

Self-reported physician practices in pulmonary arterial hypertension: Diagnosis, assessment, and referral



Susan Polanco-Briceno^{*}, Daniel Glass, Alexis Caze

Deerfield Institute, 780 Third Avenue, 37th floor, New York, NY, 10017, USA

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ABSTRACT

Background: Numerous clinical trials have contributed to rapid advancements in the diagnosis and management of pulmonary arterial hypertension (PAH), yet patients often do not undergo right heart catheterization (RHC) with vasoreactivity testing and may receive a delayed or incorrect diagnosis. Efforts to improve standards of care include the designation of Pulmonary Hypertension Association (PHA)-Accredited PH Care Centers (PHCCs). This study evaluated current practices in the diagnosis and assessment of PAH.

Methods: A survey of 167 physicians who had ≥ 1 claim for PAH in the past 3 months was conducted. **Results:** Of 167 respondents, 15% were affiliated with a PHCC, 40% had referred ≥ 1 patient with diagnosed PAH, and 79% had ≥ 1 patient referred to them by another physician who they then newly diagnosed with PAH. More than half (52%) reported having ≥ 1 patient who was previously misdiagnosed with PAH referred to them by another physician. RHC and vasoreactivity testing, respectively, were performed in 43% and 33% of patients with PAH who respondents referred to another physician, 86% and 67% of patients newly diagnosed by respondents, and 84% and 57% of patients who respondents considered accurately diagnosed prior to being referred to them. Respondents affiliated with a PHCC were more likely to try to refer to another physician affiliated with a PHCC, and to perform RHC and vasoreactivity testing.

Conclusions: Self-reported clinical practices often deviated from established guidelines. Future research should focus on both clinical efficacy and ways to encourage clinicians to bring their practices in line with well-supported, evidence-based recommendations.

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1. Introduction

Data from a multitude of clinical trials have contributed to rapid advancements in the management of pulmonary arterial hypertension (PAH) [1–5], and PAH is the focus of many ongoing trials [6–11]. However, the benefits of these advances for patients can be limited by the capacity of physicians to adopt practices supported by evidence from well-designed studies.

PAH is a rare type of pulmonary hypertension (PH) and is

specifically defined as increased pulmonary vascular resistance that can ultimately lead to right ventricular failure and death [2–4,12,13]. Four classes of functional status have been defined by the World Health Organization. Patients with Functional Classification (FC) Class I PH are the least affected whereas those with Class IV PH are significantly functionally impacted [14,15].

PAH is defined by hemodynamic measures, including a mean pulmonary artery pressure >25 mm Hg at rest or >30 mm Hg with exercise [2,15]. Right heart catheterization (RHC) is the diagnostic gold standard for PAH, in part because echocardiography can only provide an estimate of pulmonary artery pressure [2,13,15,16].

Accurate diagnosis of PAH and exclusion of other types of PH is crucial to optimal management [14]. PAH-specific therapies have not been shown to benefit patients with other forms of PH, and inappropriate treatment can prevent or delay the introduction of more beneficial treatment and/or directly harm the patient [13,14].

Ideally, vasoreactivity testing is done during RHC to determine whether the patient might benefit from treatment with a calcium

Abbreviations: CCB, calcium channel blocker; FC, functional classification; PAH, pulmonary arterial hypertension; PCPs, primary care physicians; PH, pulmonary hypertension; PHA, Pulmonary Hypertension Association; PHCCs, Pulmonary Hypertension Care Centers; RHC, right heart catheterization; SHS, Symphony Health Solutions.

^{*} Corresponding author.

E-mail addresses: spolanco-briceno@deerfield.com (S. Polanco-Briceno), dglass@deerfield.com (D. Glass), acaze@deerfield.com (A. Caze).

channel blocker (CCB) [2,15]. Patients who do not respond with an adequate level of vasoreactivity are unlikely to benefit from CCB therapy yet would still be at risk for treatment side effects [15]. Although only a small subset of patients with PAH will demonstrate vasoreactivity sufficient to justify CCB treatment, short-term vasoreactivity testing is currently the only method of identifying those patients [2,15].

