2023 PH Professional Network (PHPN) Symposium: Abstracts

EFFECT OF PULMONARY HYPERTENSION ON CLINICAL AND ECONOMIC OUTCOMES OF PATIENTS ADMITTED WITH ACUTE MYOCARDIAL INFARCTION IN THE UNITED STATES, A NATIONWIDE STUDY

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Category: Clinical Science
Subcategory: Diseases and Conditions Associated with PH

Background: Acute myocardial infarction (AMI) is one of the leading causes of morbidity and mortality. Pulmonary hypertension (PH) is often missed as a diagnosed comorbidity in patients admitted with AMI. We aimed to study the effect of PH (all categories) on the outcomes of patients admitted with AMI with further subclassifications into ST elevation myocardial infarction (STEMI) and non-STEMI.
Methods: Using the National Inpatient Sample Database from 2017 to 2020, a retrospective study of adult patients with principal diagnosis of AMI with secondary diagnosis with or without PH according to ICD-10 codes. Several demographics, including age, race, and gender, were analyzed. The primary endpoint was mortality, while the secondary endpoints included mechanical intubation, length of stay in days, and patient charge in dollars. Multivariate logistic regression model analysis was used to adjust for confounders, with a *P* value <0.05 considered statically significant.
Results: The study included 1830229 patients admitted with an AMI, of which 37895 of which had PH. The mean age for patients with and without PH was 72.8 and 66.7 years, respectively. In the PH group, 50% were females compared with 37% in the non-PH group. Around 70% in both groups were White. Statistically significant comorbidities noticed in the PH group included sepsis (4% versus 2%), diabetes mellitus (47% versus 40%), hypertension (89% versus 81%), acute kidney injury (36% versus 19%; $P < 0.01$). In-hospital mortality rate was higher in the PH group with statistical significance (7.2% versus 4.6%, $P < 0.01$). The adjusted odds ratio (aOR) was 0.99 without statistical significance. In the STEMI group, mortality rate was higher in the PH group with statistical significance (15.7% versus 7.8%, $P < 0.01$) similar to the non-STEMI group (5.9% versus 3.3%, $P < 0.01$). The odds ratio if in-hospital mechanical ventilation was only statistically significant in the STEMI group (aOR = 1.32, $P = 0.01$). The length of stay was longer in the PH group across the 3 groups (AMI: 6.5 versus 4.35 days, aOR = 0.87, $P < 0.01$; STEMI 6.6 versus 3.9, aOR = 0.87, $P < 0.01$; non-STEMI 6.5 versus 4.5 days, aOR = 0.88, $P < 0.01$). Patients in the PH group had a higher total charge in the 3 groups (Figures 1 and 2).
Conclusion: Patients admitted with AMI with associated PH were found to have worse clinical outcomes and a higher economic burden. Practicing clinicians should be aware of the significance of associated PH as a comorbidity in the setting of AMI.

Table 1: Demographic Characteristics			
Characteristics	Without PH	With PH	p value
AMI-PH, no(%)	1,792,334 (98)	37,895 (2)	
Female, no(%)	663,163 (37)	18,947(50)	<0.01
Age (y)	66.7	72.8	
Race,no(%)			<0.01
White	1,326,327 (74)	26,526 (70)	
Black	197,156 (11)	5,305 (14)	
Hispanic	143,386 (8)	3,031 (8)	
Asian or Pacific Islander	53,770 (3)	1,136 (3)	
Native American	8,961 (0.5)	265 (0.7)	
Other	53,770 (3)	1,136 (3)	
Charlson Comorbidity Index score, no. (%)			
1	448,083 (25)	1,894 (5)	
2	448,083 (25)	5,684 (15)	
>=3	896,167 (50)	30,316 (80)	
Median annual income in patient's zip code, US$, no. (%)			0.13
1 - 43,999	537,700 (30)	11,747 (31)	
44,000 - 55,999	501,853 (28)	10,989 (29)	
56,000 - 73,999	430,160 (24)	8,715 (23)	
74,000+	322,620 (18)	6,442 (17)	
Insurance type, no. (%)			<0.01
Medicare	1,057,477 (59)	29,179 (77)	
Medicaid	179,233 (10)	3,031 (8)	
Private Insurance	483,930 (27)	4,926 (13)	
Self-pay	71,693 (4)	757 (2)	
Hospital bed size, no. (%)			0.13
Small	304,696 (17)	7,200 (19)	
Medium	555,623 (31)	11,747 (31)	
Large	932,013 (52)	18,947(50)	
Hospital region, no. (%)			0.02
Northeast	322,620 (18)	7,200 (19)	
Midwest	394,313 (22)	8,715 (23)	
South	716,933 (40)	14,021 (37)	
West	358,466 (20)	7,957 (21)	
Teaching hospital			<0.01
Rural	125,463 (7)	2,273 (6)	
Urban Nonteaching	448,083 (25)	7,957 (21)	
Urban teaching	1,218,787 (68)	27,663 (73)	
Comorbidities, no. (%)			
Sepsis	35,846 (2)	1,515 (4)	<0.01
DMII	716,933 (40)	17,810 (47)	<0.01
HTN	1,451,790 (81)	33,726 (89)	<0.01
AKI	340,543 (19)	13,642 (36)	<0.01
BMI>40	286,773 (16)	6,442 (17)	<0.01
AMI:Acute Myocardial Infarction, PH: Pulmonay Hypertension, DMII: Diabetes Milletus II, HTN: Hypertension, AKI: Acute Kidney Injury, BMI: Body Mass Index			

Figure 1: Demographics.

In-hospital mortality rates and odds						
	Total	Without PH	With PH	p value	Adjusted Odds Ratio	p value
AMI, no (%)	85,834 (4.7)	82,506, (4.6)	2635 (7.2)	<0.01	0.99	0.98
STEMI, no (%)	39,190(7.9)	38,682(7.8)	760 (15.7)	<0.01	1.04	0.6
NSTEMI, no (%)	45,444(3.4)	42,799(3.3)	1,936(5.9)	<0.01	1.12	0.03

In-hospital mechanical ventilation odds		
	PH-Adjusted Odds Ratio	p value
AMI	1.08	0.15
STEMI	1.32	0.01
NSTEMI	1.13	0.055

Mean Length of Stay				
	Without PH	With PH	Adjusted Odds Ratio	p value
AMI, days	4.35	6.5	0.87	<0.01
STEMI, days	3.9	6.6	0.87	<0.01
NSTEMI, days	4.5	6.5	0.88	<0.01

Total Charges				
	Without PH	With PH	Adjusted Odds Ratio	p value
AMI, ($)	95,213	119,083	13,229	<0.01
STEMI, ($)	111,963	159,452	18,587	<0.01
NSTEMI, ($)	88,906	113,450	15,040	<0.01

Figure 2: Results.

PERSISTENCE AND PREDICTORS OF PERSISTENCY FOR PULMONARY ARTERIAL HYPERTENSION PATIENTS ON SELEXIPAG IN CANADA: A RETROSPECTIVE CLAIMS DATABASE STUDY

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Category: Clinical Science
Subcategory: Therapeutic Strategies

Background: Pulmonary arterial hypertension (PAH) is a serious, progressive disease that usually leads to right heart ventricular failure and death. Although treatment guidelines include recommendations for combination drug therapy with selexipag (prostacyclin receptor agonist), research examining real-world persistence and potential predictors of persistency in the Canadian population is sparse.
Methods: This retrospective claims database analysis included PAH patients (inferred) with ≥1 selexipag claim from Ontario Drug Benefits (ODB), Régie de l'assurance maladie du Québec (RAMQ), or Canadian Private Drug Plan (PDP) databases between April 2016 and July 2021. Selexipag persistence was calculated from index date (first selexipag claim) until discontinuation (no further selexipag claims) or censoring (no further claims in any database or persistent at the end of the study period). Persistence was estimated by Kaplan-Meier (KM) analyses. Four feature selection models (stepwise Cox proportional hazards, Boruta, Coxnet, and Random Survival Forest) were used to rank 28 potential predictors of persistence, including clinical and demographic variables. The top 12 (average model rank) were included in a Cox proportional hazards model for selexipag persistence.
Results: Of 311 patients identified throughout the observation period (PDP = 101, 32%; ODB = 181, 58%; and RAMQ = 29, 9%), 70% were female and 71% were aged 50–79 years. During the study period, 129 patients (41%) discontinued selexipag, including 16 (5%) who switched to intravenous prostacyclin. Another 69 patients (22%) were censored, and 113 (36%) were persistent on selexipag at the end of the study. From the KM

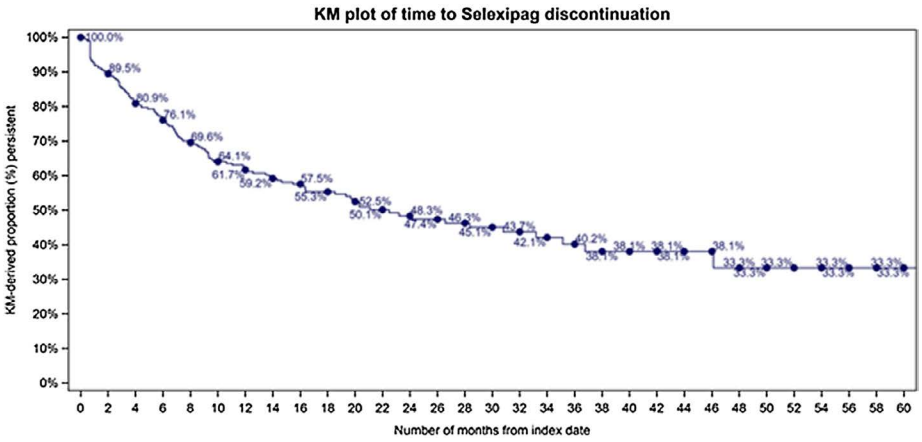

Figure 1: Kaplan-Meier derived selexipag persistence for pulmonary arterial hypertension patients between April 2016 and July 2021 discontinuations.

analysis, 62% of patients were persistent on selexipag after 1 year, 48% after 2 years, and 33% after 4 years (Figure 1). None of the predictors tested reached statistical significance level (0.05). However, 3 predictors had *P* values <0.1: baseline use of double oral combination therapy (heart rate [HR] = 0.63; 95% confidence interval [CI] = 0.38, 1.04), sildenafil monotherapy (HR = 1.92; 95% CI = 0.97, 3.58), and riociguat monotherapy (HR = 2.31; 95% CI = 0.89, 5.23).

Conclusion: This is the first Canadian retrospective claim database study to examine the persistence and predictors of persistency of PAH patients on selexipag. Persistence on selexipag in this cohort was 62% at 1 year and 33% at 4 years. However, none of the predictors of selexipag persistence tested in this study reached significance in this population. Further research into predictors of selexipag persistence is needed to help improve potential treatment outcomes and therefore benefits for PAH patients.

INPATIENT PROSTACYCLIN ACTIVITY OVER A 1-YEAR PERIOD AT A PULMONARY HYPERTENSION CENTER OF COMPREHENSIVE CARE

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Category: Clinical Science
Subcategory: Therapeutic Strategies

Background: Prostacyclins are high-risk, high-alert medications that have been shown to actually or potentially cause significant harm to the patient, even when used as intended. As a result, inpatients receiving prostacyclins require care from specially trained nurses and pharmacists. With the recent newer prostacyclin dosage formulations coming to market, in this study, we seek to provide baseline data on inpatients who receive prostacyclins at our Pulmonary Hypertension Center of Comprehensive Care.

Methods: Hospital encounters with inpatient medication orders for prostacyclins between January 1 and December 31, 2022, were identified by electronic health record. Prostacyclin route of administration, average length of stay, and average discharge dose were extracted from the electronic health record patient encounter.

Results: This study included 62 hospital encounters by 36 patients. Of 62 hospital encounters, 35 (56%) received parenteral prostacyclin, 14 (22%) received inhaled prostacyclin, and 13 (21%) received oral prostacyclin. Three patients made up 20 (32%) of the 62 hospital encounters over the 1-year period. Four (7%) of 62 encounters were for ≤1 day, and all 4 were on parenteral prostacyclin. The mean (+SD) discharge dose was 54.9 ± 17.7 ng/kg/min, and mean length of stay was

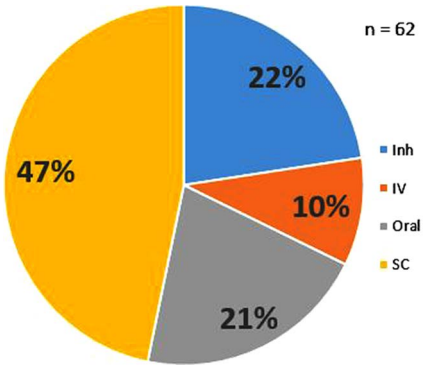

Figure 1: Hospital encounters with a prostacyclin order by route.

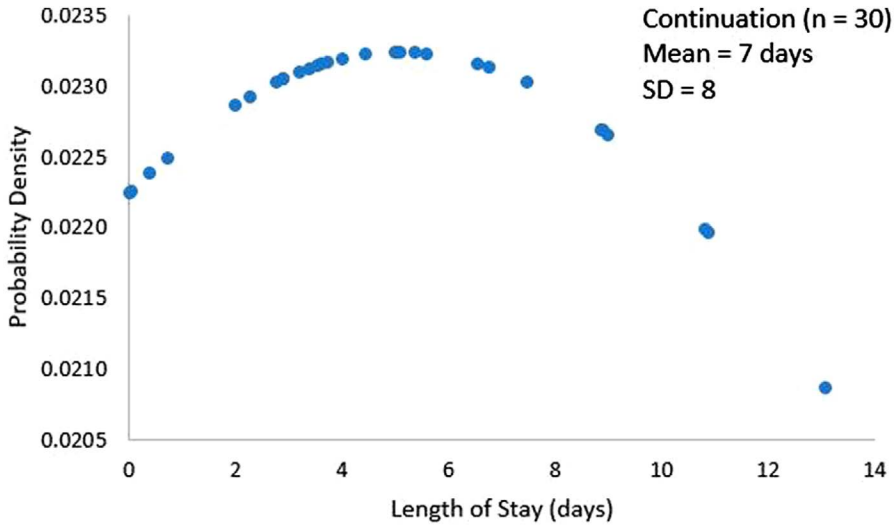

Figure 2: Mean length of stay for continuation of parenteral prostacyclin encounters.

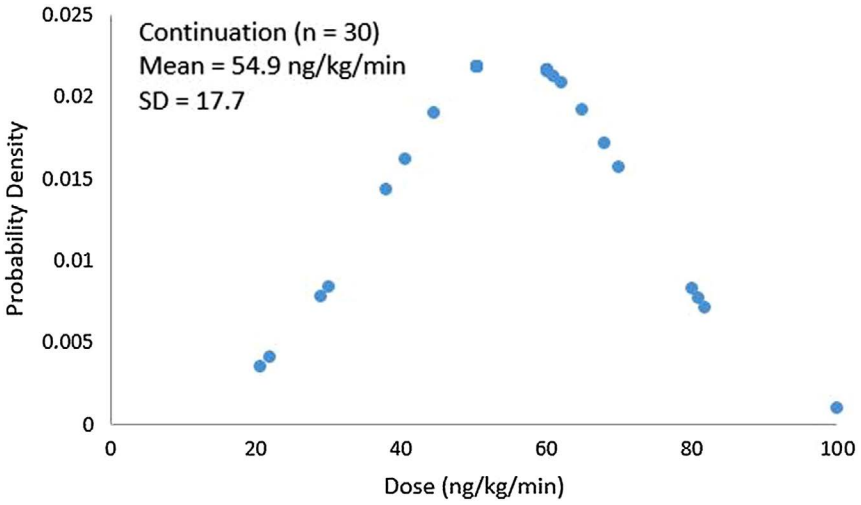

Figure 3: Mean discharge dose for continuation of parenteral prostacyclin encounters.

7 days for established patients on parenteral prostacyclin. The mean discharge dose was 20 ng/kg/min, and mean length of stay was 11 days for new patients on parenteral prostacyclin (Figures 1–3).

Conclusion: Over a 1-year period, 36 patients on prostacyclin therapy presented to the hospital 62 times. Three patients made up 20 (32%) of the 62 hospital encounters over the 1-year period. The mean length of stay for patients on parenteral prostacyclin therapy is between 7 and 11 days. Additional research will be done evaluating the difference in length of stay and cost of care between patients receiving parenteral, inhaled, and oral prostacyclin therapy.

A CASE SERIES OF COMMON VARIABLE IMMUNODEFICIENCY RELATED LUNG DISEASE WITH PRECAPILLARY PULMONARY ARTERIAL HYPERTENSION (PAH): REVIEW OF CLINICAL PRESENTATIONS AND TREATMENT CONSIDERATIONS

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Category: Case Report
Subcategory: Diseases and Conditions Associated with PH

Background: Common variable immunodeficiency (CVID) is a rare and poorly understood immunologic disease with varying criteria for diagnosis. CVID is associated with various pulmonary manifestations including lymphoid interstitial pneumonitis, bronchiectasis, granulomatous-lymphocytic interstitial lung disease (GLILD), and severe pulmonary arterial hypertension (PAH). The ideal treatment option for this rare, complex form of PAH is unknown given the sparsity of clinical data, and thus, treatment is guided by case reports. Our case series highlights the diagnosis of CVID-related PAH, varying treatment options for their PAH, and the outcomes for 3 patients with different clinical manifestations.

Methods: Retrospective chart review was performed on 3 patients previously known to the Pulmonary Hypertension program at Henry Ford Hospital in Detroit, Michigan. Our patients had CVID and were receiving active treatment or have probable CVID based off Ameratunga criteria. All included patients were demonstrated to have severe precapillary PAH by right heart catheterization (RHC) or highly likely to have pulmonary hypertension (PH) by their echocardiogram data by the 2022 European Respiratory Society guidelines, which is consistent with previous PAH described in CVID patients.

Results: Our 3 patients had the following demographics: 2:1 F/M ratio, male patient was diagnosed at age 46, and our female patients' age of diagnosis was average 28 years old. Our female patients were on oxygen therapy for a mean of 8 years prior to the diagnosis of PH. Our patients had the following echocardiographic data: median estimated pulmonary artery (PA) pressure of 83 mmHg, mean maximal tricuspid valve regurgitation velocity of 4.235 m/s, median tricuspid annular plane systolic excursion when available was 1.245 cm. Our patients' RHC data (n = 2) showed median mean PA pressure (mPAP) of 48 mmHg, median pulmonary capillary wedge pressure of 6 mmHg, median cardiac index of 2.57 L/min/m^2, median pulmonary vascular resistance of 24.49 WU. Pulmonary function testing showed severe reduction in forced expiratory volume in the first second (median 33% of predictive) and diffusing capacity after correction for alveolar volume for all patients. Median diffusing capacity for carbon monoxide (DLCO) was 24.2 mL/mmHg/min, roughly 25% of predicted, and median adjusted DLCO/alveolar volume was 4.88 mL/mHg/min/L, roughly 70% of predicted. All patients had New York Heart Association functional class III/IV dyspnea prior to PH treatment and had pulmonary symptoms, including hypoxia requiring continuous oxygen and/or frequent respiratory infection for a mean of 13 years prior to diagnosis of PAH. Regarding treatment options, all patients had variable courses for both their CVID treatment and PH treatment. Ultimately, 2 of our patients received intravenous immunoglobulin therapy for their CVID, and 1 patient was additionally treated with rituximab infusions and mycophenolic acid 2 times per day, with worsening of GLILD off mycophenolic acid and stabilization when resumed. One patient had progression to bilateral lung/liver transplantation performed in 2013 due to bronchiectasis and end-stage liver disease related to CVID. One patient with PAH symptoms was controlled with inhaled treprostinil alone

15 puffs 4 times per day, and 1 patient was on inhaled treprostinil 9 puffs 4× per day and ambrisentan 10 mg combination. **Conclusion:** CVID has a wide spectrum of presentations and likely varying pathophysiologic mechanisms leading to the development of PAH. Our cases highlight these variable clinical manifestations and the eventual development of severe precapillary PH, which is consistent with the little data published to date. More research is needed into the possible mechanisms of CVID-PAH, and more awareness is needed to reduce the mean time to diagnosis. Patients with frequent respiratory infections should have screening with serum immunoglobulins if the clinical picture fits a description of CVID. We believe a myriad of factors lead to pulmonary vascular remodeling in CVID not limited to chronic hypoxia, portal hypertension, systemic inflammation, granulomatous inflammation, lymphocytic infiltration, or a combination of them. No treatment generalizations can be made from our patients, each appearing to have a different manifestation of CVID leading to PAH; however, our series highlights that great care should be taken to solve the underlying pulmonary mechanisms which are driving the severe PAH.

A PHASE 3 STUDY TO EVALUATE THE SAFETY, TOLERABILITY, PHARMACOKINETICS, AND EFFICACY OF LIPOSOMAL TREPROSTINIL (L606) IN SUBJECTS WITH PULMONARY ARTERIAL HYPERTENSION OR PULMONARY HYPERTENSION ASSOCIATED WITH INTERSTITIAL LUNG DISEASE

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Category: Clinical Science
Subcategory: Diseases and Conditions Associated with PH

Background: Pharmosa Biopharm Inc. is developing L606, a novel sustained formulation, as an inhalation combination product in the treatment of patients with pulmonary arterial hypertension (PAH) or pulmonary hypertension associated with interstitial lung disease (PH-ILD). L606 is composed of treprostinil-encapsulated liposomes which alleviate upper airway irritation and reduce dose frequency to twice a day. In addition, a mesh-vibrating nebulizer offers a simple, convenient, and portable inhalative delivery that is a clinically meaningful improvement over the current nebulized therapy. In the Phase 1 study, L606 showed a sustained and prolonged release profile as compared with Tyvaso and is expected to reduce the time spent at subtherapeutic levels as well as frequency of inhalations per day. L606 was found to be safe and was well tolerated in healthy volunteers. This Phase 3, open-label, 2-part, multicenter study aims to demonstrate the short-term and long-term safety and efficacy of repeated doses of L606 in subjects with PAH or PH-ILD.
Methods: A single-arm, open-label, multicenter study was designed to recruit 60 patients with PAH or PH-ILD. Subjects will be recruited into 2 cohorts with different target populations: Cohort A—subjects with PAH or PH-ILD on a stable Tyvaso dose who are willing to transition to L606; and Cohort B—subjects with PAH who are not receiving a prostacyclin at the time of study entry. Subjects in Cohort A will sequentially participate in a 2-week main study and extension phase (up to 12 months). Subjects in Cohort B will sequentially participate in a 12-week main study and extension phase (up to 12 months). In Cohort A only, a subset of approximately 15 subjects will also participate in a pharmacokinetics (PK) substudy to evaluate steady-state plasma treprostinil PK after administration of Tyvaso and L606. The safety assessments include adverse effects, physical and vital signs examination, clinical laboratory tests, 12-lead electrocardiogram, and echocardiogram. Efficacy assessments includes the 6-minute walking test, Borg Dyspnea Score, PH symptoms, New York Heart Association functional class, and N-terminal prohormone B-type natriuretic peptide levels. In this study, we also evaluate the steady-state PK of L606 as compared with Tyvaso, quality of life, and treatment satisfaction with L606 in patients with PAH or PH-ILD.
Results: The enrollment of this study is currently ongoing.
Conclusion: We hypothesize that L606 will achieve similar systemic exposure but safer and more convenient than Tyvaso in patients with PAH or PH-ILD.

IMPLEMENTATION OF A PHARMACY SPECIALIST ROLE TO IMPROVE CHRONIC, PULMONARY HYPERTENSION MEDICATION MANAGEMENT AND PATIENT EXPERIENCE

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Category: Clinical Science
Subcategory: Diseases and Conditions Associated with PH

Background: A multidisciplinary approach is recommended to individualize care for patients with pulmonary hypertension (PH). Previous publications described the role of a pharmacist, however, were limited to specialty pharmacies, inpatient settings, and timeframe immediately postdischarge.
Methods: An ambulatory clinic-focused PH pharmacist was incorporated into the team. A proactive, new medication follow-up and side effect management process was created. This is a retrospective cohort analysis for the time period October 15, 2021, to July 20, 2022. Pharmacist-driven, phone follow-up encounters were included. Calls unrelated to chronic PH disease management were

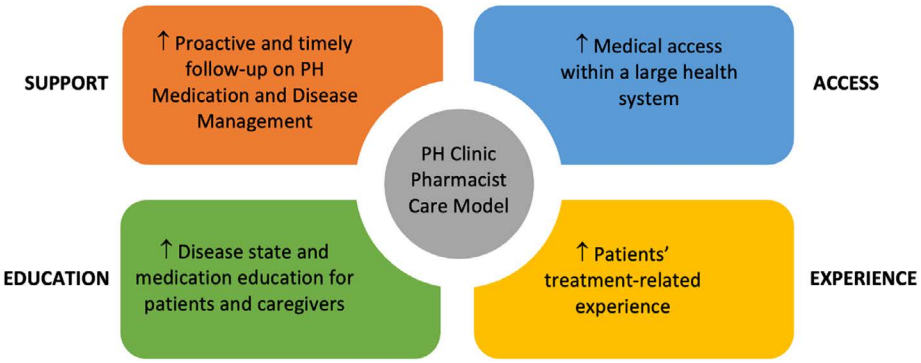

Figure 1: Summary of clinical pharmacist effect on the care of ambulatory pulmonary hypertension patients.

