Wellcome's response to the European Commission Call for Evidence on a Comprehensive Approach to Mental Health

Wellcome is a politically and financially independent global charitable foundation, focused on using science to solve major global health challenges. We work to improve health for everyone by funding research, influencing policy, leading advocacy campaigns, and building global partnerships. We fund discovery research into life, health and wellbeing, and we support research to find solutions to three health challenges: mental health, infectious disease and climate.

Our vision is a world in which nobody is held back by mental health problems. We believe that mental health science has the potential to unlock transformational progress in the understanding and treatment of anxiety, depression and psychosis – some of the conditions which cause the greatest burden of mental ill health in Europe, and globally. We, therefore, warmly welcome the European Commission's proposal to promote a comprehensive approach to mental health and hope that it will include ambitious commitments to invest in, coordinate and advance mental health research – recognising the crucial role research must play if we are to make progress.

We agree with the Commission that there is an urgent need to improve the quality, quantity and accessibility of existing mental health services and treatments, improve mental health literacy and reduce stigma. There is so much we still do not understand about how mental health conditions develop or how and why different interventions work. As a result, existing mental health treatments can have limited effectiveness. In practice, this means that identifying the right intervention for the right person can be a process of trial and error, many mental health treatments come with challenging side-effects that affect adherence rates, and for some people, existing interventions simply don't work at all.

More than 1 in 3 Europeans experience mental health problems each year, at a cost of an estimated €461 billion per year. Despite this, only €543 million or around 0.68% of the total c.€80 billion Horizon 2020 budget was allocated to mental health research. [1]

Therefore, as previously concluded in the report on the final outcomes of the Conference on the Future of Europe, the EU must prioritise investments to "improve understanding of mental health issues and ways of addressing them".[2] Without supporting mental health science, the EU cannot achieve its goal of delivering evidence-based, innovative, personalised and effective treatments that will improve the quality of life for everyone facing mental health challenges, particularly those from vulnerable and disadvantaged groups.

As a leader for research and innovation, with some of the best scientists and strongest research environments in the world, we believe the EU is well placed to drive global progress in mental health science. The opportunity for progress is rich. The latest research includes using machine learning based on individuals' digital footprint to help personalise treatment for depression,[3] avatar therapy to improve quality of life for voice hearers[4] and a brand-new treatment for Schizophrenia that has higher effectiveness and fewer side-effects than the current options.[5]

A fully-funded, ambitious, multi-disciplinary EU mental health strategy that capitalises on the EU 'Health in All Policies' approach and allies cutting-edge science with lived experience could be the catalyst for a transformational breakthrough in our ability to effectively treat those with mental health conditions across Europe and around the world.

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[1] European Commission. EU research in public health. [accessed 13 02 2023].
[2] European Union. Conference on the Future of Europe: Report on the Final Outcome. 2022.
[3] Daniel Z et al. Exploring the digital footprint of depression: a PRISMA systematic literature review of empirical evidence. BMC Psychiatry. 22. 421 (2022).
[4] AVATAR2 Therapy. AVATAR2 Therapy Trial. [accessed 10 02 2023].
[5] Bisland L. A new approach for treating schizophrenia. [accessed 13 02 2023].

Recommendation 1: The EU must invest in mental health science to develop new and improved interventions

The EU and all member states should commit to doubling investment in mental health science and research by 2030, in line with the WHO Comprehensive Mental Health Action Plan. To maximise the impact of this investment, the EU should explore the potential for a new EU Mission on Mental Health as part the Horizon Europe Strategic Plan 2025-2027.

The need for a Mental Health Mission centred on research.

