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High-Cost Treatments, Value Assessments, Innovation, and More at ISPOR 2017

The International Society for Pharmacoeconomics and Outcomes Research (ISPOR) met May 20-24, 2017, for its 22nd Annual International Meeting in Boston, Massachusetts. Many topics of conversation concerned rising drug prices, ways of addressing rising prices, and the future of healthcare delivery as policy changes under the new presidential administration.

ISPOR kicked off with a plenary session delivered by 2 speakers who have advised Republicans —Gail Wilensky, PhD, of Project HOPE, and Joseph R. Antos, PhD, of the American Enterprise Institute—and 2 who have advised Democrats—Jonathan Gruber, PhD, of the Massachusetts Institute of Technology, and David M. Cutler, PhD, of Harvard University.

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Real-World Evidence Comparing Cost and Resource Utilization on Novel Oral Anticoagulants

In a study that is one of the first of its kind, researchers conducted a head-to-head comparison of all-cause healthcare costs and healthcare resource utilization (HCRU) associated with use of 3 novel oral anticoagulants (NOACs) in patients with newly diagnosed nonvalvular atrial fibrillation (NVAF) receiving a NOAC for the first time. Cost outcomes in patients receiving dabigatran (Pradaxa), rivaroxaban (Xarelto), and apixaban (Eliquis) were evaluated.

Researchers presented the results of the study at the International Society for Pharmacoeconomics and Outcomes Research 22nd Annual International Meeting, which convened May 20-24, 2017, in Boston, Massachusetts. Study authors Jessica Franchino-Elder, PhD, MPH, and Azhar Ahmad, MBBS, both of Boehringer Ingelheim, discuss the study design, outcomes, and what the results mean.

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High-Cost Treatments (Continued from page 1)

They discussed the current state of the Affordable Care Act (ACA) and efforts by Republicans to repeal the law through the American Health Care Act, which passed the House of Representatives on May 4, and legislation is still being created in the Senate.

Wilensky voiced her concern that as Republicans work to repeal parts of the ACA, the inroads made in reducing the number of people without insurance in the United States will be lost.

"There are other issues to deal with, but I'm somebody who strongly believes that having insurance coverage is important," she said. "Whatever we do going forward, I don't want to lose ground."

Antos said that Republicans missed out on "fairly straightforward changes" that could have been made to stabilize the market in favor of bigger changes to the ACA. He labeled "questionable" claims that the ACA marketplaces were in a death spiral. All panelists agreed that any turmoil in the ACA markets was "induced" by the Republican Party.

Cutler noted that the insurance markets had begun stabilizing in 2016, with some insurers making profits as they corrected for beneficiary characteristics.

According to Cutler, "the Trump administration has created an enormous amount of confusion" by threatening to not fund the cost-sharing reductions and by not requiring people to report on their tax returns if they had insurance. He added, "Insurers are now thinking again that every change out of Washington will cause them to lose money."

Gruber added that Republicans are making the situation worse for themselves. When the ACA was first drafted, Republicans were on committees to draft the bill. "There are still parts of Obamacare that were put in by Olympia Snowe [former Republican senator from Maine] and her staff," he noted. It was only once Republicans went to town halls, where their constituents were furious, that all Republicans jumped ship and refused to vote for the bill, he explained. According to Gruber, at the present time, Democrats are not being engaged at all.

Drug Pricing

Because of President Trump's announcement during the 2016 campaign that he was interested in letting Medicare negotiate drug pricing, the concept has gained new traction. A panel at ISPOR discussed the complexities of allowing Medicare to negotiate prices and whether or not it would actually produce savings.

Currently, Medicare is prohibited by law from negotiating drug prices; however, recurring interest in the idea has led to the Congressional Budget Office (CBO) weighing in on the potential savings that might be realized. According to Juliette Cubanski, PhD, MPP, MPH, of Kaiser Family Foundation, those savings might not be as large as some would expect. Part of the reason the CBO believes savings would be negligible is because private plans already do a fairly good job of negotiating prices, and there is little reason to believe that the Health and Human Services (HHS) secretary could do better, she explained.

Still, some legislation is in development that would allow Medicare to negotiate. One bill would not only allow Medicare to negotiate drug prices, but also provides a fallback. In the event that no agreement is reached after 1 year of negotiations, the price would be what the Department of Veterans Affairs pays. In addition, the HHS secretary would be directed to establish formularies.

Dana P. Goldman, PhD, of the University of Southern California, added to the discussion that he believed that any savings that come from allowing Medicare to negotiate prices might not be worth pursuing. While negotiations might result in lower prices in the near term, the policy would likely negatively affect innovation in the long run, he said.

