Personalized Treatments

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This newsletter explores the topic of personalised treatments for mental illness and the barriers to their inclusion in standardised healthcare. While there are different classes of antidepressants, even drugs within the same class can have different effects on people with the same mental illness. This variation in response can be due to a number of factors, including genetic make-up, environmental influences, and personal circumstances. The development of personalised treatments that take these factors into account could greatly improve outcomes for people with mental illness. However, there are several challenges to implementing this approach, including the need for more research and the high cost of developing personalised treatments. Despite these challenges, personalised medicine has the potential to transform mental health care and improve the lives of millions of people. This article was first published in Subkiton on February 01, 2023 (https://www.subkit.com/pernillebuelow/posts/personalized-treatments).

Personalized Treatments

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Abstract

This newsletter explores the topic of personalised treatments for mental illness and the barriers to their inclusion in standardised healthcare. While there are different classes of antidepressants, even drugs within the same class can have different effects on people with the same mental illness. This variation in response can be due to a number of factors, including genetic make-up, environmental influences, and personal circumstances. The development of personalised treatments that take these factors into account could greatly improve outcomes for people with mental illness. However, there are several challenges to implementing this approach, including the need for more research and the high cost of developing personalised treatments. Despite these challenges, personalised medicine has the potential to transform mental health care and improve the lives of millions of people.
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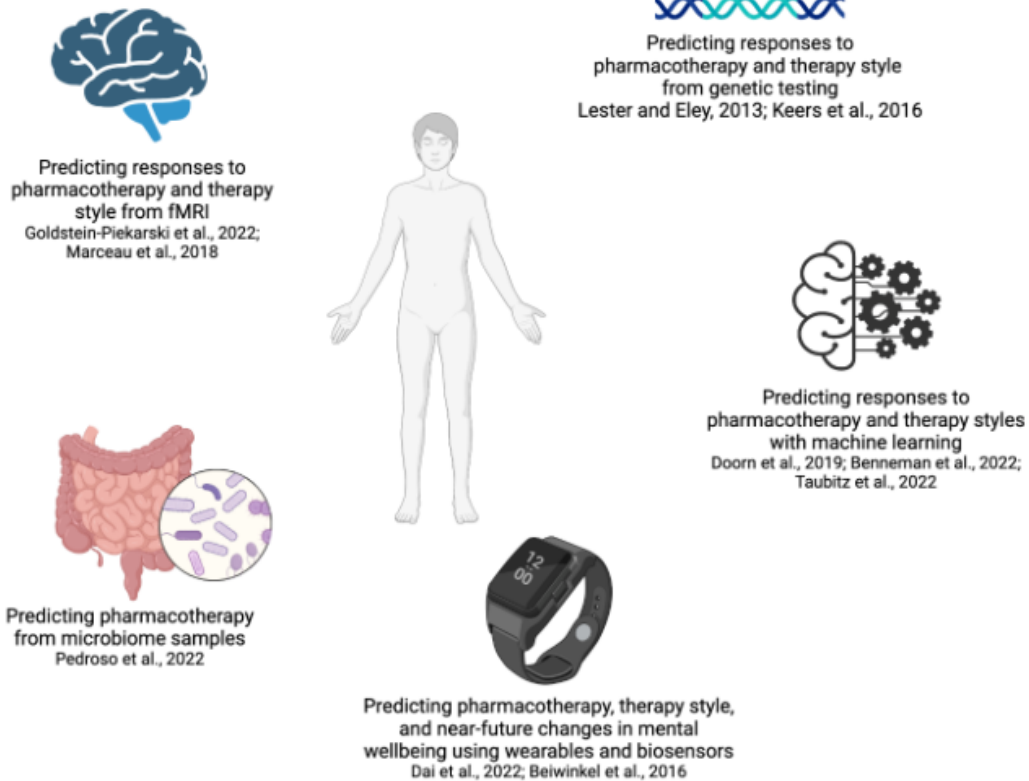
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Have you ever wondered why there are so many antidepressants on the market? (if you feel like being overwhelmed, check out a complete list of all the antidepressants available in the US here and here).

