CUTTING EDGE TECHNOLOGIES THAT ARE CHANGING THE WAY WE TREAT DEPRESSION

HOW DNA TESTING AND TRANSCRANIAL MAGNETIC STIMULATION (TMS) ARE BECOMING GAME CHANGERS IN THE FIGHT AGAINST DEPRESSION

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Disclaimer: While Assurex Health and Neuronetics do not compensate me for any of my talks, I do use both technologies on a daily basis in my office and will be using examples from my experience with them.

(World Health Organization, 2012)

WHAT IS THE DSM-5 CRITERIA FOR MAJOR DEPRESSIVE DISORDER?

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure

Note: Do not include symptoms that are clearly attributable to another medical condition.

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report

2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation.)

3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. (Note: In children, consider failure to make expected weight gain.)

4. Insomnia or hypersomnia nearly every day.

5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).

6. Fatigue or loss of energy nearly every day.

7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).

8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).

9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

(American Psychiatric Association, 2013, p. 94-95)

DIAGNOSTIC CRITERIA (CONT'D)

B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

C. The episode is not attributable to the physiological effects of a substance or to another medical condition.

Note: Criteria A-C represent a major depressive episode

Note: Responses to a significant loss (e.g., bereavement, financial ruin, losses from a natural disaster, a serious medical illness or disability) may include the feelings of intense sadness, rumination about the loss, insomnia, poor appetite, and weight loss noted in Criterion A, which may resemble a depressive episode. Although such symptoms may be understandable or considered appropriate to the loss, the presence of a major depressive episode in addition to the normal response to a significant loss should also be carefully considered. This decision inevitably requires the exercise of clinical judgment based on the individual's history and the cultural norms for the expression of distress in the contest of loss.

D. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders.

E. There has never been a manic episode or a hypomanic episode

Note: This exclusion does not apply if all of the manic-like or hypomanic-like episodes are substance-induced or are attributable to the physiological effects of another medical condition

(American Psychiatric Association, 2013, p. 94-95)

COMMON TREATMENTS FOR DEPRESSION

- Medications
  - SSRIs (ex: Celexa, Lexapro, Prozac, Paxil, Zoloft, Viibryd)
  - SNRI's (ex: Cymbalta, Effexor XR, Pristiq, Fetzima)
  - Atypical Antidepressants (ex: Wellbutrin, Remeron, Trazodone, Trintellix)
  - Tricyclic (ex: Tofranil,Elavil,Doxepin)
  - MAOIs (ex: Emsam, Nardil, Marplan, Parnate)
  - Augmentation with mood stabilizers, antipsychotics, or anti-anxiety medication
- Psychotherapy
- Transcranial Magnetic Stimulation (TMS)
- Electroconvulsive Therapy (ECT)

(Mayo Clinic, 2018)

STATISTICS FOR MAJOR DEPRESSIVE DISORDER

- Major Depressive Disorder Affects 14 Million People in the United States
- 7.2 Million People in the United States are treated for Major Depressive Disorder
- 4 Million of those treated are poorly served
- This is due to inadequate response and intolerance to side-effects of medication

(Kessler et al., 2003, p. 3095-3105)

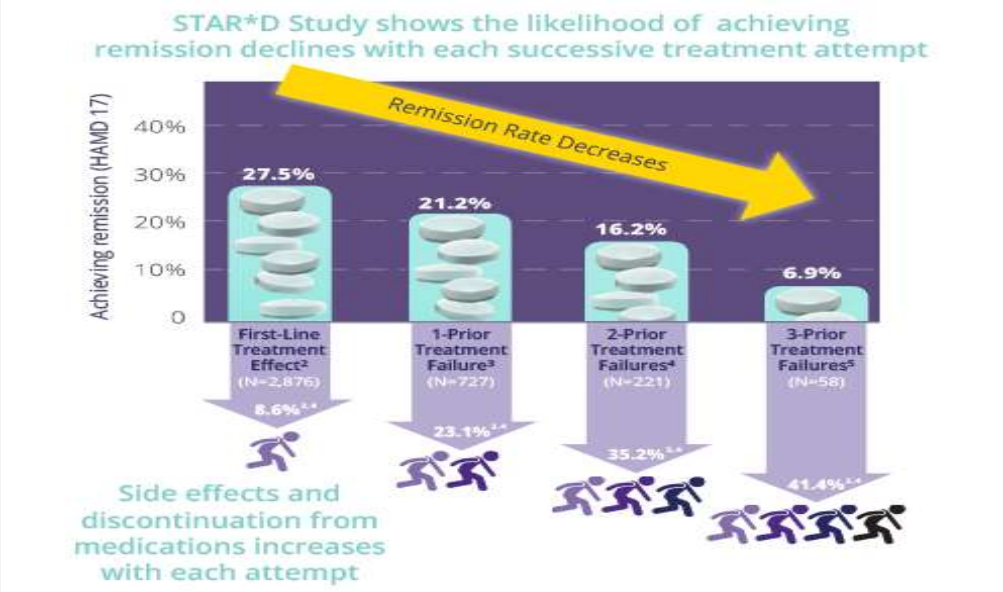
With so many people with Major Depressive Disorder being underserved in the community, what tool can we use to help better manage medications being prescribed to these individuals?

