11 ideas on innovative enrichment strategies for mental disorders using objective, quantifiable predictive biomarkers

IHI received 11 almost-identical ideas from 11 separate organisations / individuals. As they are extremely similar, the SIP assessed them together and we are publishing them together here, as follows.

Idea title: Innovative enrichment strategies for mental disorders using objective, quantifiable predictive biomarkers for therapeutic interventions

Reference numbers of the ideas: TI_001225, TI_001224, TI_001223, TI_001222, TI_001221, TI_001233, TI_001232, TI_001231, TI_001230, TI_001226

Idea title: Enrichment strategies for mental disorders using objective, quantifiable biomarkers towards the development of preventive, diagnostic or therapeutic discoveries

Reference number of the idea: TI_001219

Topic Idea to IHI - Reference Number: TI_001219

Are you submitting the idea:
☐ **in your personal capacity?**
☒ **on behalf of an organisation?**

Please indicate the name of the group organisation: Inserm

Please select from the list below the type of stakeholders your organization represents:
Research/higher or secondary education organisation (private or public)

1 Title of your idea

Please provide a short title that accurately reflects the objective(s) of your idea:
ENRICHMENT STRATEGIES FOR MENTAL DISORDERS USING OBJECTIVE, QUANTIFIABLE BIOMARKERS TOWARDS THE DEVELOPMENT OF PREVENTIVE, DIAGNOSTIC OR THERAPEUTIC DISCOVERIES

2 Scope

Explain the specific challenges/problems to be addressed by your idea and how these affect relevant stakeholders, taking into account what is already known and/or available in the field:
Current therapeutics for major psychiatric disorder lead to remission in approximately one third of patients and partial remission in another third. This heterogeneity in treatment outcomes is thought to reflect heterogeneity of current categorical diagnosis. In addition, a large fraction of patients are not diagnosed or with delay, while clinical trials fail because of absence of objective endpoints to asses efficacy.

Developing enrichment strategies will aid academic and industry to optimise prevention, diagnosis and trial designs by guiding selection of the most appropriate patient population and outcome measures, using objective, measurable, quantifiable biomarkers based on uni or mutli-modal biomarkers such as cognition, omics, brain imaging, electrophysiology…. This will enable more precise diagnostic and therapeutic strategies and increase interest among industry to initiate RCTs for psychiatry.

This can be done through re-analysis of existing cohorts or of previous trial data, or through new large RCTs in enriched or stratified populations.

The goal of this call would thus to develop and validate enrichment biomarkers to be added to current diagnostic categories, possibly across psychiatric disorders, based on previously identified abnormalities such as pharmacogenomics to predict drug responses, electrophysiology to identify brain circuits, brain stimulation using brain imaging, immune dysfunctions targeting inflammation, metabolism, gut dysbiosis, mitochondria... These enrichment strategies will optimise future clinical trials, and improve treatment outcomes and prognosis of patients with mental disorders, known to be the principal global cause of handicap (WHO, 2020) and to represent a large unmet clinical need.

Please indicate which IHI specific objective(s) (SO), as described in the IHI Strategic Research and Innovation Agenda (SRIA), your idea addresses:

["SO1: contribute towards a better understanding of the determinants of health and priority disease areas"
"SO2: integrate fragmented health research and innovation efforts bringing together health industry sectors and other stakeholders, focusing on unmet public health needs, to enable the development of tools, data, platforms, technologies and processes for improved prediction, prevention, interception, diagnosis, treat- ment and management of diseases, meeting the needs of end-users"]

Please select the keywords that are most relevant to your idea:
["Mental health"
"Diagnosis"
"Treatment"]

In alignment with the IHI specific objective(s) selected above, specify the objectives of your idea:

Following the established principles of precision psychiatry, innovation should improve clinical trials' successes towards the development of mechanisms-based treatment solutions targeting homogeneous patient's subgroups defined by objective biomarkers, thus helping reduction of individual suffering and of economic cost. Mental disorders represent the leading source of years lost to disability and constitute five of the top ten causes of disability. In the EU, it is estimated that over 27% of the general population will experience some form of mental disorders inducing a total cost across Europe above 4% of GDP (over 600 billion €).

This project will :
1. Contribute to the creation of an EU-wide Brain and Mental Health research and innovation ecosystem that will facilitate translation of scientific knowledge into diagnostic and therapeutic innovations
2. Foster the development of safe, effective, people-centred and cost-effective predictive enrichment strategies that respond to strategic unmet public health needs across psychiatric disorders.
3. Drive cross-sectoral health innovation for a globally competitive European health industry
4. Create mentorship and capacity development opportunities to facilitate sustainability and implementation

3 Expected <u>impacts</u> to be achieved by your idea

Briefly describe the expected impacts to be achieved by your idea, ensuring that they contribute to IHI general and relevant specific <u>objectives</u>, as described in the IHI SRIA:

Impacts are wider long-term effects on society (including the environment), the economy and science, enabled by the outcomes of R&I investments. Impacts generally occur sometime after the end of the project, e.g. successful implementation of digital solutions supporting people-centred care.

IHI general objectives: 1. contribute towards the creation of an EU-wide health research and innovation ecosystem that facilitates translation of scientific knowledge into innovations, notably by launching at least 30 large-scale, cross-sectoral projects, focussing on health innovations; 2. foster the development of safe, effective, people-centred and cost-effective innovations that respond to strategic unmet public health needs, by exhibiting, in at least 5 examples, the feasibility of integrating health care products or services, with demonstrated suitability for uptake by health care systems. The related projects should address the prevention, diagnosis, treatment and/or management of diseases affecting the EU population, including contribution to 'Europe's Beating Cancer Plan'; 3. drive cross-sectoral health innovation for a globally competitive European health industry and contribute to reaching the objectives of the new Industrial Strategy for Europe and the Pharmaceutical Strategy for Europe.

