Retrospective analysis of the documentation of results from combinatorial psychiatric pharmacogenetic testing

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Background

- Pharmacogenetics (PG) focuses on the interaction between a patient's genetics and medication pharmacokinetics and pharmacodynamics.
- PG testing and information is increasingly used to guide prescribing in various medical specialties, including psychiatry.
- A growing list of widely-used medications are known to have gene-drug interactions.
- Combinatorial pharmacogenetic (CPG) tools use multiple genotypes in proprietary algorithms to generate medication recommendations.
- Ordering and resulting of CPG products' results happens outside Electronic Health Records (EHR).

Objectives

- Evaluate the current documentation of CPG panel results in an academic hospital system.
- Characterize the incidence of post-CPG prescriptions with known gene-drug interactions.
- Understand which medical specialties prescribe medications that are affected by the genes on the CPG panel.

Materials & Methods

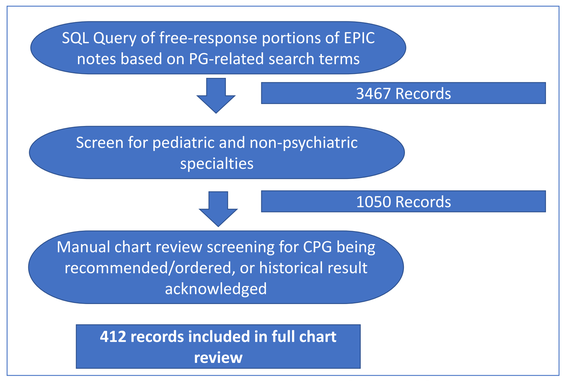
- Retrospective review of patient records in the EHR
- An SQL query searching clinical note text for PG-relevant search terms identified patients with CPG testing.
- Inclusion criteria for chart review:
  - CPG testing was ordered by provider, or provider was given historical CPG results
  - Patient over 18 years old
  - Treated by an adult psychiatry service
- Demographic, medication history, and diagnoses were extracted from each index record.
- Follow-up visits from index record to present were reviewed for new prescriptions with actionable guidance per the Clinical Pharmacogenetics Implementation Consortium and FDA (Table 1).

Table 1. Gene-Drug interactions included on Pharmacogenetic Panel

Gene	Medications					
CYP2B6	efavirenz	methadone				
CYP2C19	amitriptyline	citalopram	clopidogrel	escitalopram	lansoprazole	sertraline
	belzutifan	clobazam	dexlansoprazole	flibanserin	omeprazole	trimipramine
	brivaracetam	clomipramine	doxepin	imipramine	pantoprazole	voriconazole
CYP2C9	acenocoumarol	erdafitinib	fosphenytoin	meloxicam	siponimod	
	celecoxib	flurbiprofen	ibuprofen	phenytoin	tenoxicam	
	dronabinol	fluvastatin	lornoxicam	piroxicam	warfarin	
CYP2D6	amitriptyline	clomipramine	fluvoxamine	metoclopramide	pitolisant	tramadol
	amphetamine	clozapine	gefitinib	nortriptyline	propafenone	trimipramine
	aripiprazole	codeine	hydrocodone	oliceridine	risperidone	tropisetron
	atomoxetine	desipramine	iloperidone	ondansetron	tamoxifen	valbenazine
	brexpiprazole	deutetrabenazine	imipramine	paroxetine	tetrabenazine	venlafaxine
	carvedilol	doxepin	lofexidine	perphenazine	thioridazine	vortioxetine
	cevimeline	eliglustat	meclizine	pimozide	tolterodine	
*HLA-A*31:01*	carbamazepine					
*HLA-B*15:02*	carbamazepine	phenytoin	fosphenytoin	oxcarbazepine		

Results

Figure 1. Patient record sampling and screening for inclusion criteria



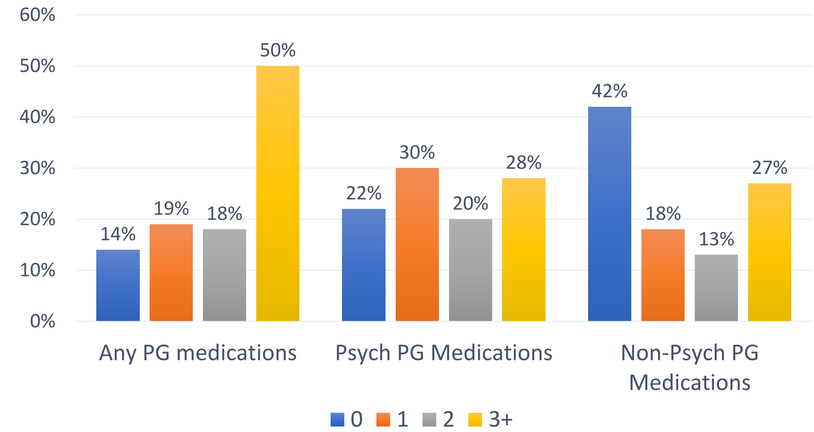
Sample Demographics

- 341 (83%) had documented confirmation that CPG testing was completed.
- The mean age was 37 years (range 28-53).
- The sample was 64% female, 73% white.
- 73% of patients were treated in an intensive outpatient therapy program.
- 55% of patients had greater than 1 psychiatric diagnosis (Table 2).
- 55 psychiatric prescribers were represented. One individual comprised 54% of the cases.