Pharmacogenomic Testing (DNA Testing)

WHY DNA TESTING?

- DNA testing cuts down on the trial and error common with medication management
- By cutting down on trial and error, DNA testing also cuts down on delays in treatment
- DNA testing leads to better medication management which leads to patients feeling better, spending less time on sick leave, being more productive, and it ultimately costs less for society and insurance in the long run
- Patients just like it. It is an easy test that validates patient's struggles with medications

(Kehr, 2017)



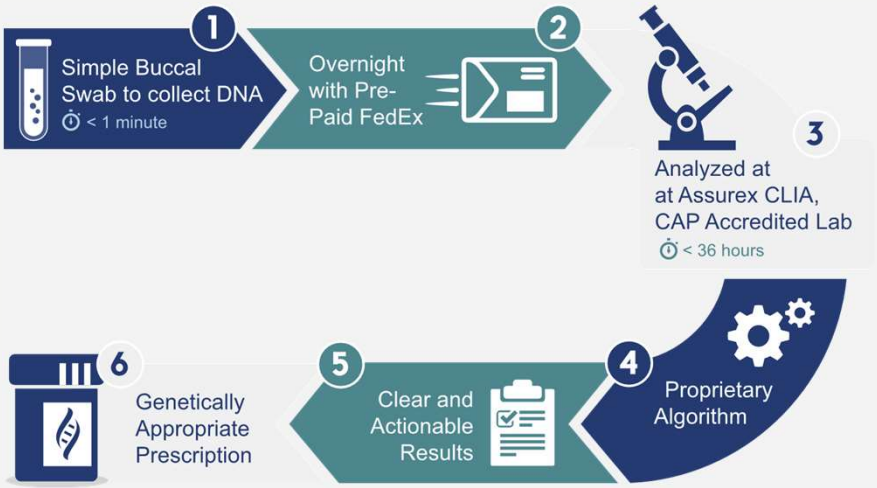
(Neuronetics, 2018)

SO HOW DOES DNA TESTING WORK?

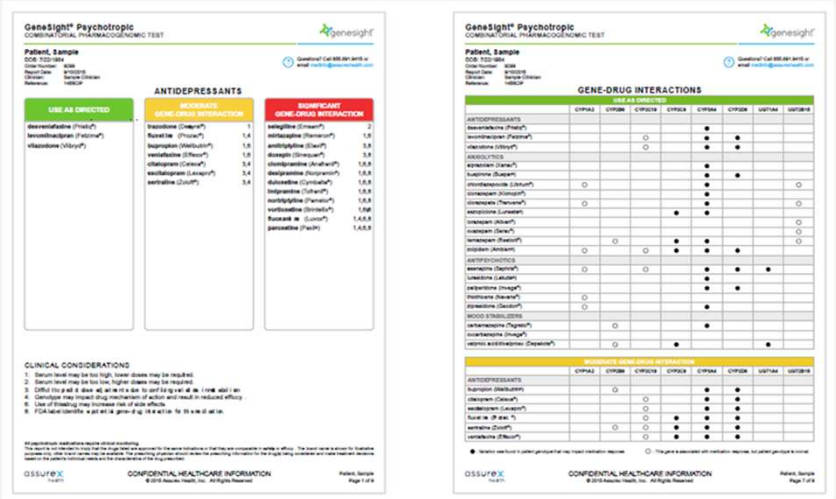
- Pharmacogenomics is defined as the study of gene expression on the body's ability to break down medications
- Gene expression refers to the way your genes influence medication response
- Genes direct the production of enzymes needed to metabolize the medications you take
- Enzymes have a large role in how effective the medication will be and how likely there are to be negative side effects
- A genotype is a unique combination of genes. A person's genotype can tell if they will make more or less enzymes that other people.
- Enzymes help medications to break down into more easily excreted substances. The amount and ability of enzymes to breakdown medication dictates if the medication will be broken down easily or if the medication will be broken down into harmful substances causing negative side effects
- Other factors such as smoking, pregnancy, age, diet, gender, medications, and other medical problems also affect how the body metabolizes medications

(Manzi, 2016)

TESTING PROCESS



DNA REPORTS



What Happens When Medications are STILL Not Working For Depression??????

Transcranial Magnetic Stimulation (TMS)

WHAT IS TRANSCRANIAL MAGNETIC STIMULATION (TMS) AND HOW DOES IT WORK?

- TMS is a noninvasive procedure that uses an MRI like coil to stimulate parts of the brain that are underperforming during depression
- The brain has several parts that play a role in mood regulation. These areas are connected via neuronal pathways. These pathways communicate to each other via neurotransmitters
- When there are enough neurotransmitters in these pathways, communication is good between these areas and mood regulation is optimal.
- When patients are depressed, the level of neurotransmitters in these pathways changes or sometimes the neurons become dysfunctional. This disrupts communication and affects mood
- Since neurons are electrochemical cells, the TMS magnet creates pulsed magnetic fields that depolarize the neurons and increases the number of neurotransmitters being released into the synapse
- The increase in neurotransmitters boosts communication between areas of the brain that play a role in mood regulation

(Neuronetics, 2017)

WHAT HAPPENS DURING TMS?