Developing innovative predictive enrichment strategies focusing on targeted treatments for specific subgroups of mental disorders is based on reinforced private-public collaboration towards

- Discovery and validation of objective, quantifiable, targetable and/or mechanism-based stratification biomarkers using re-analysis of existing data on treatment response (longitudinal cohort studies or clinical trials) data from Europe and beyond
- Selection, development and testing of mechanisms-based treatments in stratified homogeneous subgroups of patients using existing European networks of expert/excellence centers for psychiatric disorders
- Development of an international platform facilitating and supporting innovative clinical trial designs to assess the safety, health outcomes and health-economic impact of innovative treatment paradigms
- Discussion with regulatory agencies, consumers to share the results
- Improvement of patient's prognosis and reduction of overall cost

4 Why should your idea become an IHI call topic?

Explain why collaboration through a cross-sectoral and multidisciplinary public private partnership is needed in particular:

Why does it require collaboration among several industry sectors (*e.g.* pharma, vaccines, biotech, medical devices, in vitro diagnostics, radiotherapy, medical imaging health ICT)?

Why does it require collaboration between private (industry) and public partners (*e.g.* academia, healthcare practitioners, patients, regulators)?

Developing objective, quantifiable biomarkers for enrichment strategies require public-private partnerships and patient-centric efforts. This can be achieved in Europe thanks to pre-existing databases (clinical trials, cohorts) as well as networks of academic/clinical centers specialised and organized in national and international networks, sharing similar assessments tools which can be used to discover and validate signatures using clinical and digital tools, blood based and brain imaging biomarkers for stratifying psychiatric disorders. This project will reinforce collaboration between scientists, industrials and patients on the discovery and validation of biomarkers. Regulators should also be included to discuss innovative diagnostic strategies, and clinical trials design, requirements to validate biomarkers for stratification or to be used as endpoints. Patient's associations are already associated with academic entities on the challenges of Precision Psychiatry, and they will be participating to the research and clinical designs.

Why is the contribution of industry needed to achieve the expected impacts?

Industry contribution is needed to develop enrichment biomarkers to identify subgroups of patients and appropriate endpoints for future clinical trials. This should increase study efficiency, produces larger effect sizes, and permits the use of a smaller study population.

The industry is needed to develop blood-based biomarkers based on proteomics, metabolomics, cell-based assay, brain imaging, digital assessments and/or to explore biomarkers predicting efficacy in past clinical trials. By leveraging the combined strengths of academia, research institutions, and healthcare industry, this project can significantly accelerate the development of new diagnostic tools and personalized therapies for mental disorders. Both established enterprises and start-ups that focus on the fields of biomarker discovery, drug development or repurposing, will greatly benefit from this project.

Topic Idea to IHI - Reference Number: TI_001221

Are you submitting the idea:
☐ **in your personal capacity?**
☒ **on behalf of an organisation?**

Please indicate the name of the group organisation: INSERM

Please select from the list below the type of stakeholders your organization represents:
Research/higher or secondary education organisation (private or public)

1 Title of your idea

Please provide a short title that accurately reflects the objective(s) of your idea:
INNOVATIVE ENRICHMENT STRATEGIES FOR MENTAL DISORDERS USING OBJECTIVE, QUANTIFIABLE PREDICTIVE BIOMARKERS FOR THERAPEUTIC INTERVENTIONS

2 Scope

Explain the specific challenges/problems to be addressed by your idea and how these affect relevant stakeholders, taking into account what is already known and/or available in the field:
Current therapeutic interventions for major psychiatric disorders only lead to remission in approximately one third of patients and partial remission in another third. This heterogeneity in treatment outcomes is thought to reflect the low accuracy of current categorical diagnostic frameworks. In addition, a large fraction of patients are not diagnosed or with delay, while clinical trials fail because of absence of objective endpoints to asses efficacy.
Developing predictive enrichment strategies will aid academia and industry to optimise future trial designs by guiding selection of the most appropriate patient population and outcome measures, using objective, measurable, quantifiable, valid biomarkers based on uni- or multi-modal patient-centered data such as cognitive batteries, blood-based omics, brain imaging, and electrophysiology, which can be used to predict treatment responses. By shifting away from the traditional one-size-fits-all approach, innovative enrichment strategies will enhance the signal-to-noise ratio of existing or new therapeutic strategies, and
The goal of this call would thus be to develop and validate robust, reproducible, sensitive to clinical changes, predictive biomarkers to be added to current diagnostic categories, possibly across psychiatric disorders, based on previously identified abnormalities. This can be done through re-analysis of existing cohorts or previous trial data, or through the development of new cohorts or RCTs in enriched or stratified populations. Examples include pharmacogenomics to predict drug responses, electrophysiology to identify brain circuits, brain stimulation using brain imaging, immune dysfunctions targeting inflammation, metabolism, gut dysbiosis, mitochondria...
In summary, mental disorders represent the principal global cause of handicap (WHO, 2020) and a large unmet clinical need. The proposed enrichment strategies will optimise future clinical trials, thereby increasing interest among industry to (re-)enter the field and tackle these needs.