Depression, anxiety, and psychosis are holding millions of people back every day. We still know far too little about how and why these conditions develop, and how they can best be resolved. While a range of interventions can be effective for treating or managing mental health conditions, there are also limitations to existing options that are available. For example:

1. **We lack the understanding to predict which treatments will work best for different people so people often have to try lots of options before finding something that works:** While various sociodemographic and clinical factors have been linked to outcomes in depression and psychosis, there is still a lot we don't understand about who will respond to which interventions and why.[6] This means it is not possible to predict who is most likely to benefit from which interventions and so decisions are made on a trial-and-error basis.[7] As a result, people often try many interventions, with little benefit, before finding a combination that works for them.
2. **Even where treatments do help symptoms associated with the mental health condition**, **this sometimes comes with difficult side effects that impact daily life**.[8] Individuals, therefore, have to weigh up benefits and drawbacks and make trade-offs when making treatment decisions. Factors such as side effects can play an important role in treatment adherence, which has been found to be only around 50% for psychotropic medication.[9]
3. **For many people, the existing treatments simply don't work:** Evidence suggests that almost 50% people treated for depression do not achieve symptomatic remission during initial acute treatment[10] and only half of people respond to antipsychotics, with fewer experiencing a 'full' response.[11] Over the long-term, many individuals relapse. One study suggests that 25% to 40% of patients who recover after treatment for depression will have another depressive episode within 2 years, reaching 85% after 15 years.[12]

Without investment in mental health science and coordinated action to maximise the impact of that science, the EU cannot deliver on the strategic priority of evidence-based, innovative, promising and personalised approaches and interventions, effective treatments and high-quality care.

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[6] Bozzatello P, Bellino S, Rocca P. Predictive Factors of Treatment Resistance in First Episode of Psychosis: A Systematic Review . Front Psychiatry. 10:67 (2019); Rost N, Binder EB, Brückl TM. Predicting treatment outcome in depression: an introduction into current concepts and challenges. Eur Arch Psychiatry Clin Neurosci. (2022).

[7] Lally J, MacCabe J. H. Personalised approaches to pharmacotherapy for schizophrenia. BJPsych Advances. 22.2 (2016); ABPI. Stratified medicine in the NHS: An assessment of the current landscape and implementation challenges for non-cancer applications. 2014. [accessed 23 01 2023].

[8] Schofield P et al. Patients' views of antidepressants: from first experiences to becoming expert. Br J Gen Pract. 61.585 (2011); Cuijpers P., Stringaris A., Wolpert M. Treatment outcomes for depression: challenges and opportunities. The Lancet Psychiatry. 7:11 (2020).

[9] Kraus C. et al. Prognosis and improved outcomes in major depression: a review. Translational Psychiatry. 9.127 (2019).

[10] Fusar-Poli P. et al. The lived experience of psychosis: a bottom-up review co-written by experts by experience and academics. World Psychiatry. 21.2 (2022).

[11] Semahegn A et al. Psychotropic medication non-adherence and its associated factors among patients with major psychiatric disorders: a systematic review and meta-analysis. Systematic Reviews. 9:17 (2020).

[12] Cuijpers P., Stringaris A., Wolpert M. Treatment outcomes for depression: challenges and opportunities. The Lancet Psychiatry. 7:11 (2020).

Mental Health Research Priorities

The EU is a global leader in research and innovation and European researchers have already demonstrated their ability to deliver health breakthroughs that have the potential to improve the lives of millions of people in the EU and beyond.

A dedicated commitment to mental health science has the potential to contribute to global efforts to:

1. **Better predict what will work, for whom:** Research can help us to understand why some people respond to certain interventions and others do not. Research can also help to identify markers that will better predict response to treatment. This would allow us to better target interventions and help people more quickly identify interventions that will work for them. This is already a reality for some other diseases, such as cancer, where it is more common to use factors about the individual and the specific nature of the condition to guide treatment decisions.[13]
2. **Better detect and screen for mental health conditions:** Research can help us unpick the complex interplay between biological, psychological, and social determinants of mental health problems so that we can intervene earlier and take a more preventative and personalised approach.
3. **Identify and develop new treatments that are more effective than those currently available**: Research can support the development of new interventions that target different biological mechanisms, cultural contexts and individual preferences. These could involve things that an individual does for themselves, are provided by a healthcare professional, or are supported by policies or practices in wider society. With a greater choice of interventions to try, individuals are more likely to find interventions that work for them.

Recommendation 2: The EU should position itself as a world-leader on mental health.

The EU should use its global convening power to catalyse more ambitious and coordinated global action on mental health by setting pioneering regional goals, bringing together global leaders and revitalising commitments to a shared set of mental health priorities and targets – and establishing an unequivocal consensus that there is no health without mental health.

