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**ORIGINAL ARTICLE**

**Retrospective Study**

- 39 Clinical utilities and end-user experience of pharmacogenomics: 39 mo of clinical implementation experience in an Australian hospital setting

*Moxham R, Tjokrowidjaja A, Devery S, Smyth R, McLean A, Roberts DM, Wu KHC*

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## Retrospective Study

# Clinical utilities and end-user experience of pharmacogenomics: 39 mo of clinical implementation experience in an Australian hospital setting

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## Abstract

### BACKGROUND

Pharmacogenomics (PG) testing is under-utilised in Australia. Our research provides Australia-specific data on the perspectives of patients who have had PG testing and those of the clinicians involved in their care, with the aim to inform wider adoption of PG into routine clinical practice.

### AIM

To investigate the frequency of actionable drug gene interactions and assess the perceived utility of PG among patients and clinicians.

### METHODS

We conducted a retrospective audit of PG undertaken by 100 patients at an Australian public hospital genetics service from 2018 to 2021. *Via* electronic surveys we compared and contrasted the experience, understanding and usage of

results between these patients and their clinicians.

## RESULTS

Of 100 patients who had PG, 84% were taking prescription medications, of which 67% were taking medications with actionable drug-gene interactions. Twenty-five out of 81 invited patients and 17 out of 89 invited clinicians completed the surveys. Sixty-eight percent of patients understood their PG results and 48% had medications changed following testing. Paired patient-clinician surveys showed patient-perceived utility and experience was positive, contrasting their clinicians' hesitancy on PG adoption who identified insufficient education/training, lack of clinical support, test turnaround time and cost as barriers to adoption.

## CONCLUSION

Our dichotomous findings between the perspectives of our patient and clinician cohorts suggest the uptake of PG is likely to be driven by patients and clinicians need to be prepared to provide information and guidance to their patients.

**Key Words:** Pharmacogenomics testing; Clinical adoption; Drug gene interactions; Clinician perspectives; Patient perspectives

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**Core Tip:** Pharmacogenomics (PG)-guided therapy has the potential to reduce adverse drug reactions and improve clinical outcomes of patients with mental illness. Despite increasing evidence, the uptake of PG among Australian clinicians remains low. We report for the first time on the dichotomous responses between patients and their clinician counterparts in the usage of PG: Patients were generally positive and willing to use PG compared with clinicians, suggesting that the uptake of PG in Australia is likely to be driven by patients, and that clinicians need to be prepared to provide information and guidance to their patients.

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## INTRODUCTION

Variabilities in an individual's genetic sequence may affect the pharmacokinetics and pharmacodynamics of a drug, leading to an altered therapeutic response and/or increased risk of adverse drug reactions (ADRs)[1]. Pharmacogenomics (PG) is the study of clinically relevant genetic biomarkers, or pharmacogenetic variants that can influence a person's response to therapeutic drugs[1]. The relationship between pharmacogenetic variants and drug response is termed drug-gene interaction (DGI). Recent advances in genomic technologies including Next Generation Sequencing, or Massively Parallel Sequencing, have led to an unprecedented capacity allowing multiple genes to be interrogated at once. This approach allows multiple genes that are involved in, not only different metabolising enzymes (pharmacokinetics) and drug receptors (pharmacodynamics) for a single drug, but also those of multiple drugs, to be analysed in a single test with a gene panel. Such pharmacogenomic testing can determine an individual's likely response to multiple, up to a few hundred, medications from a single sample, unlike the traditional pharmacogenetic test of a single variant and single DGI at a time[2].

PG, especially if done pre-emptively, has the potential to guide clinicians at point-of-care in choosing the right therapeutic drug and dosing that is tailored to each patient, with the potential promises of reduced adverse effects, improved tolerability, and enhanced therapeutic response[3].

Internationally, there is a growing interest for widespread adoption of PG among patients and its potential to improve their medication outcomes[4-6]. In contrast, studies on clinician perspectives of PG have highlighted barriers and challenges towards its implementation into clinical practice. These barriers include lack of education/training, confidence, and acceptability of PG by clinicians[7-10], as well as a lack of consensus between clinical guidelines and access to clinical decision support[11-14]. To date, there is limited literature on the perspectives of the Australian end-users on PG[15].

In Australia, only two genotypes are covered by the national Medicare scheme, namely, *HLA-B* 5701 for abacavir, and *TPMT* for thiopurine drugs. However, multigene panel PG is neither publicly-funded by Medicare nor covered by private health insurance schemes. Patient-pay testing can be requested by a specialist or a general practitioner (GP). Most clinical genetics services in Australia, which are funded by State-operated public hospitals, do not routinely offer multigene panel PG, with the exception of St Vincent's Hospital Sydney which is the setting of our investigation.

