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Effects of Genetic Testing on Clinical Outcomes of Patients with Obsessive Compulsive Disorder

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Abstract

Problem: The National Institute for Mental Health (NIMH) reports that only 1.2% of adults suffer from OCD, but over 50% are severe (Obsessive Compulsive Disorder (OCD), n.d.). Meier et al. (2016), found that patients with OCD faced a 40% higher chance of early mortality. Individuals with psychiatric conditions are more at risk for poor physical health, poor education, economic struggles and crime (Mental Health by the Numbers, 2019). Emergency departments claim tens of millions of visits per year related to psychiatric issues resulting in billions in costs each year (Mental Health by the Numbers, 2019). Genetic testing is becoming a more frequently used tool in the battle against mental illness, but it can be expensive and its value in improving clinical outcomes is still up for debate (What is the cost of genetic testing, n.d.).

Methods: A descriptive, observational, quality improvement project aimed at evaluating clinical outcomes among genetically tested patients with OCD.

Results: This quality improvement project included 15 patients (n=15), 6 who were genetically tested (n=6, 40%) and 9 who were not (n=9, 60%). An analysis of variance (ANOVA) was conducted based on an alpha value of 0.05 for each clinical outcome and all were insignificant.

Implications for practice: Providers and Patients should seriously consider the cost before utilizing routine genetic testing in patients with OCD. A larger sample size should be used in future studies.

Evaluating the Effects of Genetic Testing on Patients with Obsessive Compulsive Disorder

Mental health conditions pose a serious burden in the US. The National Alliance for Mental Health reports that 1 in 5 adults face mental health issues each year (Mental Health by the Numbers, 2019). In 2017, that represented over 46 million individuals (Mental Illness, n.d.). When looking at obsessive compulsive disorder (OCD) specifically, the National Institute for Mental Health (NIMH) reports that while only 1.2% of adults suffer from OCD, over 50% of those have impairment that is deemed “severe” (Obsessive Compulsive Disorder (OCD), n.d.). A Danish study in 2016 by Meier et al., found that even after accounting for associated disorders and substance abuse, patients with OCD faced a 40% higher chance of early mortality compared to the general population. Genetic testing is becoming a more frequently used tool in the battle against mental illness, but it can cost anywhere between $100-$2000 and its value in improving clinical outcomes is still up for debate (What is the cost of genetic testing, n.d.). This project will seek to answer the study question: What effect does genetic testing have on clinical outcomes such as medication changes, side effects, tolerance and therapeutic response in patients aged 18-60 being treated for OCD compared to those who only undergo traditional clinical assessment and management?

According to the NIMH, OCD affects women more than men and young adults show the highest incidence (Obsessive Compulsive Disorder (OCD), n.d.). The second leading cause of death in individuals ages 10 to 34 is suicide (Mental

Health by the Numbers, 2019). Individuals who struggle with psychiatric conditions are more at risk for deterioration of physical health as well as issues with poor education, economic struggles and crime (Mental Health by the Numbers, 2019). Emergency departments claim 10's of millions of visits per year related to psychiatric issues resulting in billions of dollars in treatment costs each year (Mental Health by the Numbers, 2019).

Treating mental health diagnoses is complex with unique challenges. Treatment is often an emotional roller-coaster as the hope of a new drug is often followed by disappointment when, after weeks of waiting, it proves ineffective or intolerable. This cycle can be repetitive resulting in despair, hopelessness and ultimately defeat leading patients to cease treatment rather than face another painful cycle. In addition, potentially life altering side effects may occur with many mental health medications leading patients to struggle with treatment adherence.

Genetic testing may offer a potential "short cut" by identifying a patient's specific genetic variations allowing the provider to select the most effective and least disruptive medication for that specific patient much sooner, reducing treatment failure and non-adherence. For example, Smits et al. (2007) showed that among patients with depression, up to 40% will be resistant to SSRI's, the current first line treatment, due to genetic variations related to Serotonin processing. Using that information in treatment selection for patients with major depression increased the 6-week remission rate by almost 5% (Smits et al., 2007).

