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Introduction

Pulmonary arterial hypertension (PAH) is a chronic disease with elevated mPAP (mean pulmonary artery pressure). PAH therapies do not reverse the disease yet improve pulmonary hemodynamics and offer symptomatic relief. Two challenges to these therapies are medication tolerance and patient compliance. Healthcare providers, particularly nurses, play a significant role in bridging the gap to improve medication adherence. Historically, in-home nurse visits have offered disease state education, discussed therapy expectations and provided support tools for patients when experiencing adverse events which might lead to therapy discontinuation. During the COVID-19 Pandemic, however, many traditional face-to-face nurse visits transitioned to remote or telephonic visits instead.

Objective

To compare adherence and compliance rates to oral and inhaled PAH therapies between patients receiving in-home or face-to-face educational nursing visits and telephonic nurse visits.

Methods

From June 2018 to December 2021, we identified patients who initiated a complex oral PAH therapy (riociguat, selexipag or treprostinil) or inhaled treprostinil, supported by a nursing program, using claims data. We defined complex oral PAH therapies as oral multi-step titratable therapies. We divided patients into two groups based on the study period; we assumed live nurse visits occurred between June 2018 and March 31, 2020. Visits between April 2020 and December 31, 2021, were defined as virtual visits.

We compared the following measures by group: Fill count: the number of distinct claims for study medications; Medication Possession Ratio (MPR): sum of the days' supply of medication/days between index fill and exhaust of last fill; First fill drop off rate (FFDR): % of patients with only one fill during the study period; Therapy persistence (TP): length of time when a patient has medication on hand; and Adverse drug event (ADE): at least one entry in the ADE database with the indicator for ADE. A logistic regression model accounted for demographic and medication factors associated with adherence.

Results

Table 1. Baseline characteristics

Variable	Overall (N=4494)	Live N(%) = 2290 (50.96)	Virtual N(%) = 2204 (49.04)	p-value
Person-Days observed (Mean[SD])*	205.94 (173.59)	211.71 (176.95)	199.95 (169.87)	0.023
Person-Days observed (Median[Q1-Q3])*	158 (55 - 323.75)	162 (55-336)	152.5 (56-311.25)	0.031
Age (Mean[SD])*	61.84 (14.95)	61.36 (15.17)	62.33 (14.72)	0.029
Age (Median[Q1-Q3])*	64 (52 - 73)	63 (51-73)	64 (52-74)	0.018
Male Gender (N[%]) [§]	1429 (31.8%)	725 (31.66%)	704 (31.94%)	0.86
Combination Therapy (N[%]) [§]	1456 (32.4%)	761 (33.23%)	695 (31.53%)	0.24
Number of concomitant medications (Mean[SD])	0.47 (0.75)	0.49 (0.76)	0.45 (0.73)	0.056

