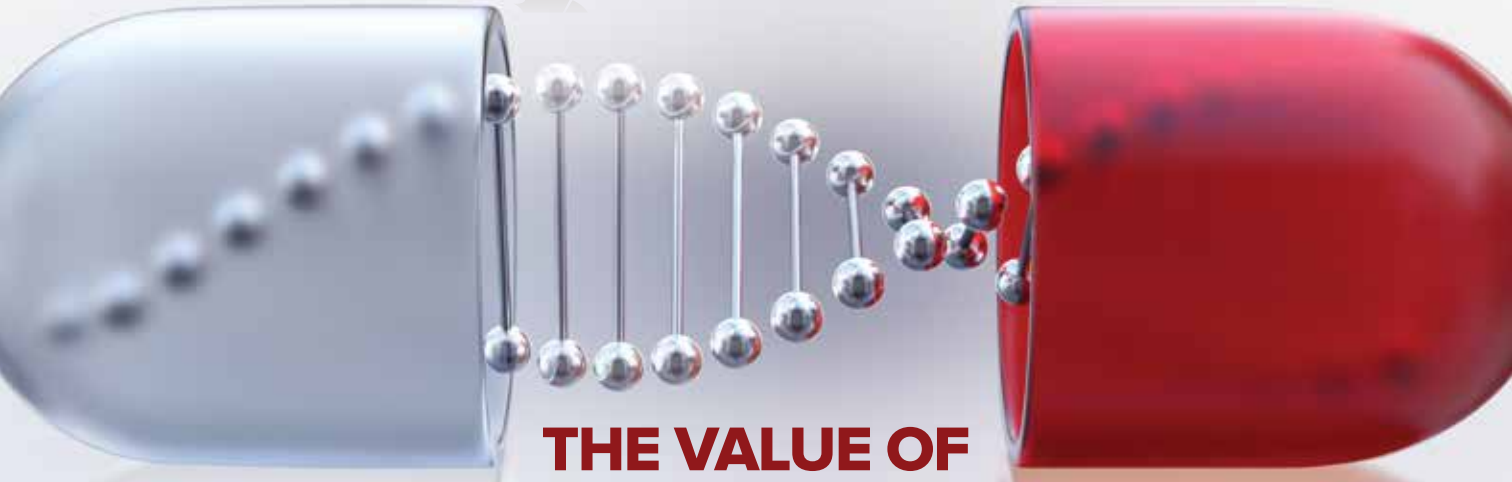


THE VALUE OF INNOVATION

How private payers can balance affordability and innovation

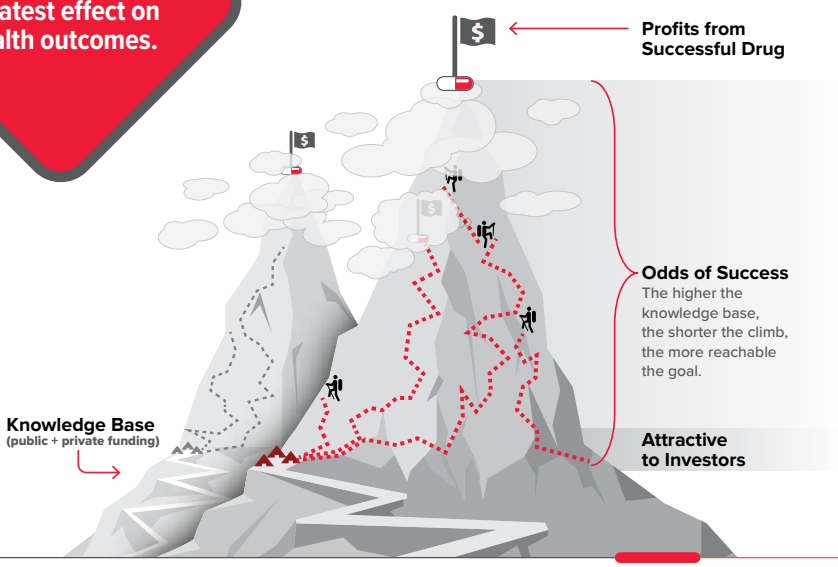
The 2022 Canadian Leadership Council on Drug Plan Partnerships brought together benefit plan advisors to discuss innovation in drug development and its impact on Canadian private drug plans. Although many drug innovations have been life-changing, plan advisors are concerned about the impact on their clients' benefit plans. Unfortunately, the lack of effective insurance often leaves plan sponsors no choice but to restrict or reduce coverage to manage their risk.