Current practices at a psychiatric outpatient clinic in a large mid-western city vary widely from provider to provider. The clinic has been utilizing the Genomind test for approximately two years. Some providers are highly motivated to use the test to guide their treatment plan, while others are unsure of the value of testing and prefer to rely on traditional clinical assessment alone. Some tests are reserved for highly treatment resistant patients, while others are targeted towards specific diagnoses. Patient input is often a determining factor as some patients are resistant to offering up their DNA while others simply “want to know”. For some patients, finding that their genetics explain why they are struggling is confirming and helpful in coming to terms with their condition. The findings of this quality improvement project may help to guide future practice.

Review of Literature

This project began with a review of the current literature as it pertained to the topic of the effectiveness of genetic testing in mental health, anxiety and OCD. The databases of PubMed, CINAHL and Google Scholar were searched for articles using various combinations of the terms mental health, behavioral health, psych*, effectiveness, anxiety, OCD, clinical outcomes, side effects, therapeutic response, medication changes, genetic and genomic testing. Articles were limited to having been published between January 1st, 2015 and the present.

Three articles discussed the basics of genetic testing and its role in anxiety disorders. McGowan (2019) explains the current status of studies relating to anxiety and genetic testing and provides evidence that multiple gene variants

could account for variations of severity of disease as well as response to medications. Tomasi et al. (2019) also discussed current knowledge of specific genetic variants as they pertained to anxiety disorders. Both articles emphasize the serotonin system. Smoller (2015) elaborates on what is and isn't known regarding the role of genetic variants in these disorders. All three articles discuss the complexity of the anxiety family of disorders and inconsistencies among current knowledge and acknowledge that while there are known genetic markers of interest, there is much room for further study specific to anxiety disorders.

One study, by Perlis et al., (2018), focused on cost effectiveness of genetic testing for anxiety patients, as the test can be as high as $2000 (What is the cost of genetic testing, n.d.). After comparing health claims between anxiety patients who received genetic testing to those who had not, it was determined that the tested group had statistically significant reductions in emergency room visits and hospitalizations resulting in an estimated savings of almost $2,000 over the 6 months (Perlis et. al, 2018). This potential savings could help justify the cost.

Three articles focused on the overall utility of genetic testing in anxiety disorder patients. A 2017 article by Tiwari et al. analyzed the Individualized Medicine: Pharmacogenetic Assessment and Clinical Treatment (IMPACT) study and the MEDCO dataset to evaluate the effectiveness of genetic testing. It was determined that there were statistically significant reductions of symptoms and benzodiazepine usage post genetic testing. Bradley et al., (2017) found statistically significant improvement in outcomes among patients with depression

and anxiety whose treatment was based on genetic testing when compared to the untested groups. The 2018 systematic review by Solomon, Cates and Li (2019) examined 16 studies between 2013 and 2018. While data was inconsistent, it was inferred that testing may benefit the population even though it may not necessarily equate to improved outcomes. Further research was recommended to determine whether the use of genetic testing translates to actual improvement in clinical outcomes.

A deeper review of the literature specifically regarding genetic testing as it pertains to OCD revealed 4 additional articles. Song et al. (2017) found that mutations within the SLITRK5 gene were implicated in OCD in both mice and humans. Other articles spoke to the role of neurotransmitters and their involvement in patient response to selective serotonin reuptake inhibitors (SSRIs). Sina, Ahmadiani, Asagi and Shams (2018) found a link between HTR2A haplotypes and therapeutic response to fluvoxamine in patients with OCD. Contrarily, Gomes et al. (2018) was unable to find a correlation with OCD and HTR2A but did find strong associations with OCD and the polymorphism in SLC6A4 STin2, another gene involved in serotonin transportation. Umehara et al. (2016) identified the calcium signaling pathway as being associated with therapeutic response to both SSRIs and SSRIs combined with antipsychotics.

In summary, genetic markers and variants among individuals can play a role in the presentation of anxiety and OCD as well as the response to medication therapy. Evidence has shown various benefits of genetic testing in

reducing medication costs and usage. There is insufficient data regarding improvement in clinical outcomes among genetically tested patients.

