

## Unlocking the potential of pharmacogenetics in South Africa

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Pharmacogenetics, often abbreviated as PGx, is the study of how an individual's genetic makeup influences their response to drugs. By utilising individual genetic data, PGx can optimise drug therapy plans, minimise adverse effects and reduce healthcare costs associated with ineffective treatments. In our article, we explain the critical role of PGx in shaping personalised medicine, with focus on South Africa region, where unique disease patterns require specialised treatments. We outline challenges such as the cost of testing, the need for more research, and the importance of education for both physicians and patients.

**Keywords:** pharmacogenetics, South Africa, practitioner's portal; personalised medicine

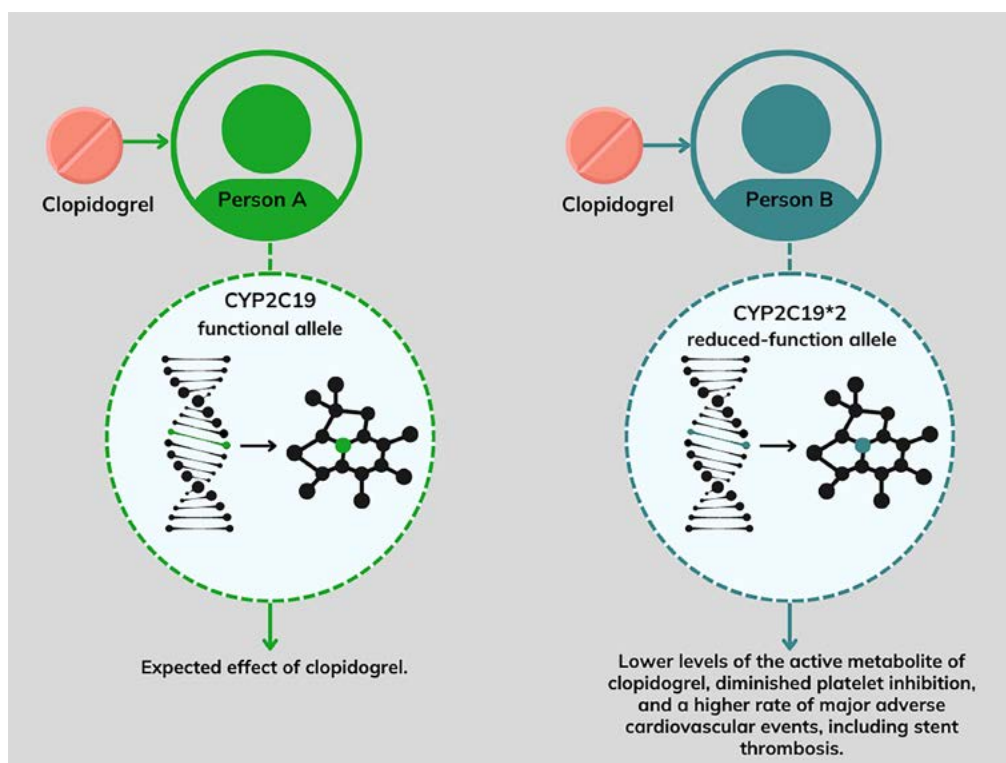
### Introduction

Within personalised medicine, genetic applications aid modern medicine in moving beyond the "one size fits all" treatment plan that is currently a norm in most healthcare systems. One of the major segments of personalised medicine is pharmacogenetics testing.<sup>1</sup>

Pharmacogenetic (PGx) testing is a burgeoning field that utilises a patient's genetic information to predict their response to various drug therapies. Using genetics to determine a course of treatment can improve patient health care by reducing the toxicity produced by the drug and the risk of adverse effects.

Also, it can improve the drug's efficacy, leading to customisation of drug treatment plans and reducing unnecessary healthcare costs associated with ineffective treatments.<sup>2</sup>

DNA acts as the instructions to make proteins such as enzymes. Of particular interest for pharmacogenetics are the enzymes that metabolise drugs. Slight variations in the genes of these enzymes can alter how effective they are in processing pharmaceuticals and other substances (Figure 1). This is the reason why one person might experience adverse effects of a medication while another person might find the same drug very effective in treating the condition. Through genetic testing, it is possible to



**Figure 1:** A single genetic variation between two people can cause alterations in the efficacy of the metabolising enzyme. Person A is a carrier of the functional *CYP2C19* allele and therefore metabolises clopidogrel as expected. Person B is a carrier of the reduced-function allele of *CYP2C19* and therefore may experience adverse effects from clopidogrel treatment.

\*Figure generated using Canva.

predict which drug will be most effective for an individual and to tailor their treatment accordingly.<sup>3</sup>

### How does pharmacogenetic testing work?

Genetic variants form the basis of pharmacogenetic testing, defining gene-drug interactions and determining drug metabolism pathways.<sup>4</sup> The most used data in pharmacogenetic tests include genotyping and next-generation sequencing (NGS) data.<sup>5,6</sup> Pharmacogenetics explains the correlation between multiple genes and how they can influence enzyme activity, affecting a drug's effectiveness or adverse effects.

A well-documented example of a gene-drug interaction that gives valuable insight into medication is the gene CYP2C19 and the antiplatelet drug clopidogrel, as seen in Figure 1. Individuals carrying CYP2C19\*2 allele metabolise clopidogrel differently, which may result in less effective prevention of cardiovascular events. Consequently, carriers of this allele might benefit from different antiplatelet therapies.<sup>7</sup> Having genotype information may help clinicians tailor medication to be effective in their patients and avoid adverse effects.

