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An Overview of Pharmacogenomic Testing for Psychiatric Disorders

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Questions or requests for information about this report can be directed to Requests@CADTH.ca

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Key Messages

- Pharmacogenomic testing is a precision medicine technology that examines genetic variation in medication metabolism. Selected for inclusion in [CADTH's 2023 Watch List](#), pharmacogenomic testing has the potential to significantly influence the landscape of health care in Canada over the next 5 years. By analyzing an individual's unique genetic profile, this testing aims to guide personalized treatment strategies that improve therapeutic outcomes, optimize the medication selection process, and enhance patient experiences. The integration of pharmacogenomic testing into clinical practice may pave the way for a more efficient and effective delivery of mental health care.
- Pharmacogenomic tests for psychiatric disorders that are available in Canada include direct-to-consumer tests – which are paid out of pocket – and tests that are offered as a laboratory service (which may or may not be paid out of pocket). These tests are quite different from each other, including the types and number of genes examined, cost of testing, and methods used for sample collection and analysis.
- Despite being available for approximately 20 years and that numerous guideline-developing groups and regulators have issued recommendations about the types of pharmacogenomic information that should be used to guide prescribing decisions, pharmacogenomic testing has yet to be integrated into most psychiatric care practices in Canada and worldwide. Although some studies suggest pharmacogenomic testing provides benefits over treatment as usual, the evidence is often conflicting and of limited quality. Concerns related to risk of bias, inconsistency across studies, reproducibility, and generalizability do not allow a clear and consistent interpretation of the results.
- This Horizon Scan provides an overview of information related to pharmacogenomic testing for psychiatric disorders, a description of some of the published studies, and a summary of some important considerations related to clinician education and training, privacy and confidentiality of health data, health equity, and laboratory capacity should testing become more widely used in Canada.

Purpose

The purpose of this Horizon Scan is to present health care stakeholders in Canada with an overview of information related to:

- the use of pharmacogenomic testing for informing the treatment of psychiatric disorders
- a description of some of the published studies
- and a summary of some important considerations related to the potential implementation of the technology.

This report is not a systematic review and does not involve critical appraisal or include a detailed summary of study findings. It is not intended to provide recommendations for or against the use of the technology.

Methods

Literature Search Strategy

An information specialist conducted a literature search on key resources including MEDLINE, Embase, PsycINFO, the Cochrane Database of Systematic Reviews, the International HTA Database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search approach was customized to retrieve a limited set of results, balancing comprehensiveness with relevancy. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. Search concepts were developed based on the elements of the research questions and selection criteria. The main search concepts were pharmacogenetics and psychiatric disorders (including but not limited to, anxiety disorders, mood disorders, personality disorders, neurodevelopmental disorders, substance use disorders, and trauma disorders). No filters were applied to limit the retrieval by study type. The search was completed on January 27, 2023, and limited to English-language documents published since January 1, 2020.

Study Selection

One author screened the literature search results and reviewed the full text of all potentially relevant studies. Studies were considered for inclusion if the intervention was pharmacogenomic testing used for people with psychiatric disorders or related conditions for which care is typically provided by a psychiatrist or psychiatric care specialist (e.g., attention-deficit/hyperactivity disorder [ADHD], autism spectrum disorder). Conference abstracts and grey literature were included when they provided additional information to that available in the published studies.

Peer Review

A draft version of this Horizon Scan was reviewed by 1 clinical expert with expertise in pharmacogenomics and precision pharmacotherapy.

Background

Psychiatric disorders encompass a wide range of conditions that impact an individual's thoughts, feelings, perceptions, behaviour, or mood. Common categories of psychiatric disorders include depressive disorders, bipolar and related disorders, anxiety disorders, trauma- and stressor-related disorders, psychotic disorders, dissociative disorders, eating disorders, and personality disorders.¹ Although each psychiatric disorder is characterized by different sets of symptoms, they are generally associated with distress, emotional problems, social dysfunction, and decreased productivity, functionality, and quality of life.²⁻⁴ Estimates suggest that approximately 1 in 5 people in Canada experience mental illness each year, and when both the direct (e.g., costs of hospitalizations, physician visits, medication) and indirect costs (e.g., costs due to loss productivity) to society are considered, the economic impact of psychiatric disorders in Canada exceeds \$50 billion per year.⁵

Treatment strategies for psychiatric disorders often involve psychotherapy and pharmacotherapy. There are more than 200 pharmacotherapies available for treating psychiatric disorders, many of which have unique cellular targets and mechanisms of action.^{6,7} Although many people with psychiatric disorders can manage their symptoms with pharmacological interventions, it can be challenging to find the most appropriate treatment for each patient due to the wide array of available drugs and the large interindividual variability in response.^{8,9} For example, it has been reported that a clinically significant response is not reached with initial antidepressant medication in as many as 50% of people with major depressive disorder.¹⁰ Consequently, many people with psychiatric disorders go through a trial-and-error process, during which drugs and doses are sequentially trialed before a suitable regimen of pharmacotherapy is found that can help adequately manage symptoms.¹¹ The trial-and-error phase is often characterized by poor symptom control and adverse side effects, which can cause dissatisfaction and treatment discontinuation.¹¹⁻¹³

Precision medicine, also known as personalized medicine, is an approach that tailors treatment decisions based on individual differences in genetics, lifestyle, and other factors.¹⁴ Pharmacogenomics, which is the study of how genes affect a person's response to particular drugs, is 1 of the core elements of precision medicine. Genetic variations can influence the absorption, distribution, metabolism, and excretion of medications.¹⁵ These variations contribute to the interindividual variability in response to psychotropic medications and are therefore particularly relevant in the field of psychiatry.^{15,16} Testing for genetic variations in genes of interest before initiating pharmacotherapy can provide clinicians with additional information to consider when making prescribing decisions. Although this approach is not a part of the current standard of care for people with psychiatric disorders in Canada, it has the potential to minimize the trial-and-error phase and improve patient experiences.¹⁷ Recognizing this, [CADTH's 2023 Watch List](#)¹⁸ acknowledges pharmacogenomic testing for mental health conditions as a top 10 precision medicine technology that has the potential to make a significant and meaningful impact in transforming health systems in Canada over the next 5 years.

This Horizon Scan provides an overview of:

- pharmacogenomic testing for psychiatric disorders
- a summary of some of the clinical and cost-effectiveness evidence
- perspectives on early considerations should emerging evidence demonstrate the value of pharmacogenomic testing.

