DECEMBER 2024

PMHW: Year in Review

STANFORD CENTER FOR PRECISION
MENTAL HEALTH & WELLNESS

4th Annual Symposium

From Data to Care: Precision Medicine in Action for Mental Health

WRITTEN BY: HOSNA OMARZAD

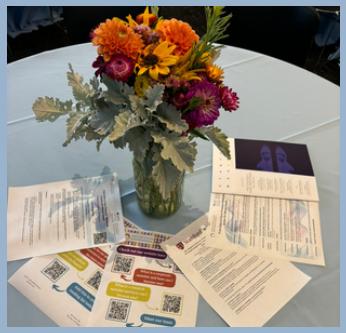
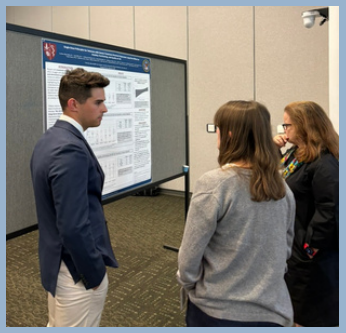
The Stanford Center for Precision Mental Health and Wellness and Stanford's Major Laboratories and Clinical Translational Neuroscience Incubator presented the 4th Annual Precision Mental Health & Wellness Symposium on Friday, September 13th.

We would like to personally thank our expert speakers, poster presenters, attendees and affiliates for joining us for a day of lively discussions and captivating advancements in precision mental health research. The success of this event would not have been possible without the participation, engagement thoughtful questions and thought provoking conversations of all those who joined.

Attendees heard how healthcare data is being leveraged for precision medicine, the selection of treatment using a precision approach to mental health and understanding subtypes of depression. They learned about new approaches to understanding individual experiences of disorders such as depression by understanding the brain, how we are starting to personalize treatments and novel therapies.

These new discoveries provide hope for the future of mental health treatment.

We are excited to announce recordings are now available on our YouTube channel here. In collaboration with the Stanford Center for Continuing Medical Education, we are excited to offer CME credits. For more information, visit the activity page here.


Leanne Williams receives $18 million National Institutes of Health grant to diagnose and treat depression

Professor of psychiatry and behavioral health Leanne Williams will lead a project to define depression's cognitive biotypes and create tools for clinicians to diagnose and treat patients.

WRITTEN BY CHRISTINA HENDRY

Leanne Williams, PhD, a professor of psychiatry and behavioral sciences, has been awarded a five-year, $18.86 million grant, part of the National Institute for Health's Individually Measured Phenotypes to Advance Computational Translation in Mental Health initiative, to develop a diagnosis and treatment tool for depressive disorders.

Williams, the Vincent V.C. Woo Professor and the director of the Stanford Center for Precision Mental Health and Wellness, will be the project leader; the co-principal investigators are Jun Ma, MD, PhD, and Olu Ajilore, MD, PhD, of the University of Illinois, Chicago. Additional Stanford Medicine investigators include Laura Hack, MD, PhD, Trevor Hastie, PhD, Booil Jo, PhD, Ruth O'Hara, PhD, Peter van Roessel, MD, PhD, and Alan Schatzberg, MD.
Only one-third of patients with depression improve with current assessment and treatment approaches. This project has the potential to double that number, Williams said.

"Our team is driven by the urgent need for better tools to understand and treat depression."

Individually Measured Phenotypes to Advance Computational Translation in Mental Health (IMPACT-MH)

"It's not just about seeing depression as a whole, but understanding how it uniquely affects each individual's brain. Imagine being able to tailor treatments based on how depression affects someone's thinking — that's the promise of this study. We're not just aiming to improve outcomes; we're aiming to transform the way depression is diagnosed and treated, one individual at a time."

Relying on a pool of more than 4,500 participants, the team will use brain imaging, computerized tests and a novel smartphone app — which measures swipe speed, keystroke dynamics and message length — to specify what they call cognitive biotypes for depression.

The researchers then plan to develop a tool that can be used at the first instance of major depression — or early as possible after diagnosis — to help pinpoint the specific type of depression (biotype), provide personalized predictions and guide treatment choices, whether by a primary care physician or a specialist. They expect to refine the tool using machine learning and artificial intelligence — making significant advancements in individualized psychiatric treatment and risk prediction.

"By advancing a clinical cognitive signature to personalize treatments, we address an urgent public need," Williams said. "Depression, with its staggering lifetime prevalence of 20.6% in the U.S. and affecting 280 million people globally, is a leading cause of disability and imposes an economic burden of $326.2 billion. With our project, we aim to develop individualized, brain-based assessments at scale, enhancing clinical decision-making and improving outcomes for millions affected by depression worldwide."