Method

Design

This project was a descriptive, observational, quality improvement project aimed at evaluating the clinical outcomes of prescribed medication changes, side effects, medication tolerance and therapeutic response among genetically tested patients with OCD compared to OCD patients who are not tested.

Framework

This project followed a Plan-Do-Study-Act (PDSA) framework. Each step is discussed further in the subsequent sections. This project evaluated the effects of genetic testing on clinical outcomes among patients with OCD. To execute this the researcher compared a convenience sample of OCD patients whose treatment was based on genetic testing to a convenience sample of OCD patients whose treatment was based only on traditional clinical diagnosis and assessment. A retrospective chart review of a 6-month period was used to evaluate each group and the effects of genetic testing on the clinical outcomes of medication changes, side effects, tolerance of medications and therapeutic response compared between the two groups.

Setting

This project took place in an outpatient psychiatric care clinic in a large mid-western city. The practice employs one physician and four nurse

practitioners and treats both pediatric and adult patients with all types of mental health conditions, including substance abuse.

Sample

In addition to obtaining the necessary approvals, the planning of the sample process was included in the *Plan* portion of the PDSA. The sample was a convenience sample of patients meeting the inclusion/exclusion criteria. Included for study were patients aged 18-60, seeking treatment for OCD whose initial visit and/or initial genetic test fell within the 12-month window between January 1st and December 31st of 2019. Excluded from the study were any patients exhibiting suicidal thoughts or intent, those with concurrent diagnoses of any personality disorders, those who were not actively being treated for OCD or related complications, and any patients who did not continue care for at least 6 months following initiation of treatment. These were divided into two groups: patients who received genetic testing within that time frame and patients who did not.

Data Collection

Data collection made up the *Do* section of the PDSA framework. Following clinic and IRB approval, read-only access to the medical records was obtained from the clinic. Data was collected via retrospective chart review. Data collected included patient demographics divided categorically to protect patient identities, initial anxiety scores based on the Patient Health Questionnaire (PHQ-9) and initial treatment recommendations among both groups. Data collected at three and six months included genetic markers/variants found, subsequent PHQ-9

scores, level of therapeutic response to initial recommended therapy (ie. no response, sub-therapeutic, therapeutic), side effects experienced (divided by category type), whether or not the side effects were tolerable, and number of medication changes. All data was collected and organized using a Word document collection tool (Appendix A) and then entered into Intellectus Statistics for analysis. All data was de-identified, coded and protected for patient privacy. Names were removed, and ages were coded by broad categories rather than actual age (ie. 18-24, 25-34, etc.). While genetic markers and variants found via testing were listed, these are found in all humans, making it impossible to utilize this data to track back to any single individual. All paper collection tools were stored in a locked filing cabinet and all records were accessed via a single, password protected laptop, both accessible to the researcher alone. Data will be secured in the same manner for 5 years, after-which it will be deleted or shredded utilizing the clinic's professional shredding service.

Data Analysis

Data Analysis made up the *Study* portion of PDSA. Data was analyzed using Intellectus Statistics. Descriptive data such as mean age group, gender, etc., was extrapolated on both groups to summarize the samples. ANOVA was utilized to compare the control group of patients receiving traditional clinical assessment-based care to OCD patients who received care guided by genetic testing to evaluate whether or not the genetic group showed significant changes in the identified clinical outcomes. These changes may have included greater reduction of PHQ9 scores, higher level or sooner reaching of therapeutic

response, less or more tolerable side effects, or less changes to medications. The *Act* portion of PDSA included any recommendations to the clinic in terms of how they utilize genetic testing which can be made based on the findings of this project.

Approval Process

An integral part of the *Plan* of PDSA, organizational approval was obtained after an in-person verbal proposal presentation given to all providers and clinic staff at the clinic's weekly provider meeting. Committee approval through UMSL was obtained after project proposal defense. UMSL IRB approval was received.

Results

A retrospective chart review of the clinic's patients who met criteria resulted in a total of 15 patients (n=15), 6 who were genetically tested (n=6, 40%) and 9 who were not (n=9, 60%). 100% (n=15) of the patients selected were female. The most frequently observed categories of age were 18-24 and 25-34, each with an observed frequency of 5 (33%).

