Magellan Rx MANAGEMENT

Utilization and Adherence Rates to Pulmonary Arterial Hypertension Medications

Pulmonary Arterial Hypertension

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Background

- Due to high costs of drug therapy and extensive utilization of ancillary medical services, patients with pulmonary arterial hypertension (PAH) can be very costly to treat.
  - It has been estimated that average annual pharmacy costs alone were $38,514 per patient per year, although this number is likely even higher today as medication costs and the use of combination therapy may have risen.
- The treatment of PAH is goal-orientated. New medications are added onto existing treatments if the patient fails to reach treatment goals.
  - Many studies have demonstrated that combination therapy with multiple medications may provide benefit over monotherapy.
- Lack of adherence to PAH medications may also contribute to suboptimal response to therapy and may be associated with increased emergency room visits, hospitalizations, and increased overall medical expenses. It is also possible that suboptimal adherence may lead to quicker use of combination medication therapy.
  - Although adherence data is limited, one study suggested that more than 50% of patients with PAH reported suboptimal adherence.

Objective

- To determine cost and utilization trends, including adherence rates and associated hospitalizations in patients using PAH medications.

Methods

- Medical and pharmacy claims data from four regional and national health plans between January 1, 2010 and December 31, 2015 were evaluated.
- Analysis included only commercial members who were continuously enrolled for at least two years with a diagnosis of PAH and had at least two pharmacy claims for a PAH medication.
  - As a proxy for continuous enrollment, patients with less than two claims and patients identified as having claims with a date of service that spanned less than 150 days during one calendar year were flagged as not being continuously enrolled for that year. This methodology is consistent with the continuous eligibility specifications detailed in the Utilization Review Accreditation Commission's (URAC) Pharmacy Benefit Management Performance Measurement Specifications.
- Adherence for PAH medications dispensed under the pharmacy benefit was measured by proportion of days covered (PDC).
- A linear regression analysis was performed to understand the relationship between adherence and hospitalization. A dichotomous cut point was created to compare the number of hospitalizations between patients who are adherent to therapy (PDC≥90%) vs. not adherent (PDC<90%). A t-test was used to detect statistical significance (α=0.05).
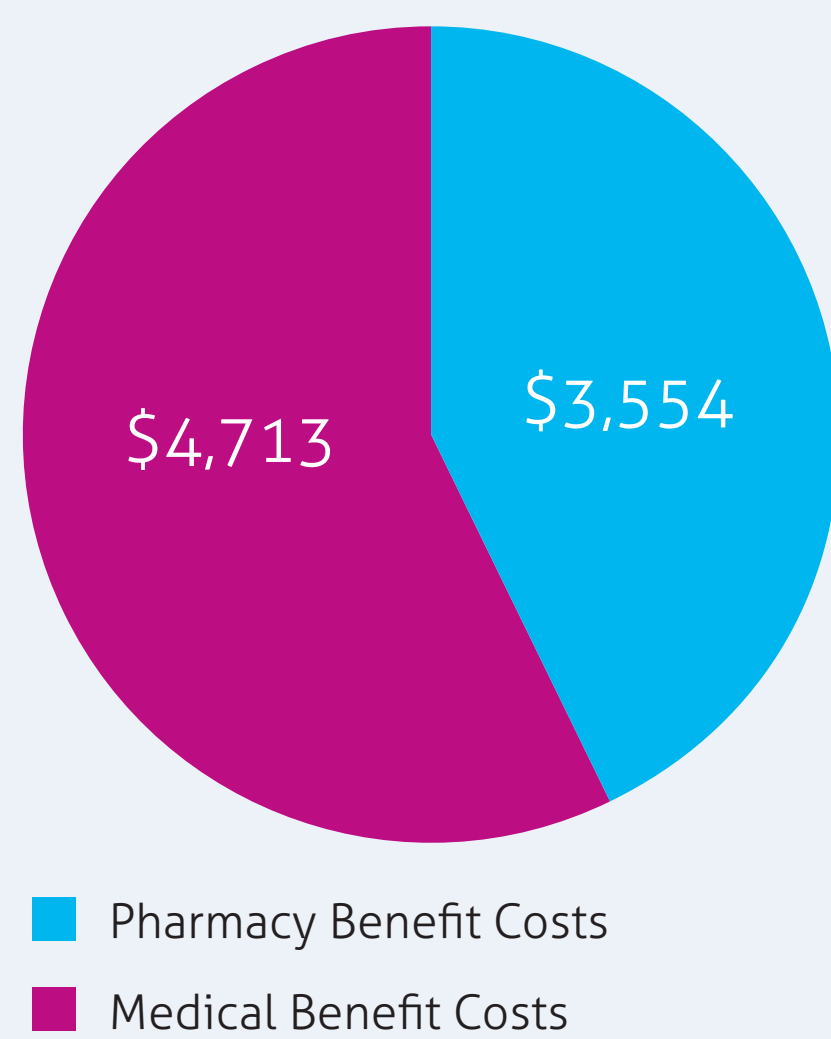
References