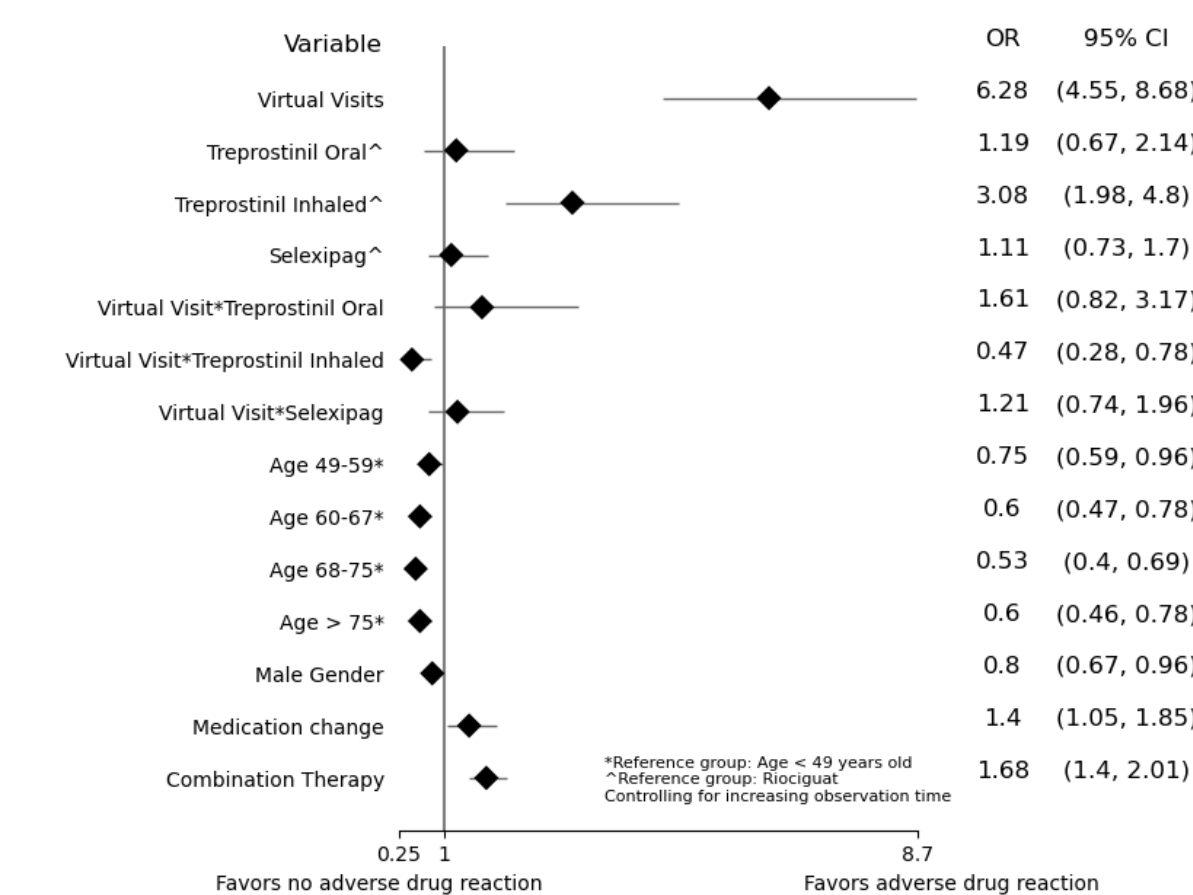
SD = standard deviation, Q1 = first quartile; Q3 = third quartile

Table 2. Whole cohort characteristics by group

Variable	Overall (N=4494)	Live N(%) = 2290 (50.96)	Virtual N(%) = 2204 (49.04)	p-value
Total Person Years (PY)	2535.64	1328.25	1207.39	
Medication Change (N[%])	362 (8.06%)	188 (8.21%)	174 (7.89%)	0.74
Incidence Rate Ratio (IRR)		1.02 (0.83-1.25)		0.87
First Fill Dropoff (N[%])	796 (17.71%)	396 (17.29%)	400 (18.15%)	0.48
Incidence Rate Ratio (IRR)		1.11 (0.97-1.28)		0.14
Optimal Adherence (N [%])	3985 (88.67%)	2029 (88.60%)	1956 (88.75%)	0.92
Gap Days (Median[Q1-Q3])	0 (-9 - 15)	0 (-8-16)	0 (-11-14)	0.0012
Max Gap (Median[Q1-Q3])	6 (0 - 16.75)	6 (0-16)	6 (0-18)	0.059
Number of Fills (Mean[SD])	7.23 (5.91)	7.39 (5.95)	7.06 (5.87)	0.066
Total Days Supplied (Median[Q1-Q3])	150 (60 - 322)	164 (60-330)	150 (58-300)	0.026
Adverse Drug Event (N[%])	773 (17.20%)	151 (6.59%)	622 (28.22%)	<0.0001
Incidence Rate Ratio (IRR)		4.82 (4.04-5.79)		<0.0001

