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RESEARCH ARTICLE

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Implementing pharmacogenomic testing in Australian general practice: an exploratory qualitative study

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ABSTRACT

Aim: To explore general practitioners' (GPs) views on implementing pharmacogenomic testing in Australian general practice.

Methods: Semi-structured interviews were conducted with nine GPs in Australia, recruited from primary care networks. Interviews were analyzed using thematic analysis. Themes were mapped onto the Consolidated Framework for Implementation Research domains.

Results: Barriers to implementation included lack of knowledge, education, standardized pharmacogenomic reports and national clinical guidelines and financial inaccessibility. Facilitators included positive exposure to pharmacogenomics, peer influences, interdisciplinary collaboration and proven clinical utility. Current uptake was minimal; however, GPs shared positive perceptions of clinical use.

Conclusion: Recommendations for successful implementation include building and disseminating clinical evidence, developing national guidelines and standardized reports, incorporation into formal education and increasing financial accessibility.

PLAIN LANGUAGE SUMMARY

What is this article about?: This article describes an original research study that examines the implementation of pharmacogenomic testing in Australian general practice. Pharmacogenomic testing applies personalized genomic information to medication prescribing, as genetic differences can affect how a person metabolizes certain medications. While there is excitement about the possibilities of using pharmacogenomics, the general uptake is slow. This study looked to understand the barriers and facilitators to implementation from the perspectives of general practitioners in Australia.

What were the results?: Through exploratory interviews with general practitioners, this study identified that barriers to implementation include a lack of knowledge, education, standardized reports and national clinical guidelines and financial inaccessibility. Facilitators include positive exposure to pharmacogenomic testing, peer influences, interdisciplinary collaboration and proven clinical utility. Current uptake was minimal; however, GPs shared positive perceptions of the potential of testing.

What do the results of the study mean?: Based on the results of this study, the following recommendations were generated for successful implementation: building and disseminating clinical evidence, developing national guidelines, incorporation into formal education, establishing accessible experts and improving financial accessibility.

TWEETABLE ABSTRACT

A qualitative study explores the barriers and facilitators to successful implementation of pharmacogenomic testing in Australian general practice.

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consolidated framework for implementation research; general practice; genetic testing; implementation; personalized genomic medicine; pharmacogenomics

1. Background

Pharmacogenomics, which considers the effect of genomic variation on drug response, presents an emerging technology that could revolutionize individualized healthcare. Through genotyping for variants in drug receptors or drug metabolism, patients can receive improved efficiency and effectiveness in clinical prescriptions. While the term 'pharmacogenetics' is often used interchangeably, it refers to the impact

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of a single gene variant on drug metabolism, whereas pharmacogenomics refers to variants across the entire genome. Despite the potential for positive use and growth in commercially available tests, the uptake of pharmacogenomic testing in clinical practice has been reportedly slow [1,2].

Clinical validity and utility in pharmacogenomic testing have been established for several commonly used medications. A well-characterized example is the anticoagulant warfarin. Response to warfarin can be highly variable, resulting in an increased risk of adverse effects and clinical trials have shown that prescribing with pharmacogenomic testing can lead to faster therapeutic results and improved outcomes [3–5]. Pharmacogenomic testing has also shown promise in psychiatry, with some United States insurance companies now providing funding for testing. Multiple published studies demonstrate evidence of the clinical utility of pharmacogenomic testing for variants in genes that affect anti-depressant metabolism, such as *CYP2D6* and *CYP2C19*, prior to prescribing for major depressive disorder [6–9]. A meta-analysis concluded that target response and remission rates were achieved faster with pharmacogenomic testing [10].

Pharmacogenomic testing is particularly relevant in primary care, as general practitioners (GPs) are often responsible for initiating prescriptions and providing the first line of care for physical and mental health [11]. Successful implementation in general practice requires understanding barriers, facilitators and strategies of implementation and a number of studies in Canada and the United Kingdom have addressed these within their respective healthcare systems [12,13]. Barriers include inconsistencies in supporting scientific evidence, a lack of randomized controlled trials (RCTs), uncertainty surrounding cost–effectiveness, undetermined ethical and social implications of genomic information, a lack of incorporation into formal education and the unclear impact of non-genetic factors such as sex and diet, which can make genotype-based prescribing difficult [12–16]. Facilitators include a positive attitude toward pharmacogenomics and interprofessional collaboration among healthcare practitioners, such as medical doctors and pharmacists [17,18].

Despite some research exploring the implementation of pharmacogenomic testing on a global scale, there is a gap in knowledge regarding its application in Australian general practice. Extrapolating implementation recommendations between countries is difficult as each presents a unique healthcare structure with distinct priorities. Differences in prevalent medical conditions and commonly used medications may influence choices made in clinical implementation. In Australia, healthcare is jointly provided by the federal, state and territory governments. Accessibility to all is a central tenet to healthcare in Australia. 'Medicare' is the national insurance scheme that gives Australian citizens and permanent residents access to free and low-cost care healthcare. In addition, many residents of Australia choose to pay into private health insurance plans. Government subsidies for health services are determined by the federal government and listed as part of the Medicare Benefits Schedule (MBS). MBS rebates currently exist for two pharmacogenomic test items, *HLA-B*57:01* for abacavir hypersensitivity and *TPMT* and *NUDT15* for thiopurines. According to the Royal Australian College of General Practitioners, while international guidelines and evidence from RCTs for clinical utility of pharmacogenomic tests may inform clinical practice, the overall incorporation and role in Australian healthcare is still undecided [19].

A report commissioned by the Australian Genomics Health Alliance in 2022 describes that despite the international exemplars of implementation research, evaluation and implementation remains one of the three research priorities for pharmacogenomics testing in Australia. This overarching category includes research that focusses on experiences of patients and practitioners, barriers and enablers and identification of implementation strategies [20]. To successfully implement routine pharmacogenomic testing into Australian general practice, it is necessary to understand the needs and views of local, practicing clinicians. Therefore, the objective of this study was to explore the perceptions of Australian GPs regarding the integration and utilization of pharmacogenomic testing in primary care. Viewpoints on the current knowledge and uptake, perceived usefulness and barriers and facilitators of implementation were discussed to gain a better understanding of how successful implementation may occur and highlight key considerations of GPs.

