The

INSIDE STORY®

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What's Inside

Personalized medicine represents a world of possibilities

SCIENTIFIC EVIDENCE WILL HELP MAKE IT REALITY

It seems like just yesterday we were excited about mobile technologies like cell phones and iPods, and now in the blink of an eye, it's all about "wearables" like Fitbits and Apple watches and Google glasses. From PVRs to Netflix…from electric cars to driverless cars…today, rapid technological change is the norm.

Fortunately, new technologies have the potential to enhance our lives in many ways—one being the potential of personalized medicine to improve health care. In fact, certain aspects of personalized medicine are now a reality—making the question no longer "can it be done?" but rather, "when should it be covered as an eligible benefit?"

First, a personalized medicine refresher

As the term implies, the concept behind personalized medicine is to individually customize medical treatment to an individual's genetic makeup. Also referred to as individualized or precision medicine, it tailors medical decisions, treatments, and products to each individual patient based on their genetic makeup to predict their response to different treatments or risk of disease.

Fascinating, eh? Especially when you think of the potential for health care to be personalized through numerous techniques—via new drugs, new technologies, new diagnostic tools, and new techniques for patient care. And the potential for health care to be personalized along all stages of care: prevention, diagnosis, treatment, and follow-up.

Maybe one day your plan members will be able to have their medications specially formulated based on their individual genetic makeup. In fact, with pharmacogenomics now possible, maybe personalized medicine is one step closer to that day becoming a reality. Let's see…

Technological innovation in action

- **Just like Wolverine and Deadpool**: Researchers used 3D printing and 3D imaging techniques to enable injured lab rats to regrow sensory and motor functions—basically they regenerated damaged nerves. Also, 3D printing is to thank for saving a man's life; he now has a 3D-printed titanium ribcage and sternum. Plus, a three-year-old girl underwent the world's first full skull-reconstruction surgery using 3D printing technology to create a new titanium skull.

- **Changing the way we look at cataracts**: To tackle cataracts—the clouded lens that grows over the eye that is the leading cause of blindness globally—researchers have developed eye drops that melt the cataracts away. Once approved for testing in humans, the treatment could mean no more eye surgeries and could decrease the risk of going blind.

- **Battling brain tumours with re-engineering**: Not only was a re-engineered polio virus successful in seeking out and killing cancerous cells, but it also avoided damaging normal cells. Development has been in the works for decades, and now the U.S. Food and Drug Administration is expected to make its decision on "breakthrough status" within the year.[1]

Pharmaco-what?

Pharmacogenomics is a type of personalized medicine where the goal 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.

Ideally pharmacogenomics helps predict who will benefit from a medication, versus who will not respond at all, versus who will experience negative side effects. 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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Here's how it works:

- A patient provides a saliva sample, which is identified only by a numeric code. The sample is sent to the lab where it's analyzed—with a focus on just the genetic variations involved in physiological processes—like drug metabolism.
- The results are sent to the patient and/or health care provider who requested the sample (i.e., doctor, pharmacist, genetic counselor). The patient can also show their test results to their pharmacist who could consider altering a medication or dosage or could discuss it with the doctor.
- The health care provider reviews the test results and determines the drug and dosage that will most likely work well for that specific person. For example, an individual with a genetic variation linked to slower metabolizing of a certain drug would need a lower dose since their body is slower in processing and eliminating it. Whereas, an individual who is a high metabolizer would need a higher dose. Alternatively, the doctor may decide that the patient should avoid the medication entirely.

This kind of genetic testing is becoming more readily available across Canada, so access is not an issue—the bigger issue will be who pays and is there a return on those dollars. One step further—should health benefits plans one day cover pharmacogenomics as an eligible benefit?

Pharmacogenomics in action...

Genetic testing to predict medication response is already routine in certain clinics and research centres. Canada's first personalized medicine clinic opened in 2008; it focuses on complex health conditions and medications like the blood-thinner warfarin, cholesterol-lowering statins, and the breast-cancer drug tamoxifen.

However, the clinical pharmacologist who established the clinic explains that adjusting medication based on genetic testing is not as easy as it is often made out to be. If it were, "every hospital in North America would be doing it." He explains that actual drug levels in the body still vary a lot even among patients with a similar genetic makeup.

