camh IMPACT
Individualized Medicine:Pharmacogenetic Assessment & Clinical Treatment

Assurex HEALTH

# IMPACT Newsletter

6th Edition | May 2016

## Introduction

The goal of the IMPACT newsletter is to provide you with exciting news, updates and study milestones. Without your referrals and continued support, we would not have been able to reach the high number of patients who have already received pharmacogenomic testing through IMPACT. Thank you for all of your support!


Meet the IMPACT team! Visit us at www.im-pact.ca.

## IMPACT Study Milestones

- The IMPACT study was initiated in June 2011 after receiving $19.5 million from the Ontario Ministry of Research and Innovation, the CAMH Campbell Family Mental Health Research Institute and Larry & Judy Tanenbaum.
- In May 2012, the first IMPACT patient was consented.
- In January 2013, for the first time in Canada, patients were able to receive genetic testing at their family physician's office; this was made possible through the IMPACT study.
- In November 2013, CAMH and Assurex Health signed a partnership agreement to bring the benefits of a personalized approach to psychiatric treatment to more Canadians.
- Beginning in November 2014, patients enrolled in the IMPACT study were tested using the Assurex Health proprietary technology, GeneSight Psychotropic.
- Since May 2012, 1,821 clinicians have completed the clinic registration process.

## Important Study Reminders

Participants are asked to provide the following information at each stage of the study:

### Baseline (Upon Consent)

- Symptoms
- Medication History
- Side effects

### Week 4

- Symptoms
- Current Medications
- Side effects

### Week 8

- Symptoms
- Current Medications
- Side effects

Symptomology is gathered through scales such as BDI and PANSS depending on the patient's diagnosis. Please discuss with your patients the importance of completing these scales at each time point of the study.

## Referral Process

Referring a patient to the IMPACT study is easy!

To refer a patient to the study, please download and complete the appropriate referral form below. The completed form is sent to the IMPACT team via email impact@camh.ca or fax 416.979.4666:

- IMPACT Adult Referral Form (16+)
- IMPACT Adolescent Referral Form (7-15)

A Research Analyst from CAMH will then contact your patient to walk him/her through the informed consent process in order to enroll him/her in the study. If you have any questions regarding the referral process please contact us at 416.535.8501 ext. 30240.

Patients who are over 16 years of age and not diagnosed with schizophrenia (as PANSS must be conducted in person) can consent online. The patient will then be prompted to choose between providing the buccal swabs in person at CAMH or having a sample collection package sent to their address (via FedEx) at no charge.

## Access to genetic reports

Once the buccal swabs are received by the laboratory and processed, the GeneSight reports can either be faxed (in black and white) or accessed online (in colour with print option). An email address for the clinician must be provided on the referral for online access.

GeneSight reports are available within 36 hours of buccal swab receipt!

## Testimonials

Please let us know if you would be interested in sharing your experiences with pharmacogenomic testing. We are always interested in feedback — reach us by email at impact@camh.ca.

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## IMPACT Study Status

As of May 2016, the IMPACT Study has enrolled 5,900 patients for pharmacogenomic testing in total, averaging over 172 patients enrolled per month in 2015-2016.