Advancements in the diagnosis and management of PAH have produced novel treatments and improved patient outcomes, and could have an even greater positive impact on healthcare [2,4,17]. However, in many cases evidence-based recommendations such as published guidelines are not followed [12,14,17–19]. A substantial delay between symptom onset and diagnosis still occurs in many patients, with the majority of patients diagnosed when they are already in FC Class III or IV, despite better outcomes being associated with FC Classes I and II [4,17,19]. Other issues include misdiagnosis and inappropriate therapy [19]. To improve standards of care, the Pulmonary Hypertension Association (PHA) has developed a program for accreditation of centers demonstrating expertise in PH, with particular emphasis on PAH [17].

The objective of this study was to evaluate actual practices in the diagnosis, assessment, and treatment of PAH. The goals were to understand: which physicians are diagnosing PAH; the methods used for diagnosis, evaluation, and treatment; how patients with diagnosed or suspected PAH are referred between physicians; and at which point in the progression of the disease patients tend to be diagnosed and/or referred.

2. Methods

2.1. Survey sample design

A universe sample frame of PAH-treating physicians in the US was created by sourcing 2013 insurance–claims activity for PAH therapies from Symphony Health Solutions (SHS). SHS is a leading source of nationally representative and comprehensive physician prescribing information in the US. A total of 2594 physicians who had at least one insurance claim for PAH were invited by postal mail and email to participate in an online study regarding PH. At this point, physicians voluntarily self-screened based on knowledge, interest, and experience level in PH. As it is unknown how many physicians successfully received, reviewed, and self-screened for this survey invitation, a true response rate cannot be calculated for this recruitment methodology. However, it is assumed that participation in this survey was random and represented basic interest and knowledge in this disease area.

In order to qualify for the survey, physicians had to personally have made treatment decisions and/or adjustments for at least one patient specifically to manage PAH in the previous three months. They also had to be willing to provide accurate responses to questions about their professional experiences.

2.2. Ethics, consent, and permission

Physicians were offered an industry-standard honorarium for their time to complete the survey. By opting in to the survey, the respondents provided consent to use their anonymized responses to the survey questions. Because this study did not involve patients or patient data, Institutional Review Board approval and patient consent were not required.

2.3. Survey and data collection

The survey was live between June 11 and July 12, 2015, and was comprised of 22 quantitative and eight qualitative questions.

Quantitative questions addressed the total volume of patients treated for PH and PAH, the type of physician who diagnosed/referred patients, tools used for diagnosing, and functional class at time of diagnosis. Additional quantitative questions that were unrelated to this analysis include volume of current patients in each functional class, current therapy (by functional class), and overall treatment approach by line of therapy; these results will not be presented here. Qualitative questions included those relating to how a diagnosis was determined among patients who did not have an RHC and why patients who did not receive vasoreactivity testing were not tested. Additional questions not included in this analysis related to the rationale for their treatment approach among FC Class I and FC Class IV patients, rationale for brand preference (if any), and rationale for whether they use PAH-specific medications to treat patients with PH. The survey also contained a short demographic section that asked respondents to provide their gender, the number of years in practice, the location and the setting of their practice, affiliation with any academic medical center, and percentage of professional time spent in direct patient care vs research and teaching vs other professional duties (e.g., hospital/practice administration).

2.4. Data analysis

All survey data were analyzed in the aggregate, and study authors were blinded to the individual identities of physician survey respondents. Responses to the closed questions were analyzed quantitatively. Responses to open-ended questions were coded into predetermined categories that were developed based on four telephone interviews with two pulmonologists and two cardiologists with current experience treating PAH. A response that addressed multiple categories was counted as multiple comments. SPSS Version 20 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.) was used to perform the appropriate statistical analyses in order to test for significant differences between two subgroups (those affiliated with a PHA-Accredited PHCC and those not affiliated with a PHA-Accredited PHCC), although the sample size for one group (those affiliated with a PHA-Accredited PHCC) was lower than ideal for this comparison. Two-sided test p-values less than 0.05 were considered statistically significant. Multiple comparisons were not adjusted.

3. Results

Of the 184 physicians who entered the screener, 136 were pulmonologists, 33 were cardiologists, 11 were primary care physicians (PCPs), and four were rheumatologists (Table 1). Of the 136 pulmonologists who entered the screener, 129 qualified and completed the survey (although one was excluded for data quality issues), two qualified but did not complete the survey, and one did not qualify due to not personally making treatment decisions or adjustments specifically to manage PAH in the past three months. A total of 32 cardiologists completed the screener, 28 qualified and completed the rest of the survey, three qualified but did not complete the rest of the survey, and one did not qualify due to not personally making treatment decisions or adjustments specifically to manage PAH in the past three months. Out of the 11 PCPs who entered the screener, eight qualified and completed the survey, one qualified but did not complete the rest of the survey, and two did not qualify due to not personally making treatment decisions or adjustments specifically to manage PAH in the past three months. Finally, all three of the rheumatologists who completed the screener qualified and completed the rest of the survey. An additional four pulmonologists, one cardiologist, and one

Table 1
Respondent disposition.