2. Materials & methods

2.1. Study design

This was an exploratory qualitative study that used semi-structured interviews with Australian GPs to understand perspectives on pharmacogenomic testing in general practice. The research philosophy underlying this study was a constructivist approach, which uses concurrent collection of inductive data and comparative qualitative analysis to identify themes and construct theories. This approach acknowledges the multiple standpoints and realities of both researchers and participants [21]. Thematic analysis was used, allowing for the generation of themes and adaptation to a wide range of datasets [22].

2.2. Ethics

Ethics and governance approval was received from The Office of Research Ethics and Integrity, University of Melbourne (2021-20766-18399-4).

2.3. Recruitment & sampling

Recruitment for the study occurred through two methods. First, research team members sent the study advertisement via email to GPs within their personal and professional networks. Second, the recruitment advertisement was included in the Victorian primary care practice-based Research and Education Network (VicREN) monthly newsletter, a resource which is sent to GPs, practice managers and other primary care providers around the Australian state of Victoria, and physicians were encouraged to forward to any GPs who may have interest. GPs who wished to learn more about the study indicated interest by emailing research team member EE, who then provided a plain language statement and written consent form. Researcher EE then scheduled remote interviews with interested participants. Purposive sampling was used to ensure diversity in participant age, years of practice, gender and location, to capture a range of viewpoints. Recruitment ended when themes appeared to be firmly grounded in empirical data and it was determined that sufficient information power had been achieved [23].

2.4. Data collection & storage

Data was collected through in-depth, semi-structured, long form interviews to allow for information richness with a small sample size. All interviews were conducted via Zoom. An interview guide was developed based on previous literature and the domains of the Consolidated Framework for Implementation Research [Supplementary File 1]. Questions were designed to encourage open discussion in four broad categories: current knowledge of pharmacogenomic testing, opinion and perceived usefulness, implementation and interdisciplinary care and perceived patient opinions. Demographic information, including age, sex, years of experience and practice location, was also collected. An example pharmacogenomic testing report for a clinically available test was pulled from Sonic Genetics online resources for the interview [https://www.sonicgenetics.com.au/media/14660/pgx-example-report-2022w2.pdf]. Sonic Genetics' example report was chosen as they are Australia's largest private genetics laboratory and therefore likely to be relevant or familiar to Australian GPs [24]. This report was shared with participants ahead of the interview and incorporated into discussion to explore potential test result delivery. After two interviews, the guide was refined to better address the questions and arising themes. Written and verbal consent were obtained prior to recording and only audio recordings were retained. Interviews were then transcribed verbatim, de-identified and coded. Field notes were taken concurrently with interviews.

2.5. Analysis

NVivo V.12 by QSR International was used to manage qualitative data [25]. First-level complete coding was carried out using an inductive approach and then codes were grouped together to unveil larger themes [26]. Systematic coding of entire transcripts ensured rigour by starting with a data-driven approach. Coding of transcripts was completed by researcher EE and co-coding of a subset of interviews to ensure rigour was performed by research team members SS and GR. As interviews and analysis took place simultaneously, the research team met frequently throughout the interview and analysis process to discuss initial coding, emerging themes and add to or adjust the interview guide questions as necessary.

2.6. Consolidated framework for implementation research

Identified themes were mapped onto the five domains of Consolidated Framework for Implementation Research (CFIR) to assess facilitators and barriers of implementation and generate recommendations. CFIR is a conceptual framework that was developed to integrate many implementation science theories into one consolidated framework. It systematically assesses 39 constructs categorized into five domains to identify variables relevant to implementation of an intervention [25]. Identification of these interacting constructs through a pragmatic structure can then be used to interpret findings and generate recommendations. The five domains of CFIR as described in the context of this project are: intervention characteristics (features of pharmacogenomic testing); inner setting (features of general practice); outer setting (features of government and healthcare systems); characteristics of individual (qualities of GPs); and implementation process (strategies that may influence implementation).

3. Results

3.1. Participants

Nine participants were interviewed. The interviews lasted from 35 to 65 min. The mean participant age was 42, and the mean years of experience as a GP was 17.5. Participants from metropolitan (major capital cities, such as Melbourne), regional (centers with a population of over

500,000 outside of major capital cities) and remote and rural locales (less populated areas outside of cities) were included (Table 1).

3.2. Themes presented within the domains of CFIR

Themes are presented according to the domains of CFIR. Each theme has been sorted into one of the five domains and then classified as a barrier or facilitator of implementation. Figure 1 shows themes mapped onto CFIR domains.

3.3. Intervention characteristics

3.3.1. Pharmacogenomic testing is perceived to be clinically useful

All participants viewed pharmacogenomic testing to possess some degree of clinical utility relevant to their practice. GPs imagined potential time and length reductions in *"the trial-and-error process of medications"* (M, 33, 5 years of experience), as well as an explanation as to why a particular medication is not effective:

> *"There are times when you are doing everything that you think is right and it's not working even when the patient is compliant…it just might explain a lot of situations where you are just guessing and trying to change from one medication to another, not really knowing."* (F, 43, 15 years of experience)

Medications for treating psychiatric illnesses, such as antidepressants, were identified as particularly useful and relevant targets for pharmacogenomic-guided prescribing. GPs noted patients *"go through a lot of medications before they find something that fits"* (F, 31, 5 years of experience) due to inconsistent efficacy, and "*patients might cycle through quite a few antidepressants"* (F, 35, 5 years of experience). They addressed the difficulties of trial-and-error prescribing and the ability of pharmacogenomics to aid this:

> *"It's actually quite traumatic going through a trial of medication you don't react to for mental health…when you're suffering with a mental health condition. Yeah, I think people are very receptive to [pharmacogenomics]."* (F, 57, 33 years of experience)

GPs also saw a means to effectively adjust medication dosage based on genotype, as they could feel confident in "*try[ing] a higher dose…before giving up on that [medication] or moving to another option,"* (F, 35, 5 years of experience).

The results of the test allowed them to feel assured in these choices.

> *"You know it's got a tick so it's relatively safe, so you could probably push it to high doses." (*F, 51, 30 years of experience*)*

Clinicians also saw value in predicting, and subsequently reducing, adverse effects, which can be *"a big cause of why people are non-adherent"* (F, 43, 15 years of experience). Being able to communicate this to their patients was also seen as valuable for instilling confidence in treatment.

