evaluatingdrugs: Apples vs ranges

By Suzanne Lepage

WHY DO some formularies cover a certain drug while other formularies do not? Don't all formulary managers review the same scientific evidence to evaluate drugs? Why don't they arrive at the same coverage decision? Most payers need a way to compare similar drugs and establish their relative value. If a drug claims to be superior, how can they determine if it is incrementally better than current therapies? How can they assess if additional costs of the new drug are justifiable vis-a-vis the reported benefits? These questions spur payers to develop methodologies to compare similar treatments.

Some studies evaluate efficacy rather than effectiveness. Efficacy reflects the degree to which the use of a drug produces a predefined benefit under carefully controlled conditions imposed by the inclusion and exclusion criteria of a clinical trial. These studies are randomized controlled trials (RCT) and are typically conducted to address safety and efficacy and meet the standards established by regulatory agencies such as Health Canada to receive marketing authorization. In contrast, effectiveness research measures the observed benefits and harms of drugs in real-world clinical settings and broader populations. Comparative effectiveness research (CER) compares a drug against its commonly used alternatives rather than against a placebo. Until CER is fully implemented in Canada, researchers are limited to comparing the effects of drugs indirectly using various statistical methods.

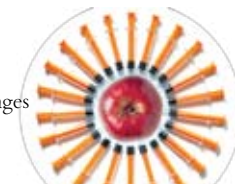
These two methodologies are analogous to the types of research available to consumers when purchasing a car. On the one hand, there are safety studies performed by car manufacturers to get approval from Transport Canada (comparable to RCT on drugs). Then there are reports from Consumer Report, Lemon Aid and Edmunds Report in which real-world drivers and experts rank the car (similar to CER).

CER is needed because the evidence generated by RCTs is often insufficient to support coverage and reimbursement decisions. Although RCTs are considered to be the gold standard of scientific evidence, they have some limitations: RCTs are conducted in an "ideal" patient which often does not represent the "average" or general patient population and may not help when making decisions for an "average" patient. An RCT may not tell us which patients will benefit most from the treatment. Moreover, an RCT does not demonstrate whether the drug is better at treating particular conditions than other drugs or if the drug is more cost effective than another drug.

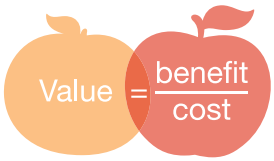
"There are many different ways to assess research like RCTs," says Mike Sullivan, president of Cubic Health, an analytics and drug plan management company. "It's not black and white. "There can be grey areas in interpreting that information." As a result, there might be a gap in what one group of researchers might conclude versus another."

There is no widespread agreement on comparative effectiveness. Comparisons between drugs are not simple because determining the value depends on the perspective of the evaluator.

The least expensive alternative is not always the most economical and may not produce an optimal outcome for both the patient and



the drug plan (see case study: Value is relative). Evaluating value as an economic calculation often depends on what we include in the formula. If you consider that value can be derived by assessing the benefit versus the cost, then the value will vary significantly depending on what factors you include in your benefit-and-cost calculations.



"There are limitations with the way drugs are currently evaluated by private drug plans," says Dr. Neil MacKinnon, a professor at the College of Pharmacy and Faculty of Medicine at Dalhousie University who researches drug benefit management and reviews drug submissions for a Canadian private drug plan. "Private formulary committees have access to good RCTs that compare new drugs against placebos, but then they are left on their own to determine how a new drug compares against existing products. That is the promise of CER: real world studies that compare effectiveness versus efficacy. A drug may work very well in a controlled trial, but how does it perform in the real world?"

"An RCT does not necessarily reflect the population that has the disease, because there are protocols that limit who can be included in the study, and those who qualify must follow a regimented treatment," explains Dr. Carter Thorne, a Newmarket, Ont., rheumatologist and director of The Arthritis Program, a unique inter/trans-disciplinary program to optimize outcomes for people who have arthritis and other rheumatic disorders. Research done by Dr. Thorne demonstrated this disconnect between RCT protocols and patients: only 18 percent of real world early rheumatoid arthritis patients would have met the criteria to be included in RCTs.[1]

One might think that it would be easy for private formulary managers to look to government drug plan decisions to guide their formulary management. One commonly referenced source is The Canadian Agency for Drugs and Technologies in Health (CADTH).[2] CADTH is a not-for-profit agency funded by Canadian federal, provincial and territorial governments to provide information about the effectiveness of drugs and other health technologies to Canadian public healthcare decision-makers. CADTH offers three main programs: Health Technology Assessment (HTA), which assesses drugs and health technologies; Common Drug Review (CDR), which conducts drug reviews and provides formulary listing recommendations; and Canadian Optimal Medication Prescribing and Utilization Service (COMPUS), which identifies and promotes optimal drug therapy. The challenge for private plans referencing CADTH is that its mandate is to provide support to Canadian government healthcare decision-makers. The principles used to manage a provincial formulary, often designed for seniors or low-income residents, are very different than those used for a private drug plan, which are intended to protect an active working population.

