EDITORIAL

Where’s the Easy Button? The Many Barriers to Care for Patients With Pulmonary Arterial Hypertension

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The estimated burden of medication nonadherence in the United States includes 10% of all hospitalizations, 100,000 deaths, and billions of dollars to the healthcare system every year. Barriers to medication adherence include lack of knowledge and insight about the disease, cognitive impairment, medication adverse effects, complexity of the medication regimen, access to pharmacies, medication availability at pharmacies, cost, and inadequate communication between the patient and the prescriber. Patients with pulmonary arterial hypertension (PAH) face additional obstacles in that their medications are frequently sourced through specialty pharmacies, are quite costly, and may be subject to additional requirements such as pregnancy testing before dispensing.

Cost-related nonadherence (CRN) occurs when the prescribed medication regimen is altered because the patient does not have the economic solvency to obtain the prescribed therapy. Typical CRN scenarios include use of a reduced medication dose or complete interruption of therapy because of delays in obtaining medication refills. Patients with diabetes and hypertension commonly report medication nonadherence caused principally by cost-related issues. Medication nonadherence directly secondary to economic problems has been associated with a 15% to 22% increased risk of all-cause mortality in patients with diabetes, hypertension, and cardiovascular disease. Data from the US Sample Adult and Sample Child National Health Interview Surveys identified ≈7% of adults with at least 1 CRN between 1999 and 2015. Of those individuals who participated in the survey, 25% of patients with diabetes reported using insulin doses lower than prescribed to delay needed refills, and almost 40% did not disclose this practice to their providers.

Factors associated with CRN among patients with chronic illnesses include low income, lack of medical insurance, high medication copays, and high out-of-pocket medication costs. However, other studies have found that lower household income and lack of health insurance are not the only determinants of CRN. Many patients with medical insurance and incomes at or above the US median incur CRN when they have complex or multiple illnesses requiring numerous medications. As expected, more expensive drugs, higher copays, and the need for multiple medications were linked to CRN.

A particularly problematic aspect of the US healthcare system is the “donut hole” of prescription coverage through Medicare part D. Patients enter the donut hole after exceeding the initial coverage limit and exit the donut hole when they reach the out-of-pocket

See Article by Schikowski et al.

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threshold. Details vary based on specific plans, but there is often a difference of several thousands of dollars between the initial coverage limit and the out-of-pocket threshold. While in the donut hole, increased copays likely lead to CRN. The Affordable Care Act in 2010 included measures to blunt the impact of the donut hole, but it remains a significant concern for patients with high out-of-pocket costs.

Another significant limitation of the US healthcare system is the lack of price transparency for everything from medications, clinic visits, diagnostic tests and procedures, surgeries, and hospitalizations from both the patient and physician perspectives. Pharmacies, hospitals and healthcare systems, independent physician groups, and independent testing centers such as medical laboratories each negotiate prices with individual insurance providers. Uninsured patients lack negotiating power and can be billed at the highest rates. To address this lack of transparency, US Centers for Medicare and Medicaid Services required hospitals to publish lists of prices for all hospital procedures and services starting in 2019, with updated requirements in 2021 and 2022. Compliance with these regulations has been incomplete at best. A recent study found that only 13% of hospitals publish the cost of a routine ECG, with charges ranging from $9 to $4325. At the time of a clinic or inpatient visit, the physician and patient rarely if ever know the costs of the interventions discussed, making it challenging at best to appropriately counsel a cost-conscious patient.

PAH is a rare and complex disease. Current median survival for a newly diagnosed patient with PAH is 7 years, and survival is significantly reduced by delays in diagnosis and treatment. Sadly, delays in diagnosis are quite common; the average time interval between symptom onset and diagnosis is more than a year, and in clinical practice it is common to encounter patients who have been erroneously diagnosed with asthma or heart failure with preserved ejection fraction before PAH. Diagnosis itself is costly as the basic evaluation of suspected PAH includes an ECG, transthoracic echocardiogram, pulmonary function testing, 6-minute walk, chest radiograph, ventilation perfusion imaging, numerous laboratory tests, cardiac catheterization, and at least 1 visit with a cardiologist or pulmonologist. Care at an accredited center is associated with reductions in hospitalizations and mortality. Although the number of centers has grown dramatically since the inception of the accreditation program in 2011, they remain limited in distribution, and 16 states have no accredited centers, which leads to significant travel costs for patients seeking comprehensive care.