GRIK1 is the glutamate receptor and is highly associated with anxiety disorders such as OCD (Terbeck, Akkus, Chesterman, & Hasler, 2015.). It can present as A/A, A/C, or C/C and the C allele is associated with alcohol addiction. C allele carriers have shown good response to Topiramate when compared with Placebo (Selfdecode, n.d.). When examining the genetic variants among the tested patients, the most frequently observed category of Grik1 was A/C (*n* = 3, 50%).

ANK3 is involved in the production of homocysteine and variations of this gene may be associated with methylenetetrahydrofolate reductase deficiency. It can present as C/C, C/T, or T/T and the presence of the T allele is associated with bipolar disorder and attention deficits (Genecards, n.d.). The most frequently observed category of ANK3 was C/C, or normal (*n* = 6, 100%).

CACNA1c is a gene involved in producing calcium channels and may be associating with learning and rewards processing and can present as A/A, A/G or G/G and the presence of an A allele is associated with bipolar disorder (Genecards, n.d). The most frequently observed category of CACNA1c was G/G (*n* = 5, 83.3%).

SL64A is a sodium-dependant transporter gene involved in the movement of serotonin between synapses (PubChem, n.d.). It has multiple alleles and can present as La/La, Lg/Lg, L/S, or S/S with the S allele being highly associated with depression. The most frequently observed category of SL64A was L/S (*n* = 4, 66.67%).

COMT is an enzyme that helps break down neurotransmitters in the pre-frontal cortex such as epinephrine and dopamine (Selfdecode, n.d.). It may present as Val/Val, which have high levels of COMT activity resulting in lower dopamine levels, Met/Val or Met/Met which has the lowest levels of activity and therefor higher levels of dopamine (GeneCards, n.d.). The most frequently observed category of COMT was Met/Val, or normal (*n* = 4, 66.67%). Frequencies and percentages are presented in Table 1.

An analysis of variance (ANOVA) was conducted based on an alpha value of 0.05 for each clinical outcome to determine whether there were significant differences between the genetically tested group and the non-tested group.

For medication changes at 3 months, the results of the ANOVA were not significant, $F(1, 13) = 1.62$, $p = .226$. For number of medication changes at 6 months, the results of the ANOVA were not significant, $F(1, 13) = 0.01$, $p = .909$.). The means and standard deviations are presented in Table 2 and Table 3, and can be visualized in Figure 1.

For medication tolerance at 3 months, the results of the ANOVA were not significant, $F(1, 13) = 0.00$, $p = 1.000$. For therapeutic response at 3 months, the results of the ANOVA were not significant, $F(1, 13) = 1.56$, $p = .234$. For side effects at 3 months, the results of the ANOVA were not significant, $F(1, 13) = 0.24$, $p = .635$. These findings indicated there were no significant differences in clinical outcomes at 3 months between the genetically tested group and the non-tested group (Table 2). The percentages and standard deviations are presented in Table 2.

For medication tolerance at 6 months, the results of the ANOVA were not significant, $F(1, 13) = 1.56$, $p = .234$. For therapeutic response at 6 months, the results of the ANOVA were not significant, $F(1, 13) = 0.04$, $p = .847$. For side effects at 6 months, the results of the ANOVA were not significant, $F(1, 13) = 0.01$, $p = .939$. These findings indicated there were no significant differences in clinical outcomes at 6 months between the genetically tested group and the non-

tested (Table 3). The percentages and standard deviations are presented in Table 3 and can be visualized in Figure 2.

An analysis of variance (ANOVA) was also conducted to determine whether there were significant differences in PHQ9 scores over time by genetic testing.

The ANOVA was examined based on an alpha value of 0.05. The results of the ANOVA were not significant, $F(1, 13) = 0.13$, $p = .720$, indicating the differences in change for the PHQ9 scores from initial to 6 months between the genetically tested group and the non-tested group were similar and not significant (Table 4). The means and standard deviations are presented in Table 5.