In Australia, the New South Wales Health Commission conducted an ‘Inquiry into the Management of Mental Healthcare Delivery’ in 2018 that identified under-utilisation of PG and recommended such testing as a key priority to improve clinical outcomes for mental health patients[16]. In order to see wider uptake, one needs to identify barriers to and facilitators of PG adoption in Australia, as perceived by patients who have had testing and clinicians who care for these patients. Such data, which remain limited to date, will inform an implementation science approach to promote the systematic uptake of PG into routine practice[17].

In this study we aim to: Investigate the potential impact of PG by determining the frequency of actionable DGIs in our patient cohort; assess within the same patient cohort, their experience of testing, as well as their understanding and usage of PG results and; assess among clinicians involved in the care of these patients, the experience, acceptability, understanding and perceived utility of PG (Figure 1).

## MATERIALS AND METHODS

### PG testing and retrospective review of results

A retrospective review was conducted on the PG reports and medication history of consecutive adult patients who were aged 18 years or older who had PG at St Vincent’s Hospital Clinical Genomics Sydney Australia between 1 August 2018 and 31 September 2021.

PG testing was conducted using a comprehensive commercial gene panel at a CLIA-certified laboratory (OneOme, Minneapolis, MN, United States), and included the following genes: *CYP1A2*, *CYP2B6*, *CYP2C9*, *CYP2C19*, *CYP2D6*, *CYP3A4*, *CYP3A5*, *CYP4F2*, *COMP*, *DPYD*, *DRD2*, *F2*, *F5*, *GRIK4*, *HLA-A*, *HLA-B*, *HTR2A*, *HTR2C*, *IFNL4*, *NUDT15*, *OPRM1*, *SLC6A4*, *SLCO1B1*, *TPMT*, *UGT1A1*, and *VKORC1*. This gene panel includes most pharmacogenes with high association evidence according to Clinical Pharmacogenetics Implementation Consortium, Dutch Pharmacogenetics Working Group and PG Knowledgebase[18].

Data collected on each patient included: age, sex, ethnicity, referring clinician and subspecialty, reason for referral, medication history, history of drug allergies and ADRs, number of high-risk and moderate-risk DGIs as shown on their PG report, number of current medications with high-risk or moderate-risk DGI.

### Patient and clinician recruitment

Consecutive patients aged 18 years or older who underwent PG testing during a 39-month period between 1 August 2018 and 31 September 2021, and clinicians involved in the care of these patients, were identified and re-contacted *via* email and invited to participate in an online survey.

### Survey development and distribution

Patient and clinician surveys were developed and created on the Research Electronic Data Capture (REDCap) software. The patient survey assessed patient experience including their understanding and usage of the PG results. The clinician survey assessed clinician experience including their knowledge, acceptability and perceived utility of PG, as well as barriers to and support needs for broader adoption of PG in clinical practice. Demographic data were collected from both surveys. The surveys were constructed using 5-Point Likert Agreement Scale for categorical response questions, as well as other single or multiple option and open-ended comment questions. Survey questions were constructed using simple sentences at a literacy level of 5<sup>th</sup> grade using the Flesch-Kincaid Readability Calculator[19].

Both surveys were pilot tested by a focus group of five laypeople randomly identified from investigator’s peers and five clinicians who were randomly identified through St Vincent’s Hospital network, who were representative of our intended survey respondents. Members of the focus groups were provided with written instructions on how to review and test the survey and their feedback was sought regarding clarity, comprehension, functionality of the branching logic and the duration of time taken to complete the survey. Adjustments were made to the surveys with the final versions taking 15-20 min to complete. The REDCap surveys were distributed electronically *via* email, or short message service (SMS), if emails were unavailable, to patients and clinicians respectively. Follow-up reminder emails or SMSs were sent two weeks after the initial invitation if no responses were received.

### Data analysis

Descriptive statistics were used to summarise categorical data ascertained from the retrospective chart review. If applicable, correlations were made between patient’s reported medication side effects/ADR and the DGI of the implicated medication. Mean, median, and standard deviation were derived using Microsoft Excel (Microsoft Corporation, 2016, version 16.0) for continuous variables such as age and number of high/moderate risk DGIs. The survey data were exported from REDCap and analysed using a regular analysis Microsoft Excel (Microsoft Corporation, 2016, version 16.0) package. Categorical data were summarised in descriptive and numerical formats using bar graphs and tables. For the 5-Point Likert scale (*e.g.* strongly agree, agree, neither agree nor disagree, disagree, strongly disagree), data was reviewed in its original form and combined into three categories (*i.e.* agree, neutral, disagree) then analysed as categorical data.

