The INSIDE STORY®

APRIL 2018

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COMPLETELY INDIFFERENT

PHARMACOGENOMICS:

PROMISE, POTENTIAL, POSSIBILITIES

NOW ALL WE NEED IS THE PROOF!

Pharmacogenomics definitely has promise, potential, and possibilities—that's why it's been on GSC's radar for years. *But…* we don't want to prematurely jump on the pharmacogenomics bandwagon. We need to look before we leap by ensuring that its use is backed by solid scientific evidence. In fact, we're even adding to the body of evidence with a new study of our own. And not just any study, a study that will fill a critical gap in the existing research. Here's the scoop…

There's the promise…
And then there's the reality – the scientific reality

There's no doubt, drug therapy is often an important part of treating health conditions. And finding the right drug at the right dose can certainly be a challenge that takes time and risks harmful side-effects. Accordingly, the promise of pharmacogenomics as a way to potentially bypass drugs that don't work and go right to the most effective option is definitely alluring.

PHARMACO-WHAT?

As you may recall from the July/August 2016 edition of *The Inside Story*…

The goal of pharmacogenomics is to guide prescribing decisions so that patients receive the most optimal drug treatment. It aims to answer the question: Does the plan member have certain genetic mutations that are known to influence their response to a drug in a certain way?

The idea is that variations in a patient's genetic profile can help determine how the patient will respond to certain medications. Based on the patient's genetic profile—revealed by a genetic test—doctors and pharmacists can potentially use the results to choose medications better suited to each individual patient.

So pharmacogenomics is specifically about determining medication tolerance and effectiveness—it is distinct from other types of genetic testing such as identifying genetic mutations that increase the risk of developing health issues that have a genetic basis or confirming a disease diagnosis when a certain health condition is suspected based on physical symptoms.

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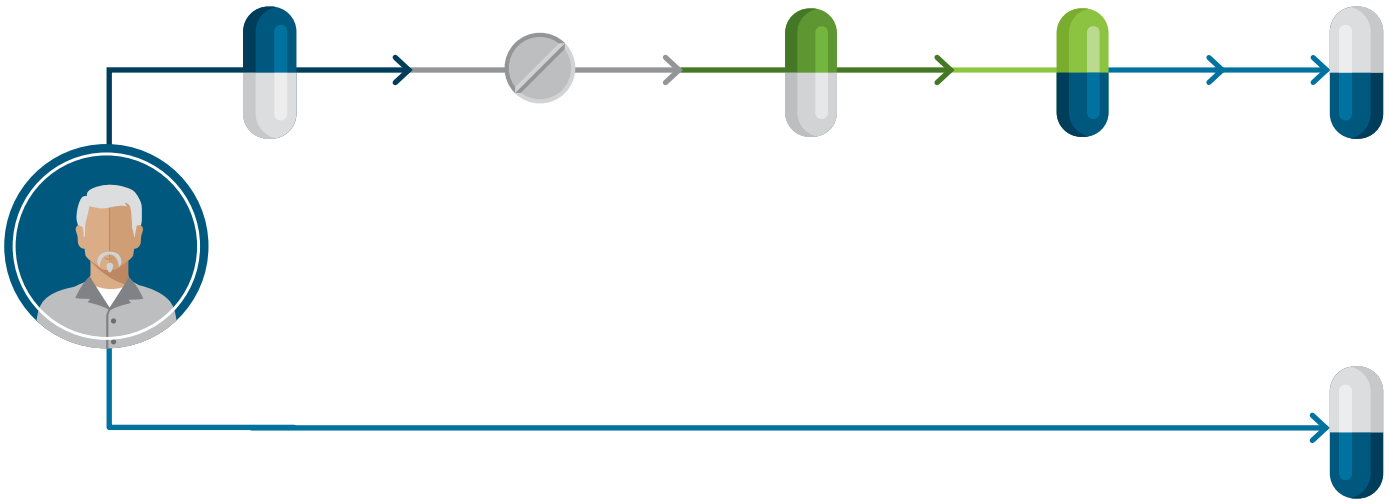
> **JUST IMAGINE BEING ABLE TO DISCOVER IN ADVANCE WHICH DRUG A PLAN MEMBER WILL RESPOND TO...**



Just imagine being able to discover *in advance* which drug a plan member will respond to... and what the right dose is… and avoid harmful side-effects… and prevent waste? In addition to having an impact on plan member health, in theory pharmacogenomics could also impact benefits plans. Definitely pharmacogenomics is something we need to keep a close eye on and approach with an open mind—but an open mind that is fueled by science.

