Cost-Effectiveness Analysis of Pharmacogenetic-Guided Treatment in Drug Resistant Depression

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Introduction

Drug side effects and ineffectiveness are a source of morbidity, significant disability, mortality, and increase the overall cost of care worldwide. Pharmacogenetic tests aim to detect specific variants in a patient's genome to enable personalized treatment in terms of drug selection and dosage, in order to optimize therapeutic efficacy and reduce treatment-related side effects. This research explores the cost-effectiveness and potential budget impact on the National Organization for Healthcare Services in Greece (EOPYY) of an in vitro diagnostic (IVD) pharmacogenetic test, iDNA PGx-CNS, for the treatment of patients with Major Depressive Disorder (MDD) who have not responded to at least 2 antidepressant treatments, i.e., Drug Resistant Depression (DRD). This test examines the proven interaction of drugs administered to patients with MDD with genetic variants, as reflected in the most recent international scientific literature and pharmacogenetic databases, for the optimal selection of the most therapeutically efficacious medication.

Methods

An economic model was developed for the financial evaluation of iDNA PGx-CNS-guided therapy of MDD. The model was designed to calculate cost-effectiveness analysis (deterministic analysis) and probabilistic sensitivity analysis (PSA), specifically employing 5,000 simulations. The study included 2 groups of patients (n=100,000 per group) and compared pharmacogenetic (PGx)-guided therapy versus Treatment-As-Usual (TAU). The time horizon of the study was defined as 12 months, through the perspective of the National Agency for the Provision of Health Services (EOPYY) in Greece. Data inputs to populate the decision tree were derived from the literature, Greek cost data sources, and a panel of psychiatry experts. Following analysis of the results, the cost-utility acceptability curve (CUAC) was derived, with the aim to systematically compare the overall costs and benefits associated with the pharmacogenetic alternative therapeutic intervention in the management of MDD.

Results

A tree diagram of all possible treatment options and their clinical outcomes, accompanied with their respective probabilities, was developed (Figure 1). For each outcome, respective probabilities of occurrence, direct costs (hospitalization, doctor visit, pharmacotherapy, and side effects costs) and patients' quality of life were estimated. The model takes into account the cost of pharmacotherapy, based on the relative frequency of use of antidepressants and the cost per drug. Finally, the model considers patients' Quality-Adjusted Life Years (QALYs) for each outcome.

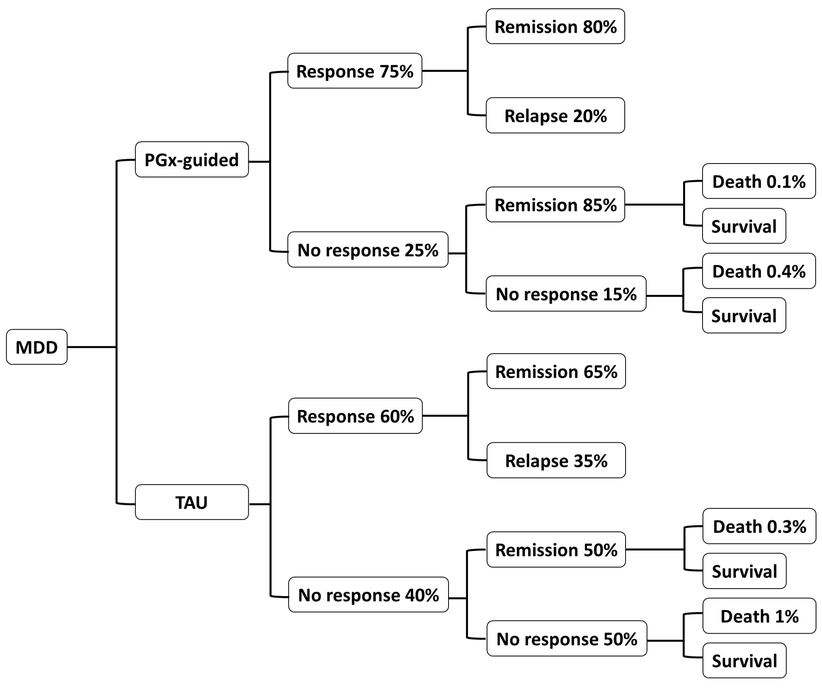

Figure 1: Decision tree for Major Depressive Disorder (MDD) therapy following PGx test or Treatment-As-Usual (TAU). The probabilities of the alternative outcomes were determined by a panel of psychiatry experts.