Ethics approval was sought and received from St Vincent’s Hospital Human Research Ethics Committee (2019-ETH12892) to conduct this study.

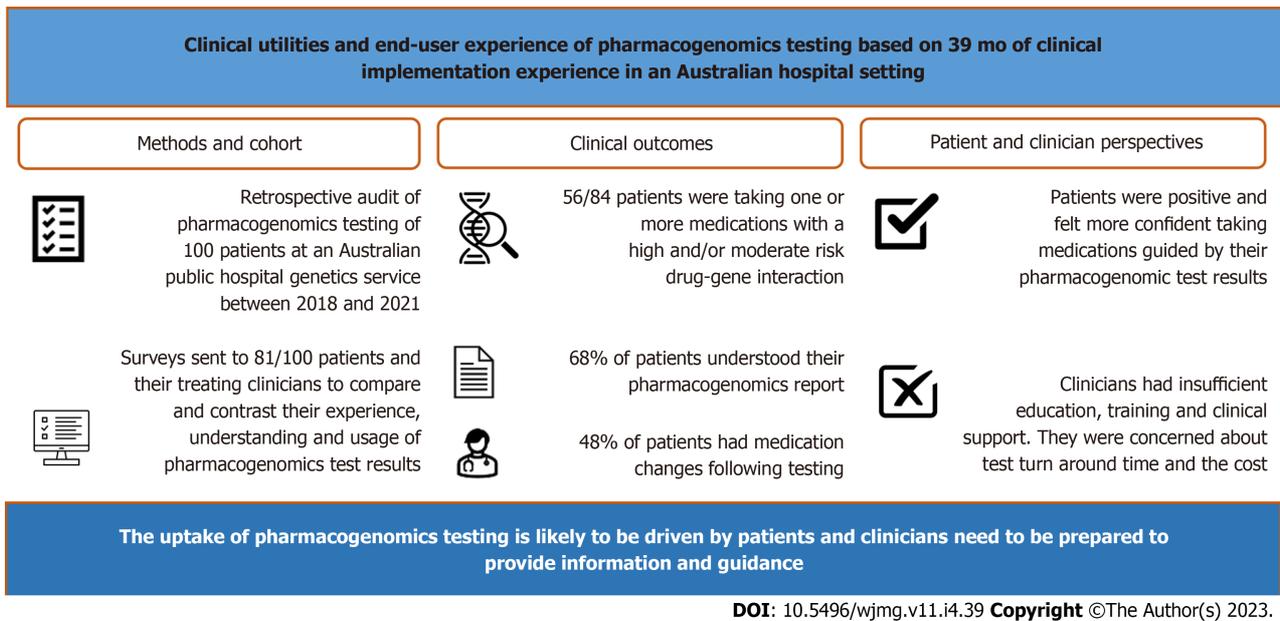


Figure 1 Graphical abstract.

## RESULTS

### Demographics of patients referred for PG testing

There were 100 patients identified during the audit period, consisting of 44 males and 56 females, with a mean age of 44.7 years +/- standard deviation 15.7 years (age range 18-75 years). Patients were referred by psychiatrists (39%), immunologists (15%), GPs (10%), neurologists (9%), transplant physicians (8%), and clinical pharmacologists (5%). The remaining 14% were referred by the following specialists: cardiologist, endocrinologist, gastroenterologist, haematologist, nephrologist, obstetrician, rheumatologist and thoracic physician; with each specialist category accounting for 2% of referrals. The referral indications were: to guide current pharmacotherapy (62%), previous history of ADRs (51%), history of polypharmacy (5%), and/or pre-emptive purpose to guide future prescription (5%). The demographics of the 100 patients are summarised in [Table 1](#).

### PG reports

The PG reports of the 100 patients showed that on average, patients had 11 high-risk DGIs (range: 0-49, SD: 13.3) and 55 moderate-risk DGIs (range: 1-149, SD: 28.1). Of the 84 patients who provided a medication history, 17 patients (20%) were taking medications implicated with high-risk +/- moderate-risk DGI, 39 patients (46%) were taking medications with a moderate-risk DGI; with 56 patients (66%) taking medications with an actionable DGI (either high-risk DGI or moderate-risk DGI). Of these, one patient was taking nine medications with an actionable DGI ([Table 2](#)).