By Suzanne Lepage

Scientific advances have improved health outcomes and increased life expectancy and patient quality of life; however, a survey of physicians published in the *Journal of Managed Care and Specialty Pharmacy* noted that "pharmaceuticals have had the greatest effect on health outcomes, above and beyond new techniques and procedures," said Joe Farago, executive director, private payers and investment, Innovative Medicines Canada.

Pharmaceuticals have had the greatest effect on health outcomes.

"Investing in drug research and development is risky", said Peter Kolchinsky, biotechnology investor, scientist and founder of No Patient Left Behind. He offered an analogy that scientific knowledge is the base camp of a mountain. Investors fund many drug development programs. They are the climbers tackling the mountain trying to reach the flag at the peak, which is the reward for coming up with a successful therapeutic. The higher the climb, the longer the odds of success. "That flag at the top needs to be big enough so the expected revenues and profits justify the expensive, risky climb," said Kolchinsky.



THE BIOTECH SOCIAL CONTRACT

Kolchinsky suggested the concept of the biotech social contract, in which today's branded drugs will be generic within 10–15 years and "will add to our arsenal of high-value, low-cost generic medications. This promise forms the core of the contract between drug developers and society." The branded price is finite, he noted, whereas the value society will enjoy is infinite.

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"It's like paying a mortgage on a home," Kolchinsky explained. "It's more expensive than rent at first, but worth it in the long run." A borrower spends 15–30

https://www.nopatientleftbehind.org/

years paying off a mortgage, and although mortgage payments may be substantial, he noted, once the property is paid off, it is lived in rent free and can be passed down to children and grandchildren.

Compared to drugs, said Kolchinsky, doctors, surgeries and non-pharmaceutical treatments are like rent and will remain expensive forever. "We can only hope to prevent the need for these expensive services with inexpensive drugs," he said.

Some patients can't afford their out-of-pocket copay costs, Kolchinsky said. "I don't think that it's right to ask only the people who need treatments today to bear the cost of rewarding innovation that will benefit society for generations to come."

Biopharma innovators are builders that are rewarded with a finite mortgage paid by society, said Kolchinsky. After the mortgage is paid off, drugs continue to provide society with value long after they have gone generic.

PORTFOLIO MANAGEMENT IN DRUG DEVELOPMENT

Investors generally invest in a portfolio of projects across a variety of disease areas because only a few will be successful, noted Kolchinsky. Unfortunately, they won't know which of them is destined to be successful. "Ideally an investor wants to only go after the big winners, but that requires a crystal ball that nobody has."

Only a few projects may be those winners and generate considerable revenue, whereas others may be modest contributors that generate only sufficient revenue to cover their development costs. "If we clip the prices of the big winners," said Kolchinsky, "the whole portfolio becomes unattractive" and investors may reduce their investment in new drug research and development or choose to invest elsewhere. "We don't just lose the big winners," he continued, "we lose all the drugs that might have been developed in that portfolio." If investors conclude that the investment isn't worth it, "patients won't get new treatments. And by patients, I mean all of us," said Kolchinsky.

NEW COST-EFFECTIVENESS ANALYSIS

Some health economists have said there's a lot of different values to consider when assessing the cost effectiveness of a drug, said Kolchinsky. For example, they don't just help the patients get better, they may also allow their caregivers to be more productive.

"The trouble is that conventional cost-effectiveness models do not take this societal perspective into consideration," he said. They also don't consider that the drug will eventually go generic or face biosimilar competition, which will drive down prices.

The value of a medications is much higher than their list price, just like the value of the home is greater than the mortgage payments.

To understand a drug's true value, Kolchinksy suggested that assessments consider each person that it will help as a branded drug in the present and as a generic in the future. "If we were to add up the benefits that these drugs continue to generate, even once they are generic," he explained, and credit them back at that point of invention, "we would see that they were really a lot more worth inventing than we gave them credit for when we judged them only by their price when they first launched."