Please indicate which IHI specific objective(s) (SO), as described in the IHI Strategic Research and Innovation Agenda (SRIA), your idea addresses:

["SO1: contribute towards a better understanding of the determinants of health and priority disease areas"
"SO2: integrate fragmented health research and innovation efforts bringing together health industry sectors and other stakeholders, focusing on unmet public health needs, to enable the development of tools, data, platforms, technologies and processes for improved prediction, prevention, interception, diagnosis, treat- ment and management of diseases, meeting the needs of end-users"]

Please select the keywords that are most relevant to your idea:
["Immune system diseases"
"Mental health"
"Metabolic diseases"
"Prediction"
"Prevention"
"Diagnosis"
"Treatment"
"Disease management"
"Digital health"
"Health technology"]

In alignment with the IHI specific objective(s) selected above, specify the objectives of your idea:

Following the established principles of precision psychiatry, innovation should improve discovery and validation of enrichment biomarkers to development robust, reproducible and sensitive biomarkers to improve diagnosis and clinical trials. This should reduce individual suffering and economic cost. Mental disorders constitute five of the top ten causes of disability. It is estimated that over 27% of the general population will experience mental disorders inducing a total cost across Europe above 4% of GDP.
This project will
1. contribute to the creation of an EU-wide Brain and Mental Health research and innovation ecosystem that will facilitate translation of scientific knowledge into diagnostic and therapeutic innovations
2. foster the development of safe, effective, people-centred, cost-effective predictive enrichment strategies that respond to strategic unmet public health needs across psychiatric disorders.
3. drive cross-sectoral health innovation for a globally competitive European health industry
4. create mentorship and capacity development opportunities to facilitate sustainability and implementation

3   Expected <u>impacts</u> to be achieved by your idea

Briefly describe the expected impacts to be achieved by your idea, ensuring that they contribute to IHI general and relevant specific <u>objectives</u>, as described in the IHI SRIA:

Impacts are wider long-term effects on society (including the environment), the economy and science, enabled by the outcomes of R&I investments. Impacts generally occur sometime after the end of the project, e.g. successful implementation of digital solutions supporting people-centred care.

IHI general objectives: 1. contribute towards the creation of an EU-wide health research and innovation ecosystem that facilitates translation of scientific knowledge into innovations, notably by launching at least 30 large-scale, cross-sectoral projects, focussing on health innovations; 2. foster the development of safe, effective, people-centred and cost-effective innovations that respond to strategic unmet public health needs, by exhibiting, in at least 5 examples, the feasibility of integrating health care products or services, with demonstrated suitability for uptake by health care systems. The related projects should address the prevention, diagnosis, treatment and/or management of diseases affecting the EU population, including contribution to 'Europe's Beating Cancer Plan'; 3. drive cross-sectoral health innovation for a globally competitive European health industry and contribute to reaching the objectives of the new Industrial Strategy for Europe and the Pharmaceutical Strategy for Europe.

Developing innovative predictive enrichment strategies focusing for homogeneous subgroups of mental disorders is based on reinforced private-public collaboration towards
-         Discovery and validation of objective, quantifiable, targetable, robust, reproducible biomarkers ,with operational delivery stratification biomarkers using existing data or future data collection from longitudinal cohort studies or clinical trials data from Europe and beyond
-         In silico selection, of mechanisms-based treatments to be tested in stratified homogeneous subgroups of patients
-         Setting up European infrastructures to facilitate and support enrichment strategies in clinical trials based on the construction of a European Network of expert/excellence centers for mental disorders and on a robust data infrastructure allowing data sharing.
-         Discussion with regulatory agencies, consumers to share the results
-         Improvement of patient's prognosis and reduction of overall cost

4   Why should your idea become an IHI call topic?

Explain why collaboration through a cross-sectoral and multidisciplinary public private partnership is needed in particular:

Why does it require collaboration among several industry sectors (*e.g.* pharma, vaccines, biotech, medical devices, in vitro diagnostics, radiotherapy, medical imaging health ICT)?

Why does it require collaboration between private (industry) and public partners (*e.g.* academia, healthcare practitioners, patients, regulators)?

Developing objective, quantifiable biomarkers for enrichment strategies require public-private partnerships and patient-centric efforts. This can be achieved in Europe thanks to pre-existing databases (clinical trials, cohorts) as well as networks of academic/clinical centers specialised and organized in national and international networks, sharing similar assessments tools which can be used to discover and validate signatures using clinical and digital tools, blood based and brain imaging biomarkers for stratifying psychiatric disorders. This project will reinforce collaboration between scientists, industrials and patients on the discovery and validation of biomarkers. Regulators should also be included to discuss innovative diagnostic strategies, and clinical trials design, requirements to validate biomarkers for stratification or to be used as endpoints. Patient's associations are already associated with academic entities on the challenges of Precision Psychiatry, and they will be participating to the research and clinical designs.

Why is the contribution of industry needed to achieve the expected impacts?

Industry contribution is needed to develop enrichment biomarkers to identify subgroups of patients and appropriate endpoints for future clinical trials. This should increase study efficiency, produces larger effect sizes, and permits the use of a smaller study population

The industry is needed to develop blood-based biomarkers based on proteomics, metabolomics, cell-based assay, brain imaging, digital assessments and/or to explore biomarkers predicting efficacy in past clinical trials. By leveraging the combined strengths of academia, research institutions, and healthcare industry, this project can significantly accelerate the development of new diagnostic tools and personalized therapies for mental disorders. Both established enterprises and start-ups that focus on the fields of biomarker discovery, drug development or repurposing, will greatly benefit from this project.