### Demographics of survey respondents

Of the 100 patients identified and included in the retrospective review, 81 patients were invited to participate in the patient survey, after excluding those with no contact details and those who had indicated they did not wish to be contacted for future research. Of the 81 patients invited, 25 patients (31%) responded and completed the survey. Patient survey respondents were mostly female, aged 40-49 years with a tertiary level of education. A total of 89 clinicians, including 29 subspecialist clinicians and 60 GPs, involved in the care of the same patient cohort were identified and invited to participate in the clinician survey. Of those invited, 17 clinicians (19%) responded and completed the survey. Clinician survey respondents were mostly male, practicing in psychiatry, with a medical degree attained after the year 2000, who encountered patients in the hospital setting and had referred or discussed PG with their patients in the preceding 12 mo. A summary of survey respondent demographics for both patient and clinician surveys is shown in [Table 3](#).

### Clinician knowledge and training sources of PG

Responses from clinician survey ( $n = 17$ ) showed that clinicians have different levels of knowledge and sources of education for PG. The majority of clinicians (94.1%) knew that individuals respond differently to medications based on genetic factors. Their knowledge of how many drugs have a PG impact varied significantly. None of the clinicians had completed any formal training in PG, with the majority (52.9%) reporting not feeling confident in discussing and/or answering questions about PG with their patients. The primary sources of knowledge about PG for clinicians were medical colleagues (75%), scientific journals (62.5%), conferences and scientific meetings (25%), publicly available online resources (25%) and/or commercial providers such as pathology laboratories (18.8%).

**Table 1 Demographics of 100 patients included in the retrospective review of pharmacogenomics result**

Patient characteristics	
Sex	(%)
Male	44
Female	56
Age (yr)	(%)
18-29	23
30-39	12
40-49	29
50-59	17
60-69	14
> 70	5
Referring specialists	(%)
Psychiatrists	39
Immunologists	15
General practitioners	10
Neurologists	9
Transplant physicians	8
Clinical pharmacologists	5
Others <sup>1</sup>	14
Indications for referral	(%)
To guide pharmacotherapy	62
Previous drug reactions	51
Polypharmacy <sup>2</sup>	5
Pre-emptive testing	5
Did not specify	5

<sup>1</sup>Cardiologist, endocrinologist, gastroenterologist, haematologist, nephrologist, psychologist, obstetrician, rheumatologist and thoracic physician referred.

<sup>2</sup>Patient taking  $\geq 5$  prescription medications. Referring clinicians could list more than one indication for pharmacogenomics testing.

**Patient experience:** Patient respondents ( $n = 25$ ) were generally positive in their experience with PG. The majority of patients (68%) agreed with the statement “I have a good understanding of my PG results”. Nineteen (76%) and 17 (68%) patient respondents agreed that PG has helped them understand which medications were safe, and effective, for them respectively. Likewise, 17 patients (68%) agreed with the statement “I feel more confident in a new medication chosen by my doctor according to my PG results”; and 15 patients (60%) agreed with the statement “The results of my PG test results helped explain my experiences with medications”. Nine patients (36%) agreed with the statement “My doctor was able to address my questions regarding my PG results” (Figure 2).

**Clinician perspective:** Clinician respondents ( $n = 17$ ) were generally ambivalent in their perception of PG utility, with 50% reporting that PG has benefitted some of their patients, while 37.5% and 6.3% reported that PG has benefitted little, or none, of their patients, respectively; while 6.3% reported it has benefitted most of their patients. In addition, 17.7% of respondents disagreed with, and 35.3% were neutral to, the statement “PG has guided me in choosing the right medication and/or dosage for my patients”. When asked about the likelihood of utilising PG in the next 12 mo, 64.7% clinicians reported likely, 23.5% reported unlikely, and 11.8% were ambivalent about using it in the next 12 mo. Seven (41.2%) clinicians agreed that “PG can help reduce overall costs for patients”, while nine (52.9%) were neutral to the same statement. There was an equal distribution among clinicians who agreed with (31.3%), were neutral to (31.3%), or disagreed with (37.6%), the statement that PG was too expensive for their patients. Most clinicians (88.2%) agreed that they were more likely to order PG testing if Medicare covered the cost (Figure 2).

**Table 2** Number of patients (*n* = 56) taking medications found to have high- and/or moderate-risk drug-gene interaction against the number of such medications, in those whose medication history was available (*n* = 84), *n* (%)

Number of medications with implicated DGI	Number of patients taking medications with high-risk +/- moderate-risk DGI implicated	Number of patients taking medications with moderate-risk DGI implicated only	Number of patients taking medications with an actionable <sup>1</sup> DGI
1	5 (6)	20 (24)	25 (30)
2	7 (8)	11 (13)	18 (21)
3	3 (4)	7 (8)	10 (12)
4	1 (1)	0 (0)	1 (1)
5	0 (0)	1 (1)	1 (1)
6	0 (0)	0 (0)	0 (0)
7	0 (0)	0 (0)	0 (0)
8	0 (0)	0 (0)	0 (0)
9	1 (1)	0 (0)	1 (1)
10	0 (0)	0 (0)	0 (0)
Total	17 (20)	39 (46)	56 (66)

<sup>1</sup>Either high-risk drug-gene interaction (DGI) or moderate-risk DGI.  
DGI: Drug-gene interaction.