Invited	2594
Entered screener	184
Pulmonologists	136
Completed the screener	133
Qualified and completed the survey (1 later excluded for data quality issues)	129
Qualified but did not complete the survey	2
Did not qualify	1
Cardiologists	33
Completed the screener	32
Qualified and completed the survey	28
Qualified but did not complete the survey	3
Did not qualify	1
Primary care physicians	11
Qualified and completed the survey	8
Qualified but did not complete the survey	1
Did not qualify	2
Rheumatologists	4
Completed the screener	3
Qualified and completed the survey	3

rheumatologist started the screener but did not complete all of the questions to verify their qualification for the survey.

A total of 167 qualified physicians (physicians who referred or personally made treatment decisions or adjustments for at least one patient with PAH in the three months prior to the survey) provided responses. The majority of qualified respondents were male (84%), and the mean number of years in practice was 16.5. Most (77%) were pulmonologists (Table 2). A small percentage of respondents were affiliated with a PHA-Accredited PHCC (15%, $n = 25$). However, most were not affiliated with a PHA-Accredited PHCC (72%, $n = 120$), some were familiar with this accreditation but were not sure if their center was accredited (8%, $n = 14$), and a few (5%, $n = 8$) reported being unfamiliar with this type of accreditation.

Respondents had managed a mean of 31 patients with PAH in the three months prior to the survey. Ninety-six percent of respondents had diagnosed PAH in a patient and 99% had made treatment decisions for patients with PAH. Most patients with PAH seen by respondents were FC Class II (32%) or FC Class III (38%).

3.1. Referral patterns

Referrals among physicians were relatively common; 21% of respondents had referred at least one patient with suspected PAH to another physician and 40% had referred at least one patient with diagnosed PAH (Fig. 1). The majority of respondents (79%) had at least one patient referred to them by another physician who they then newly diagnosed with PAH. Although 65% of respondents reported having at least one patient with correctly diagnosed PAH referred to them by another physician, more than half (52%) reported having at least one patient who was previously misdiagnosed with PAH referred to them by another physician. Overall, an average of 10 patients were either referred to respondents by another physician for PAH or newly diagnosed with PAH by respondents in the three months prior to the survey. Of those, 31% had been accurately diagnosed with PAH before referral, 19% were misdiagnosed with PAH before referral, and 49% were newly diagnosed with PAH by respondents.

Of patients who were first evaluated for and diagnosed with PAH by respondents, 60% of patients had slightly more severe

Table 2
Respondent characteristics.

	All qualified respondents (N = 167)
Specialty	
Internal Medicine	5%
Pulmonology	77%
Cardiology	17%
Rheumatology	2%
Number of patients with PAH managed in the last 3 months	
Mean	31
Median	25
WHO functional classification of patients seen	
FC Class I	15%
FC Class II	32%
FC Class III	38%
FC Class IV	14%
Respondents who, in the last 3 months:	
Diagnosed PAH	96%
Made treatment decisions for PAH	99%
Affiliated with a PHA-Accredited PHCC	
Yes	15%
No	72%
Familiar with accreditation, but unsure if affiliated centers are accredited	8%
Unfamiliar with accreditation	5%

Abbreviations: FC, Functional Classification; PAH, pulmonary arterial hypertension; PHA, Pulmonary Hypertension Association; PHCC, Pulmonary Hypertension Care Center; WHO, World Health Organization.