The Technology

Pharmacogenomic testing analyzes target genes for polymorphisms that affect the function of proteins identified as playing a role in drug metabolism, including drug metabolizing enzymes, receptor proteins, and drug transporting enzymes.¹⁹ Genetic polymorphisms are naturally occurring changes in the nucleotide sequence of the DNA. Although many polymorphisms do not cause any changes to the proteins that the DNA sequence codes for, some polymorphisms can result in altered protein function and have physiologic consequences.²⁰ Information from pharmacogenomic testing can be incorporated into the prescribing

process because an individual's genetic profile may predict which medications are most likely to result in desired outcomes (e.g., treatment response) or to have the lowest risk of adverse events.²¹

A classic example of genetic variation leading to observable changes in the way medications are metabolized is the cytochrome P450 superfamily of enzymes. Depending on the genetic polymorphisms present, individuals can be classified as poor metabolizers, intermediate metabolizers, extensive metabolizers, or ultra-rapid metabolizers.²² Poor metabolizers are more likely to experience adverse reactions from drugs that are processed by cytochrome P450 enzymes, while ultra-rapid metabolizers are more likely to not respond at all to normal doses because the drug is rapidly cleared from their system.²²

Pharmacogenomic tests use a sample of saliva, blood, or a buccal (cheek) swab as a source of genetic material. Once collected, the sample is processed through a series of steps that result in DNA extraction, purification, and genotyping.²³ The results of genotyping are then relayed to the care provider. Pharmacogenomic tests can be performed on single genes or can provide an analysis of multiple genes at once. Using proprietary algorithms, many pharmacogenomic tests that include multigene panels provide colour-coded assessments of the suitability of medications based on results of testing.²⁴ For example, medications categorized as green can be prescribed as directed and yellow-coded drugs have the potential for moderate gene-drug interactions.²⁴

Pharmacogenomic testing has applications in many fields of medicine, including cardiology, endocrinology, gastroenterology, hematology, immunology, neurology, oncology, and psychiatry.²⁵ For the purpose of this report, we aimed to summarize information on pharmacogenomic testing for psychiatric conditions (e.g., depressive disorders, anxiety disorders, psychotic disorders) and other related conditions for which care is typically provided by a psychiatrist or psychiatric care specialist (e.g., ADHD, autism spectrum disorder). Information on other conditions, such as those that would primarily be managed by a neurologist or other clinical specialty (e.g., tic disorders, epilepsy, dementia, cancer, cardiovascular disorders), was considered out of scope.

Availability and Guidelines

Although widespread implementation and adoption of pharmacogenomic testing for informing the treatment of psychiatric disorders has not yet occurred,^{17,26} several health facilities in Canada offer clinical pharmacogenomic testing through research programs, including the Hospital for Sick Children, BC Children's Hospital, the University of Montreal, Western University, the University of Calgary, the University of Alberta, and the Centre for Addictions and Mental Health.^{17,27} In addition to these programs, there are a wide range of commercial pharmacogenomic testing options available in Canada as direct-to-consumer tests.¹⁷ A description of some pharmacogenomic tests available in Canada with applicability in mental health is provided in [Appendix 1, Table 2](#).

Regulations

The regulation of pharmacogenomic tests is complex and can be under the purview of federal or provincial authorities, depending on the nature of the test.²⁸ Commercial pharmacogenomic tests that are marketed as test kits and that qualify as in vitro diagnostic devices (i.e., diagnostic tests performed using medical equipment and accessories on clinical samples, such as blood, urine, saliva, and tissue derived from the human body) are required to have regulatory approval by Health Canada as a Class III medical device.²⁸⁻³⁰ To qualify as an in vitro diagnostic device, the test kit includes the reagents required to process the sample and receive the test result, similar to most pregnancy tests (i.e., the sample is not sent to a laboratory for analysis).²⁸ However, there are currently no pharmacogenomic tests for psychiatric disorders that meet these criteria in Canada, meaning that commercially available tests are not subject to regulatory approval by Health Canada. Tests that are offered as laboratory services, or that were developed in-house at hospitals or other clinical settings, are subject to regulation by provincial authorities.^{28,29} Alternatively, pharmacogenomic tests that are processed in a laboratory outside of Canada (i.e., the sample is collected in Canada and sent outside of Canada for analysis) do not undergo any regulatory scrutiny in Canada.²⁹

Guidelines on the Clinical Implementation of Pharmacogenomic Testing

To facilitate the implementation of pharmacogenomic testing into clinical practice, several organizations and professional societies have produced evidence-based guidelines that offer recommendations about when testing is appropriate and provide guidance about how an individual's genotype status can be used to inform treatment selection or dosing decisions. This guidance is particularly important because pharmacogenomic testing is relatively uncommon in routine clinical practice, and many clinicians may not have the specialized knowledge and expertise in genetics and pharmacology needed to interpret test results accurately and effectively incorporate them into treatment decisions.³¹

The most comprehensive pharmacogenomic testing guidelines available are published by the Clinical Pharmacogenetics Implementation Consortium (CPIC) and the Dutch Pharmacogenetics Working Group (DPWG).³² Although these guidelines do not recommend any specific pharmacogenomic tests, they serve as a resource for clinicians to gain an understanding of what pharmacogenomic information is clinically actionable during the prescribing process. The advice from these guidelines is based on findings from studies that have examined the associations between genetic variants and pharmacokinetic and pharmacodynamic parameters or clinical outcomes.

The CPIC guidelines are designed to help clinicians understand how available genetic test results should be used to optimize drug therapy. The international consortium of experts has produced more than 25 guidelines that provide recommendations on various gene-drug interactions,³³ including guidelines on:

- selective serotonin reuptake inhibitors³⁴
- tricyclic antidepressants³⁵
- atomoxetine³⁶
- and mood stabilizers.³⁷

Similarly, the DPWG is a multidisciplinary team that includes clinical pharmacists, physicians, clinical pharmacologists, clinical chemists, epidemiologists, and toxicologists who aimed to develop pharmacogenomic-based therapeutic dose recommendations that could be integrated into drug prescription and medication surveillance systems.³⁸ The group published their original guidelines in 2008³⁹ and subsequently updated their guidelines in 2011.³⁸ Since 2011, the DPWG have maintained and updated their guidelines on their [Farmacogenetica](#) website as the evidence continues to evolve. Relevant to the field of psychiatry, their guidelines include dosing recommendations on various antidepressants (e.g., amitriptyline, citalopram, escitalopram, paroxetine) and antipsychotics (e.g., aripiprazole, brexpiprazole, risperidone, zuclopenthixol).³⁸

Guidelines produced by CPIC and the DPWG have received endorsements from a number of professional associations in Canada and internationally, including the Canadian Paediatric Society,⁴⁰ the American Society of Health-System Pharmacists,⁴¹ the American Society for Clinical Pharmacology & Therapeutics,⁴² the European Association for Clinical Pharmacology and Therapeutics,⁴³ and the European Association of Hospital Pharmacists.⁴³

Guidelines on the appropriate use of pharmacogenomic testing in psychiatry have also been published by the International Society of Psychiatric Genetics and the Dutch Clinical Psychiatric Association. In 2021, a group of experts convened by the International Society of Psychiatric Genetics described when the use of pharmacogenomic testing to inform medication selection and dosing of several commonly used antidepressant and antipsychotic medications is supported by evidence and key considerations and limitations related to the use of pharmacogenomic testing in psychiatry.²⁷ Their guidelines suggest that pharmacogenomic testing to guide treatment selection and dosing is supported in several clinical contexts, including for antidepressants, antipsychotics, anticonvulsants, and the ADHD medication atomoxetine.²⁷ Similarly, the Dutch Clinical Psychiatric Association have published guidance on how to best use genotyping in clinical psychiatric practice, including when to genotype, how to request genotyping, which genes to investigate, and how to interpret genotype results.⁴⁴