**Table 3** Patient and clinician survey respondent demographics, *n* (%)

Patient respondents ( <i>n</i> = 25)		Clinician respondents ( <i>n</i> = 17)	
Sex		Sex	
Male	9 (36.0)	Male	11 (64.7)
Female	16 (64.0)	Female	6 (35.3)
Patient age (yr)		Clinician attained medical degree	
18-29	4 (16.0)	Before 1980	2 (11.8)
30-39	2 (8.0)	1981-1990	2 (11.8)
40-49	7 (28.0)	1991-2000	3 (17.6)
50-59	6 (24.0)	After 2000	10 (58.8)
60-69	5 (20.0)		
> 70	1 (4.0)		
Patient education level		Clinician specialty	
Did not finish high school	1 (4.0)	Psychiatry	5 (29.4)
High school	6 (24.0)	Clinical pharmacology	3 (17.6)
Certificate or diploma	5 (20.0)	Immunology	2 (11.8)
Bachelor's degree	11 (44.0)	Neurology	2 (11.8)
Master's degree or doctorate	2 (8.0)	General practitioner	1 (5.9)
		Other <sup>1</sup>	7 (41.2)

<sup>1</sup>Rheumatology, respiratory, endocrinology, nephrology, gastroenterology.  
Clinician respondents could list more than one area of specialty.

### Usage and sharing of PG results

As shown in [Figure 3](#), the majority of patient respondents (92%) have shared their PG results with their health care providers; and 12 patients (48%) reported having had their medications changed over 17 clinical encounters following PG testing. Of the seventeen medication changes reported by patient respondents, nine instances (53%) of medication changes were made by their specialist, seven (41%) by their GP, and one instance (6%) was made by the patient themselves.

### Clinician support needs and barriers for adoption of PG

As shown in [Figure 2](#), clinicians were ambivalent towards the adoption of PG. The majority of clinician respondents (70.6%) thought that PG requires more evidence for it to be clinically useful. The majority of respondents (70.6%) did not agree that the information generated from PG was easy to understand; the majority (52.9%) did not feel confident in discussing and answering questions about PG. When asked if support is needed before clinicians feel comfortable in requesting PG, the responses were fairly equally distributed, between agree (35.3%), neutral (23.5%), and disagree (41.2%). The majority of clinician respondents (52.9%) reported not having easy access to resources to help manage their patients; and 52.9% respondents would like support from genetic professionals to help manage patients who have undergone PG testing.

In regards to whom clinicians thought would be the most appropriate person to discuss and return PG results to patients, the responses were equally divided between: Specialist ordering the test (52.9%), and clinical geneticists/genetic counsellors (47.1%); with no responses for GPs or pharmacists.

Barriers to adoption of PG were identified from our clinician cohort whose patients have had PG testing. The single most important barrier as reported by clinician respondents includes one of: A lack of clinical decision aids (29.4%), cost factor for patients (23.5%), timeliness of results (23.5%), lack of access to information (11.8%), patient expectations (5.9%) and difficult logistics in organising testing (5.9%). If barriers were overcome, most but not all clinicians (76.5%) agreed there was value in PG for their patients, with 17.6% providing a neutral response and 5.9% disagreeing to the statement.

## DISCUSSION

Despite recent advances in genomic testing, the increasing knowledge of DGIs, and the availability of dosing guidelines based on actionable DGIs[20], PG remains under-utilised in Australia. There have been several PG implementation projects undertaken in the US and Europe; such initiatives are limited in Australia[21].

Our study highlighted the potential utility of PG in identifying high- and/or moderate-risk, or actionable, DGIs that may trigger a change in prescription. Our audit showed a wide range of variabilities in the number and degree of DGIs among patients, supporting the rationale for individualised prescribing based on genetic characteristics. Additionally, our results indicated that a significant proportion of patients, 66%, were taking a medication implicated to have an actionable DGI at the time of PG testing, highlighting the potential utility of PG in guiding prescription and reducing the incidence of adverse drug effects[22].