Clinic Visit and Pharmacist Follow-up Calls	
Total number of clinic visits, n=91	**115**
Clinic visits since referral per patient, median (Q1,Q3) Range: Min-Max	2 (1,2) Range: 0-5
Total number of pharmacist phone follow-up encounters, n=91	**265**
Pharmacist follow-up visits per patient, median (Q1,Q3) Range: Min-Max	2 (1,3) Range: 1-11
Pharmacist follow-up within 30 days of clinic appointment, n (%)	60 (65.9)

Figure 2: Clinic visit and pharmacist phone follow-up encounters.

Side Effect Management Encounters (n=28)	
Side Effect Resolved, n (%)	25 (89.3)
In progress, n (%)	1 (3.6)
Complicated by COVID infection, n (%)	1 (3.6)
Lost to follow-up, n (%)	1 (3.6)
Medication Titration Encounters (n=18)	
At goal, n (%)	14 (77.8)
Not at goal*, n (%)	2 (11.1)
In progress, n (%)	1 (5.6)
Lost to follow up, n (%)	1 (5.6)
Diuretic Management Encounters (n=28)	
Euvolemia, n (%)	22 (78.6)
Uncontrolled hypervolemia^, n (%)	5 (17.9)
Lost to follow up, n (%)	1 (3.6)

**1 patient passed away, 1 patient abruptly discontinued medication independently*
^4 patients required admission and 1 patient was noncompliant to medication adjustments and laboratory follow-up

Figure 3: Pharmacist medication management outcomes for the total cohort.

excluded. Outcomes included number of clinic visits, pharmacist phone follow-up encounters, patients with pharmacist follow-up within 30 days of clinic appointment, type of pharmacist follow-up, and pharmacist medication management outcomes, ie, side effect resolution, medication titrated to goal, and euvolemic status.

Results: Ninety-one patients received pharmacist follow-up; 265 pharmacist follow-up phone encounters were completed (median, 2 per patient). These patients completed 115 traditional clinic visits during the study period, yielding a >2:1 ratio of pharmacist interactions to physician visits. In addition, 60% of patients had a pharmacist follow-up within 30 days of clinic visit. For medication management, 25 of 28 patients (89%) reached an acceptable level of side effect improvement, 14 of 18 patients (78%) with pharmacist-driven titration plans reached goal doses, and 22 of 28 patients (78.6%) reached euvolemia (Figures 1–3).

Conclusion: The integration of a PH ambulatory pharmacist has led to side-effect mitigation, achievement of goal medication doses, and improved volume status in patients. Medication-related issues are proactively addressed sooner than may have been addressed at a traditional clinic practice model.

ASSESSING THE READABILITY OF PULMONARY HYPERTENSION DRUG PRODUCT PATIENT PACKAGE INSERTS

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Category: Clinical Science
Subcategory: Quality of Life

Background: The currently recommended reading level for patient education materials is at a fifth grade level. Despite this, it has been shown that many patient package inserts for drug products contain information that is of a much higher reading level. Patients with lower health literacy levels may find these materials to be unreadable or may even misinterpret the information leading to poor outcomes.
Methods: Three patient package inserts for drug products within the nitric oxide pathway were included in this analysis. Four student pharmacists independently appraised each of the patient package inserts using the Simple Measure of Gobbledygook (SMOG) criteria and Fry readability formula. Data are checked randomly by the research group to ensure precision and accuracy. Descriptive statistics were used for the display of results.
Results: Preliminary data suggested the reading level of patient package inserts within the nitric oxide pathway to be between the 11th and 13th grade reading levels.
Conclusion: Based on preliminary data, the research group strongly recommends that patient package inserts for pulmonary arterial hypertension drug products be updated to increase compliance to recommended reading level and improve readability. Results and conclusion will be finalized and presented at the Pulmonary Hypertension Professional Network Symposium 2023.

ENHANCING KNOWLEDGE, ATTITUDES, AND WILLINGNESS TO DISCUSS CLINICAL TRIALS AND REGISTRIES WITH PULMONARY ARTERIAL HYPERTENSION PATIENTS: A QUALITY IMPROVEMENT PROJECT

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Category: Basic Science
Subcategory: Databases and Registries

Background: Research clinical trials (RCTs) and registries are necessary to advance science and bring novel therapies to patients, particularly in rare disease. Success of an RCT or registry depends heavily upon the success of patient recruitment. However, despite multiple efforts to improve patient involvement in clinical research, participation in RCTs remains low. The lack of clinical trial diversity is also evident in the literature. Diverse subsets of clinical trial participants improve equity of care and are essential in determining the efficacy and safety of new therapies for the populations who will ultimately be using them. Despite that most patients regardless of race or ethnicity have expressed interest in participating in RCTs if approached by a trusted clinician, these conversations are not happening on a consistent basis, if at all. Pulmonary arterial hypertension (PAH) is a progressive, life-threatening disease characterized by an elevation of pulmonary artery pressure and pulmonary vascular resistance, leading to right ventricular failure and death. PAH is classified as a rare disease, with an estimated 40000–100000 patients globally. Adequate enrollment strategies are even more important in rare diseases given that available data are already limited due to the small number of patients available for participation. Subsequently, obtaining sufficient and diverse datasets in rare diseases can take years, which can delay access to potentially life-saving therapies and hinder the generalizability of the data to diverse populations of patients. Recent literature has identified that PAH patients would be willing to participate in clinical trials but are not consistently being approached by their clinicians. Nurses and nurse practitioners (NPs) spend a substantial amount of time with their patients and thus are in a prime position to discuss the option of RCTs and registries. However, nurse professionals often lack the awareness and education to feel empowered to have these discussions. Misunderstanding, lack of confidence or awareness of clinical trials and registries available for patients may prevent nurses and NPs from discussing clinical trials and registries as an option for their patients, thereby creating a missed opportunity for speedy enrollment with a diverse and representative population. Targeted education around enhancing the patient-provider discussion around clinical trials and registries may increase the number of conversations occurring with PAH patients and thus help improve the problem of lack of diversity in clinical trials.
Methods: Ten to 20 nurse professionals who belong to the Pulmonary Hypertension Association Pulmonary Hypertension Resource Network (PHPN) email listserv will be invited to participate in a survey and virtual educational intervention. Participants must be 18 or older and be actively caring for patients with PAH. The survey is an adapted tool from the IMPACT study, which has been validated for use with oncology nurses and has been adapted for the purposes of this project.
Results: Results will be updated upon project completion. Anticipated completion date is February 2023.
Conclusion: Conclusions will be updated upon project completion. Anticipated completion date is February 2023.

MINDFULNESS MEDITATION FOR PULMONARY HYPERTENSION PROGRAM FOR SYMPTOM SELF-MANAGEMENT: QUALITATIVE THEMATIC ANALYSIS FROM PATIENTS' PERSPECTIVE

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Category: Clinical Science
Subcategory: Quality of Life

Background: Patients with pulmonary hypertension (PH) face many challenges in symptom self-management. Despite pharmacologic advancement, patients experience dyspnea, anxiety, depression, and poor quality of life, leading to suboptimal medical treatment adherence and clinical outcomes. Preliminary evidence demonstrates that complementary health approaches (CHAs) positively affect symptom reduction in PH. However, in-person participation has proven to be physically challenging and can contribute to an increased risk of infection exposure, particularly during the COVID-19 pandemic. A technology-assisted mindfulness meditation for PH (MMPH) program can potentially improve intervention adherence through better acceptance and acceptability. In-depth knowledge of how patients accept, embrace, and adopt Web-based-delivered CHA is needed.
Methods: A qualitative design was used. Participants included 12 patients with PH who completed an MMPH intervention program in a randomized pilot trial (October 11 to December 8, 2022). The MMPH program included 8 weekly 60-minute intervention sessions, including mindfulness concepts, application to the PH experience, and mindful practices (breathing, movement, positioning, and meditation) designed for the virtual delivery method. It incorporated 3 technology-delivery methods: Zoom (Weeks 1 and 4), videos, and the MMPH app daily use. The interviews were conducted individually over Zoom (October 11 to December 8, 2022). Example interview questions were (1) "Describe your experience with the MMPH study," and (2) "What do you like and do not like about the MMPH Zooms, videos, and app?" Recorded interview sessions were transcribed verbatim. We analyzed the interview transcripts for thematic content through open coding/labeling of ideas that emerged employing constant comparison.
Results: Participants were predominantly females (83%), aged 35–72, and 2–46 years living with PH. Six major themes emerged, reflecting what participants determined as remarkable about the intervention (Table 1). These themes included overall positive experiences in symptom management, enhanced understanding of mindfulness, incorporating mindfulness into daily practice, perceived facilitators of mindfulness app, barriers to app use, and distinguishing features of MMPH video use.

"It's a great program. It does relax you. It makes you feel better."

"The idea is to notice what you are thinking, to know that, and to go back to your breath. If you have to do that 10 times in a 10-minute sit, that's what the practice is."

"I noticed that, if I started practicing mindfulness and paying attention to what I was doing in the breathing exercises, my anxiety lessened, and I've noticed my stress levels have gone down. So it helped me."

Table 1. Participants Perceptions of MMPH Intervention

Theme No.	Qualitative themes	Theme definitions	Participants count (N = 12)
#1	MMPH study impression	Positive comments and feelings about the program	●●●●●●●●●●●●
#2	MMPH study effect on mindfulness knowledge	Descriptions about increased awareness of thoughts, body sensations	●●●●●●●●●●●●
#3	MMPH study effect on mindfulness integration	Descriptions of self-care practices by integrating mindfulness knowledge	●●●●●●●●●●●●
#4	MMPH app facilitators	Preference descriptions of app features; aspects of the app that enhance app use	●●●●●●●●●●
#5	MMPH app barriers	Descriptions of app design, functionality, or user interface that lessen app use	●●●●●●●●●
#6	MMPH video as a mindfulness anchor	Descriptions of how visual learning serves as an anchor in mindfulness practice	●●●●●●●●●●●●

Abbreviation: MMPH = mindfulness meditation for pulmonary hypertension.

"Yeah, for one reason, the voice on the video is so calming. I can't even begin to tell you. It's almost like a warm blanket wrapped around you. It's just so calming."

"It's the visual aspect. Seeing it, seeing a person, my mind doesn't wander as much when I watch a video compared to listening to audio."

Conclusion: Our MMPH intervention demonstrates acceptability and feasibility for participants with PH. Patients perceive its benefit in psychological stress and symptom reduction, with exemplars of real-life integration into their routine PH self-management practice.

PARENTERAL TREPROSTINIL INDUCTION FACILITATES RAPID ACHIEVEMENT OF THERAPEUTIC DOSES OF ORAL TREPROSTINIL: RESULTS FROM THE EXPEDITE STUDY

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Category: Clinical Science
Subcategory: Diseases and Conditions Associated with PH

Background: Oral treprostinil slows disease progression and improves exercise capacity in pulmonary arterial hypertension (PAH), yet titration can be lengthy. Data from clinical studies and real-world analyses suggest that prostacyclin-naïve patients achieve a mean daily oral treprostinil dose around 6 mg by Week 16 (W16), while those on prior parenteral treprostinil reached higher doses at the same timepoint. EXPEDITE (NCT03497689), an open-label multicenter study, assessed the efficacy of rapid parenteral treprostinil induction to rapidly achieve higher doses of oral treprostinil in patients with PAH.

Methods: Parenteral treprostinil was titrated over 2–8 weeks. Subjects transitioned to oral treprostinil, which was titrated through W16. The primary endpoint was percent of subjects reaching a daily oral treprostinil dose ≥12 mg at W16. Secondary endpoints included changes in clinical measurements from baseline (BL) to W16. BL was defined as prior to parenteral treprostinil initiation.

Results: Twenty-nine eligible prostacyclin-naïve subjects were included in these analyses. Patients had to have a REVEAL 2.0 Risk Score <10 with either World Health Organization (WHO) functional class (FC) II or III symptoms and could be on 0, 1, or 2 PAH therapies. At W16, the mean daily oral treprostinil dose was 16.4 mg with 79% of subjects meeting the primary endpoint. WHO FC improved in 68% of subjects ($P < 0.0001$); 46% achieved FC I, and 39% achieved FC II. From BL to W16, median NT-proBNP improved from 415 to 212 ng/L, with a median change of –134 ng/L ($P = 0.0041$). Median 6-minute walk distance improved from 363 to 395 m, with a median change of +25 m ($P = 0.0078$). Median right atrial area improved from 20.3 to 17.5 cm^2, with a median change of –2.9 cm^2 ($P = 0.0102$). Statistically significant improvements were also seen in Borg Dyspnea Score ($P = 0.0009$) and the emPHasis-10 quality of life (QOL) questionnaire ($P = 0.0001$). Favorable trends were seen in risk stratification, additional echocardiography parameters, PAH symptoms, and treatment satisfaction.

Conclusion: Short-course parenteral treprostinil allowed for over twice the dose oral treprostinil previously reported in de novo initiations. Significant improvements were seen in clinical parameters, risk status, echocardiography, and QOL. These results support rapid parenteral treprostinil induction as a useful approach to quickly reach effective doses of oral treprostinil.

Sponsored by United Therapeutics.

THE IMPLEMENTATION OF A PULMONARY HYPERTENSION PROGRAM AT A COMMUNITY HEALTH SYSTEM

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Category: Clinical Science
Subcategory: Therapeutic Strategies

Background: Pulmonary hypertension (PH) is a complex, resource intensive disease state. As the incidence increases and more patients require treatment in community health systems, standardization of program development and implementation will be essential for optimal patient care. Prior to program implementation, in fiscal year 2020, our health system had roughly 3000 patients with a diagnosis of PH who were hospitalized for a variety of medical problems over 4100 times. **Methods:** The development of a PH program at our institution began in September 2020 with a presentation to hospital administrators. A PH work group was created that included an advanced heart failure cardiologist as program medical director, pulmonary and critical care physician, administrator, clinical pharmacist, respiratory therapist, advanced practice provider, nurse navigator, and both inpatient and outpatient nursing representation. This interdisciplinary group met monthly throughout the program development and implementation process. **Results:** Focused education was completed with core team members including inpatient nursing staff and providers within the advanced heart failure, pulmonary, critical care, and hospital medicine service lines. Emergency departments across the health system were made aware of resources available to care for this patient population. The pharmacy department was trained on how to safely process PH therapies including the risk evaluation and mitigation strategy, home dosing, and medication compounding. Lectures provided for inpatient and outpatient nursing, physicians, and rehabilitation providers were recorded for future reference. Oral pulmonary vasodilator therapy was added to the hospital formulary in September 2021. In December 2021, a protocol was developed for delivery of inhaled epoprostenol to treat patients with decompensated PH. A comprehensive prostacyclin therapy guideline and nursing policy was implemented for continuous infusion prostacyclin therapy in December 2022. As part of this initiative, a comprehensive order set was built into the electronic medical record to ensure safe patient management. In January 2023, a PH clinic was established for ongoing collaboration of care between advanced heart failure cardiology and pulmonology. A multidisciplinary case conference is conducted monthly for case review and quality improvement. Future initiatives for this program include creation of a perioperative management guideline, development of a pharmacist-directed medication titration program, construction of a PH dashboard within the electronic medical record, and application for Pulmonary Hypertension Association accreditation. **Conclusion:** As the incidence of PH increases, due in part to heightened awareness as a serious medical problem, many patients will be evaluated and treated within community health systems. This framework for PH program development can be used to implement new programs resulting in improved access to quality care.

FINDING THE "NEW BEST NORMAL": HEALTH CARE RE-ENTRY AND ADHERENCE

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Category: Case Report
Subcategory: Effect of COVID and Telemedicine on PH Management

Background: The COVID-19 pandemic has created obstacles to established approaches to managing pulmonary hypertension (PH) patients' care, including impeding in-facility appointments, testing, and prescribing behaviors. We commissioned an independent research and consulting firm to conduct an online quantitative study of PH patients that measured behaviors, awareness, and attitudes to establish benchmarks for use in detecting subsequent changes in patient care. In this study, we also aimed to uncover prospective drivers of and barriers to care use and medication adherence among PH patients. **Methods:** We developed a quantitative questionnaire to distribute to Pulmonary Hypertension Association constituents (with sample files of n = 7883 patients and n = 8000 friends). The questionnaire included questions regarding past care use during the previous 3 months and projected care use over the next 3 months. We sent an initial email and up to 2 follow-up emails inviting the sampled individuals to take part in the online study, resulting in n = 530 completed questionnaires. We

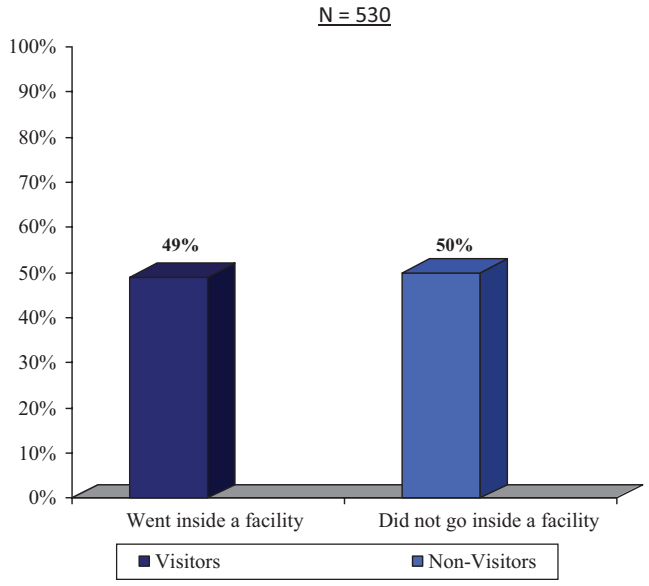

Figure 1: Whether participant went inside a health care treatment facility to receive care for pulmonary hypertension (PH) or chronic thromboembolic PH (CTEPH) in the past 3 months.

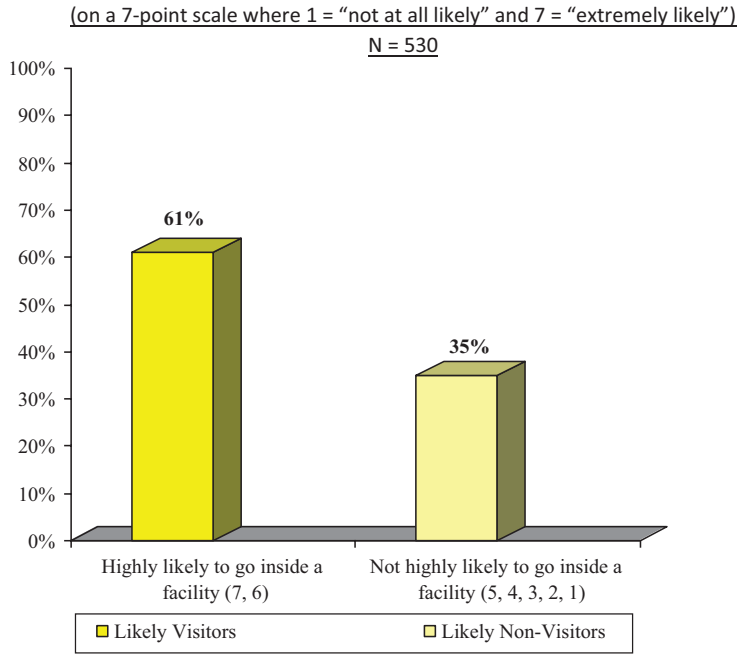

Figure 2: Rating of participants' likelihood to go inside a health care treatment facility to receive care for pulmonary hypertension (PH) or chronic thromboembolic PH (CTEPH) in the next 3 months.

were able to define various care use segments to consider in analyzing the data for patterns of statistically significant differences in PH patients' care behaviors including past in-facility visits, past telehealth participation, likelihood to make an in-facility visit, likelihood to participate in telehealth, in-facility care use, past care demand, and projected care demand.

Results: The questionnaire results showed that, among the 530 respondents, 49% had recently entered a health care treatment facility to receive care, and 61% qualified as likely visitors in the next 3 months. The most cited reason for those who were not likely to enter a facility in the next 3 months was that visits were not medically necessary, or they had no set appointment. The results also showed that 28% of respondents had received care for PH in the past 3 months via telehealth, and 44% said they were highly likely to use telehealth in the next 3 months. We further analyzed the results through segmentation analysis into drivers of care use behavior such as in-facility visits (persistents, periodics, potentials, and absentees) and the number of different medications participants' health care providers had prescribed (5+, 3–4, 1–2, and 0). The number of different medications was revealed to be a constant driver of care use behavior; 56% of respondents who were persistents (visitors + likely visitors) had 5+ different medications versus 11% of respondents who were absentees (nonvisitors + likely nonvisitors). Also, only 17% of respondents who were persistents had 0 medications versus 50% of absentees who had the same (Figures 1–5).

Conclusion: The COVID-19 pandemic did not show a major influence on PH patient in-facility care use, and PH patients will continue to return to care. The results of the study lead us to conclude that individual patients are not the main decision maker regarding seeking in-facility or telehealth care, but the care management system (and health care providers' medication prescribing

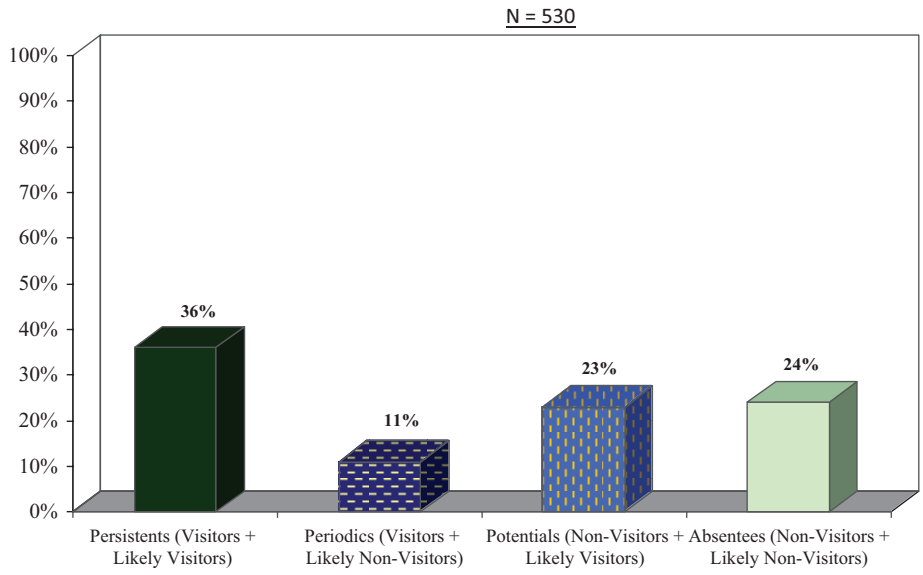

Figure 3: In-facility care use segments (did/did not go inside a health care facility in the past 3 months + highly likely/not highly likely to go inside a health care facility in the next 3 months).

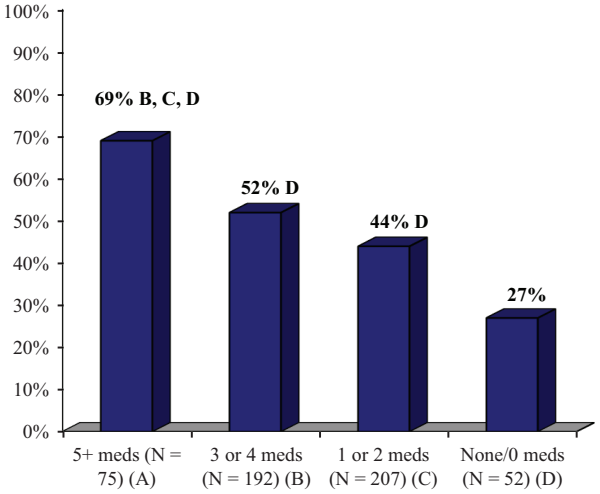

Figure 4: Percent of participants in the visitors care use segment: by number of different pulmonary hypertension (PH) or chronic thromboembolic PH (CTEPH) medications for which participant has a current prescription.