In addition to clinical guidelines, product labels from regulatory agencies, such as the FDA, Health Canada, the Swiss Agency for Therapeutic Products, the European Medicines Agency, and the Pharmaceuticals and Medical Devices Agency in Japan, provide recommendations on when pharmacogenomic information should be considered when making treatment selection or dosing decisions.²⁷

Pharmacogenomics Prescribing Information Knowledgebase

Information from clinical guidelines and products labels is available on the [Pharmacogenomics Knowledgebase \(PharmGKB\)](#) website, which is a resource funded by the US National Institutes of Health that collects, curates, and disseminates pharmacogenomic evidence.^{16,45} A list of gene-drug pairs with variant-specific prescribing guidance supported by a high level of evidence (i.e., level of evidence of 1A according to the PharmGKB annotation scoring system) is provided in [Table 1](#).^{16,31,46,47}

Despite the numerous guidelines and product labels that can be used to help clinicians decide which genetic polymorphisms are clinically actionable, there is little to no guidance available on who should be tested

and when it is most appropriate to test (e.g., before starting a first-line medication, following inadequate response or side effects from medication).³¹ Additional guidance on who should be tested and when they should be tested may encourage further adoption of pharmacogenomic testing into psychiatric practices.

Table 1: Gene-Drug Pairs With Actionable Recommendations From CPIC, DPWG, Health Canada, and the FDA^a

Gene	Psychotropic drug	Variant-specific prescribing guidance ^b			
		CPIC	DPWG	FDA	HC
CYP2B6	Sertraline	Yes	No	No	No
CYP2C9	Fosphenytoin	Yes	No	Yes	No
	Phenytoin	Yes	Yes	No	No
CYP2C19	Amitriptyline	Yes	No	No	No
	Citalopram	Yes	Yes	Yes	Yes
	Clomipramine	Yes	Yes	No	No
	Doxepin	Yes	No	Yes	No
	Escitalopram	Yes	Yes	Yes	Yes
	Imipramine	Yes	Yes	No	No
	Sertraline	Yes	Yes	No	No
	Trimipramine	Yes	No	No	No
CYP2D6	Amitriptyline	Yes	Yes	Yes	No
	Aripiprazole	No	Yes	Yes	Yes
	Atomoxetine	Yes	Yes	Yes	Yes
	Clomipramine	Yes	Yes	Yes	No
	Desipramine	Yes	No	Yes	No
	Doxepin	Yes	Yes	Yes	No
	Fluvoxamine	Yes	No	Yes	No
	Haloperidol	No	Yes	No	No
	Imipramine	Yes	Yes	Yes	No
	Nortriptyline	Yes	Yes	Yes	Yes
	Paroxetine	Yes	Yes	No	No
	Risperidone	No	Yes	No	No
	Trimipramine	Yes	No	Yes	No
	Venlafaxine	Yes	Yes	Yes	No
	Vortioxetine	Yes	No	Yes	Yes
Zuclopenthixol	No	Yes	No	No	
CYP3A4	Quetiapine	No	Yes	No	No

Gene	Psychotropic drug	Variant-specific prescribing guidance ^b			
		CPIC	DPWG	FDA	HC
<i>HLA-A</i>	Carbamazepine	Yes	Yes	Yes	Yes
<i>HLA-B</i>	Carbamazepine	Yes	Yes	Yes	Yes
	Fosphenytoin	Yes	No	Yes	Yes
	Lamotrigine	No	Yes	No	No
	Oxcarbazepine	Yes	Yes	Yes	Yes
	Phenytoin	Yes	Yes	Yes	Yes

CPIC = Clinical Pharmacogenetics Implementation Consortium; DPWG = Dutch Pharmacogenetics Working Group; HC = Health Canada.

^aOnly gene-drug combinations with a high level of evidence supporting the association that have prescribing guidance for specific variants in a current clinical guideline annotation or an FDA-approved drug label were included (i.e., level of evidence of 1A according to the PharmGKB annotation scoring system).

^bVariant-specific prescribing guidance from CPIC, DPWG, FDA, and HC were identified from the Pharmacogenomics Knowledgebase (PharmGKB). Drug labels from the FDA and HC coded as “actionable,” “testing recommended,” or “testing required” in the Pharmacogenomics Knowledgebase were considered actionable (i.e., labels coded as “informative” were not considered actionable).

Cost

The costs associated with pharmacogenomic testing differ across tests and can be affected by factors such as the methods of sample collection (e.g., blood drawn versus self-collected saliva), the complexity of genetic analysis (e.g., single gene versus multigene), and how the test results are communicated.^{48,49}

A 2020 Canadian study¹⁷ examined the cost of 13 pharmacogenomic tests relevant to psychiatry that were available in Canada. The study reported that the cost for each test ranged from \$199 to \$2,310, with a median cost of \$499.¹⁷ These prices did not include any costs associated with the interpretation of the test results by a clinician for prescribing decisions or any additional expenses, such as applicable taxes or shipping fees. The study did not investigate the factors responsible for the variability in test pricing. The authors noted that at the time of the study, pharmacogenomic testing was not covered by health insurance plans in Canada, but that many employer-based health-spending accounts list pharmacogenomic testing as an eligible expense and were piloting the use of pharmacogenomic testing for individuals with mental health-related disability claims, suggesting that it may become eligible for reimbursement in the future.¹⁷

Who Might Benefit and Potential Impact

The use of pharmacogenomic testing has the potential to benefit a wide variety of people who are starting a new pharmacological treatment for psychiatric disorders, including people with treatment-resistant conditions, with a family history of poor response to specific medications, who are using multiple medications and may be at risk for drug-drug interactions, and who have experienced serious treatment-related side effects in the past.^{50,51} Although the proportion of people in Canada who are diagnosed with psychiatric disorders and have clinically actionable gene variants (as defined by the available guidelines) is unclear, 1 in 5 people in Canada experience mental illness each year, and approximately 75% of people with a mood or anxiety disorder diagnosis have reported that they are receiving treatment with psychotherapeutic

drugs.⁵² One study⁵³ estimated that genetic testing for *CYP2C19* and *CYP2D6* variants could influence treatment decisions in up to one-third of individuals receiving pharmacotherapy for depression in Canada. In 2021, more than 120 million prescriptions for antidepressants, anxiolytics, antipsychotics, and psychostimulants were dispensed in Canadian community pharmacies for various psychiatric disorders.⁵⁴ The significant number of individuals in Canada undergoing pharmacotherapy for psychiatric disorders highlights the potential role that pharmacogenomic testing could play in many treatment decisions.^{5,55,56}

Summary of the Evidence

We aimed to review the published literature that assessed the comparative clinical effectiveness and cost-effectiveness of pharmacogenomic tests for guiding the treatment of psychiatric disorders compared with treatment as usual (i.e., no pharmacogenomic testing to guide medication selection). Additionally, we sought studies that have evaluated patients' perspectives and experiences related to pharmacogenomic testing. Because the clinical evidence about the use of pharmacogenomic testing varies by patient population, the findings are presented by psychiatric disorder. When available, the emerging evidence summarized in published health technology assessments (HTAs) or systematic reviews was prioritized. If there were no HTAs or systematic reviews identified for a condition, the findings from primary clinical studies (both randomized and nonrandomized) were described.