> *"I can certainly think of instances where you've had patients that are either avoiding taking medications because they're so worried about potential side effects or have had negative experiences with a certain medication and then are really reluctant to try other options, that might be really helpful in order to be able to alleviate some anxieties."* (F, 33, 8 years of experience)

3.3.2. Financial access prevents beneficial care

All participants raised concerns regarding the cost of pharmacogenomic testing, as it is currently self-funded in Australia, except for two MBS items: abacavir and thiopurines. One GP stated, *"the cost to the patient is going to be really relevant" (*F, 51, 30 years of experience) and another that *"cost is a barrier"* (F, 57, 33 years of experience). Many recognized the *"huge socioeconomic inequalities [faced] in general practice"* and felt that paying several hundred dollars for a medical test meant that *"even if that information might be valuable, it might be inaccessible*" (F, 33, 8 years of experience). There was concern about how some socioeconomic classes may be affected differently:

> *"If you're working in more affluent suburbs, we see that cost doesn't mean so much. But I think for the general population…people would be more hesitant to pay."* (M, 33, 5 years of experience)

GPs also felt that patients would be deterred from testing if it was self-funded, as *"when tests…require payment, patients are generally more hesitant"* (M, 33, 5 years of experience). Some felt that if they were able to provide evidence to justify the clinical use of pharmacogenomic testing, patients would be more willing to pay out-of-pocket.

> *"If you're going to save twelve months of trial and error then I guess a lot of people would be happy to pay $200."* (F, 31, 5 years of experience)

A history of patients paying out-of-pocket for other tests suggested to GPs that *"if patients can sort of see the benefits of that then they're often happy to pay those costs"* (F, 33, 8 years of experience). While the fee paid after any healthcare rebates are applied caused concern, the long-

Table 1. Participant demographics. (n = 9).

Sex		
Male	1	11%
Female	8	88%
Age		
25–34	4	44%
35–44	2	22%
45–54	1	11%
55–64	1	11%
65+	1	11%
Years of experience		
0–5	3	33%
6–10	2	22%
11–20	1	11%
21–30	1	11%
31+	2	22%
Practice location		
Metropolitan	6	66%
Regional	1	11%
Remote and rural	2	22%

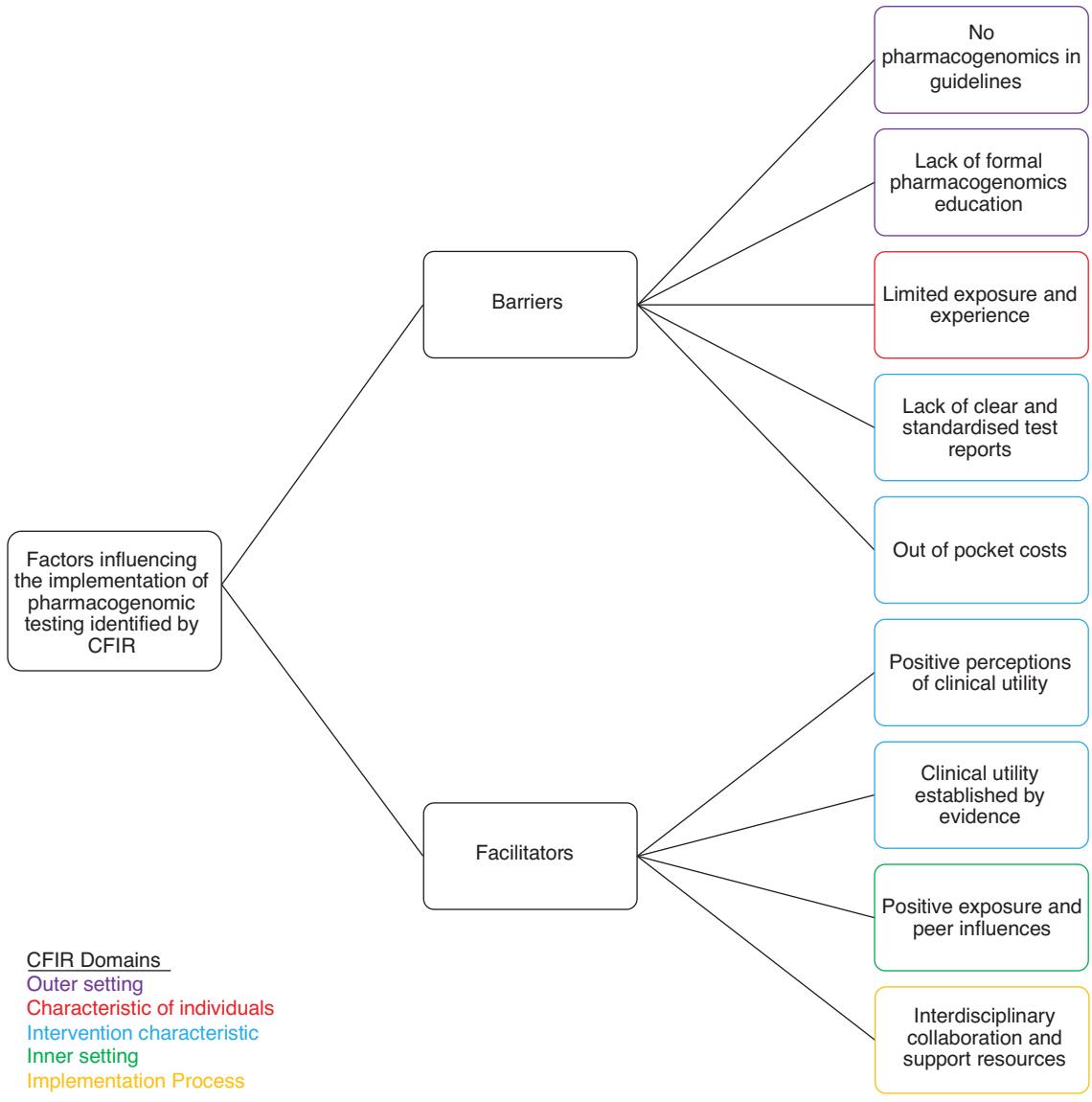

Figure 1. Themes mapped onto the five domains of CFIR.

term financial benefits could justify the costs, for example by "*doing this test on a lot of people to save on this one person who has to stay in hospital a couple extra days*" (F, 57, 33 years of experience), or for the patients themselves as *"it would save time for the patient, and [so] it would save money for the patient"* (F, 43, 15 years of experience).

GPs working in rural locations had concerns specific to their patient population. They reflected on the difficulty of accessing specialty centers which can affect patients' decisions, as "*rural patients are happier seeing [GPs] or want to avoid going to a specialist if not necessary due to where they're located and the costs associated*" (F, 35, 5 years of experience). For all patients, in rural or metropolitan areas, they "*have to pay a lot to see private specialists and that's a barrier*" (F, 57, 33 years of experience).