His opinion is that pharmacogenomic testing can be a useful tool but that it requires specialized knowledge: "This should not be something we jump at as a broad, big-hammer approach."[2]

To cover or not to cover, that *will be* the question

Vendors offering pharmacogenomic genetic testing convey numerous reasons for adopting it as an eligible benefit. In theory, an enhanced ability to prescribe drugs that are a better fit with each patient should decrease adverse drug reactions and hospitalizations. In addition, it should reduce the need for a trial and error approach to finding the most effective therapy, during which time patients' conditions can worsen.

In turn—and again, in theory—by avoiding inappropriate medications, pharmacogenomics should improve plan member health outcomes and therefore productivity, absenteeism, and disability. And this should result in lower drug costs due to less medication waste and reduced costs associated with absenteeism and disability. That's the potential "return" we ask about.

It's exciting to consider what pharmacogenomics could potentially mean for enhancing plan member health. So to get a more in-depth perspective on where pharmacogenomics is currently at, we turned to the science.

So what does the science say?

A number of studies have examined the association between a specific genetic mutation and drug therapy outcomes with findings that tend to be inconclusive or inconsistent. For example, several studies show that patients who are considered poor and intermediate metabolizers have a higher incidence of adverse effects when taking a specific antidepressant. However, an equal number of studies do not show statistically significant associations.

As Ned Pojskic, GSC's pharmacy strategy leader explains, "It's great to see that the fundamental scientific methodology behind pharmacogenomic testing is sound; however, the scientific evidence isn't clear yet as to whether it is a viable drug management option for plan sponsors. And, as such, further evidence is needed before embracing routine pharmacogenomic testing en masse."

And what about the broader context of the patient's health? For example, age, sex, diet, smoking status, drug interactions, and co-morbidities are just some of the many other factors that need to be taken into consideration when interpreting test results because they affect how a patient metabolizes and responds to medications. And then there may also be factors in the patient's environment that could influence their response.

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Ned advises, "It's important to recognize that a patient's individual genetic makeup is only one of many factors that influence how the patient will respond to a particular drug. In fact, there is evidence that a patient's individual genetic makeup explains only a small percentage of the variance in response to a particular drug."

So what does it all mean? Ok, here goes:

The presence of a genetic mutation does not guarantee an adverse response to a drug.
…And the absence of the mutation does not mean the adverse response will not occur.

Did you catch that? It may take a couple of reads, but basically, the take-home message is that although genetic testing has a lot of potential to enhance drug management, sound prescribing decisions should not be based on genetic testing alone. Genetics is just one factor in the mix.

A lot of potential...But not ready for primetime yet

Insufficient scientific evidence means that pharmacogenomics isn't there yet in terms of warranting coverage as an eligible benefit in 2016. Experts explain that, "Despite the rapid pace of discovery and test development, the routine use of pharmacogenetic testing is stymied by the lack of data demonstrating clinical utility, or evidence that use of the test will improve health outcomes for a given patient. While randomized controlled trials remain the gold standard for clinical evidence, very few have been performed in pharmacogenetics."[3] (By the way, just when you figured out how to say pharmacogenomics—another name for it is pharmacogenetics.)

Take the drug warfarin for instance, which is one of the most commonly prescribed cardiovascular medications worldwide, but also one with a high risk of adverse drug reactions. Research findings conclude that "although genetic status can greatly influence an individual patient's warfarin dosing requirement, routine prospective pharmacogenomic testing is not endorsed by the FDA or by other expert panels because there is currently insufficient evidence to recommend for or against it."[4]

But what about other drug categories? Since there is ongoing research regarding the use of pharmacogenomics and prescribing antidepressants, we reached out to a leading Canadian psychiatrist. Here's what Michael Rosenbluth MD FRCPC, chief, Department of Psychiatry, Toronto East General Hospital and associate professor, University of Toronto had to say:

"Pharmacogenetic testing is an exciting, relatively new area that one day will hopefully bear fruit and contribute to our efforts to achieve optimal outcomes for our patients. However, from reviews of the literature, at this time there are no large-scale randomized controlled trials to examine the utility of routine pharmacogenetic testing. The poor correlation between genetics and clinical response precludes the current utility of pharmacogenetic testing in antidepressant prescribing."

And here's what Health Canada has to say in terms of pharmacogenomics now and in the future: "Pharmacogenomics is not yet a major field of study in Canada. However, the need to reduce adverse drug reactions and costs for the health care system may encourage pharmacogenomic research programs by both private enterprises and government."[5]

So far all the evidence points to the same conclusion: pharmacogenomics is promising but still early days in terms of warranting coverage in benefits plans. However, with pharmacogenomics showing real potential, what could be better than helping build the body of evidence around its use?