For example, CADTH recently conducted a therapeutic review pilot project to evaluate the comparative

case study:

Value is relative

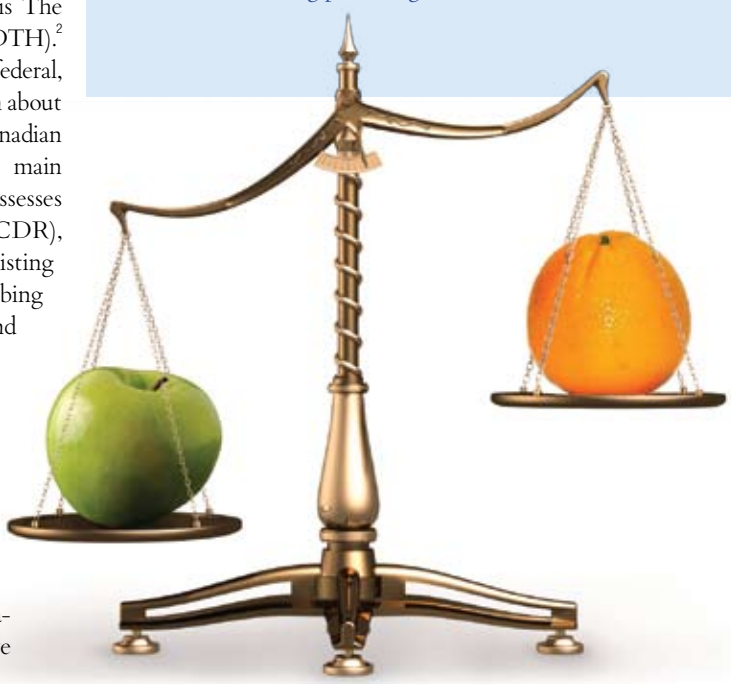
Consider a situation in which two treatments are available for a particular condition. Both are identical in safety and efficacy. One treatment is an intravenous (IV) infusion that would be delivered in hospital. The other is an oral medication that can be taken at home.

How would different stakeholders value each treatment?

- The patient may prefer to receive the treatment at home rather than being hospitalized, since it would be more convenient and less intrusive.
- The physician may prefer to see the patient treated in hospital, allowing for easier monitoring for complications.
- The hospital may prefer to have the treatment taken at home to reduce pressure on hospital resources.

How would these values change if the IV infusion is funded by the hospital and the oral medication is not?

- A low income single parent with no insurance may prefer the IV hospital treatment because it does not require out-of-pocket payment.
- A busy executive may prefer the oral treatment because it can be taken at home without having to squeeze hospital visits into a busy schedule. In addition, this individual may be able to afford to pay for the treatment out of pocket or may have a private drug plan that will cover the cost.
- The private drug plan manager might prefer the IV hospital treatment versus funding the treatment out of their drug plan budget.
- The hospital or public drug plan manager may prefer to have the treatment taken at home versus funding the treatment out of their drug plan budget.



effectiveness, harms and cost-effectiveness of biological response modifier agents for adults with rheumatoid arthritis.

"The CADTH report only considered clinical trials," explains Dr. Thorne, "and unfortunately clinical trials don't reflect all types of patients or situations we treat. Often specialists will have to use good clinical judgment to select the appropriate treatment based on real-world experience with medications."

Although RCTs can demonstrate that some drugs may have similar outcomes, real-world use of a drug often identifies important factors, such as dose escalation, which are not included in the RCT data but appear to be happening in actual practice. "This is why evaluating the impact of drugs can be quite complex," says Sullivan.

"CADTH reports are tailored with a public payer end user in mind," says Dr. MacKinnon. "When asking the question, 'Is this drug cost effective?' CADTH may consider the impact on hospitalizations and the healthcare system. They are not looking at things like workplace productivity and absenteeism that might be of more interest to private payers.

"Reports prepared for consideration by government drug plans, such as the CADTH therapeutic review, are one of many sources of information that private plans can consult," continues Dr. MacKinnon. He suggests that when private formularies consult external or government reports to evaluate drugs, they should consider the following:

1. Who conducted the research? Who is the study's intended end user? Do they value the same thing you value?
2. What costs are included? Are these costs relevant to you?
3. What benefits are considered? Are these benefits for you?

Looking south

WellPoint, a leading U.S. health benefits company, uses clinical efficacy and clinical effectiveness real-world data to make formulary decisions. "At WellPoint we recognize that there are circumstances in which RCTs may not be sufficient alone for decision-making and that CER data may complement RCT data by providing data on outcomes achieved in a real-world setting," says Jeff White, director, Drug Evaluation and Clinical Analytics.

WellPoint's goal is to improve clinical health outcomes, quality of life and productivity, and reduce total cost of care. "A more expensive medication can be less expensive overall if the member's health is improved," says White. For example, WellPoint discovered that by assessing outcomes for medications for chronic obstructive pulmonary disease, the drug with the highest price tag was actually the most cost effective for the plan to cover.