3.3.3. GPs prefer a targeted approach for test results

GPs were prompted to give feedback on the example report as a method for returning results. A consistent view regarding the report was it was *"too distracting to have a whole panel"* and a *"targeted approach"* would be preferred for incorporation into general practice (F, 51, 30 years of experience). Concern was shared regarding *"the length of the report, 18 pages"* as GPs were *"not sure how or when [they would] be able to read [it]"* (F, 30, 7 years of experience). GPs wanted a report with clarity and sufficient information within a manageable amount of reading.

> *"I'd be very reluctant to order that [test] if I'm going to get something back like that."* (F, 66, 42 years of experience)
>
> *"I haven't read it in detail but that is definitely not a good block of text to put in front of a GP, that will put them off ordering this test."* (F, 57, 33 years of experience)

Simplicity was also important for patient comprehension, as GPs *"would be using this information to explain it to patients, and patients will have a copy of this test"* (F, 57, 33 years of experience). *"Making it more tailored information"* (F, 33, 8 years of experience) or *"tailoring to the medications that are commonly used"* (M, 33, 5 years of experience) and having a *"targeted panel"* (F, 33, 8 years of experience) were all noted as important for GPs.

3.4. Inner setting

3.4.1. Positive exposure & peer influence increase uptake

While experience with pharmacogenomic testing for many GPs was minimal, exposure and positive peer anecdotes help to encourage uptake.

> *"The more you are exposed to it and somebody you know uses it, it's kind of like how wildfire spreads. I think more people would be likely to get on board if more people were using it."* (F, 31, 5 years of experience)

Experiencing successful applications of pharmacogenomics could increase future use as well, as *"if [pharmacogenomic testing] was really effective for one patient then [GPs] may say, look, it's worth doing earlier"* (M, 33, 5 years of experience), and "*if [they] knew for example that one of [their] peers was doing it…and found it really helpful and really useful then [they] would start to use it*" (F, 30, 7 years of experience). GPs felt hesitant to be early adopters and instead have been *"watching and waiting to see what others are doing"* (F, 57, 33 years of experience). Positive experiences from trusted sources such as specialists or peers were encouraging for GPs to try using pharmacogenomic testing in their own practice.

> *"I guess the more I saw it from trusted resources like psychiatrists, the more likely I would be to use it. As soon as I realized our psychiatrist uses this with a lot of patients I was like, oh okay, well it's obviously worth it, for these patients at least."* (F, 31, 5 years of experience)

GPs *"tend to follow what the people who are specializing in that area do"* as pioneering new technology or methods *"can be a dangerous thing for a GP to do"* (F, 51, 30 years of experience). Younger participants felt that watching senior clinicians successfully use pharmacogenomics would motivate them to do the same, as *"a lot of [their] practice is really influenced by what some senior colleagues do"* (F, 33, 8 years of experience).

3.5. Outer setting

3.5.1. Guidelines & policy influence practice

GPs discussed how institutional guidelines influenced their practice. Recommendations generated by pharmacogenomic reports often include prescribing doses outside of usual guidelines, which GPs felt they *"would not be in favour of doing"* (M, 33, 5 years of experience). Prescribing in *"high quantities"* would cause GPs to be *"thinking twice"* (F, 30, 7 years of experience).

> *"We're not currently using these reports and with that then you're going to be like, 'well one of them could lead to risks around doing these tests, and what are the implications for my patients, but also for me.'"* (F, 30, 7 years of experience)

GPs stressed the *"need [to] have guidelines…around how we manage all this, not just ordering these tests"* (F, 66, 42 years of experience). To address this, GPs saw potential

in *"[integrating] into existing guidelines in a way that might make…that information more accessible"* (F, 33, 8 years of experience). Suggestions were also made to create strongly evidenced guidelines which would be based upon a *"very good synthesis of literature [that is] translated to a really good resource"* (F, 57, 33 years of experience). GPs saw guidelines as a *"protective sort of blanket"* which provided *"something to lean on if there's a problem"*, which was a reason why if pharmacogenomics was *"built into a guideline in terms of when to use it then people would be more likely to"* (M, 33, 5 years of experience).

> *"The more automatic or the more embedded it is in the technology and how the institution works, then it's easier for people to just use it."* (F, 43, 15 years of experience)

3.5.2. Education & upskilling are required prior to use

Regardless of when participants had graduated from medical school they had *"never [encountered pharmacogenomics] coming through the general practice curriculum"* (M, 33, 5 years of experience), as it *"hasn't been actively taught in our general practice curriculum"* (F, 33, 8 years of experience). GPs felt a lack of formal training reduced their confidence in using pharmacogenomic testing.

> *"It's something completely outside of what we've learned about, what medical students do. It's not in our training, so how do we use it properly?" (F, 57, 33 years of experience)*

A need for standardized education on pharmacogenomics was highlighted, as GPs *"need to know what the benefit is for patients [and] be able to tell them"* (F, 30, 7 years of experience), and have an "*understanding of how to support a patient once we get the results back"* (F, 51, 30 years of experience). Some felt delivery through a formal education program, such as *"through general practice training to start with"* (M, 33, 5 years of experience), during medical school, or through professional development opportunities, would be helpful for incorporation.

Others reflected on their priorities in professional development being *"driven by the sort of work [they're] doing"* and *"often [being] done in the evenings or weekends"* (F, 66, 42 years of experience). Providing resources such as *"short messages, short letters…podcasts, webcasts"* was noted to be helpful for self-driven skill development (F, 51, 30 years of experience).

3.6. Characteristics of individuals

3.6.1. GPs lack exposure & experience with pharmacogenomic testing

All GPs reflected on their personal experience with pharmacogenomic testing. While all participants had some theoretical knowledge, most had never had a clinical encounter with pharmacogenomic testing before. Having *"never ordered a pharmacogenomics test for one of [their] patients"* there was a lack of confidence in knowing *"how [to] do it"* (F, 30, 7 years of experience).

> *"Definitely knew it was out there and it has been sort of thrown around I'm sure for the last ten years, but never really in practice."* (F, 51, 30 years of experience)

Several GPs were unaware that pharmacogenomic testing was *"available other than as a research tool"* (F, 51, 30 years of experience) and could be used in the clinical space.