"The value of medications is much higher than their list price, just like the value of the home is greater than the mortgage payments," he noted.

MULTIPLE TREATMENTS FOR ONE CONDITION MEET PATIENTS' DIVERSE NEEDS

When we suddenly get many new treatments for one condition, said Kolchinsky, "we may wonder what are the odds that they all came to market at about the same time?"

If we look back, he explained, sometimes a decade or more, there was a starting line, such as the discovery of a particular new concept or the development of a new animal model or scientific discovery that made it possible for developers to start making their way up the mountain. As years went by, developers were doing clinical trials and racing for that flag at the peak.

If we paused at a given point in time, there would be several drugs in different phases of development. "At that point, we wouldn't be able to identify which one is going to be the first to market and which ones might be me-too drugs," said Kolchinsky. They all thought that they could be better than the other drugs. Some might look like they're the best, to the point that maybe all others should concede defeat. Yet, according to Kolchinsky, some will fail and fall off the mountain and potentially someone else had the better drug.

When similar drugs come to market at the same time, it doesn't increase the cost to society because the number of patients who need treatment and the unmet need were already there.

All of them were innovative before they were approved, he noted, but one company gets to market first. "They all hustled to make it to the top of the mountain," but whoever was first got the credit for introducing the world to the great breakthrough.

The Patented Medicine Prices Review Board (PMPRB) refers to many new drugs as having slight or no improvement over the first in a class; however, according to Farago, "That's a bit of a misrepresentation." For example, if a new product is a cure for a disease where there previously had been no cure, this drug may receive breakthrough status. However, every subsequent drug that's also a cure for this same disease may then be classified as having slight or no improvement over the first drug in the class, even though it's also a cure.

When similar drugs come to market at the same time, Kolchinsky said, it doesn't increase the cost to society because the number of patients who need treatment and the unmet need were already there.

When there are multiple treatments for one condition, they are often not identical by design, he said. To justify continuing to pursue the development of a drug when others are ahead, investors will focus on the residual unmet need to get into the market. The first in class is not always the best in class, said Farago, because there continues to be incremental innovation in new treatments that are brought to market.

This is an opportunity to play the companies off one another and save money.

Drugs don't always work the same way for everyone. Differences in individual genetic makeup can lead to variability in treatment response, which is why there is a need for a variety of treatment options for a condition.

Additional drugs may offer improved outcomes due to improved target specificity or reduced side effects and drug interactions, said Farago. Some products improve dosing, which may increase compliance. He also noted that for many conditions, the first drug doesn't always work, so there needs to be additional therapeutic alternatives.

"We also need more drugs to deal with potential drug supply shortages," said Farago. "If you recall during the pandemic, there was a real fear about shortages." If only one or two drugs are on the market for a condition and those are in short supply, that doesn't leave many options for patients.

This is an opportunity, noted Kolchinksy, to play the companies off one another and save money. Prices often drop significantly in competition for market share. "You don't need price controls when you've got this kind of competition."

"Covering multiple treatments is not going to cost more," said Kolchinsky. Payers can choose a preferred drug by seeing which manufacturer will give the best price. They can make that drug the first-line treatment and when a person's not benefiting from that drug anymore, the payer can give them access to another therapy.

"Approving multiple treatments is not going to increase the number of people with the condition," said Kolchinsky. Patients can generally be treated with only one drug at a time, and many drugs are not intended be given on top of another drug.

When a patient doesn't benefit from the covered drugs and there aren't any alternatives, then the cost is an untreated or inadequately treated plan member. Kolchinsky noted, "Plans aren't saving money, it's simply a different cost being incurred."

If a plan covers multiple drugs in the same class, it can treat people who previously would have had no treatment or people for whom the first few lines of therapy would have failed and whose condition would have kept progressing. "There are benefits to these additional treatments for people who need them," said Kolchinsky.