There are good, but sometimes overlooked, reasons for this. As you may already know, there are different 'classes' of antidepressants. Some prevent the reuptake of serotonin or norepinephrine while others inhibit the activity of enzymes that would normally break down or reabsorb various neurotransmitters, including serotonin, dopamine, and norepinephrine. In general, the scientific purpose is the same: to increase the availability of neurotransmitters in the synaptic cleft, but the way they achieve this can have very different effects on people's symptoms and wellbeing.

This difference in effects is not only due to the unique actions of the various categories of antidepressants. Even the same type of drug can have distinct effects on two people that are struggling with the same mental illness. One person with depression might find that a drug, perhaps the Selective Serotonin Reuptake Inhibitor (SSRI) Lexapro, benefits them greatly, while another person with depression experiences no benefit at all, in worst case scenarios they may just experience the negative side effects. Why is that?

Technologies to personalize drug and psychotherapeutic treatments

Predicting responses to pharmacotherapy and therapy style from fMRI
Goldstein-Piekarski et al., 2022; Marceau et al., 2018

Predicting responses to pharmacotherapy and therapy style from genetic testing
Lester and Eley, 2013; Keers et al., 2016

Predicting responses to pharmacotherapy and therapy styles with machine learning
Doorn et al., 2019; Benneman et al., 2022; Taubitz et al., 2022

Predicting pharmacotherapy from microbiome samples
Pedroso et al., 2022

Predicting pharmacotherapy, therapy style, and near-future changes in mental wellbeing using wearables and biosensors
Dai et al., 2022; Beiwinkel et al., 2016

Drugs, genetics, and gut culture

One reason is the beast of genetics. Although we (usually) are all born in the same human shape with two legs and one nose, our genetic composition can vary considerably. These variations give rise to differences in personality, eye color, vocal sound, and the likelihood of developing certain diseases, such as cancer and mental illness. These genetic variations also influence how certain drugs affect us. One of my clients recently had genetic testing done to assess which antidepressant would work best for her. Prior to the test, she had tried five different antidepressants but each time she would experience adverse reactions, for example, a severe full-body rash or a chronic activation of her sympathetic nervous system. After the fifth drug and adverse reaction, she gave up on drug treatments. Her journey had been exhausting and demoralizing, and she was ready to call it quits. While she continued working with her treatment team (including a psychotherapist, a dietitian, and a physical therapist), she did not reach her desired treatment goal, and although the negative experiences still lingered, she started reconsidering pharmacological options. In the interim, she transitioned to a new primary doctor,

and this doctor suggested something others had not: **How about getting a genetic test done before deciding on which antidepressant to try?** Hopeful of the idea that a genetic test could help tailor her drug therapy, she paid the necessary 300$ out of pocket fee for the genetic test. It turns out that she lacks a specific gene (MTFHR) which disrupts her body's ability to process neurotransmitters and this gene is linked to deficient responses to many antidepressants (Halaris et al., 2021). But a solution was readily available: a simple prescription supplement – and this supplement might be all she needed to also improve her mental health. Shockingly, around 10% have the same genetic mutation as my client (Halaris et al., 2021). Clearly, many people experience the same struggles as her. I am going to return to her story, in the meantime, you can linger on the question of why genetic testing was not offered sooner, perhaps before she even tried the first antidepressant.

Another factor to consider in differential drug responses is your gut culture (Clapp et al., 2017). If you have followed the news, you know that there is a well-documented connection between your gut and brain (which has given rise to a whole new version of pop-science and nutrition). I even talked about this in the context of [whether semen might be good for your mental health](#) (a less studied, but considerably more entertaining topic). The gut-brain connection signifies how changes in your gut can affect your brain and vice versa. There are more serotonin receptors in the gut than in the brain, and it is hypothesized that some of the major effects of antidepressants that regulate serotonin receptors act through the gut. Researchers have also found that specific gut bacteria correlate with higher rates of anxiety and depression (Pedroso et al., 2021). Just like our genetics, our guts vary. The variation in receptor expression and gut microbiome can personalize how you react to a drug. Even if everything else is identical, two people with different gut cultures can have significantly different symptoms and drug reactions. Companies, such as [Digbi Health](#), are now using recent technological advances to evaluate a person's genetics and gut microbiome to identify appropriate therapies for various diseases, including mental illness. **Yet again I am struck by the question why personalized treatment strategies is not a part of standard medical care?**