> *"I've got no clinical experience with using pharmacogenomics at all. I'm not aware of any of my colleagues that have used it or are using it either. I think I was sort of more aware of it as a kind of emerging technology that is in the process of development."* (F, 33, 8 years of experience)

For the few GPs with patients who had testing, the only area in which pharmacogenomic testing had been used was psychiatry. GPs who had encountered *"pharmacogenomic testing for complex psychiatric illnesses"* in the clinic had seen results from tests ordered by other professionals, as *"[pharmacogenomic testing] has always been specialist driven"* (F, 31, 5 years of experience), but had never ordered a test themselves. Additionally, some GPs had patients ask about pharmacogenomic testing, but felt unable to proceed with ordering due to their lack of experience.

> *"Some patients have come in inquiring about [pharmacogenomic testing] but I don't think I've got enough knowledge, I didn't at the time, to know well how do we go about it? Where do we send you?"* (F, 51, 30 years of experience)

3.7. Implementation process

3.7.1. Interdisciplinary collaboration & resources are needed for support

GPs wanted to be able to *"ask somebody…like a special pharmacist"* questions regarding testing, *"especially [for] using higher than recommended doses"* (F, 35, 5 years of experience). New technologies require *"backup support until [there is] an understanding"* (F, 51, 30 years of

experience), and establishing a collaborative healthcare team could be beneficial in combining *"the expertise of different kinds of groups of health professionals to support the patient overall"* (F, 33, 8 years of experience). Having *"everyone involved in a patient's care"* was seen to be *"always beneficial"* (F, 31, 5 years of experience). Other potential healthcare professionals for clinical pharmacogenomics collaboration included psychiatrists, pharmacists and genetic counsellors.

> *"[A pharmacogenomic testing report] might have some numbers to contact which would open the door to some genetic counsellors of pharmacists."* (F, 51, 30 years of experience)
>
> *"If pharmacists were included [to] work out the best way to present results and they are involved in considering alternatives…or this is unavailable in Australia why is it in the report…that would be useful."* (F, 57, 33 years of experience)

4. Discussion

This study is the first to explore Australian GPs views on implementation of pharmacogenomic testing in general practice. We found that although current uptake was limited due to various reasons, the Australian GPs who took part in this study shared positive perceptions of the potential clinical applications of pharmacogenomic testing. However, barriers exist that must be addressed prior to incorporation, including a lack of education, standardized test reports and national guidelines for clinical use, as well as financial inaccessibility. Conversely, facilitators of implementation included perceived clinical utility, positive exposure and collaboration with peers, allied health professionals and specialists. Viewing data through the lens of CFIR allowed for identification of factors that hinder or facilitate implementation. While studies on the implementation of pharmacogenomic testing have been conducted in other countries, understanding factors that pertain to Australia's unique healthcare system is essential in facilitating successful national implementation. With a combined public and private healthcare system that strives to provide access to all, as well as a diverse geographical and socioeconomic landscape, the Australian healthcare faces unique challenges that must be understood prior to implementation of pharmacogenomic testing.

4.1. Barriers to implementation of pharmacogenomic testing in general practice

A barrier to implementation found in this research is that the GPs in this study had little experience of pharmacogenomic testing in general practice. A lack of exposure to pharmacogenomics has been echoed in other research, such as a qualitative study conducted in Quebec, Canada, which found that while most GPs had a general idea of theoretical pharmacogenomics, very little had any clinical experience [12]. In the United Kingdom, one study found that many GPs had never even heard of the term pharmacogenomics before [13]. Furthermore, GPs consider their lack of experience to be a cause for anxiety when anticipating an incoming 'tidal wave' of patients wanting pharmacogenomic testing [27].

Our study found that hesitation to use pharmacogenomic testing also appears to be in part due to a lack of formal education. While a recent analysis of worldwide health programs, including some in Australia, found that pharmacogenomics education was being incorporated into most medical, pharmacy and nursing school programs, the participants of our study, all of whom had graduated at least 5 years prior, reported no official education on the subject; indicating that incorporation may have been very recent [28]. Increasing general genetics education for GPs internationally has been highlighted as necessary to keep current with the progression of genetics in primary care [29].

A lack of clear and standardized reports was another identified barrier to implementation. To standardize clinical use of pharmacogenomic testing, a report delivery system that is concise, clear, consistent and translatable between the laboratory, practitioners and patients is needed. When assessing the sample pharmacogenomic testing report currently being used by a private laboratory in Australia, GPs felt unsure of how to translate information to their patients and reluctant or unable to read the full report due to the excessive length and amount of information. Another Australian study found that pharmacogenomics reports need to be 'user friendly', as GPs often do not have extensive training on the background and delivery [11]. An alternative method for delivery could be incorporation of a clinical decision support system with integrated report data into an already existing electronic medical record system that GPs use. Such a system has been trialled in research with some success in Canada, a country with a healthcare system that is similar to Australia's [30]. The Genomic Prescribing System, an interactive online system for physicians, has been shown to be useful in the USA, while other studies note that clinical decision tools are effective for prescribing [31–33].

For implementation of pharmacogenomic testing on a national level, cost to patients and accessibility must be considered. GPs who serve rural populations had particular concerns about the cost and time it takes to access tests. Regardless of practice location or patient demographics, GPs reiterated that financial access would

be a significant barrier for their patients. In Australia, apart from genetic testing for cancer treatment, there are only two pharmacogenomic testing related items on the Medicare Benefits Schedule (MBS): abacavir hypersensitivity (item 73323) and thiopurines dosing (item 73327). All other testing is self-funded, and a full panel, such as the Sonic Genetics example, would cost approximately $200 AUD. Prohibitive out of pocket costs may deter patients from accessing the benefits of pharmacogenomic testing. In addition, GPs noted that financial barriers may be particularly challenging for those of a lower socioeconomic class. While the Australian universal healthcare system aims to provide accessible healthcare to all people regardless of socioeconomic status, a 2020 study by Pulok et al. found there to be a pro-rich bias in accessing general practice [34]. Addressing financial barriers in pharmacogenomic testing is essential in preventing a gap in healthcare accessibility from dividing further.