- The TMS magnetic coil is put over the left prefrontal cortex of the brain. Studies have shown that this area is the most underserved during depression

(Neuronetics, 2014)

(TMS Centre, 2017)

- The TMS magnet delivers 3000 pulses to the targeted area between 18-37 minutes depending on the type of TMS machine and coil used

(Neuronetics, 2018)

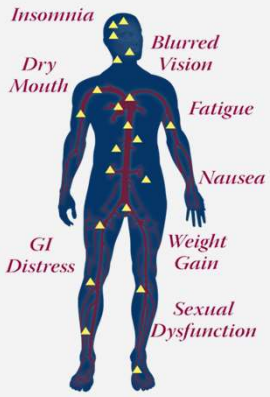
(Magstim, 2018)

- TMS treatments typically take less than 20 minutes with an updated coil and does not require any sedation
- Typical TMS Treatments are everyday, five days a week, for six weeks. Then, the treatment is tapered to three treatments the next week, two treatments the following week, and one treatment the final week. The overall therapy is 36 sessions
- TMS is FDA-cleared for the treatment of depression
- Used at over 365 centers including leading teaching institutions
- Specifically for patients with depression who have not benefited from their initial antidepressant medication

TMS THERAPY AVOIDS SIDE EFFECTS EXPERIENCED WITH MEDICATION

DRUG THERAPY

OTHER ADVERSE EVENTS
Nervousness
Weakness
Abnormal Ejaculation
Constipation
Anxiety
Impotence
Diarrhea
Increased Appetite
Dizziness
Sweating
Decreased Appetite
Tremor
Drowsiness
Decreased Sexual Interest
Headache/Migraine
Treatment Discontinuation Side Effects



TMS THERAPY

OTHER ADVERSE EVENTS
Eye Pain
Toothache
Muscle Twitching
Facial Pain
Pain of Skin

In clinical trials, fewer than 5% of patients discontinued treatment with NeuroStar TMS Therapy due to adverse events.

From product labeling for currently marketed antidepressant medications; adverse events occurring at an incidence >5% incidence and 2x the rate of placebo treatment (Neuronetics, Inc, data on file)

TMS THERAPY A SAFE TREATMENT

- Safety verified in multiple clinical trials
- Patients are awake and alert throughout treatment- no need for anesthesia or sedation
- Thinking and memory are not affected
- Technology similar to MRI which has a long-term safety record
- There is a rare risk of seizure associated with TMS (1 in 30,000 treatments)
- Over 200,000 treatments demonstrate safety
- Many people treated with TMS experience significant benefits
- In clinical trials, after 4 to 6 weeks of treatment:
  - 1 in 2 improved significantly
  - 1 in 3 were free of symptoms

(Demitrack & Thase, 2009)

Q & A?

References

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders: DSM-5*. Arlington, VA: Author.

Demitrack, M. A., & Thase, M. E. (2009). Clinical significance of transcranial magnetic stimulation (TMS) in the treatment of pharmacoresistantdepression: synthesis of recent data. *Psychopharm Bull*, *42*(2), 5-38.

Kehr, B. (2017, March 8). Genetic testing improves patients' lives through precision medicine. Retrieved from https://drbrucekehr.com/genetic-testing-improves-patients-lives-through-precision-medicine/

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K., Rush, A. J., … Walters, E. E. (2003). The epidemiology of major depressive disorder results from the national comorbidity survey replication. *Journal of the American Medical Association*, *283*(23), 3095-3105. Retrieved from chrome-extension://oemmndcbldboiebfnladdacbdfmadadm/https://pdfs.semanticscholar.org/1de7/eadfba10ce1ded6325e97fdb6e506c8a068f.pdf

Magstim. (2018). [Photograph]. Retrieved from https://www.magstim.com/clinical-solution/0/rapid2-therapy-system

Manzi, S. (2016, December 15). Can genetic testing help determine the best medications for you? [Web log post]. Retrieved from https://www.health.harvard.edu/blog/can-genetic-testing-help-determine-the-best-medications-for-you-2016121610888

Mayo Clinic. (2018, February 3). Depression (major depressive disorder). Retrieved from https://www.mayoclinic.org/diseases-conditions/depression/diagnosis-treatment/drc-20356013

Neuronetics. (2014). [Photograph]. Retrieved from https://www.medscape.com/viewarticle/831860

Neuronetics. (2017, July 20). *NeuroStar advanced therapy* [Video file]. Retrieved from https://www.youtube.com/watch?v=S847k2dTb0U

Neuronetics. (2018). [Photograph]. Retrieved from https://neurostar.com/neurostar-tms-depression-treatment/how-neurostar-tms-works/

TMS Centre. (2017, August 21). [Photograph]. Retrieved from https://www.rtmscentre.co.uk/patient-tms-review/

World Health Organization. (2012, October 2). *I had a black dog, his name was depression*[Video file]. Retrieved from https://www.youtube.com/watch?v=XiCrniLQGYc