A review of the scientific evidence around pharmacogenomics reveals a range of issues. The least of which is that there simply isn't a lot of research to draw on. And of the research that does exist—as well as some research in progress—there could potentially be bias depending on the organizations involved. In addition, although some pilot projects are already underway, it's not clear yet whether pharmacogenomics testing has a positive effect on patient outcomes or not. And without that, what we have been seeing in the flood of articles and presentations in our industry may be more hype, and hope, over real-world evidence. We need higher-quality research.

For example, a high-quality process-oriented study (and award-winning!) is the Canadian study—*The Innovative Canadian Pharmacogenomic Screening Initiative in Community Pharmacy (ICANPIC) study*.[1] It found that not only are community pharmacists receptive to adopting pharmacogenomics screening into practice, but they also have the skills to interpret pharmacogenomics results and intervene to try to improve patient outcomes.

We had a chance to touch base with the study author, and community pharmacist, John Papastergiou, who explained the findings. "After reviewing the study participants' pharmacogenomics testing reports, the pharmacists identified clinically significant drug therapy problems and forwarded recommendations for optimizing medications to the study participants' doctors."

This paves the way for future research to shift gears away from a focus on process issues toward a focus on whether pharmacogenomics influence patient outcomes. As John explains, "this study shows that it is viable for pharmacists to use pharmacogenomics testing to intervene in patient care in the community pharmacy setting. So new research needs to take the discussion to the next level; it needs to focus on whether intervention based on pharmacogenomics testing makes a difference in terms of patient outcomes."

It's clear that there is a gap in the research. In fact, a big gaping hole regarding the inherent value of pharmacogenomics in influencing patient outcomes. Time to fill the gap!

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RANDOMIZED CONTROLLED TRIALS MEAN GOING FOR GOLD

Of course, no surprise here that GSC believes—like most scientists, researchers, and clinicians—that decision-making that relies on the best available evidence is ideal. But how do we know what the best available evidence is? How do we know what the gold standard is? We can assess the available evidence by placing research studies into what is known in the research world as a hierarchy of evidence.

There isn't one universally agreed-upon hierarchy as some include more detail in terms of the number of levels and/or the types of studies that fall within each level. However, there is broad agreement that systematic reviews and randomized controlled trials fall in the highest levels. This is because they use methodologies that most effectively protect against bias and in some cases, may show a causal link between the intervention and the clinical outcome.

By contrast, case studies and expert opinions are often considered as falling in the lowest levels. This is because they can be biased by the author's opinions or experience and there is no control of any number of factors that could influence the results.[2]

Going for gold…
The gold standard in evidence

As you know we're always talking (OK, nagging and insisting) about the importance of basing coverage decisions on high-quality scientific evidence. But we don't just talk-the-talk, we also walk-the-walk by not just reviewing research, but also by doing actual studies as Ned Pojskic, GSC's pharmacy strategy leader, explains:

"While monitoring the emerging evidence, we are encouraged by the pilot projects going on out there because this type of testing will contribute to the overall body of evidence. However, these pilots will not conclusively answer the fundamental question around the inherent value of pharmacogenomics testing. This is because, as helpful as pilots are, they are geared to investigating operational aspects like implementation best practices. Although those running pilots will often say that, as part of the pilot, they will investigate what happens, they are not structured to achieve this.

"By contrast, to conclusively answer the value question requires a study design that is considered the gold standard in scientific research—a randomized controlled trial. So that's where GSC is jumping in with our new study that aims to answer the fundamental question: Does intervening with pharmacogenomics testing affect patient outcomes?"