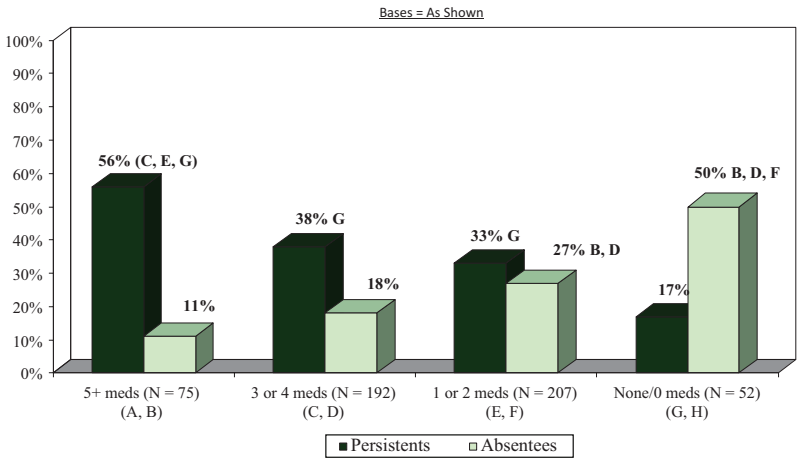

Figure 5: Percent of participants in selected in-facility care use segments (persistents and absentees): by number of different pulmonary hypertension (PH) or chronic thromboembolic PH (CTEPH) medications for which participant has a current prescription.

behaviors) were correlated with in-facility and telehealth care usage. The health care system is just beginning to come to terms with the major changes in care delivery resulting from the COVID-19 pandemic. For PH and chronic thromboembolic PH patients specifically, care has evolved to encompass in-facility visits, telehealth, and/or adjunctive methods, such as smartphone apps and wearables. While adoption of and reliance on various care delivery methods will continue to change, future investigation will be needed to explore the optimal mix of care delivery methods for PH.

HELPING ACUTE PULMONARY EMBOLISM (PE) PATIENTS PHACE THE FUTURE: DEVELOPMENT OF AN ACUTE PE FOLLOW-UP CLINIC

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Subcategory: Diseases and Conditions Associated with PH

Background: Current literature suggests that the incidence of chronic thromboembolic pulmonary hypertension (CTEPH) and chronic thromboembolic disease (CTED) is underestimated for multiple reasons. One of those reasons is a lack of follow up after acute pulmonary embolism (PE). In turn, this leads to a missed opportunity to detect a developing disease process or underlying disease that may have contributed to the sentinel PE event. In early 2021, our PH care team recognized a low incidence of CTEPH and CTED diagnoses in relation to our pulmonary arterial hypertension World Health Organization Group 1 patient population. We also received some referrals for patients who had persistent symptoms following an acute PE event >3 years prior. To increase local awareness of the disease process and improve our effectiveness in identifying such patients, we developed an acute PE follow-up protocol with the collaboration of our inpatient pulmonary embolism response team (PERT) colleagues.

Methods: Beginning in July 2021, we developed a plan for outpatient follow up for acute PE patients but lacked an efficient referral process and noticed poor patient adherence to the follow-up plan. Barriers included lack of an efficient referral process, poor patient and caregiver understanding, and inability to contact patients following discharge. We collaborated with our inpatient PERT colleagues to develop a workflow that allowed for improved patient adherence to the follow-up plan. The key elements of improving our process included creating an Epic order for consultation, creating of an information packet explaining the follow-up process, standardizing follow-up appointments, and working with our care management team to streamline communication with each patient.
Results: As a result, we appreciated a significant increase in patient adherence to the follow-up plan and were able to identify many more patients with CTEPH and CTED than prior years. Some other unexpected but favorable outcomes included identification of hypercoagulable conditions and coordinating hematology consultation, diagnosis of other disease processes that contributed to the venous thromboembolism, assisting with medication refills, and financial assistance to avoid a treatment gap, securing or discontinuing supplemental oxygen therapy, and receiving referrals from outside health care systems as local awareness increased.
Conclusion: Likewise, we identified some challenges including managing care for patients who do not live near our geographic

location, obtaining approval for repeating a ventilation perfusion scan and/or echocardiogram imaging on occasion, and developing new anticoagulation protocols. We now have a streamlined process in place for each acute PE patient and have started working with the local Emergency Departments to identify patients who may not be identified using our current process. Overall, developing this process has allowed our PH team to meet a need for this often-overlooked patient population.

RISK FACTORS ASSOCIATED WITH PEDIATRIC PULMONARY HYPERTENSION WITHIN THE NATIONAL 2016 KIDS' INPATIENT DATABASE (KID)

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Category: Clinical Science
Subcategory: Pediatrics

Background: Pediatric patients with untreated obstructive sleep apnea (OSA) are at risk for development of pulmonary hypertension (PH), a rare but serious outcome. By identifying clinical and demographic risk factors associated with PH, primary care providers can better direct prompt screening and specialty referral in high-risk children, such as those with OSA.
Methods: Retrospective cross-sectional cohort study analyzing weighted discharges from the 2016 Kids' Inpatient Database (KID). Demographic, procedural, and continuous variables were examined. Mean and median levels of continuous variables were estimated and compared between patients with and without PH using the 2-sample *t* test or Wilcoxon rank sum test. Bivariate analysis was conducted, followed by a multivariable logistic regression model to investigate risk factors associated with PH among the overall cohort using odds ratios (ORs) and 95% confidence intervals (CIs). PH was the primary outcome and was identified via diagnostic ICD-10 codes recorded in the KID.
Results: A total of 6081132 weighted discharges were included. The mean age was 3.8, and 48.9% were males. The prevalence of PH was 0.21% (12777 patients). There were 37631 patients with OSA, and the prevalence of PH among this cohort was 3.3%. Risk factors associated with PH included chronic lung disease of prematurity (OR = 21.3; 95% CI = 19.3, 23.4), congenital heart disease (OR = 16.0; 95% CI = 14.8, 17.2), Down syndrome (OR = 11.2; 95% CI = 10.1, 12.3), asthma (OR = 2.0; 95% CI = 1.8, 2.2), OSA (OR = 4.9; 95% CI = 4.4, 5.5), central sleep apnea (OR = 2.1; 95% CI = 1.4, 3.3), hypertension (OR = 4.9; 95% CI = 4.4, 5.4), sickle cell disease (OR = 3.9; 95% CI = 3.4, 4.5), obesity (OR = 1.3; 95% CI = 1.1, 1.5), Asian or Pacific Islanders (OR = 1.2; 95% CI = 1.1, 1.4), Blacks (OR = 1.2; 95% CI = 1.1, 1.3), Native Americans (OR = 1.3; 95% CI = 1.0, 1.7), enrollment in government-sponsored health insurance (OR = 1.4; 95% CI = 1.4, 1.5), patient age (OR = 1.014; 95% CI = 1.010, 1.02), hospital admission in the Western US region (OR = 1.2; 95% CI = 1.1, 1.3), and male gender (female gender was protective [OR = 0.93; 95% CI = 0.89, 0.98]; Figure 1).
Conclusion: The prevalence of PH among patients with OSA was 3.3%, which is over 10 times greater than the overall prevalence of PH in the 2016 KID (0.21%). Several risk

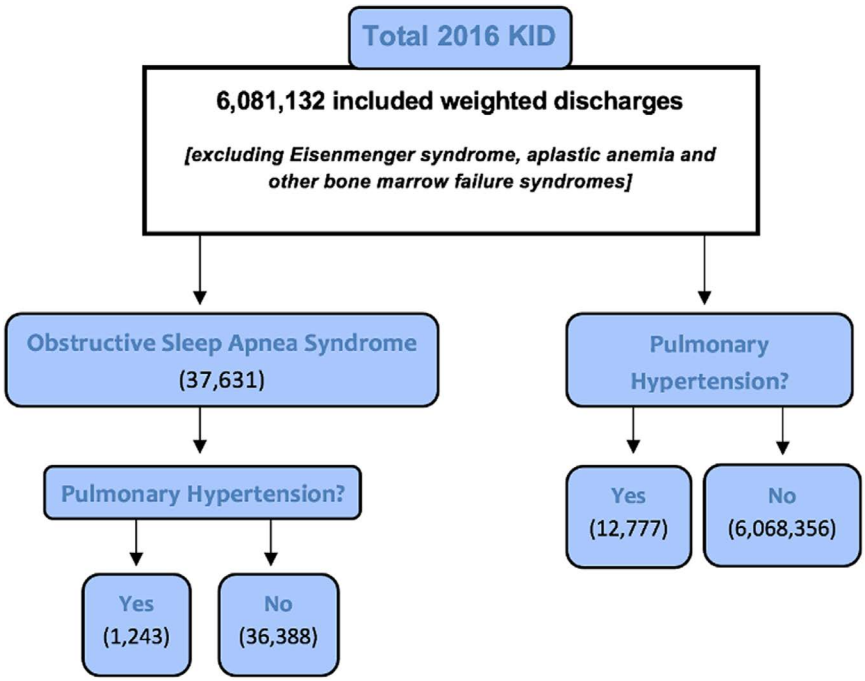

Figure 1: 2016 Kids' Inpatient Database (KID) pulmonary hypertension and obstructive sleep apnea weighted discharges.

factors were independently associated with PH. Considering that the KID only includes in-patient admission data, future multi-institutional prospective studies are needed to further evaluate the relationships between specific clinical and demographic risk factors, such as OSA, obesity, insurance status, and other potential risk factors for development of pulmonary hypertension.

PREDICTION OF PULMONARY HYPERTENSION ASSOCIATED WITH BRONCHOPULMONARY DYSPLASIA IN PRETERM INFANTS USING MIRNAS IN EARLY TRACHEAL ASPIRATE SAMPLES

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Category: Clinical Science
Subcategory: Pediatrics

Background: Pulmonary hypertension (PH) associated with bronchopulmonary dysplasia (BPD) is a severe complication of preterm birth associated with high mortality. However, because the clinical signs and symptoms of BPD-PH overlap with that of BPD, a high level of suspicion needs to be employed to perform tests to diagnose BPD-PH. Hence, the current clinical practice is to screen for BPD-PH via echocardiogram at 36 weeks in preterm infants with BPD. Identifying at-risk preterm infants will help early diagnosis. We have previously identified a panel of 20 miRNAs in tracheal aspirate (TA) differentially expressed in BPD-PH. The objective of the study is to analyze the predictive value of target specific miRNA panel in early TA samples in extreme preterm infants.
Methods: We collected TA samples from 22 preterm infants born <28 weeks of gestation within the first 7 days of age. The samples were frozen at –80°C until analysis. The samples were then thawed, RNA extracted using Norgen miRNA purification kit, and miRNA was analyzed using small RNA-sequencing libraries prepared from 5–25 ng total RNA, the resulting high throughput sequencing data using the QIAseq miRNA Library kit (QIAGEN). Of the original 20 miRNAs, only 16 were expressed in the 7-day-old samples in our new cohort. Logistic regression was calculated for the 16 miRNAs (hsa-miR-29a-3p, hsa-miR-542-3p, has-miR-624-5p, hsa-miR-183-5p, hsa-miR-3131, hsa-miR-501-3p, hsa-miR-101-3p, has-miR-101-5p, hsa-miR-3128, hsa-miR-128-3p, hsa-miR-628-3p, hsa-miR-24-3p, hsa-miR-1255b-5p, hsa-miR-205-5p, hsa-let-7i-3p, and has-let-7i-5p) to calculate receiver operating characteristic (ROC) area under the curve.

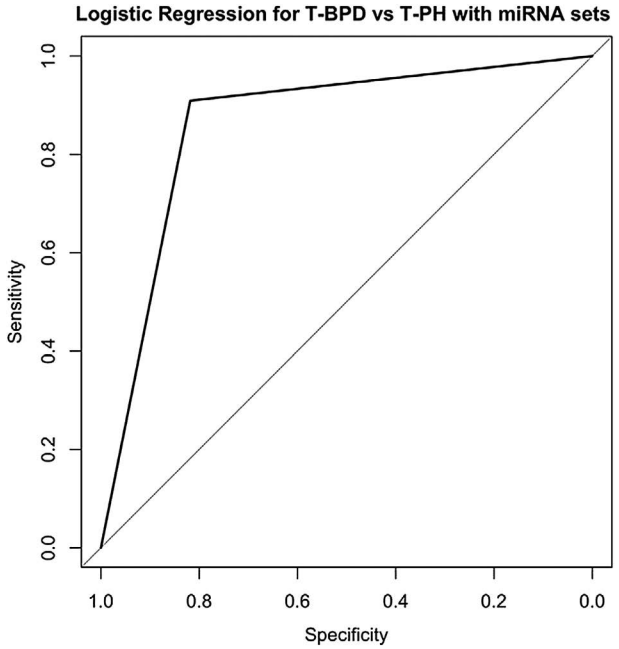

Figure 1: Predictive value of 16 mIRNAs in early tracheal aspirates in extreme preterm infants show receiver operating characteristic (ROC) area under curve = 0.86 and sensitivity of 83% and specificity of 82%.

Results: Of the 22 infants, 11 of them were diagnosed with BPD-PH at 36–40 weeks of gestation based on their echocardiogram findings, and 11 of them with Grade 2–3 BPD (2019 National Institute of Child Health and Human Development [NICHD]/Neonatal Research Network [NRN] classification). Logistic regression calculation (Table 1) of the 16 miRNAs comparing infants who went on to develop BPD-PH versus BPD at 36 weeks of PMA revealed area under the curve ROC = 0.86 with sensitivity and specificity of 83% and 82%, respectively (Figure 1), of predicting BPD-PH in those with high risk of developing BPD.
Conclusion: A panel of 16 miRNAs expressed in early TA samples has significant predictive value in identifying extreme preterm infants that are at high risk for developing BPD-PH at 36 weeks PMA. This panel once validated in a larger cohort has the potential as a clinical tool to closely monitor high-risk infants for pulmonary vascular disease and intervene as needed with target oxygen saturations, optimize nutrition and fluid goals, and early echocardiogram to screen for BPD-PH.

PULMONARY HYPERTENSION-RELATED AGE-ADJUSTED MORTALITY RATES AND TRENDS BY URBANIZATION CATEGORY IN THE UNITED STATES

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Category: Clinical Science
Subcategory: Databases and Registries

Background: Pulmonary hypertension (PH) is a progressive disease and is associated with high mortality regardless of the subtype. Despite therapeutic advances, the overall age-adjusted PH mortality rate increased significantly from 1999 to 2019. However, rural-urban disparities in PH-related mortality and trends have not been studied.
Methods: We analyzed adjudicated death certificate data from the Centers for Disease Control and Prevention Wide Ranging Online Data for Epidemiological Research Multiple Cause of Death Database for PH-related deaths in the US from 2005 to 2019. We identified PH-related deaths using ICD-10 codes. We divided the cohort into large metropolitans (>1 million), medium/small metropolitans (50000–999999), and rural (<50000) areas. Poisson regression modeling was used to calculate mortality rate ratios and to analyze temporal trends from 2005 to 2019.
Results: There were 346452 PH-related deaths between 2005 and 2019. Of these, 46.9% of decedents were from large metropolitans, 34.4% from medium/small metropolitans, and 18.7% from rural areas. The age-adjusted mortality rates (AAMRs) from PH per 1 million population were 60.3 in large metropolitans, 73.4 in medium/small metropolitans, and 72.2 in rural areas. From 2005 to 2019, AAMRs increased 26.6% in large metropolitans, 35.0% in medium/small metropolitans, and 33.6% in rural areas. The absolute difference in PH-related AAMRs per 1 million population almost doubled from 2005 to 2019 between large metropolitans and medium metropolitans (9.1 to 18.4) and between large metropolitans and rural areas (9.9 to 19.4; Figure 1).
Conclusion: Between 2005 and 2019, there was an increase in PH-related deaths within all urbanization categories. However, the absolute difference between large metropolitans and rural/medium/small metropolitans nearly doubled over time. The disparities noted are likely due to demographic differences; varying risk factors; and a combination of social, economic, and geographic barriers to health care. Further investigations focused on the causes for these differences are needed to reduce the disparities and decrease the burden of deaths from PH. As an extension of these data, we will be investigating demographic differences (sex, age groups, and race) in PH-related mortality rates/trends between urbanization categories.

	Number of Deaths	Age-Adjusted Mortality Rate per 1,000,000 (95% CI)	Mortality Rate Ratio (95% CI)	% Rate Change from 2005-2019
Overall	346452	66.5 (66.2-66.7)	-	+29.4 (22.4-36.4)*
Large Metropolitan	162426	60.3 (60.0 to 60.6)	Reference	+26.6 (19.6-33.6)*
Medium/Small Metropolitan	119250	73.4 (73.0 to 73.9)	1.21 (1.18-1.25)*	+35.0 (28.0-40.6)*
Rural	64776	72.2 (71.7 to 72.8)	1.20 (1.17-1.23)*	+33.6 (26.6-39.2)*

*P = <0.001

Figure 1:

CORRELATION OF WORLD HEALTH ORGANIZATION FUNCTIONAL CLASS AND PATIENT-REPORTED OUTCOME MEASURES IN ADULTS WITH PULMONARY ARTERIAL HYPERTENSION

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Category: Clinical Science
Subcategory: Quality of Life

Background: The World Health Organization Functional Classification (WHO-FC) measures pulmonary arterial

hypertension (PAH) symptom severity and physical activity limitations. Patient-reported outcome (PRO) instruments are increasingly used to monitor other aspects of patient health such as treatment satisfaction, overall wellbeing, and disease burden. In this study, we aimed to understand the correlation between WHO-FC and PRO measures in patients with PAH.
Methods: In this study, we analyze data for adults with PAH on oral treprostinil enrolled in the ADAPT Registry. Assessments were obtained for select PRO measures at registry enrollment: Treatment Satisfaction Questionnaire for Medication (TSQM), emPHasis-10, and Short-Form-12v2 Health Survey (SF-12). WHO-FC was assessed by clinician or patients using the Pulmonary Hypertension Functional Classification Self-Report (PH-FC-SR). Authors of previous work have shown high agreement between clinician-assessed WHO-FC and PH-FC-SR. WHO-FCs completed within 30 days of registry enrollment were used. Pearson or Spearman correlation coefficients were used to assess strength of association.
Results: Eighty-six patients met inclusion criteria for this analysis. Patients had a mean ± SD age of 55.4 ± 13.4, 67 (78%) were female, and 67 (78%) were white. Thirteen (15%) patients were WHO-FC Class I, 43 (50%) Class II, and 30 (35%) Class III. For all 4 domains of TSQM, mean scores worsened with higher WHO-FCs. Mean ± SD emPHasis-10 scores worsened from WHO-FC Class I (18.2 ± 11.4) to Class II (23.0 ± 12.1) to Class III (34.1 ± 11.2). WHO-FC and emPHasis-10 overall scores were strongly correlated ($\rho = 0.45$; $P < 0.01$). SF-12 physical aggregate scores worsened with higher WHO-FCs, but mean ± SD SF-12 mental aggregate scores were similar across WHO-FC Class I (51.9 ± 10.5), Class II (50.5 ± 10.7), and Class III (49.8 ± 12.3). WHO-FC was strongly correlated with aggregate SF-12 physical score ($\rho = -0.58$; $P < 0.01$), but there was no correlation with aggregate SF-12 mental score ($\rho = -0.07$; $P = 0.60$).
Conclusion: WHO-FC strongly correlates with emPHasis-10 and SF-12 aggregate physical scores, but there are aspects of patient health that it does not reflect, such as mental health. Holistic patient health may not be adequately monitored in routine care for patients with pulmonary arterial hypertension.

CASE STUDY: CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

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Category: Case Report
Subcategory: Diseases and Conditions Associated with PH

Background: The case study to be presented is on chronic thromboembolic pulmonary hypertension (CTEPH). This describes a patient our team is following and workup which led to definitive treatment of the disease condition.
Methods: We reviewed several cases and chose 1 to be presented.
Results: The patient underwent pulmonary endarterectomy with success.
Conclusion: The case chosen for this case study continues to be followed in clinic.

INPATIENT TRANSITIONS OF PARENTERAL PROSTACYCLINS AND SELEXIPAG: A 6-YEAR, ACADEMIC MEDICAL CENTER EXPERIENCE

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Category: Clinical Science
Subcategory: Therapeutic Strategies

Background: The University of Cincinnati Medical Center, a Pulmonary Hypertension Center of Comprehensive Care, uses thorough medication guidance to outline the medication use process of parenteral prostacyclins and other pulmonary arterial hypertension (PAH)-targeted pharmacotherapy in the inpatient setting. These guidelines include a specific appendix that contains recommended transition processes between select medications. All transitions to or from a parenteral prostacyclin are completed during an inpatient admission. Prostacyclin infusions are only administered in designated units. Medical Step Down is the preferred unit for medication transitions with the Medical Intensive Care Unit as an alternative based on bed availability or severity of illness. All nurses in these units complete initial and ongoing education and competency related to disease state and administration of targeted pharmacotherapy. PAH providers and pharmacists use these transition processes as a general guide for developing individualized patient transition plans. Each process includes information specific to the medications included in the transition, a transition checklist, and a transition process. The transition checklist includes necessary items for medication administration. Examples include (but are not limited to)

required type of intravenous (IV) access, calculation references (such as for parenteral to oral treprostinil), dose rounding, and dosing weight selection. The transition process describes information such as time between transition steps, medication overlap (if required), whether central line priming is required, typical duration of transition (in hours), recommendations for long-term intravenous access (such as tunneled catheters), and general line/site care (such as withdrawal of medication from central line prior to removal).
Methods: Selexipag has been approved for inpatient administration since 2016. We reviewed all inpatient transitions, including planned admissions and unplanned transitions, from a data query of the electronic medical record. Patients were included if they completed a transition between selexipag and parenteral treprostinil or epoprostenol (either to or from). A single patient was included multiple times if he or she experienced >1 medication transition (ie, from IV epoprostenol to selexipag, then later from selexipag back to IV epoprostenol).
Results: From July 2016 to December of 2022, 49 patients were transitioned between selexipag and a parenteral prostacyclin. Median (IQR) transition time was 36 (24–48) hours. The most frequent transition periods were 24 (n = 12) and 36 (n = 12) hours, and most (77.6%) occurred over <48 hours. The shortest transition occurred over 12 hours (n = 4), and the longest transition was a duration of 156 hours (n = 2). Thirty-two of the 49 patients (65.3%) transitioned from a parenteral prostacyclin to selexipag. Of those patients, 16 (50%) transitioned from epoprostenol and 16 (50%) to treprostinil. Seventeen patients (34.7%) transitioned from selexipag to a parenteral prostacyclin; 23.5% (n = 4) to epoprostenol, and 76.5% (n = 13) to treprostinil. Most patients were discharged from the hospital; however, 3 patients died during the hospital stay after completing the transition. Of the 46 patients who were discharged, 69.6% (n = 32) were discharged with selexipag, and 30.4% (n = 14) were discharged with parenteral prostacyclin (71.4% with treprostinil and 28.6% with epoprostenol).
Conclusion: A guideline-based approach is effective to support inpatient transitions between oral and parenteral prostacyclin pathway medications in patients with PAH.

DIRECT PROSTACYCLIN TRANSITION IN PEDIATRIC PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION

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Category: Case Report
Subcategory: Pediatrics

Background: Pediatric patients with pulmonary arterial hypertension (PAH) are commonly treated with the prostacyclin analog treprostinil in intravenous, subcutaneous, inhaled, or oral form or the prostacyclin receptor agonist selexipag. Patients who transition between these medications often follow recommendations for gradual up and down titrations that take place over several days in the hospital or several weeks as an outpatient. However, hospital resources are limited, and long transitions are inconvenient for patients and families. Our center has previously had experience with rapid 1-day transitions, so we hypothesized that direct prostacyclin transitions in pediatric PAH patients would be safe and effective.
Methods: Eight pediatric patients with PAH transitioned directly between prostacyclins with no overlapping doses. Direct medication transitions occurred in the Cardiac Intensive Care Unit, at home, and in Cardiology Clinic. Equivalent doses for selexipag were estimated using information extrapolated from experience and published materials.
Results: All patients completed direct transition as planned and remained on transition dose for at least 1 week. In most cases, selexipag was up titrated at home after establishing initial transition dose. Please see Figure 1 for transition data.
Conclusion: In selected patients, direct prostacyclin transition in pediatric patients with PAH is safe, effective, convenient for families and reduces the use of hospital resources.

Age (years)	Weight (kg)	From	To	Location
15	58	SQ treprostinil 116 ng/kg/min	IV treprostinil 116 ng/kg/min	Clinic
4	13	IV treprostinil 34 ng/kg/min	Selexipag 400 mcg BID	CICU
2	16	SQ treprostinil 76 ng/kg/min	Selexipag 800 mcg BID	CICU
14	85	SQ treprostinil 50 ng/kg/min	Selexipag 1600 mcg BID	CICU
15	55	Inhaled treprostinil 6 breaths (_ mcg) QID	Selexipag 200 mcg BID	Home
14	56	Oral treprostinil 6 mg TID	Selexipag 1000 mcg BID	Home
12	38	Selexipag 1600 mcg	SQ treprostinil 40 ng/kg/min	CICU
14	85	Selexipag 1600 mcg	SQ treprostinil 50 ng/kg/min	Home

Figure 1: Transition data.

