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FRANCE 2030 PROGRAMME DE RECHERCHE PRECISION PSYCHIATRY

2nd Global Summit for Precision Psychiatry

Moving Towards Better Care in Psychiatry

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About this report

This paper summarises the discussions at the 2nd World Summit of Precision Psychiatry, which took place in Brussels in May 2024. Organised by the FondaMental Foundation, in collaboration with the PEPR PROPSY (Programme-Project in Precision Psychiatry, France 2030) and ECNP (the European College of Neuropsychopharmacology), the event served as an opportunity to share various perspectives on precision psychiatry and raise awareness of the field and its challenges. The summit's overall objective was to facilitate open dialogue and discussion among all stakeholders, including regulatory and funding agencies, patient and caregivers' associations, policymakers and decision makers, industry and academia.

Science|Business is ultimately responsible for the content of this report.

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Context

Severe mental illnesses, such as major depression disorders, including treatment-resistant depression, bipolar disorder, and psychotic disorders, are among the greatest challenges of the 21st century. They affect more than one in six people and constitute the leading cause of disability and the second cause of deaths worldwide. In Europe alone, over 84 million citizens are estimated[1] to experience some form of mental disorder. Psychiatric disorders not only lead to significant suffering, but are also contribute to a notable increase in somatic comorbidities, including cardiovascular disorders, accounting for 22% of the reduction in overall life expectancy. They also come with costs of over €600 billion[2], making them more costly than cancer and diabetes combined.

Last year, the European Commission launched a Comprehensive Approach to Mental Health programme, reflecting the growing importance being attached to high quality and affordable mental healthcare across the EU.

Current psychiatric treatments are mostly non-specific, and drug development is hampered by diagnostic categories lacking distinct pathophysiological boundaries, as well as sensitivity, and specificity. Patients are being treated with non-specific drugs, which have largely been discovered by serendipity, and whose mechanisms remain poorly understood. These drugs are effective only for certain groups of patients, and clinicians do not have access to the necessary tools for predicting in which cases they will be effective. There is an urgent need to personalise the treatment for the individual patient instead of relying on trials and errors.

Precision psychiatry represents a different approach to improve prevention, diagnosis, and treatment of psychiatric disorders. It aims to better understand the underlying biological mechanisms of the disease, identify associated biomarkers, and to develop targeted therapeutic strategies. In simple terms, rather than prescribing generic drugs with uncertain efficacy to patients, precision psychiatry aims to identify the precise biological factors underlying a specific patient's symptoms. This approach allows for accurate diagnosis and tailored treatment of the patient's disorder

Main conclusions from the event:

> Precision psychiatry needs to work towards biology-based frameworks to establish more precise diagnosis and treatment of mental disorders.

> It is necessary to collect and analyse large amounts of clinical, biological, digital and environmental data in order to identify the specific biological mechanisms and develop suitable therapeutic solutions.

> Clinical trials and treatment related to mental disorders should be based on greater patient stratification. To achieve this, it's necessary to identify stratification biomarkers associated with the specific disease subtype.

> As precision psychiatry is patient-centred, patients and caregivers need to be involved early in the process of research.

> The Diagnostic and Statistical Manual of Mental Disorders, the current classification methodology used to diagnose mental disorders, is now in its sixth version and is set to evolve further to represent the current scientific realities.

> To make progress, it is necessary to address the lack of resources and funding in the field of mental disorders, as well as to convince regulatory agencies, health industry and healthcare professionals that the current diagnostic entities are too broad. To this end, one of the outputs of this Summit is to write a policy brief for European policy and decision makers.

1 - Source: https://www.consilium.europa.eu/en/policies/mental-health/
2 - Source: https://www.oecd-ilibrary.org/sites/health_glance_eur-2018-4-en/index.html?itemId=/content/component/health_glance_eur-2018-4-en

From one-size-fits-all to haute couture

There is a large heterogeneity among patients who suffer from the same mental disorder, meaning that the same disorder can be caused by many different biological mechanisms. Therefore, a more personalised approach in psychiatric diagnosis and treatment is required. “In precision psychiatry, we want to move away from “one-size-fits-all” fashion to “haute couture” that addresses the needs of every specific patient,” explained Marion Leboyer, psychiatry professor at the University Paris-Est Créteil, and CEO of FondaMental.