Goldman believes that the best way to curb drug prices is to support value-based pricing. Patricia M. Danzon, PhD, of the University of Pennsylvania, outlined a possible way Medicare could use value-based pricing to negotiate drug pricing.

She proposes allowing an independent agency to assess the value of new drugs, and tasking Medicare with establishing reimbursement levels for new drugs—up to the independent agency's pricing threshold. Any cost above the threshold would be paid for by the plan and the patient.

"In this way, Medicare's value-based price is constraining the actual reimbursed price; it's not trying to negotiate rebates off of an unlimited price, but rather it's constraining the reimbursed price," she explained.

Outcomes-Based Risk-Sharing Agreements

A recent survey found that only 24% of health plans had an outcomes-based contract in place, but another 30% are in the process of negotiating one. However, of those currently using outcomes-based agreements, only 9% view them as being very successful, and 50% said they are somewhat successful, according to Kathleen E. Hughes, MBA, of Avalere Health, which conducted the survey.

The therapeutic areas in which payers see the most opportunity for outcomes-based contracts are endocrinology (eg, diabetes), infectious disease (eg, hepatitis C), and cardiovascular medicine (eg, hypercholesterolemia, atrial fibrillation). Jim Clement, MHA, of Aetna, explained that many of Aetna's contracts focus on "disease states that will actually impact population health." Its top 3 therapeutic areas are diabetes, respiratory, and cardiovascular.

Aetna has found that to be successful with these contracts, flexibility is necessary—with which Michael L. Ryan, PharmD, of Bristol-Myers Squibb (BMS), agreed. These contracts must work for both parties, he said, which is why BMS has both contracts with downside risk only and contracts with upside-downside risk.

And as these contracts proliferate and begin to work, more and more pharmaceutical companies are open to trying them, said Michael S. Sherman, MD, MBA, MS, of Harvard Pilgrim Health Care, which now has 11 value-based agreements in place.

However, not all proposed value-based contracts have been successful. For example, Harvard Pilgrim has pursued value-based contracting opportunities with pharmaceutical companies, but no agreements have been signed to date. Even so, discussions between pharmaceutical companies and payers can still be beneficial. These discussions encourage both insurers and pharmaceutical stakeholders to think about value-based contracts and how they might work.

"This is relatively new, uncharted territory, and let's face it: We're making it up as we go along," Sherman said.

Potential and Challenges of Gene Therapies

Gene therapies may have tremendous potential for improving patient outcomes, but according to panelists, questions remain about the cost, ethics, and practicality of these treatments.

There are currently 23 gene therapies in active phase 3 development in the United States, and a small number have already reached market in Europe, explained Bill Dreitlein, PharmD, BCPS, of the Institute for Clinical and Economic Review. However, warned Dreitlein, gene therapies that have reached the European market have yet to achieve any real success.

Adrian Towse, MA, MPhil, of the Office of Health Economics in London, highlighted Glybera, which is on the market in Europe. This treatment, with a price tag of more than 1 million Euros per patient, treats a rare inherited disorder that can cause severe pancreatitis. However, only 1 patient has been treated so far, and faced with the lack of use and other challenges, the manufacturer is not renewing its marketing authorization.

> "The best way to curb drug price is to support value-based pricing."

Despite these challenges, American manufacturers such as bluebird bio remain excited about the potential of gene therapies. "We really believe in the potential of gene therapies to transform patient lives," said Clark Paramore, MSPH, of bluebird bio.

Paramore noted that he understands concerns that since gene therapies are so new, it is still unclear what their long-term benefits will be. As a result, he believes a value-based payment model makes the most sense in this area.

A value-based model or a way to pay over time for gene therapies would help alleviate some of the concerns over the unknowns of how these therapies will actually work, said John Watkins, PharmD, MPH, BCPS, of Premera Blue Cross.

Beyond figuring out how to pay for these therapies, there are other ethical concerns. For instance, will there need to be a prioritization of who gets treated?

"If we cannot afford to pay for it for everyone, where do we draw the line?" Watkins asked.

Moving forward with gene therapies will require buy-in in the United States, said Paramore. Industry will lead the way, but payers will have to work to remove barriers, providers will need to change the way they think about treating patients, and patients will need to demand these new therapies.