PATIENTS LIVING WITH PULMONARY ARTERIAL HYPERTENSION (PAH) PROVIDE ESSENTIAL INSIGHTS FOR DRUG DEVELOPMENT

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Category: Case Report
Subcategory: Quality of Life

Background: The voices of patients and patient representatives are essential in improving health outcomes, including drug development. A patient advisory meeting was held to gain insights into experiences with pulmonary arterial hypertension (PAH) and to inform early-stage clinical research and development, disease management, and patient advocacy programs.
Methods: A virtual patient advisory meeting was conducted with 6 US patients (4 women, 2 men), ages 24–69, living with PAH. Participants reported a range of functional classes (FCs), including 1 person in FC 1, 3 people in FC 2, and 2 people in FC 3. Diagnoses included idiopathic PAH and familial PAH. The meeting included interactive polls, a chatroom, and featured a live illustration of patients' experiences with PAH.
Results: The patients shared their experiences with PAH, which are collated into 6 themes below: (1) Symptoms: Shortness of breath, fatigue, and lack of energy are primary physical complaints. This inhibits their ability to execute basic activities of daily living. (2) Diagnosis: Patients report varied experiences with diagnoses, with some being diagnosed shortly after experiencing symptoms, while others' diagnoses were delayed for years. Female participants reported that their symptoms were attributed to other common causes, like obesity or asthma. (3) Effect on Life: Mental and emotional health are the biggest challenges participants face, and this is exacerbated by the isolation they feel from family and friends. Participants noted that their disease is invisible yet has an overt effect, particularly economic. (4) Health Wishlist: Ideal outcomes from treatment would enable patients to have more energy to participate in normal everyday activities. Patients want to remain active for as long as possible. (5) Desired Treatments: Some approved treatment options can be cumbersome and place limitations on patients' mobility and agility. Patients shared that oral medications could help them live with more freedom. (6) Seeking Care: Patients are highly interested in clinical trials but are concerned about inclusion criteria. Other challenges cited are need for time off work, being placed on placebo, and drug reactions. On approved medications, patients said they can experience stability; however, disease progression can be unpredictable and rapid (Figure 1).
Conclusion: This exchange revealed a need for patient-friendly resources for the newly diagnosed, psychosocial support, improved diagnostics, and patient input into clinical trial designs to help speed the development of new treatment options.

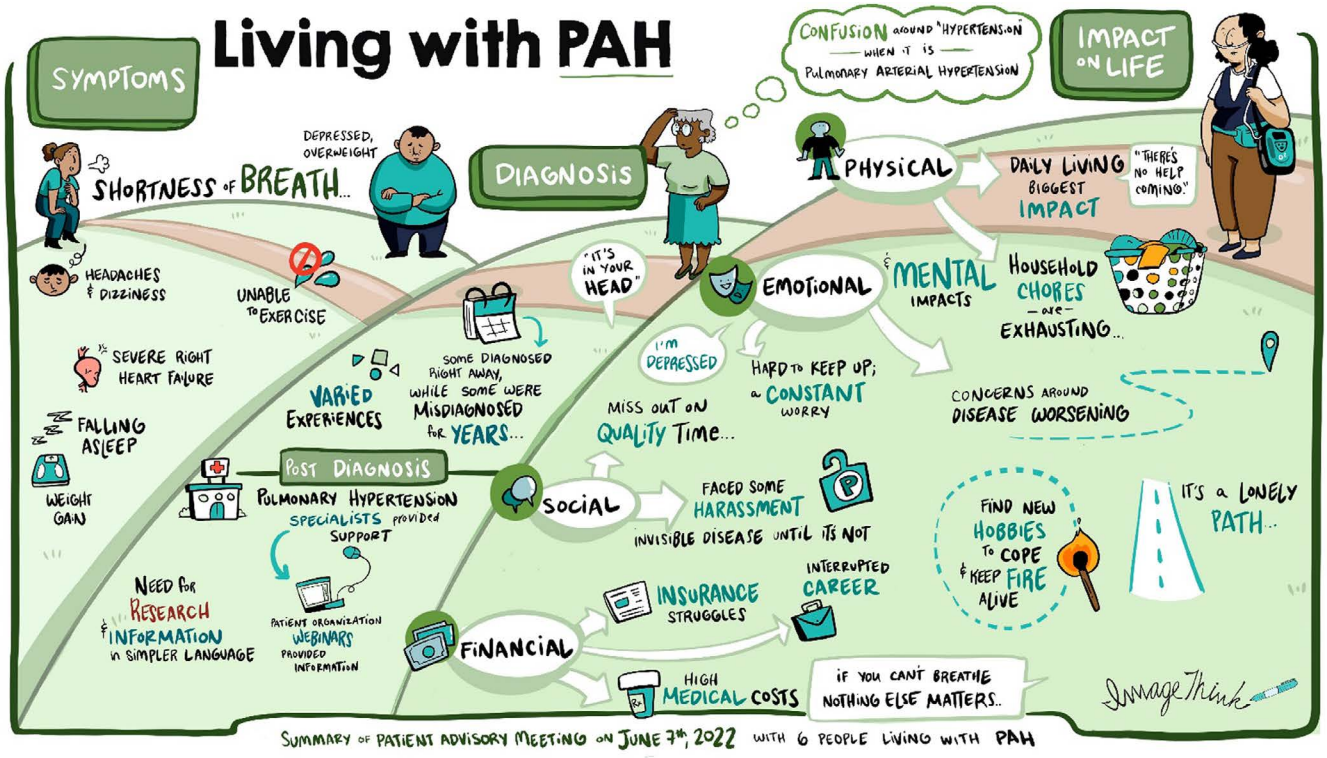

Figure 1: Illustration of PAH patient journey from patient advisory board meeting.

CASE REPORT: CANNABIDIOL (CBD) FOR TREATMENT OF REMODULIN® SITE PAIN

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Category: Case Report
Subcategory: Therapeutic Strategies

Background: Cannabidiol (CBD) has been used for pain management in other disease states and other indications but has not been studied for pain relief from subcutaneous (SC) site pain related to SC treprostinil use. CBD is known to interact with some pathways through which the body initiates inflammation. Transdermal administration efficiently delivers medication directly to the local area where it is applied, thereby possibly reducing the dosage needed, decreasing side effects, and removing the need for systemic treatment.

Methods: We conducted case reports by following/evaluating 2 patients from the Pulmonary Hypertension Center who experienced site pain while on SC treprostinil and used topical CBD for pain management. These patients had previously tried various other suggested methods to mitigate the site pain but were unsuccessful. Therefore, topical CBD was tried as an alternative.
Results: The 2 patients that were followed/evaluated in the Pulmonary Hypertension Center while using topical CBD for site pain relief reported favorable results regarding mitigating their site pain.
Conclusion: CBD, which is nonpsychoactive and nonaddictive, may be considered a viable option for site pain mitigation with the use of SC treprostinil.

CLINICIAN'S GUIDE TO MANAGE PULMONARY HYPERTENSION USING CARDIOPULMONARY EXERCISE TESTING

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Category: Clinical Science
Subcategory: Therapeutic Strategies

Background: Traditional methods of diagnosing pulmonary hypertension (PH) include invasive measures of cardiopulmonary hemodynamics acquired from right and left heart catheterization, which are typically performed at rest. However, since most patients are asymptomatic at rest, diagnostic tests in this state may underappreciate the patient's condition where dyspnea and abnormal physiologic processes only manifest during higher levels of exertion. Cardiopulmonary exercise testing (CPET) is a noninvasive means to quantify patient effort, aerobic capacity, and ventilation to perfusion (V/Q) matching during exercise. Variables from CPET have been related with pulmonary vascular pressure and aid in the diagnosis of PH, accurately reflect disease severity, predict adverse events, and reflect the response to therapeutic interventions.
Methods: Patients with PH tend to be exercise limited due to the inimical remodeling of the pulmonary vasculature, which leads to increases in vascular resistance and alveolar hypoperfusion. As a result, patients require increased ventilation pertaining to a certain degree of V/Q mismatch with increased dead space ventilation. Moreover, right ventricular wall thickness and chamber size increase in patients with established PH, which reduces left ventricular chamber size and causes decreased filling, compliance, and stroke volume. Failure of oxygen to be appropriately delivered to working skeletal muscle because of reduced oxygen diffusion and diminished left-sided cardiac output is reflected by lowered peak oxygen consumption during CPET.
Results: Excessive increases in ventilation relative to the demands of the work rate are described as ventilatory inefficiency and usually caused by V/Q mismatch, elevated chemoreceptor and muscle-receptor sensitivity, early lactate accumulation, and/or elevated pulmonary pressures. The ventilation to carbon dioxide output slope is associated with the degree of ventilatory inefficiency, and PH patients display higher ratios in accordance with the increase in pulmonary artery pressures (PAPs). Additionally, end-tidal CO_2 has been shown to have an inverse relationship at rest and at anerobic threshold with elevated PAP (Figure 1).
Conclusion: CPET provides the unique ability to noninvasively assess PH in patients primarily through aerobic capacity and V/Q coupling within the pulmonary system. This is of particular importance when attempting to identify PH early, as V/Q mismatching progressively worsens as pulmonary pressures continue to rise. Increased clinical acceptance of CPET in the assessment of pulmonary hemodynamics may decrease undiagnosed patients, allowing clinicians to implement early treatment plans and therapeutic options.

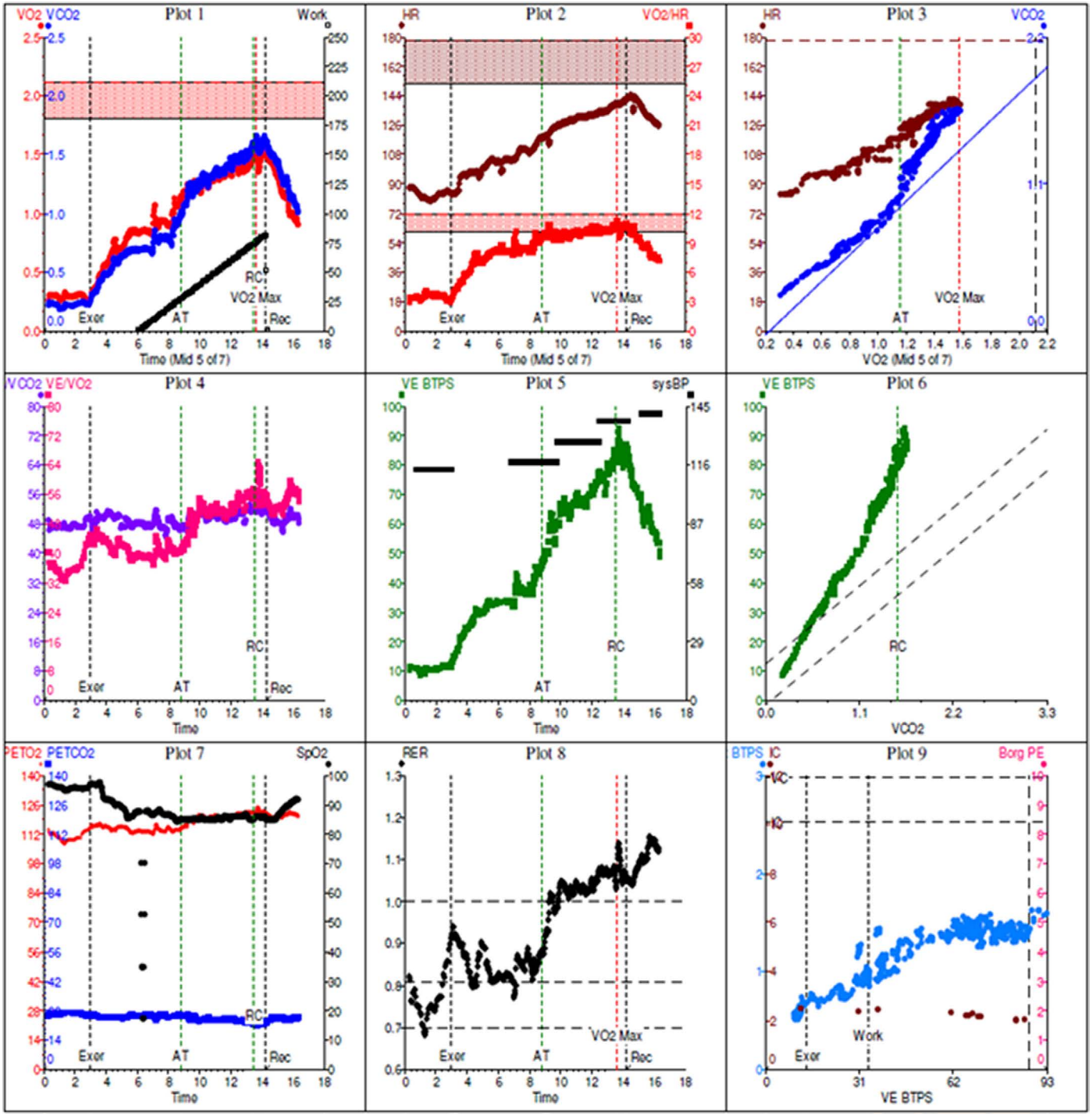

Figure 1: Nine-panel plot of a patient with known pulmonary hypertension.

PULMONARY HYPERTENSION ASSOCIATION REGISTRY (PHAR): A STATUS UPDATE AND RESOURCE FOR RESEARCH

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Category: Clinical Science
Subcategory: Databases and Registries

Background: The Pulmonary Hypertension Association Registry (PHAR) is the largest active longitudinal registry of patients diagnosed with World Health Organization diagnostic Group 1 pulmonary arterial hypertension or Group 4 chronic thromboembolic pulmonary hypertension. The principal purpose of the PHAR was to measure and improve adherence to published guidelines and quality of care for patients with pulmonary hypertension (PH) and subsequently improve outcomes. To facilitate that aim, the data repository has been leveraged for ongoing research by PHAR investigators.
Methods: Demographic and clinical data were collected from the PHAR data repository as of October 2022. Research proposals were reviewed and assessed by committee. Both abstracts and manuscripts were quantitated with focused areas highlighted.
Results: Of 82 accredited PH Care Centers (PHCCs), 67 (83%) participated in PHAR, and 65 (79%) centers have enrolled at least 1 patient, with over 2200 patients total (Table 1). Most were White women in their mid-50s. Less than 2% were age <18. The majority were Group 1 pulmonary arterial hypertension, somewhat evenly split between idiopathic and associated (Figure 1). Most were modified New York Heart Association Functional Class III with average 6-minute walk distance nearly 340 m (Table 2). Mean pulmonary artery pressure was moderately elevated, and pulmonary vascular resistance was just under 10 Wood units (Table 3). Most of the PHAR participants were on combination therapy with the most common agents being phosphodiesterase-5 inhibitors and endothelin receptor blockers (Table 4). The average emPHasis-10 score was 25.1 ± 12.3. As of January 2023, 41 proposals for research were submitted and reviewed, resulting in 35 (85%) approvals and 14 manuscripts published to date. There were also 24 abstracts, 4 of which were for 2023 national society meetings. The primary focus of the published

Table 1. Demographics of PHAR Participants

Description	All (N = 2247)
Sex	
Male	623 (27.7%)
Female	1594 (70.9%)
Missing	30 (1.3%)
Age	
Mean ± SD	54.86 ± 17.04
Median (IQR)	54.9 (43.2, 67.8)
Missing	12 (0.5%)
Race	
Chinese	12 (0.5%)
Filipino	31 (1.4%)
Japanese	2 (0.1%)
Korean	3 (0.1%)
Vietnamese	7 (0.3%)
Other Asian	13 (0.6%)
Black or African American	301 (13.4%)
Native Hawaiian/Pacific Islander	8 (0.4%)
White	1639 (72.9%)
American Indian	21 (0.9%)
Asian Indian	20 (0.9%)
More than one race	42 (1.9%)
Unknown/not reported	137 (6.1%)
Missing	11 (0.5%)
Ethnicity	
Hispanic or Latino	14 (4.4%)
Not Hispanic or Latino	288 (90.3%)
Unknown/not reported	17 (5.3%)
Missing	0 (0%)
Health insurance	
Private health insurance	1124 (50%)
Medicare	927 (41.3%)
Medicaid	351 (15.6%)
Medi-Gap	46 (2%)
SCHIP	3 (0.1%)
Military health care (TRICARE/VA, Champ-VA)	81 (3.6%)
Indian Health Service	7 (0.3%)
State-sponsored health plan	169 (7.5%)
Other government program	69 (3.1%)
Single service plan (eg, dental, vision, prescription)	38 (1.7%)
No coverage	43 (1.9%)
Education	
Under 18 years old	42 (1.9%)
Did not graduate high school	146 (6.5%)
High school/GED/vocational education graduate	675 (30%)
Some college or university	373 (16.6%)
Graduated from college or university	574 (25.5%)
Professional training beyond 4-year college or university	229 (10.2%)
Missing/do not know	15 (0.7%)

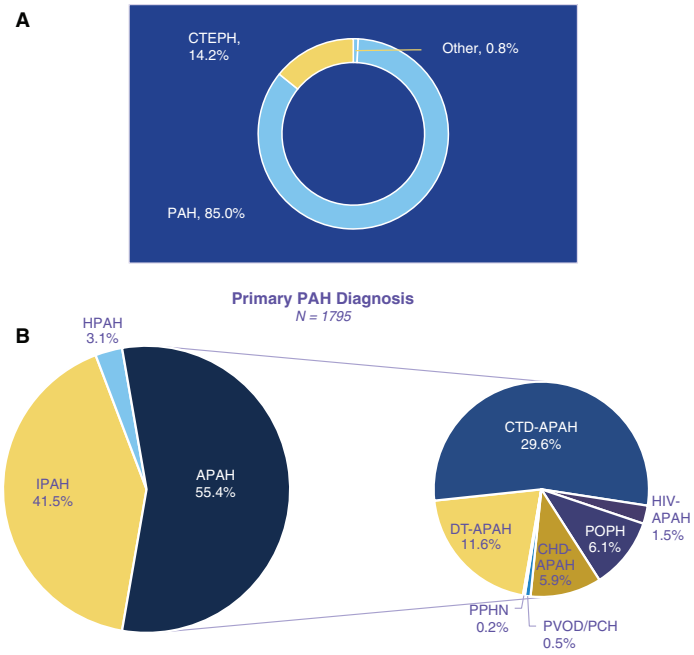

Figure 1: Diagnostic group classification of Pulmonary Hypertension Association Registry participants.

Table 2. Baseline Clinical Characteristics of PHAR Participants

Baseline characteristic	All (N = 2247)
6-minute walk distance, m	
Mean ± SD	335.41 ± 125.23
Median (25%ile, 75%ile)	340 (247, 420)
Missing	418 (18.6%)
NYHA/WHO Functional Class	
I	181 (8.1%)
II	778 (34.6%)
III	1005 (44.7%)
IV	135 (6%)
Missing	148 (6.6%)

Abbreviations: NYHA, New York Heart Association; WHO, World Health Organization.

manuscripts was distributed as follows: cause-related outcome 3, health care disparities 3, demographics 2, quality of life 2, treatment 2, and hospitalization/mortality 2. There have been 4 ancillary studies: 1 completed, 3 in progress potentially including those PHAR participants (79%) who agreed to additional research. Pharmaceutical companies have used PHAR data in support of drug delivery and development.

Conclusion: The PHAR represented a collaborative effort of the majority of PHCCs that enrolled a significant number of patients diagnosed with either Group 1 or Group 4 PH. The data collected represented demographic and clinical characteristics of those patients along with prospectively collected outcomes. Investigators at PHAR sites submitted multiple proposals for data queries with a broad range of research aims that resulted in several published manuscripts over the last 3 years. Ancillary and industry-related studies offer ongoing opportunities.

Table 3. Baseline Clinical Characteristics of PHAR Participants

Hemodynamics	All (N = 2247)
Right atrial pressure, mmHg	
Mean ± SD	9.85 ± 6.12
Median (IQR)	9 (5, 13)
Missing, No.(%)	146 (6.5%)
Pressure (mPAP), mmHg	
Mean ± SD	48.29 ± 13.66
Median (IQR)	48 (39, 57)
Missing	96 (4.3%)
Pulmonary artery wedge pressure (PAWP), mmHg	
Mean ± SD	11.09 ± 5.63
Median (IQR)	10 (7, 14)
Missing	188 (8.4%)
Left ventricular end-diastolic pressure (LVEDP), mmHg	
Mean ± SD	11.8 ± 4.98
Median (IQR)	11.5 (8, 14.25)
Missing	1827 (81.3%)
Pulmonary vascular resistance (PVR), Wood units	
Mean ± SD	9.72 ± 5.42
Median (IQR)	8.81 (5.76, 12.36)
Missing	325 (14.5%)
Cardiac output (CO), L/min	
Mean ± SD	4.35 ± 1.51
Median (IQR)	4.1 (3.3, 5.15)
Missing	217 (9.7%)
Cardiac index (CI), L/min/m^2	
Mean ± SD	2.31 ± 0.79
Median (IQR)	2.17 (1.79, 2.7)
Missing	260 (11.6%)

Table 4. Medication Patterns for PHAR Participants

PH-targeted treatment baseline, PAH patients	N = 2247
PH medications now	
None	404 (18.0%)
1	677 (30.1%)
2	848 (37.7%)
3	308 (13.7%)
≥4	10 (0.4%)
Medications at enrollment (w/in 6 months)	
Endothelin receptor antagonists (ERA)	1128 (50.2%)
Phosphodiesterase-5 (PDE-5) inhibitors	1549 (68.9%)
Soluble guanylate cyclase (sGC) stimulators	246 (10.9%)
Prostanoid (inhaled)	133 (5.9%)
Prostanoid (oral)	193 (8.6)
Prostanoid (parenteral)	493 (21.9%)
Prostanoid (any)	722 (32.1%)

NOVEL USE OF A PDE-5I DURING COVID-19

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Category: Clinical Science
Subcategory: Therapeutic Strategies

Background: Pulmonary hypertension (PH), specifically pulmonary arterial hypertension (PAH), is a rare and chronic disease, requiring life-long management with expensive medications that are typically difficult to tolerate from a side-effect standpoint. The peak of the COVID-19 pandemic was especially challenging when adding PH-targeted therapies and medications needed to manage patients' side-effect profiles. A phosphodiesterase-5 inhibitor (PDE-5i) is usually first-line therapy for management of newly diagnosed PAH, whether prescribed as monotherapy or upfront with an endothelin receptor antagonist (ERA). Adcirca, now commercially available in generic formulation, is particularly preferred because of its once-daily dosing and lack of pill burden as compared with generic Revatio, which may require up to 80 mg (4 tablets) 3 times daily (ie, 12 tablets per day). To circumvent or delay adding PH-targeted therapies, for those on monotherapy with a Food and Drug Administration-approved dose of tadalafil 40 mg daily or for those maximally treated on triple therapy, patients were supplemented an afternoon dose of tadalafil 20 mg as follows: 40 mg in the morning and 20 mg in the late afternoon.
Methods: This is a retrospective quality improvement study on patients' responses to an additional dose of a PDE-5i. Data were reviewed from October 2021 to January 2023 on patients' demographics, subjective tolerance, hospital admission, Crt, 6-minute walking test, brain natriuretic peptide, initiation of prostacyclin therapy, and cost analysis of obtaining additional dose of the PDE-5i.
Results: Current analysis of the data is in progress and will be updated once it is completed. A total of 50 patients' charts was reviewed.
Conclusion: Current analysis of the data is in progress, and the conclusion will be updated once it is completed.

ANXIETY AND DEPRESSION SCREENING TO IDENTIFY AT-RISK YOUTH: A QUALITY IMPROVEMENT PROJECT IN AN OUTPATIENT PULMONARY HYPERTENSION CLINIC

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Category: Clinical Science
Subcategory: Pediatrics

Background: Pulmonary hypertension (PH) is a disease associated with significant morbidity and mortality. It can negatively affect a child's ability to grow, develop, and perform normal tasks of daily living. Children with chronic diseases are thought to have higher rates of anxiety and depression (AD) than their healthy peers. However, there is a gap in evidence for the prevalence of AD and screening practices in children diagnosed with PH.
Methods: All eligible patients were identified in the preclinic huddle. A process map was created and reviewed with the PH team (nurses, providers, and social workers). Patients were given the questionnaires before the provider began the visit. The W.K. Kellogg Foundation logic model was adapted to understand planned work and objectives. The Centers for Disease Control and Prevention Framework for Program Evaluation aided the evaluation of the project.
Results: Thirty patients out of 47 eligible were screened, reaching 64% of the eligible population. Screening identified AD in 14 of the 30 patients, prompting further social work assessment and intervention, resulting in mental health service referrals and follow-up. The average total GAD-7 score was 4.9 (range, 0–16), and the average total PHQ-9 score was 4.8 (range, 0–20). Eighteen females were screened with an average age of 15.4 years, and 12 males were screened with an average age of 14.4 years. Females were found to have higher PHQ-9 scores of 5.6 ± 5.1 ($P = 0.001$) and GAD-7 scores of 5.7 ± 4.6 ($P = 0.002$) than males (3.2 and 3.5, respectively). A total of 4 patients required an additional suicide assessment due to findings from the screens (Figures 1 and 2).

