Precision Psychiatry
Boehringer Ingelheim Mental Health
1 in 10 people globally live with a mental health condition
Redefining management of mental health
Moving beyond the constraints of a syndrome-based paradigm
A wider spectrum of support
Complementing pharmacotherapy with digital therapeutics

Precision psychiatry: Taking individual variability into account
Identifying brain activation patterns common across disorders
Connecting symptoms to specific brain circuit dysfunctions
Connecting CIAS to NMDAR hypofunction
Aiming to address previously untreatable aspects of mental health
Working to put mental healthcare on the path to precision psychiatry

Evolving treatment to benefit people with mental health conditions

CIAS, cognitive impairment associated with schizophrenia; NMDAR, N-methyl-D-aspartate receptor.
Globally, almost 800 million people live with a mental health condition, making up approximately 10.7% of the population.

### Schizophrenia
- **Point prevalence:** 0.46%²
- **Lifetime prevalence:** 0.4%²
- **Incidence:** 15.2 per 100,000 people²
- Over 19 million people live with schizophrenia globally³
- Burden and prevalence expected to increase⁴

### Major depressive disorder (MDD)
- **Lifetime prevalence:** 12%⁴
- Over 163 million people have MDD across the world³
- Highest prevalence of MDD found in Europe⁵
- Third highest source of burden of disease⁴
- MDD twice as prevalent in women than men⁶

### Borderline personality disorder (BoPD)
- **Point prevalence:** 1.6%⁷
- **Lifetime prevalence:** 5.9%⁷
- In clinical settings, the ratio of women to men has been reported as 3:1⁷
- No significant difference in rates of BoPD between women and men in the general population⁷

### Post-traumatic stress disorder (PTSD)
- **Lifetime prevalence:** up to 9%, depending on region⁸
  - Japan: 1.3%
  - Spain: 2.2%
  - South Africa: 2.3%
  - Italy: 2.4%
  - Northern Ireland: 8.8%

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BoPD, borderline personality disorder; MDD, major depressive disorder; PTSD, post-traumatic stress disorder.

Redefining the management of mental health

**Technology**
Boehringer Ingelheim is using technology to achieve better patient outcomes by exploring ways to combine digital technologies with innovative medicines.

**Digital phenotyping**
We have three main approaches:
- Complex data sets
- Artificial intelligence
- Smart devices

**Digital therapeutics**
We are working towards providing non-pharmaceutical tools to enhance the efficacy of future medicines; the aim is to maximize the potential of our medicines.

**Solutions**
We remain committed to finding new solutions for people living with mental illness.

Moving beyond the constraints of a syndrome-based paradigm

Despite advances in the field of psychiatry over the past half century, significant challenges and unmet needs remain. Advances in our understanding of mental health conditions are beginning to bridge the gap between neurobiology and psychiatry, allowing us to move away from the constraints of syndrome-based diagnosis and treatment. Diagnosis and treatment of mental health conditions can be challenging because any one symptom may be present in several syndromes. Through our greater understanding of the brain, we are now in a better position to start deciphering the circuits that combine to affect behavior. Despite advances in the field of psychiatry over the past half century, significant challenges and unmet needs remain.

A wider spectrum of support

BI Mental Health is innovating beyond medications to provide patients with a wider spectrum of support\(^1\)

- Early detection of disease
- Ongoing psychosocial interventions
- Digital therapeutics

There is a need for a more **holistic and integrated approach** to treating mental health conditions that encompasses the **social, psychological, and biological** aspects of these conditions\(^2\)

Recent studies have shown that integrative care is often the most beneficial for psychiatric disorders:\(^2\)

It has been suggested that combined pharmacological intervention, cognitive remediation therapy, and psychosocial intervention may improve cognitive impairments and functional outcomes in people with mental health conditions\(^3,\!^4,\!^5\)

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Complementing pharmacotherapy with digital therapeutics

BI Mental Health is looking to the future of care in mental health by developing digital therapeutics to complement pharmacotherapy.  