BALANCING INNOVATION AND AFFORDABILITY

The council members said that although they see the value of innovative medications, it's often not about the value; rather, it's the affordability for plan sponsors. Reimbursement becomes a budgetary problem and a risk-management challenge because of the perceived lack of effective insurance and risk pooling for high-cost drugs for Canadian plan sponsors.

"Drug manufacturers have created a lot of innovation; the problem is the speed of drug innovation has outpaced the speed of innovative reimbursement," said Farago. What are some innovative solutions that don't just restrict access for new drugs? "Sometimes the benefits industry is a little afraid of the innovation, said Paul Crossdale, CEO and president, benefitsConnect Inc. "I think we need to show less fear and continue with the innovation in our marketplace."

The speed of drug innovation has outpaced the speed of innovative reimbursement.

"I don't think anybody argues that drug innovations have been life-changing for patients," said Farago. "If you or a family member had one of these conditions, you'd want the most effective treatment."

"My grandfather had very bad Parkinson's and he suffered dearly," said Bianca Krimberg, senior advisor, Health Benefit Trust of Alberta, Alberta Health Services. She noted the advances in research and innovation being done for Parkinson's and wished that her grandfather would have been able to have access to them.

"I know somebody who required a $2 million drug that treats an incredibly horrible condition," said Jason Faulkner, consultant, Advocate Benefits Inc. He asked, "How's that going to get to the market without a

How can the industry pool risk so that these valuable new treatments can benefit everyone?

true insurance model? How do they or their employer's benefit plan pay for them?"

Canadian plan sponsors don't think they can afford new drugs and remain sustainable, and they find the existing insurance and pooling models lacking.

"I have been involved in a case with a drug claim exceeding $700,000 per year," said Tim Foster, consultant, Luedey Consultants Inc. That impacted the plan financially and limited options to market the plan. "The question is, if they keep paying for this drug, will they need to cut benefits for the rest of their members?" Foster asked, "How can the industry pool risk so that these valuable new treatments can benefit everyone?"

"I don't feel that the average employer has access to a real insurance plan that allows those sorts of products to be contemplated in their benefits package," said Faulkner.

Elaine Yedlin, COO, corporate benefits, Johnston Shaw Inc., felt that "there is really no transparency in Canadian stop-loss programs, and an EP3 [extended health policy protection plan] doesn't help plan sponsors control their costs or help with the underlying pools."

Kolchinsky said there is a need for better insurance models to make drugs affordable to all who need them. "Insurance works best when it's applied across a very large population."

"Some orphan drugs that are particularly expensive are threatening because of the incredible risk that a plan may have a patient who needs one," he noted.

Kolchinsky asked, "Is there a better model that would allow them to share that risk and get the benefits of large numbers?" He proposed that an ideal model would cost very little per plan member to offer them the benefit of peace of mind of knowing "that if they or a family member have one of these conditions, they'll get the treatment they need."

The council agreed that there is a need for a different model in Canada for insurance and pooling.

The overall growth of drugs has been about 5% across the entire private market, noted Farago, "and that's manageable. What's unmanageable are smaller plans when they win the lottery and get a high-cost drug claim."