Key Process Measure Data Summary

	June – August	September - December	Project Total
Screened	22	8	30
Eligible	37	47	47
Females screened	13	5	18
Average age (years)	*15.9*	*14*	*15.4*
Males screened	9	3	12
Average age (years)	*15*	*13.3*	*14.4*

Figure 1: Key process measure data summary.

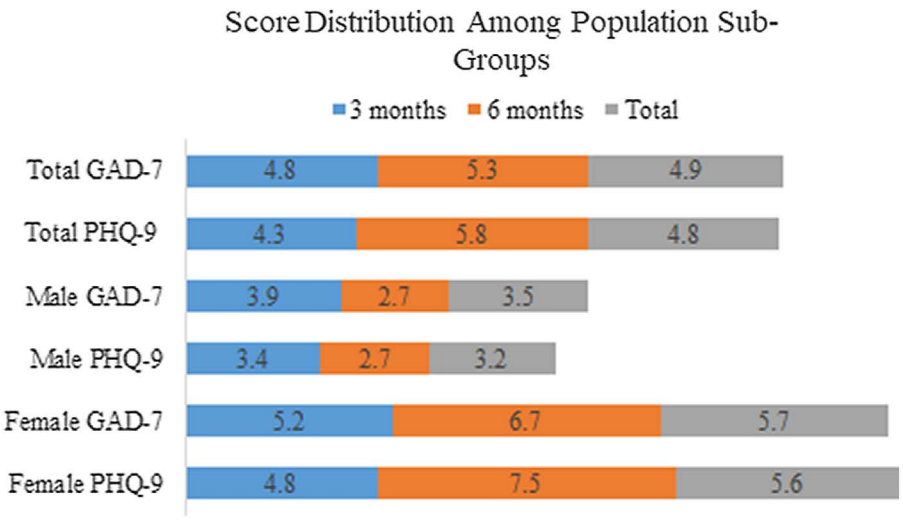

Figure 2: PHQ-9/GAD-7 score distribution.

Conclusion: In this targeted population, there was a high prevalence of unrecognized AD, necessitating the activation of institution-specific assessment and intervention protocols. Given these results, this project supports continued AD screening and response to fill a population need for improved mental health support.

INTEGRATED GENETIC COUNSELING IN A MULTIDISCIPLINARY PEDIATRIC PULMONARY HYPERTENSION CLINIC ENABLES HIGH-YIELD GENETIC TESTING AND FAMILY-BASED CARE

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Category: Clinical Science
Subcategory: Pediatrics

Background: Incorporation of a genetic counselor (GC) in a multidisciplinary pediatric pulmonary hypertension (PPH) clinic enables family-based care and high-yield genetic testing. GCs can triage patients to determine those most likely to benefit from both genetic counseling and genetic testing and

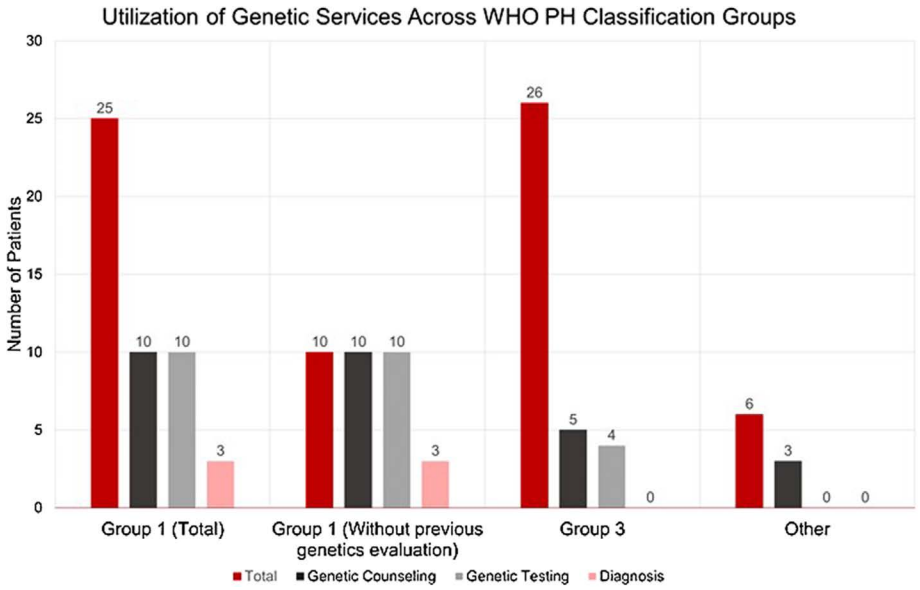

Figure 1: Number of patients who received genetic counseling, genetic testing, and a genetic diagnosis between clinical pulmonary hypertension classification groups as defined by the World Symposium on Pulmonary Hypertension (WSPH).

enable family-based care by providing family testing and screening recommendations.

Methods: For a 12-month period, from July 2021 to July 2022, all unique patients in the PPH clinic at Riley Hospital for Children were analyzed to determine if they had formal genetic counseling, had genetic testing, and/or received a genetic diagnosis. Patients were analyzed according to their clinical pulmonary hypertension classification, as defined by the World Symposium on Pulmonary Hypertension (WSPH).

Results: Sixty-three unique patients were analyzed. Of those, 23 (36.5%) saw a GC, 18 had genetic testing (28.6%), 15 (23.8%) had a comprehensive pedigree completed, and 5 received a genetic diagnosis (7.9%). Family screening and/or cascade genetic testing recommendations were provided to 7 patients (11.1%). For the 25 patients clinically classified as Group 1 (pulmonary arterial hypertension [PAH]), 15 had previous genetic diagnoses and were evaluated outside of the PPH clinic. The remaining 10 all received formal genetic counseling and had genetic testing (100%), with a formal molecular diagnosis in 3 (33%) of the 10 patients (Figure 1). Comparatively, for 26 patients clinically classified as Group 3 (pulmonary hypertension due to lung diseases and/or hypoxia), 5 (19.2%) had formal genetic counseling, 4 (15.4%) had genetic testing, and 0 (0%) received a molecular diagnosis (Figure 1).

Conclusion: GC integration in the PPH clinic facilitates genetic testing in appropriate patients, yielding to a high level of genetic diagnosis (30%) in Group 1 (PAH) patients. GC integration allowed for family-based care by providing family screening and genetic testing recommendations for 11.1% of patients seen.

UTILITY OF INTEGRATED GENETICS TO CREATE A GENETIC TESTING PRACTICE MODEL FOR A PEDIATRIC PULMONARY HYPERTENSION CLINIC

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Category: Clinical Science
Subcategory: Pediatrics

Background: Genetic counseling and, if indicated, genetic testing are recommended by most professional societies for patients with idiopathic and heritable pulmonary arterial hypertension (IPAH and HPAH, respectively) and their first-degree relatives (FDRs). Genetic counselors (GCs) provide support in pretest counseling, posttest counseling, and determination of test use management. Continued evaluation and inclusion of genes newly associated with pulmonary arterial hypertension (PAH) on genetic testing panels can increase genetic testing yield. Ongoing evaluation of genetic testing recommendations, evaluation of literature supporting new PAH-associated genes, and evaluation of available genetic testing panels are advantages of an integrated GC within a pediatric pulmonary hypertension (PPH) clinic. Currently, there is no evidence on how to best integrate a GC and a genetic testing model within a multidisciplinary PPH clinic.

Methods: Relevant PAH consensus guidelines were reviewed to determine recommendations for genetic counseling, genetic testing, and to determine important candidate genes. This along with clinical experience informed the creation of a genetic counseling/testing clinic model.

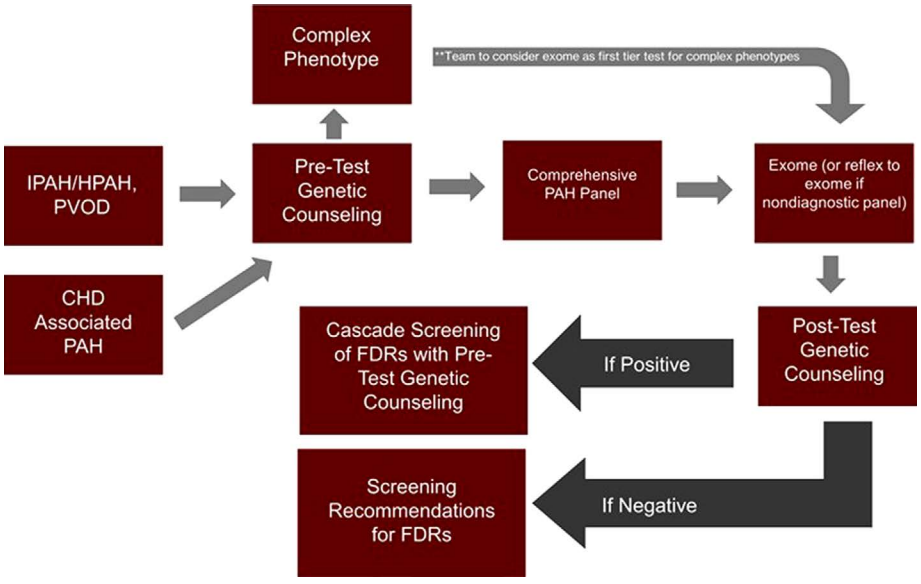

Figure 1:

Results: All major professional guidelines recommend pretest and posttest genetic counseling for individuals with HPAH and IPAH as well as FDRs for whom familial variant testing is available. Additionally, individuals with both PAH associated with congenital heart disease and pulmonary venoocclusive disease benefit from genetic testing. Comprehensive PAH genetic testing panels are recommended as a first-line test, and individuals with a nondiagnostic PAH panel may benefit from exome sequencing to identify novel and possible de novo causes of PAH.
Conclusion: Our evidence-based genetic testing model (Figure 1) ensures equitable and high-quality care for all patients. A GC embedded in clinic allows for regular evaluation of this model by reviewing published recommendations, investigating new candidate genes, and providing insight into the nuanced differences between the varied genetic testing panels.

TRANSITION OF INTRAVENOUS EPOPROSTENOL TO ORAL TREPROSTINIL IN A PATIENT WITH PULMONARY ARTERIAL HYPERTENSION: A PATIENT CASE REPORT

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Category: Case Report
Subcategory: Therapeutic Strategies

Background: Prostacyclin therapy is commonly used for management of pulmonary arterial hypertension (PAH). Historically, prostacyclin therapies have only been available in parenteral or inhaled formulations; however, new oral formulations have emerged. Patients' clinical course and preferences may require transition from one formulation to another, but limited guidance exists regarding how to successfully transition from one formulation to another. We present our experience in transitioning a patient with Group 1 PAH from intravenous (IV) epoprostenol to oral (PO) treprostinil.
Methods: A 43-year-old female with a history of PAH associated with drugs and toxins, congestive heart failure, atrial fibrillation, coronary artery disease, acute lymphoblastic leukemia, and obesity presented to the hospital for a planned transition from IV epoprostenol to PO treprostinil. The patient has been on IV epoprostenol since May 2016. At the time of admission, she was stable at a dose of 60 ng/kg/min with a dosing weight of 100 kg. Epoprostenol was infused via CADD-Legacy® ambulatory infusion pump through a tunneled central catheter. The transition from IV epoprostenol to PO treprostinil was pursued for patient satisfaction and ease of medication administration. Patient was directly converted from IV epoprostenol to PO treprostinil with a target PO treprostinil dose of 14 mg 3 times a day (TID).
Results: The patient was able to undergo a direct transition from IV epoprostenol to PO treprostinil over the course of 72 hours while being monitored in the Cardiac Intensive Care Unit. The target dose of PO treprostinil was established by considering manufacturing conversion guidance for IV epoprostenol to IV treprostinil and IV treprostinil to PO treprostinil, as well as the patient's recent 10% weight loss. After switching the patient from her home CADD-Legacy ambulatory infusion pump to the hospital's IV infusion pump, the IV epoprostenol was titrated down twice daily by 9 ng/kg/min while simultaneously the PO treprostinil dose was increased by 2 mg with each infusion adjustment. The patient was able to tolerate the transition well and was discharged home after a 5-day hospital admission with the new PO treprostinil regimen following successful discontinuation of IV epoprostenol.
Conclusion: Despite limited guidance regarding how to successfully transition from IV epoprostenol to PO treprostinil, we report a successful direct conversion from IV epoprostenol to PO treprostinil with no resulting adverse effects at our institution.

EXERCISE-INDUCED PULMONARY ARTERIAL HYPERTENSION IN SELECT PATIENTS WITH KNOWN ATRIAL SEPTAL DEFECT/PATENT FORAMEN OVALE: SINGLE CENTER EXPERIENCE

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Category: Case Report
Subcategory: Diseases and Conditions Associated with PH

Background: A small subset of patients with unexplained dyspnea was identified in a select at-risk population for exercised-induced pulmonary arterial hypertension (PAH) with suspected or previously identified atrial septal defect/patent foramen ovale. Early detection of PAH, meeting Group I criteria using 2022 European Society of Cardiology/European Respiratory Society clinical guidelines is critical to

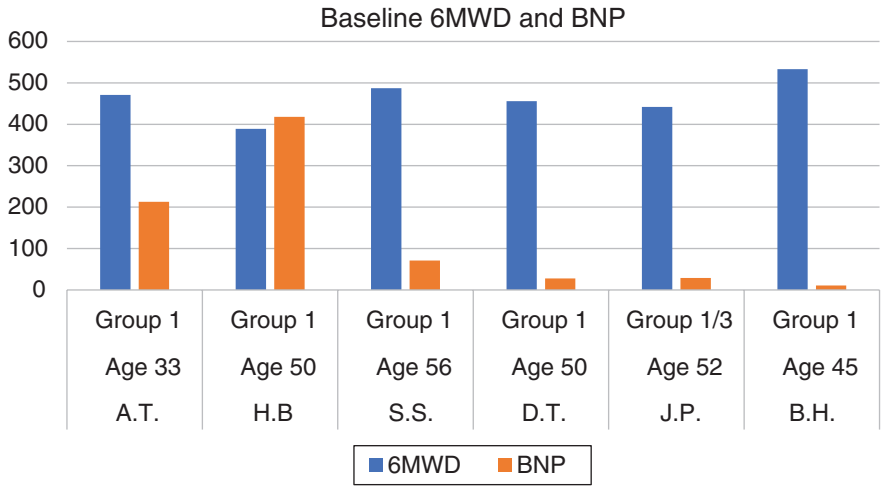

Figure 1: Charted changes noted after right heart catheterization (RHC) with exercise protocol.

implement targeted PAH therapy when appropriate to delay PAH disease progression.

Methods: Data collection was obtained and reviewed from medical records using system electronic medical record. Measurements were charted based on values obtained from studies (echocardiogram/right heart catheterization). Evaluated relationships and variables between cases.
Results: Although a small sample size, we can potentially identify similar patients from our select community who could benefit from thorough review and comprehensive screening for PAH to avoid delays in initiation of appropriate PAH targeted therapies.
Conclusion: We are using a multidisciplinary practice group to develop and implement protocols to comprehensively study and subsequently identify appropriate subset of patients/Group I PAH that may potentially benefit from PAH targeted therapies.

HANK THE HEART AND PULMONARY HYPERTENSION (PH) MEDICATION MANAGEMENT: CHARACTER STORYTELLING ANIMATIONS DIGITAL MEDIA TOOL TO FURTHER EDUCATE AND ENGAGE PATIENTS AND FAMILIES WITH PH

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Category: Case Report
Subcategory: Pediatrics

Background: Pulmonary hypertension (PH) is a rare, complex disease affecting both children and adults. Efforts to provide health education are imperative as patients/caregivers can feel overwhelmed or confused by the complexity of the disease and treatment options. Health literacy affects a patient's/caregiver's capacity to acquire, process, and understand health information and make informed health decisions. Enhancing health literacy improves the patient/caregiver knowledge about illness, can alleviate anxiety about the disease, and plays a significant role in determining the degree of overall adherence to recommended therapies. An abundance of adult-centric patient educational materials, formatted as handouts and online readable materials are available, but there is a scarcity of pediatric specific material. YouTube™ videos accommodate visual and auditory learners, which increases engagement from both children and their caregivers. It is also free, which allows ease of access for anyone with internet capabilities. Our first video about PH in a series of planned educational videos received over 20000 views. Given this, we established the goal of developing content to include more educational topics for our patient population.
Methods: Cincinnati Children's Media Lab is an established animation team and multimedia lab which partners with institutional specialties to create brief, informative, and visually engaging animated educational videos. The PH team partnered with the Media Lab to create a series of character-based animations specific to PH. The animations were designed to be educational and engaging for the child and adult learner with content vetted and set at the sixth-grade fluency level by the organizational health literacy team. From idea to final product, the PH team collaborated with the Media Lab to assemble topic specific educational content, followed by development of a main character

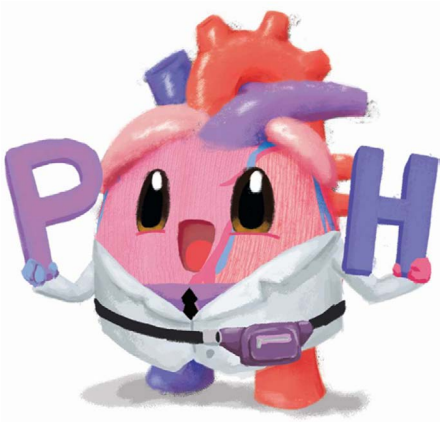

Figure 1: Prespecified subgroup analysis demonstrated consistent benefit of seralutinib on pulmonary vascular resistance (PVR) across subgoups.

(ie, Hank the Heart) and supporting scenes. A rough draft storyboard was assimilated where content, both audio and visual, could be edited. The final visual product was rendered with background music and voiceover added by sound engineers and a voice actor. Once complete, content can be uploaded and electronically shared.
Results: See Conclusion.
Conclusion: The advent and availability of consumer technologies offers access to online educational materials as an alternative teaching tool for clinicians while educating both pediatric patients and their caregivers. This is a unique opportunity for our institution to partner with the Media Lab and develop such content. We expect that offering this unique education at an acceptable health literacy fluency level will motivate the patient and family to understand and adhere to recommended therapies. In addition, we anticipate it will alleviate anxiety about the disease and treatment while empowering patients and their caregivers to make informed health decisions.

TONGUE TWISTER OR PULMONARY HYPERTENSION SUBSPECIALTY COORDINATION SPECIALIST

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Category: Case Report
Subcategory: Pediatrics

Background: Patients with pulmonary hypertension (PH) and their families have complex medical needs and are challenged with ongoing issues in access to care, decreased personalization of care, and individual health disparities. Our pediatric PH Care Center team serves patients over a 4-state region Washington, Alaska, Montana, and Idaho. We recognized our pediatric patients and families were struggling with issues related to ability to access care, decreased personalization of care, inability to coordinate complex diagnostic testing across multiple departments (cardiopulmonary exercise testing [CPET], cardiac magnetic resonance imaging [cMRI], pulmonary function testing [PFT], echocardiograms, sleep studies, swallow studies, genetics clinic, pulmonary clinic, etc), distance from our center, financial concerns, and social stressors. We wanted to address these patient disparities and yet improve the work for our team members. We identified a need to support our patients and our PH program with a coordinator role that did not require provider or registered nurse (RN) involvement and allow the MA the ability to work to the fullest extent of licensure and expand job parameters beyond rooming and obtaining diagnostic studies.
Methods: We used multiple quality improvement (QI) processes and direct observation to examine the needs of our patients and needs in our PH program. The outcome of these processes and assessment of current staffing allowed for identification and need for the creation of this role. We initially started by selecting 1 area which we could monitor with a QI using the plan-do-check-act process: creation and maintenance of a PH patient database by use of a clinic MA. We saw immediate improved patient tracking and outpatient follow-ups. We were able to track inpatient consults and new outpatient referrals efficiently. With the success of the database trial, we approached the Heart Center Administration with the request for a dedicated MA and designated time to work with our PH team and provide basic clinical support. With the support of administration, we continued to expand the MA role to increase MA involvement within our program and added responsibilities within the licensure of our MA but beyond the standard scope of practice of an MA. Over time, the position evolved into a nonnursing coordinator role.
Results: The development of this role has benefited our patients across all aspects of care. Some of the identified areas supported by this role include complex appointment coordination with diagnostic testing (cMRI, computed tomography angiography, CPET, PFT, sleep studies, and videofluoroscopic swallowing studies), coordination of specialty clinics (pulmonary, genetics, nutrition, etc), working with cardiac surgery coordinators for cardiac catheterizations and cardiac surgery, knowledge of hospital and ambulatory processes (admission and discharge), ability to track and enter monthly labs, enter REMs reporting and counseling, and participate in RedCap data entry. Orders are pended and verified in a timely manner to perform testing such as electrocardiograms, 6-minute walking distance, cardiac monitor placement, clinical intake, and discharge. Patients have benefited from increased face-to-face interaction and involvement with our team. RNs are freed from lower-level clinical work and able to focus on higher-acuity patient needs and education. Providers can delegate minor clinical administrative tasks including the tracking of patients and are notified of patient needs and discrepancies. This role has improved interpersonal contact with patients and families before they come to clinic and when they are in clinic, assisting in identifying and escalating social determinants of health needs. Patients experience improved access and follow-up. The position has allowed us to work with the families who live outside a 3-hour drive to our facility to streamline their clinic visits. Our coordinator has initiated a process with our team where we work with local providers and cardiologists to bring PH care to the families in their local communities when possible. We are better able to identify and addressing cultural disparities for families who live 2000 miles away in remote villages in Alaska and assisting them to make a clinical visit to Seattle smoother and less stressful when possible. We have improved the disconnect between the inpatient wards and the ambulatory side with the discharge of at-risk infants and patients and coordination of follow-up appointments with complex scheduling across departments. We have used and integrated the knowledge of an MA who was experienced with the complexities of caring for cardiac patients with PH and created a position to address gaps in our program.

Conclusion: The successful integration of this role within the subspecialty PH program has led the single ventricle/Fontan and electrophysiology subspecialties to replicate this position for their programs in the Heart Center at Seattle Children's Hospital. Other PH programs may benefit from exploring this position and building a similar role for their programs. Using the knowledge and clinical skills of a nonnursing coordinator with direct face-to-face interactions with families could help to bridge gaps between the needs of the patients, RNs, providers and clinic and assist in tasks that are often overlooked and not in the scope of existing roles. This role can help to improve access to care for patients and families, personalizing and individualizing care by identifying needs or issues patients and families encounter.

SELEXIPAG USE IN PEDIATRIC PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION

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Category: Clinical Science
Subcategory: Therapeutic Strategies

Background: Selexipag, a prostacyclin receptor agonist, is approved for use in adult patients with pulmonary arterial hypertension (PAH). There is an ongoing clinical trial to determine optimal dosing for pediatric patients. Currently available published literature describing dosing practices in pediatric patients is limited, with the largest study including 15 patients.
Methods: This is a retrospective chart review of patients <18 years old with diagnosed PAH who were prescribed selexipag between September 20, 2020, and October 21, 2022. Patients were identified using a database maintained by the institution's PAH team. The primary objectives were to describe selexipag dosing strategies used by the PAH team and any changes in concomitant PAH therapies (phosphodiesterase-5 inhibitors, endothelin receptor agonists, and prostacyclin derivatives) during the selexipag titration period. Secondary objectives were to describe the efficacy (changes in catheterization, echocardiogram, and/or 6-minute walk test [6MWT] results) and safety (reason for dose reductions or discontinuations) of selexipag. All results are descriptive in nature.
Results: Twenty-seven patients aged 1–17 years, weighing 10–63 kg, started a median dose of oral selexipag 100 mcg twice daily. Therapy was increased by a median of 100 mcg twice daily every 6 days to a maximally tolerated median dose of 800 mcg twice daily. All 24 patients on another prostacyclin derivative were able to discontinue therapy at their maximum tolerated selexipag dose; other concomitant PAH therapies did not change. No patient had catheterization data collected before and after selexipag initiation. Changes in echocardiogram data and 6MWT results were variable. No patient discontinued selexipag; 4 patients received decreased doses due to flushing (n = 1), drug interactions (n = 2), or increased frequency of nose bleeds (n = 1).
Conclusion: Selexipag use in pediatric patients appears to be safe and well tolerated. The titration regimen used at the institution resulted in patients being able to discontinue another prostacyclin derivative. No other PAH medication changes were made with selexipag therapy.