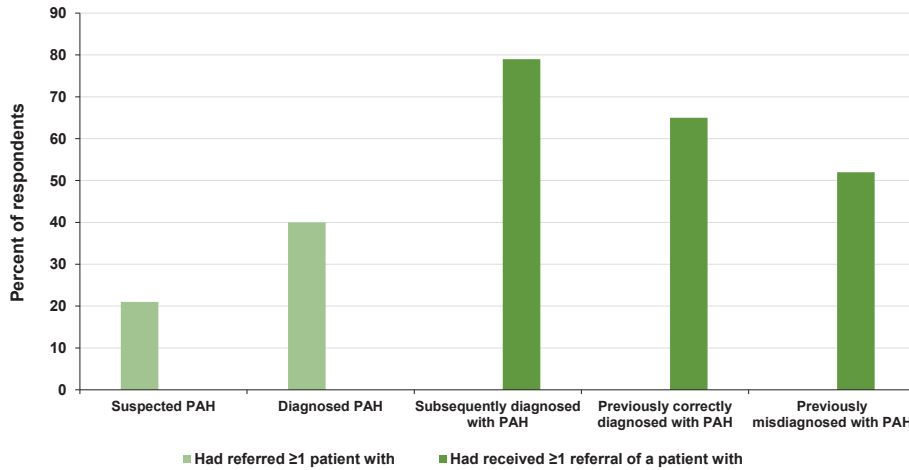


Fig. 1. Referral patterns.

illness (FC Class III - 41%, FC Class IV - 19%, Fig. 2). Similarly, 51% of patients who were first diagnosed by respondents after being referred by another physician were FC Class III or IV. Overall, patients who were referred out for PAH tended to have slightly more severe illness, with 71% of patients in FC Class III or IV at the time they were referred.

As noted earlier, a small proportion of respondents reported that they were affiliated with a PHA-Accredited PHCC (15%, n = 25). Most respondents reported that they were not affiliated with a PHA-Accredited PHCC (72%, n = 120), and the remaining were either unsure if sure if their center was accredited or were unfamiliar with this type of accreditation. Of those who identified as being affiliated with a PHA-Accredited PHCC, 92% (23 of 25) reported making an effort to refer patients to a physician who was also affiliated with a PHA-Accredited PHCC, which was significantly greater than the proportion of respondents who identified as not being affiliated with a PHA-Accredited PHCC who did likewise (48%, 68 of 142) ($p < 0.001$).

3.2. Diagnostic testing – right heart catheterization

More than half (57%) of patients with PAH who respondents referred to another physician did not have an RHC (Fig. 3). Most respondents reported that the diagnosis of PAH among these patients had been made based on tests such as echocardiogram, often in combination with clinical symptoms.

A total of 14% of patients who were newly diagnosed with PAH by respondents, and 16% of patients accurately diagnosed with PAH by another physician before being referred to respondents, had not had RHC. A smaller percentage of patients who were newly diagnosed with PAH by respondents affiliated with a PHA-Accredited PHCC had not had an RHC (4%) compared with those not affiliated with a PHA-Accredited PHCC (17%), although this difference was not significant ($p = 0.484$). Physicians were asked an open-ended question regarding why these patients had not undergone an RHC to confirm the diagnosis of PAH; responses were coded using predetermined categories. Of respondents who had at least one patient who had not had an RHC (n = 45), 84% reported that

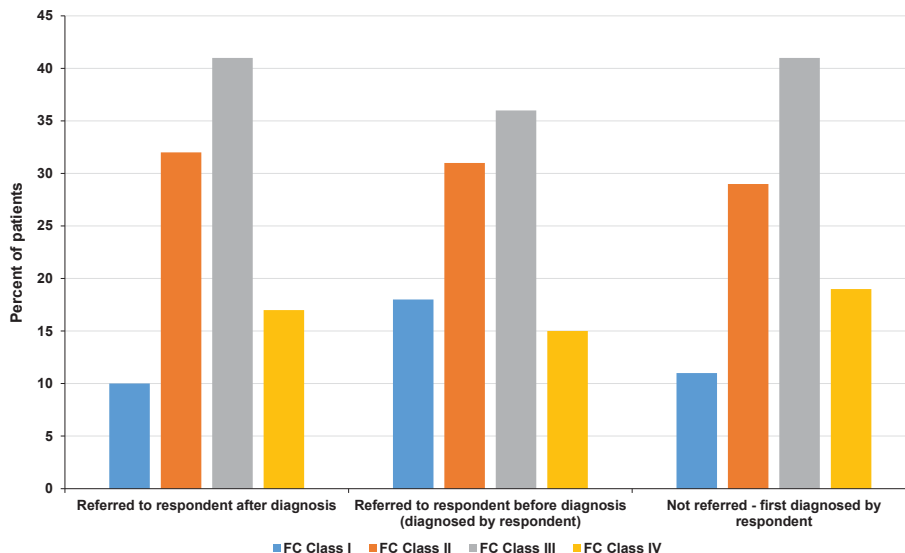


Fig. 2. Disease severity at time of referral, Abbreviation: FC, Functional Classification.

