Supplementary Information

Clinical implementation of preemptive pharmacogenomics in psychiatry

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Table S1. Costs of medical interventions to treat ADRs.

Medical Interventions*	Costs (€)**
Adverse Drug Reactions	
Weight gain	2,599
Extrapyramidal disorder	1,670
Gastrointestinal pain	323
Fatigue	1,245
Mania	2,568
Musculoskeletal and connective tissue disorders	1,203
Tremor	1,152
Skin disorder	181
Suicidal Attempt	2,568
Sepsis	2,316
Surgical procedure	3,000
Diarrhea	323
Examination Costs	
CT upper and lower abdomen	71.11
Echocardiogram	70
Electrocardiogram	10
Laboratory Tests costs	
CPK	5.02
Prolactine blood test	12.38
Follow up assessments	
Therapist consultations	48
Visit to General practitioner/neurologist, cardiologist	10
Genetic testing costs	
PGx testing	120

*It refers to all procedures done due to adverse events and adverse drug reactions. ** All costs data derived from Greek Ministry of Health, EOPPY, DRGs official page: http://kenicd.e-healthnet.gr/%CE%91%CF%81%CF%87%CE%B9%CE%BA%CE%B7.aspx
CT: computerised tomography, Echo: echocardiogram, CPK: creatine phosphokinase, PGx: Pharmacogenomics

Table S2. Frequency of ADRs, stratified by their respective NCI-CTCAE severity grade on the entire study population. Each patient could have presented with multiple ADRs that are included in this table.

	Control N = 528[1]	PGx-guided N = 545[1]	p-value[2]	q-value[3]
Cardiac disorders Grade 1	1 (0.19%)	0 (0.00%)	0.5	0.8
Cardiac disorders Grade 2-5	3 (0.57%)	0 (0.00%)	0.12	0.4
Ear and labyrinth disorders Grade 1	0 (0.00%)	2 (0.37%)	0.5	0.8
Ear and labyrinth disorders Grade 2-5	0 (0.00%)	1 (0.18%)	>0.9	>0.9
Endocrine disorders Grade 2-5	1 (0.19%)	0 (0.00%)	0.5	0.8
Eye disorders Grade 1	0 (0.00%)	2 (0.37%)	0.5	0.8
Eye disorders Grade 2-5	0 (0.00%)	1 (0.18%)	>0.9	>0.9
Gastrointestinal disorders Grade 1	19 (3.60%)	11 (2.02%)	0.12	0.4
Gastrointestinal disorders Grade 2-5	15 (2.84%)	4 (0.73%)	0.009	0.076
General disorders and administration site conditions Grade 1	2 (0.38%)	3 (0.55%)	>0.9	>0.9
General disorders and administration site conditions Grade 2-5	11 (2.08%)	3 (0.55%)	0.027	0.2
Immune system disorders Grade 2-5	0 (0.00%)	1 (0.18%)	>0.9	>0.9
Infections and infestations Grade 2-5	2 (0.38%)	0 (0.00%)	0.2	0.7
Investigations Grade 1	29 (5.49%)	25 (4.59%)	0.5	0.8
Investigations Grade 2-5	26 (4.92%)	28 (5.14%)	0.9	>0.9
Metabolism and nutrition disorders Grade 1	5 (0.95%)	4 (0.73%)	0.7	>0.9
Metabolism and nutrition disorders Grade 2-5	5 (0.95%)	2 (0.37%)	0.3	0.8
Musculoskeletal and connective tissue disorders Grade 1	0 (0.00%)	1 (0.18%)	>0.9	>0.9
Musculoskeletal and connective tissue disorders Grade 2-5	1 (0.19%)	11 (2.02%)	0.004	0.066
Neoplasms Grade 2-5	0 (0.00%)	1 (0.18%)	>0.9	>0.9
Nervous system disorders Grade 1	17 (3.22%)	24 (4.40%)	0.3	0.8
Nervous system disorders Grade 2-5	34 (6.44%)	15 (2.75%)	0.004	0.066
Psychiatric disorders Grade 1 *	17 (3.22%)	8 (1.47%)	0.057	0.3

