

JOINT MEDIA RELEASE

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IMH-NTU study identifies blood-based markers that may help predict development of psychosis in at-risk Asian youths

A new study by researchers from NHG Health's **Institute of Mental Health (IMH)** and **Nanyang Technological University, Singapore's (NTU Singapore) Lee Kong Chian School of Medicine (LKCMedicine)** has identified blood-based proteomic biomarkers that may help predict who among the at-risk group is at increased risk of developing psychosis. These biomarkers refer to specific patterns of proteins circulating in blood plasma, which reflect underlying biological processes and may provide objective indicators of disease risk.

Psychosis is a serious mental health condition that typically emerges in adolescence to early adulthood and can significantly impact a person's ability to function. It is characterised by symptoms such as hallucinations, delusions and disorganised thinking. In Singapore, 1 in 43 individuals aged 18 and up has had a diagnosis of psychosis (which includes schizophrenia) in their lifetime¹. Given its early onset and long-term impact, there is a critical need for more reliable tools to identify individuals at risk and enable earlier intervention.

The study utilised data from IMH's "**Longitudinal Youth at Risk Study**" (LYRIKS), a landmark Singapore study initiated in 2008 that laid the foundation for subsequent research in psychosis. LYRIKS was designed to comprehensively assess the social, clinical, and biological risk factors associated with youths at ultra-high risk of developing psychosis.

Ultra-high risk of psychosis refers to a clinical state in which an individual shows early warning signs or risk factors that significantly increase the likelihood of developing psychosis.

Associate Professor Jimmy Lee, Group Chief Research and Innovation Officer, NHG Health, and Senior Consultant and Clinician-Scientist, IMH, who led the LYRIKS study said, "Psychosis is a debilitating condition, but early intervention can shape the disease progression trajectory to produce good recovery outcomes. Diagnosing psychosis is, however, inherently challenging because symptoms might take time to fully manifest. These biomarkers could potentially complement clinical assessments in identifying those at risk of developing psychosis. Among youths who are at ultra-high risk of

¹ Singapore Mental Health Study 2016

psychosis, about 20% develop psychosis within two years. Our objective is to identify ways to pinpoint, and follow up more closely on that 20%, or perhaps intervene even earlier or more aggressively to prevent the onset of psychosis."

Dr Lee who is also an **Associate Professor (Clinical Practice) at NTU's LKCMedicine** said LYRIKS followed 173 young people aged 14-29 of whom 65 participants were identified as being at ultra-high risk of developing psychosis. Over a two-year follow-up period, 13 of these individuals were diagnosed with psychosis.

Current diagnosis of psychosis relies primarily on clinical assessments and behavioural observations. Yet individuals can experience early, subtle warning signs that might develop over time into psychosis, posing a challenge to early detection and intervention.

Findings from this IMH-NTU study, published in *Translational Psychiatry*, an authoritative journal that focuses on bridging neuroscience research with novel treatments for psychiatric disorders, were gathered using data from LYRIKS. The paper, titled "[*Blood plasma proteomic biomarkers for forecasting transition to psychosis in an Asian cohort*](#)", highlights the potential of integrating biological markers into current clinical assessment framework. It demonstrates how population-specific models may improve the accuracy of psychosis risk predictions in Asian populations.

Study Findings

Using mass spectrometry-based proteomic analysis, the researchers examined 1,757 different proteins. The team focused on three main questions:

- a) Can protein patterns previously found in Caucasian groups also work for Asian populations?
- b) Can protein patterns identified from this study improve how accurately we can predict outcomes?
- c) Do people from both Caucasian and Asian backgrounds show the same biological changes when developing psychosis?

The research team created and tested five models to predict whether high-risk patients might develop psychosis using advanced machine learning methods.

Two models were based on protein patterns identified in earlier studies on Caucasian groups, while the remaining **three models** were developed using the LYRIKS dataset, with proteins selected through machine learning and statistical approaches. The models were designed to predict whether high-risk patients might develop psychosis.

The research team found that models based on the Caucasian protein patterns achieved accuracy levels of 75% to 81% on the LYRIKS dataset. In comparison, models developed using the LYRIKS dataset performed better, reaching **accuracy levels of up to 96%**.

Although the specific proteins identified differed between the LYRIKS and Caucasian groups, similar biological processes - such as immune function - were observed in both.

First author, Dr Chan Wei Xin, Research Fellow, LKCMedicine, said, “These observations suggest that while psychosis risk prediction models benefit when tailored to specific populations, protein biomarkers identified in Caucasian populations were comparable to an Asian population. The protein biomarkers largely belong to the same key immune-related pathways and protein families, supporting recent evidence that dysregulation of these pathways plays a role in psychosis.”

Assoc Prof Lee said, “As Singapore's only national specialist psychiatric institution, IMH is committed to advancing mental health care through research. Research like this helps deepen understanding of complex psychiatric conditions, uncover their biological basis, and support the development of more effective diagnostic tools. This will ultimately improve recovery outcomes for patients.”

Assistant Professor Wilson Goh, from LKCMedicine and the NTU Centre of AI in Medicine, who co-led the study said, “The findings were encouraging as they showed that protein signatures identified in Caucasian populations could be applied more broadly, while also providing insight into how an Asian-specific signature looks and performs. This moves the field closer to molecular-based profiling that can support existing clinical approaches, bringing us a step closer to more personalised, biology-based care.”

Future Plans

While the findings are promising, the researchers acknowledge that these findings need to be validated in larger, independent studies across different populations before clinical implementation. The team also notes that the study focused only on proteins present in most blood samples, which means some important but lower-expressed proteins in the blood that might also be biologically relevant may have been missed, which future research could explore.

The research team believes that advances in studies on the biological processes behind psychosis will open the door to more targeted treatments and the potential development of new drugs that can better improve patients' lives in future.

Assoc Prof Lee said, “Our research marks meaningful progress towards a more personalised approach to psychiatry, where treatment can be tailored to an individual's biological profile rather than a one-size-fits-all model, bringing us closer to the day when these findings can be translated into real clinical benefit for patients.”

Asst Prof Goh said, “There is significant potential to go beyond proteins by combining different types of data, such as genomics, metabolites and social factors, to improve predictive accuracy. Integrating these approaches with explainable artificial intelligence

could also help both doctors and patients better understand diagnoses. The future of mental health care is likely to be increasingly supported by AI to deliver better outcomes.”

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About the Institute of Mental Health (IMH)

The Institute of Mental Health (IMH), a member of NHG Health, is the only tertiary psychiatric care institution in Singapore. Located on the sprawling 23-hectare campus of Buangkok Green Medical Park in the north-eastern part of Singapore, IMH offers a multidisciplinary and comprehensive range of psychiatric, rehabilitative and therapy services in hospital-based and community-based settings. The 2,000-bedded hospital aims to meet the needs of three groups of patients – children and adolescents (aged below 19 years), adults and the elderly. Besides providing clinical services, IMH dedicates resources to carry out mental health promotion and raise mental health literacy. IMH also leads in mental health research and training the next generation of mental health professionals in Singapore. For more information, please visit www.imh.com.sg

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NTU is also home to world-renowned autonomous institutes – the National Institute of Education and S Rajaratnam School of International Studies – and various leading research centres such as the Earth Observatory of Singapore, Nanyang Environment & Water Research Institute, Energy Research Institute at NTU, and Singapore Centre for Environmental Life Sciences Engineering.

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