Building on the EU's global leadership during the COVID-19 pandemic and the new the EU Global Health Strategy, the EU now has an opportunity to act as a world-leader on mental health. This should include building on existing momentum in other global, national and regional strategies and pushing further to set high targets for post 2025.

The WHO Comprehensive Mental Health Action Plan offers a clear and comprehensive set of global targets for collective action on mental health. Wellcome is particularly supportive of efforts to uphold Objective 4[14]:

- Global target 4.1: 80% of countries will be routinely collecting and reporting at least a core sent of mental health indicators every two years through their national health and social information systems by 2030.

- Global target 4:2 The output pf global research on mental health doubles by 2030.

Building on the aligned WHO European Framework for Action on Mental Health 2021-2025,[15] the EU should aim to galvanise global collective action in alignment with these important goals whilst setting its own goals for a post-2025 framework that is even more ambitious. For example, the WHO Action Plan

[13] ABPI, 2014

[14] World Health Organisation. Comprehensive Mental Health Action Plan 2013-2030. Geneva, 2021.

[15] World Health Organisation. Regional Office for Europe. WHO European Framework on Action for Mental Health 2021-2025. 2021.

proposes efforts to 'develop and promote a prioritized and funded national research agenda in the area of mental health, based on consultation with all stakeholders.' Maximising these ambitions, a new EU Mission on Mental Health could include the development and delivery of a regional or even a global agenda setting process for mental health research.

Utilising key global fora such as the Berlin-hosted World Health Summit and with the Italian presidency of the G7 in 2024, this Communication is a timely opportunity to set a bold Team Europe approach to mental health that can deliver a heightened level of ambition globally, calling for better interventions so that nobody is held back by a mental health condition in Europe or around the world.

Crucially, the EU's comprehensive approach to Mental Health should also include partnerships with stakeholders in low- and middle-income countries where there is significant mental health burden, a recognised need for research and investment and a commitment to action. For example, the Africa CDC Non-Communicable Diseases, Injuries Prevention and Control and Mental Health Promotion Strategy (2022-26)[16] lays out clear ambition on mental health action across the African continent including prioritisation of context-specific research and innovation. Important collaborative initiatives such as the European Union-African Union Summit and the EU-WHO partnership to assist the African Union in reaching its target for increasing local vaccine production in Africa have shown the positive potential impact that the EU can have in partnering with other regions on shared priorities. A comprehensive approach to mental health should include similar ambitious global partnerships.

Recommendation 3: The EU should capitalise on its 'Health in All Policies' approach to drive strengthen interdisciplinary and inter-sectoral action.

The EU should integrate mental health priorities into policy areas beyond health policy by promoting collaboration within and across diverse expert teams and involving those with lived experience of mental health conditions within agenda-setting.

Wellcome firmly supports the Commission's 'Health in All Policies' approach, the EU Global Health Strategy's prioritisation of 'tackling the root causes of ill health' and the Commission's recognition that "to effectively reduce human suffering and bring benefits to our societies and economies, EU action needs to go beyond health policy and include all policies with an impact on mental health." [17]

Building on these commitments, and as the WHO Comprehensive Mental Health Action Plan advises, mental health should be more explicitly mainstreamed both within other priority health programmes, as well as within other relevant sectors' policies and laws. This should include but not be limited to education, R&D, housing, poverty reduction, climate, social protection, technology, employment, disability, the judicial system, and human rights.

In order to design and deliver effective policy change across this diverse range of sectors, an interdisciplinary approach is essential. This should include collaboration, inclusive decision-making and spaces for shared learning that involves mental health professionals, lived experience experts, patient organisations, social services and scientists across a range of disciplines.

Examples of an interdisciplinary 'Mental Health in All Policies' approach

As recognised in the EU Global Health Strategy, "Global Health is being impacted by the triple planetary crisis of climate change biodiversity and pollution."[18] We are only just beginning to understand the extent of

[16] African Union. Africa CDC. Africa CDC Non-Communicable Diseases, Injuries Prevention and Control and Mental Health Promotion Strategy (2022-26) . Addis Ababa, 2022.
[17] European Commission. EU Global Health Strategy: Better Health for All in a Changing World. 2022.
[18] Ibid

the impact of climate change on mental health: ranging from the impact of higher temperatures on those taking anti-depressants[19]; and how air pollution increases the incidence of anxiety and depression[20]; to the mental health impact of catastrophic weather events[21]. To build a truly comprehensive approach to mental health, there is an urgent need for additional research at the intersection of mental health and climate science and for better communication and collaboration between scientists and policy-makers across a range of policy areas including health, energy, transport and social protection.

