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Research Article

Exploring Pharmacogenetic Testing for Depression in Primary Care in the UK: A Five-Year Longitudinal Study of Patient Outcomes

Bhimpuria M[1*], Roser A[2], Roser T[3]

[1]*GP, Alconbury and Brampton Surgeries, Huntingdon, Cambridgeshire, UK*
[2]*GP, Alconbury and Brampton Surgeries, Huntingdon, Cambridgeshire, UK*
[3]*Psychologist and Assistant Professor, Loughborough University, Loughborough, UK*

Corresponding Author: Malav Y Bhimpuria, MB BS BSc (HONS) FRCGP DCH DRCOG PGCert (Med Ed). Alconbury and Brampton Surgeries, Huntingdon, Cambridgeshire, UK, E-mail: malav.bhimpuria@nhs.net

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Abstract

Depression is commonly managed in primary care. However, not every antidepressant is effective in every patient and clinicians typically use a "trial-and-error" approach to optimise treatment until the right medication is found for a particular patient. This process however can be time-consuming, leading to suboptimal outcomes with many side-effects. Pharmacogenetic testing (PGT) refers to a genetic test that identifies certain genetic differences that are associated with variable drug responses, thus enabling tailored drug treatment to the patient's unique genetic makeup, thereby improving patient outcomes.

Aim: To explore how pharmacogenetic testing for antidepressants can be embedded in primary care as part of "usual care" and ascertain if any subsequent treatment changes are sustainable over several years.

How this study fits in Previous research has shown that up to 50% of patients treated with antidepressants fail therapy. PGT can be undertaken in primary care, but it has not been established if it can occur as part of "usual care" or if these changes are sustainable in the long-term.

Method: 23 patients with depression had PGT to ascertain if they were extensive (normal) metabolisers to antidepressants, intermediate, poor or ultra-rapid metabolisers on the CYP2C19 and CYP2D6 pathways. They were reviewed at 1 week and at 4 years and then at 5 years.

Results: On the CYPC219 pathway, 5 patients were ultra-rapid metabolisers and had their antidepressants changed. On the CYP2D6 pathway, 2 were poor metabolisers and had treatments changed. The changes were sustained at 4 and at 5 years.

Conclusion: PGT for depression in primary care works and results are sustainable. It can lead to actionable insights that are adopted in primary care.

Keywords: *Pharmacogenetics; Depression; Primary Care*

Introduction

Depression is commonly managed in primary care, with choice of drug treatment determined by national guidelines. However, not every antidepressant is effective in every patient. Up to 50% of patients treated with antidepressants fail therapy [4]. Clinicians typically use a 'trial-and-error' approach to optimise treatment until the right medication and treatment plan can be found for a particular patient. This process can be time-consuming, costly and lead to suboptimal treatment outcomes. On average, it may take 3-4 months to put a patient on the right antidepressant, requiring a number of GP appointments to review medications, make dose adjustments, issue new prescriptions and make referrals to other healthcare specialists.

Further, a 'trial-and-error' approach may put patients at increased risk due to ineffective treatment or side effects. In addition to health and economic factors there are also important non-clinical factors we need to consider (e.g. GP issues sick note, the patient cannot work; impact on family members; lower productivity levels increased suicide risk in society; poor compliance to treatment).

Pharmacogenetic testing (PGT) refers to a genetic test that identifies certain genetic differences that

are associated with variable drug response [6].

Personalised prescribing entails using pharmacogenetics to tailor drug treatment to the patient's unique genetic makeup and thereby improve drug adherence and outcomes.

Meta-analyses of randomised controlled trials (RCTs) show that individuals receiving pharmacogenetic-guided therapy are significantly more likely to achieve symptom remission relative to individuals who receive treatment as usual [2].

Aim

To explore how pharmacogenetic testing for antidepressants can be embedded in primary care as part of "usual care" and ascertain if any subsequent treatment changes are sustainable over several years.

Method

23 patients with a known diagnosis of depression were recruited from Alconbury Surgery, Huntingdon in 2019 and had genetic testing via a cheek swab to ascertain if they were extensive (normal) metabolisers to common antidepressants, intermediate metabolisers, poor metabolisers or ultra-rapid metabolisers. They were tested on the CYP2C19 pathway and CYP2D6 pathway. Results were conveyed to the patients by their GP within a week and the patients further reviewed at 4 years (in 2023) and at 5 years (in 2024) to see if any treatment changes were sustainable.

Results

On the CYP2C19 pathway, 10 patients were extensive (normal) metabolisers, 8 intermediate metabolisers, 0 poor metabolisers and 5 ultra-rapid: all these 5 had their antidepressants changed at one-week review.

At 4-year review 20 out of 23 patients were still on the correct treatment, 2 patients had treatment discontinued as they were clinically better and 1 was commenced on treatment that was not compatible with their genetic makeup. This treatment was subsequently changed by the GP and this change was sustained at 5-year follow-up.

On the CYP2D6 pathway, 19 patients were extensive metabolisers, 1 intermediate and 2 poor: these two patients had their treatment changed at one-week review.

At 4-year review, 19 patients were still on the correct treatment, 2 had their treatment stopped as were better and 2 were commenced on treatment that was incompatible with their genetic makeup. This treatment was subsequently changed by the GP and this change was sustained at 5-year follow-up.

Conclusion

Pharmacogenetic testing (PGT) is increasingly utilised in clinical practice as a tool to aid the optimization of antidepressant use with pharmacogenetic strategies [8, 3]. Making this information available enables better prescribing, monitoring and clinical outcomes [5]. Instead of a 'trial-and-error' and 'one-size-fits-all' approach, PGT can enable more targeted treatments with a view to prescribing the right drug the first-time round [1, 7].

Pharmacogenetic testing for depression in primary care works, patients and GPs are engaged and the results are sustainable at four and five years with 95% of patients on the CYP2C19 pathway still on the correct drugs and 90% of patients on the CYP2D6 pathway still on the correct drugs. However, numbers were small and more research is needed to see if this is replicable at scale. Additionally, in this study, GPs were the only health care professional who undertook the consenting and testing. Other members of the wider primary healthcare team, such as clinical pharmacists embedded in primary care, could play a crucial role if PGT is to be scaled up and rolled out to a wider patient population.

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Ethical approval

Was not required as it was classified as an implementation project.

Competing interests

None.

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