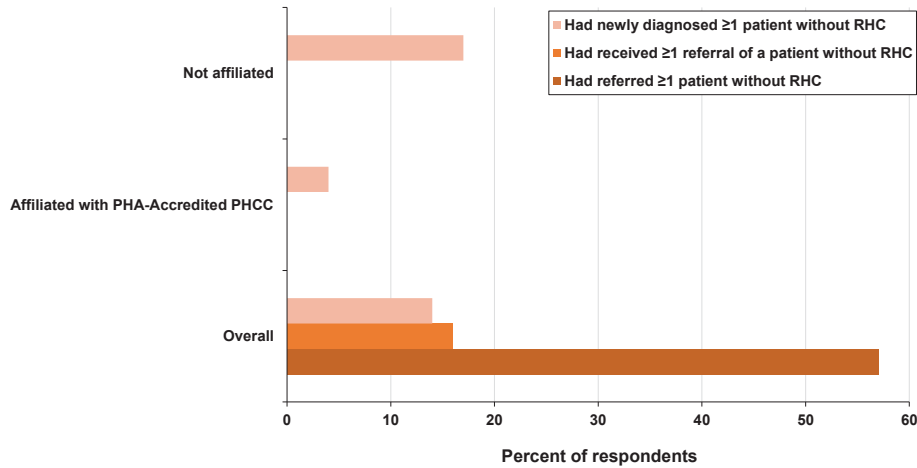


Fig. 3. RHC patterns.

they would confirm their diagnosis of PAH using an echocardiogram/2-D echo Doppler.

3.3. Diagnostic testing – vasoreactivity testing

Respondents reported that a larger proportion of patients newly diagnosed by them (either whose first discussion about PAH was with them or who were referred by another physician who had not yet diagnosed them) were tested for vasoreactivity (67%) compared with those referred to them by another physician who had already accurately diagnosed them with PAH (57%) (Fig. 4). In addition, most patients (67%) referred out by respondents had not received vasoreactivity testing specifically to determine candidacy for CCBs. A smaller proportion of patients diagnosed by respondents affiliated with a PHA-Accredited PHCC (22%) did not have vasoreactivity testing compared with those not affiliated with a PHA-Accredited PHCC (28%), although this difference was not significant ($p = 0.608$). Physicians were asked an open-ended question regarding why these patients had not undergone vasoreactivity testing and responses were coded using predetermined categories. Of those respondents who personally diagnosed at least one patient who had not undergone vasoreactivity testing, 25% reported they do not routinely test because they do not believe that CCBs are effective in treating PAH, and 11% felt that testing was unnecessary

due to the low probability of finding a candidate for CCB treatment (with a net of 31% mentioning either one of those reasons). The next most common reason, reported by 25% of physicians, was that the patient was referred and re-doing the RHC for the vasoreactivity testing would not be worthwhile. Other reasons included lack of capability/cardiologist who performed it (mentioned by 16%), patient contraindications (mentioned by 16%), bypassing the test by empirically trying CCBs (mentioned by 9%), suspicion of etiology not supporting candidacy for CCBs (mentioned by 7%), patient refusal (mentioned by 3%), and cost/insurance issues (mentioned by 3%).

4. Discussion

PAH is a rare condition, particularly compared with the relatively common larger category of PH [2,13,15]. RHC is required to confirm a PAH diagnosis, with associated vasodilator testing necessary to evaluate patient suitability for CCB treatment [2,13,15]. Differences in diagnosis and treatment between types of PH make accurate diagnosis of PAH of paramount importance in effective patient treatment [14].

Although only a small proportion of patients with PAH will benefit from CCB therapy, the potential benefit to those patients is substantial [2,15]. However, due to the rarity of substantial

