (5.3)	5 (4.9)	0.869
Charlson comorbidity score, mean (SD)	3.3 (2.0)	3.3 (2.0)	3.4 (2.0)	0.865
Charlson comorbidity score, n (%)				
0	31 (1.9)	30 (2.0)	1 (1.0)	0.485
1–2	498 (30.4)	464 (30.2)	34 (33.3)	0.509
3–4	729 (44.5)	683 (44.5)	46 (45.1)	0.906
> 5	379 (23.2)	358 (23.3)	21 (20.6)	0.526
Common comorbidities, n (%)				
Lower respiratory disease[a]	1,500 (91.6)	1,404 (91.5)	96 (94.1)	0.349
Systemic hypertension[a]	1,317 (80.5)	1,235 (80.5)	82 (80.4)	0.987
Lipid metabolism disorder[a]	903 (55.2)	854 (55.6)	49 (48.0)	0.135
Connective tissue disease[a]	698 (42.6)	653 (42.5)	45 (44.1)	0.755
Type 2 diabetes[b]	641 (39.2)	609 (39.7)	32 (31.4)	0.096
Sleep apnea[b]	609 (37.2)	**581 (37.9)**	**28 (27.5)**	**0.035**
Respiratory failure or insufficiency[a]	521 (31.8)	487 (31.7)	34 (33.3)	0.736
Thyroid disease[b]	381 (23.3)	353 (23.0)	28 (27.5)	0.303
Depression[b]	218 (13.3)	199 (13.0)	19 (18.6)	0.103
CV medication, n (%)				
Diuretics	1,184 (72.3)	1,115 (72.6)	69 (67.7)	0.275
Anticoagulants	796 (48.6)	749 (48.8)	47 (46.1)	0.595
Digoxin	211 (12.9)	200 (13.0)	11 (10.8)	0.512

[a]Defined using AHRQ Clinical Classifications Software.
[b]Identified from ICD-9-CM codes on claims during the baseline period.
Comb., combination; CV, cardiovascular; SD, standard deviation.

Healthcare resource utilization

- Healthcare resource utilization was substantial during both the baseline and follow-up periods; nearly 100% of patients had an ambulatory visit, and emergency room visits and inpatient stays were common (Table 2).
- In both the baseline and follow-up periods:
  - A higher percentage of MAPD vs commercial enrollees had inpatient stays (Table 2).
  - The percentage of patients with inpatient stays was higher in the combination therapy cohort than in the monotherapy cohort (Table 2).

Table 2. All-cause healthcare resource utilization

Resource	Total		Monotherapy		Combination therapy	
	Commer. (n = 746)	MAPD (n = 891)	Commer. (n = 684)	MAPD (n = 851)	Commer. (n = 62)	MAPD (n = 40)
Ambulatory visit, n (%)						
Baseline	743 (99.6)	884 (99.2)	681 (99.6)	844 (99.2)	62 (100.0)	40 (100.0)
Follow-up	745 (99.9)	890 (99.9)	683 (99.9)	850 (99.9)	62 (100.0)	40 (100.0)
ER visit, n (%)						
Baseline	319 (42.8)	494 (55.4)	284 (41.5)	473 (55.6)	35 (56.5)	21 (52.5)
Follow-up	540 (72.4)	703 (78.9)	493 (72.1)	669 (78.6)	47 (75.8)	34 (85.0)
Inpatient stay, n (%)						
Baseline	354 (47.5)	474 (53.2)	321 (46.9)	452 (53.1)	33 (53.2)	22 (55.0)
Follow-up	459 (61.5)	626 (70.3)	417 (61.0)	595 (69.9)	42 (67.7)	31 (77.5)

Commer., commercial; ER, emergency room; MAPD, Medicare Advantage with Part D.

Results (continued)

Healthcare costs

- Per-patient-per-month (PPPM) total healthcare costs and medical costs were higher among commercial enrollees vs MAPD enrollees (Figure 2, Table 3).
- PPPM total healthcare costs showed only small differences between baseline and follow-up for the monotherapy cohort, but increased more than 2-fold for both commercial and MAPD enrollees in the combination therapy cohort (Figure 2).

Figure 2. PPPM ±SD total all-cause healthcare costs

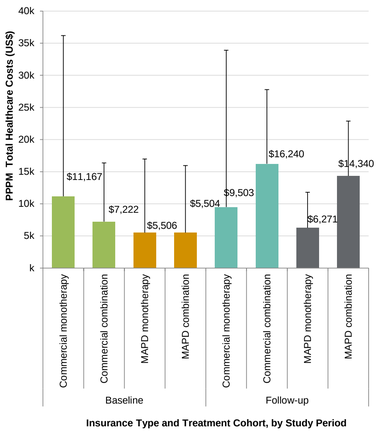


Table 3. PPPM all-cause medical costs (US$)

Category, mean (SD)	Total		Monotherapy		Combination therapy	
	Commer. (n = 746)	MAPD (n = 891)	Commer. (n = 684)	MAPD (n = 851)	Commer. (n = 62)	MAPD (n = 40)
Ambulatory						
Baseline	1,949 (2,724)	946 (1,023)	1,923 (2,766)	943 (1,028)	2,231 (2,215)	1,018 (913)
Follow-up	1770 (4458)	746 (990)	1,788 (4,620)	737 (945)	1,572 (1,839)	936 (1,692)
ER						
Baseline	50 (123)	112 (240)	51 (127)	114 (244)	40 (65)	65 (95)
Follow-up	32 (70)	112 (299)	32 (72)	114 (305)	27 (33)	80 (81)
Inpatient						
Baseline	7,514 (21,952)	3,777 (11,072)	7,824 (22,775)	3,781 (11,104)	4,086 (8,043)	3,690 (10,497)
Follow-up	3434 (20,440)	1553 (3389)	3,451 (21,216)	1,532 (3,338)	3,247 (7,463)	1,995 (4,348)

Comm., commercial; ER, emergency room; MAPD, Medicare Advantage with Part D.

Study Limitations

- This study was conducted in a large US managed care population and may not be generalizable to other populations.
- Because the ICD-9-CM did not have a unique code for PAH, patients were identified using an algorithm based on diagnostic and pharmacy codes, which may have impacted the sensitivity in some cases.
- Medications provided as part of a clinical trial may not be accounted for in claims data.
- This study did not incorporate healthcare costs paid by other payers, which may have resulted in lower cost estimates.

Conclusions

- The population of patients with PAH is heterogeneous and fragile; patients frequently presented with complex comorbidity profiles, consistent with previously published data.[3]
- Most patients had 2 or more years of follow-up, and initiated PAH treatment with monotherapy rather than combination therapy.
- Healthcare resource utilization was substantial, with higher percentages of inpatient stays in the combination therapy cohort vs the monotherapy cohort, and among MAPD enrollees vs commercial enrollees.
- Patients initiating with combination therapy vs monotherapy may have had more severe underlying comorbidities, as evidenced by higher healthcare resource utilization and costs during the follow-up period.
- Further research should be conducted to examine clinical outcomes associated with different PAH-related medication treatments.

References

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2. McGoon MD, Miller DP. Eur Respir Rev. 2012;21(123):8-18
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Presented at the PHA/NIH Joint Symposium, May 19, 2017, Bethesda, MD.
This study was funded by Actelion Pharmaceuticals US, Inc. Medical writing assistance was provided by Yvette Edmonds, PhD, an employee of Optum.