- Grady, D., et al. Adherence to pulmonary arterial hypertension targeted therapies. European Respiratory Journal 2015 46: PA3786
- Sikirica M, et al. The economic burden of pulmonary arterial hypertension (PAH) in the US on payers and patients.BMC Health Serv Res. 2014 Dec 24;14:676.
- Simonneau G, Rubin LJ, Galiè N, Barst RJ, Fleming TR, Frost AE, Engel PJ, Kramer MR, Burgess G, Collings L, Cossons N, Sitbon O, Badesch DB, PACES Study Group: Addition of sildenafil to long-term intravenous epoprostenol therapy in patients with pulmonary arterial hypertension: a randomized trial. Ann Intern Med. 2008, 149: 521-530.
- McLaughlin VV, Oudiz RJ, Frost A, Tapson VF, Murali S, Channick RN, Badesch DB, Barst RJ, Hsu HH, Rubin LJ: Randomized study of adding inhaled iloprost to existing bosentan in pulmonary arterial hypertension. Am J Respir Crit Care Med. 2006, 174: 1257-1263.

Disclosures

- This research was conducted by MagellanRx Management, Newport, RI, without external funding.

Results

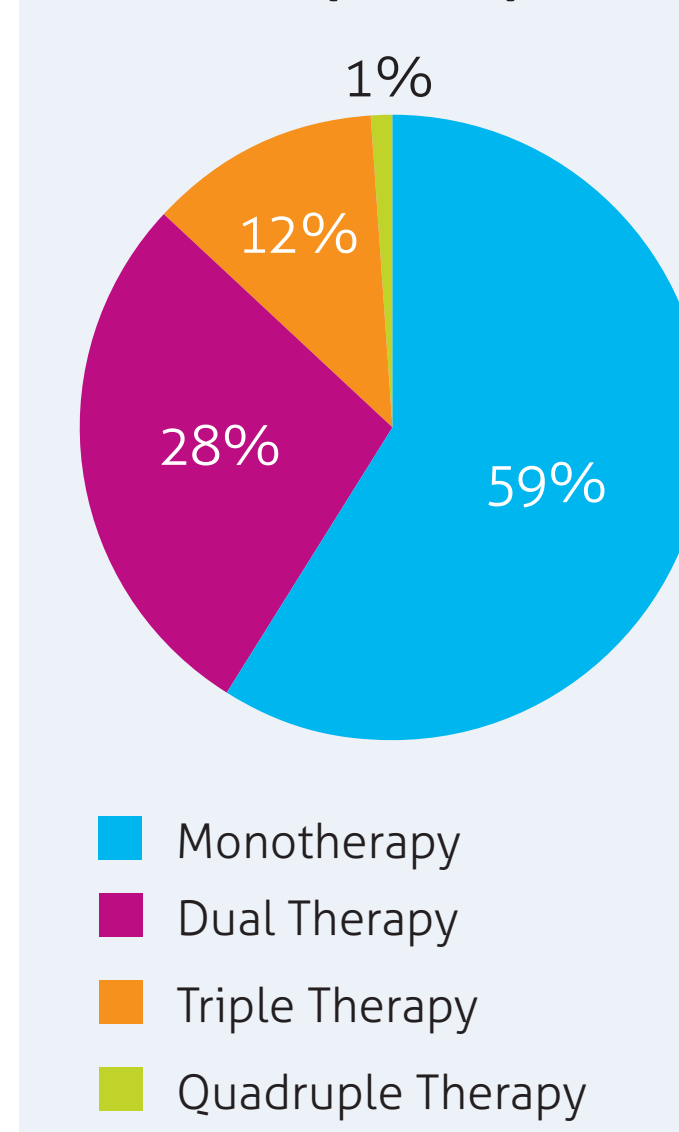### Average Total Health Care Costs Per Member Per Month (N=441)