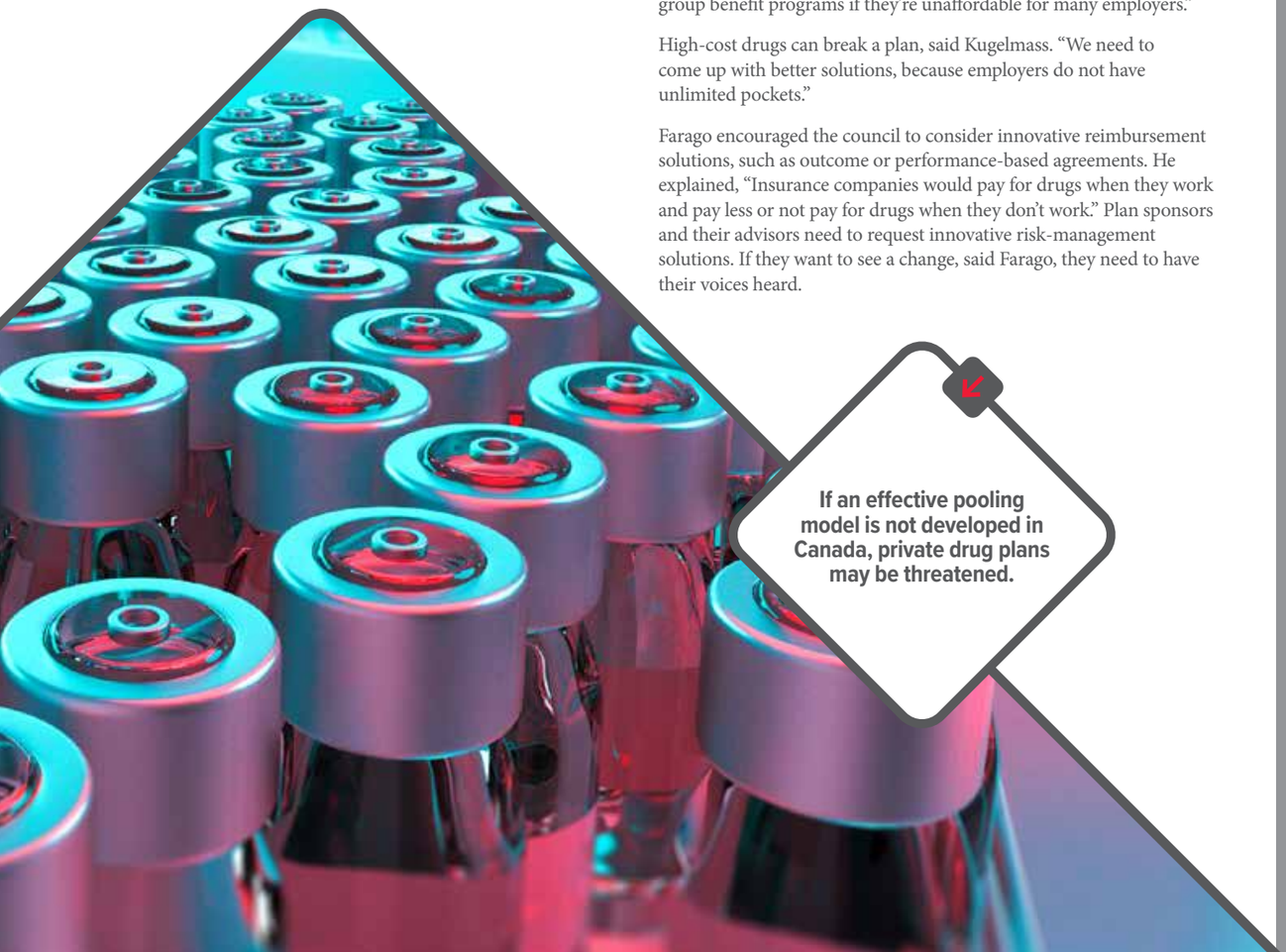
Some advisors suggested that the US has a better-stop loss market. Plans can shop stop-loss, said Yedlin, and have their benefits with one provider, then find a different provider to meet their stop-loss insurance needs.

Some expressed concern that if an effective pooling model is not developed in Canada, private drug plans may be threatened. Unless we can work toward true transparency with stop-loss pooling arrangements, said Caroline Kugelmass, owner, Excel Benefit Consulting Inc., "We're going to have no choice but to move to more of an American model with high deductibles and maximums because plan sponsors are not going to continue to pay these costs."

Employer-sponsored benefit programs "were never intended to pay for these kinds of treatments," said Laura Cabral, consultant, Eckler Ltd. "Something is going to suffer, and it could be the disappearance of group benefit programs if they're unaffordable for many employers."

High-cost drugs can break a plan, said Kugelmass. "We need to come up with better solutions, because employers do not have unlimited pockets."

Farago encouraged the council to consider innovative reimbursement solutions, such as outcome or performance-based agreements. He explained, "Insurance companies would pay for drugs when they work and pay less or not pay for drugs when they don't work." Plan sponsors and their advisors need to request innovative risk-management solutions. If they want to see a change, said Farago, they need to have their voices heard.