Since John Papastergiou's ICANPIC study demonstrated that community-based pharmacies are ideally suited to leveraging pharmacogenomics testing, the pharmacy setting is exactly where we are setting up our new study. It is being run out of two large, urban, high-volume pharmacies in downtown Toronto meaning the study results will reflect the use of pharmacogenomics in a real-world setting—pharmacies with large customer bases and broad demographics. And of course, we're going for the gold standard…

Randomized – Blinded – Long term

Here's how it works… First, the pharmacists enrol study participants based on a screening questionnaire that asks about their satisfaction with their current medication. John shared with us the importance of having a screening tool. "Use of a screening tool will make sure that patients actually have an issue with their medication by, for example, asking questions like: Do you feel your medication is working? Are you experiencing any side-effects? Are you looking for more from your therapy?" Based on the screening, a patient is successfully enrolled if they are currently on a psychiatric drug, are having issues with their current medication, and provide informed consent. We're aiming for over 200 participants.

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And, as John explains, the community pharmacy setting should produce a good cross-section of participants, not just retirees who have the time to get involved. "We know from my previous research that the community pharmacy actually draws a good mix of the older and younger generations. In addition, as a pharmacy owner myself, I see interaction with the pharmacist across generations first hand. The young populations are drawn into the pharmacy due to two main drivers: convenience and accessibility. With long business hours, they can have immediate access to a pharmacist and also conveniently access services like quickly getting their flu shot. The new study should be able to draw this kind of cross-section from young to old."

John also explains how the new study's focus on psychiatric drugs is especially important. "The evidence around early optimization of therapy, particularly for depression, shows that the earlier patients are on the right therapy for them, generally the better they do down the road. We also find that patients on psychiatric medications receive a high degree of intervention usually due to the drugs' side-effects. So if a pharmacogenomics test can help get a patient on the right therapy quicker with less trial and error in prescribing, that is a very important tool."

Next, our researchers randomly assign each participant to either a control group or an intervention group. It's **randomized**—assignment to each group is not influenced by any factors. Technically, this is referred to as a randomized controlled trial. And it's **blinded**—participants don't know which group they are in. This all goes on behind the scenes.

Then *all* participants—whether control group or intervention group—do a pharmacogenomics test. This ensures no potential bias is introduced by one group perceiving they received more care than other participants. The pharmacist receives the results in about a week.

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The actual test is a simple process where the participant supplies a cheek swab and a lab analyzes the DNA cells collected by the swab. The DNA analysis indicates things like whether the person's genetic makeup will or will not tolerate certain types of drugs. In addition, it indicates variables like whether the patient is a slow or fast metabolizer, which influences how quickly a drug works. This in turn will influence what should be considered the most appropriate dose and frequency of dosage.

Next, all participants meet with a pharmacist to receive what is considered the "standard of care." This includes activities like a medication review and, as needed, working with the participant's doctor to optimize drug therapy. However, the pharmacist only reviews the intervention group's pharmacogenomics tests. As a result, if the pharmacist has medication modification recommendations for the participant's doctor, they are based on the pharmacogenomics test. By contrast, although the control group receives the identical standard of care from the pharmacist as the intervention group, any medication modification recommendations are *not* based on the pharmacogenomics test. There is no access to the control group's test results by the pharmacist or participant until *after* the study.

Finally, the participant meets with the pharmacist at one, three, and six months making it a **long-term trial**. And voilà, by the end of 2018 we hope to have all the data in! Then we'll get cracking on the analysis to see if intervention by way of pharmacogenomics testing had an impact on patient outcomes. (Be sure to catch John discussing the study in this *Inside Story*'s **companion podcast**.)

Let the evidence speak for itself

As it is well established by the hierarchy of evidence that anecdotal evidence is at the bottom of that hierarchy and systematic reviews are at the very top, our study methodology—a randomized controlled study—ensures that it meets the criteria as the "best available evidence." In addition, the long-term nature of the study will allow us to fill the gap in the research and accurately assess whether pharmacogenomics testing did—or did not—have a unique contribution in influencing patient outcomes. That unique aspect is the key to this study. A great deal of evidence has already shown that when community pharmacies deliver clinical services, patient outcomes improve. The question then is whether pharmacogenomics testing can improve patient outcomes over and above those very valuable pharmacy services.

Pharmacogenomics definitely holds promise with lots of potential and possibilities. And now it won't be too long until we have the proof regarding the inherent value of pharmacogenomics in influencing patient outcomes. And in turn, we'll have additional insight to help guide coverage decisions. As John sums it up, "This study's setting with actual patients at community pharmacies should help address what is lacking in the research, which is the ability to apply results in the real world regarding whether pharmacogenomics influences patient outcomes or not." Say goodbye to the research gap and say hello to decision-making based on the best available evidence!