- $4,713 (Medical Benefit Costs)
- $3,554 (Pharmacy Benefit Costs)

■ Pharmacy Benefit Costs
■ Medical Benefit Costs

Total Utilization and Spend for PAH Medications*

Drug Name	Unique Utilizers†	Average Annual Cost per Utilizer
Sildenafil Citrate	258	$21,403
Tadalafil	179	$21,574
Bosentan	127	$80,505
Ambrisentan	123	$77,357
Treprostinil	26	$165,415
Macitentan	25	$82,770
Iloprost	10	$180,416
Riociguat	9	$94,032
Treprostinil Diolamine	5	$222,482

*Medications dispensed under pharmacy benefit only
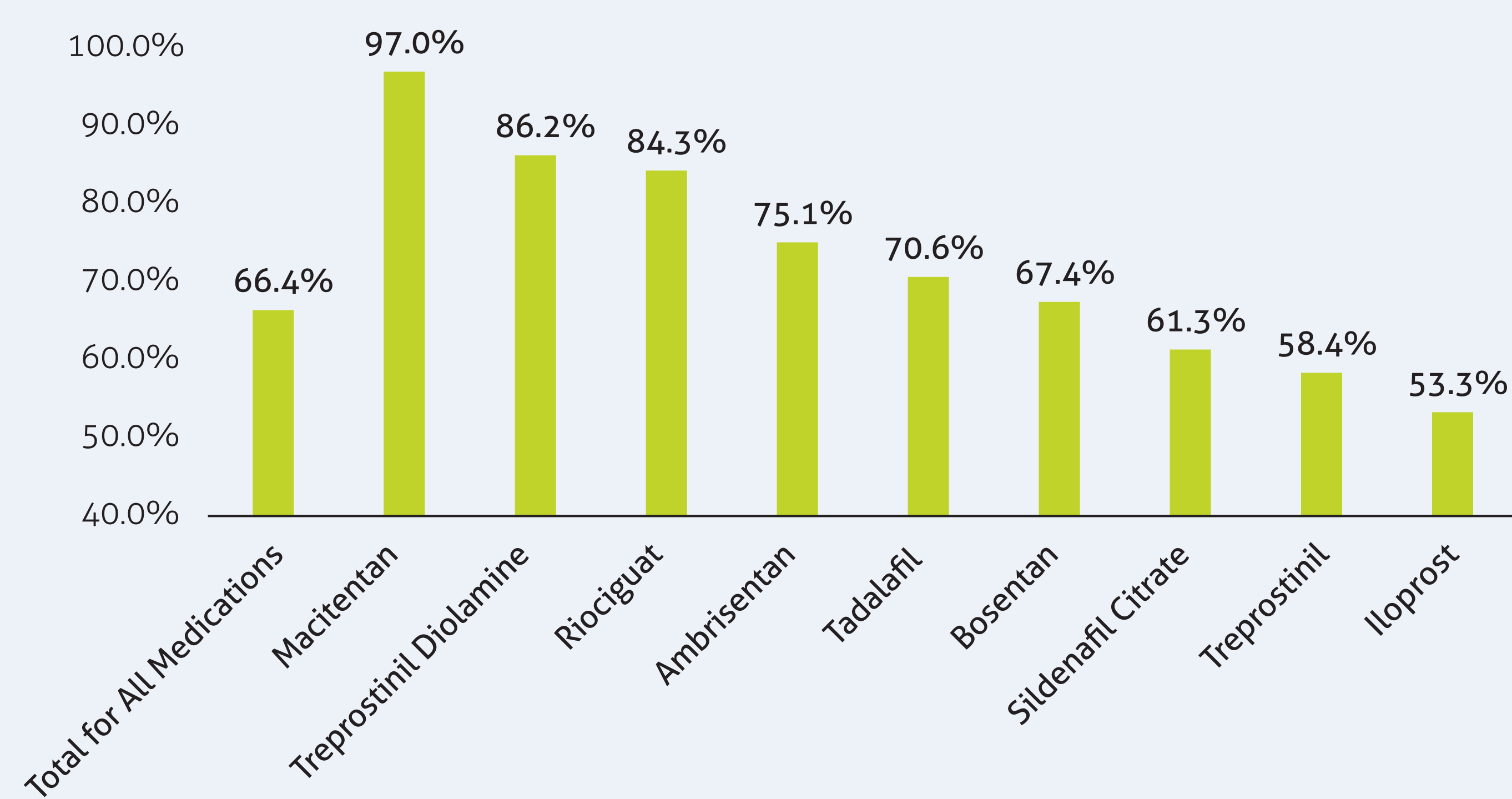†Unique utilizers over 5 years