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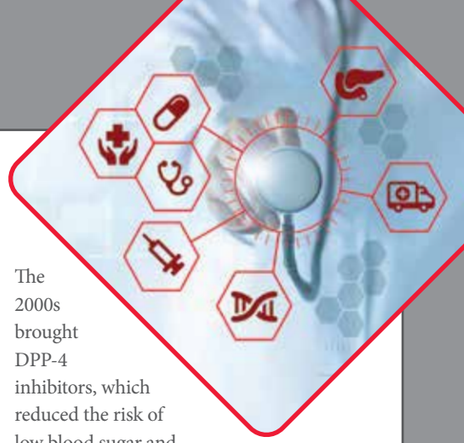
INNOVATION IN ACTION



Incremental innovation in type 2 diabetes grows alongside disease knowledge

Type 2 diabetes accounts for 90% of Canadian diabetes cases, according to Godfrey Mau, senior patient access manager at Novo Nordisk.

It is characterized by high blood sugar, which is detected by an elevated HbA1c, which is an average of blood glucose levels over the previous three months and is used to manage diabetes. The target value of less than 7% is recommended by the Diabetes Canada Clinical Practice Guidelines to avoid long-term complications; however, according to Mau, it is estimated that over 40% of Canadians living with type 2 diabetes are not achieving this target, which underscores the need for additional treatments.

"It's important to get to target quickly," said Mau. The guidelines recommend that patients hit the 7% target within three to six months, because for every year that blood sugars are elevated, there is an increased risk and incidence of complications, which include cardiovascular, kidney and eye disease.

The evolution of the treatment for type 2 diabetes, explained Mau, demonstrates innovation that aligns with the growing medical understanding of the condition. For example, we now know that type 2 diabetes impacts multiple organ systems within the body – from the brain and how it regulates appetite to the kidneys and their role in regulating glucose levels. With this knowledge, researchers have been able to develop newer treatment options, which can modify the disease. Each of these treatment classes work differently and have different side effect profiles.

In the 1970s, metformin was one of the first noninsulin treatment options for type 2 diabetes. It is good at blood glucose lowering and is still recognized as a first-line treatment option.

However, diabetes is a progressive condition, noted Mau, and as time goes on, patients will need additional medications to manage their condition.

In the 1990s, the introduction of a new class, sulfonylureas, offered blood glucose control but had potential risks of low blood sugar (hypoglycemia) and weight gain, which could negatively impact patient adherence.

The 2000s brought DPP-4 inhibitors, which reduced the risk of low blood sugar and weight gain as side effects but are not as effective as metformin and sulfonylureas in reducing blood glucose.

The 2010s saw the introduction of two new classes, SGLT-2 inhibitors and GLP-1 receptor agonists, both of which provide strong A1C reduction, minimal risk of low blood sugar and weight loss as a side effect, which could improve patient adherence.

As this evolution continues, said Mau, "We are starting to recognize type 2 diabetes as a cardiometabolic disease and we now have drugs that not only control blood sugar, but have an impact on comorbidities and a reduction of cardiovascular and kidney risk. These new drugs are wrapped up in relatively easy modes of administration such as daily pills, once-weekly injections, or a drug available in an oral form that had previously been given as an injection."

Discovery of gene spurred innovation in treatment of metastatic breast cancer

Five percent of the estimated 28,000 new breast cancer cases in Canada are diagnosed as advanced or metastatic, where the cancer has spread to other organs, such as the lungs, liver or brain, and to the bones, said Priscilla Nykoliation, senior manager, payer engagement and strategic partnerships, private market, AstraZeneca Canada. Unfortunately, 30% to 40% of early breast cancer patients will also advance to metastatic breast cancer.

Different cancers have different treatment regimens, said Nykoliation, and although there are more limited options for metastatic breast cancer, "We've seen some great incremental innovation due to the advances made in science and research."

Approximately 14% of metastatic breast cancer tumours are HER2-positive, which tend to grow and spread more aggressively than HER2-negative tumours. Although metastatic breast cancer is not curable, according to Nykoliation, HER2-targeted therapies have substantially improved patients' survival outcomes.