	Control N = 528[1]	PGx-guided N = 545[1]	p-value[2]	q-value[3]
Psychiatric disorders Grade 2-5 *	14 (2.65%)	3 (0.55%)	0.006	0.066
Renal and urinary disorders Grade 1	1 (0.19%)	2 (0.37%)	>0.9	>0.9
Renal and urinary disorders Grade 2-5	4 (0.76%)	1 (0.18%)	0.2	0.7
Reproductive system and breast disorders Grade 1	2 (0.38%)	4 (0.73%)	0.7	>0.9
Reproductive system and breast disorders Grade 2-5	8 (1.52%)	3 (0.55%)	0.12	0.4
Respiratory, thoracic and mediastinal disorders Grade 2-5	0 (0.00%)	2 (0.37%)	0.5	0.8
Skin and subcutaneous tissue disorders Grade 1	3 (0.57%)	4 (0.73%)	>0.9	>0.9
Skin and subcutaneous tissue disorders Grade 2-5	1 (0.19%)	0 (0.00%)	0.5	0.8
Social circumstances-related disorders Grade 1	0 (0.00%)	1 (0.18%)	>0.9	>0.9
Surgery and medical procedure-related disorders Grade 1	0 (0.00%)	2 (0.37%)	0.5	0.8
Vascular disorders Grade 2-5	0 (0.00%)	1 (0.18%)	>0.9	>0.9

[1]n (%)

[2]Fisher's exact test; Pearson's Chi-squared test

[3]Benjamini & Hochberg correction for multiple testing

* Psychiatric disorders symptoms considered as ADRs include: Agitation, Anorgasmia, Anxiety, Confusion, Delayed orgasm, Delirium, Delusions, Depression, Euphoria, Hallucinations, Insomnia, decreased/increased Libido, Mania, Personality change, Psychosis, Restlessness, Suicidal ideation, Suicide attempt

Table S3. Frequency of ADRs, stratified by their respective NCI-CTCAE severity grade within actionable patients. Each patient could have presented with multiple ADRs that are included in this table.

	Control, N = 126[1]	PGx-guided, N = 135[1]	p-value[2]	q-value[3]
Gastrointestinal disorders Grade 1	6 (4.76%)	5 (3.70%)	0.7	>0.9
Gastrointestinal disorders Grade 2-5	4 (3.17%)	1 (0.74%)	0.2	0.6
General disorders and administration site conditions Grade 2-5	6 (4.76%)	1 (0.74%)	0.059	0.3
Immune system disorders Grade 2-5	0 (0.00%)	1 (0.74%)	>0.9	>0.9
Investigations Grade 1	3 (2.38%)	7 (5.19%)	0.3	0.8
Investigations Grade 2-5	8 (6.35%)	5 (3.70%)	0.3	0.8
Metabolism and nutrition disorders Grade 1	0 (0.00%)	1 (0.74%)	>0.9	>0.9
Metabolism and nutrition disorders Grade 2-5	1 (0.79%)	1 (0.74%)	>0.9	>0.9
Musculoskeletal and connective tissue disorders Grade 2-5	0 (0.00%)	1 (0.74%)	>0.9	>0.9
Neoplasms Grade 2-5	0 (0.00%)	1 (0.74%)	>0.9	>0.9
Nervous system disorders Grade 1	2 (1.59%)	4 (2.96%)	0.7	>0.9
Nervous system disorders Grade 2-5	10 (7.94%)	2 (1.48%)	0.013	0.12
Psychiatric disorders Grade 1	**8 (6.35%)**	**0 (0.00%)**	**0.003**	**0.047**
Psychiatric disorders Grade 2-5	6 (4.76%)	2 (1.48%)	0.2	0.6
Renal and urinary disorders Grade 2-5	1 (0.79%)	0 (0.00%)	0.5	>0.9
Reproductive system and breast disorders Grade 1	0 (0.00%)	1 (0.74%)	>0.9	>0.9
Reproductive system and breast disorders Grade 2-5	4 (3.17%)	0 (0.00%)	0.053	0.3
Skin and subcutaneous tissue disorders Grade 1	2 (1.59%)	2 (1.48%)	>0.9	>0.9

[1]n (%)

[2]Pearson's Chi-squared test; Fisher's exact test

[3]Benjamini & Hochberg correction for multiple testing

Table S4. Number of patients receiving at least 2 antipsychotic drugs.

	Control	PGx-guided	p-value[2]
Entire study population	**N = 529[1]** **98 (18.53%)**	**N = 547[1]** **71 (12.98%)**	**0.012**
Actionable patients	N = 126[1] 20 (15.87%)	N = 136[1] 15 (11.03%)	0.2

[1]n (%)
[2]Pearson's Chi-squared test