Sources:

[1] The Innovative Canadian Pharmacogenomic Screening Initiative in Community Pharmacy (ICANPIC) study, John Papastergiou, Peter Tolios, Wilson Li, and Jane Li, Journal of the American Pharmacists Association, September – October 2017. Retrieved March 2018: http://www.japha.org/article/S1544-3191(17)30685-4/fulltext.

[2] "The hierarchy of evidence: Levels and grades of recommendation," BA Petrisor and M Bhandari, Indian Journal of Orthopaedics, Jan-March 2007. Retrieved March 2018: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2981887/.

What's UP...

NOVA SCOTIA HELPING WITH COST OF TAKE-HOME CANCER DRUGS

Cancer patients in Nova Scotia who are prescribed take-home cancer drugs as part of their treatment may be eligible for a new Take-Home Cancer Drug Fund. The fund covers take-home cancer drugs included in Nova Scotia Pharmacare programs including: chemotherapy, hormonal therapies, and immunotherapies. It does not cover supportive care drugs such as anti-nausea and pain medications.

The government has committed $846,000 this fiscal year and $2 million in each of the next three years. The Nova Scotia Health Authority is currently administering the fund while the government explores a longer-term solution. The new fund is retroactive to April 1, 2017, with the deadline of September 30, 2018, for retroactive reimbursement applications.

Resources such as cancer patient navigators and social workers will work with patients to help them access the fund. To be eligible a patient must be a Nova Scotia resident and have a valid Nova Scotia health card. They must also have a prescription for take-home cancer drugs and out-of-pocket expenses for eligible take-home cancer drugs greater than 4% of their net family income. In addition, patients must register with the Nova Scotia Family Pharmacare Program and meet any coverage criteria associated with the specific drug prescribed.

What does this mean for your plan? As the fund is last payor—patients must access all other sources of financial assistance available first, including private benefits plans—there should be no impact to GSC plans.

For more information, visit www.nshealth.ca/news/fund-help-patients-cost-take-home-cancer-drugs.

STUDY SHOWS MULTIPLE CHRONIC CONDITIONS WHEN ONTARIANS DIE

A new study—*Accumulation of Chronic Conditions at the Time of Death Increased in Ontario from 1994 to 2013*—focused on multimorbidity of chronic conditions, which is when an individual has two or more chronic conditions at the same time. Conducted by the Institute for Clinical Evaluative Sciences, the researchers examined more than 1.6 million deaths registered in Ontario from 1994 to 2013 and linked each death to the province's patient health data. They found that for people with multimorbidity when they died, these conditions were most commonly present: hypertension, osteoarthritis and other arthritis, mood disorder, cancer, chronic obstructive pulmonary disorder (COPD), chronic coronary syndrome, congestive heart failure, diabetes, non-mood mental health disorder, and stroke.

The study findings include that the prevalence of multimorbidity at time of death rose from 80% in 1994 to 95% in 2013. In addition, by 2013, two in three people who died in Ontario had more than five or more chronic conditions. In terms of decline, the presence of chronic coronary syndrome, congestive heart failure, and stroke declined by almost 2% each from 2004 to 2013.

The researchers also found that the types of chronic conditions that Ontarians accumulated varied by socioeconomic status. People that lived in low-income neighbourhoods were more likely to die with COPD, mental health disorders, and diabetes. Whereas, it was more common for people who lived in high-income neighbourhoods to have cancer and dementia when they died.

To access the study, visit https://www.ices.on.ca/Publications/Journal-Articles/2018/March/Accumulation-of-chronic-conditions-at-the-time-of-death-increased-in-Ontario-from-1994-to-2013.

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UPDATE ON OPIOIDS

New guideline recommends prescribing medication for opioid addiction

To help curb deaths from opioids, a new Canadian guideline recently published in the *Canadian Medical Association Journal*—"Management of opioid use disorders: a national clinical practice guideline"—recommends against using withdrawal management, such as referral to a short-term detox centre, as an isolated strategy. Instead, the guideline recommends that whenever possible, family doctors and emergency physicians should treat opioid addiction by prescribing medication as part of an evidence-based and longer-term strategy.