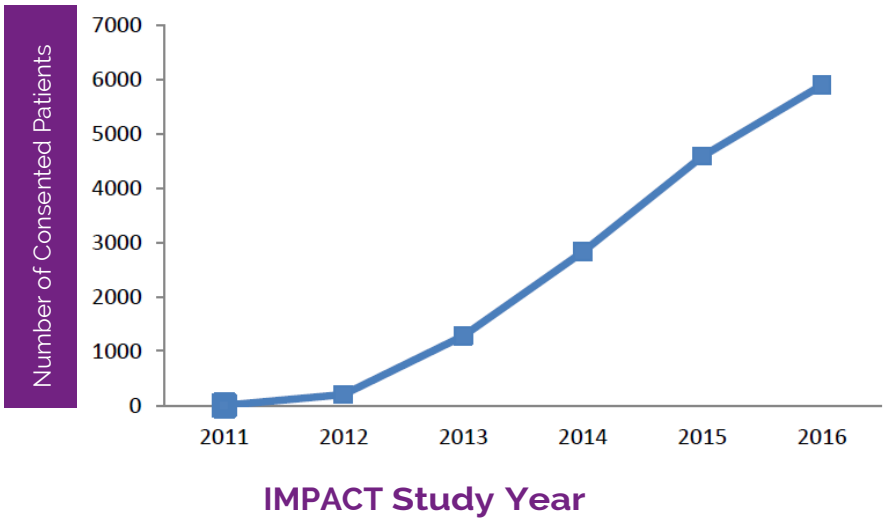



FIGURE 1 Number of patients consented to participate in the IMPACT Study.

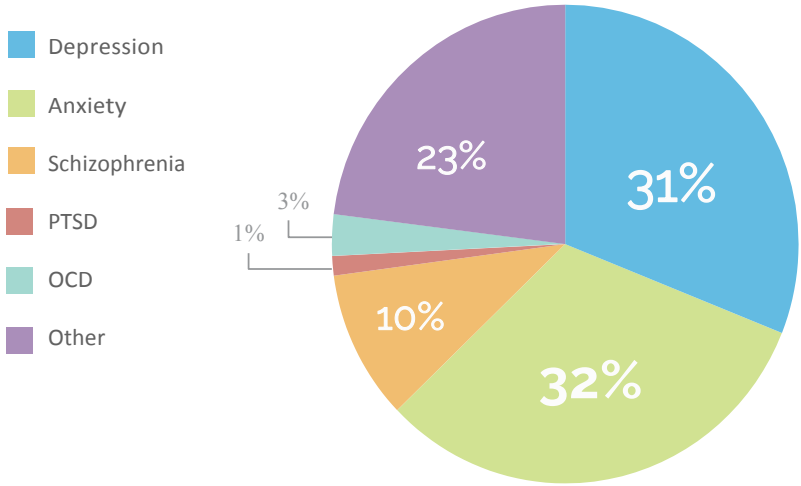



FIGURE 2 Percentage of IMPACT study participants with a primary diagnosis of depression, anxiety, schizophrenia, PTSD, OCD or other. Patients may have a secondary diagnosis

## Gene Spotlight

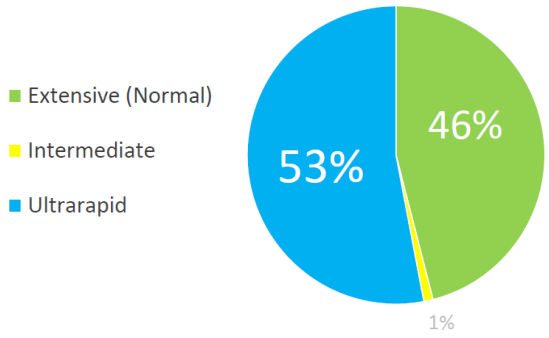
### Drug metabolizer CYP1A2

CYP1A2, located on chromosome 15, encodes a liver enzyme involved in the metabolism of medications. CYP1A2 is involved in the metabolism of 32% of all medications on the GeneSight test. CYP1A2 is considered a low-affinity, high-capacity enzyme, and a significant metabolic clearance pathway for chlorpromazine, clozapine, duloxetine, fluvoxamine, imipramine, mirtazapine, olanzapine, and thioridazine.

The associations between CYP1A2 and drug metabolism were assessed in eight studies. Study populations consisted of patients with major depression or schizophrenia and other psychiatric disorders. The most commonly studied medications included olanzapine and clozapine because CYP1A2 plays a dominant role in their metabolism. Among these eight studies, only two of the studies found a significant association.