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>
> Marion Leboyer

Building on this point, the summit participants discussed the need for a new diagnosis framework for mental disorders. Martien Kas, professor of behavioural neuroscience at the University of Groningen, and President of ECNP, explained biology-based frameworks are required to establish more precise diagnosis and treatment for mental disorders. “There is clearly a lack of understanding of underlying mechanisms of psychiatric and neurological disorders. We need to understand the biology of the patient and use this understanding for new treatments,” stated Kas. Biology-based frameworks are also necessary in order to conduct successful and accurate clinical trials, stressed Andrew Miller, professor of psychiatry at Emory University. “The way we conduct clinical trials is based on the past,” warned Miller. As such, clinical trials generally involve a highly heterogeneous population, which often doesn’t lead to any significant findings. To make progress, patients should be divided into subgroups based on specific mechanisms that drive their symptoms.

The progress towards greater precision

Precision medicine has been successfully applied in other fields, specifically neurology and oncology. Professor Wiesje van der Flier, scientific director of the Alzheimer Centre Amsterdam, highlighted the benefits of precision medicine in neurology. She explained that there has been a major improvement in the diagnosis and definition of Alzheimer’s disease thanks to the use of brain imaging and biomarkers. While Alzheimer’s used to be considered a syndrome, it is now considered to be a biological disease that is not defined by its symptoms. “There is a large role for imagining and biomarkers in personalised medicine for many diseases,” said Van der Flier. “They help us recognise the disease before clinical manifestation, provide evidence of process we aim to target, offer patient stratification, can measure if the drug does what it should do, and understand mechanism of the disease.”

Marion Leboyer

From left to right: Brenda Penninx, Martien Kas, Andrew Miller, Marion Leboyer.

Oncology is another field that has been revolutionised by precision medicine. Laurence Zitvogel, professor of immunology and biology at Université de Paris Sacla, described how, in the past decades, oncology has moved from cell-centred to patient-centred medicine. As with mental disorders, the understanding of cancer used to be very different, explained Zitvogel. Cancer used to be considered a local disease, while it is now known to be systemic. Thanks to the development and recognition of targeted therapy and immunotherapy, oncology has been completely reformed.

Examples of successes of precision medicine can also be found in the field of psychiatry itself. Carmine Pariante, professor of biological psychiatry at the Institute of Psychiatry at King's College, talked about the link between the immune system and mental health. By using biomarkers, studies have shown that (some forms of) depression could be caused by inflammation. To properly understand and target this cause, however, it is essential to apply precision medicine and target only those patients that display the biomarkers associated with inflammation. Brenda Penninx, professor at the Department of Psychiatry at Amsterdam MC and the Vrije Universiteit, also highlighted that recent evidence suggests that anti-inflammatory treatment could be used for depression. Like her colleagues, however, Penninx stressed that one type of treatment cannot be effective for all patients and stressed the importance of integrating mental health and somatic health.

Neuroimaging can also help to advance the field of precision psychiatry. Charles Laidi, associate professor in psychiatry at Paris University Hospitals, explained that neuroimaging could be very useful for patient stratification, as well as for simulating the effect of medication on the brain. He described a trial with personalised targeting which has shown outstanding results, demonstrating the effect of precise intensive treatment on patients with severe depression.

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>
> Lynn Durham

Another real-life application of precision psychiatry was presented by Lynn Durham, CEO and founder of STALICLA. The company has developed a neurodevelopmental precision medicine platform that matches patients with the right treatment options. "We want to recognise and break through one-size-fits-all diagnostics," said Durham. "Just as the lived experiences of people diagnosed with neurodevelopmental disorders are unique, conditions that currently fall under the same disease category, e.g. autism spectrum disorder, have very different biological bases."

Innovative techniques, advanced technologies, new tools

Steps are being taken to develop better tools for precision psychiatry. This includes research into biomarkers, as well as the use of proteomics, the use of risk factors interplay, artificial intelligence (AI) and machine learning, as well as digital tools – all of which were presented at the summit.

Alessio Travaglia, director of neuroscience at the Foundation for the National Institutes of Health (FNIH), introduced the biomarkers consortium, which aims to identify biomarkers and other drug development tools to accelerate the development of new therapeutics and health technologies. One method for identifying relevant biomarkers and gaining better understanding of neuropsychiatric disorders is proteomics. Anne-Li Lind, scientific liaison for neuroscience at Olink Proteomics, explained that blood proteomics analysis has revealed potential biomarkers associated with autism spectrum disorder, psychosis patients, bipolar disorder, as well as proteins associated with schizophrenia.