MAKING A SPLASH… IN SEARCH OF A SAFE WAY TO SUBMERGE ON SUBCUTANEOUS TREPROSTINIL THERAPY

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Category: Clinical Science
Subcategory: Quality of Life

Background: Subcutaneous (SQ) site maintenance is burdensome for patients on continuous treprostinil therapy. Patients self-administer a small catheter via a needle injection device under the skin. Setting each new site often results in 5–7 days of debilitating pain and erythema, often referred to as "hell week." Promoting longevity of sites up to 3 months is therefore of utmost importance. Although the Remunity pump itself may be submerged for a short time under water, it is the site that is most difficult to maintain. Patients frequently report that the supplies allotted from the specialty pharmacies to protect sites from water during showering/bathing are often ineffective. To achieve a more normal lifestyle, some patients have been noted to interrupt their continuous infusions to shower or swim. With a half-life of 4 hours, patients have a false sense of security that they are safe to disconnect from their treprostinil pumps without complications. Our patient herein admits to having previously disconnected the pump to swim after reading on social media sites that other patients disconnect to submerge. This is not only against medical advice but also dangerous. Unfortunately, not enough research has been performed on best practices to waterproof SQ sites. Our patient took it upon herself to find a better solution and found that the Allevyn Life dressing afforded reliable waterproofing.
Methods: The existing SQR site is covered by an IV3000 dressing. The site, tubing, and pump are secured with tape for extra support. A test strip which detects the presence of moisture is placed beside the SQR site. The Allevyn Life dressing (8.25 × 8.25 in) is applied, smoothed out completely with no wrinkles or buckles, and the patient will submerge in water for 20 minutes. Upon exiting the pool, the Allevyn Life dressing is removed. The IV3000 dressing over the existing SQR site is

shown to be completely dry. The test strip shows no evidence of moisture, thereby demonstrating the waterproof capability of the Allevyn Life dressing.
Results: The Allevyn Life dressing by Smith & Nephew was successfully used by 1 patient to reliably waterproof her pump and site while submerging in water.
Conclusion: Pending institutional review board approval, we intend to further investigate the reliability of this dressing by having other patients on SQ therapy use it to submerge in water in a controlled setting. Moisture strips will be used to ensure that the dressing is occlusive. Surveys of trial patients will be conducted before and after using the dressing to assess satisfaction with the Allevyn dressing compared with current dressings. The surveys will also gauge the effect on quality of life as patients may now submerge in water.

A MULTI-INSTITUTIONAL RESPONSE TO PROMOTING CAREGIVER EDUCATION IN PEDIATRIC PULMONARY HYPERTENSION: DEVELOPMENT OF 3 EDUCATIONAL BROCHURES

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Category: Case Report
Subcategory: Pediatrics

Background: As part of the PPHNet, the Advanced Practice Provider and Nursing (APPN) Committee identified 2 main areas of focus for educational brochures to develop: subcutaneous (SQ) treprostinil management and World Health Organization (WHO) Group 3 associated pulmonary hypertension (PH). For children diagnosed with severe PH, the use of continuous prostacyclin therapy is often used for aggressive pulmonary vasodilation. This therapy may be associated with changes to quality of life related to SQ site pain and management. A SQ treprostinil guide was created with experienced parent/patient input as a resource for new SQ parents/patients including pain and site management troubleshooting, practical advice from patients and parents, and basic medication information. Patients with WHO Group 3 associated PH make up a large portion of pediatric PH patients. In the setting of this diagnosis, there is limited patient and caregiver educational materials, both printed and electronic. The APPN committee identified 2 types of lung diseases that are often associated with PH to focus on: bronchopulmonary dysplasia (BPD) and congenital diaphragmatic hernia (CDH). Representatives from 6 PPHNet centers (6 total APPNs) volunteered to develop a caregiver educational flyer specific to BPD and CDH-associated PH describing the definition, prevalence, risk factors, assessment/testing, treatment, and long-term follow-up to be used to help support caregiver education.
Methods: A review of the published literature available for all 3 topics, SQ treprostinil management, PH in BPD, and PH in CDH, was completed by members of the APPN Committee in the project. During monthly meetings, the educational brochures were outlined and edited to meet user readability, both in reading level (average ninth grade) and graphic layout. The content was derived from the published literature and expert practice.
Results: The APPN Committee produced 3 brochures that enable patients and families to have access to concise written educational documents. These documents have also been translated into Spanish and Arabic and will be reviewed at 2-year intervals.
Conclusion: Using available literature and professional expertise from multiple institutions, centers can produce well-written and visually pleasing educational brochures. These brochures fill a gap in written literature available to pediatric PH patients and caregivers. Future plans include posting the brochures to the PPHNet Website for wider availability.

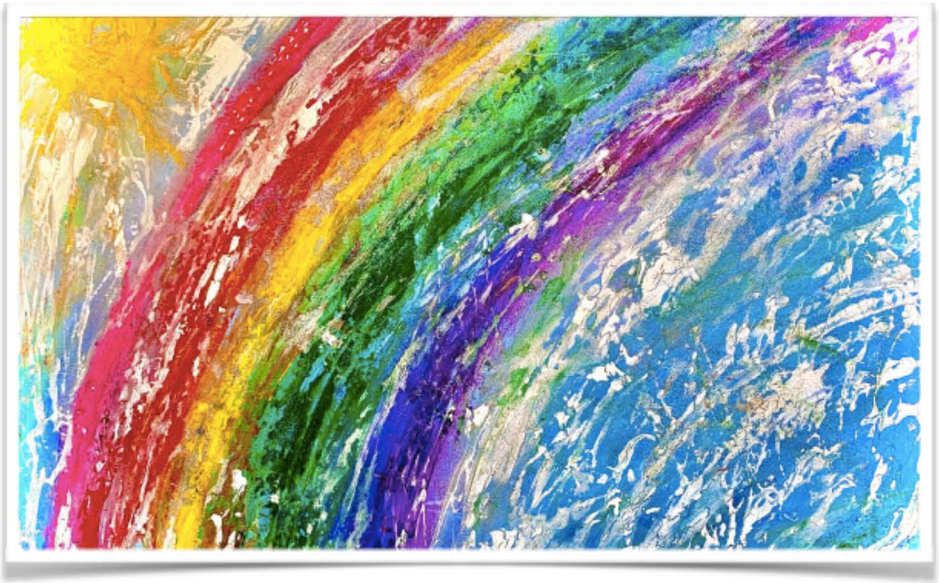
"SQ" Prostacyclin Therapy A guide for new medication starts

Bronchopulmonary Dysplasia & Pulmonary Hypertension: A Guide for Patients & Families.

"SQ" Prostacyclin Therapy

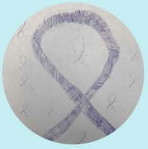
A guide for new medication starts

BY: ELISE WHALEN, NP, CLAIRE PARKER NP, ERIN ELY, RN, MELISSA MAGNESS, NP, & KATY TILLMAN, NP ON BEHALF OF PPHNET NURSING COMMITTEE



Pulmonary Hypertension
An overview of the disease, symptoms, & testing

Treatment options



Pain Management Strategies

Frequently Asked Questions: Things I Wish I knew

Pulmonary Hypertension: What is it?

An overview

Pulmonary hypertension (PH) is another name for high blood pressure in the lungs. It is a big word, but let's break it down. "Pulmonary" means lungs, and hypertension means "high blood pressure." The high blood pressure in the lungs occurs because the arteries narrow down causing higher blood pressures. This higher pressure in the lungs makes the right side of the heart work harder to push blood through the lungs. This extra work causes the heart to become less flexible and even get bigger over time.

SYMPTOMS

Symptoms may include being unable to perform exercise or do activities that are normal for age. Increased tiredness, shortness of breath, dizziness, upset stomach, decreased appetite, and swelling of the face hands, and feet are commonly seen.

TESTING

Your doctor may order an echocardiogram (ultrasound of the heart), chest x-ray, or MRI (pictures of the heart by a magnetic field and radio waves). They could order a cardiac catheterization. This procedure directly measures the pressures and flow in the heart.

Figure 1:

Bronchopulmonary Dysplasia & Pulmonary Hypertension: A Guide for Patients & Families

By: Melissa Magness, NP, Anna Brown, NP, Elizabeth Colglazier, NP, Alicia Grenolds, NP, Emma Jackson, NP, & Elise Whalen, NP on behalf of the PPHNet APP and Nursing Committee

Did you know?

- Between 10-60% of children with BPD develop PH.
- Echocardiography screening for PH is recommended for all infants with moderate to severe BPD at 36 weeks

What is bronchopulmonary dysplasia (BPD)?

Bronchopulmonary dysplasia (BPD) is a condition of halted lung development that is primarily seen in children born prematurely (typically born < 30 weeks gestation and birthweight < 2 pounds). BPD can range from mild to severe and can improve as the child grows. Some patients with BPD may need long-term oxygen therapy and breathing help from machines like ventilators, even after they go home.

What is pulmonary hypertension (PH)?

Some children with moderate to severe BPD may be diagnosed with PH which is high blood pressure in the lungs. In BPD, PH is caused by small or abnormal development of blood vessels in the lungs. High blood pressure in the lungs can put extra stress on the right side of the heart, which can affect its ability to pump blood well.

RISK FACTORS DURING PREGNANCY

- Preeclampsia
- Fetal Growth Restriction
- Infection
- Oligohydramnios (low/absent amniotic fluid)
- Genetic Conditions

RISK FACTORS AFTER BIRTH

- Prolonged mechanical ventilation
- Infection
- Hypoxemia
- Presence of cardiac shunts (abnormal connections in the heart)
- Aspiration (accidental breathing in of fluid into lungs)

Figure 2:

IMPROVING NURSING KNOWLEDGE AND SELF-EFFICACY WITH INTRAVENOUS PROSTACYCLIN ADMINISTRATION

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Category: Clinical Science
Subcategory: Therapeutic Strategies

Background: Management of intravenous (IV) prostacyclin administration in the inpatient setting introduces significant challenges. IV prostacyclins are high-risk, low-frequency medications that pose a significant risk to patient safety if used in error. A lack of standardized procedures and education related to the nursing administration of IV prostacyclins has led to a knowledge gap among nurses responsible for its infusion.
Methods: A convenience sample of registered nurses (N = 21) from a medical intensive care unit of a teaching hospital was used. The project used a 1-group presurvey and postsurvey design that compared nursing knowledge of IV prostacyclins and self-efficacy with IV administration. Satisfaction with the intervention was also assessed. The intervention was a 30-minute online module incorporating didactic and audiovisual modes of instruction. Optional teach-back sessions were also provided.
Results: The effectiveness of the educational intervention was statistically significant for improved nursing knowledge of IV prostacyclins ($P < 0.01$) and cognitive ($P < .001$) and psychomotor self-efficacy of IV prostacyclin administration ($P < 0.05$). Affective self-efficacy was not statistically significant. There were no significant differences in knowledge or all self-efficacy domains for participants who attended the optional teach-back session. Participants overwhelmingly reported satisfaction with its accessibility, appropriateness for level of experience, and improved knowledge from training.
Conclusion: The findings suggest that the implementation of an online educational module is an effective training strategy to improve nursing knowledge and self-efficacy with IV prostacyclin administration. Online didactic and audiovisual methods of instruction are an effective way to affect nursing knowledge and self-efficacy with IV medication management.

TRANSITION FROM TD300 INHALATION DEVICE TO DRY-POWDER INHALER FOR TREPROSTINIL ADMINISTRATION: COMPARING DOSING, TOLERABILITY, AND REASON FOR CONVERSION

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Category: Clinical Science
Subcategory: Therapeutic Strategies

Background: The objective was to evaluate tolerability, patient-reported adverse events, and reason for conversion in patients who used a TD300 inhalation device and then transitioned to a dry-powder inhaler (DPI) to administer inhaled treprostinil. The design is a retrospective, crossover comparison of patients on inhaled treprostinil who used the TD300 device for at least 12 months before converting to a DPI and used the inhaler for at least 6 months.
Methods: A review of the electronic medical records was conducted to evaluate patient maintenance dose postconversion, reported reason for conversion, and patient-reported adverse events related to patients using inhaled treprostinil for pulmonary arterial hypertension (PAH) treatment. Inclusion criteria included patients aged 18–89 and carried a diagnosis of either World Health Organization (WHO) Group 1 PAH or WHO Group 3 pulmonary hypertension (PH) associated with interstitial lung disease (ILD). Patients were included if they completed 12 months of therapy using a TD300 device followed by 6 months using a DPI. Patients started with inhaled treprostinil via TD300 inhalation after March 2, 2020, and the DPI after July 20, 2022. Exclusion criteria included any patient who displayed a gap in therapy at any point during the review period or who transitioned >1 time from a TD300 device to DPI or from a DPI to the TD300 device. Records were reviewed to interpret the reason for transition, dose equivalence on conversion to DPI, and patient-reported adverse events experienced on either inhalation device.
Results: The sample size of 32 patients reviewed showed that 91% (29/32) of patients initiated a conversion to DPI due to ease of use (78% [25/32] for convenience and 13 [4/32] due to desire for less complex regimen). Three patients (9% [3/32])

resulted in an unknown reason for transition. Twenty-one patients (66% [21/32]) were able to convert to an equivalent treprostinil dose and frequency using the DPI. Six patients (19% [6/32]) were able to achieve a higher dose upon transition, and 5 patients (15% [5/32]) achieved a lower maintenance dose. Side-effect data were collected for both inhalation devices for the first 6 months the patient was on service with each device. While on the TD300 device, the most common side effects (>10%) included cough, headache, increased shortness of breath, diarrhea, congestion, dizziness, hypotension, nausea, muscle/joint pain, upset stomach, and edema. Administration with a DPI resulted in side effects (>10%) aligning with those in the package insert, including cough, increased shortness of breath, congestion, and edema.

Conclusion: Conversion from a TD300 inhalation device to a DPI was well tolerated wmosty of patients achieving an equivalent dose of inhaled treprostinil. This coupled with the reported ease-of-use advantage of the DPI makes transitioning a viable option for patients treating PAH and PH-ILD with inhaled treprostinil.

TOLERABILITY OF TREPROSTINIL DRY-POWDERED INHALER IN PATIENTS WITH PULMONARY HYPERTENSION RELATED TO FIBROSING INTERSTITIAL LUNG DISEASE AT A LARGE RESPIRATORY REFERRAL CENTER

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Category: Clinical Science
Subcategory: Therapeutic Strategies

Background: Inhaled treprostinil is approved for pulmonary arterial hypertension (PAH) and pulmonary hypertension associated with interstitial lung disease (PH-ILD). A dry-powdered inhaler formulation (treprostinil DPI) was Food and Drug Administration approved in March 2022 for

Table 1: Patient Demographics

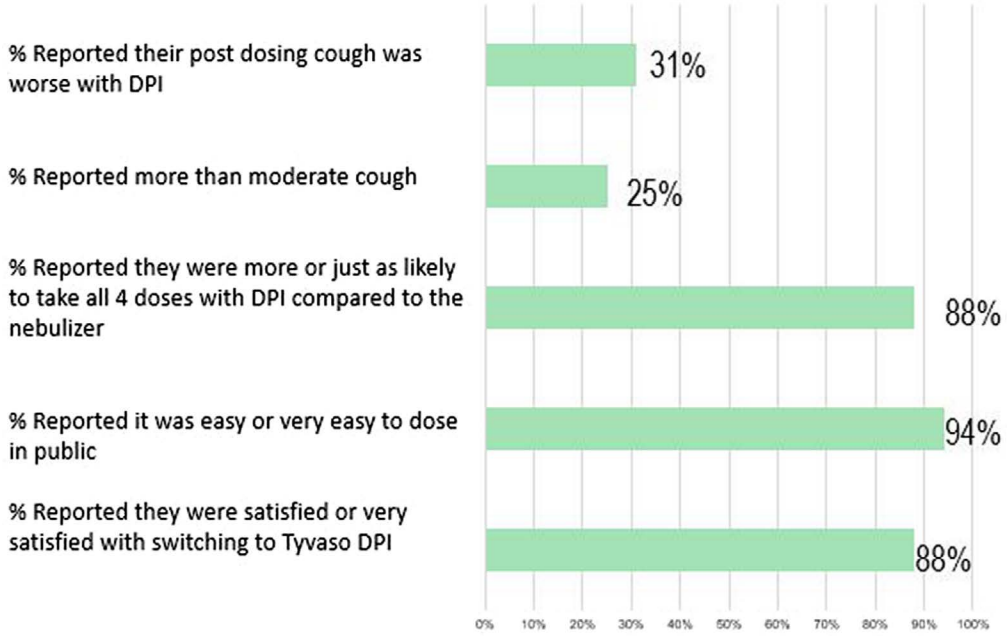
Number of patients	23
Age (years), median (range)	76 (49-82)
Sex	
Male	13
Female	10
ILD type	
CTD-ILD	12
IPF	4
CPFE	3
Chronic organizing pneumonia	1
Chronic HP	1
Granulomatous lymphatic ILD	1
LIP	1
Treprostinil neb dose (breaths), median (range)	12 (9-18)
Starting Tyvaso DPI dose (mcg), median (range)	64 (48-80)
Functional Class	
II	13
III	10
Pre-treprostinil PVR (WU), mean (SD)	5.29 (± 1.9)
FVC (% predicted), mean (SD)	73 (± 23)
DLCO (% predicted), mean (SD)	37 (± 16)
BNP (pg/mL), median (SD)	67.5 (155.9)
6 MWD (m), mean (SD)	299.81 (± 113.9)
Distance saturation product (DSP) – 6MWD x SpO2 nadir (m%), mean (SD)	255.5 (± 98.4)

Table 2: Pretransition and Posttransition Data

	Pre-Transition	Post-Transition
FVC (% predicted), mean (SD)	73 (± 23)	71 (± 23) 14
DLCO (% predicted), mean (SD), n*	37 (± 16)	42 (± 16) 13
BNP (pg/mL), median (CI)	67.5 (33.2-151.8)	84.4 (43.2-110.9) 14
6MWD (m), mean (SD)	299.8 (±113.9)	293.2 (± 113.2) 16
RVSP (mmHg), mean (SD)	47.91 (± 17.8) 21	54.57 (± 18.7) 14
TAPSE (cm), mean (SD)	2.17 (± 0.43)	2.16 (± 0.43) 13
DSP (m%)	255.5 (±98.4)	240.8 (± 96.9) 16
Change in 6MWD (m)		51.36 (±67) 16
Change in DSP (m%)		5.43 (± 58.3) 16

* n listed if < 23 (data collection ongoing)
Note: All pre-transition data were reported when patients were on nebulized treprostinil

Table 3: Patient Survey Data (n = 16)



patients with PAH or PH-ILD based on a recent clinical trial (BREEZE); however, the safety and tolerability of the DPI formulation was only evaluated in patients with PAH. Patients with PH-ILD were excluded in this study and only studied on inhaled nebulizer during the INCREASE trial. Tolerability of Tyvaso DPI has not been formally studied in patients with PH-ILD who possess altered breathing mechanics.

Methods: Upon commercial availability of treprostinil DPI, patients on nebulized treprostinil were given the option to switch during regular follow-up. Data on pretransition and posttransition 6-minute walking distance, brain natriuretic peptide, echocardiogram, hemodynamics, and spirometry were collected within 3–6 months of first use of the DPI. A patient-experience questionnaire was designed and administered to patients posttransition.

Results: Between July 2022 and April 2023, 23 patients with fibrosing ILD were transitioned from the nebulized form of inhaled treprostinil to DPI, with 4 patients planned for transition in the coming weeks. At baseline, patients were on a mean dose of 12 breaths 4 times daily and transitioned successfully to 64 mcg 4 times daily. No change in baseline PH-related therapy occurred during this transition. Table 1 summarizes the baseline characteristics of the patients that completed the transition. A survey answered by 7 patients at the time of submission indicated they were all *very satisfied* with the transition and that treprostinil DPI was well tolerated and was *very easy* to use. All patients reported a cough with treprostinil DPI that, when compared with treprostinil nebulizer, was better in 38% of patients, the same in 31%, and worse in 31%. Patients reported they were more (44%) or as likely (44%) to take all 4 doses of treprostinil DPI compared with the nebulized formulation. Only 12% of patients reported they were less likely to take a dose compared with the nebulizer. Five patients (21.7%) who were transitioned to the DPI discontinued taking it. Three of the 5 discontinued due to side effects and transitioned back to

Table 4: Patient Satisfaction and Symptom Survey

	Very dissatisfied, I regret the change 1	Dissatisfied 2	Neutral, neither satisfied nor dissatisfied 3	Satisfied 4	Very Satisfied, I am glad I made the change 5
1. How satisfied are you with making the change from nebulizer to DPI? Please choose on a scale of 1 - 5.	○	○	○	○	○
	Very Difficult - so difficult that I don't use it outside of my home 1	Difficult - hard to use it when I leave home 2	Moderately challenging - I have to plan around taking the medication when outside my home 3	Easy - it is not a problem 4	Very Easy - I can take it outside of the home without concerns. 5
How easy is it to use Tyvaso DPI in public? Please choose on a scale of 0 - 5.	○	○	○	○	○
Are you more likely to take all 4 doses per day with Tyvaso DPI than with Tyvaso nebulizer?	○ Yes, more likely to take all 4 doses with DPI than with nebulizer ○ Same, just as likely to take all 4 doses with DPI as with nebulizer ○ No, less likely to take all 4 doses with DPI than with nebulizer				
	I always missed a dose 1	I almost always missed a dose 2	50% of the days I took 4 doses 3	I almost never missed a dose 4	I never missed a dose 5
On a scale of 1-5, how often were you taking all 4 doses with Tyvaso nebulizer each day (before switching to DPI)?	○	○	○	○	○
	No cough 1	Almost no cough 2	Some cough 3	A lot of cough 4	Severe cough 5
Are you coughing after taking DPI?	○	○	○	○	○
Is your post-treatment cough changed since the change from Tyvaso nebulizer to DPI?	○ It's better ○ It's the same ○ It's worse				

the nebulizer. Two discontinued completely, 1 due to lung transplant and the other due to hypotension (Tables 2–4). **Conclusion:** In this analysis of patients with PH-ILD, transition from nebulized treprostinil to DPI was well tolerated. Most patients preferred the DPI formulation. More data need to become available regarding long-term safety and tolerability in a larger cohort. Data collection is ongoing.

STUDY DESIGN OF THE DECENTRALIZED, PATIENT-CENTRIC EVOLVE STUDY EVALUATING REAL-WORLD USE OF NEXT GENERATION INFUSION PUMPS TO DELIVER PARENTERAL TREPROSTINIL IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION

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Category: Clinical Science
Subcategory: Databases and Registries

Background: With recent Food and Drug Administration guidance and advocacy groups encouraging more patient-focused drug development and incorporation of the patient voice, there has been a shift from traditional clinical trials to those collecting direct patient feedback, or patient-centric trials. This is especially important in rare diseases, such as pulmonary arterial hypertension (PAH). In combination with advancing digital health technologies, therein lies an opportunity for a virtual trial directly engaging with patients and reducing patient burden for participation. Parenteral treprostinil is indicated for the treatment of PAH and available via continuous intravenous or subcutaneous (SC) infusion delivered by an external infusion pump. For almost 20 years, 1 pump has been available to patients in the US for the delivery of SC treprostinil, highlighting a need for newer, next-generation infusion pumps to improve patient experience. One such pump, the Remunity® Pump for Remodulin (treprostinil) injection, has been specifically developed to be used by patients with PAH; however, there is a need for data on its real-world use.
Methods: The EVOLVE (NCT05060315) study is a virtual, observational, patient-centric study to evaluate the real-world use of Remunity, following approximately 60 patients for up to 8 weeks after beginning use of their next-generation infusion pump and consists of remote and electronic assessments completed by patients via a mobile application. Two cohorts of patients will be enrolled: 1 cohort new to parenteral prostacyclin-class therapy and 1 cohort currently receiving SC treprostinil via another infusion pump (ie, previous generation infusion pump) and transitioning to a next-generation infusion pump. The primary objective is to observe and assess drug administration activities, time spent on drug administration activities, and patient-reported outcomes, including quality of life, treatment satisfaction, and patient perception of devices. The secondary objectives are to assess infusion site pain/reaction relief strategies/medications in patients receiving SC treprostinil and collect information related to the dosing of SC treprostinil. Specifically, in those transitioning from a previous-generation infusion pump, secondary objectives are to observe transition mechanics from previous-generation to next-generation infusion pumps and to compare patient perception, treatment satisfaction, and time spent on drug administration activities with next-generation to previous-generation pumps to administer SC treprostinil, where available.
Results: This study is currently open to enrollment. Results forthcoming.
Conclusion: Conclusions forthcoming.