Similarly, it is well known that an individual's mental health impacts their financial outcomes.[22] and that there are significant economic benefits from investing in the mental health of those living in poverty.[23] However, deliberate or targeted action in this area is currently lacking.[24] Delivering effective interventions at the intersection of mental health and poverty requires interdisciplinary partnerships between policymakers working in multiple sectors including health, housing, social protection. It also requires collaboration and involvement of psychiatrists, economics, sociologists and those with lived experience of poverty and mental health conditions.

An interdisciplinary 'Mental Health in All Policies' approach in action

Wellcome supports the EU's plans to build a new, joined-up way of working that will improve coordination across all policy areas relevant to health.[25] Wellcome encourages efforts to ensure mental health is given fair consideration within this effort and encourages consideration of a new EU mission on Mental Health as a powerful mechanism to ensure the necessary join-up and maximise impact. Wellcome also encourages the EU to identify and support opportunities for agencies and bodies working on relevant policy areas at Member state and EU level to take innovative approaches to integration and interdisciplinary working, to evaluate the impact of the 'health in all policies' approach and to share learnings with the goal of enabling a stronger, more diverse and more impactful mental health policy field.

Annex: Case Studies

Case study 1: Ground-breaking discovery offers a new way to treat schizophrenia more effectively

The following case study was adapted from an article, authored by Lynsey Bilsland, Wellcome Trust.[26]

What is the problem we are trying to solve?

Schizophrenia is a severe, long-term mental health condition that affects around 1 in 300 people worldwide. Symptoms include hallucinations, delusions, muddled thoughts, loss of interest in everyday activities and social withdrawal.

Antipsychotic drugs are commonly used to treat the condition; however, they don't work for everyone. Historically, these drugs have focused on the neurotransmitter dopamine. They work to block some of the dopamine receptors in the brain, which can lead to problematic side effects. These side effects mean that some people stop taking the medication, causing them to relapse. Moreover, between 20% and 33% of patients don't respond to dopamine-targeting drugs at all.

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[19] Rackham A. Some antidepressants may make heatwave challenging. BBC News . 13 08 2022. [accessed 13 02 2023].
[20] Xu G et al. Long-Term Air Pollution, Genetic Susceptibility, and the Risk of Depression and Anxiety: A Prospective Study in the UK Biobank Cohort. Environ Health Perspect. 131.1 (2023).
[21] World Health Organisation . Mental Health in Emergencies. 16 March 2022. [accessed 13 02 2023].
[22] Ridley M et al. Poverty, depression, and anxiety: Causal evidence and mechanisms. Science. 370.6522 (2020).
[23] Lund C et al. Poverty and mental disorders: breaking the cycle in low-income and middle-income countries. The Lancet. 378.9801 (2011).
[24] Ridley M et al. (2020).
[25] European Commission. EU Global Health Strategy: Better Health for All in a Changing World. 2022.

[26] Bisland L. A new approach for treating schizophrenia. [accessed 13 02 2023].

What can research do about it?

A biotech organisation called Karuna Therapeutics Inc. has developed a new combination drug called KarXT. The KarXT trial is the first positive phase three trial for an investigational medicine that does not directly rely on dopaminergic or serotonergic pathways in the brain in approximately seventy years. KarXT works in a completely new way.

While current therapies for schizophrenia can be effective in managing select positive symptoms, like hallucinations and delusions – they do not address other life-limiting symptom areas. For example, negative symptoms like social withdrawal and cognitive symptoms like memory problems. KarXT has the potential to address all three symptom areas associated with schizophrenia (positive, negative and cognitive).

What does the future look like?

There are three ongoing trials evaluating the short and long-term effectiveness of KarXT in treating schizophrenia and how safe it is to use over a long period. Following their completion, Karuna aims to file a New Drug Application with the Food and Drug Administration (FDA) for KarXT in schizophrenia in mid-2023.