GPs lacking access to any national guidelines was identified as another barrier to implementation, as trusted clinical guidance is essential for GPs. Australian general practice guidelines that describe how or when pharmacogenomic prescribing should be used do not yet exist. International groups such as the Clinical Pharmacogenetics Implementation Consortium and the Dutch Pharmacogenetic Working Group have published extensive work assigning levels of actionability to drug-gene interactions based on current evidence [35]. The Pharmacogenomics Knowledge Base (PharmGKB.org) is another resource which presents curated information on gene-drug pairs with recommended guidelines for clinical use. These may be a useful starting point for clinicians seeking recommendations; however, factors such as drug availability and variant frequencies will differ between countries, so creating Australia specific recommendations is essential. As identified in this study as well as others, consistent and relevant guidelines that are endorsed and disseminated by Australian organizations such as the Royal Australian College of General Practitioners, or incorporating information into platforms such as *Therapeutic Guidelines*, a consolidated tool for local Australian medical practice, could help Australian GPs confidently use pharmacogenomic testing [11].

4.2. Facilitators of implementation of pharmacogenomic testing in general practice

A facilitator of implementation that GPs in our study highlighted was positive experiences of pharmacogenomics testing and recommendations from peers, especially those with seniority or specialization. For example, some psychiatrists have implemented pharmacogenomic testing for antidepressant prescribing, a drug category whose application is supported by strong evidence from clinical trials [9,36]. Increasing GP exposure to experienced specialists using pharmacogenomic testing, such as psychiatrists, may be a way to encourage preliminary uptake. Continued support, such as access to a hotline or expert for questions would make introducing pharmacogenomic testing into clinical practice more appealing for GPs. Collaboration with other healthcare practitioners, such as genetic counsellors, may provide an avenue for support and expertise. Distributing responsibilities among healthcare practitioners has been shown to result in increasing the number of patients seen, improving resource management and reducing inappropriate testing [36–38].

Whether or not GPs in this study had practical experience with pharmacogenomic testing, it was perceived to have clinical utility and relevant applications to practice, despite GPs being unfamiliar with actual existing clinical evidence. Other healthcare professionals, such as pharmacists and genetic counsellors, also perceive pharmacogenomic testing to be of value [39,40]. Evidence of clinical utility has been established with some medications, such as warfarin and abacavir and various psychiatric drugs [41–43]. However, a 2017 review by Klein et al. suggested that a lack of RCTs proving clinical utility has caused healthcare providers to be reluctant of uptake, and other literature examining implementation of pharmacogenomics has echoed this sentiment [12,14,41]. Perceived utility by interested partners, in this case GPs, can assist in determining the value of testing where large RCTs may not have yet been conducted, which is the current state for some gene-drug pairings [44–46]. Continuing to expand the body of evidence with gold-standard RCTs for drug-specific clinical utility, then effectively disseminating this information to GPs, will encourage uptake.

4.3. Recommendations

Based on the barriers and facilitators identified through analysis with CFIR, there are several actions we would recommend for successful implementation of pharmacogenomic testing in Australia. To address the lack of education on the principles and uses of pharmacogenomic testing, we suggest that pharmacogenomics is incorporated into formal Australian medical education, and accessible professional development resources are provided for already graduated GPs. Additionally, GPs are hesitant to adopt technologies that are not used by peers, as they cannot access support when needed. We recommend establishing accessible experts for early adopters, increasing exposure between disciplines and increasing collaboration with specialists to expose GPs

to clinical pharmacogenomics use. Continuing research of clinical utility for more gene-drug interactions is also integral, so we recommend conducting more RCTs and disseminating results to GPs in Australia.

In this study, we found that result delivery can affect GPs willingness to use tests. Therefore, a clear, concise and consistent report for pharmacogenomic testing should be developed that is comprehensible for GPs and patients. Data can be incorporated into a clinical decision-making tool that already exists in electronic medical systems for ease of access. A lack of Australian guidelines was also deterring GPs from using pharmacogenomic testing, so we recommend development of formal national guidelines on clinical use of pharmacogenomic testing within Australia with instructions for how and when to use testing. Finally, out-of-pocket costs create financial barriers to test access when there may be patient and healthcare system cost benefits. Financial accessibility can be improved upon by lobbying the government for more Medicare rebates linked to pharmacogenomic tests with proven clinical utility.

4.4. Strengths & limitations of the study

Although purposive sampling was used to include participants with diverse characteristics, there was some skewing of categories, which may limit transferability. For example, only one out of nine participants interviewed identified as male. However, the distribution of participants across rural, regional and metropolitan locations within Australia was balanced, giving a diverse range of geographical views within the state. A bias may have existed toward positive viewpoints on pharmacogenomic testing, as it is possible GPs who would take part in this study did so because of an already established interest in the subject.

In-depth, semi-structured interviews allowed for information-rich, insightful exploration, given the current dearth of Australian evidence. Future research would be well placed to explore the generalizability of our findings to Australian general practice more broadly. Incorporation of CFIR into our analysis allowed for recommendation generation based on the perspectives of GPs who are key in primary care. Using CFIR also allowed for the identification of high-priority factors influencing implementation, thereby providing a comprehensive overview of barriers and facilitators of implementation.

5. Conclusion

This study examined the implementation of pharmacogenomic testing in primary care through the perceptions of Australian GPs. We sought to explore participants' current levels of experience with pharmacogenomic testing, which was found to be preliminary or theoretical only. While participating GPs possessed some knowledge regarding pharmacogenomics, their formal education on the subject was minimal and upskilling was individually driven. Despite limited interactions, the GPs who took part in this study had positive views surrounding the perceived clinical utility of pharmacogenomic testing in their practice. Based on the identified factors that influence implementation, we have generated recommendations for Australian general practice including increasing formal education, peer support, exposure and clinical trials; as well as developing standardized reports and national guidelines, and improving financial accessibility.

Article highlights

- Pharmacogenomic testing provides an opportunity to tailor drug prescriptions to individuals, which can possibly increase adherence and reduce adverse effects, time to successful treatment and costs.
- Understanding the implementation of pharmacogenomic testing in general practice is important as GPs are often the first contact patients will have in the medical care system, and are also the healthcare professionals who are prescribing medication.
- This study used exploratory interviews with GPs to understand their perceptions of pharmacogenomic testing, including perceived barriers and facilitators to implementation.
- Themes were generated through analysis and considered under the five domains of the Consolidated Framework for Implementation Research.
- While perceptions surrounding pharmacogenomics were positive, current use by GPs was low.
- Barriers to implementation included lack of knowledge, education, standardized pharmacogenomic reports and national clinical guidelines and financial inaccessibility. Facilitators included positive exposure to pharmacogenomics, peer influences, interdisciplinary collaboration and proven clinical utility.
- Recommendations for implementation were generated, including building and disseminating clinical evidence, developing national guidelines, incorporation into formal education, establishing accessible experts and improving financial accessibility.