Topic idea to IHI - Reference Number: TI_001222

Are you submitting the idea:
☐ **in your personal capacity?**
☒ **on behalf of an organisation?**

Please indicate the name of the group organisation: Amsterdam UMC

Please select from the list below the type of stakeholders your organization represents:
Research/higher or secondary education organisation (private or public)

1   Title of your idea

Please provide a short title that accurately reflects the objective(s) of your idea:
INNOVATIVE ENRICHMENT STRATEGIES FOR MENTAL DISORDERS USING OBJECTIVE, QUANTIFIABLE PREDICTIVE BIOMARKERS FOR THERAPEUTIC INTERVENTIONS

2   Scope

Explain the specific challenges/problems to be addressed by your idea and how these affect relevant stakeholders, taking into account what is already known and/or available in the field:
Current therapeutic interventions for major psychiatric disorders only lead to remission in approximately one third of patients and partial remission in another third. This heterogeneity in treatment outcomes is thought to reflect the low accuracy of current categorical diagnostic frameworks. In addition, a large fraction of patients are not diagnosed or with delay, while clinical trials fail because of absence of objective endpoints to asses efficacy.

Developing predictive enrichment strategies will aid academia and industry to optimise future trial designs by guiding selection of the most appropriate patient population and outcome measures, using objective, measurable, quantifiable, valid biomarkers based on uni- or multi-modal patient-centered data such as cognitive batteries, blood-based omics, brain imaging, electrophysiology,….which can be used to predict treatment responses. By shifting away from the traditional one-size-fits-all approach, innovative enrichment strategies will enhance the signal-to-noise ratio of existing or new therapeutic strategies, and

The goal of this call would thus be to develop and validate robust, reproducible, sensitive to clinical changes, predictive biomarkers to be added to current diagnostic categories, possibly across psychiatric disorders, based on previously identified abnormalities. This can be done through re-analysis of existing cohorts or previous trial data, or through the development of new cohorts or RCTs in enriched or stratified populations. Examples include pharmacogenomics to predict drug responses, electrophysiology to identify brain circuits, brain stimulation using brain imaging, immune dysfunctions targeting inflammation, metabolism, gut dysbiosis, mitochondria...

In summary, mental disorders represent the principal global cause of handicap (WHO, 2020) and a

large unmet clinical need. The proposed enrichment strategies will optimise future clinical trials, thereby increasing interest among industry to (re-)enter the field and tackle these needs

Please indicate which IHI specific objective(s) (SO), as described in the IHI Strategic Research and Innovation Agenda (SRIA), your idea addresses:

["SO1: contribute towards a better understanding of the determinants of health and priority disease areas"
"SO2: integrate fragmented health research and innovation efforts bringing together health industry sectors and other stakeholders, focusing on unmet public health needs, to enable the development of tools, data, platforms, technologies and processes for improved prediction, prevention, interception, diagnosis, treat- ment and management of diseases, meeting the needs of end-users"]

Please select the keywords that are most relevant to your idea:

["Mental health"
"Prediction"
"Prevention"
"Immune system diseases"
"Disease management"
"Treatment"
"Metabolic diseases"
"Digital health"
"Health technology"]

In alignment with the IHI specific objective(s) selected above, specify the objectives of your idea:

Following the established principles of precision psychiatry, innovation should improve discovery and validation of enrichment biomarkers to development robust, reproducible and sensitive biomarkers to improve diagnosis and clinical trials. This should reduce individual suffering and economic cost.
Mental disorders constitute five of the top ten causes of disability. It is estimated that over 27% of the general population will experience mental disorders inducing a total cost across Europe above 4% of GDP.
This project will
1. contribute to the creation of an EU-wide Brain and Mental Health research and innovation ecosystem that will facilitate translation of scientific knowledge into diagnostic and therapeutic innovations
2. foster the development of safe, effective, people-centred, cost-effective predictive enrichment strategies that respond to strategic unmet public health needs across psychiatric disorders.
3. drive cross-sectoral health innovation for a globally competitive European health industry
4. create mentorship and capacity development opportunities to facilitate sustainability and implementation

3   Expected <u>impacts</u> to be achieved by your idea

Briefly describe the expected impacts to be achieved by your idea, ensuring that they contribute to IHI general and relevant specific <u>objectives</u>, as described in the IHI SRIA:

Impacts are wider long-term effects on society (including the environment), the economy and science, enabled by the outcomes of R&I investments. Impacts generally occur sometime after the end of the project, e.g. successful implementation of digital solutions supporting people-centred care.

IHI general objectives: 1. contribute towards the creation of an EU-wide health research and innovation ecosystem that facilitates translation of scientific knowledge into innovations, notably by launching at least 30 large-scale, cross-sectoral projects, focussing on health innovations; 2. foster the development of safe, effective, people-centred and cost-effective innovations that respond to strategic unmet public health needs, by exhibiting, in at least 5 examples, the feasibility of integrating health care products or services, with demonstrated suitability for uptake by health care systems. The related projects should address the prevention, diagnosis, treatment and/or management of diseases affecting the EU population, including contribution to 'Europe's Beating Cancer Plan'; 3. drive cross-sectoral health innovation for a globally competitive European health industry and contribute to reaching the objectives of the new Industrial Strategy for Europe and the Pharmaceutical Strategy for Europe.