**Digital therapeutics**

- Software driven
- Evidence based
- Not restricted by time or location
- Personalized
- Able to monitor responses to treatment
- Cost-effective
- More readily available than some F2F therapies

Combining the benefits of psychosocial treatments with the accessibility of mobile technology has been shown to:

1. Improve adherence to medication
2. Reduce self-reported psychological symptoms
3. Improve remission rates
4. Improve functional and cognitive symptoms
5. Improve patients’ knowledge of their disorder and treatment

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F2F, face to face.

Precision psychiatry: Taking individual variability into account

Traditional approach

Stratification

Precision psychiatry

Heterogenous group of patients with the same DSM-5 diagnosis

Grouping of patients by clinical features

Treatment for a specific symptom dimension and neural circuit

Taking into account genes, environment, lifestyle, physiology, individual preferences

Developing treatments that can target underlying neurobiological processes is at the center of this approach

Seeking to provide more specific symptom control, supported by a rich development pipeline

Identifying brain activation patterns common across disorders

Behavioral symptoms associated with amygdala dysfunction

A meta-analysis of neuroimaging studies supported the role of amygdala dysfunction across disorders, with behavioral alterations linked to abnormal amygdala activity and dysfunctional interaction with cortical regions.

This precision psychiatry approach has potential clinical benefits: data-driven identification of subpopulations who are more likely to respond to the MoA of a given medication.

BoPD, borderline personality disorder; MDD, major depressive disorder; MoA, mode of action; PTSD, post-traumatic stress disorder.

Connecting symptoms to specific brain circuit dysfunctions

Precision psychiatry rests on evidence that mental health conditions can be described as neurobehavioral phenotypes.

**Neuroimaging meta-analysis design:**
- 298 studies
- 5,427 people with mental health conditions including schizophrenia, bipolar disorder, and unipolar depression
- 5,491 control participants

**Key results:**
- Activation likelihood estimation meta-analysis revealed a pattern of neurocircuit disruption across multiple mental health conditions.
- Disruption affected regions key to emotional processing including the amygdala, hippocampal/parahippocampal gyri, and prefrontal regions.

With advancements in neurobiology, we are uncovering associations between specific brain circuit dysfunctions and the emotions and behaviors experienced by a person with a mental health condition.

Connecting CIAS to NMDAR hypofunction

Evidence suggests the neural underpinnings of CIAS involve aberrant NMDAR-mediated synaptic plasticity. Normal NMDAR functioning has a key role in learning and memory.

By drawing on insights from research to connect symptoms to specific brain-circuit dysfunctions, we can target the underlying neurobiological processes.

References:

Aiming to address previously untreatable aspects of mental health

Example: schizophrenia

**POSITIVE SYMPTOMS**
- e.g. hallucinations, delusions, disorganized speech, agitative/repetitive movements, abnormal behavior

**NEGATIVE SYMPTOMS**
- e.g. alogia, avolition, social isolation, anhedonia, flattened affect

**COGNITIVE SYMPTOMS**
- e.g. poor memory, disorganized thinking, poor attention, poor comprehension, difficulty expressing thoughts

Pharmacologic treatments available, primarily antipsychotics

No robust pharmacologic treatments yet

In mental health conditions such as schizophrenia, there is a considerable unmet need for treatments for symptoms with a significant impact on quality of life

Working to put healthcare on the path to precision psychiatry

Working closely with research initiatives and academia, using multiple and combined methods

Research partners

- Psychiatry Consortium
- University of Oxford
- Earlham Institute

Behavioral tasks

Challenge studies

Neuroimaging techniques

Our goal is to translate these lessons into practice and bring precision psychiatry into the clinic to alleviate the burden on people with mental health conditions, their loved ones, and society.
Evolving treatment to benefit people with mental health conditions

- From treating psychiatric disorders
- From a focus on pills
- From DSM 5 indication-driven

To providing mental health solutions
- To a holistic approach: Pill + DTx + support
- To Precision Psychiatry

DSM-5, Diagnostic and Statistical Manual of Mental Disorders, 5th edition; DTx, digital therapeutics.