The psychological effects of having a progressive and terminal disease diagnosis can create an additional barrier to care. An estimated 30% of patients with PAH struggle with comorbid psychiatric diagnoses such as anxiety and depression. Patients with PAH and moderate to severe anxiety or depression experience worse quality of life, although fortunately there was no association with mortality in 1 study. The impact of anxiety and depression on medication adherence has not been studied in PAH, but in a chronic obstructive pulmonary disease cohort adherence to treatment of major depressive disorder has been linked to improved pulmonary medication adherence and reductions in emergency department visits and hospitalizations.

Once the diagnosis of PAH is made, the direct cost per patient per month is 4 to 5 times higher than matched controls by age, sex, geographical area, and annual income. Clinical trial and meta-analysis data support early initiation of combination therapy with a phosphodiesterase type 5 inhibitor (PDE5) and an endothelin receptor antagonist (ERA), resulting in a significant reduction in morbidity and mortality. As the disease progresses, so does the pharmacy cost because of the increased number and complexity of medications such as prostanoids (oral, inhaled, or parenteral) and soluble guanylate cyclase stimulators. A study examining claims to managed care plans found that the pharmacy costs of patients with PAH increased with the escalation of medical therapy during a 12-month period. However, the increase in pharmacy costs was balanced by a reduction in costs for hospitalizations and ambulatory visits. One would expect this trend to eventually reverse as patients approach end stage, at which point all costs increase until the patient undergoes lung transplantation, enrolls in hospice, or dies.

In this issue of the Journal of the American Heart Association (JAH), Schikowski and colleagues sought to understand the association between medication copays and adherence in patients with PAH, with particular attention to the impact of household income. To answer these questions, they used a deidentified claims database that includes US patients with commercial insurance and Medicare Advantage plans; this database is proprietary and commercially licensed to the researchers. As predicted, increased copays were associated with decreased medication adherence for prostanoids and combination therapy (defined as ERA and PDE5), although surprisingly higher copays were associated with increased compliance with PDE5s. Unexpectedly, household income did not impact medication adherence for any medication class at any copay level. Soluble guanylate cyclase stimulators trended toward improved compliance with lower copays but did not reach statistical significance. No clear associations were noted between copays and compliance with ERAs. It is interesting that less than a quarter of patients in this database were treated with combination therapy despite the overall trend of PAH care during the past decade in this direction. Unfortunately,
insufficient details were available in the database to permit the inclusion of patients treated with parenteral prostacyclins. There is no mention of patients treated with alternative medication combinations, such as ERA and soluble guanylate cyclase stimulators as 1 example. In clinical practice, prostacyclin monotherapy is uncommon, suggesting that pulmonary vasodilator prescriptions were incompletely captured.

It is tempting to focus on the expected findings of this study, increased copays are associated with decreased medication adherence. However, the full picture is more complex in that the opposite held true for PDE5s, numerically the largest group in the study accounting for more than half of the included patients. Both PDE5s used to treat PAH (sildenafil and tadalafil) are available as generics, although some prescribers and patients prefer the brand name medications, perhaps patients motivated to purchase brand name medications at higher copays have higher adherence. Two ERAs are available as generics while the third is only available as brand name, as with PDE5s some patients may be willing to accept higher copays for brand name medications confounding the relationship between copay and adherence. Unfortunately, the study did not distinguish between generic and brand name medications to help answer these questions. Another unexpected finding is the lack of association between household income and medication adherence for any medication at any level of copay. Financial assistance programs were not considered in this data set, and these programs are frequently targeted at lower income patients and likely improve adherence for eligible patients. Overall, the study results suggest more complex relationships between copay, household income, and medication adherence than predicted and calls for further study.

All patients with chronic diseases face barriers to care, and those with rare diseases such as PAH face added barriers such as delays in diagnosis, limited access to comprehensive care, and costly medications only available through specialty pharmacies. Shah and colleagues described their experience prescribing PDE5s for PAH at an academic medical center with an integrated specialty pharmacy. They were able to achieve excellent medication adherence at low out-of-pocket costs, truly an “easy button” for their patients, with a corresponding reduction in adverse events. Although this model is not available to all patients with PAH or other rare diseases, it does highlight the benefits of integrated care.

ARTICLE INFORMATION

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Disclosures
None.