For the PGx-guided arm, use of the iDNA PGx-CNS pharmacogenetic test was explored. This panel examines Single Nucleotide Polymorphism (SNP) variants in 13 genes associated with well-established gene-drug interactions (Table 1), explicitly developed for drugs of the Central Nervous System (CNS) [**1,2**]. To estimate costs, hospitalization data for MDD per year (Table 2) and indicative drug compensation costs by the EOPYY were used (Table 3). The pharmacogenetic test was offered at 139 €, while 90.35 € were assumed covered by the EOPYY. To estimate the cost of medical visits, the frequency of visits was taken into consideration, as well as the cost of 10 € per visit.

Table 1: Panel of genes and Single Nucleotide Polymorphisms (SNPs) examined in the iDNA PGx-CNS Kit.

Gene	SNP
ANKK1, DRD2	rs1800497
CYP2C19	rs12248560, rs28399504, rs4244285, rs4986893
CYP2C9	rs1057910, rs1799853
CYP2D6	rs1065852, rs28371725, rs35742686, rs3892097, rs5030655, rs5030656
DRD2	rs1799978
DRD3	rs963468
EPHX1	rs1051740, rs2234922
FKBP5	rs4713916
GRIK1	rs2832407
HTR2C	rs1414334
MC4R	rs17782313, rs489693
SCN1A	rs3812718
UGT2B7	rs7668258

Table 2: Average number of hospitalizations and average days of hospitalization following PGx and Treatment-As-Usual (TAU).

	PGx-guided	TAU	Source
Average number of hospitalizations per year	2,000 (2%)	5,000 (5%)	Panel of psychiatry experts
Average number of hospital days per hospitalization	15 days	25 days	Panel of psychiatry experts

Table 3: List of medicines primarily used in the treatment of MDD and corresponding costs.

Active substance	Content per tablet (or per ml)	Tablets (or ml) per pack	Cost per pack
Escitalopram	10 mg	14	2.46 €
Citalopram	20 mg	28	4.32 €
Venlafaxine	150 mg	28	5.72 €
Sertraline	100 mg	30	7.13 €

Based on utility data derived from the literature [**3,4**] and according to a panel of psychiatry experts (Table 4), the results of the cost-utility analysis showed that the average cost per patient with MDD is 263 € for patients receiving PGx-guided therapy, and 259 euros for patients receiving TAU. In addition, the PGx-guided therapy was associated with 0.712 QALYs and TAU therapy with 0.651 QALYs. From the above it was then calculated that the marginal cost-utility ratio is 55 € per QALY gained (Table 5).

Table 4: Utility data derived from the literature and according to the data obtained from a panel of psychiatry experts.

Utilities	Value	95% CI	Source
Response	0.81	-	Groessl *et al.*, 2018
No response	0.57	-	Groessl *et al.*, 2018
Remission	0.8	0.76	Sluiter *et al.*, 2018
Relapse	0.48	0.38	Sluiter *et al.*, 2018
Suicide	0	-	-

Table 5: Results of cost-utility analysis.