There are many gene-drug association studies that examine the relationship between genetic polymorphisms and response to pharmacotherapies for various disorders, including depression,⁵⁷⁻⁵⁹ bipolar disorder,^{60,61} substance use disorders,⁶²⁻⁶⁵ schizophrenia spectrum disorders,⁶⁶ ADHD,⁶⁷⁻⁶⁹ obsessive-compulsive disorder,⁷⁰ anxiety disorders,^{71,72} autism spectrum disorder,^{73,74} post-traumatic stress disorder (PTSD),⁷⁵ and alcohol withdrawal syndrome.⁷⁶ Although these studies may be informative for the development of pharmacogenomic tests because they identify genes of potential interest, these studies were not reviewed in this report.

This Horizon Scan report is not a systematic review of the evidence, the studies included were not critically appraised, and it does not endorse any information, pharmacogenomic test, or technology.

Clinical Effectiveness

Mood Disorders

Relative to other psychiatric disorders, the clinical effectiveness of pharmacogenomic testing for mood disorders, including major depressive disorder, bipolar disorder, and other depressive disorders, appears to have the largest volume of clinical studies published to date.

Major Depressive Disorder

Ontario Health conducted a HTA²⁹ on multigene pharmacogenomic testing that includes decision-support tools to guide medication selection for major depression. The clinical evidence review included 14 interventional studies that evaluated 6 unique multigene pharmacogenomic tests compared with treatment as usual in a total of 3,262 participants.²⁹ The findings suggested that the use of multigene

pharmacogenomic testing to guide medication selection for major depression showed inconsistent effectiveness.²⁹ Overall, testing resulted in little to no difference in depressive symptoms compared with treatment as usual.²⁹ However, some specific tests may improve response to treatment or remission from symptoms.²⁹ The authors indicated that these tests are a heterogeneous class of interventions and that each individual test has different effectiveness compared with treatment as usual.²⁹ Additionally, the authors noted that the evidence was uncertain, and that these observed effects may not reflect the true effects of the intervention.²⁹ After consideration of the evidence described in the HTA and based on the guidance of the Ontario Health Technology Advisory Committee, Ontario Health recommended against publicly funding multigene pharmacogenomic testing that includes decision-support tools for guiding medication selection for people with major depression.⁷⁷

More recently, a systematic review and meta-analysis by Skryabin et al. (2022)⁷⁸ included 5 randomized controlled trials (RCTs) (N = 2,200) that examined the effects of pharmacogenomic decision-support tools in people undergoing pharmacotherapy for major depressive disorder. The results of the meta-analysis suggested that people who received therapy guided by pharmacogenomic testing experienced improved response rates and remission rates after both 8 and 12 weeks of therapy compared with those who received unguided pharmacotherapy.⁷⁸

Mixed Depressive Disorders

A systematic review with meta-analysis⁷⁹ published in 2023 examined the effectiveness of pharmacogenomic tests that include *CYP2D6* and *CYP2C19* genomic variants for guiding the treatment of mixed depressive disorders. Based on evidence from 12 RCTs that included a total of 5,685 participants, the authors concluded that the use of pharmacogenomic testing that includes *CYP2D6* and *CYP2C19* genomic variants for guiding the treatment of depressive disorders improved depressive symptoms, response rates, and remission rates compared with treatment as usual.⁷⁹ Similar results were described in other systematic reviews,^{80,81} including a 2022 systematic review and meta-analysis by Brown and colleagues,⁸⁰ which included data from 4,767 participants of 13 primary studies. The authors concluded that pharmacogenomic-guided antidepressant therapy is associated with a modest but significant increase in depressive symptom remission compared with treatment as usual in adults with major depressive disorder.⁸⁰

One systematic review⁸² analyzed studies of patients with major depressive disorder and bipolar disorder separately, conducting a meta-analysis for each patient group. The findings from the meta-analysis for patients with major depressive disorder, which included data from 3,462 participants enrolled in 6 primary studies, indicated that people who were treated using therapies guided by pharmacogenomic testing experienced significantly higher response rates and remission rates.⁸² For patients with bipolar disorder, the findings from the meta-analysis (which included a total of 223 participants from 2 studies) indicated that there were no significant differences between treatment guided by pharmacogenomic testing and treatment as usual with respect to efficacy.⁸²

In addition to these systematic reviews, CADTH previously conducted 2 Rapid Reviews^{83,84} on the clinical effectiveness of pharmacogenomic testing for people with depression. Findings of these previous reports suggested that the available evidence was inconclusive because the included studies reported mixed results

(i.e., some studies suggested pharmacogenomic testing improved outcomes while others suggested there was no difference between pharmacogenomic testing and treatment as usual).^{83,84} Additional details on the methodology and findings of these CADTH reports are available in the reports.^{83,84}

It is important to take into consideration the significant overlap in the primary studies that are included in these reviews when interpreting their findings. The inclusion of data from primary studies across multiple evidence syntheses could cause double counting of data from the same primary studies, leading to a biased interpretation of the results.

Schizophrenia

In a single-blind RCT,⁸⁵ 311 people aged 18 years or older who were diagnosed within the schizophrenia spectrum were randomized to receive antipsychotic drug treatment guided by pharmacogenomic testing, antipsychotic drug treatment guided by structured clinical monitoring, or treatment as usual. Within the pharmacogenomic testing group, attending psychiatrists were provided information on patients' cytochrome P450 2D6 and 2C19 (*CYP2D6* and *CYP2C19*) genotype, which could be used to inform prescription decisions based on the CYP guidelines.⁸⁵ Participants within the structured clinical monitoring group were assessed for treatment effects, adverse effects, and attitudinal and behavioural factors influencing patient adherence routinely, which could be used to adjust treatment selection or dosing if deemed appropriate.⁸⁵ Participants in the control group received standard care, assessment of symptoms at fixed time points was not required, and the CYP test results were concealed.⁸⁵ The study found that there was no significant difference in antipsychotic drug persistence (i.e., the time in days to the first modification of the initial antipsychotic treatment) between the pharmacogenomic-guided group and the control group, suggesting the prescribing that was guided by pharmacogenomic testing did not improve tolerability or effectiveness.⁸⁵

Autism Spectrum Disorders

An observational cohort study by Arranz and colleagues⁸⁶ examined the effectiveness of a pharmacogenomic intervention that evaluated genetic variants in *CYP1A2*, *CYP2C19*, *CYP2D6*, and *SLC6A4* genes in people with autism spectrum disorders. A total of 42 individuals with treatment-resistant autism spectrum disorders were included in the intervention group, while 62 individuals with autism spectrum disorders were included in the control group that received no pharmacogenomic intervention.⁸⁶ Of the 42 individuals in the pharmacogenomic testing group, 39 (93%) experienced improvement in their Clinical Global Impression (CGI) scores, and 37 (88%) experienced improvement in their Children's Global Assessment Scale (CGAS) scores. The proportion of people who experienced treatment response was higher in the intervention group than in the control group, in which 41 individuals (66%) were classified as responders (i.e., they had improvements in CGI and CGAS scores after treatment).⁸⁶

Mixed Populations

Several studies have examined the clinical effectiveness of pharmacogenomic testing in patient populations with a variety of psychiatric disorders or comorbid disorders.

