

# Pharmacogenetic (PGx) Testing

## to Improve Patient Mental Health Outcomes During a Pandemic

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The COVID-19 pandemic is contributing to unprecedented levels of stress, intensifying existing symptoms of depression and anxiety for some, and causing new symptomatology in others. Mass quarantine and social isolation measures have led to widespread fear, anxiety, depression, and sleep disorders, not only in those infected with SARS-CoV-2, but their family members, close contacts, the general public, and of particular concern, front line workers and healthcare professionals<sup>1,2</sup>

The stress caused by isolation is being further exacerbated by factors related to our health like, lack of exercise or inability to engage in routine activities, concerns regarding impacts on our children's education, and financial/job security. Large-scale disasters are almost always accompanied by increases in mental and behavioral disorders, domestic violence, and child abuse.<sup>3</sup> Depression and anxiety levels have surged after other crises, such as the 9/11 attacks and the SARS-CoV-1 epidemic, which was also associated with increases in PTSD, and stress disorders in both patients and clinicians.<sup>4</sup> Researchers suggest the current pandemic could also lead to an increase in suicide rates due to economic stress and isolation. During February–March 2020, utilization of mental health services through apps/virtual means increased 50–150%, with companies offering these services struggling to meet the explosion in demand<sup>5</sup>. As early as mid March, 'Kids Help Phone Canada' was reporting a 350% increase in young people reaching out, due to fears related to COVID-19.<sup>6</sup> 'Crisis Services Canada' and 'Distress and Crisis Ontario' are also experiencing a significant increase in calls from people experiencing extreme anxiety at this time<sup>5</sup>.

The Centers for Disease Control acknowledges the inevitable mental health impact of the COVID-19 outbreak<sup>7</sup>, and stress that people who may respond more strongly to the stress of this crisis include:

- Elderly
- Children and teens
- Those with mental health conditions, chronic diseases or substance use disorders
- Front-line workers/responders including doctors, nurses, paramedics, pharmacists and other healthcare providers

According to analytics company GlobalData, global sales for drugs treating mental health disorders are expected to reach US\$27.4 billion in 2020, an increase of US\$717 million from 2019. Health systems need to develop efficient and expeditious mechanisms for patient assessment and delivery of essential treatments, including psychiatric medicines. Delivering the most effective, least resource-heavy treatment to patients in need before attempting more resource-intensive treatment will prove critical.<sup>8</sup>

**Pharmacological treatment of mental health conditions typically involves months of "trial and error" before finding effective medication(s), leading to delays in recovery, extended disability, medication waste, and the risk of substance abuse:**

Approximately 25% of adults suffer from some form of mental health condition, and at least half will develop one in their lifetime.<sup>9</sup> Drug treatment for mental health conditions is rarely straightforward. Due to genetics, individual variation in drug responses can be significant, and common drugs can be ineffective or cause unacceptable side effects in more than half of patients. Over 95% of individuals carry gene variants that cause an altered response to certain drugs<sup>10–13</sup>, and genetic variants are estimated to affect between 20 – 95% of individual response variability.<sup>14,15</sup> As a result, up to two thirds of patients with major depressive disorder fail their first antidepressant trial, necessitating additional "trial and error" in an effort to find an effective regimen.<sup>16,17</sup> Remission

rates are as low as 28 – 37.5%.<sup>18,19</sup>, and chances of remission are reduced with each subsequent drug trial<sup>20,21</sup>. Those who experience side effects with their first drug trial also suffer from reduced rates of remission<sup>20</sup>. Cycling through multiple drugs is time-consuming, costly, and often leads to additional mental anguish, discouragement, and drug discontinuation/resistance to trialling new agents. Thirty per cent of prescriptions are never filled, and only 50% of patients take medications as prescribed. Reasons for non-adherence include perceived/expected lack of efficacy, fear of side effects and depression<sup>22</sup>. This translates into significant drug wastage, delays in recovery and/or missed work.