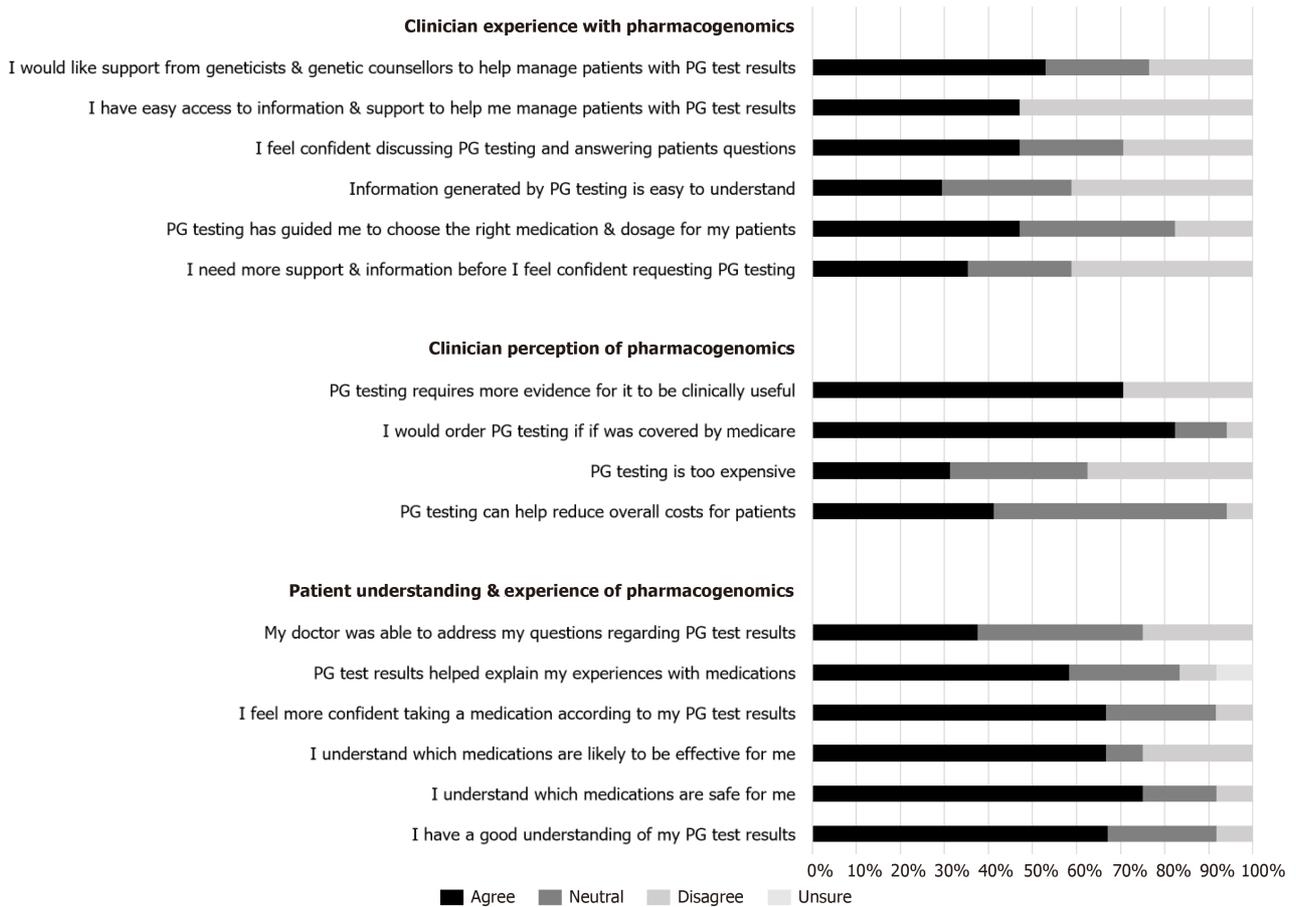
Although our patients who have had testing were generally in favour of the utility of PG on improving their medication experience, the perception of PG among clinicians who care for these patients was however reserved with hesitancy and/or skepticism. Over half of our patient respondents (68%) reported feeling more confident in medications when their PG results were taken into consideration by their healthcare providers when prescribing. This echoes the limited literature showing that PG may increase medication adherence among patients[23]. In contrast to patient perception, and consistent with previous studies on clinician attitudes towards PG[24,25], a significant proportion of our clinician cohort was more cautious on the utility of PG and would like to see more evidence published and challenges addressed before using PG in their routine practice. Our dichotomous findings between the perspectives of our patient and clinician cohorts may suggest that the uptake of PG is likely to be driven by patients and that clinicians need to be prepared to deal with the information and provide guidance to their patients. This is a valuable finding as there are no recent studies investigating among or contrasting between the end-users in their perception and understanding of PG using the current multi-variant testing technology.