Parameters	PGx-guided	TAU
Total cost (€)	263	259
QALYs	0.712	0.651
Additional cost of PGx-guided therapy versus TAU (€)	-	3
Additional QALYs of PGx-guided therapy versus TAU (€)	-	0.062
ICER of PGx-guided therapy versus TAU (€/QALY gained)	-	55

The dispersion of incremental cost-effectiveness ratios (ICERs) (Figure 2) are in the upper right and lower right quadrants of the scatterplot, indicating that the very large majority of simulations are either dominant or cost-effective. The cost-utility acceptance curve (CUAC) (Figure 3) suggests that PGx-guided therapy appears to be the most cost-effective, with a probability of 100% at the average price (€34,242) and the lowest price (€17,121) of the acceptance range threshold.

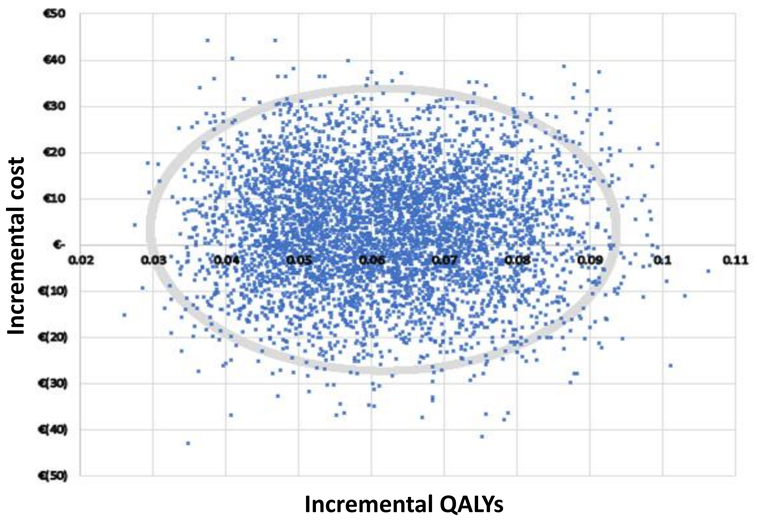

Figure 2: Scatterplot derived from the probabilistic sensitivity analysis (PSA) following 5,000 simulations.

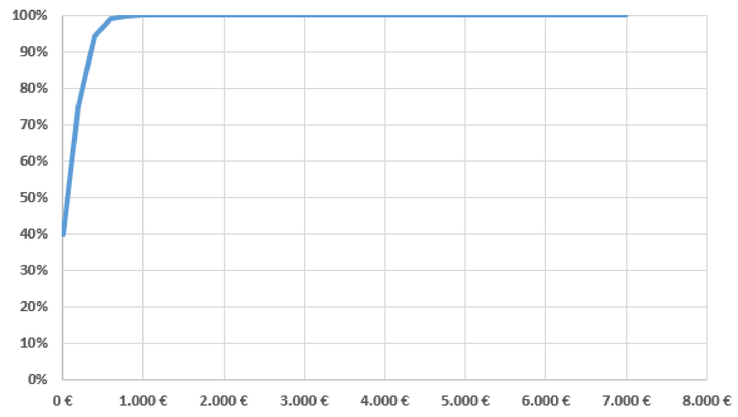

Figure 3: Cost-utility acceptance curve (CUAC) of pharmacogenetic-guided therapy in MDD.

Discussion

In comparison to conventional treatment, pharmacogenetic-guided treatment with the iDNA PGx-CNS was found to be a cost-effective intervention with ICER 55 €/QALY, which is almost minimal compared to the conventional average (€ 34,242) and the lowest ratio (€ 17,121). Furthermore, its impact is rather limited on the EOPYY's budget, as even in the hypothetical scenario of the use of the iDNA PGx-CNS by all patients with DRD, the 5-year cumulative total financial burden does not exceed 1 million €. The analysis also showed a significant reduction in suicides, specifically 638 fewer deaths from patient suicide in 5 years, in the pharmacogenetic-guided arm. Hence, pharmacogenetic guidance is cost-effective and advances the individualized choice of the most effective, safe, and tolerable medication for each patient.

References

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