"Gene therapies are coming, and they're going to be expensive, so it's time to start thinking about them," Dreitlin said. ●

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***AJMC®*: How does this study differ from previous real-world studies on the use of NOACs in patients with NVAF?**

Jessica Franchino-Elder, PhD, MPH: This study is one of the first matched direct comparison of healthcare costs, and HCRU data among NOACs. I think this is a key differentiator that readers will want to understand, especially given the increasing amount of real-world evidence that's being generated right now. There have been published studies that assess clinical costs and healthcare resource utilization, outcomes in a real-world setting with NOACs versus warfarin. There have also been studies evaluating real-world evidence of safety and efficacy with NOACs.

This study is the first propensity score-matched direct comparison among the NOACs that looks at all-cause costs and HCRU using real-world data of commercial and Medicare populations. Not only is it the first of its kind, but we also are able to conduct a study in a population of over 70,000 NVAF patients.

> "This is the first matched, direct comparison between dabigatran and rivaroxaban, and dabigatran and apixaban, that compares all-cause costs and HCRU outcomes."

***AJMC®*: What is the burden of nonvalvular atrial fibrillation among the US population?**

JFE: According to the CDC, it is estimated that there are between 3 million and 6 million people in the United States with atrial fibrillation, and that there are over 750,000 hospitalizations and 5 million office visits per year. This costs the healthcare system almost $6 billion annually.

***AJMC®*: What were the main findings from the study?**

JFE: One of the key takeaways from the study is the findings. By direct comparison, between dabigatran and rivaroxaban, among those newly diagnosed and newly treated with NVAF, dabigatran had significantly lower total, inpatient, and outpatient pharmacy all-cause adjusted cost, as well as lower HCRU, compared with rivaroxaban. Then, compared with apixaban, the total inpatient and outpatient pharmacy costs were similar. Dabigatran did have more all-cause outpatient and pharmacy HCRU than apixaban, but had similar [results in terms of] all-cause hospitalizations.

***AJMC®*: What finding from the study surprised you the most?**

JFE: Based on other real-world evidence that we've seen, we actually weren't surprised. With that being said, this was a critical study for us to conduct in order for us to validate our thinking. We were able to do so using a large, real-world evidence sample. While other oral anticoagulant real-world evidence studies have been conducted comparing NOACs and warfarin, this is the first matched, direct comparison between dabigatran and rivaroxaban, and dabigatran and apixaban, that compares all-cause costs and HCRU outcomes. For the primary outcome of cost, this study found that adjusted all-cause costs are lower with dabigatran than with rivaroxaban, and they are similar between dabigatran and apixaban.

***AJMC®*: What follow-up is recommended for patients on NOACs, such as dabigatran, and what should clinicians be looking for?**

Azhar Ahmad, MBBS: For patients who are on NOACs, the main difference is that you don't need any routine coagulation monitoring. Patients still need to go for their regular check-up with their physician, so it's basically standard follow-up with the physician. The focus would be to make sure that the patients are taking the medication because I think adherence is always a big topic and with NOACs and warfarin especially. We really do want to make sure that they are compliant and taking their medication.

I think the key is always about understanding of the disease and I don't think we spend enough time making sure that the patient really understands their disease and the reason that they are taking the medication, especially when it is related to prevention. So, when you don't really feel the benefit of the drug until what they think we are trying to prevent happens, it is really hard sometimes for the patient to understand why they are taking medication. I think the main thing is understanding and education for the patient.

***AJMC®*: What is the reversal agent for dabigatran and how does it work?**

AA: The reversal agent for dabigatran is called Praxbind, or idarucizumab. This is a specific reversal agent that has been developed only for Pradaxa (dabigatran). It is an antibody that binds directly to dabigatran, and when it does that, it basically neutralizes dabigatran. It has now been on the market in the United States for nearly 2 years, and is widely available across the country. The main indication is for emergency use only, so it has to be for a patient with life-threatening or uncontrollable bleeding, or for a patient coming in with an emergency and requiring some urgent procedure or urgent surgery. ●

Head-to-Head Matched Comparison of Cost and Resource Utilization of Pradaxa, Xarelto, and Eliquis in Patients With NVAF

In the United States, it has been estimated that costs related to nonvalvular atrial fibrillation (NVAF) total more than $6 billion each year, including the burden of approximately 750,000 hospitalizations and 5 million office visits. Considering the high costs of NVAF, it is important to recognize the differences in healthcare-related costs among patients receiving different novel oral anticoagulant (NOAC) agents.[1]

Previous studies of NOACs have demonstrated important advantages over the traditional anticoagulant warfarin, including improved efficacy in prevention of NVAF-related events and reduced monitoring requirements versus warfarin.[2,5]