Documentation of CPG results (n=341**)**

- 97 (28%) patients had no genotype or phenotype results documented at all.
- 101 (30%) had results documented for only some genes on the CPG panel.
- 143 (42%) had results documented for every gene on the CPG panel.
- CPG testing results were documented in the following locations:
  - 57% under "Media" as scanned document.
  - 48% mentioned in free-text narrative portions of notes.
  - <1% of patients documented under the problem or allergy lists. No patients had discrete pharmacogenomic results documented in their chart.

Figure 2. % Patients Receiving 0-3+ PG Medications after CPG testing



Prescribing after completing CPG testing, in patients with >1 year follow-up (n=228)

- 86.4% were prescribed CPG-relevant medications (Figure 2).
- Non-psychiatric services frequently ordered medications with actionable guidance (Figure 3).
- Widely-used medications with gene-drug interactions were frequently prescribed after CPG testing (Figure 4).

Figure 3. Frequency of Specialties Prescribing PG-relevant Medications

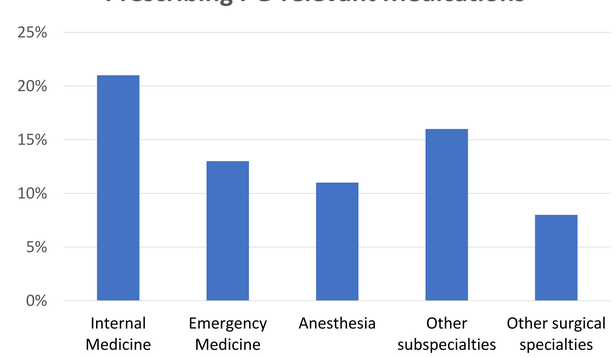


Figure 4. Most Frequent PG-relevant Medications Prescribed post-CPG testing

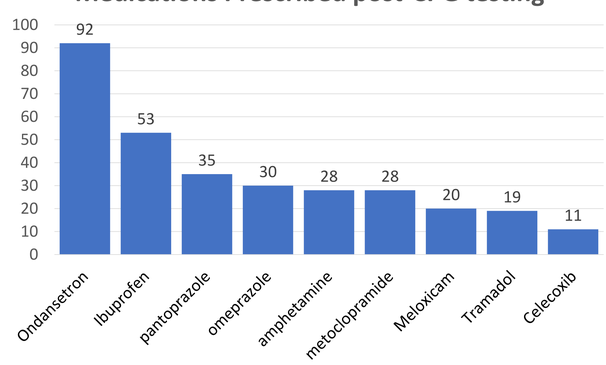


Table 2. Frequency of Psychiatric diagnoses & ICD-10 codes (%)

Major depressive and persistent mood disorders (F33, F34, F39)	196 (57%)
Anxiety disorders including panic disorder (F41)	119 (35%)
Obsessive compulsive disorder (F42)	74 (22%)
Bipolar disorder (F31)	70(21%)
Stress disorders (F43)	54 (16%)
All other anxiety disorders (F40-49)	29 (9%)
Attention deficit hyperactivity disorder (F90)	29 (9%)
Schizophrenia, other psychotic disorders (F20-29)	26 (8%)
Personality disorders (F60)	14 (4%)
None, or not specified MH diagnosis (F99)	10 (3%)

Discussion

- CPG testing results are inconsistently documented.
- When CPG results are documented, it is often in a way that is not readily available to other providers.
- PG-relevant medications are frequent prescribed by providers from other specialties than the ordering provider (psychiatry, in the present sample)
- PG testing holds the benefit of having life-long and static results. Hosting them in the EHR is therefore beneficial so it can accompany a patient across services.
- Having discrete pharmacogenetic results available in EHRs will be important for allowing clinical decision support alerts, facilitating research and evaluation, and preventing adverse drug reactions.

Future Directions

- Analysis of genotype information for patients who did receive CPG testing
- Characterize the prevalence of actionable genotypes in this sample
- Explore the prevalence of adverse drug reactions that are potentially avoidable with access to CPG testing results.

Acknowledgements

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