Psychotherapy – it worked for them, but not for me

While the personalization of drug therapy has been coined its own name ('personal medicine'), psychotherapy, and the personalization of this, has been vastly overlooked. Like the example of antidepressants, there are many different types of psychotherapies. Some focus on your interpersonal relationships while others focus

on changing your coping skills. As is true for drugs, some psychotherapeutic styles work for some, but not for others. Why?

A psychotherapeutic strategy is often geared to one type of mental illness. For example, cognitive behavioral therapy (often referred to as 'CBT') is exceptionally effective for people struggling with various anxiety disorders, while dialectical behavioral therapy is particularly good for people struggling with emotion regulation. Thus, your mental illness may inform which psychotherapy is better for you, and **yet, many people that suffer from the same mental illness do not all benefit from the same psychotherapeutic approach**.

Just like genetic variations can contribute to drug responses, genetics can also influence how you respond to certain psychotherapeutic treatments (Lester and Eley, 2013). Most of the studies on this topic use candidate gene approaches to evaluate response to one therapeutic style. In other words, they focus on how one known gene may modify a person's response to a specific type of psychotherapy. This scientific method makes sense in the context of our knowledge on 'susceptibility' genes to mental illness, i.e. that carrying certain genetic variants can render you more likely to developing mental illness. Unfortunately, this candidate gene approach has offered limited and sometimes contradictory results (Lester and Eley, 2013). The lack of results suggests that an unbiased genome-wide assessment is necessary. In contrast to a candidate gene approach, genome-wide assessments evaluate the entire genetic composition to identify meaningful genetic patterns that may hold diagnostic or predictive value. Albeit being expensive and laborious process, one study identified genome-wide correlations between treatment response to cognitive behavioral therapy and environmental sensitivity in children with anxiety (Keers et al., 2016). Using a genome-wide approach removes the pressure on finding the holy grail of genes and shifts the focus to appreciate that a combination of low-risk genes collectively confers personalized responses to treatments (and risk to mental illness).

But we do not even have to look for genes to parse out personalized psychotherapy responses. Last year, I wrote an [article](#) for Science Connected Magazine summarizing and discussing a recent study using functional magnetic resonance imaging (fMRI) to investigate how people with mental illnesses would benefit from various drugs and psychotherapies (Goldstein-Piekarski et al., 2022). The researchers observed that a person's brain activity prior to any treatment could predict whether they would respond better to a specific drug or a certain type of psychotherapeutic intervention. In other words, using brain imaging, researchers

could tell which treatment would benefit you the most and the fastest. Studies using a similar approach have identified a predictive relationship between treatment outcome and brain activity in people with bipolar disorder (Marceau et al., 2018).

Digitalization of personalized treatments

A new wave of personalized treatment is emerging through wearables, biosensors, and apps. By tracking your own physiological metrics and filling out self-assessments (either through surveys or video diaries) researchers and providers can now get a **quantified holistic insight into your mental wellbeing every day and every hour**. These developments can be used to diagnose and predict changes in mental state, and, one day, inform which psychotherapy (or drug) would benefit you the most. Smartwatches, wristbands, and smartphones hold immense potential in helping people figure out which psychotherapy works best for them. While some companies are already leveraging this technology (Check out Sentio Solutions and Cognition Kit), much more research is needed to clarify what technology provides reliable and meaningful data. Outside of identifying drugs and therapy style, apps and smart-devices hold their own promise of being a therapeutic device in itself, whether that be helping you fall asleep or engaging coping skills at the right times (also called 'Just In Time' therapy). While Just In Time therapy holds tremendous promise, research on and development of effective platforms is still scarce (Nahum-Shani et al., 2018).