Discussion

Genetic testing is becoming increasingly available to providers and patients to aid in guiding treatment for mental health conditions. While the literature suggests that genetic testing may offer many insights into the functioning of various systems as they relate to mental health disorders, this quality improvement project aimed to see if testing translated to improved clinical outcomes. No significant differences in clinical outcomes were found among the genetically tested group compared to the group that was treated with traditional diagnosis and management. Of note, all variables showed considerably better outcomes at the 6 months compared to at 3 months, regardless of testing group suggesting that effective treatment of mental health takes time, persistence, and patience.

Upon reflection, several factors may have contributed to the lack of statistical significance. Despite reviewing one year of patients seen, the sample size was very small. This was due to the researcher's efforts to find the most accurate, homogenous sample. The study did not account for practice differences among the five providers and differences in how they utilize the genetic findings in their treatment plans. Finally, the PHQ9 screening tool, while helpful in gauging generalized data on patient progress with depression, may not have been the most accurate tool in reflecting progress with OCD symptoms.

Conclusion

This quality improvement project did not find evidence to suggest that clinical outcomes are improved after genetic testing. Recommendations for future practice would include discouraging routine genetic testing for OCD patients as traditional diagnosis and management showed similar clinical outcomes compared to the genetically tested group in this project. Any discussion regarding genetic testing should be done thoughtfully between patient and provider when considering treatment options. Given the potentially high cost of genetic testing to patients and the healthcare system as a whole, providers should take great care before choosing to utilize genetic testing in this patient population. Future studies evaluating clinical outcomes as they relate to genetic testing in patients with OCD should consider utilizing a larger sample size, controlling for practice methods by focusing on a single provider and utilizing a screening tool specific for OCD.

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Table 1.

Frequency Table for Nominal Variables

Variable	*n*	*%*
Age		
18-24	5	33.33
25-34	5	33.33
35-44	3	20.00
45-54	1	6.67
55-60	1	6.67
Sex		
female	15	100.00
Genetic Testing		
yes	6	40.00
no	9	60.00
Grik1		
C/A	3	50.00
C/C	2	33.33
A/A	1	16.67
ANK3		
C/C	6	100.00
CACNA1c		
A/A	1	16.67
G/G	5	83.33
SL64A		
La/La	2	33.33
L/S	4	66.67
COMT		
Met/Met	2	33.33
Met/Val	4	66.67

Note. Due to rounding errors, percentages may not equal 100%.

Table 2.

ANOVA for 3 months			Genetically tested				Not tested			
Variable	***F***	***p***	**%**	***M***	***SD***	***n***	**%**	***M***	***SD***	***n***
Number of Med Changes	1.62	0.226		1.83	1.94	6		3.44	2.65	9
Tolerability	0	1			0.52	6			0.5	9
yes			33.33				66.67			
no			66.67				33.33			
Therapeutic Response	1.56	0.234			0.52	6			0.5	9
none			0				11.11			
sub			66.67				77.78			
therapeutic			33.33				0			
Side Effects	0.24	0.635			1.26	6			1.32	9
none			66.67				77.78			
sleep			16.67				11.11			
weight			16.67				0			
mood			0				0			
headaches			0				11.11			
GI			0				0			

Table 3.

ANOVA for 6 Months				Genetically Tested					Not Tested			
Variable	***F***	***p***		**%**	***M***	***SD***	***n***		**%**	***M***	***SD***	***n***
Number of Med Changes	0.01	.909			1.67	2.25	6			1.78	1.48	9
Tolerability	1.56	.234				.41	6				0.00	9
yes				83.33					100.00			
no				16.67					0			
Therapeutic Response	0.04	.847			.55	0.52	6				.53	9
none				0					0			
sub				50.00					44.44			
therapeutic				50.00					55.56			
Side Effects	0.01	.939				.55	6				1.67	9
none				50.00					88.89			
sleep				50.00					0			
weight				0					0			
mood				0					0			
headaches				0					0			
GI				0					11.11			

Table 4.