Approval and roll-out of this new drug has the potential to offer life-changing benefits to people with schizophrenia.

Case study 2: Using digital technologies to predict mental health relapse

This case study is based on research by A Cohen et.al. 2023[27].

What is the problem we are trying to solve?

Even if initial treatment works, people with schizophrenia are often at risk of experiencing a relapse, where symptoms return. When this happens, it's important to act as early as possible to have the best chance of responding effectively.

Without early intervention, relapse can hamper recovery and even contribute to the risk of treatment-resistant schizophrenia. More broadly, relapse is known to increase risks of self-harm, homelessness and broader social, educational and employment-related impacts.

Unfortunately, predicting a relapse is challenging because there is a wide range of unique social, personal and environmental triggers involved. Therefore, finding ways to predict relapse more effectively is an important and complex clinical priority.

What can research do about it?

Innovative new research is helping to scale-up a digital solution for predicting relapse based on a method known as 'digital phenotyping'. This method uses sensors in smartphones to capture a range of useful data such as green space exposure, amount of social contact, sleep habits and screen time. This data can then be combined with self-reported survey data about symptoms and medication adherence also collected through a digital app.

Research led by Professor John Torous using a smartphone app called MindLAMP has found a way of applying an algorithm to digital phenotyping data to help detect significant anomalies. This research has shown that it is possible to use this smartphone tool to accurately predict relapse one month after significant anomalies have been detected.

[27] Cohen A et al. Relapse prediction in schizophrenia with smartphone digital phenotyping during COVID-19: a prospective, three-site, two-country, longitudinal study. Schizophrenia. 9:6 (2023).

Through the most recent research conducted in diverse settings, it has also been shown that this approach is effective in different and diverse contexts and cultures. This means that there is significant potential to roll the tool out globally.

What does the future look like?

MindLAMP, is an open access tool, co-created in partnerships with patients, family members and clinicians based in the areas of the study and available worldwide on android and iOs. The tool is currently being used in 523 global sites as part of another study, which will help create even greater understanding of how it works in different contexts.

Given the limited access to care for people living with schizophrenia in many countries, this new smartphone app has the potential to play a vital part in contributing to relapse prevention efforts around the world.

Case study 3 The role of research in ensuring mental health interventions work effectively

This case study is based on the MYRIAD project.[28]

What is the problem we are trying to solve?

There are many suggested ways to intervene in schools to try to address burgeoning rates of anxiety and depression which often first manifest in adolescence. However, we don't yet know which are the most effective. Mindfulness has been found to help adults with anxiety and depression, but we don't know if it can help children when rolled out as part of a large-scale school based preventive intervention.

What can research do about it?

The MYRIAD (MY Resilience in ADolescence) project was a highly rigorous, eight-year project involving more than 28,000 children aged 11-14 years and 650 teachers across 100 schools across the UK.

MYRIAD gathered 20 million data points with the goal of understanding if schools-based mindfulness training is an effective, cost-effective, accessible and scale-able way to promote mental health and well-being in adolescence. Ultimately, the study did not find that mindfulness was an effective way to help young people's mental health or well-being in schools.

Whilst many might consider this finding to be disappointing, research like this is very important for ensuring that we prioritise interventions that work for the people they are seeing to help before investing funding in significant large-scale universal roll-out.

What does the future look like?

This study suggests policy makers in the UK would not be advised to invest in large scale implementation of mindfulness training as an approach in schools to prevent anxiety and depression in 11–14-year-olds.

This frees up funds to be used on other initiatives that have been shown to improve mental health such as physical exercise and poverty reduction.

[28] University of Oxford. MYRIAD: MY Resilience in ADolesence. 2008-2023. [accessed 13 02 2023].

Bibliography

ABPI. Stratified medicine in the NHS: An assessment of the current landscape and implementation challenges for non-cancer applications. 2014. [accessed 23 01 2023]. <https://www.abpi.org.uk/publications/stratified-medicine-in-the-nhs/>.

African Union. Africa CDC. Africa CDC Non-Communicable Diseases, Injuries Prevention and Control and Mental Health Promotion Strategy (2022-26) . Addis Ababa, 2022.

AVATAR2 Therapy. AVATAR2 Therapy Trial. [accessed 10 02 2023]. <https://www.avatartherapytrial.com/>.