Research study anyone?

GSC jumped at the opportunity to become one of the funders of phase two of a British Columbia Pharmacy Association study called *Genomics for Precision Drug Therapy in the Community Pharmacy.*

Phase one laid the groundwork for this first-of-its kind study of pharmacogenomics at the community pharmacy level. It involved 33 community pharmacists in rural and urban British Columbia who recruited 200 volunteer patients to provide saliva samples.[6]

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Researchers at the University of British Columbia finished sequencing the samples in January and will do a retrospective analysis of DNA information to learn how genetics would have altered the drug dosage patients were prescribed. Other foundational work in phase one included developing procedures for the collection of patient saliva samples, processing and sequencing of DNA, and creating educational tools used by pharmacists for patient awareness.

Building on the foundation established in phase one, phase two is expected to begin this fall and will take about a year and a half to complete. The focus of phase two is on drug categories for mental health, cardiovascular, pain, and possibly respiratory conditions (COPD and asthma). It will involve collecting saliva samples from 1,000 volunteer patients in participating pharmacies in Vancouver, Winnipeg, Toronto, and Halifax.[7]

A lot of valuable insights are coming our way; in addition to determining how the testing could influence prescribing, the study will also assess whether prescribers were able to act on the genetic information, and whether their medication or dosage was altered or discontinued. We will also learn whether pharmacogenomics at community pharmacies is a viable service, which will help determine what the financial impact could be on private drug plans.

We're on it!

Taking a proactive approach by supporting the emerging evidence will help us monitor developments in pharmacogenomics. We'll be at the forefront of new developments—which means that so will you.

OUT & ABOUT... EVENTS NOT TO MISS

CPBI Regional Conference – Quebec & Ontario – September 12-14, 2016

Fairmont Tremblant, Mont-Tremblant, Quebec

http://www.cpbi-icra.ca/Events/Details/Québec/2016/09-12-2016-CPBI-Regional-Conference-Quebec

Sources:

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[2] "Your pharmacist's secret weapon: How your DNA can help perfect your medication," Adriana Barton, February 14, 2016, The Globe & Mail. Retrieved July 2016: www.theglobeandmail.com/life/health-and-fitness/health/researchers-seek-to-personalize-medicine-by-unlocking-secrets-in-dna/article28745033/

[3] "Pharmacogenetic testing: current evidence of clinical utility," Jivan Moaddeb and Susanne B. Haga, August 2013, National Center for Biotechnology Information. Retrieved July 2016: www.ncbi.nlm.nih.gov/pmc/articles/PMC3765014/

[4] "Pharmacogenomic testing: Relevance in medical practice, Why drugs work in some patients but not in others," Joseph P. Kitzmiller, David K. Goen, Mitch A. Phelps, Wolfgang Sadee, May 14, 2012, National Center for Biotechnology Information. Retrieved July 2016: www.ncbi.nlm.nih.gov/pmc/articles/PMC3351041

[5] Pharmacogenomics, Science and Technology, Health Canada. Retrieved July 2016: www.hc-sc.gc.ca/sr-sr/tech/biotech/about-apropos/pharma-eng.php

[6] "B.C. pharmacies complete role in first-of-its-kind genomics project," British Columbia Pharmacy Association, January 27, 2016. Retrieved July 2016: www.bcpharmacy.ca/genome

[7] "BC Genomics Project moves to second phase, BCPhA expanding its cutting edge genomics project to cities across Canada," British Columbia Pharmacy Association, June 7, 2016. Retrieved July 2016: www.bcpharmacy.ca/files/news/1465406091.pdf

COMMUNITY GIVING PROGRAM

HERE'S HOW WE **ADD** TO THE **GREATER GOOD**…

Paving the way for a brighter future
Take a look at how our grant recipients are making a difference

Frontline care—like dental services, vision care, prescription drugs, disease management, and mental health supports—can act as a catalyst for change. That's why the GSC Community Giving Program is focused on supporting organizations and initiatives that provide frontline care for underinsured or uninsured populations. And all grant recipients include a navigator component—this means ongoing positive change as clients are referred to any additional services they may need.

This year, GSC is granting $2.5 million to 29 organizations across Canada—coast to coast—from Yellowknife to Moncton.