Utilization of Combination Regimens

Proportion of Patients Using Combination Regimens (N=441)

- 59% Monotherapy
- 28% Dual Therapy
- 12% Triple Therapy
- 1% Quadruple Therapy

■ Monotherapy
■ Dual Therapy
■ Triple Therapy
■ Quadruple Therapy

Most Frequent Combination Regimens

Drug Name	Unique Utilizers	Percent of Total Dual-Therapy Utilizers
Ambrisentan+Tadalafil	13	10%
Bosentan+Sildenafil Citrate	13	10%
Ambrisentan+Sildenafil Citrate	10	8%
Tadalafil+Ambrisentan	9	7%
Tadalafil+Bosentan	9	7%
Sildenafil Citrate+Ambrisentan	7	6%
Bosentan+Tadalafil	8	5%

PDC by PAH Medication

- Total for All Medications: 66.4%
- Macitentan: 97.0%
- Treprostinil Diolamine: 86.2%
- Riociguat: 84.3%
- Ambrisentan: 75.1%
- Tadalafil: 70.6%
- Bosentan: 67.4%
- Sildenafil Citrate: 61.3%
- Treprostinil: 58.4%
- Iloprost: 53.3%

PDC by Threshold and Associated Hospitalizations

PDC By Threshold

PDC Threshold	Proportion of Patients
≥90%	27.9%
<90%	72.1%
<80%	60.0%
<70%	48.5%
<50%	26.8%

Mean Hospitalizations

PDC	N	Mean # of Hospitalizations	Standard Deviation
<90%	282	1.47	2.52
≥90%	80	0.86	1.58
Difference	-	0.61 (p=0.0097)	-