INTEGRATION OF REVEAL LITE 2 RISK CALCULATOR INTO EPIC

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Category: Basic Science
Subcategory: Therapeutic Strategies

Background: Current best-practice guidelines for pulmonary hypertension (PH) treatment recommends patients receive an objective risk assessment at time of diagnosis and at routine intervals to evaluate disease progression. PH risk calculator tools have been proven useful in enabling clinicians to predict clinical outcomes and escalate treatment as needed. We recognized the need to integrate a formal PH risk assessment tool into the electronic health record at our institution.
Methods: We chose to integrate the REVEAL Lite 2 Risk Calculator based on ease of use, streamlined noninvasive scoring criteria, and proven ability to predict long-term outcomes and detect response to treatment. We collaborated with our EPIC analyst to design a REVEAL Lite 2 Calculator prototype which we applied to our EPIC system. Aspects of the calculator were modified and revised as needed until we achieved a working embedded calculator. A smart phrase was then created to allow for efficient addition of the risk calculator to medical doctor progress note.
Results: We successfully integrated a fully operational REVEAL Lite 2 Risk Calculator into our EPIC system. The addition of this formal risk assessment tool has proven to be an invaluable enhancement to our clinical workflow. We now have a validated PH risk stratification tool allowing rapid performance of a PH risk assessment.

Conclusion: The integration of a formal PH risk assessment tool into the electronic record allows for initial and longitudinal risk assessment for PH patients. Embedding PH risk assessment tools into EPIC has a positive effect on clinical workflow by allowing for enhanced data-driven clinical decision making in a rapid fashion and ultimately optimizing patient care. The PH risk assessment tool has become an additional vital sign.

SUCCESSFUL TRANSITIONS FROM ORAL TREPROSTINIL TO SELEXIPAG IN 2 PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION IN A RURAL CARE SETTING: CASE SERIES

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Category: Case Report
Subcategory: Therapeutic Strategies

Background: Oral prostacyclin agents have been the standard therapy for pulmonary arterial hypertension (PAH) in addition to nitric oxide pathway agents and endothelin receptor antagonists. Currently, oral treprostinil and selexipag are available as oral synthetic prostanoid agents. However, oral treprostinil may cause severe uncontrolled headaches and diarrhea, and transitions to selexipag are considered to mitigate these adverse effects. However, limited evidence exists regarding how to down-titrate oral treprostinil and up-titrate selexipag without rebound effects.
Methods: We present 2 PAH patients who successfully transitioned from oral treprostinil to selexipag. Due to the limited literature for this transition, the transition schedule was made based on the estimated dose equivalence between parenteral and oral treprostinil products and the approximate conversion ratio between parenteral treprostinil and selexipag.
Results: Patient 1 is a 58-year-old female with a history of idiopathic pulmonary hypertension (PH) who was electively admitted to the hospital for the transition from oral treprostinil to selexipag due to abdominal pain and intolerance to higher doses of oral treprostinil. The patient had World Health Organization (WHO) Functional Class 2 symptoms, and the baseline 6-minute walk distance (6MWD) was 273 m. Her PAH medication regimen included riociguat 0.5 mg 3 times daily, ambrisentan 10 mg once daily, and oral treprostinil 8.5 mg twice daily. The patient was successfully transitioned to selexipag 1000 mcg twice daily over 8 days during the hospitalization and discharged. At outpatient, selexipag was further titrated up to 1600 mcg twice daily over 2 months after discharge. Her symptoms and 6MWD were stable at 274 m, and there was no evidence of clinical decline. Her adverse effects were also significantly improved after the transition to selexipag. She remained a WHO Functional Class 2. Patient 2 is a 48-year-old female with a history of PAH who experienced severe migraine headaches and diarrhea due to oral treprostinil. Her PAH medication regimen was sildenafil 20 mg 3 times daily and oral treprostinil 3.5 mg 3 times daily. The patient developed severe lower extremity edema due to macitentan. Her baseline 6MWD was 285 m and WHO Functional Class 3. Due to her significant adverse effects of the previous regimen and relatively current stable course, her oral treprostinil was transitioned to selexipag at an outpatient setting over 2 months without clinically significant deterioration. She experienced minor headaches, nausea, and diarrhea during the transition, but her migraine and diarrhea significantly improved.
Conclusion: Two patients with PAH were successfully transitioned from oral treprostinil to selexipag without clinically significant deterioration. Our 2 patient cases demonstrated practical titration examples in both inpatient and outpatient settings. Further details in the transition schedule and clinical course will be discussed in the poster presentation.

THE PITFALLS OF SPECIFIC THERAPY IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION ASSOCIATED WITH CONGENITAL HEART DEFECTS

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Category: Clinical Science
Subcategory: Therapeutic Strategies

Background: Pulmonary arterial hypertension (PAH) in patients with Eisenmenger syndrome (ES) and PAH after defect closure is included in the clinical classification of PAH associated with congenital heart defects (PAH-CHD).
Methods: There were 42 patients: 25 patients with PAH-CHD and ES and 17 patients with PAH after defect closure evaluated in our pulmonary hypertension center according to the data of Russian National Registry of Patients With Pulmonary Arterial Hypertension (NCT03707561). Patients were followed for 24 months.
Results: The duration of PAH therapy in patients with PAH-CHD is estimated at 3.0 (2.0, 5.0) years. There were no

differences in groups in the duration of therapy. In assessing the duration of specific therapy with various drugs by 24 months, it was found that the duration of sildenafil therapy was 3.5 (2.0, 5.0) years in the group with ES and 3.0 (2.0, 5.0) years in patients with PAH after defect closure. The duration of bosentan therapy was 4.0 (2.0, 5.0) years and 3.0 (2.0, 7.0) years, respectively. The duration of macitentan therapy was 1.0 (1.0, 1.0) years and 1.0 (1.0, 1.0) years, respectively. The duration of riociguat therapy was 1.0 (1.0, 1.5) years and 2.0 (2.0, 2.0) years, respectively. Duration of therapy with iloprost was 1.5 (1.0, 2.0) years and 2.5 (1.0, 5.0) years, respectively. During analyzing the changes in PAH therapy for 2 years, it was found that, in the group with ES (n = 25), by the 24th month, 52% of patients received combined specific therapy. In patients with PAH after defect closure (n = 17), by the second year of follow-up, combination therapy occurred in 67% of patients, which indicates the illness severity in this group.
Conclusion: Our data suggest that adults with PAH after defect closure have a more severe course of the disease that requires combination therapy.

STREAMLINING CLINICAL TRIAL RECRUITMENT WITH AUTOMATED PRESCREENING WORKFLOWS: A SOLUTION TO OVERCOMING RESOURCE CONSTRAINTS

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Category: Clinical Science
Subcategory: Diagnosis/Screening and Physiologic Studies

Background: Clinical trial recruitment significantly affects the success of clinical trials, with prescreening constituting a crucial step in identifying potentially eligible patients. However, constraints such as inadequate staffing and insufficient time for comprehensive prescreening due to personnel stretched thin across multiple responsibilities often pose substantial barriers to patient recruitment.
Methods: To address this, we designed an automated screening workflow using widely accessible Microsoft Office tools. Our strategy employs electronic surveys which feed data into datasheets that automatically prescreen patients and indicate their general eligibility for specific studies based on their requirements.
Results: Applying these automated workflows showed promising results by significantly reducing the staff time spent in the prescreening process. It eliminated the need to repeatedly review patient records to assess eligibility criteria for multiple studies, allowing for a more efficient approach to patient recruitment.
Conclusion: Automated prescreening workflows can expedite the patient referral process, potentially accelerating recruitment into clinical trials. This approach offers a feasible solution to mitigate the challenges presented by resource constraints in the prescreening phase of clinical trial recruitment. Additionally, it allows an easy method for physicians to refer patients to a study site for potential participation in active trials as well as for a wider pool of potential patients to be screened in the same timeframe. Our experience with automation of prescreening underscores the potential of digital tools to improve the efficiency and effectiveness of recruitment in clinical trials, thus further diversifying our participant pool.

SERALUTINIB FOR THE TREATMENT OF PULMONARY ARTERIAL HYPERTENSION: RESULTS FROM THE PHASE 2 TORREY TRIAL

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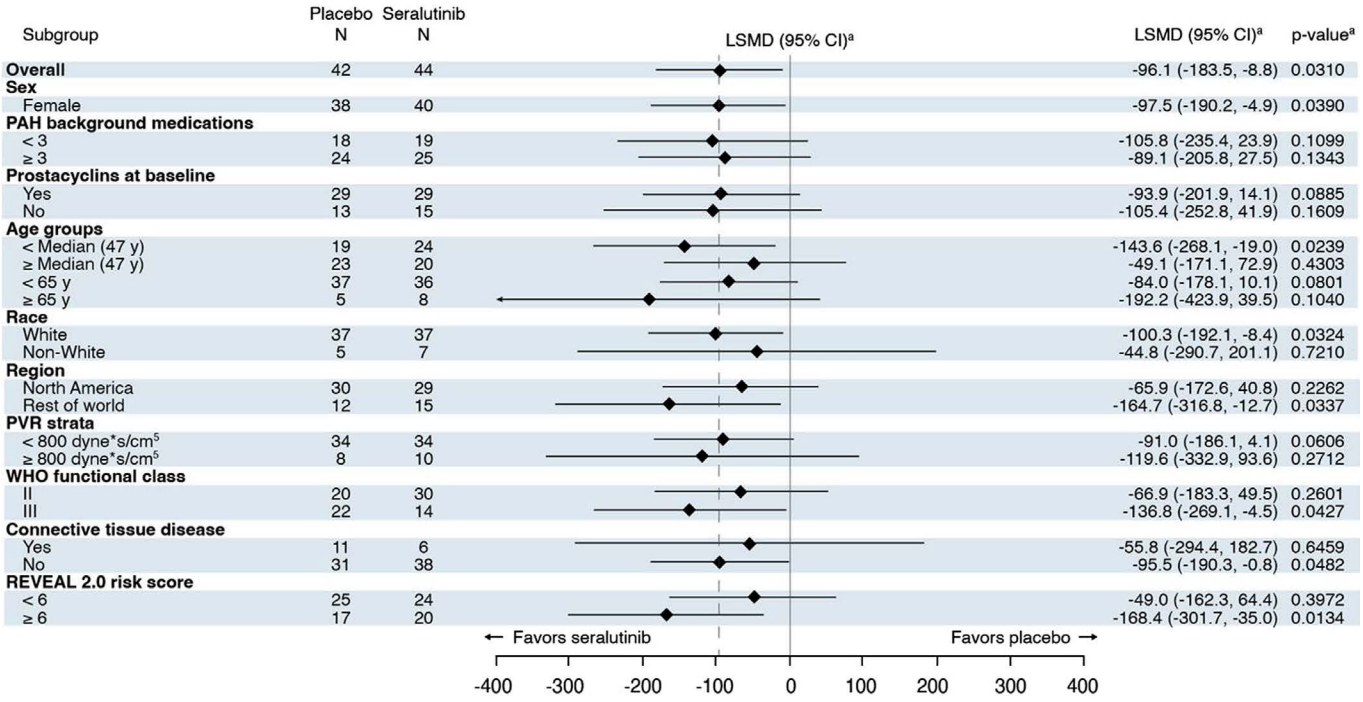
Category: Clinical Science
Subcategory: Therapeutic Strategies

Background: PDGFR, CSF1R, and c-KIT kinase pathways play key roles in the inflammation, proliferation, and fibrosis that drive pulmonary arterial vascular remodeling in pulmonary arterial hypertension (PAH). Seralutinib is a novel, potent kinase inhibitor designed for dry powder inhalation to reach the deep lung and target these dysfunctional pathways.
Methods: TORREY, a Phase 2, randomized, double-blind, placebo-controlled, multicenter study, evaluated the efficacy and safety of inhaled seralutinib in PAH over 24 weeks. Eligible subjects (World Health Organization [WHO] Group 1 pulmonary hypertension [PH], Functional Class [FC] II or III) on standard background therapy were randomized 1:1 to seralutinib 90 mg or placebo by dry powder inhaler twice daily. The primary endpoint was change from baseline to Week 24 in pulmonary vascular resistance (PVR) by right heart catheterization. Secondary and exploratory endpoints included change in 6-minute walk distance (6MWD) and NT-proBNP. Safety was assessed during scheduled visits.
Results: Eighty-six subjects were randomized to treatment (seralutinib, n = 44; placebo, n = 42) at 40 sites worldwide; 80 subjects completed the study. Seralutinib and placebo groups were balanced except for WHO FC: seralutinib, 68%/32% FC II/III; placebo, 48%/52% FC II/III. At baseline, most subjects (96.5%) received ≥2 PAH medications; 44.2% were receiving parenteral prostacyclin. At Week 24, PVR was significantly decreased by seralutinib, with a placebo-corrected reduction of 14.3% (95% CI = –183.5, –8.8; $P = 0.0310$). Among FC



[a] Based on an ANCOVA model with multiple imputation. ANCOVA, analysis of covariance; LSMD, least squares mean difference; PAH, pulmonary arterial hypertension; PVR, pulmonary vascular resistance; REVEAL, Registry to Evaluate Early and Long-Term PAH Disease Management; WHO, World Health Organization.

Figure 1: Prespecified subgroup analysis demonstrated consistent benefit of seralutinib on pulmonary vascular resistance (PVR) across subgoups.

III subjects, the effect on PVR was more pronounced, with a placebo-corrected reduction of 20.8% (95% CI = –269.1, –4.5; $P = 0.0427$). Prespecified subgroup analyses demonstrated a strong concordance of benefit across seralutinib-treated subgroups (Figure 1). Reductions in NT-proBNP were significant at Weeks 12 (LSMD[SE]: –309.6[119.76]; $P = 0.0116$) and 24 (LSMD[SE]: –408.3[120.86]; $P = 0.0012$). 6MWD improved directionally overall (+6.5 m, P = NS) and significantly in FC III subjects (+37.3 m, $P = 0.0476$). At Week 24, worsening to FC IV was observed in 3 placebo-treated subjects and no seralutinib-treated subjects. The most common adverse event in the seralutinib group was mild-moderate cough (43.2% versus 38.1% for placebo).

Conclusion: The TORREY study met its primary endpoint by demonstrating a significant reduction in PVR in the seralutinib group. This is the first clinical trial to show a reduction in PVR by a novel inhaled PDGFR, CSF1R, and c-KIT kinase inhibitor in PAH. Prespecified subgroup analyses showed strong concordance of seralutinib benefit. The reduction in PVR is meaningful in the context of the associated reduction in NT-proBNP. Inhaled seralutinib was well tolerated in this study population. Based on these results, a Phase 3 study is planned. RPF, VVM contributed equally to this work. This abstract was previously presented at the ATS 2023 International Conference (Frantz RP et al. Am J Respir Crit Care Med. 2023;207:A6726).

EFFECTS OF INHALED SERALUTINIB ON RIGHT VENTRICULAR-PULMONARY ARTERIAL COUPLING AND RIGHT HEART FUNCTION IN PULMONARY ARTERIAL HYPERTENSION

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Category: Clinical Science
Subcategory: Therapeutic Strategies

Background: Impaired right ventricular-pulmonary arterial (RV-PA) coupling portends a poor prognosis in pulmonary arterial hypertension (PAH), and right ventricular free wall strain/systolic pulmonary artery pressure (RVFWS/sPAP) has been reported as a measure of RV-PA coupling. Furthermore, increased RVFWS and right atrial area (RAA) as well as decreased pulmonary artery compliance (PAC) are associated with increased mortality risk in PAH. Seralutinib is a novel, small-molecule kinase inhibitor that targets PDGFR, CSF1R, and c-KIT administered via dry powder inhaler. TORREY, a Phase 2, double-blind, randomized, placebo-controlled study of inhaled seralutinib in patients with PAH (NCT04456998) met its primary endpoint, demonstrating a significant reduction in pulmonary vascular resistance (PVR) from baseline (BL) to Week 24 compared with placebo. In addition, seralutinib significantly decreased NT-proBNP.
Methods: Eighty-six patients with World Health Organization (WHO) Group 1 pulmonary hypertension (PH; Functional Class II, III), ages ≥ 18 years, PVR ≥ 400 dyne·s/cm^5, and on stable PAH standard-of-care therapy (the majority of whom were on double and triple therapy with approved PAH medications) were enrolled. Right heart catheterization (RHC) and full echocardiography were performed at BL and Week 24 and at BL, Week 12, and Week 24, respectively; both were analyzed in a blinded central laboratory. To calculate RVFWS/sPAP, the sPAP from RHC was used. PAC was calculated from RHC data with the formula (SV/[PAS – PAD]). Statistical analysis was performed using analysis of covariance (ANCOVA).
Results: At Week 24, the change in RVFWS/sPAP was lower in the seralutinib group than placebo (Table 1). The changes in RVFWS and RAA were lower in the seralutinib group versus placebo at Weeks 12 and 24 (Table 1). Change

Table 1: Echocardiography Changes From Baseline at Weeks 12 and 24

Week 12

Parameter	Placebo		Seralutinib			
	n	LS Mean Change ± SE	n	LS Mean Change ± SE	LS Mean Difference (SE)	p-value
RAA (cm^2)	40	3.36 ± 0.808	38	1.24 ± 0.831	-2.12 (1.037)	0.0442
RVFWS (%)	39	3.39 ± 0.965	40	0.09 ± 0.938	-3.3 (1.201)	0.0076

Week 24

Parameter	Placebo		Seralutinib			
	n	LS Mean Change ± SE	n	LS Mean Change ± SE	LS Mean Difference (SE)	p-value
RAA (cm^2)	41	3.36 ± 0.693	36	1.36 ± 0.725	-1.99 (0.897)	0.0293
RVFWS (%)	41	3.74 ± 0.985	37	1.11 ± 1.005	-2.62 (1.240)	0.0377
RVFWS/sPAP	41	0.054 ± 0.016	35	0.002 ± 0.017	-0.051 (0.020)	0.0123

LS, least squares; RAA, right atrial area; RVFWS, right ventricular free wall strain; sPAP, systolic pulmonary arterial pressure; all p values are nominal.

in NT-proBNP correlated with change in RAA ($r = 0.43$). At Week 24, change in PAC was greater in the seralutinib group (–0.02 ± 0.085 placebo, 0.19 ± 0.089 seralutinib; LSMD: 0.22 [0.104]; $P = 0.04$). There was no effect of seralutinib on left ventricular ejection fraction.

Conclusion: Treatment with seralutinib was associated with a significant reduction of RVFWS/sPAP. In addition, significant differences in RVFWS itself, RAA, and PAC were observed. These treatment effects support improved RV-PA coupling and right heart function. In conjunction with concordant reductions in PVR and NT-proBNP, these data suggest potential favorable effects of seralutinib in PAH. Seralutinib is in clinical development as a potential new treatment option for patients with PAH.

This abstract was previously presented at the ESC Congress 2023 (Frantz RP et al. Eur Heart J. 2023;44(suppl).

SERALUTINIB IMPROVES PULMONARY ARTERIAL BLOOD VESSEL VOLUME DISTRIBUTION IN PULMONARY ARTERIAL HYPERTENSION: RESULTS OF THE TORREY PHASE 2 IMAGING SUBSTUDY

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Category: Clinical Science
Subcategory: Therapeutic Strategies

Background: Seralutinib, a novel, inhaled kinase inhibitor with anti-inflammatory and antiproliferative effects, met the primary endpoint of reduction in pulmonary vascular resistance in the Phase 2 TORREY trial in pulmonary arterial hypertension (PAH; NCT04456998) and has the potential to treat pulmonary vascular remodeling. This abnormal remodeling includes distal pruning and proximal pulmonary arterial dilation. Quantitative analysis of these features is possible with computed tomography (CT) imaging.
Methods: The TORREY CT substudy used thin-section, volumetric noncontrast chest CTs followed by automated pulmonary vascular segmentation to evaluate the reverse remodeling potential of seralutinib. Baseline and Week 24 blood vessel volumes (BVVs) were determined at distinct levels defined by vessel cross-sectional area (CSA) in 19 subjects on a background of 2–3 approved PAH therapies. BVVs of pulmonary arteries with a CSA < 5 mm^2 (BV5A) and > 10 mm^2 (BV10A) were calculated. The BV5A to BV10A ratio (BV510ARATIO) was used to express relative redistribution of pulmonary arterial BVV. Linear regression was used to model the treatment effect.
Results: The BV510ARATIO increased from baseline to Week 24 in the seralutinib group (n = 7) versus placebo (n = 12; $P = 0.028$), and BV510ARATIO changes correlated with changes in stroke volume ($R = 0.65$, $P = 0.0033$) and pulmonary artery compliance ($R = 0.56$, $P = 0.016$).
Conclusion: In heavily treated PAH subjects, adding seralutinib for 24 weeks led to a significant redistribution of pulmonary arterial BVV to smaller vessels. These data visualize and quantify seralutinib's treatment effect on the pulmonary arterial vasculature in PAH.

CASE SERIES—PARTIAL ANOMALOUS PULMONARY VENOUS CONNECTIONS

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Category: Case Report
Subcategory: Pediatrics

Background: Partial anomalous pulmonary venous connections (PAPVCs) are rare congenital anomalies in which some of the pulmonary veins are erroneously connected to the right atrium rather than the left. Scimitar syndrome (SS) is a specific type of PAPVC in which the anomalous connection is typically to the inferior vena cava and is additionally associated with atrial septal defects and hypoplasia of the right lung and pulmonary artery. There are 2 forms: a more severe infantile form and a milder adult form, which will be discussed in this case study. The adult form is often asymptomatic and is rarely severe enough to require surgical correction. Here, we present a case of adult SS and PAPVC severe enough to lead to pulmonary hypertension and right-sided congestive heart failure.
Methods: The patient is a 41-year-old female who presented for evaluation for shortness of breath along with some swelling in lower extremities. Patient had prior history of smoking and methamphetamine usage. She had elevated d-dimer at 687 so had computed tomography scan of chest with contrast to rule out pulmonary embolism (PE), which was negative for PE but showed abnormal pulmonary venous return with enlarged right ventricle. Patient underwent right heart catheterization (RHC), which revealed severe precapillary pulmonary hypertension secondary to anomalous pulmonary venous return. Her echocardiogram revealed a right ventricular systolic pressure of 90 mmHg, severely dilated right atrium, and ventricle with systolic flattening of interventricular septum and severe tricuspid regurgitation. The patient was started on oral dual combination therapy and was set to be evaluated at a tertiary care center for

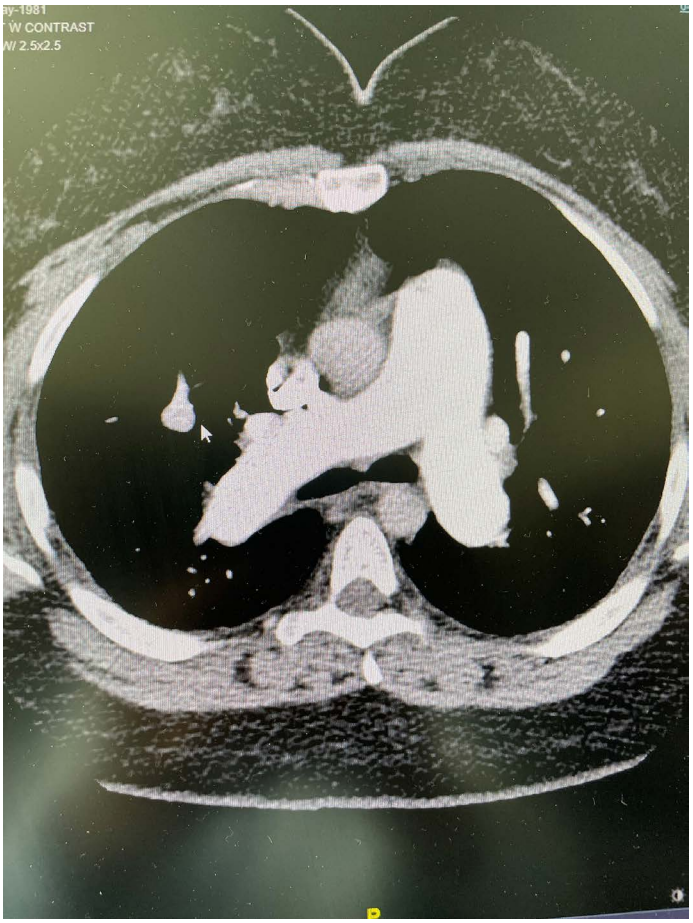

Figure 1: Partial anomalous pulmonary venous return (PAPVR) computed tomography (CT) chest.