Half of the patient respondents in our study reported having their medications changed following PG, highlighting the potential impact of PG on treatment decisions. Additionally, our patient survey showed that the majority of respondents have discussed their PG results with their GPs; and of those who had medication changes, half of the respondents had their medications changed by their GPs. These findings suggest the importance of primary care engagement and involvement in the wider adoption and implementation of PG in Australia.

We identified a lack of education and training, and a lack of clinical decision aids and support as the major barriers to routine adoption of PG among our clinician cohort who was involved in the care of patients who underwent PG testing. The majority of our clinicians have not completed any formal training in PG; have expressed complexities of incorporating results in their patient care; and have expressed the need for support from trained health professionals to manage these results. Similar to initiatives in various healthcare settings in the United States[26-28], our findings could inform an interdisciplinary care model approach in Australia. Such an approach would incorporate the expertise of genetics professionals, clinical pharmacologists and pharmacists providing training and education to primary care providers, the patient's nominated specialists and/or pharmacists[29].

Other barriers to uptake of PG identified in our study include time limitations and cost of testing. The long turnaround time for results highlights the importance of testing in a pre-emptive setting so that results are available at future point-of-care. In Australia, Medicare currently covers only two DGIs (*HLA-B 5701* for abacavir, *TPMT* for thiopurine drugs).

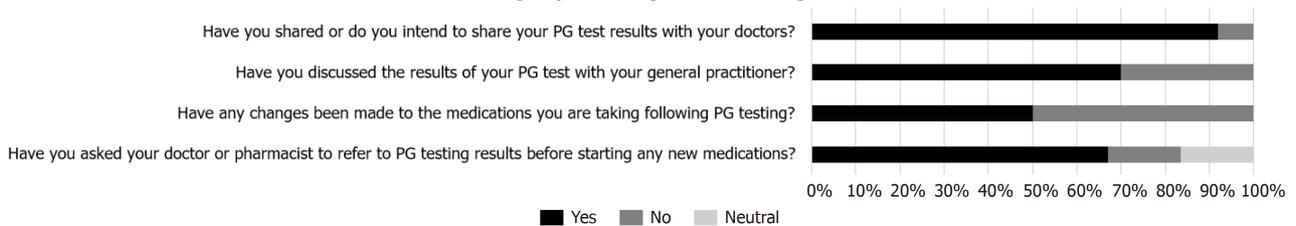
**Clinician and patient survey responses on pharmacogenomics testing**



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**Figure 2 Patient and clinician perspectives on the utility and application of pharmacogenomics testing.** PG: Pharmacogenomics.

**Patient sharing of pharmacogenomics testing results**



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**Figure 3 Sharing of pharmacogenomics testing results by patients.** PG: Pharmacogenomics.

Most clinicians would like to see more PG tests covered by Medicare and reported that they are more likely to order a test if there was public funding. From the patient perspective, our patient survey did not capture cost implications as testing was undertaken at no charge to patients. To date, economic studies have suggested that PG testing can be cost-effective and that the cost of testing could be offset by its cost-savings from reduced time wastage on medication trial-and-error, enhanced therapeutic response, and mitigation of ADRs[30-32]. Future studies that explore the cost implications of PG-informed prescription should capture data on, not only individual patients, but also the overall healthcare system, to inform public funding for mainstream implementation in Australia.

The present study is limited by a lack of generalizability of our survey results, due to the small sample size, with 72% of patient respondents having a tertiary qualification or higher, and recruitment bias through a single tertiary genetics service. Similarly, our clinician respondents represent a small niche cohort who mostly work in a tertiary hospital setting. Our survey response rate of 31% from patients and 19% from clinicians in a sample size smaller than 500 can be considered sufficient to conclude estimates but is still below the average online survey response rate of 44.1% and is therefore best considered as observatory and exploratory[33]. Furthermore, our study had limited, 5.9%, survey response rate from GPs, which may be attributable to the coronavirus disease 2019 pandemic impact during the time of the survey. This makes it difficult to draw perspectives from this clinician cohort who is potentially a frontline user and adopter of

PG. As a Cronbach's Alpha Test was not performed to assess the reliability or internal consistency of the survey questions these surveys were not considered validated[34]. Finally, recall bias is an inherent limitation of survey research into past experiences, in particular, patient recall of medication changes, as well as understanding and sharing of PG results.

## CONCLUSION

This study provides not only Australia-specific data, but also the perspectives of patients who have had PG and those of the clinicians involved in their care, which can inform future research into the implementation and the wider adoption of PG in Australia. Through an audit of 100 patients who have had testing, we found a significant proportion, 66%, of patients were taking a medication with an actionable DGI. Our paired end-user surveys highlighted dichotomous perspectives on PG between patients and their clinicians. Patients were generally positive and willing to use PG compared with clinicians, suggesting that patients may play a significant role in driving change and promoting the uptake of PG in clinical care.