**Recovering from this pandemic will be achieved through a combination of approaches including psychotherapy, financial assistance, and a targeted approach to pharmaceutical therapy that expedites connecting individuals with treatments that are both effective and tolerable. Individual genetic compatibility with drug treatment promises to be of critical importance in these efforts.**

**PGx profiling offers a personalized treatment approach that has been demonstrated to increase response rates, improve symptoms, reduce side effects, and ultimately increase chances of remission. Additional benefits include minimization of drug wastage/costs, reduced hospitalizations/healthcare utilization costs, and significant potential savings to employers and insurers:**

When selecting a PGx test to assist in treatment strategies, several factors should be considered:

- 1) **Is the test specifically designed for mental health vs. a "general pharmacogenetic panel"?**

While a test may seem to evaluate an impressive number of genes, if it does not include all of the specific

variants shown to impact metabolism of mental health drugs, the resulting report will not be a useful treatment guidance tool. The more variants targeted to mental health, the more complete the resulting guidance will be. Although some genetic variants are rare, they occur more frequently among certain ethnicities, and omitting them would significantly alter results for those who carry them. Many tests include only variants most common in populations of European descent, resulting in potential for false negatives for non-Europeans. This is important in populations with ethnic diversity like Canada.

Some tests primarily include pharmacokinetic variants (affecting how a drug is broken down/eliminated), however it is critical that pharmacodynamic variants (impacting how the body will respond to the drug once processed based on number/effectiveness of transporters, receptors, etc.) are also included.

"The more alleles (gene variants) a test includes with a functional impact on a gene, the more confidence one should have in the predicted phenotype and associated drug selection and dosing advice"<sup>23</sup>.

The list of mental health specific drugs evaluated by the test should also be comprehensive to ensure the majority of drugs for mental health conditions are included. Cannabis, now widely used in various mental health disorders, can also interact with other medications, thus should also be included in the PGx panel being considered.

## 2) Is the test accurate and does it abide by standards set by regulating agencies?

Pharmacogenetic tests and reports should not only be developed by qualified genetic experts, but it is critical that the lab and the tests themselves be certified by an independent

accrediting body. Quality controls ensure the test can accurately predict responses to specific drugs. Unlike the US, regulation and quality control of pharmacogenetic companies in Canada is as yet largely absent, with many PGx testing companies operating without oversight, rendering quality procedures and accountabilities unclear. Additionally, some companies contract out their pharmacogenetic testing services, which does not allow for full control and oversight at each stage of the process.

CLIA\* certification, a Health Canada Medical Device Establishment License as well as The College of American Pathologists (CAP) accreditation are important in ensuring the highest level of quality control and test result accuracy/reliability.

*\*CLIA stands for Clinical Laboratory Improvement Amendments. The Centers for Medicaid and Medicare Services (CMS) regulates laboratory testing through the CLIA certification program. The objective of CLIA is to ensure the accuracy, reliability, and timeliness of patient test results through quality laboratory standards.*

## 3) Accessibility: Is the test easy to take, affordable, and the results easily comprehensible?

The value of PGx testing is realized when it successfully enables the right treatment decision as efficiently as possible. Results should be easily interpreted by patients, clinicians and other members of the healthcare team. Pharmacists can assist patients in selecting a reputable PGx testing company based on their particular needs, keeping the aforementioned elements in mind.

*Complete references can be accessed at [opatoday.com/TOP](http://opatoday.com/TOP).*

# Impacts of PGx Testing

## Improved remission and response rates with decreased side effects:

After 8 weeks, patients using genetic testing to guide treatment experienced 50% increased remission and 30% increased response. Side effects were reduced by 60%<sup>24</sup>

## Symptom improvement in less time:

Greater than 4-fold improvement in depressive symptoms and time to symptom relief<sup>25</sup>

## >\$1000/year reduction in medication costs per patient:

Genetic testing saved an average of \$1036 per patient per year in medication costs. Pharmacy cost savings averaged \$2774.53 for patients who were changed to a PGx congruent medication regimen, compared to those who were not. In addition, medication adherence improved by 17% and polypharmacy was reduced by 20%<sup>26</sup>

## Healthcare costs increase more than \$5000/year when patients take medications that are incompatible with their genetic profile:

A retrospective study demonstrated that patients who had not undergone genetic testing/were using medications that should have been avoided based on their genetic profile had a 69% increase in total healthcare visits, 4 times the number of disability claims, and 3-fold increase in medical absences<sup>27</sup>

**For further information on personalized medicine for your patients visit [inagene.com](http://inagene.com).**