More about the launch of our study inside:

LAUNCH OF IMPACT-MH - 3



Launch of IMPACT-MH

Accelerating Cognition-guided signatures to Enhance translation in Depression (ACE-D)

WRITTEN BY HOSNA OMARZAD

In July of 2024, Leanne Williams, PhD, Stanford professor of psychiatry and behavioral sciences, the project lead team at the Stanford Center for Precision Mental Health and Wellness, Stanford Medicine investigators: Laura Hack, MD, PhD, Trevor Hastie, PhD, Booil Jo, PhD, Ruth O'Hara, PhD, Peter van Roessel, MD, PhD, and Alan Schatzberg, MD along with University of Illinois, Chicago co-principal investigators Jun Ma, MD, PhD, and Olu Ajilore, MD, PhD, and the UIC research team met to officially launch the **A**ccelerating **C**ognition-guided signatures to **E**nhance translation in **D**epression (ACE-D) study funded under the National Institute for Health's Individually Measured Phenotypes to Advance Computational Translation in Mental Health initiative, to develop a diagnosis and treatment tool for depressive disorders. The research team of experts in the field, met at the Stanford campus to launch this large-scale study that will have lasting impacts on the field of precision psychiatry and the treatment of mental health.

The team looks forward to sharing study outcomes and more on how you can get involved. To learn more about our studies and register as a participant, visit our research registry here.


Six distinct types of depression identified in Stanford Medicine-led study

Brain imaging, known as functional MRI, combined with machine learning can predict a treatment response based on one's depression "biotype."

WRITTEN BY RACHEL TOMPA

In the not-too-distant future, a screening assessment for depression could include a quick brain scan to identify the best treatment.

Brain imaging combined with machine learning can reveal subtypes of depression and anxiety, according to a new study led by researchers at Stanford Medicine. The study, published June 17 in the journal Nature Medicine, sorts depression into six biological subtypes, or "biotypes," and identifies treatments that are more likely or less likely to work for three of these subtypes.

Better methods for matching patients with treatments are desperately needed, said the study's senior author, Leanne Williams, PhD, the Vincent V.C. Woo Professor, a professor of psychiatry and behavioral sciences, and the director of Stanford Medicine's Center for Precision Mental Health and Wellness. Williams, who lost her partner to depression in 2015, has focused her work on pioneering the field of precision psychiatry.

Around 30% of people with depression have what's known as treatment-resistant depression, meaning multiple kinds of medication or therapy have failed to improve their symptoms. And for up to two-thirds of people with depression, treatment fails to fully reverse their symptoms to healthy levels.

That's in part because there's no good way to know which antidepressant or type of therapy could help a given patient. Medications are prescribed through a trial-and-error method, so it can take months or years to land on a drug that works — if it ever happens. And spending so long trying treatment after treatment, only to experience no relief, can worsen depression symptoms.

"The goal of our work is figuring out how we can get it right the first time," Williams said. "It's very frustrating to be in the field of depression and not have a better alternative to this one-size-fits-all approach."

Biotypes predict treatment response

To better understand the biology underlying depression and anxiety, Williams and her colleagues assessed 801 study participants who were previously diagnosed with depression or anxiety using the imaging technology known as functional MRI, or fMRI, to measure brain activity. They scanned the volunteers' brains at rest and when they were engaged in different tasks designed to test their cognitive and emotional functioning. The scientists narrowed in on regions of the brain, and the connections between them, that were already known to play a role in depression.

Using a machine learning approach known as cluster analysis to group the patients' brain images, they identified six distinct patterns of activity in the brain regions they studied.

The scientists also randomly assigned 250 of the study participants to receive one of three commonly used antidepressants or behavioral talk therapy. Patients with one subtype, which is characterized by overactivity in cognitive regions of the brain, experienced the best response to the antidepressant venlafaxine (commonly known as Effexor) compared with those who have other biotypes. Those with another subtype, whose brains at rest had higher levels of activity among three regions associated with depression and problem-solving, had better alleviation of symptoms with behavioral talk therapy. And those with a third subtype, who had lower levels of activity at rest in the brain circuit that controls attention, were less likely to see improvement of their symptoms with talk therapy than those with other biotypes.