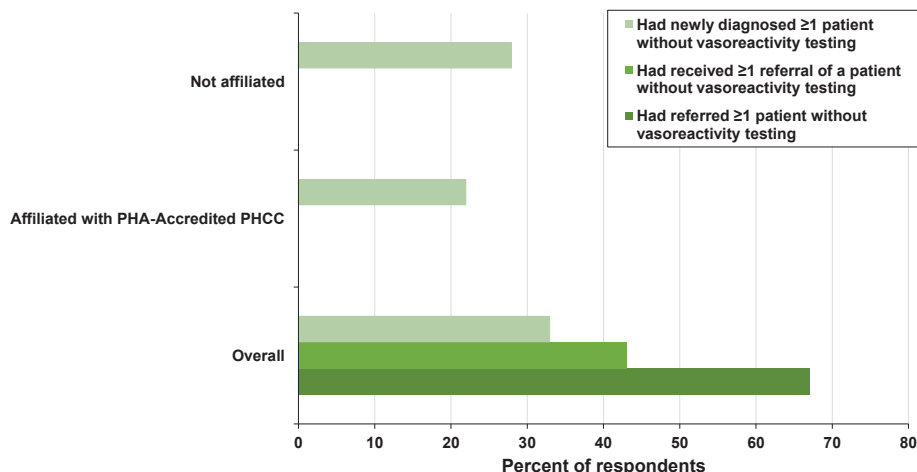


Fig. 4. Vasoreactivity testing patterns.

vasoreactivity and suitability for CCB treatment, empiric therapy with CCBs in untested patients is very likely to fail, thus delaying effective treatment [2].

Respondents in this study had managed an average of 31 patients with PAH in the previous three months, making diagnoses as well as treatment decisions. Although rates of RHC usage were relatively high among this experienced group, it was less likely to be done in patients they had referred to other physicians. Vasoreactivity testing was performed in only about one third of patients.

Referrals of patients with suspected or diagnosed PAH were common, with respondents seemingly more likely to receive referrals than to refer patients with PAH to other physicians themselves. Respondents were not asked to report on any misdiagnoses of their own that they had been made aware of, but more than half reported having at least one patient who was previously misdiagnosed referred to them by another physician.

In this study, the majority of respondents were pulmonologists and only 5% were not aware of the existence of PHA-Accredited PHCCs. The requirements for PHA-Accredited PHCCs include a cardiac catheterization laboratory as well as an echocardiography laboratory. Staff at these centers must follow available diagnosis and treatment consensus guidelines when possible, must have experience with acute vasodilator testing, and be proficient with PAH therapies [20]. Respondents affiliated with a PHA-Accredited PHCC were more likely to try to refer to a physician also affiliated with a PHA-Accredited PHCC, as well as to follow established evidence-based guidelines by performing RHC and vasoreactivity testing.

The limitations of this study include possible enrollment bias and the inherent limitations of self-reported data. Cause and effect cannot be established from these data. For example, where physician behavior deviated from guideline recommendations, it is not known whether the physician was unaware of the recommendations, did not agree with the recommendations, or had patients who were justifiably outside of the scope of the recommendation (e.g., patients in whom vasoreactivity testing was contraindicated). In addition, the small sample size of respondents who were affiliated with a PHA-Accredited PHCC ($n = 25$, 15%) may account for the lack of statistical significance in some of the statistical comparisons.

Despite the many advances made in the management of PAH, the need for improvements remains. Patients with PAH cannot benefit from the knowledge gained in clinical studies if clinicians do not incorporate these findings into their practices. The results reported here are in concordance with other reported findings of suboptimal PAH management [12,14,17,18], and indicate that future research should focus not only on clinical efficacy but also on ways to encourage clinicians to bring their practices in line with well-supported, evidence-based recommendations. Potential methods for improving adherence among physicians at the individual level could include education on current evidence-based recommendations made easily accessible and possibly including CME activities to encourage participation. In addition, incentives for physicians should be based on following best practices. Physicians should also be made aware of the existence of PHA-Accredited PHCCs and encouraged to refer patients to such centers. At the institutional level, efforts should be made to encourage healthcare facilities with a high volume of patients with PH or PAH to move towards fulfilling the standards to become a PHA-Accredited PHCC. Finally, reimbursement should be designed to reflect evidence-supported best practices.

5. Conclusions

Deviations from established, evidence-based guidelines were self-reported by a group of physicians selected for experience with

PAH and who had substantial involvement in PAH diagnosis and treatment. Affiliation with a PHA-Accredited PHCC was associated with better practices, indicating that further education and efforts to change physician behavior are likely to be effective in improving outcomes for patients with PAH.

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Competing interests

The authors declare that they have no competing interests.

Author contribution

All of the authors contributed to the conception and design of the study and analysis methods. SPB and DG collected and analyzed the data and drafted the manuscript. AC supervised all aspects of the study. All of the authors contributed to interpreting the data, critically revised the manuscript for important intellectual content, and approved the final version of the submitted manuscript.

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