Developing innovative predictive enrichment strategies focusing for homogeneous subgroups of mental disorders is based on reinforced private-public collaboration towards
-        Discovery and validation of objective, quantifiable, targetable, robust, reproducible biomarkers ,with operational delivery stratification biomarkers using existing data or future data collection from longitudinal cohort studies or clinical trials data from Europe and beyond
-        In silico selection, of mechanisms-based treatments to be tested in stratified homogeneous subgroups of patients
-        Setting up European infrastructures to facilitate and support enrichment strategies in clinical trials based on the construction of a European Network of expert/excellence centers for mental disorders and on a robust data infrastructure allowing data sharing.
-        Discussion with regulatory agencies, consumers to share the results
-        Improvement of patient's prognosis and reduction of overall cost

4   Why should your idea become an IHI call topic?

Explain why collaboration through a cross-sectoral and multidisciplinary public private partnership is needed in particular:

Why does it require collaboration among several industry sectors
(*e.g.* **pharma, vaccines, biotech, medical devices, in vitro diagnostics, radiotherapy, medical imaging health ICT)?**

Why does it require collaboration between private (industry) and public partners
(*e.g.* **academia, healthcare practitioners, patients, regulators)?**

Developing innovative predictive enrichment strategies focusing for homogeneous subgroups of mental disorders is based on reinforced private-public collaboration towards
-        Discovery and validation of objective, quantifiable, targetable, robust, reproducible biomarkers ,with operational delivery stratification biomarkers using existing data or future data collection from longitudinal cohort studies or clinical trials data from Europe and beyond
-        In silico selection, of mechanisms-based treatments to be tested in stratified homogeneous subgroups of patients
-        Setting up European infrastructures to facilitate and support enrichment strategies in clinical trials based on the construction of a European Network of expert/excellence centers for mental disorders and on a robust data infrastructure allowing data sharing.
-        Discussion with regulatory agencies, consumers to share the results
-        Improvement of patient's prognosis and reduction of overall cost

Why is the contribution of industry needed to achieve the expected impacts?

Industry contribution is needed to develop enrichment biomarkers to identify subgroups of patients and appropriate endpoints for future clinical trials. This should increase study efficiency, produces larger effect sizes, and permits the use of a smaller study population

The industry is needed to develop blood-based biomarkers based on proteomics, metabolomics, cell-based assay, brain imaging, digital assessments and/or to explore biomarkers predicting efficacy in past clinical trials. By leveraging the combined strengths of academia, research institutions, and healthcare industry, this project can significantly accelerate the development of new diagnostic tools and personalized therapies for mental disorders. Both established enterprises and start-ups that focus on the fields of biomarker discovery, drug development or repurposing, will greatly benefit from this project.

Topic Idea to IHI - Reference Number: TI_001223

Are you submitting the idea:
☐ **in your personal capacity?**
☒ **on behalf of an organisation?**

Please indicate the name of the group organisation: CIBER

Please select from the list below the type of stakeholders your organization represents:
Research/higher or secondary education organisation (private or public)

1 Title of your idea

Please provide a short title that accurately reflects the objective(s) of your idea:
INNOVATIVE ENRICHMENT STRATEGIES FOR MENTAL DISORDERS USING OBJECTIVE,
QUANTIFIABLE PREDICTIVE BIOMARKERS FOR THERAPEUTIC INTERVENTIONS.

2 Scope

Explain the specific challenges/problems to be addressed by your idea and how these affect relevant stakeholders, taking into account what is already known and/or available in the field:
Current therapeutic interventions for major psychiatric disorders only lead to remission in approximately one third of patients and partial remission in another third. This heterogeneity in treatment outcomes is thought to reflect the low accuracy of current categorical diagnostic frameworks. In addition, a large fraction of patients are not diagnosed or with delay, while clinical trials fail because of absence of objective endpoints to asses efficacy.
Developing predictive enrichment strategies will aid academia and industry to optimise future trial designs by guiding selection of the most appropriate patient population and outcome measures, using objective, measurable, quantifiable, valid biomarkers based on uni- or multi-modal patient-centered data such as cognitive batteries, blood-based omics, brain imaging, electrophysiology,….which can be used to predict treatment responses. By shifting away from the traditional one-size-fits-all approach, innovative enrichment strategies will enhance the signal-to-noise ratio of existing or new therapeutic strategies.
The goal of this call would thus be to develop and validate robust, reproducible, sensitive to clinical changes, predictive biomarkers to be added to current diagnostic categories, possibly across psychiatric disorders, based on previously identified abnormalities. This can be done through re-analysis of existing cohorts or previous trial data, or through the development of new cohorts or RCTs in enriched or stratified populations. Examples include pharmacogenomics to predict drug responses, electrophysiology to identify brain circuits, brain stimulation using brain imaging, immune dysfunctions targeting inflammation, metabolism, gut dysbiosis, mitochondria...
In summary, mental disorders represent the principal global cause of handicap (WHO, 2020) and a large unmet clinical need. The proposed enrichment strategies will optimise future clinical trials, thereby increasing interest among industry to (re-)enter the field and tackle these needs. The ultimate goal is to bring the right treatment to the right patient at the right time, achieving better health

outcomes and reducing the personal, societal and economic burden of mental illnesses.

Please indicate which IHI specific objective(s) (SO), as described in the IHI Strategic Research and Innovation Agenda (SRIA), your idea addresses:

["SO1: contribute towards a better understanding of the determinants of health and priority disease areas"
"SO2: integrate fragmented health research and innovation efforts bringing together health industry sectors and other stakeholders, focusing on unmet public health needs, to enable the development of tools, data, platforms, technologies and processes for improved prediction, prevention, interception, diagnosis, treat- ment and management of diseases, meeting the needs of end-users"]

Please select the keywords that are most relevant to your idea:

["Metabolic diseases"
"Mental health"
"Prediction"
"Prevention"
"Diagnosis"
"Treatment"
"Disease management"
"Digital health"
"Health technology"
"Immune system diseases"]

In alignment with the IHI specific objective(s) selected above, specify the objectives of your idea:

Following the established principles of precision psychiatry, innovation should improve discovery and validation of enrichment biomarkers to development robust, reproducible and sensitive biomarkers to improve diagnosis and clinical trials. This should reduce individual suffering and economic cost.
Mental disorders constitute five of the top ten causes of disability. It is estimated that over 27% of the general population will experience mental disorders inducing a total cost across Europe above 4% of GDP.
This project will
1. contribute to the creation of an EU-wide Brain and Mental Health research and innovation ecosystem that will facilitate translation of scientific knowledge into diagnostic and therapeutic innovations
2. foster the development of safe, effective, people-centred, cost-effective predictive enrichment strategies that respond to strategic unmet public health needs across psychiatric disorders.
3. drive cross-sectoral health innovation for a globally competitive European health industry
4. create mentorship and capacity development opportunities to facilitate sustainability and implementation

3 Expected impacts to be achieved by your idea

Briefly describe the expected impacts to be achieved by your idea, ensuring that they contribute to IHI general and relevant specific objectives, as described in the IHI SRIA:

Impacts are wider long-term effects on society (including the environment), the economy and science, enabled by the outcomes of R&I investments. Impacts generally occur sometime after the end of the project, e.g. successful implementation of digital solutions supporting people-centred care.

IHI general objectives: 1. contribute towards the creation of an EU-wide health research and innovation ecosystem that facilitates translation of scientific knowledge into innovations, notably by launching at least 30 large-scale, cross-sectoral projects, focussing on health innovations; 2. foster the development of safe, effective, people-centred and cost-effective innovations that respond to strategic unmet public health needs, by exhibiting, in at least 5 examples, the feasibility of integrating health care products or services, with demonstrated suitability for uptake by health care systems. The related projects should address the prevention, diagnosis, treatment and/or management of diseases affecting the EU population, including contribution to 'Europe's Beating Cancer Plan'; 3. drive cross-sectoral health innovation for a globally competitive European health industry and contribute to reaching the objectives of the new Industrial Strategy for Europe and the Pharmaceutical Strategy for Europe.

Developing innovative predictive enrichment strategies focusing for homogeneous subgroups of mental disorders is based on reinforced private-public collaboration towards
-        Discovery and validation of objective, quantifiable, targetable, robust, reproducible biomarkers ,with operational delivery stratification biomarkers using existing data or future data collection from longitudinal cohort studies or clinical trials data from Europe and beyond
-        In silico selection, of mechanisms-based treatments to be tested in stratified homogeneous subgroups of patients
-        Setting up European infrastructures to facilitate and support enrichment strategies in clinical trials based on the construction of a European Network of expert/excellence centers for mental disorders and on a robust data infrastructure allowing data sharing.
-        Discussion with regulatory agencies, consumers to share the results
-        Improvement of patient's prognosis and reduction of overall cost.

4 Why should your idea become an IHI call topic?

Explain why collaboration through a cross-sectoral and multidisciplinary public private partnership is needed in particular:

Why does it require collaboration among several industry sectors
(*e.g.* **pharma, vaccines, biotech, medical devices, in vitro diagnostics, radiotherapy, medical imaging health ICT)?**

Why does it require collaboration between private (industry) and public partners
(*e.g.* **academia, healthcare practitioners, patients, regulators)?**

Developing objective, quantifiable biomarkers for enrichment strategies require public-private partnerships and patient-centric efforts. This can be achieved in Europe thanks to pre-existing databases (clinical trials, cohorts) as well as networks of academic/clinical centers specialised and organized in national and international networks, sharing similar assessments tools which can be used to discover and validate signatures using clinical and digital tools, blood based and brain imaging biomarkers for stratifying psychiatric disorders. This project will reinforce collaboration between scientists, industrials and patients on the discovery and validation of biomarkers. Regulators should also be included to discuss innovative diagnostic strategies, and clinical trials design, requirements to validate biomarkers for stratification or to be used as endpoints. Patient's associations are already associated with academic entities on the challenges of Precision Psychiatry, and they will be participating to the research and clinical designs.

Why is the contribution of industry needed to achieve the expected impacts?

Industry contribution is needed to develop enrichment biomarkers to identify subgroups of patients and appropriate endpoints for future clinical trials. This should increase study efficiency, produces larger effect sizes, and permits the use of a smaller study population

 The industry is needed to develop blood-based biomarkers based on proteomics, metabolomics, cell-based assay, brain imaging, digital assessments and/or to explore biomarkers predicting efficacy in past clinical trials. By leveraging the combined strengths of academia, research institutions, and healthcare industry, this project can significantly accelerate the development of new diagnostic tools and personalized therapies for mental disorders. Both established enterprises and start-ups that focus on the fields of biomarker discovery, drug development or repurposing, will greatly benefit from this project.

Topic Idea to IHI - Reference Number: TI_001224

Are you submitting the idea:
☐ **in your personal capacity?**
☒ **on behalf of an organisation?**

Please indicate the name of the group organisation: Università degli Studi di Milano

Please select from the list below the type of stakeholders your organization represents:
    Research/higher or secondary education organisation (private or public)

1   Title of your idea

Please provide a short title that accurately reflects the objective(s) of your idea:
INNOVATIVE ENRICHMENT STRATEGIES FOR MENTAL DISORDERS USING OBJECTIVE,
    QUANTIFIABLE PREDICTIVE BIOMARKERS FOR THERAPEUTIC INTERVENTIONS