The interplay of our genes and the environment can shape our risk for psychiatric disorders. According to Elisabeth Binder, the director of the Department of Translational Research of the Max Planck Institute of Psychiatry, psychiatric genetics have made tremendous progress and seem to be strong predictors of risk, but the interplay of factors cannot be ignored. Mechanistic understanding of risk factors could support patient stratification and inform prevention and treatment strategies.

Advances in AI could also support the development of more precise psychiatry. Emmanuel Bacry, research director at Paris-Dauphine University, spoke about the possible uses of AI for health. These include using supervised AI as a diagnostic aid, surgeon aid, and for precision medicine. While AI could be applied in psychiatry, Bacry warned that the field first needs to overcome "the data challenge" and improve access to data, data distribution and interoperability. "The revolution of AI in health is mainly the revolution of data," said Bacry. This point was echoed by Paris Lalousis, lecturer in AI in mental health at King's College London, whose talk focused on using machine learning to extract new trans diagnostic categories of mental disorders. Machine learning and AI could be used to identify clinical biomarkers related to a disease, but large sets of data are needed in order to perform this type of AI analysis.

> *Data collected via smartphones can allow us to view symptoms as dynamic patterns and look at mental disorders in a much more detailed way*
>
> Inez Myin-Germys

Another technology that could be used for more precise diagnosis and treatment of mental disorders can already be found in everyone's pocket. Inez Myin-Germys, professor of Contextual Psychiatry at KU Leuven, explained that smartphones could be a valuable tool in this regard. "Data collected via smartphones can allow us to view symptoms as dynamic patterns and look at mental disorders in a much more detailed way," said Myin-Germys. It can help clinicians to create personalised targets for treatment, and to better evaluate their progress.

Building a better understanding of patients

In the past, drug discovery in neuropsychiatry has not followed a rational path and often happened through serendipity, according to Hugh Marston, Head of Global CNS Disease Research at Boehringer Ingelheim. Noting that innovation in neuropsychiatry is "an area of great unmet medical need", he stressed that innovation should be done through understanding the patient better. "We used to ask experts what to do. What we should do is to ask the patients – what they'd need to make their lives better, but also what their biology tells us."

Understanding patients and moving toward greater stratification in psychiatry, however, requires an industrial scale database of real-world data evidence (RWDE), pointed out Nawal Roy, founder of data science company HOLMUSK. With access to large sets of patient RWDE data, it's possible to achieve better clinical trial simulation, guide pipeline strategy, and clinical targeting.

Machine learning and data mining can indeed be transformative for precision psychiatry, agreed Andreas Meyer-Lindenberg Mannheim, psychiatrist and professor at Heidelberg University. Thanks to big progress in machine learning, it's now possible to discover complex data patterns and data sets. Before data mining, however, more relevant data needs to be collected, noted Marston: "It's not only about data mining, but also about data collection in a pragmatic and systematic way." There was also a call to develop more precise clinical development programmes, and to shorten the timeline of bringing new drugs to the market. Vikas Mohan Sharma, global head of neuroscience and ophthalmology at Fortrea, stressed the need to find the right innovative trial design and reduce the number of required study participants. Current procedures should be replaced with simpler, patient-centric protocols. Patients should be involved in clinical trials early

> ***Patients are open to co-creation and being involved in research, we need to find ways to make this happen***
>
> Peter Keri

on and interventions should be designed based on patients' needs. "Medicine started wrong – it was top down," Sharma cautioned. "It was always wise men trying to solve the problems of patients without asking the patients what they need."

This view was reinforced by Peter Keri, president of Global Alliance of Mental Illness Advocacy Networks-Europe (GAMIAN-Europe), who offered the patient's perspective on precision psychiatry. He agreed that patients should be involved in the design and implementation of mental health programs and policies. "Patients are open to co-creation and being involved in research," said Keri. "We need to find ways to make this happen."

Given the lack of innovative drugs and viable ways to treat psychiatry patients, the field should come up with more precise drug development for a specific population, added Florence Butlen-Ducuing of the European Medicines Agency. "Patients are waiting, we need to find a way to develop treatments that work."

In summary, there was a clear consensus at the summit that policymakers in the EU and elsewhere need to step up efforts to move toward more patient-centred and personalised psychiatry. Mental health and somatic health are not independent of one another, and more biology-based evidence needs to make its way into psychiatric research, diagnosis and treatment. However, to make these steps, it is necessary to convince policymakers of the importance of precision psychiatry and its benefits for society, and to secure more resources and funding.

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