Analysis of Variance Table for change over time for PHQ9 from initial to 6 months by genetic testing

Term	*SS*	*df*	*F*	*p*	η_p^2
Genetic testing	7.51	1	0.13	.720	0.01
Residuals	726.22	13			

Table 5.

Mean, Standard Deviation, and Sample Size for change over time by genetic testing

Combination	*M*	*SD*	*n*
Yes	-8.33	9.22	6
No	-6.89	6.13	9

Figure 1.

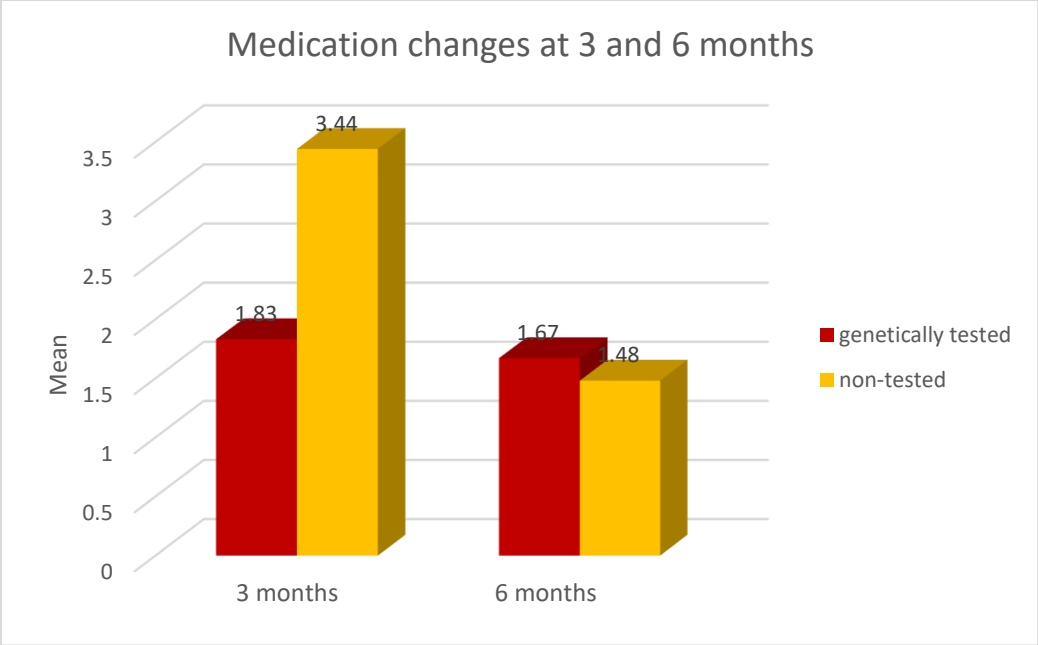
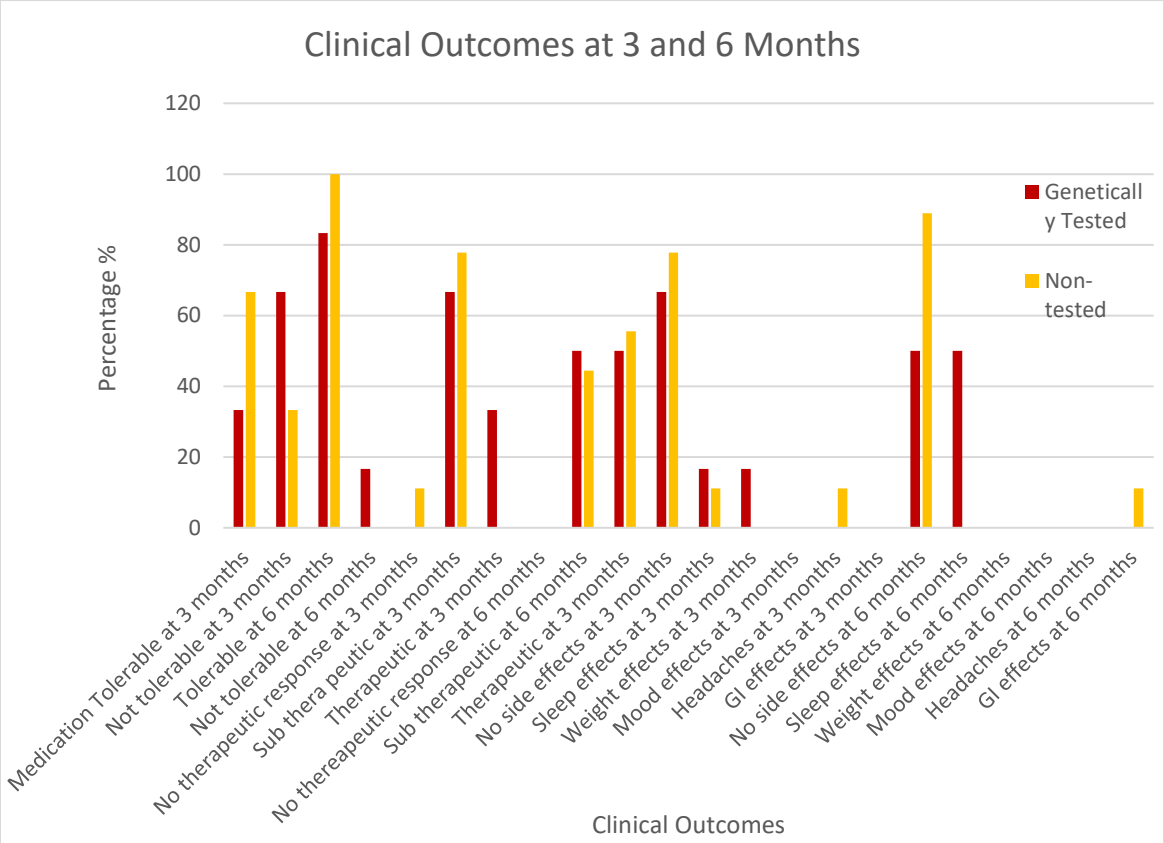
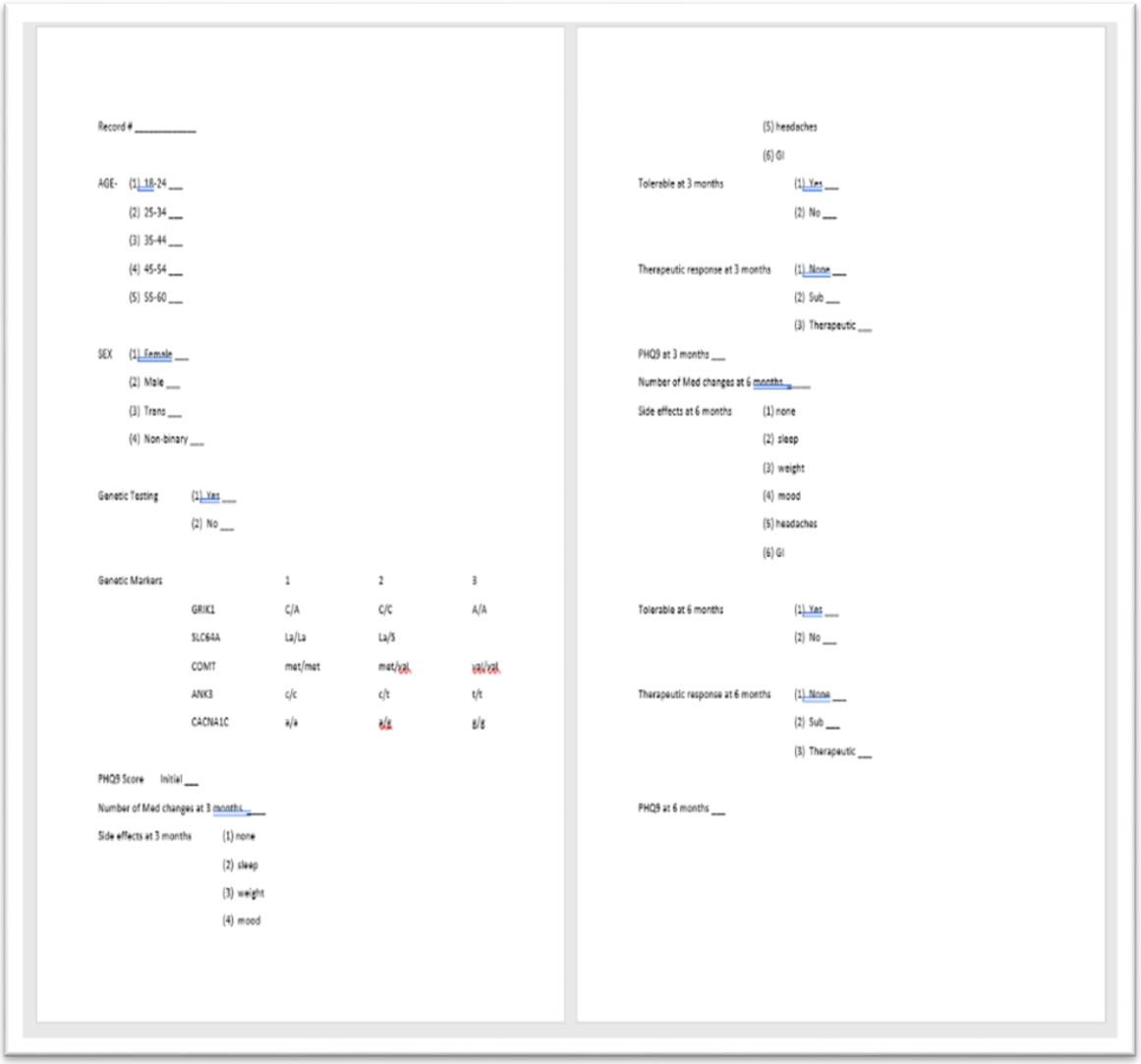