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Author contributions

E Ewasiuk: conceptualization; data curation; formal analysis; writing – original draft, review and editing; investigation; methodology. S Saya: methodology; writing – review and editing, conceptualization; formal analysis; supervision. G Reid:

writing – review and editing; formal analysis; supervision. J Emery: conceptualization; methodology; writing – review and editing; supervision; project administration. All authors reviewed and gave final approval for this version of the work to be published.

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Competing interests disclosure

The authors have no competing interests or relevant affiliations with any organization or entity with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

Writing disclosure

No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

The authors have obtained institutional board approval from the University of Melbourne for the research described (ID 20766). All participants gave verbal and written informed consent prior to interviews for the study.

Data availability statement

The data from this study is not publicly available due to privacy restrictions. Data that supports the finding of this study is available upon request of the corresponding author.

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References

Papers of special note have been highlighted as: • of interest; •• of considerable interest

1. Muflih S, Bleidt B, Laffery L, Shawaqfeh M, Alvarez G. Measuring knowledge and attitudes towards the utilization of pharmacogenetic testing among physicians. J Pharmaceut Health Serv Res. 2019;2:227–234. doi:10.1111/jphs.12289
2. Amara N, Blouin-Bougie J, Bouthillier D, Simard J. On the readiness of physicians for pharmacogenomics testing: an empirical assessment. Pharmacogenom J. 2018;18:308–318. doi:10.1038/tpj.2017.22
3. Relling MV, Evans WE. Pharmacogenomics in the clinic. Nature. 2015;526(7573):343–350. doi:10.1038/nature15817
4. Daly AK. Pharmacogenetics: a general review on progress to date. Br Med Bull. 2005;124:65–79.
5. Dean L. Wafarin therapy and *VKORC1* and *CYP* genotype. In: Medical Genetics Summaries [Internet] Pratt VM, Scott SA, Pirmohamed M, et al., editors. Bethesda, MD, USA: National Center for Biotechnology Information; 2012.
6. Perez V, Salavert A, Espadaler J, et al. Efficacy of prospective pharmacogenetic testing in the treatment of major depressive disorder: results of a randomized, double-blind clinical trial. BMC Psychiatry. 2017;17:250. doi:10.1186/s12888-017-1412-1
7. Han C, Wang S-M, Bahk W-M, et al. Pharmacogenomic-based antidepressant treatment for patients with major depressive disorder: results from an 8-week, randomized, single-blinded clinical trial. Clin Psychopharmacol Neurosci. 2018;16:469–480. doi:10.9758/cpn.2018.16.4.469
8. Espadaler J, Tuson M, Lopez-Ibor JM, et al. Pharmacogenetic testing for the guidance of psychiatric treatment: a multicenter retrospective analysis. CNS Spectr. 2017;22:315–324. doi:10.1017/S1092852915000711
9. Bousman CA, Stevenson JM, Ramsey LB, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6, CYP2C19, CYP2B6, SLC6A4, and HTR2A genotypes and serotonin reuptake inhibitor antidepressants. Clin Pharmacol Ther. 2023;114(1):51–68. doi:10.1002/cpt.2903
10. Wang X, Wang C, Zhang Y, Zhuoling A. Effect of pharmacogenomics testing guiding on clinical outcomes in major depressive disorder: a systematic review and meta-analysis of RCT. BMC Psych. 2023;23(1):334. doi:10.1186/s12888-017-1493-x
11. Polasek TM, Kym M, Graeme S. Pharmacogenomics in general practice: 'the time has come'. Aust J Gen Pract. 2019;48(3):100–105. doi:10.31128/AJGP-10-18-4733
12. Frigon M, Blackburn M, Dubois-Bouchard C, et al. Pharmacogenetic testing in primary care practice: opinions of physicians, pharmacists, and patients. Pharmacogenomics. 2019;20(8):589–598. doi:10.2217/pgs-2019-0004
13. Rafi I, Crinson I, Dawes M, et al. The implementation of pharmacogenomics into UK general practice: a qualitative study exploring barriers, challenges, and opportunities. J Comm Genet. 2020;11:269–277. doi:10.1007/s12687-020-00468-2
• A similar qualitative study that explores implementation of pharmacogenomic testing in UK primary care. Results found that were different to our study include social implications of testing and concerns of electronic capture of genomic information and data sharing.
14. Drozda K, Pacanowski MA. Clinical trial designs to support clinical utility of pharmacogenomic testing. Pharmacotherapy. 2017;37(9):1000–1004. doi:10.1002/phar.1971
15. Verbelen M, Weale ME, Lewis CM. Cost–effectiveness of pharmacogenetic-guided treatment: are we there yet? Pharmacogenomics J. 2017;17:395–402. doi:10.1038/tpj.2017.21
16. Limaye N. Pharmacogenomics, theranostics and personalized medicine - the complexities of clinical trials: challenges in the developing world. Appl Transl Genom. 2013;2:17–21. doi:10.1016/j.atg.2013.05.002
17. Lanting P, Drenth WH, Boven LG, et al. Practical barriers and facilitators experienced by patients, pharmacists,