At the International Society for Pharmacoeconomics and Outcomes Research 22nd Annual Meeting in Boston, Massachusetts, May 20-24, 2017, Gilligan et al presented head-to-head comparisons of all-cause healthcare costs and healthcare resource utilization (HCRU) between similar patients receiving dabigatran (Pradaxa) and rivaroxaban (Xarelto), and dabigatran and apixaban (Eliquis).[1]

In this retrospective comparison of cost outcomes for newly diagnosed propensity score-matched patients with NVAF, investigators found that use of dabigatran was associated with lower inpatient, outpatient, and total HCRU costs than the use of rivaroxaban. No significant differences between dabigatran and apixaban were identified on these cost outcomes, however.[1]

This study represents one of the first to evaluate dabigatran in a head-to-head study to assess cost and HCRU against other NOACs. The primary objective was to compare all-cause healthcare costs among patients with a new diagnosis of NVAF receiving a NOAC as initial therapy. In a secondary analysis, authors also compared all-cause HCRU with dabigatran versus rivaroxaban and with dabigatran versus apixaban.[1]

Authors analyzed data on patients 18 years and older with at least 1 inpatient or outpatient claim for atrial fibrillation who were treated with a NOAC. Patients were followed for up to 12 months.[1]

Each of 26,592 patients receiving dabigatran was individually paired with a patient receiving rivaroxaban based on clinical characteristics through propensity score matching. Similarly, in the dabigatran–apixaban comparison, 8857 matched participants were studied. The majority of patients in each arm were insured through Medicare (57% - 59%), slightly more than one-third (37%) of patients were female, and the mean patient age was 68 years.[1]

In the comparison of outcomes in patients receiving dabigatran versus rivaroxaban, patients receiving dabigatran had lower average per patient per month (PPPM) total costs in both descriptive ($4145 vs $4605, P <.001) and multivariate-adjusted outcomes ($4093 vs $4636, P <.001). On multivariate-adjusted outcomes, inpatient costs ($1476 vs $1862, P <.001), outpatient medical costs ($2016 vs $2121, P <.01), and outpatient pharmacy costs ($634 vs $645, P <.05) were all significantly lower with dabigatran versus rivaroxaban.[1]

In the comparison of outcomes in patients receiving dabigatran versus apixaban, patients receiving dabigatran had lower average PPPM total costs, but the costs were not notably different in both descriptive ($3862 vs $3998) and multivariate-adjusted outcomes ($3886 vs $3951). There were no significant differences between groups in terms of inpatient costs, outpatient medical costs, or outpatient pharmacy costs.[1]

> “...Investigators found that use of dabigatran was associated with lower inpatient, outpatient, and total HCRU costs than the use of rivaroxaban.”

These results show that, in patients with newly diagnosed and newly treated NVAF receiving a NOAC, patients using dabigatran incur lower overall healthcare spending than patients receiving rivaroxaban, and incur similar overall healthcare spending to patients receiving apixaban. Although these data were generated through a retrospective study, these findings are worthy of consideration in formulary decision making for managed care professionals. ●

REFERENCES

1. Gilligan A, Franchino-Elder J, Song X, et al. Comparison of all-cause healthcare resource utilization (HCRU) and costs among patients with non-valvular atrial fibrillation (NVAF), newly treated with novel oral anti-coagulants (NOACs). Poster presented at: International Society for Pharmacoeconomics and Outcomes Research 22nd Annual International Meeting; May 20-24, 2017; Boston, MA.

2. Sarich TC, Seltzer JH, Berkowitz SD, et al. Novel oral anticoagulants and reversal agents: considerations for clinical development. *Am Heart J*. 2015;169(6):751-757. doi: 10.1016/j.ahj.2015.03.010.

3. Fernandez MM, Wang J, Ye X, et al. Systematic review and network meta-analysis of the relative efficacy and safety of edoxaban versus other nonvitamin K antagonist oral anticoagulants among patients with nonvalvular atrial fibrillation and CHADS2 score ≥2. *SAGE Open Med*. 2015;3:2050312115613350. doi: 10.1177/2050312115613350.

4. Seeger JD, Bykov K, Bartels DB, Huybrechts K, Zint K, Schneeweiss S. Safety and effectiveness of dabigatran and warfarin in routine care of patients with atrial fibrillation. *Thromb Haemost*. 2015;114(6):1277-1289. doi: 10.1160/TH15-06-0497.

5. Graham DJ, Reichman ME, Wernecke M, et al. Cardiovascular, bleeding, and mortality risks in elderly Medicare patients treated with dabigatran or warfarin for nonvalvular atrial fibrillation. *Circulation*. 2015;131(2):157-164. doi: 10.1161/CIRCULATIONAHA.114.012061.

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