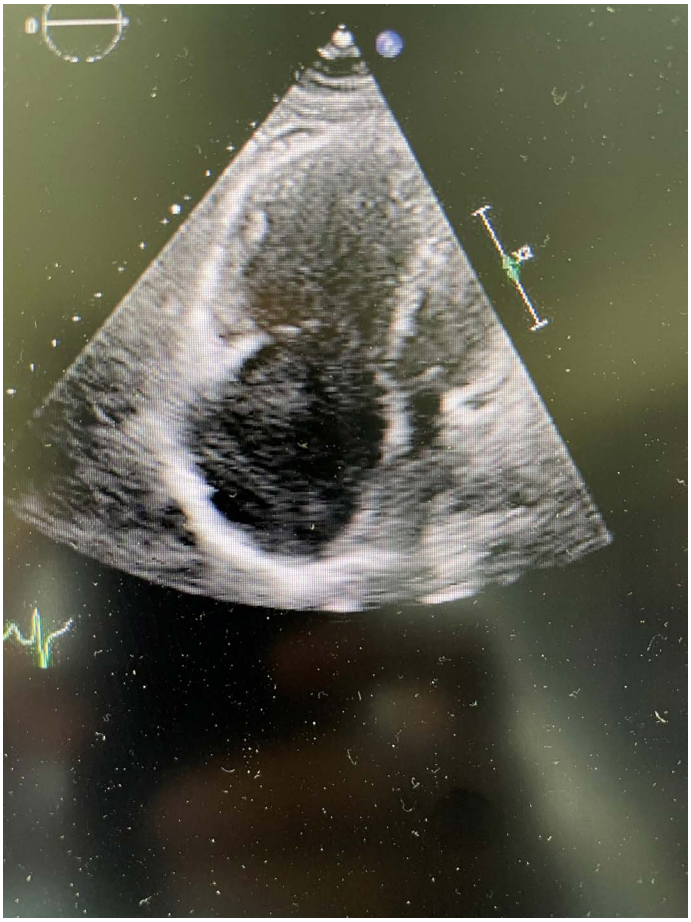

Figure 2: Partial anomalous pulmonary venous return (PAPVR) echocardiogram (ECHO).

evaluation of the shunt. Due to poor compliance, she failed to follow up and represented with much worsening symptoms in 14 months also including skin rash. She was additionally evaluated by dermatology for a chronic history of livedo vasculopathy with poorly healing ulcerations. On arrival, she was noted to have diffuse livedo reticularis and multiple areas of ulcers with necrosis across the extremities, worse in the lower limbs. Autoimmune and oncologic workups were negative, and ulcers were thought to be due to a combination of poor perfusion leading to necrosis and chronic methamphetamine use with associated skin changes. Biopsies demonstrated erosion of the skin with underlying superficial vascular ectasia and fat necrosis. The patient due to worsening hemodynamics was started on parenteral prostacyclin therapy. She was transferred to the Medical University of South Carolina for management and surgical evaluation. She underwent another RHC which demonstrated precapillary pulmonary hypertension with mean pulmonary artery pressures of 46 mmHg, transpulmonary gradient 27 mmHg, diastolic pressure gradient 14 mmHg, and pulmonary vascular resistance of 3.47 Wood units. It also

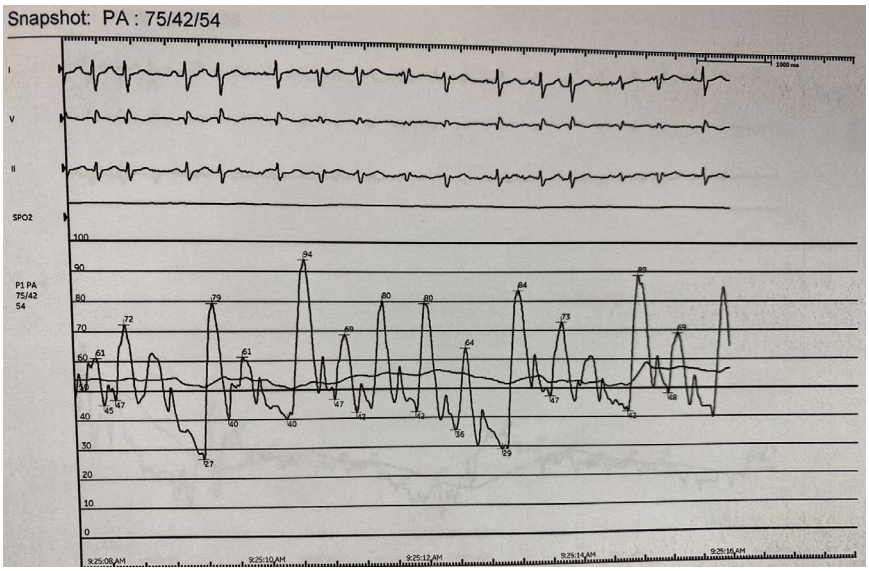

Figure 3: Partial anomalous pulmonary venous return (PAPVR) right heart catheterization (RHC).

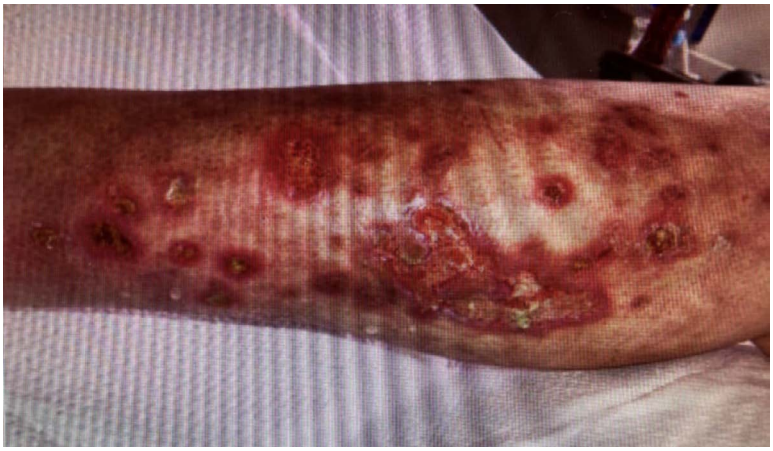

Figure 4: Partial anomalous pulmonary venous return (PAPVR) skin.

revealed a low pulmonary artery pulsatility index of 1.44, indicating poor right ventricular function. Due to her chronic and severe pulmonary hypertension, she is currently a poor candidate for surgical correction because of the increased likelihood of poor outcomes postoperatively and is maintained on triple pulmonary vasodilator therapy.

Results: SS is an extremely rare congenital anomaly, estimated to only occur in 2 in every 100000 births. The condition has been described in autopsies since 1836 and was not found in a live patient until 1949. Though the exact mechanisms are not yet fully understood, it is thought that the syndrome occurs from a persistence of embryologic vasculature and a failure of right pulmonary artery development. There are 2 main anomalies seen in SS: 1 in which both the right upper and lower pulmonary veins drain into the inferior vena cava (IVC) and 1 in which there is partial or complete right lower pulmonary vein draining to the IVC. The latter form was seen in this patient along with symptoms typical of a more severe presentation: fatigue, exertional dyspnea, and pulmonary hypertension. These symptoms are more often seen in the more severe infantile form but can be found in adults with SS, especially if other congenital cardiorespiratory anomalies are present. In this patient though, there were no other anomalies; the extensive history of smoking methamphetamine and tobacco likely exacerbated her condition and led to her decline. In adults, medical intervention is preferred, and surgery is generally reserved for severely symptomatic patients or patients with a Q_P/Q_S ratio >1.5, which would indicate significant shunting. The patient's ratio was 1.7. There are 2 main pathways for surgical SS correction: either resecting the part of the lung connected to the anomalous vein or rerouting flow of the anomalous vein to the left atrium; any other defects would need to be repaired as well. Several procedures can be used depending on the extent of aberrant circulation and lung hypoplasia. However, all procedures carry a high risk of thrombosis due to the low-velocity flow in venous circulation. The skin findings in this patient could be a unique manifestation of chronic cardiopulmonary disease. Plexiform lesions can be seen in patients with severe pulmonary hypertension but are typically found in lung tissue when samples are available. However, the pathology demonstrated is remarkably like that seen in this patient's biopsies, especially the vessel dilation and thickening. Additionally, the necrosis and poor healing could indicate decreased perfusion and even thrombi from the lungs due to the widespread and chronic pulmonary endothelial inflammation (Figures 1–4).

Conclusion: Though rare, it may be useful to consider the diagnosis of partial anomalous pulmonary venous return and SS in patients with pulmonary hypertension of unknown etiology, especially if severe and with cyanosis at presentation. Surgical correction is possible, and patients should be evaluated rapidly in addition to receiving appropriate medical treatment. While the adult form is rare, finding this underlying condition and altering the patient's care as needed could help prevent future health deterioration and heart failure.

PRACTICES AFFECTING MACITENTAN AND SELEXIPAG PATIENT PERSISTENCE RATES USING PULMONARY ARTERIAL HYPERTENSION CLINICAL SITE AND PATIENT PERSPECTIVES: A US QUALITATIVE RESEARCH ANALYSIS (PERSIST)

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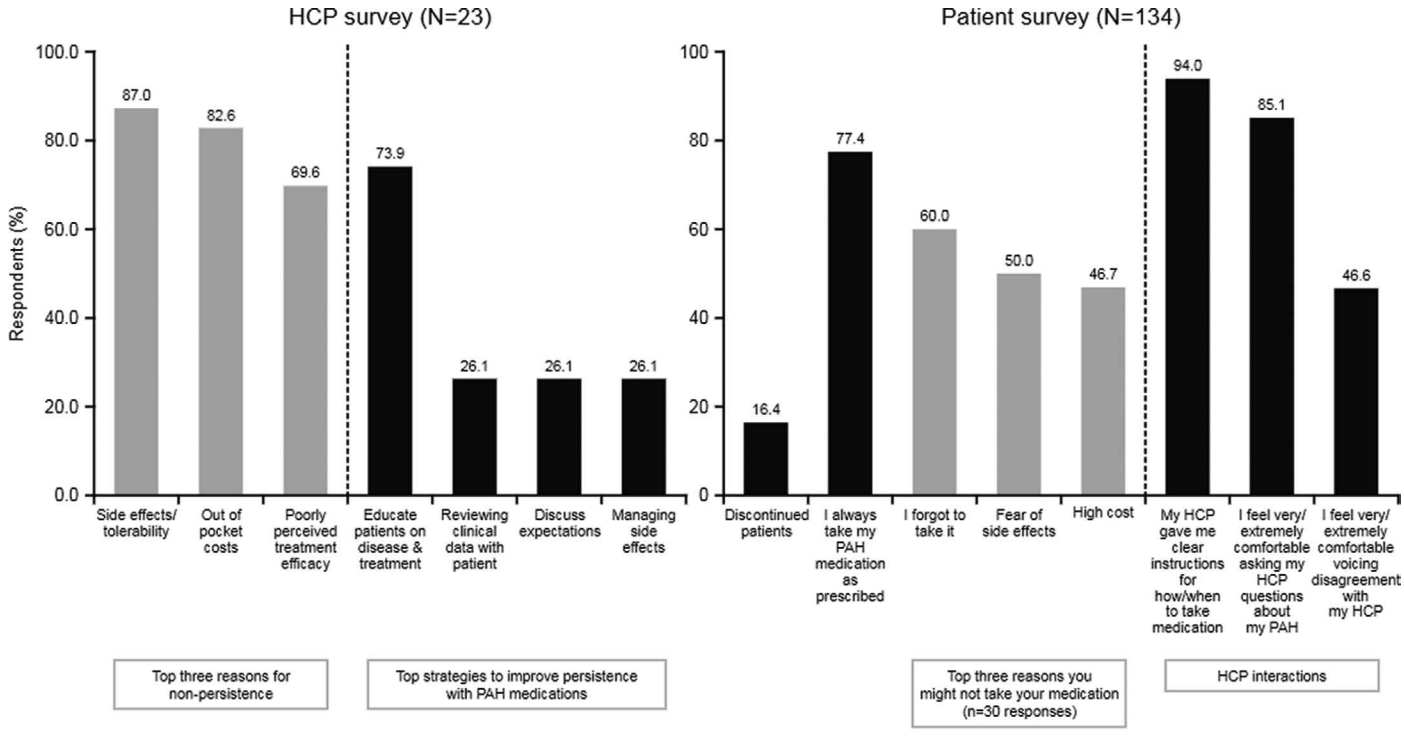
Category: Clinical Science
Subcategory: Diseases and Conditions Associated with PH

Background: Macitentan and selexipag reduce the risks of disease progression and hospitalization for patients with pulmonary arterial hypertension (PAH). Medication

persistence is important for optimizing patient outcomes but may be suboptimal in PAH. PERSIST (Protocol AC-055-513), a cross-sectional US real-world study, aimed to explore factors affecting macitentan and selexipag persistence.
Methods: PERSIST captured health care professional (HCP) and patient perspectives (November 2019 to August 2022) using a 1-time interview (HCPs) or survey (patients). HCPs were recruited from sites with high and low specialty pharmacy shipment rates during a recent 12-month period and ≥8 selexipag or ≥10 macitentan patient exposures. PAH patients self-reporting macitentan and/or selexipag use over the last 12 months were eligible. Persistent users had received macitentan for ≥3 months or stable selexipag dose for ≥1 month (without interruption >30 days), and discontinued users had stopped medication for >30 consecutive days during the last 12 months.
Results: HCPs surveyed (N = 23) perceived the most common reasons for nonpersistence to be side effects/tolerability (87% responses), treatment cost (83%), and perceived insufficient efficacy (70%). Strategies to improve persistence included educating patients about PAH and its treatment (74%), reviewing objective data (assessments, tests) with patients (26%), discussing expectations at first visit (26%), and managing side effects (26%). At low medication shipment rate sites, there was disconnect between HCP perception of persistence (86%) versus ≤40% medication shipment. Patients (N = 134) included 78 macitentan users (71 persistent; 7 discontinued) and 56 selexipag users (41 persistent; 15 discontinued). Based on patient responses, the most common reason for not taking medication as prescribed was forgetfulness in persistent patients (15/18 [83%]) and fear of side effects in discontinued patients (8/12 [67%]). Patient-cited barriers to persistence included perceived insufficient treatment efficacy and insurance coverage/out-of-pocket costs. Most frequently cited reasons for taking PAH medication were symptom improvement in persistent patients (79/111 [71%]) and HCP instruction in discontinued patients (12/22 [55%]). Most patients discussed treatment choices with their HCP (112/134 [84%]). Some were uncomfortable asking questions, and only half (62/133 [47%]) felt very/extremely comfortable disagreeing with HCP recommendations (Figure 1).
Conclusion: Results indicate that HCPs perceive persistence to be higher than indicated by medication shipment data and highlight the importance of continuous patient engagement, improvement of patient/HCP communication, disease and treatment education, and early management of side effects. Barriers such as patients' discomfort communicating with HCPs should be addressed to facilitate persistence.



HCP, healthcare professional; PAH, pulmonary arterial hypertension.

Figure 1: Key findings from health care professional (HCP) and pulmonary arterial hypertension (PAH) patient surveys in the PERSIST study.

PRELIMINARY COMPARISON OF EFFECTIVENESS OF PULMONARY VASODILATORS BETWEEN PRECAPILLARY AND COMBINED PRECAPILLARY AND POSTCAPILLARY PULMONARY HYPERTENSION PATIENTS

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Category: Clinical Science
Subcategory: Therapeutic Strategies

Background: Authors of previous studies expressed improved functional capacity in precapillary pulmonary hypertension (PH) patients—such as pulmonary arterial hypertension-prescribed PH-specific medications and in patients with combined precapillary and postcapillary PH (Cpc-PH)—managed with pulmonary vasodilators. PH medical therapy leads to pulmonary vasodilation and a decrease in pulmonary vascular resistance, which may contribute to better functional capacity. We aim to understand the clinical effect of pulmonary vasodilators in Cpc-PH compared with precapillary PH patients.
Methods: Demographic, clinical, and exercise capacity data derived from the University of Michigan Pulmonary Hypertension Patient Registry was obtained at the time of diagnosis and at 1-year follow-up for patients undergoing an evaluation for PH. Information including that of right heart catheterization, 6-minute walk (6MW), functional class, and brain natriuretic peptide (BNP) levels were assessed between groups. Patients with information on baseline and 1-year follow-up data who had documented prescriptions of PH medication were included in the study. The medications given consisted of phosphodiesterase-5 (PDE-5) inhibitors (Pre: 94.2%, Cpc: 96.2%), endothelin receptor antagonists (Pre: 52.9%, Cpc: 38.5%), and prostacyclin analogs (Pre: 37.9%, Cpc: 34.6%).
Results: Of 474 PH patients in the database, 82 precapillary, and 21 Cpc-PH patients were included. Precapillary patients were defined as those with pulmonary capillary wedge pressure (PCWP) ≥ 15 mmHg and classified as Group I, while the Cpc-PH patients had a PCWP > 15 mmHg and were classified as Group II. In terms of baseline hemodynamics for precapillary and Cpc patients, respectively, median RA was 10 mmHg versus 14 mmHg, median pulmonary artery (PA) 46 mmHg versus 52.5 mmHg, median PCWP 12 mmHg versus 19mmHg, and pulmonary vascular resistance (PVR) 7.1 WU versus 7.8 WU. Precapillary PH patients showed improvement in World Health Organization (WHO) Functional Class, with 31.7% of patients in groups I and II at baseline versus 47.6% at follow-up ($P = 0.005$). Cpc-PH patients changed from 38.1% to 57.1% groups I and II, although this did not reach statistical significance ($P = 0.102$). The difference in change to WHO groups I and II between precapillary and Cpc-PH patients from baseline to 1 year was 3.2% ($P = 0.792$, effect size = 0.084). BNP levels in the precapillary group were reduced at 1 year but not in patients with Cpc-PH. Additionally, Cpc-PH patients demonstrated significantly increased 6MW distance ($P = 0.01$). The difference in improvement

Table 1: Baseline Versus FU Difference in Precapillary Group Versus Difference in CpcPH Group

	Pre-Capillary PH, n = 82			Cpc-PH, n = 21		
	Baseline	Follow-Up	*p-value	Baseline	Follow-Up	*p-value
WHO Class, I/II, %	31.7	47.6	0.005	38.1	57.1	0.102
WHO Class, III/IV, %	68.3	52.4	0.005	61.9	42.9	0.102
BNP Level	483.0	213.2	0.001	182.5	210.8	1.000
6MW Distance, m	342.8	364.4	0.075	300.3	364.9	0.01

between Cpc-PH and precapillary PH patients was 43.1 m in favor of the Cpc-PH group ($P = 0.091$, effect size = 0.444). **Conclusion:** Although PH-targeted therapy in Cpc-PH patients is associated with a trend toward functional capacity improvement at 1-year follow-up, this change was blunted compared with patients with precapillary PH. Moreover, there was not a significant difference in BNP levels in patients with Cpc-PH. However, the Cpc-PH group demonstrated improvement in 6MW distance. This small sample size of highly selected Cpc-PH patients indicates further study of the safety and efficacy of pulmonary vasodilators in this cohort is warranted.

ROLE OF GENETIC TESTING IN PULMONARY ARTERIAL HYPERTENSION EVALUATION: A PATIENT AND CLINICIAN SURVEY RESULTS

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Category: Clinical Science
Subcategory: Diagnosis/Screening and Physiologic Studies

Background: A well-known association exists between genetic mutations and the development of pulmonary arterial hypertension (PAH). The BMPR2 gene is a well-documented culprit mutation in the disease. Patients with genetic mutations tend to be diagnosed earlier but have worse outcomes than other forms of PAH. Despite guidelines recommending genetic testing, it remains underused. We conducted a survey of patients with PAH and PAH experts from expert care centers to understand their respective views toward genetic testing.
Methods: From May 2022 to October 2022, 2 separate institutional review board-approved surveys were sent to patients with PAH and clinicians who treat PAH. The patient survey included 22 questions targeted to assess their experience, knowledge, and expectations about genetic testing. The clinician survey consisted of 25 separate questions to understand their views of and barriers to obtaining genetic testing. Both

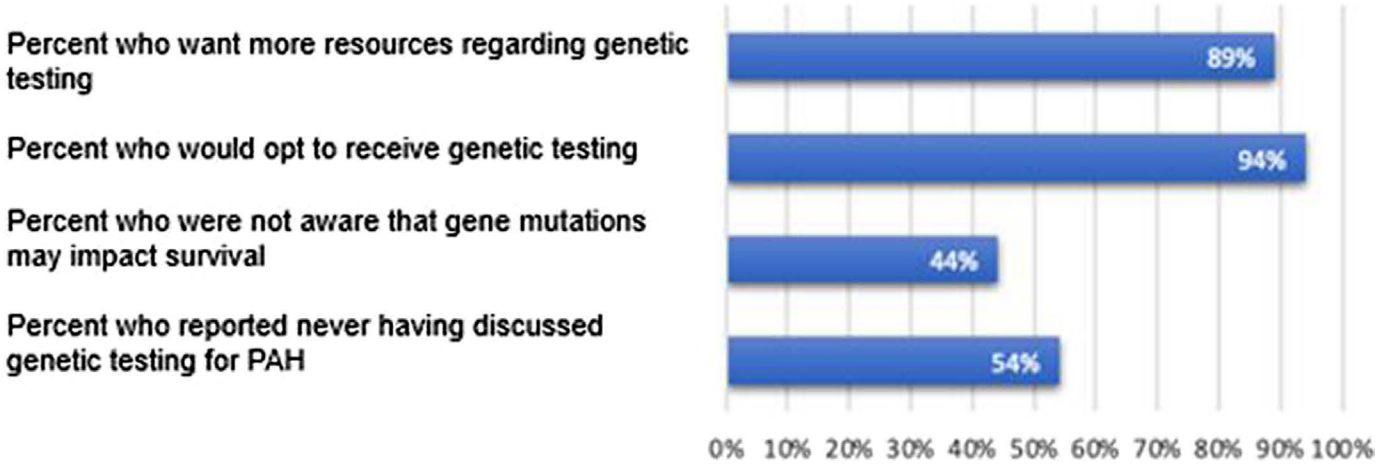

Figure 1: Patient survey results (n = 233).

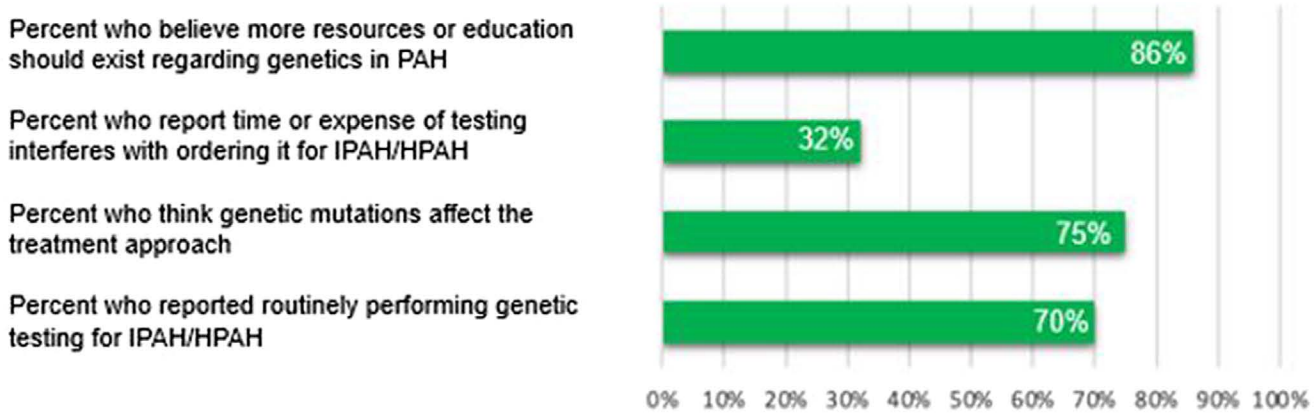

Figure 2: Clinician survey results (n = 38).

surveys were disseminated via pulmonary hypertension (PH) support groups, social media, and through the Pulmonary Hypertension Association (PHA), which provided PH clinician and researcher emails.
Results: A total of 235 patients completed the survey, 91% of whom were women. Eighty percent had self-reported World Health Organization (WHO) Group 1 disease; 12% were confirmed heritable PAH (HPAH), and 48% were confirmed idiopathic PAH (IPAH). Forty-eight percent of respondents did not know that PAH can be caused by genetic variation. While 81% responded that they would consider undergoing genetic testing, only 28% reported they were offered genetic testing (Figure 1). Fifty-two clinicians completed the survey. About two-thirds of clinicians reported awareness of current guidelines for genetic testing (Figure 2). Seventy-five percent indicated that identification of genetic mutations affected treatment approaches, but only 70% of providers reported performing genetic testing routinely during IPAH or HPAP evaluations. Eighty-five percent of clinicians cited cost of the test as a barrier to testing, while 49% cited time taken to navigate genetic testing referral as barriers to testing. However, despite the potential out-of-pocket costs, 34% of patients reported a desire to obtain genetic testing. Overall, 89% of patients and 86% of clinicians agreed that additional information and resources regarding genetic education were needed.
Conclusion: Common barriers to testing included cost as reported by both patients and clinicians and time to refer as reported by clinicians. Patients and clinicians indicated a desire for more education and access to additional information regarding genetic testing.