Papastergiou and colleagues conducted a single-blind RCT⁸⁷ that evaluated the impact of pharmacogenomic-guided therapy versus standard antidepressant therapy in 213 adult outpatients diagnosed with major

depressive disorder or generalized anxiety disorder. After measuring outcomes of depression, anxiety, disability, and treatment satisfaction at baseline and at up to 6 months postrandomization, the authors concluded that participants who received pharmacogenomic-guided treatment (N = 103) experienced greater improvements in depressive symptoms, generalized anxiety symptoms, and disability than those who received standard treatment (N = 108).⁸⁷

A single-centre, double-blind RCT by Zastrozhin et al. (2020)⁸⁸ included 118 male participants with affective disorders and comorbid alcohol use disorder. After recruitment, participants were randomized to receive treatment with fluvoxamine, mirtazapine, or carbamazepine in doses recommended by pharmacogenomic testing (N = 70) or treatment as usual (N = 48), in which the treating physicians were provided a report for each patient that indicated the individual had normal genotypes. After 16 days of treatment, there were statistically significant between-group differences in self-reported depressive symptoms and side effects that favoured the pharmacogenomic-guided group.⁸⁸

A single-centre RCT by Claudio-Campos and colleagues⁸⁹ allocated 49 people (younger than 20 years) **attending a child psychiatric clinic** to receive care that was guided by pharmacogenomic testing (N = 25) or treatment as usual (N = 24). Participants had a primary diagnosis of ADHD, anxiety, depression, or obsessive-compulsive disorder. The authors concluded that the implementation of pharmacogenomic testing was feasible and well accepted by families and physicians; however, there were no significant between-group differences in global impairment, antidepressant-related adverse events, depressive symptoms, obsessive-compulsive symptoms, or anxiety symptoms over the 12-week follow-up period.⁸⁹

Similar findings were observed in 2 nonrandomized studies.^{90,91} In a single-centre, retrospective case-control study⁹⁰ of **children and adolescents** between the ages of 4 and 18 years with various psychiatric disorders, including major depressive disorders, ADHD, generalized anxiety disorder, or multiple disorders, the authors found no difference in clinical improvement between the group who received care guided by pharmacogenomic testing (N = 126) and the treatment as usual control group (N = 129).⁹⁰ King and colleagues conducted a single-centre, open-label, prospective cohort study⁹¹ that included 75 adult inpatients at a short-term acute care unit for severe depression and anxiety. Participants were diagnosed with a wide range of psychiatric disorders, including depressive disorders, bipolar disorder, panic disorder, obsessive-compulsive disorder, PTSD, adjustment disorder, eating disorders, substance use disorders, and borderline personality disorder. Participants were assigned to receive care guided by a pharmacogenomic assay or treatment as usual. After the 3-month follow-up period, there were no significant between-group differences in any of the 3 primary outcome measures (i.e., depressive symptoms, anxiety symptoms, readmission).⁹¹

Cost-Effectiveness

Many clinical studies have examined the utility of pharmacogenomic testing for informing treatment selection in people with psychiatric disorders; however, there is a high level of uncertainty about the clinical effectiveness of pharmacogenomic testing due to the heterogeneity of tests, patient populations, and outcome measures and the mixed or conflicting results reported in clinical trials, which may limit the reliability of subsequent economic evaluations. Regardless, cost-effectiveness evidence may be useful to

health care decision-makers, particularly economic evaluations that are conducted using parameters from Canadian settings.

A 2021 systematic review⁹² of economic evaluations included 18 studies published between 2005 and 2019 that assessed the cost-effectiveness of pharmacogenomic testing to inform pharmacological treatment (including antidepressants and antipsychotics) versus treatment as usual in adults with psychiatric illness. Included studies assessed several populations, including people with:

- major depressive disorder (7 studies)
- schizophrenia (4 studies)
- depression and anxiety (3 studies)
- a variety of psychiatric disorders (4 studies).⁹²

The majority of the included studies (11 of 18) were by authors in the US. Twelve of the studies examined pharmacogenomic tests that examined a panel of multiple genes, including commercially available tests (e.g., GeneSight, NeuroIDgenetix, IDgenetix), whereas 6 studies evaluated pharmacogenomic interventions that analyzed single genes for clinically actionable polymorphisms, most often the *CYP2D6* or *CYP2C19* genes. Of the 18 studies included in the systematic review, 17 drew conclusions in favour of pharmacogenomic testing. Among them, 10 studies indicated that pharmacogenomic testing was likely to be cost-effective, while 7 studies reported that it could lead to cost savings.⁹² These 17 studies were specific to populations with major depressive disorder, schizophrenia, or a variety of psychiatric disorders.⁹² However, 1 study reported that pharmacogenomic testing was not cost-effective for individuals with major depressive disorder.⁹² The authors of the systematic review suggested that pharmacogenomic testing can contribute to reducing health care costs by decreasing:

- adverse drug reactions
- the number of drug switches and recurrent dose adjustments
- the time until disease remission
- disease burden and related costs.⁹²

Within the 18 included studies, there was a high degree of variation with respect to study designs, population characteristics, model structures, time horizon, perspectives, sources of clinical inputs, sources of cost data, methods for expressing currency and price data, and willingness-to-pay thresholds.⁹²

The generalizability of these findings to Canadian settings is unclear because the cost-effectiveness of pharmacogenomic testing is expected to be context-specific and to be influenced by many factors, including but not limited to the local costs associated with administering and interpreting pharmacogenomic testing and the prescribing practices of clinicians who provide psychiatric care.

To determine the cost-effectiveness of pharmacogenomic testing in Canada, Tanner and colleagues⁹³ conducted an economic evaluation on the use of combinatorial pharmacogenomic testing (which uses weighted algorithms) to guide the treatment of moderate to severe major depression compared with treatment as usual from the Canadian public payer perspective. Using a 5-year time horizon, the base-case

model projected that patients whose treatment was informed by combinatorial pharmacogenomic testing would gain an additional 0.17 quality-adjusted life-years and would result in cost savings of \$2,431 compared with those who received treatment as usual.⁹³ The study concluded that combinatorial pharmacogenomic testing was less costly and more effective (i.e., dominant) compared with treatment as usual for moderate to severe major depression.⁹³

Patients' Perspectives and Experiences

Studies exploring patients' perspectives and experiences have suggested that people are generally optimistic toward the potential for therapeutic benefit from pharmacogenomic testing in the field of psychiatry.⁹⁴⁻⁹⁷ However, patients have expressed some concerns, such as fear of discrimination, reliance on medication, and difficulty related to being informed of the potential for poor treatment response due to genetic profile.