2   Scope

Explain the specific challenges/problems to be addressed by your idea and how these affect relevant stakeholders, taking into account what is already known and/or available in the field:
Current therapeutic interventions for major psychiatric disorders only lead to remission in approximately one third of patients and partial remission in another third. This heterogeneity in treatment outcomes is thought to reflect the low accuracy of current categorical diagnostic frameworks. In addition, a large fraction of patients are not diagnosed or with delay, while clinical trials fail because of absence of objective endpoints to asses efficacy.
Developing predictive enrichment strategies will aid academia and industry to optimise future trial designs by guiding selection of the most appropriate patient population and outcome measures, using objective, measurable, quantifiable, valid biomarkers based on uni- or multi-modal patient-centered data such as cognitive batteries, blood-based omics, brain imaging, electrophysiology,….which can be used to predict treatment responses. By shifting away from the traditional one-size-fits-all approach, innovative enrichment strategies will enhance the signal-to-noise ratio of existing or new therapeutic strategies, and
The goal of this call would thus be to develop and validate robust, reproducible, sensitive to clinical changes, predictive biomarkers to be added to current diagnostic categories, possibly across psychiatric disorders, based on previously identified abnormalities. This can be done through re-analysis of existing cohorts or previous trial data, or through the development of new cohorts or RCTs in enriched or stratified populations. Examples include pharmacogenomics to predict drug responses, electrophysiology to identify brain circuits, brain stimulation using brain imaging, immune dysfunctions targeting inflammation, metabolism, gut dysbiosis, mitochondria...
In summary, mental disorders represent the principal global cause of handicap (WHO, 2020) and a large unmet clinical need. The proposed enrichment strategies will optimise future clinical trials, thereby increasing interest among industry to (re-)enter the field and tackle these needs.

Please indicate which IHI specific objective(s) (SO), as described in the IHI Strategic Research and Innovation Agenda (SRIA), your idea addresses:

["SO1: contribute towards a better understanding of the determinants of health and priority disease areas"
"SO2: integrate fragmented health research and innovation efforts bringing together health industry sectors and other stakeholders, focusing on unmet public health needs, to enable the development of tools, data, platforms, technologies and processes for improved prediction, prevention, interception, diagnosis, treat- ment and management of diseases, meeting the needs of end-users"]

Please select the keywords that are most relevant to your idea:
["Mental health"
"Immune system diseases"
"Metabolic diseases"
"Prediction"
"Diagnosis"
"Treatment"
"Disease management"
"Digital health"
"Health technology"]

In alignment with the IHI specific objective(s) selected above, specify the objectives of your idea:

Following the established principles of precision psychiatry, innovation should improve discovery and validation of enrichment biomarkers to development robust, reproducible and sensitive biomarkers to improve diagnosis and clinical trials. This should reduce individual suffering and economic cost.
Mental disorders constitute five of the top ten causes of disability. It is estimated that over 27% of the general population will experience mental disorders inducing a total cost across Europe above 4% of GDP.
This project will:
1. contribute to the creation of an EU-wide Brain and Mental Health research and innovation ecosystem that will facilitate translation of scientific knowledge into diagnostic and therapeutic innovations;
2. foster the development of safe, effective, people-centred, cost-effective predictive enrichment strategies that respond to strategic unmet public health needs across psychiatric disorders;
3. drive cross-sectoral health innovation for a globally competitive European health industry;
4. create mentorship and capacity development opportunities to facilitate sustainability and implementation.

3   Expected <u>impacts</u> to be achieved by your idea

Briefly describe the expected impacts to be achieved by your idea, ensuring that they contribute to IHI general and relevant specific <u>objectives</u>, as described in the IHI SRIA:

Impacts are wider long-term effects on society (including the environment), the economy and science, enabled by the outcomes of R&I investments. Impacts generally occur sometime after the end of the project, e.g. successful implementation of digital solutions supporting people-centred care.

IHI general objectives: 1. contribute towards the creation of an EU-wide health research and innovation ecosystem that facilitates translation of scientific knowledge into innovations, notably by launching at least 30 large-scale, cross-sectoral projects, focussing on health innovations; 2. foster the development of safe, effective, people-centred and cost-effective innovations that respond to strategic unmet public health needs, by exhibiting, in at least 5 examples, the feasibility of integrating health care products or services, with demonstrated suitability for uptake by health care systems. The related projects should address the prevention, diagnosis, treatment and/or management of diseases affecting the EU population, including contribution to 'Europe's Beating Cancer Plan'; 3. drive cross-sectoral health innovation for a globally competitive European health industry and contribute to reaching the objectives of the new Industrial Strategy for Europe and the Pharmaceutical Strategy for Europe.

Developing innovative predictive enrichment strategies focusing for homogeneous subgroups of mental disorders is based on reinforced private-public collaboration towards:
-        discovery and validation of objective, quantifiable, targetable, robust, reproducible biomarkers ,with operational delivery stratification biomarkers using existing data or future data collection from longitudinal cohort studies or clinical trials data from Europe and beyond;
-        in silico selection, of mechanisms-based treatments to be tested in stratified homogeneous subgroups of patients;
-        setting up European infrastructures to facilitate and support enrichment strategies in clinical trials based on the construction of a European Network of expert/excellence centers for mental disorders and on a robust data infrastructure allowing data sharing;
-        discussion with regulatory agencies, consumers to share the results;
-        improvement of patient's prognosis and reduction of overall cost.