and physicians to the implementation of pharmacogenomic screening in Dutch outpatient hospital care – an explorative pilot study. J Pers Med. 2020;10(4):293. doi:10.1101/2020.11.11.20229211
18. Bishop JR. Pharmacists as facilitators of pharmacogenomic guidance for antidepressant drug selection and dosing. Clin Transl Sci. 2021;14(4):1206–1209. doi:10.1111/cts.13057
19. Royal Australian College of General Practitioners. Genomics in general practice. (2023). https://www.racgp.org.au/getattachment/a7b97d5a-5b5f-4d4b-ab3b-efa9c08b1d6d/Genomics-in-general-practice.aspx
20. Australian Genomics. Research priorities for Australian pharmacogenomics: final report from the Pharmacogenomics Incubator Project working group. Australia (2022). https://www.australiangenomics.org.au/wp-content/uploads/2022/11/Pharmacogenomics-Incubator-Project-Report_30Aug2022-.pdf
21. Charmaz K. Constructivist grounded theory. J Posit Psychol. 2016;12:299–300. doi:10.1080/17439760.2016.1262612
22. Thomas DR. A general inductive approach for analyzing qualitative evaluation data. Am J Eval. 2006;27(2):237–246. doi:10.1177/1098214005283748
23. Malterud K, Siersma VD, Guassora AD. Sample size in qualitative interview studies: guided by information power. Qualitative Health Res. 2015;26(13):1753–1760. doi:10.1177/1049732315617444
24. Sonic Healthcare. Sonic PGx panel example report (Version 1.1) (2021). Available at: https://www.sonicgenetics.com.au/media/Multisite8698/pgx-example-watermark-report-sept-2019.pdf (Accessed: April 30, 2021).
25. Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. Implement Sci. 2009;4(50):1–15. doi:10.1186/1748-5908-4-50
• An explanation of the creation of the Consolidated Framework for Implementation Research, a pragmatic structure for approaching multi-level implementation evaluation.
26. Braun V, Clarke V. Thematic analysis in psychology. Qual Res Psychol. 2006;3(2):77–101. doi:10.1191/1478088706qp063oa
27. Carroll JC, Makuwaza T, Manca DP, et al. Primary care providers' experiences with and perceptions of personalized genomic medicine. Can Fam Physician. 2016;10(62):626–635.
• A Canadian study using focus groups to explore primary care providers experiences and perceptions of personalized medicine, focusing specifically on cancer.
28. Kuzelicki NK, Zitnik IP, Gurwitz D, et al. Pharmacogenomics education in medical and pharmacy schools: conclusions of a global survey. Pharmacogenomics. 2019;20(9):643–657. doi:10.2217/pgs-2019-0009
• A worldwide survey of pharmacogenomics in educational programs of a variety of health specialties.
29. Carrol JC, Allanson J, Morrison S, et al. Informing integration of genomic medicine into primary care: an assessment of current practice, attitudes, and desired resources. Front Genet. 2019;10:1189. doi:10.3389/fgene.2019.01189
30. Dawes M, Aloise MN, Sidney Ang J, et al. Introducing pharmacogenetic testing with clinical decision support into primary care: a feasibility study. CMAJ Open. 2016;4(3):528–534. doi:10.9778/cmajo.20150070
•• Cohort study where adults with a common disease underwent pharmacogenomic testing and had reports sent to evidence-based prescribing decision support system.
31. Chen T, O'Donnell P, Middlestadt M, et al. Implementation of pharmacogenomics into inpatient general medicine. Pharmacogenet Genomics. 2023;33(2):19–23. doi:10.1097/FPC.0000000000000487
•• A project that implemented strategies into actual clinical practice at several institutions in Chicago, USA. They discuss retrospectively the barriers to implementation that were encountered.
32. Lemke AA, Hutten Selkirk CG, Glaser NS, et al. Primary care physician experiences with integrated pharmacogenomic testing in a community health system. Personalized Med. 2017;14(5):389–400. doi:10.2217/pme-2017-0036
33. Van der wooden CH, Swen JJ, Samwald M, Mitropoulou C, Schwab M, Guchelaar H-J. A brighter future for the implementation of pharmacogenomic testing. Eur J Hum Genet. 2016;24:1658–1660. doi:10.1038/ejhg.2016.116
34. Pulok MH, van Gool K, Hall J. Horizontal inequity in the utilizations of healthcare services in Australia. Health Policy. 2020;124(11):1263–1271. doi:10.1016/j.healthpol.2020.08.012
35. Relling MV, Klein TE. CPIC: clinical pharmacogenetics implementation consortium of the pharmacogenomics research network. Clin Pharmacol Ther. 2010;89(3):464–467. doi:10.1038/clpt.2010.279
36. Bousman CA, Arandjelovic K, Mancuso SG, Eyre HA, Dunlop BW. Pharmacogenetic tests and depressive symptom remission: a meta-analysis of randomized controlled trials. Pharmacogenomics. 2019;20(1):37–47. doi:10.2217/pgs-2018-0142
37. Miller CE, Krautscheid P, Baldwin EE, et al. Genetic counselor review of genetic test orders in a reference laboratory reduces unnecessary testing. Am J Med Genet A. 2014;164(5):1094–1101. doi:10.1002/ajmg.a.36453
38. Wakefield E, Keller H, Mianzo H, Nagaraj CB, Tawde S, Ulm E. Reduction of health care costs and improved appropriateness of incoming test orders: the impact of genetic counselor review in an academic genetic testing. Laboratory. 2018;27:1067–1073. doi:10.1007/s10897-018-0226-8
39. Helm BM, Freeze SL, Spoonamore KG, Ware SM, Ayers MD, Kean AC. The genetic counselor in the pediatric arrhythmia clinic: review and assessment of services. J Genet Counseling. 2018;27:558–564. doi:10.1007/s10897-017-0169-5
40. Tuteja S, Haynes K, Zayac C, Sprague J, Bernhardt B, Pyeritz R. Community pharmacists' attitudes towards clinical utility and ethical implications of pharmacogenetic testing. Personalized Med. 2013;10(8):793–800. doi:10.2217/pme.13.85
41. Klein ME, Parvez MM, Shin J-G. Clinical implementation of pharmacogenomics for personalized precision

medicine: barriers and solutions. Sci. 2017;106(9):2369–2379. doi:10.1016/j.xphs.2017.04.051
42. Wang X, Wang C, Zhang Y, An Z. Effect of pharmacogenomics testing guiding on clinical outcomes in major depressive disorder: a systematic review and meta-analysis of RCT. BMC Psychiatry. 2023;23(334):1–12. doi:10.1186/s12888-023-04756-2
43. Mallal S, Nolan D, Witt C, et al. Association between presence of HLA-B*5701, HLA-DR7, and HLA-DQ3 and hypersensitivity to HIV-1 reverse-transcriptase inhibitor abacavir. Lancet. 2002;359(9308):727–732. doi:10.1016/S0140-6736(02)07873-X
44. Van der wooden CH, Swen JJ, Samwald M, Mitropoulou C, Schwab M, Guchelaar H-J. A brighter future for the implementation of pharmacogenomic testing. Eur J Hum Genet. 2016;24:1658–1660. doi:10.1038/ejhg.2016.116
45. Altman RB. Pharmacogenomics: "Noninferiority" is sufficient for initial implementation. Clin Pharmacol Ther. 2011;89(3):348–350. doi:10.1038/clpt.2010.310
46. Pirmohamed M, Hughes DA. Pharmacogenetic tests: the need for a level playing field. Nat Rev Drug Discov. 2012;12:3–4. doi:10.1038/nrd3921