A survey-based study⁹⁵ of 170 veterans with depressive symptoms in the US aimed to assess motivations and attitudes around pharmacogenomic testing. Although the authors noted that pharmacogenomic testing in patients with treatment-refractory depression is largely well tolerated, some patients experienced fear of discrimination based upon the test results.⁹⁵ For example, participants expressed concerns that identifying a gene linked to serious mental health illness could potentially affect their family's access to health insurance or lead to employment-related consequences.⁹⁵ Additionally, respondents indicated that they may have difficulty coping with genetic test results because it could be overwhelming to be informed that poor treatment response is likely given an individual's genetic profile.⁹⁵

Participants of a qualitative study⁹⁶ that interviewed 17 residents of British Columbia with a history of depression and antidepressant use suggested there is a need for an authority (e.g., the BC Ministry of Health) to evaluate the evidence on the benefits and harms of pharmacogenomic testing and to provide oversight to ensure testing is provided in a safe and regulated manner.⁹⁶ Furthermore, patients expressed concerns that pharmacogenomic testing might lead to an over-reliance on medication rather than exploring nonpharmacological interventions, which would limit the opportunity for patients to contribute to treatment decisions.⁹⁶

Issues to Consider

Uncertain Evidence and Inconsistent Guidelines

One of the most commonly cited barriers to the implementation of pharmacogenomic testing into psychiatric care practices is the overall paucity of high-quality, published evidence validating gene-drug interactions and assessing the clinical utility of pharmacogenomic testing in guiding treatment decisions.^{31,98-100}

Methodological Limitations

Pharmacogenomic tests are marketed to people with a wide range of psychiatric and related disorders, including depression, bipolar disorder, anxiety disorders, schizophrenia, psychosis, PTSD, ADHD, obsessive-compulsive disorder, and autism spectrum disorders; however, there is a lack of high-quality reproducible evidence validating the utility of pharmacogenomic testing to guide treatment for each of these conditions.¹⁰⁰

For example, a 2020 review¹⁷ indicated that of 13 pharmacogenomic tests available in Canada, only 2 had had been evaluated in RCTs. It is also common that multiple studies assessing pharmacogenomic testing in similar patient populations have contradictory results (i.e., some studies suggest there is a clinical benefit while others do not).^{98,101} This has been attributed to methodological limitations in their study designs, such as inadequate blinding of care providers, small sample sizes, use of heterogeneous tests and outcome measures, and lack of controlling for differences in demographic, clinical, and environmental factors in patient cohorts.^{77,98,102} In some cases, pharmacogenomic tests incorporate genes that do not have any clinical guidelines or rigorous evidence supporting their clinical validity for predicting treatment outcomes.¹⁰³ Data from higher quality clinical studies that address these methodological limitations and knowledge gaps could better inform clinical and policy decisions regarding the role of pharmacogenomic testing in psychiatric care.

Generalizability and the Need for Diversity in Research

The generalizability of the available evidence has also been criticized because studies evaluating the utility of pharmacogenomic testing have primarily been conducted in populations of European ancestry.^{100,101,104} Although this is a common issue that affects many fields of scientific research,¹⁰⁵ it is particularly concerning in pharmacogenomic research because genetic variation across geographic regions and ethnic groups can have a major influence on the outcomes of drug treatment for psychiatric conditions.^{101,104} For example, 2 gene variants of the *PTPRD* (protein tyrosine phosphatase receptor type D) gene have been associated with increased risk of antipsychotic-induced weight gain in Han Chinese people with schizophrenia;¹⁰⁶ however, the presence of these variants could not be validated to predict the risk of antipsychotic-induced weight gain in European or African American patients.¹⁰⁷ Future research on the clinical utility of pharmacogenomic testing in diverse populations is warranted to ensure the implementation of pharmacogenomic testing results in equitable access to care that can be considered universally applicable.^{100,107} Furthermore, the clinical utility of pharmacogenomic testing for initial drug selection and dosing decisions is uncertain because most studies conducted to date have focused on people with major depressive disorder who did not respond to initial pharmacotherapy or developed adverse drug reactions, limiting the generalizability of their findings to other populations or clinical scenarios.³¹

Inconsistent Recommendations

Uncertainties in the clinical literature have contributed to varied interpretations of the evidence, including inconsistencies in pharmacogenomic recommendations published by the CPIC and the DPWG, regulatory agencies (e.g., FDA, Health Canada), and professional societies.¹⁰⁸⁻¹¹⁰ In many cases, 1 source may suggest modifications to the dosing of pharmacotherapy based on the presence of a gene variant, whereas another source may not deem the same gene-drug pair as clinically actionable.^{108,109} One study has suggested that nearly half of pharmacogenomic recommendations from reporting sources in the US (e.g., CPIC and the FDA) were inconsistent.¹⁰⁷ Consistent and clear information from regulators and guideline-producing organizations might facilitate proper implementation of pharmacogenomic testing in clinical practice.¹⁰⁸⁻¹¹⁰

Clinician Education and Training

Improved clinician education and training have been identified as essential for the successful implementation of pharmacogenomic testing in psychiatric care settings.^{31,100,111-116} A mixed methods study conducted in 4 long-term care homes in Ontario following the implementation of a pharmacogenomic testing program reported that physicians' limited familiarity with pharmacogenomics and CPIC prescribing guidelines acted as a barrier to the implementation of the testing program.¹¹¹ Similar findings were described in a survey-based study conducted in Alberta, in which pediatric psychiatrists and pediatricians were asked about their pharmacogenomic testing knowledge and attitudes.¹¹⁷ Generally, respondents indicated they had limited familiarity with pharmacogenomic testing, and that they would be interested in education and training opportunities that could facilitate the implementation of pharmacogenomic testing into their practice, particularly opportunities that would provide information on how testing results should be interpreted and the current recommendations for prescribing.¹¹⁷ Several studies conducted in other jurisdictions, including Brazil¹¹² and the US,^{113,114} have also suggested that clinicians who provide psychiatric care want to increase their understanding of pharmacogenomic testing to implement testing in a clinically meaningful way.^{100,116}

Clinician education and training for physicians in training could be addressed by incorporating additional pharmacogenomic testing into medical school curricula and medical residency programs.^{113,117} To aid in the education and training of practising clinicians, continuing medical education opportunities about emerging clinical trial data, best practices for communicating test results to clients, treatment algorithms, and dosing recommendations from CPIC and other expert bodies may help to facilitate the appropriate adoption of pharmacogenomic testing.^{100,113,114,116}

Potential to Amplify Existing Health Inequities

For many people in Canada, pharmacogenomic testing for psychiatric disorders is not covered by public or private health insurance plans, meaning that testing is an out-of-pocket expense.^{17,31} Clinicians and patients have expressed concerns that the cost of testing could exacerbate health inequities because people with the ability to pay could have access to higher quality care than those who cannot.^{31,94,96,117,118} Furthermore, there is potential for pharmacogenomic tests to provide inequitable benefits to patients if they have not been validated in diverse populations. Race, ethnicity, ancestry, age, gender, and other factors have been cited as important considerations during the development of pharmacogenomic tests to reduce bias and support equitable outcomes for all.⁹⁶ People at the intersections of having the ability to pay and who are from groups that are underrepresented in clinical trials of pharmacogenomic tests have greater potential for experiencing widening health inequities.