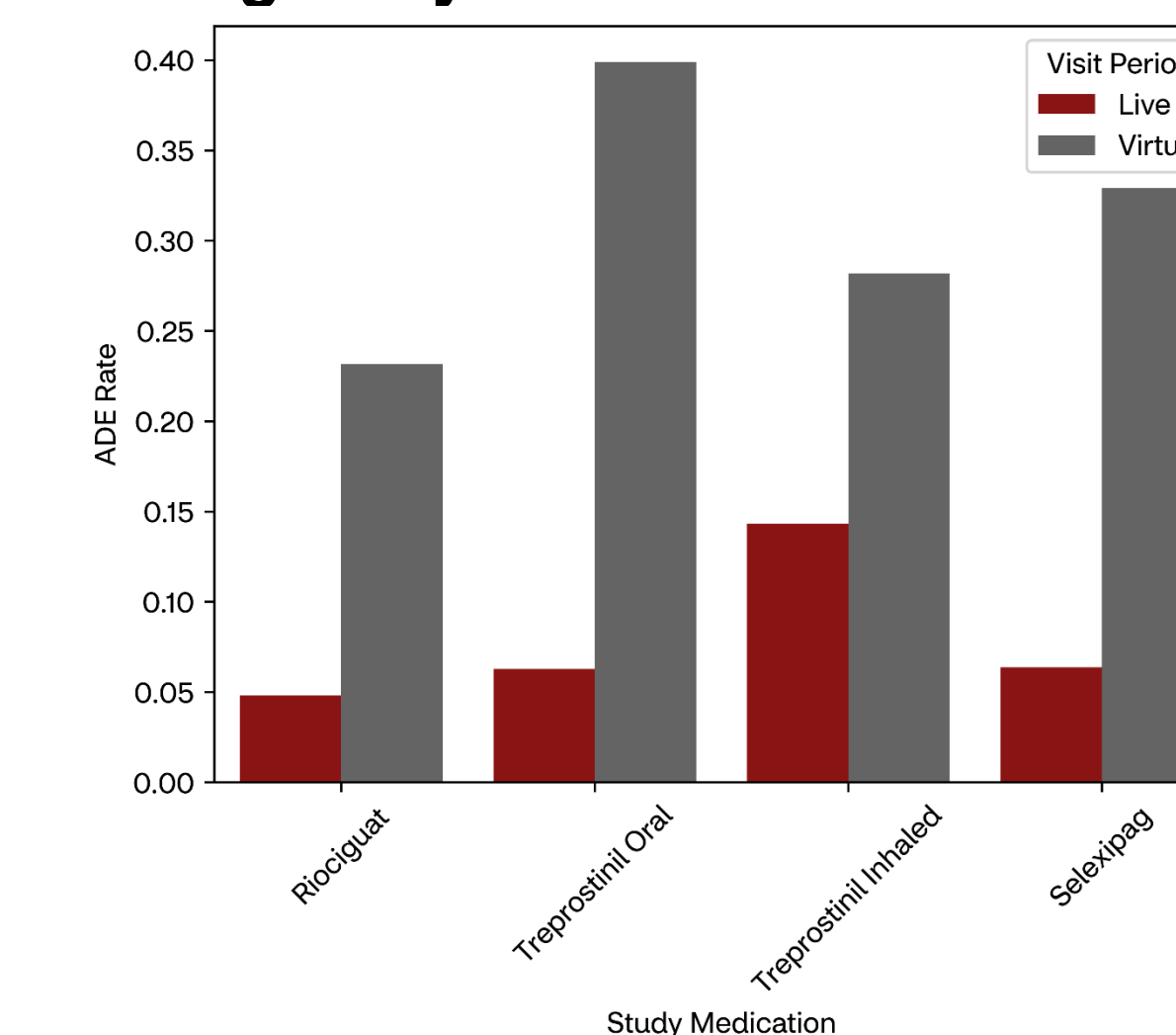
Q1 = first quartile; Q3 = third quartile

Figure 1: Odds ratio forest plot for adherence model



OR = odds ratio; CI = confidence interval

Figure 2: Adverse drug event rates among study medications



We identified 2,290 patients in the live visit group and 2,204 in the virtual visit study group. After a median of 174 person-days observed, patients in the live nursing group reported 0.33 more 30-day fills (7.39 vs. 7.06; p = 0.66) and slightly lower MPR (88.6% vs. 88.75%; p=0.92). The FFDR was 0.86% lower among patients in the live visit group than in the virtual visit group (17.29% vs. 18.15%; p = 0.48). The live visit group reported fewer ADEs (151 vs. 622; p<0.0001) than the virtual visit group.

Conclusion

Patients receiving live nursing visits for the indexed oral and inhaled PAH therapies in an educational nursing program demonstrated a similar outcome on overall medication compliance as those patients receiving virtual nursing visits. Assumptions of live vs. virtual nursing visits were made based on the suggested cutoff date of April 1, 2020, which marked the transition to primarily virtual nursing visits. While our study assumed virtual visits for the latter half of the observation period, April 1, 2020, to December 31, 2021, 10 to 40% of nursing education visits for riociguat, selexipag, oral treprostinil and inhaled treprostinil were live visits. One notable difference between the live and virtual study groups was the higher incidence of ADEs in the virtual visit setting. While our study did not compare the direct impact of nursing visits vs. not receiving visits, we had previously observed a higher MPR (86.4% vs. 75%; p<0.01) and improved persistency (72% vs. 60.6%; p<0.05) in patients on oral therapies receiving nursing support (riociguat, selexipag, treprostinil) vs. those patients on oral PAH therapies not supported by nursing (ambrisentan, bosentan and macitentan) demonstrating that a multidisciplinary patient support approach contributed to improved patient outcomes.

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