Innovation began in the 1980s when scientists discovered the HER2 gene, a driver of metastatic breast cancer, said Nykoliation. In the late 1990s, the introduction of a monoclonal antibody for HER2-positive metastatic breast cancer led to increased survival rates.

Subsequent research and development led to the first antibody drug conjugate in 2013, with a unique mechanism that targeted cancer cells. Unfortunately, said Nykoliation, it also attacked healthy cells, and although a

patient's cancer was treated, their overall health would deteriorate.

This treatment, explained Nykoliation, served as a building block for the introduction of a more sophisticated antibody drug conjugate that solely targets cancer cells and improves the side effect profile and tolerability of the treatment.

It was the discovery of the HER2 gene and the first monoclonal antibody treatment that drove innovation that led to the discovery of treatments that are more potent, targeted and tolerable for patients. Nykoliation said, "The introduction of antibody therapies has transformed the lives of HER2-positive patients with metastatic breast cancer."

These innovative therapies to treat metastatic breast cancer are administered intravenously. Based on insights from private payers, such as insurers, they are considered hospital drugs and therefore have limited to no access on private health benefit plans. In fact, these therapies, explained Nykoliation, are predominantly administered in private clinics at least until public reimbursement is achieved. Because this type of cancer typically affects a younger patient population that is in the workforce, it would be beneficial if private health benefit policies would be updated so that plan members have access to infused cancer medication options.

Evolution in IBD treatment objectives offer improved outcomes

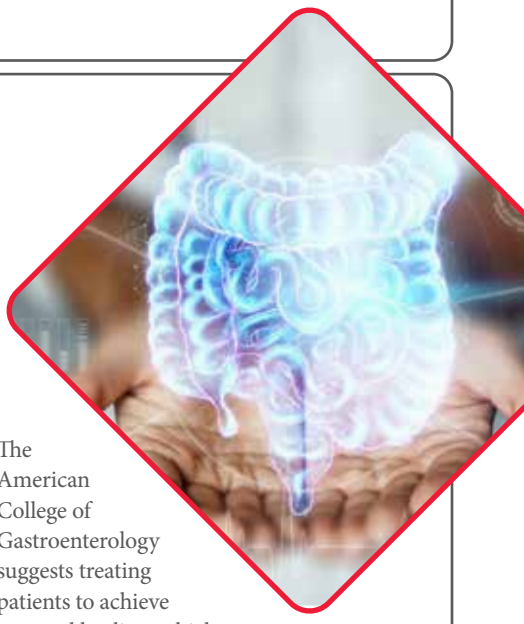
Inflammatory bowel disease (IBD) is a group of disorders that causes inflammation, pain and swelling in the intestines and includes Crohn's disease and ulcerative colitis, explained Marx Ruiz-Wilson, market access and HEOR manager, immunology, AbbVie. IBD is usually diagnosed between 15 and 30 years of age and is a condition patients live with for the rest of their lives.

Patients may have to go to the bathroom 20 times per day and often experience rectal bleeding, fatigue, diarrhea and vomiting, he said. They have high rates of hospitalizations and surgeries and face an increased risk of colon cancer. These conditions can make a patient feel isolated and induce anxiety. On average, patients miss 16.1% of work time and experience work impairment 34.8% of the time they are at work.

"Treatment objectives for IBD have evolved over time, as medical understanding of IBD has grown and drug development has evolved," noted Ruiz-Wilson. Historically, IBD treatment goals focused on controlling symptoms. Although steroids were effective to treat symptoms, they came with unwanted side effects.

As treatments evolved, the objective became remission. Early biologics provided antibody treatments that gave way to clinical remission; however, steroids continued to be a part the treatment. Fortunately, said Ruiz-Wilson, the next generation of biologics offered steroid-free remission.

Mucosal healing, the complete absence of any mucosal ulcerations in the patient's ileum or colon, is now recognized as a long-term treatment goal, said Ruiz-Wilson.



The American College of Gastroenterology suggests treating patients to achieve mucosal healing, which will increase the likelihood of sustained steroid-free remission, prevent surgery and hospitalizations, and offer patients a higher quality of life. "New medications will need to demonstrate effectiveness in achieving mucosal healing, which is now the gold standard in IBD treatment," he said.