## ARTICLE HIGHLIGHTS

### Research background

In Australia, the New South Wales Health Commission conducted an 'Inquiry into the Management of Mental Healthcare Delivery' in 2018 that identified under-utilisation of pharmacogenomics (PG) and recommended such testing as a key priority to improve clinical outcomes for mental health patients. In order to see wider uptake, one needs to identify barriers to and facilitators of PG adoption in Australia, as perceived by patients who have had testing and clinicians who care for these patients. Such data, which remain limited to date, will inform an implementation science approach to promote the systematic uptake of PG into routine practice.

### Research motivation

PG-guided therapy has been shown to significantly enhance clinical outcomes in the field of mental health. Currently, two-thirds of patients with a major depressive disorder fail to achieve remission during the first treatment level; and many require multiple different medications sequentially on a trial-and-error basis. In addition, it has been shown that the odds of remission diminish with every additional medication trial-and-error iteration; and that a window of therapeutic opportunity for major depressive disorder appears to be within the first 2 sequential treatments. PG-guided pharmacotherapy, which aims at giving the right drug at the right dosage to the right person at the right intervention time, has the potential to enhance both patient outcomes and health cost savings in the Australian mental health system. Despite the evidence, Australia has been slow in adopting PG testing to guide therapy. To facilitate widespread clinical implementation of PG it is necessary to know and understand the attitudes and acceptability of PG, as well as the support and resource requirements, amongst potential end-users, including clinicians and patients. This information can contribute to the development of a model of care, enhance the feasibility and clinical utility of PG to ensure successful implementation of PG-guided pharmacotherapy into routine clinical care of patients with mental illness.

### Research objectives

The objectives were to evaluate retrospective file data of patients participating in PG testing in Australia and to re-contact patients and their general practitioners (GPs)/clinicians to assess the impact of PG both on treatment options and patient/clinician reported outcomes.

### Research methods

A retrospective audit was undertaken of the PG results of 100 patients who underwent testing as part of their routine clinical care between 1 August 2018 and 31 September 2021 at an Australian public hospital genetics service. Specifically designed and pilot-tested surveys were used to assess clinician knowledge, acceptability and perceived utility of PG in the care of patients and evaluate patients knowledge of PG results, as well as, how the PG has impacted their pharmaceutical care and overall mental and physical health. Data was analysed using descriptive statistics to summarise categorical data ascertained from the retrospective chart review where correlations were made between patient's reported medication side effects/adverse drug reaction (ADR) and the drug-gene interaction (DGI) of the implicated medication. Categorical data from clinician and patient surveys were summarised in descriptive and numerical formats with bar graphs and tables.

### Research results

Through an audit of 100 patients who have had PG testing at St Vincent's Hospital Clinical Genomics Sydney, we found 67% of patients were taking a medication with an actionable DGI at the time of testing. The importance of our work is that *via* paired end-user surveys it highlighted dichotomous perspectives on PG between patients and their clinicians (psychiatrists, immunologists, neurologists, transplant physicians, clinical pharmacologists and GPs). Patients were generally in favour of the utility of PG on improving their medication experience, the perception of PG among clinicians who care for these patients was however reserved with hesitancy and/or skepticism. This suggests that the uptake of PG

is likely to be driven by patients, and clinicians need to be prepared to provide information and guidance to their patients.

### Research conclusions

Our research identifies barriers to the clinical implementation of PG and suggests strategic solutions that could be put in place to support a wider adoption in routine medical practice. The majority (70%) of our patient participants have discussed their PG results with their GP; and of those who had medication changes following testing, half of the respondents had their medications changed by their GP. These findings suggest the importance of primary care involvement in the wider adoption and implementation of PG in Australia.

### Research perspectives

To date, economic studies have suggested that PG testing can be cost-effective and that the cost of testing could be offset by its cost-savings from reduced time wastage on medication trial-and-error iterations, enhanced therapeutic response, and mitigation of ADRs. Future studies that explore the cost implications of PG-informed prescription should capture data on, not only individual patients, but also the overall healthcare system, to inform public funding for mainstream implementation in Australia.

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## FOOTNOTES

**Author contributions:** Moxham R and Tjokrowidjaja A recruited patients, collected and analysed data; Tjokrowidjaja A drafted the original research report and Moxham R drafted and prepared the manuscript for publication; Devery S, Smyth R and McLean A recruited patients, collected and analysed data; Roberts DM advised on clinician recruitment and data analysis; Wu KHC as the coordinating principal investigator was responsible for the study design and overall project supervision, manuscript editing and review; all authors contributed to manuscript revision, read and approved the submitted version.

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