Privacy and Confidentially

Pharmacogenomic testing involves the collection and storage of massive amounts of sensitive health data, and the privacy and security of these data are essential. To ease concerns related to the handling of data, providers of pharmacogenomic testing should seek informed consent before testing, ensure high standards for data security and protection are upheld, adhere to laws and regulations relevant to the privacy of personal information (e.g., the *Privacy Act*, the *Personal Information Protection and Electronic Documents Act*, and the

Freedom of Information and Protection of Privacy Act), and only use data for purposes that are relevant to patient care and for which patient consent has been obtained.^{96,119}

The Privacy Commissioner of Canada provides a description of the key privacy risks associated with direct-to-consumer genetic tests and a list of questions for consumers to consider before participating in testing.¹²⁰

Final Remarks

Pharmacogenomic testing is an emerging technology with the potential to optimize the therapeutic benefit of medications based on an individual's genetic profile. In the field of psychiatry, it can serve as a useful tool to minimize the trial-and-error phase of psychotropic prescribing, which could reduce adverse events and improve patient experiences.¹⁷ Despite being available for approximately 20 years and that numerous recommendations from guideline-developing groups and regulators have been issued about the types of pharmacogenomic information that should be used to guide prescribing decisions, pharmacogenomic testing has yet to be integrated into most psychiatric care practices in Canada and worldwide.^{17,27,121} This limited uptake of the technology has been partly attributed to the scarcity of high-quality studies that have provided a reliable assessment of the clinical and cost-effectiveness of these tools.⁹⁸⁻¹⁰⁰

Given the high prevalence of psychiatric disorders, their impact on the lives of people living with mental illness, the substantial economic burden associated with untreated or poorly treated mental illness (exceeding \$50 billion annually in Canada),⁵ and the potential for pharmacogenomic testing to optimize medication selection, additional research is warranted to validate the utility of pharmacogenomic testing for psychiatric disorders. Specifically, robustly designed studies are needed to overcome the limitations associated with the current evidence, including concerns related to risk of bias, reproducibility, and generalizability. Findings from ongoing investigator-initiated trials¹²²⁻¹²⁶ may provide valuable insights and help overcome some of the identified limitations of the current evidence.

Health inequities exist across health care systems, particularly in mental health, including access to care, use of care services, and outcomes achieved through care.^{127,128} Although pharmacogenomic testing has not been widely adopted in Canada, there are numerous pharmacogenomic tests available on the commercial market. Considering the potential for mental health to make people vulnerable or to further increase their vulnerability to systemic inequities, pharmacogenomic testing services may already be exacerbating existing inequities, an issue that could be amplified if the broad implementation of testing occurs without care.

As the evidence regarding the use of pharmacogenomic testing for psychiatric disorders continues to evolve, implementors of this technology should consider issues related to clinician education and training, privacy and confidentiality of health data, and the potential for testing to exacerbate existing health inequities. Should pharmacogenomic testing be widely adopted, it has potential applicability in a high volume of treatment decisions. Health systems may need to consider expanding testing capacities by augmenting existing laboratory infrastructure, including testing equipment and personnel to conduct and interpret pharmacogenomic tests.

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Appendix 1: Pharmacogenomic Tests for Psychiatric Disorders Available in Canada

Table 2: Examples of Pharmacogenomic Tests for Psychiatric Disorders Available in Canada

Test	Availability	Target conditions	Genes analyzed	Medications included in the test results
23andMe Pharmacogenetics Reports (23andMe, Inc., US)	Available in Canada as a direct-to-consumer test ¹²⁹	Depression ¹²⁹	<i>CYP2C19, DPYD, SLC01B1</i> ¹²⁹	Citalopram ¹²⁹
BiogeniQ Kit: All Pharma Profiles (BiogeniQ Inc., Canada)	Available in Canada as a direct-to-consumer test ¹⁷	Psychiatric disorders, including ADHD ¹³⁰	<i>CESI, CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, CYP3A4, CYP3A5, LPHN3, OPMR1, POR, SLC01B1, TH, VKORC1</i> ¹⁷	Psychostimulants (e.g., amphetamine, dextroamphetamine), atypical antidepressants (e.g., bupropion), tricyclic antidepressants, SSRIs, benzodiazepines, atypical antipsychotics (e.g., risperidone, quetiapine), antipsychotics, alpha-2 adrenergic agonists (e.g., clonidine, guanfacine), noradrenaline reuptake inhibitor (e.g., atomoxetine), and hypnotics (e.g., zolpidem) ¹³⁰
CNSDose (Incite Health Pty Ltd., Australia)	Available in Canada as a direct-to-consumer test ¹³¹	Psychiatric disorders, patients with general medical conditions, patients with polypharmacy, and patients with depression and co-occurring conditions ^{81,131}	15 genes, including <i>ABCB1, ABCC1, CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, CYP3A5, SLC01B1, and UGT1A1</i> ^{81,131}	Anti-ADHD agents, antidepressants, antipsychotics, anxiolytics, hypnotics, mood stabilizers, anticonvulsants, other psychotropics, and non-psychotropics ^{81,131}
Colour Extended (Colour Health Inc., US)	Available in Canada as a direct-to-consumer test ¹⁷	Analyzes genes associated with cancers, cardiac conditions, and medication metabolism ¹³²	<i>CYP1A2, CYP2C19, CYP2C9, CYP2D6, CYP3A4, CYP3A5, CYP4F2, DPYD, F5, IFNL3, NUDT15, SLC01B1, TPMT, VKORC1</i> ^{17,132}	Unclear which medications are included in the test results
Genecept Assay (Genomind, US)	Available in Canada through a health care provider ¹⁷	Depression, anxiety, OCD, ADHD, bipolar disorder, PTSD, autism spectrum disorder, schizophrenia, chronic pain, and substance abuse	<i>CYP2C19, CYP2C9, CYP2D6, CYP2B6, CYP1A2, CYP3A4, CYP3A5, SLC6A4, CACNA1C, ANK3, 5HT2C, MC4R, DRD2, COMT, ADRA2A, MTHFR, BDNF, OPRM1, GRIK1</i> ⁸¹	Many pharmacotherapies, including SSRIs, atypical antidepressants, SNRIs, antipsychotics, mood stabilizers, stimulants, and topiramate ¹³³