The biotypes and their response to behavioral therapy make sense based on what they know about these regions of the brain, said Jun Ma, MD, PhD, the Beth and George Vitoux Professor of Medicine at the University of Illinois Chicago and one of the authors of the study. The type of therapy used in their trial teaches patients skills to better address daily problems, so the high levels of activity in these brain regions may allow patients with that biotype to more readily adopt new skills. As for those with lower activity in the region associated with attention and engagement, Ma said it's possible that pharmaceutical treatment to first address that lower activity could help those patients gain more from talk therapy.

"To our knowledge, this is the first time we've been able to demonstrate that depression can be explained by different disruptions to the functioning of the brain," Williams said. "In essence, it's a demonstration of a personalized medicine approach for mental health based on objective measures of brain function."

CONTINUED PG. 5

In another recently published study, Williams and her team showed that using fMRI brain imaging improves their ability to identify individuals likely to respond to antidepressant treatment. In that study, the scientists focused on a subtype they call the cognitive biotype of depression, which affects more than a quarter of those with depression and is less likely to respond to standard antidepressants. By identifying those with the cognitive biotype using fMRI, the researchers accurately predicted the likelihood of remission in 63% of patients, compared with 36% accuracy without using brain imaging. That improved accuracy means that providers may be more likely to get the treatment right the first time. The scientists are now studying novel treatments for this biotype with the hope of finding more options for those who don't respond to standard antidepressants.

For example, in research published July 5 in Nature Mental Health, Williams' team showed that transcranial magnetic stimulation was particularly effective for the cognitive biotype. The study enrolled 43 veterans, with 26 identified by fMRI as having the cognitive biotype. After 30 daily sessions of transcranial magnetic stimulation that targeted the cognitive control circuit, veterans with the cognitive biotype recovered the deficits in their brain connectivity and improved on tests of cognitive control. Most of the improvement occurred within the first five days of treatment. The findings further demonstrate the promise of using biotypes to take the guesswork out of depression treatment.

Further explorations of depression

The different biotypes also correlate with differences in symptoms and task performance among the trial participants. Those with overactive cognitive regions of the brain, for example, had higher levels of anhedonia (inability to feel pleasure) than those with other biotypes; they also performed worse on executive function tasks. Those with the subtype that responded best to talk therapy also made errors on executive function tasks but performed well on cognitive tasks.

One of the six biotypes uncovered in the study showed no noticeable brain activity differences in the imaged regions from the activity of people without depression. Williams believes they likely haven't explored the full range of brain biology underlying this disorder — their study focused on regions known to be involved in depression and anxiety, but there could be other types of dysfunction in this biotype that their imaging didn't capture.

Williams and her team are expanding the imaging study to include more participants. She also wants to test more kinds of treatments in all six biotypes, including medicines that haven't traditionally been used for depression.

Her colleague Laura Hack, MD, PhD, an assistant professor of psychiatry and behavioral sciences, has begun using the imaging technique in her clinical practice at Stanford Medicine through an experimental protocol. The team also wants to establish easy-to-follow standards for the method so that other practicing psychiatrists can begin implementing it.

"To really move the field toward precision psychiatry, we need to identify treatments most likely to be effective for patients and get them on that treatment as soon as possible," Ma said

"Having information on their brain function, in particular the validated signatures we evaluated in this study, would help inform more precise treatment and prescriptions for individuals."

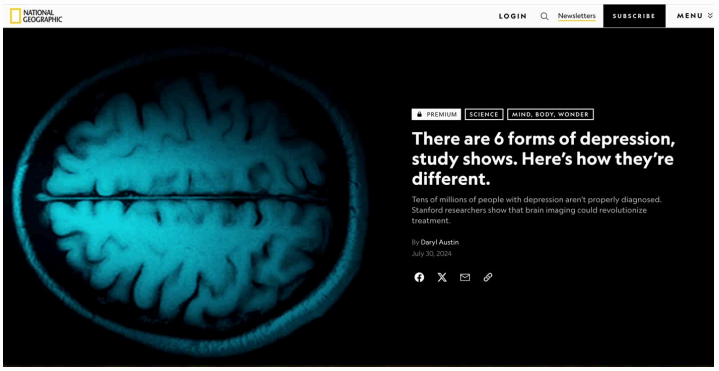
Researchers from Columbia University; Yale University School of Medicine; the University of California, Los Angeles; UC San Francisco; the University of Sydney; the University of Texas MD Anderson; and the University of Illinois Chicago also contributed to the study.

Datasets in the study were funded by the National Institutes of Health (grant numbers R01MH101496, UH2HL132368, U01MH109985 and U01MH136062) and by Brain Resource Ltd.