Specifically, the guideline recommends what is known as a stepped-care approach with Suboxone as the first-line treatment, and if necessary, moving to methadone as second-line treatment, followed by slow-release oral morphine with the support of a specialist for patients that do not respond, or have a contraindication, to Suboxone or methadone. In addition, the guideline identifies the importance of continually adjusting treatment based on individual needs and circumstances over time. It also recognizes that many people may benefit from moving between treatments.

Prescribing medication, such as Suboxone or methadone, is recommended because this is in sync with the growing body of scientific evidence that shows the superiority of these drugs in terms of retention in treatment, sustained abstinence from illicit opioid use, and reduced risk of death. Suboxone is preferred over methadone because it has a safety profile six times greater than methadone in terms of overdose risk. In addition, compared to methadone, Suboxone has benefits such as fewer side-effects, it's not easy to crush or inject, and can be taken easily at home.

This approach is based on provincial guidelines developed by the British Columbia Centre on Substance Use that were piloted in B.C. last year. The Canadian Research Initiative in Substance Misuse received funding from the Canadian Institutes of Health Research to develop the new guideline which included an extensive analysis of the addiction research by a national review committee made up of 43 primary-care physicians, addiction medicine specialists, registered nurses, and other health care professionals.

To access the guideline, visit www.cmaj.ca/content/190/9/E247.

New campaign promotes discussions about opioid use

A new national campaign called *Opioids Wisely* aims to encourage more discussion between health care providers and their patients to explore options for pain management to reduce harms associated with opioid prescribing.

The campaign materials include a set of 14 recommendations for when it is unsafe to prescribe opioids. For example, one recommendation is that for postoperative pain, patients should not continue on opioids beyond the immediate period after surgery, which is typically three days or less and not typically more than seven days. Another example is the recommendation to not prescribe opioids for patients with non-cancer pain unless the prescriber has already supported the patient to try non-drug therapies, as well as drug therapies that are not opioids. Accordingly, to help manage pain after dental surgery, the prescriber is encouraged to first prescribe a non-opioid drug and only if it is ineffective, to then consider an opioid but limit the number of pills dispensed.

This campaign is part of an even larger national campaign supported by over 30 organizations called *Choosing Wisely Canada*. Its goal is to help patients and health care providers engage in conversations about unnecessary tests and treatments and make smart and effective care choices.

For more information, visit www.ChoosingWiselyCanada.org/opioid-wisely.

OUT & ABOUT... *Events not to miss*

CPBI Western Regional Conference 2018

April 11–13, 2018 – Rimrock Resort Hotel, Banff, Alberta

Leila Mandlsohn, GSC's pharmacy strategy consultant, will deliver a presentation explaining the ideas behind Value-based Pharmacy.
www.cpbi-icra.ca/Events/Details/Southern-Alberta/2018/04-11-CPBI-Western-Regional-Conference-2018

Benefits Canada 2018 Benefits & Pension Summit

April 16–17, 2018 – Ritz-Carlton Hotel, Toronto, Ontario

Ned Pojskic, GSC's leader, pharmacy & health provider relations, will be participating in a panel on medical cannabis.
www.benefitscanada.com/conferences/benefits-and-pension-summit

Face to Face Drug Plan Management Vancouver

May 1, 2018 – Fairmont Waterfront Hotel, Vancouver, B.C.
www.benefitscanada.com/conferences/face-to-face-drug-plan-management-vancouver

Calgary Benefits Summit

May 29 – Fairmont Palliser Hotel, Calgary, Alberta
www.benefitscanada.com/conferences/calgary-benefits-summit

April Haiku

Just try getting the
Word pharmacogenomics
Into a haiku

FITBIT WINNER

Congratulations to **Q. TONG HE**, of **OTTAWA, ON**, the winner of our monthly draw for a Fitbit. Through this contest, one name will be drawn each month from plan members who have registered for Plan Member Online Services for that month.

Windsor	1.800.265.5615	**Vancouver**	1.800.665.1494
London	1.800.265.4429	**Montréal**	1.855.789.9214
Toronto	1.800.268.6613	**Atlantic**	1.844.666.0667
Calgary	1.888.962.8533	**Customer Service**	1.888.711.1119

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