Medication changes at 3 and 6 months
Mean
3.5
3
2.5
2
1.5
1
0.5
0
1.83
3.44
1.67
1.48
3 months
6 months
genetically tested
non-tested

Figure 2.


Clinical Outcomes at 3 and 6 Months
120
100
80
60
40
20
0
Percentage %
Geneticall y Tested
Non-tested
Medication Tolerable at 3 months
Not tolerable at 3 months
Tolerable at 6 months
Not tolerable at 6 months
No therapeutic response at 3 months
Sub thera peutic at 3 months
Therapeutic at 3 months
No thereapeutic response at 6 months
Sub therapeutic at 6 months
Therapeutic at 3 months
No side effects at 3 months
Sleep effects at 3 months
Weight effects at 3 months
Mood effects at 3 months
Headaches at 3 months
GI effects at 3 months
No side effects at 6 months
Sleep effects at 6 months
Weight effects at 6 months
Mood effects at 6 months
Headaches at 6 months
GI effects at 6 months
Clinical Outcomes

Appendix A

Data Collection Tool



Record # _____

AGE- (1) 18-24 ___
(2) 25-34 ___
(3) 35-44 ___
(4) 45-54 ___
(5) 55-60 ___

SEX (1) Female ___
(2) Male ___
(3) Trans ___
(4) Non-binary ___

Genetic Testing (1) Yes ___
(2) No ___

Genetic Markers	1	2	3
GRIK1	C/A	C/C	A/A
SLC64A	La/La	La/S	
COMT	met/met	met/val	val/val
ANK3	c/c	c/t	t/t
CACNA1C	a/a	a/g	g/g

PHQ9 Score Initial ___

Number of Med changes at 3 months ___

Side effects at 3 months (1) none
(2) sleep
(3) weight
(4) mood
(5) headaches
(6) GI

Tolerable at 3 months (1) Yes ___
(2) No ___

Therapeutic response at 3 months (1) None ___
(2) Sub ___
(3) Therapeutic ___

PHQ9 at 3 months ___

Number of Med changes at 6 months ___

Side effects at 6 months (1) none
(2) sleep
(3) weight
(4) mood
(5) headaches
(6) GI

Tolerable at 6 months (1) Yes ___
(2) No ___

Therapeutic response at 6 months (1) None ___
(2) Sub ___
(3) Therapeutic ___

PHQ9 at 6 months ___