And here is the list of our 2016 Community Giving Program grant recipients:

Cerebral Palsy Association of British Columbia
Community Counselling and Resource Centre (CCRC)
Dr. Borna Meisami Commemorative Foundation / Project Restoring Smiles
Encompass Support Services Society
Essex County Dental Society
Halton Peel Dental Association (HPDA)
Hamilton Health Sciences Foundation
Homeless Connect Toronto
Hope Place Centres
Horizons for Youth
Inn From the Cold Society
Jubilation Residential Centres Inc.
Maryvale
Mississauga Parent-Child Resource Centres
MukiBaum Accessibility Centre
Northern Alberta Home for Women Society (NAHWS)
Pine River Foundation
Project SHARE of Niagara Falls Inc.
Salvus Clinic Inc.
Sanguen Health Centre
Saskatoon Student Wellness Towards Community Health (SWITCH)
SPOT Clinique communautaire de santé et d'enseignement
Square One Older Adult Centre (SOOAC)
The Downtown Mission of Windsor
The Umbrella Multicultural Health Co-operative
United Way of St. Catharines & District
Veith House
Youth Without Shelter
YWCA of Yellowknife

GSC frontline care™

What's UP...

REPORT SUMMARIZES THE FIRST HEALTHY CANADA CONFERENCE

The Canadian Alliance for Sustainable Health Care (CASHC) has released a summary of the first Healthy Canada conference: Financial Models and Fiscal Incentives in Health and Health Care. The conference and associated report is the first in a series of Healthy Canada conferences organized by the CASHC.

The conference focused on what motivates behaviour from a financial and fiscal perspective and, as the report summarizes, it provides practical insight and evidence-based solutions regarding how to leverage financial models and tax incentives to improve population health and the sustainability of our health care system.

Key messages from the conference include that although controlling health care costs is complex, there are innovative financial and funding models out there. In addition, barriers to implementing the models are not insurmountable; a better understanding of the barriers will help stakeholders find ways to overcome them. For example, a main way to make progress in implementing innovative approaches and to overcoming barriers is to break down funding silos.

To access the report—Financial Models and Fiscal Incentives: Proceedings From the Healthy Canada Conference—visit the Conference Board website at *http://www.conferenceboard.ca/elibrary/abstract.aspx?did=8039&utm_source=facebook&utm_medium=social&utm_campaign=share*

The power of nudging

The report shares examples from conference participants about how they are promoting healthy lifestyles through rewards:

- A loyalty app that rewards users with points for educating themselves about their health and wellness and encourages them to make positive lifestyle choices.
- An employee wellness program that uses a three-pronged approach—awareness, opportunities for engagement, and financial incentives to strategically achieve wellness plan goals.
- An online health management portal that uses loyalty points and financial rewards to nudge plan members toward healthier choices.

Sound familiar? The third example is our very own Change4Life portal which recognizes that rewards can be motivating. Did you know that plan members can earn 100 points just by registering? Then they can use their points to bid on rewards. But we're getting ahead of ourselves. Be sure to check out *The Inside Story* in September when we'll be focusing on Change4Life.

ANTIDEPRESSANT RESEARCH IN THE NEWS...

Antidepressants prescribed for range of off-label uses

The use of antidepressants in North America has continued to rise over the last two decades. Researchers from McGill University in Montreal suspected that the reason for this trend may be more prescriptions for antidepressants to treat conditions other than depression. Little research existed on the topic, so the researchers decided to do a study with the aim of examining exactly why antidepressants are being prescribed.

The study's findings include that only 55% of antidepressant prescriptions were prescribed for depression. Physicians also prescribed antidepressants for anxiety disorders (18.5%), as well as for a range of issues like insomnia, pain, pain disorders, migraine, attention-deficit/hyperactivity disorder, digestive system disorders, and certain symptoms of menopause.

The researchers feel that the findings indicate the presence of an antidepressant prescription does not necessarily indicate treatment for depression, and that there is a need for additional research into off-label antidepressant use.