Linear Relationship Between PDC and Hospitalizations

Slope = - 0.91417

Every 46% increase in PDC results in 0.5 less hospitalizations per patient
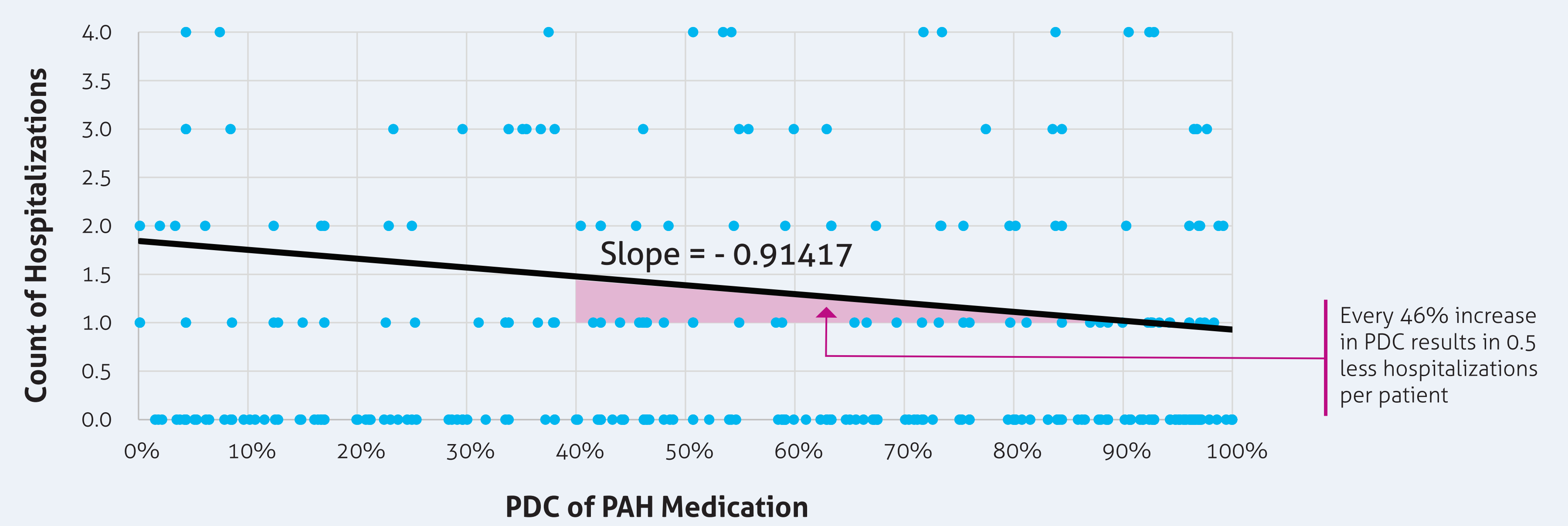
Discussion

- There was significant diversity among the 441 patients in regards to the medication regimen used including 90 unique combination regimens utilized. Of these combination regimens, 62 regimens included agents with differing routes of administration.
  - The most frequently used medications in order were sildenafil (58%), tadalafil (40%), bosentan (29%), and ambrisentan (28%) and the most commonly seen dual therapy combinations in order were ambrisentan+tadalafil (3%), bosentan+sildenafil (3%), and ambrisentan+sildenafil (2%).
- Low adherence rates were observed consistently for the majority of PAH medications with only 27.9% of patients achieving a PDC of 90% or higher. Patients with a PDC <90% were significantly more likely to have a higher rate of hospitalization compared to patients with a PDC≥90% (p=0.0097).
- Linear regression found PDC to be inversely related to hospitalization (p=0.02); patients who were more adherent to treatment were less likely to experience hospitalizations.
- Annualized total health care cost per patient was $99,204 with $56,556 and $42,648 coming from the medical and pharmacy benefits, respectively.
  - Low adherence rates is likely contributing to higher medical costs as these patients experience more associated hospitalizations.
- Limitations to this study include:
  - Due to the rarity of this condition, five years of data from multiple health plan data sets had to be pulled to achieve a meaningful study population size.
  - PDC was only able to be measured for medications dispensed under the pharmacy benefit and thus, excluded medications dispensed under the medical benefit.

Conclusion

- PAH is a complicated condition to manage from both a provider and payer perspective with significant health care utilization and spend across the medical and pharmacy benefits.
  - Adherence was consistently low for the majority of medications dispensed under the pharmacy benefit with an overall PDC of 66.4%.
- As adherence to PAH medication therapy decreases, the rate of hospitalization increases. Further study is warranted to understand the impact of low adherence on additional clinical outcomes. Patients not meeting adherence goals, for example, may be more likely to need additional combination medication therapy in the future.
- Due to the complexity of treatment for PAH, which often requires patients to utilize multiple medication therapies with differing routes of administration, dosing schedules, and safety profiles, it is recommended that health care payers and pharmacies focus attention on development of patient outreach and engagement programs in this population to ensure appropriate use of therapy.