To better understand the practical implications of pharmacogenetics testing, let's consider a hypothetical case study. Suppose a patient must undergo heart surgery and is prescribed clopidogrel as a postoperative measure to prevent clot formation. Pharmacogenetic testing reveals the patient is a poor metaboliser due to the variant of the CYP2C19 gene they have. Instead of risking ineffective treatment, the doctor prescribes an alternative drug that is more suited to their genetics, thereby reducing the potential risk of cardiovascular complications. This decision, guided by pharmacogenetics, potentially saves the patient's life.<sup>8</sup>

It is also important to mention some limitations, such as the cost and access to testing, the need for larger confirmatory studies, confidence in clinical utility of pharmacogenetics tests, and the need for detailed knowledge of pharmacology for clinical implementation.<sup>9,10</sup> However, while the example provided above shows the potential benefits of pharmacogenetics testing, its predictive power will only continue to grow as genetic sequencing technologies continue to advance and our understanding of gene-drug interactions deepens.

### Why is pharmacogenetic testing essential, and what are the main benefits?

Two main benefits of pharmacogenetic testing include: (i) improved patient outcomes through personalised medicine and (ii) considerable cost savings by reducing unnecessary healthcare costs associated with ineffective treatments and adverse drug reactions.<sup>11</sup>

### Pharmacogenetic testing improves patient outcomes

The first and most important aspect of using pharmacogenetic testing is its potential to improve patient outcomes. Various studies have recently reported the positive effects of pharmacogenetic testing. Elliott et al. reported that in a randomised controlled trial, pharmacogenetic testing of polypharmacy patients (patients

that simultaneously use multiple medicines for their conditions) aged 50 and older, considerably reduced re-hospitalisations and emergency department visits at 60 days following enrolment. As a result, pharmacogenetic testing decreased health resource utilisation and improved health care.<sup>12</sup> Another critical aspect of the pharmacogenetics application is the improvement of postoperative recovery. Following this, Senagore et al. reported that patients receiving pharmacogenetic guided treatment for postoperative therapy had fewer narcotic and NSAID (nonsteroidal anti-inflammatory drug) modifications, resulting in a 50% reduction in narcotic consumption and reduced incidence of analgesic-related adverse effects.<sup>13</sup> Additionally, using a combinatorial pharmacogenetic test significantly improves outcomes among patients with major depressive disorder who had at least one prior medication failure.<sup>14</sup> Combinatorial pharmacogenetic tests are based on an algorithmic assessment of multiple genes to predict gene-drug interactions. We believe that future research will further support the advantages of pharmacogenetic testing and favourable patient outcomes.

### Pharmacogenetic testing reduces unnecessary healthcare costs

The next significant promise of pharmacogenetic testing is the reduction of unnecessary healthcare costs associated with ineffective treatments and adverse drug reactions.<sup>15-17</sup> The comprehensive review by Verbelen et al. reported that over half of 44 economic evaluations favoured the PGx-guided strategy.<sup>18</sup> Only one in four economic evaluations reported that pharmacogenetic testing is not cost-effective. Still, this is an encouraging finding, with an even bigger projected benefit under low-cost genetic typing, suggesting that PGx testing has the potential to be a cost-effective or even cost-saving intervention.<sup>18</sup>

### How can pharmacogenetic testing be implemented in general practice?

Countries in Northern America and Europe are already successfully implementing pharmacogenetic testing.<sup>17</sup> Very little is documented regarding the implementation of pharmacogenetic testing in any other part of the world.<sup>19</sup>

South Africa has many population groups, among which there are unique disease patterns. These unique disease patterns, especially, necessitate tailored medicine prescription and intervention through pharmacogenetic testing. However, the implementation of pharmacogenetic testing still needs to be popularised in this region.<sup>17</sup>

Pharmacogenetic testing can be implemented in the traditional healthcare setting. Additionally, with new telemedicine advances and the accessibility of testing and secure data-sharing platforms, the technology enables pharmacogenetics implementation in all environments, including virtual health care.

Pharmacogenetic testing does not require patients to set aside time or travel to a doctor, laboratory, or testing centres. Patients can order tests online from the comfort of their homes as testing kits are delivered, collected from the patients' doors, and taken

to the laboratory for analysis by courier services. Patients can very easily collect their own DNA samples needed for further processing.

With the logistics in place for an at-home, simple DNA sample collection method, and the safely encrypted accessibility of the report from anywhere, location is not a factor in keeping anyone from utilising the tests, being a physician or a patient.

Since the benefits of pharmacogenetic testing are undeniable, it is the implementation thereof that requires attention.<sup>20,21</sup> Various authors have noted that the education and training of physicians involved in applying pharmacogenetics are crucial.<sup>22,23</sup> In fact, a significant lack of physician education on pharmacogenetic testing adds a considerable blockage to bringing the implementation thereof into clinical practice. Many doctors may not be familiar with the availability of the tests, are sceptical of the tests, or may not know how to implement the genetic data confidently.<sup>19,22</sup> This limitation may be overcome. For instance, BioCertica offers an online CPD course on genetics and pharmacogenetic basics, worth 5 CPD points.

Patient education is also critical. Physicians should spend time explaining pharmacogenetic testing, the implications thereof on the prescription of medication, and the testing's risks, benefits, and limitations. Patients should only undergo testing after they have an adequate understanding and realistic expectations, and they should be informed on how their medication prescriptions should be altered according to their pharmacogenetic test results.<sup>23</sup>

The inaccessibility of pharmacogenetic testing is becoming a smaller challenge against the implementation thereof, with more private companies providing these testing services. On the other hand, pharmacogenetic testing can save considerable medical costs in the long term, reducing out-of-pocket costs due to inappropriate drugs being prescribed.<sup>23</sup>

Although there are challenges regarding the wider implementation of pharmacogenetic testing, companies have made pharmacogenetic testing even more accessible and interpretable by physicians.

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