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To access the study—"Treatment Indications for Antidepressants Prescribed in Primary Care in Quebec, Canada, 2006-2015"—visit the Journal of the American Medical Association at jama.jamanetwork.com/article.aspx?doi=10.1001/jama.2016.3445

Most antidepressants ineffective for children and teens but more research necessary

Researchers recently did a review and analysis of all published and unpublished randomized clinical trials comparing the effects of 14 antidepressants in children and teens with major depressive disorder. Findings include that most antidepressants are ineffective, and some may be unsafe, for children and teenagers with major depression. The results showed that:

- → Fluoxetine was the only antidepressant where the benefits outweighed the risks.
- → Nortriptyline was "significantly less effective" than seven other antidepressants and a placebo pill.
- → Imipramine, venlafaxine, and duloxetine were rated lowest for tolerability.
- → Venlafaxine was also linked with an increased risk of suicidal thoughts or attempts.

However, the researchers rated the risk of bias and overall quality of the clinical trials included in their analysis. They found that the majority of studies had a high risk of bias and very low quality of evidence so the results have limited implications for clinical practice. In addition, they caution that the true effectiveness and potential for harm of antidepressants in young people remains unclear because only a limited amount of research has been done on antidepressant use in children and teens.

The researchers also note that because young people's brains are still developing, there is a cautious approach when prescribing medications. International treatment guidelines for major depression recommend starting with non-drug approaches like cognitive behavioural or interpersonal therapy, which evidence shows are effective.

To access the study—"Comparative efficacy and tolerability of antidepressants for major depressive disorder in children and adolescents: a network meta-analysis"—visit *The Lancet* at www.thelancet.com/journals/lancet/article/PIIS0140-6736(16)30385-3/abstract

SMOKING CESSATION RESEARCH IN THE NEWS…

There are lessons to be learned from two recent American research studies as Canada is also trying to decrease smoking through a range of interventions including graphic images on cigarette package.

Decrease smoking, decrease health care costs

A recent U.S. study found that regions with lower smoking rates had substantially lower medical costs from 1992 through 2009. In addition, states that have public policies to reduce smoking have substantially lower medical costs and those that don't, have higher medical costs.

In addition, the study found that changes in health care costs begin to be observed quickly after changes in smoking behaviour. State and national policies that reduce smoking are not only good public policy in the long run, they should also be considered an important part of short-term health care cost containment. Investing in tobacco control saves lives and saves money.

The researchers conclude that the findings add to the evidence showing that tobacco-control interventions pay off.

To access the study—"Smoking Behavior and Healthcare Expenditure in the United States, 1992–2009: Panel Data Estimates"—visit PLOS Medicine at http://journals.plos.org/plosmedicine/article?id=10.1371/journalpmed.1002020

So what's new with GSC's smoking cessation program?

We're so glad you asked! We launched some enhancements in February 2016 to our program that uses pharmacists to deliver smoking cessation services to plan members. The program—which became standard on all plans last year—is now:

- → Available in pharmacies across Canada (except Saskatchewan and Alberta where public programs exist)
- → Standardized in structure and reimbursement model with the Ontario Pharmacy Smoking Cessation Program which enables more streamlined delivery
- → Accessible as pharmacy counselling and/or drug therapy giving plan members more choice
- → Not subject to closed enrolment allowing plan members to take part when they are ready to quit

Gruesome images on cigarette packs help some quit smoking

Smoke emerging from a hole in the neck, unhealthy lungs, badly stained teeth, a patient near death—gruesome smoking-related photos aim to encourage smokers to quit. Results from a new study add to extensive evidence from around the world that large, graphic warnings are effective. More than 89 countries now require visual warnings, including Canada, Australia, and nations in the European Union—but not yet the United States.

In the study, more than 2,000 smokers in California and North Carolina were randomly assigned to receive cigarette packages either with just text warnings or packages that also included photos—described as "large and ghastly"—on the fronts and backs.

The findings include that 40% of smokers whose cigarette packs had visual warnings were likely to try to quit, compared with 34% of those whose packs only had text warnings. By the end of the study, almost 6% of the group with the packs with images had quit for a week, compared with about 4% of those who received text-only warnings on their packs.

The researchers said that the visuals worked—not because the smokers felt more at risk, or that they thought smoking was any more dangerous; they worked because the smokers couldn't get the images out of their heads; they couldn't stop thinking about the harms of smoking.

To access the study—"Effect of Pictorial Cigarette Pack Warnings on Changes in Smoking Behavior: A Randomized Clinical Trial"—visit JAMA Internal Medicine at https://archinte.jamanetwork.com/article.aspx?articleid=2526671

July/ August Haiku

July August sigh
Too hot to write poetry
Cut us some slack please

Winner of the draw for a Fitbit

Congratulations to **V. REVENKO** of **Calgary, Alberta** 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.

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