All studies investigated the *1F, *1D, *1C, *1E, and *1K alleles. The *1F and *1D alleles account for inducible enzymatic activity while *1C accounts for variable inducible activity, *1K has decreased enzymatic activity, and *1E has yet to be functionally characterized. One of these studies found an association in the direction opposite than expected between these polymorphisms and PK outcome: the UM CYP1A2 genotype was associated with the greatest circulating clozapine to N-desmethylclozapine ratio. The association of circulating olanzapine was in the expected direction to the inducible CYP1A2 enzyme associated with the *1F/*1F genotype. Among the remaining studies, those that investigated the fluvoxamine–metabolite ratio, or circulating clozapine or olanzapine exposures did not find associations with CYP1A2 genotype (Altar et al., 2013).

**CYP1A2 Phenotype Frequency***




*Phenotype frequency is based on internal Assurex Health data of over 100,000 tested patients.

## Webinars

Assurex Health offers educational webinars that provide treating information about GeneSight technology and pharmacogenomics in general.

If you are interested in participating, register by visiting: http://genesight.com/educational-webinars.

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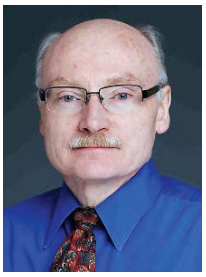
## GeneSight Psychotropic

GeneSight Psychotropic is a clinically validated, laboratory developed test that analyzes how eight genes may affect a patient's metabolism and response to 33 Health Canada approved antidepressants and antipsychotics. GeneSight testing includes genotyping of six pharmacokinetic genes from the Cytochrome P450 family and two pharmacodynamic genes related specifically to the serotonin system. GeneSight differs from other pharmacogenomic testing in that it is combinatorial and integrates information from Health Canada approved labels, published literature and clinical pharmacology with the patient's genetics to predict his/her response and tolerability to a medication. For more information, visit: www.genesight.com.

## In The News

### A lecture by Dr. James Kennedy on the use of Genetic Tests

On March 30th, 2016, Assurex Health LTD. welcomed Dr. James Kennedy, M.D., Director of Molecular Science Program at CAMH, in Mason, Ohio. Dr. Kennedy gave a lecture in city of Mason Municipal building about "The Use of Genetic Tests to Decide on Specific Medication and Dosage for Psychiatric Patients".



Dr. James Kennedy, MD

## The following information was provided by Assurex Health:

### Combinatorial Versus Individual Gene Pharmacogenomic Testing

What is the difference between traditional "single gene" testing and Genesight's combinatorial approach?

In multiple previous studies, GeneSight, a multigene combinatorial pharmacogenomics powered by CPGx™ technology, has shown an ability to predict poorer antidepressant outcomes and to help guide healthcare providers to more genetically optimal medications, leading to improved patient outcomes. The GeneSight test employs a proprietary and wholly unique method of predicting patient medication response using a combinatorial pharmacogenomic method. Combinatorial pharmacogenomics uses knowledge of each medication's unique set of pharmacokinetic and pharmacodynamic characteristics to incorporate and appropriately weight genetic variation at multiple loci to produce more accurate predictions of patient response than testing solely for the primary metabolic pathway of a medication. This differentiation, validated by multiple published clinical outcomes trials, has led the Center for Medicare and Medicaid Services to release a specific coverage policy for the GeneSight test that is separate from its policies for individual gene testing (e.g. CYP2D6).

Assurex Health presents research on Combinatorial Versus Individual Gene Pharmacogenomic Testing in Mental Health: A Perspective on Context and Implications on Clinical Utility (Winner & Dechairo, 2015).

Pharmacogenomic testing in mental health has not yet reached its full potential. An important reason for this involves differentiating individual gene testing (IGT) from a combinatorial pharmacogenomic CPGx™ approach. With IGT, any given gene reveals specific information that may, in turn, pertain to a smaller number of medications. CPGx™ approaches attempt to encompass more complete genomic information by combining moderate risk alleles and synergistically viewing the results from the perspective of the medication. This manuscript discusses IGT and CPGx™ approaches to psychiatric pharmacogenomics and reviews the clinical validity, clinical utility, and economic parameters of both. For more information, visit: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4654186/

### For More Information

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