Test	Availability	Target conditions	Genes analyzed	Medications included in the test results
GeneSight Psychotropic (Myriad Neuroscience, US)	Available in Canada through a health care provider ¹⁷	Depression, anxiety, ADHD, and other mental health conditions	<i>CYP2D6, CYP2C19, CYP2C9, CYP3A4, CYP2B6, CYP1A2, UGT1A4, UGT2B15, SLC6A4, HTR2A, HLA-A*3101, HLA-B*1502</i> ⁸¹	More than 60 psychotropic medications ¹³⁴
Invitae Mental Health Pharmacogenomics Panel (Invitae Corporation, US)	Available in Canada as a direct-to-consumer test ¹³⁵	Depression, anxiety, and other mental health disorders ¹³⁵	<i>COMT, CYP1A2, CYP2B6, CYP2C19, CYP2C9, CYP2D6, CYP3A4, CYP3A5, GRIK4, HLA-A, HLA-B, HTR2A, HTR2C, MTHFR, UGT2B15, UGT2B15</i> ¹³⁵	Unclear which medications are included in the test results
MatchMyMeds Drug Compatibility Test (DNALabs Canada Inc., Canada)	Available in Canada as a direct-to-consumer test ¹⁷	Analyzes genes related to drugs used for pain and migraine, oncology, psychiatry, gastroenterology and immunology ¹³⁶	<i>CYP2C19, CYP2C9, CYP2D6, CYP3A5, F5, SLC01B1, VKORC1</i> ¹⁷	Unclear which medications are included in the test results
myDNA Medication Test Kit (myDNA Life Ltd., Australia)	Available in Canada through a health care provider ¹⁷	Mental health conditions, pain, cardiovascular conditions, and gastrointestinal disorders ¹³⁷	<i>CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP3A4, CYP3A5, OPRM1, SLC01B1, VKORC1</i> ¹⁷	Unclear which medications are included in the test results
Neuropharmagen (InSource Diagnostics, US)	Available in Canada through a health care provider ¹⁷	Psychiatric disorders, including major depression, psychotic disorders, generalized anxiety disorder, and bipolar disorder ^{138,139}	<i>CYP2C19, CYP2C9, CYP2D6, CYP2B6, CYP1A2, CYP3A4, CYP3A5, SLC6A4, CACNA1C, ANK3, 5HT2C, MC4R, DRD2, COMT, ADRA2A, MTHFR, BDNF, OPRM1, GRIK1</i> ⁸¹	59 psychotropic medications ⁸¹
Personalized Insights Precision Pain & Mental Health (Inagene Diagnostics Inc., Canada)	Available in Canada as a direct-to-consumer test ¹⁴⁰	Pain and mental health conditions, such as ADHD, depression, and anxiety disorders	Unclear which genes are analyzed	More than 140 medications for pain and mental health ¹⁴⁰
Pillcheck (GeneYouIn Inc., Canada)	Available in Canada through a health care provider ¹⁷	A wide range of conditions, including psychiatric disorders, cardiovascular conditions, gastroenterology conditions, and other chronic conditions ^{81,141}	<i>ABCG2, ADRB2, CYP1A2, CYP2B6, CYP2C19, CYP2C8, CYP2C9, CYP2D6, CYP3A4, CYP3A5, DPYD, F2, F5, G6PD, NAT2, NUDT15, OPRM1, SLC01B1, TPMT, UGT1A1, UGT2B15, VKORC1</i> ^{81,141}	More than 230 medications, including 63 psychotropic medications ¹⁴¹

Test	Availability	Target conditions	Genes analyzed	Medications included in the test results
RightMed Comprehensive Test (OneOme, LLC., US)	Available in Canada through a health care provider ¹⁷	A wide range of conditions, including ADHD, anxiety, depression, and psychosis ¹⁴²	<i>CYP1A2, CYP2B6, CYP2C</i> Cluster, <i>CYP2C9, CYP2C19, CYP2D6, CYP3A4, CYP3A5, CYP4F2, DPYD, DRD2, F2, F5, GRIK4, HLA-A, HLA-B, HTR2C, HTR2A, IFNL4, NUDT15, OPRM1, SLC6A4, SLC01B1, TPMT, UGT1A1, VKORC1</i> ^{17,142}	More than 300 medications, including many used for psychiatric disorders ¹⁴²
RxReport: Psychiatry & Pain (Personalized Prescribing Inc., Canada)	Available in Canada as a direct-to-consumer test ¹⁴⁰	Pain and psychiatric disorders, including ADHD, anxiety, depression, autism spectrum disorder, and bipolar disorder ¹⁴³	<i>ABCB1, ADRA2A, ADRB1, ADRB2, APOE, BDNF, CACNA1C, CNR1, CNRNB2, COMT, CSMD1, COQ2, CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, CYP3A4, CYP3A5, DRD2, DRD4, F5, FAAH, FKBP5, GNB3, GRIA1, GRIK4, HLA-B, HSPG2, HTR1A, HTR1B, HTR2A, HTR2C, MC4 R, MTHFR, NEDD4 L, OPRD1, OPRM1, POLG, PRKCA, RGS4, SACM1 L, SCN1A, SCN2A, SLC01B1, SLC6A2, SLC6A4, TPH1, TPH2, TPMT, UGT1A4, UGT2B15, VKORC1, YEATS4, ZNF804A</i> ¹⁷	Unclear which medications are included in the test results
TreatGx ^{plus} (LifeLabs Genetics, Canada)	Available in Canada through a health care provider ¹⁷	Cardiovascular, endocrine, gastrointestinal, genitourinary renal, musculoskeletal, neurology, pain, respiratory, and mental health, including ADHD, anxiety disorders, bipolar disorder, depression, and schizophrenia ¹⁴⁴	<i>ABCG2, ADD1, ADRB2, ANKK1, COX1(PTGS1), CYP2B6, CYP2C19, CYP2C9, CYP2D6, CYP2A6, CYP3A5, DPYD, F2, F5, FKBP5, GNB3, GRIK4, HLA-A, HLA-B, HTR2A, HTR2C, IFNL3, KCNIP4, MC4R, MTRNR1, NUDT15, OPRM1, PRKCA, SLC01B1, TCF7L2, TNF, TPMT, VKORC1, YEATS4</i> ¹⁷	A wide range of medications, including amitriptyline, aripiprazole, asenapine, atomoxetine, carbamazepine, cariprazine, chlorpromazine, citalopram, clonazepam, clozapine, diazepam, escitalopram, fluvoxamine, haloperidol, imipramine, lamotrigine, lurasidone, olanzapine, oxcarbazepine, paliperidone, paroxetine, quetiapine, risperidone, sertraline, tamoxifen, venlafaxine, vortioxetine, and ziprasidone ¹⁴⁴

ADHD = attention-deficit/hyperactivity disorder; OCD = obsessive-compulsive disorder; PTSD = post-traumatic stress disorder; SNRI = serotonin and norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor.

Note: Information presented in this table is based on published literature and a review of manufacturers' websites and may not reflect the most recent versions of these pharmacogenomic tests. Manufacturers have not been contacted directly to verify this information.