Bisland L. A new approach for treating schizophrenia. [accessed 13 02 2023]. <https://wellcome.org/news/potential-new-treatment-for-schizophrenia-KarXT>.

Bozzatello P, Bellino S, Rocca P. Predictive Factors of Treatment Resistance in First Episode of Psychosis: A Systematic Review . Front Psychiatry. 10:67 (2019).

Cohen A et al. Relapse prediction in schizophrenia with smartphone digital phenotyping during COVID-19: a prospective, three-site, two-country, longitudinal study. Schizophrenia. 9:6 (2023).

Cuijpers P., Stringaris A., Wolpert M. Treatment outcomes for depression: challenges and opportunities. The Lancet Psychiatry. 7:11 (2020).

Daniel Z et al. Exploring the digital footprint of depression: a PRISMA systematic literature review of empirical evidence. BMC Psychiatry. 22. 421 (2022).

European Commission. EU Global Health Strategy: Better Health for All in a Changing World. 2022.

European Commission. EU research in public health. [accessed 13 02 2023]. <https://research-and-innovation.ec.europa.eu/research-area/health/public-health-research_en#:~:text=More%20than%201%20in%203,can%20help%20meet%20their%20needs.>.

European Union. Conference on the Future of Europe: Report on the Final Outcome. 2022.

Fusar-Poli P. et al. The lived experience of psychosis: a bottom-up review co-written by experts by experience and academics. World Psychiatry. 21.2 (2022).

Griffiths S.L. et al. Heterogeneity in treatment outcomes and incomplete recovery in first episode psychosis: does one size fit all? Translational Psychiatry. 12.485 (2022).

Herrman H. et al. Time for united action on depression: a Lancet–World Psychiatric Association Commission. The Lancet. 339.10328 (2022).

Kraus C. et al. Prognosis and improved outcomes in major depression: a review. Translational Psychiatry. 9.127 (2019).

Lally J, MacCabe J. H. Personalised approaches to pharmacotherapy for schizophrenia. BJPsych Advances. 22.2 (2016).

Leucht S, et al. Sixty Years of Placebo-Controlled Antipsychotic Drug Trials in Acute Schizophrenia: Systematic Review, Bayesian Meta-Analysis, and Meta-Regression of Efficacy Predictors. am J Psychiatry. 174.10 (2017).

Lund C et al. Poverty and mental disorders: breaking the cycle in low-income and middle-income countries. The Lancet. 378.9801 (2011).

Patel V et al. The Lancet Commission on global mental health and sustainable development. The Lancet. 392.10157 (2018).

Rackham A. Some antidepressants may make heatwave challenging. BBC News . 13 08 2022. [accessed 13 02 2023]. <https://www.bbc.co.uk/news/health-62496985>.

Ridley M et al. Poverty, depression, and anxiety: Causal evidence and mechanisms. Science. 370.6522 (2020).

Rost N, Binder EB, Brückl TM. Predicting treatment outcome in depression: an introduction into current concepts and challenges. Eur Arch Psychiatry Clin Neurosci. (2022).

Schofield P et al. Patients' views of antidepressants: from first experiences to becoming expert. Br J Gen Pract. 61.585 (2011).

Semahegn, A., Torpey, K., Manu, A. et al. Psychotropic medication non-adherence and its associated factors among patients with major psychiatric disorders: a systematic review and meta-analysis. Systematic Reviews. 9:17 (2020).

University of Oxford. MYRIAD: MY Resilience in ADolesence. 2008-2023. [accessed 13 02 2023].. <https://myriadproject.org/>.

World Health Organisation . Mental Health in Emergencies. 16 March 2022. [accessed 13 02 2023]. <https://www.who.int/news-room/fact-sheets/detail/mental-health-in-emergencies>.

World Health Organisation. Comprehensive Mental Health Action Plan 2013-2030. Geneva, 2021.

World Health Organisation. Regional Office for Europe. WHO European Framework on Action for Mental Health 2021-2025. 2021.

Xu G et al. Long-Term Air Pollution, Genetic Susceptibility, and the Risk of Depression and Anxiety: A Prospective Study in the UK Biobank Cohort. Environ Health Perspect. 131.1 (2023).