Machine learning (ML), the application of artificial intelligence to identify patterns in large data sets, holds an astounding promise for all kinds of personalized treatments. Using a variety of data points, ranging from socio-demographics to symptomatology to family history, ML can predict treatment outcomes, treatment barriers, and responders vs non-responders to various drugs and even therapeutic styles (Bennemann et al., 2022, Taubitz et al., 2022). Companies such as Spring Health are leveraging ML to **provide personalized treatment plans that do not just address which drug or therapy to start, but also identifies whether a person may be at risk for not completing treatment**. ML already has a large amount of peer-reviewed data, and though the accuracy is not 100%, the error rate is miniscule compared to the traditional trial-and-error approach (there is, of course, much more nuance to this debate and I encourage you to read this review (Aafjes-van Doorn et al., 2019) for an in depth discussion). Personally, I am excited about when we can start applying ML to large datasets collected from wearables

and smart devices (as some researchers are starting to, see Saito et al., 2022). Imagine what we can do then.

Why is personalized treatment not a part of our standard healthcare?

Money and insurance policies appear to be the major barrier in standardizing personalized medicine. A 300$ bill for a genetic test could have saved my client the personal and physical hassle of going through five, in her case, useless drugs. Her mental wellbeing could have flourished by now, instead she is only now starting the treatment that science is telling us is right for her. While tests to address personalized psychotherapy are still in progress, genetic tests for various pharmacotherapeutic drugs are readily available. **But only to the people that have the money, the resources, and the knowledge of them.** Many doctors do not mention to their patients that genetic tests are available to them, either out of lack of knowledge of their existence or their purpose. Even if a patient learns of the possibility for genetic testing or other forms of personalized treatment, they may not have the money the out-of-pocket fee demands or the structural resources to access it.

What else could we do? Something as simple as making smart devices (e.g. smartwatches) an insurance covered expense could transform people's healthcare experience. Doctors are already promoting this technology to support patient health (see for example how Northwest Primary Care thinks about smartwatches in healthcare), and companies like Videra Health are creating platforms to digitize remote patient monitoring for various illnesses, including mental health.

That our standard healthcare system fails people with mental illness is not a new idea. And it is encouraging that technology is advancing what we can already now do to personalize treatments, whether for drugs or psychotherapy. Yet, it is difficult not to feel frustrated and discouraged when clients repeatedly tell you of their issues with receiving proper care for their mental illness. Whether the care be for proper psychotherapy or drug treatments, their exhaustion is real. Many end up giving up on finding a treatment. To them, it is not worth adding yet another stressor into their lives. They are already exhausted, frustrated, and scared, and without guidance and support we lose them. **Personalized treatment is not just a matter of developing new technologies but also of making them easily accessible to the people who need them most.**

If people knew that the first line of treatment for mental illness would be based on an evidence-based, personalized approach, maybe we could slowly start

- Breaking stigma about mental illness being a **fundamental flaw** in one's personality

- Breaking stigma of mental illness being something you **never recover from**

- Breaking the stigma of **not speaking up** about mental illness

- Breaking stigma on **not seeking help** when struggling with mental health challenges

Just imagine.

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Pernille Bülow is a neuroscientist, research consultant and writer. Originally from Denmark, she moved to the U.S. to finish her B.S. in psychology at UC Berkeley, followed by a PhD at Emory University and a subsequent Post-doctoral fellowship at Harvard Medical School/Massachusetts General Hospital (MGH). Pernille is an expert on brain development and mental health research, topics on which she consults and writes. She currently lives in Boston with her two cats and guinea pig. Pernille writes for Psychology Today and has a monthly newsletter on neuroscience research and mental health (https://www.subkit.com/pernillebuelow). Pernille is the founder of the non-profit Mind Blossom Inc, and an Advisor and Board Member for companies that tackle mental illness and neurodevelopmental disorders. Read more about Pernille on her website: www.pernillebuelow.com.