Analyzing your own drug plan data

"Drugs are only one piece of the puzzle," says Linda Lines, vice-president of external relations with IMS Brogan, a leading Canadian pharmaceutical consulting and research firm. "They are a good place to start, but ideally plan sponsors should also consider other health benefits, disability and absenteeism to better understand their benefit plan usage and compare costs to outcomes."

promising

developments in CER in Canada....

The Drug Safety and Effectiveness Network (DSEN) was established by the federal government in 2007 to increase availability of evidence on drug safety and effectiveness to regulators, policymakers, healthcare providers and patients and to increase capacity within Canada to undertake high-quality post-market research in this area. The Canadian government is investing a total of $32 million over five years and $10 million per year ongoing.[3]

The Ontario Biologics Research Initiative (OBRI) was developed in 2005 through the cooperative efforts of patients, rheumatologists and researchers to help improve the treatment and outcomes of Ontarians living with rheumatoid arthritis (RA). The OBRI mission is to improve the quality of care and clinical outcomes of RA patients by gathering long-term information on the therapies used in the treatment of a wide cross section of people in usual day-to-day circumstances.[4]

RAPPORT (Rheumatoid Arthritis Pharmacovigiliance Program and Outcomes Research in Therapeutics) conducts post-approval surveillance and outcomes assessment of biologic drugs in partnership with Alberta Health and Wellness, Alberta Health Services, the Institute of Pharmaco-Economics, and the pharmaceutical industry. Approximately 8,000 Albertans receive care through this program and examples of successful outcomes are: 70% increase in quality of life, 40% reduction in orthopaedic surgery, 50% reduction in doctor visits, 70% improvement of work productivity, and 40% reduction in sick leave.[5]

Sullivan concurs: "At the end of day, the only real-world data that matters to an employer is their own absence and disability and drug-spend portfolio. "Until a plan sponsor integrates these data sets, they cannot measure the value of the outcomes or assess effectiveness in their own environment."

When comparing the relative cost of medications, there is much more than the price tag to look at. "What is required is the actual cost to treat a patient, and there are many challenges in standardizing data to ensure you have comparable values," says Lines. Since biologics often have multiple indications, drug spend should be isolated by indication, which can often be determined by other medications taken by the patient.

It is also important to understand how drugs are used before you evaluate them. For example, a new drug therapy may be used quite frequently in the first year and then less often in subsequent years. Another drug in the same therapy class may be used more evenly over the same period. As a result, if you look at only one calendar year to compare these drugs, you may not get an accurate picture of their relative costs. "Ideally, you'd like to look back over a five-year period to annualize the cost of a drug," says Lines.

Sullivan agrees: "There is a systemic problem if plan sponsors don't look at the big picture over a long enough time frame. A plan sponsor who only analyzes their current renewal year instead of two to four years of data will not be able to identify meaningful drug trends."

Lines reminds plan sponsors, "once you understand your own data, it is important to benchmark your data to see how you compare to industry norms."

In addition, plan sponsors should not be too quick to pat themselves on the back if they reduce drug costs. "Lower drug costs may not always be a good thing – it could be a sign of poor adherence," says Lines. Sullivan, too, emphasizes the importance of adherence to therapy: "Why would anyone invest $100 in a new drug if the employee is not going to take it or use it appropriately? There is actually no value, and you would have been better off lighting that $100 bill on fire."

Best practices: Drug submissions and evaluations

There is currently no best practice for drug submission dossier format or methods to evaluate drugs for private plans in Canada. "Very few new drug submissions that I receive for a private payer in Canada are tailored to private plans," says Dr. MacKinnon. "There is an opportunity for private payers to get together, even if they are competitors, and define what they want to see in submissions and economic calculations from pharmaceutical companies."

There are a few examples of standardized assessments from the United States. WellPoint believes in a transparent drug coverage evaluation process and is the first health benefits company to publish its health technology assessment guidelines and standardized comparative effectiveness research guidelines to provide guidance to pharmaceutical companies looking to offer meaningful information to health benefits companies.

Similarly, the Academy of Managed Care Pharmacy (AMCP) developed the AMCP Format for Formulary Submissions in October 2000. It is intended as a template for pharmaceutical manufacturers' submissions of drug products for consideration by managed care organizations and establishes a standardized process of evaluation on the basis of sound scientific evidence. Dr. MacKinnon is eager to see something similar in Canada. "It would ensure the data coming is in a common format, so you are comparing apples to apples."

Although formulary managers may review the same scientific evidence to evaluate drugs, they may not arrive at the same coverage decision. There are many other considerations that can influence drug evaluation decisions, such as the way managers assess cost, value, benefit, efficacy and effectiveness. Depending on the perspective, expertise, evidence, tools and data used by each formulary manager, the outcome of the evaluation can differ significantly. ■

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