Media coverage related to this publication:

- ***A study identified 6 types of depression. Here's why that matters***, *By Kristen Rogers, CNN*
- ***There are 6 forms of depression, study shows. Here's how they're different***, *By Daryl Austin, National Geographic*
- ***Beyond One-Size-Fits-All: Precision Psychiatry Is Here***, *By Megan Brooks, Medscape*

For more coverage, visit our Center Media Page here.



Events highlighting how biotypes are now improving the lives of people experiencing depression and anxiety

In a record year, researchers at the Stanford Center for Precision Mental Health and Wellness had monumental scientific outcomes in precision mental health and personalized treatment.

PBS 'Tell Me More with Kelly Corrigan'

Dr. Williams joins 'Tell Me More with Kelly Corrigan' to discuss the stigmas around depression and how to move forward.

Season 7 Episode 4 'Bad Days, Tough Seasons or Clinical Depression?'

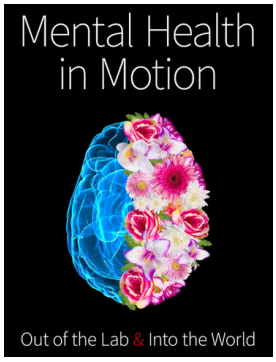
Watch Here

Stanford Medicine's Frontiers in Medicine AI in Bloom: A New Age in Human Health

Frontiers in Medicine is Stanford Medicine's annual marquee event. In 2024, in the Bing Concert Hall, we explored medicine's next frontier—artificial intelligence—and its potential to transform human health.

From improving patient care to decoding complex biological systems and personalizing treatment choices, the applications for AI in medicine are boundless. Learn how Stanford Medicine is leading the effort to ensure its responsible use across research and patient care from Dean Lloyd Minor, MD, and Stanford Health Care President and CEO David Entwistle. The evening began with a showcase of student-driven science and a lively musical performance. Experience a night of discovery, inspiration, and possibility.

Watch Here

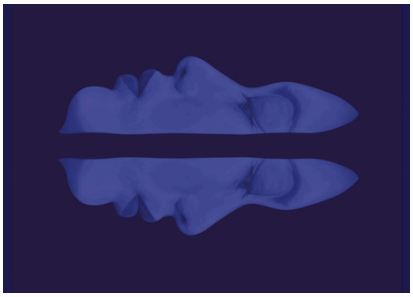


Leanne Williams - 2024 Mental Health in Motion

Leanne Williams presents 'Unlocking Precision Mental Health' at the Stanford 2024 Mental Health in Motion Event

'Out of the Lab & Into the World'

Watch Here



STANFORD MEDICINE
MAGAZINE

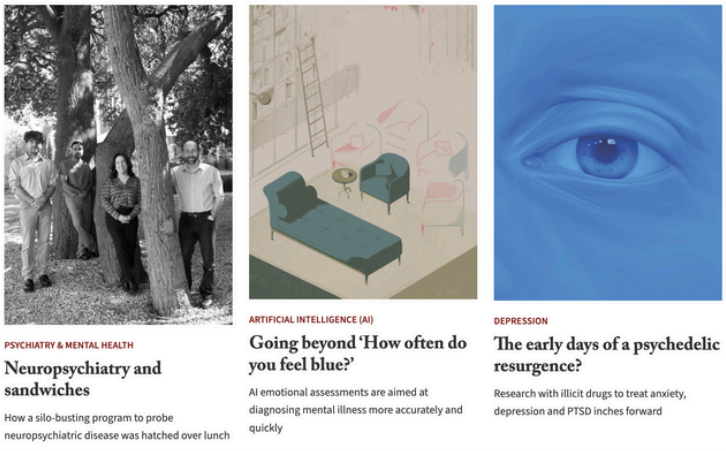
Psychiatry's new frontiers

Hope amid crisis

This new issue of Stanford Medicine magazine reports on emerging research and innovative treatments to improve mental health.

Cover Illustration by Jules Julien

Research Highlights from our Center Research Members



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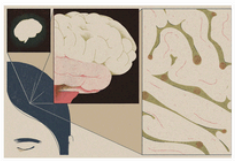

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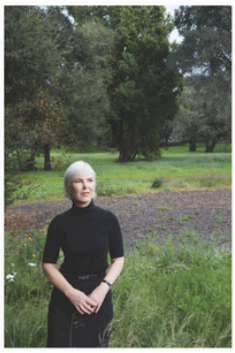

DEPRESSION

Let's talk about it

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