4   Why should your idea become an IHI call topic?

Explain why collaboration through a cross-sectoral and multidisciplinary public private partnership is needed in particular:

Why does it require collaboration among several industry sectors
(*e.g.* **pharma, vaccines, biotech, medical devices, in vitro diagnostics, radiotherapy, medical imaging health ICT)?**

Why does it require collaboration between private (industry) and public partners
(*e.g.* **academia, healthcare practitioners, patients, regulators)?**

Developing objective, quantifiable biomarkers for enrichment strategies require public-private partnerships and patient-centric efforts. This can be achieved in Europe thanks to pre-existing databases (clinical trials, cohorts) as well as networks of academic/clinical centers specialised and organized in national and international networks, sharing similar assessments tools which can be used to discover and validate signatures using clinical and digital tools, blood based and brain imaging biomarkers for stratifying psychiatric disorders. This project will reinforce collaboration between scientists, industrials and patients on the discovery and validation of biomarkers. Regulators should also be included to discuss innovative diagnostic strategies, and clinical trials design, requirements to validate biomarkers for stratification or to be used as endpoints. Patient's associations are already associated with academic entities on the challenges of Precision Psychiatry, and they will be participating to the research and clinical designs.

Why is the contribution of industry needed to achieve the expected impacts?

Industry contribution is needed to develop enrichment biomarkers to identify subgroups of patients and appropriate endpoints for future clinical trials. This should increase study efficiency, produces larger effect sizes, and permits the use of a smaller study population.

The industry is needed to develop blood-based biomarkers based on proteomics, metabolomics, cell-based assay, brain imaging, digital assessments and/or to explore biomarkers predicting efficacy in past clinical trials. By leveraging the combined strengths of academia, research institutions, and healthcare industry, this project can significantly accelerate the development of new diagnostic tools and personalized therapies for mental disorders. Both established enterprises and start-ups that focus on the fields of biomarker discovery, drug development or repurposing, will greatly benefit from this project.

Topic Idea to IHI - Reference Number: TI_001225

Are you submitting the idea:
☐ **in your personal capacity?**
☒ **on behalf of an organisation?**

Please indicate the name of the group organisation: Fondation FondaMental

Please select from the list below the type of stakeholders your organization represents:
Charity/foundation

1 Title of your idea

Please provide a short title that accurately reflects the objective(s) of your idea:
INNOVATIVE ENRICHMENT STRATEGIES FOR MENTAL DISORDERS USING OBJECTIVE, QUANTIFIABLE PREDICTIVE BIOMARKERS FOR THERAPEUTIC INTERVENTIONS.

2 Scope

Explain the specific challenges/problems to be addressed by your idea and how these affect relevant stakeholders, taking into account what is already known and/or available in the field:
Current therapeutic interventions for major psychiatric disorders only lead to remission in approximately one third of patients and partial remission in another third. This heterogeneity in treatment outcomes is thought to reflect the low accuracy of current categorical diagnostic frameworks. In addition, a large fraction of patients is not diagnosed or with delay, while clinical trials fail because of absence of objective endpoints to assess efficacy. Developing predictive enrichment strategies will aid academia and industry to optimise future trial designs by guiding selection of the most appropriate patient population and outcome measures, using objective, measurable, quantifiable, valid biomarkers based on uni- or multi-modal patient-centered data such as cognitive batteries, blood-based omics, brain imaging, electrophysiology, which can be used to predict treatment responses. By shifting away from the traditional one-size-fits-all approach, innovative enrichment strategies will enhance the signal-to-noise ratio of existing or new therapeutic strategies. The goal would thus be to develop and validate robust, reproducible, sensitive to clinical changes, predictive biomarkers to be added to current diagnostic categories, possibly across psychiatric disorders, based on previously identified abnormalities. This can be done through re-analysis of existing cohorts or previous trial data, or through the development of new cohorts or RCTs in enriched or stratified populations. Examples include pharmacogenomics to predict drug responses, electrophysiology to identify brain circuits, brain stimulation using brain imaging, immune dysfunctions targeting inflammation, metabolism, gut dysbiosis, mitochondria. The proposed enrichment strategies will optimise future clinical trials, increasing interest among industry to (re-)enter the field and tackle these needs.

Please indicate which IHI specific objective(s) (SO), as described in the IHI Strategic Research and Innovation Agenda (SRIA), your idea addresses:

["SO1: contribute towards a better understanding of the determinants of health and priority disease areas"
"SO2: integrate fragmented health research and innovation efforts bringing together health industry sectors and other stakeholders, focusing on unmet public health needs, to enable the development of tools, data, platforms, technologies and processes for improved prediction, prevention, interception, diagnosis, treat- ment and management of diseases, meeting the needs of end-users"]

Please select the keywords that are most relevant to your idea:
["Digital health"
"Health technology"
"Disease management"
"Treatment"
"Diagnosis"
"Prediction"
"Prevention"
"Mental health"
"Metabolic diseases"
"Immune system diseases"]

In alignment with the IHI specific objective(s) selected above, specify the objectives of your idea:

Following the established principles of precision psychiatry, innovation should improve discovery and validation of enrichment biomarkers to development robust, reproducible and sensitive biomarkers to improve diagnosis and clinical trials. This should reduce individual suffering and economic cost. Mental disorders constitute five of the top ten causes of disability. It is estimated that over 27% of the general population will experience mental disorders inducing a total cost across Europe above 4% of GDP.
This project will
1. contribute to the creation of an EU-wide Brain and Mental Health research and innovation ecosystem that will facilitate translation of scientific knowledge into diagnostic and therapeutic innovations
2. foster the development of safe, effective, people-centred, cost-effective predictive enrichment strategies that respond to strategic unmet public health needs across psychiatric disorders.
3. drive cross-sectoral health innovation for a globally competitive European health industry
4. create mentorship and capacity development opportunities to facilitate sustainability and implementation.

3   Expected <u>impacts</u> to be achieved by your idea

Briefly describe the expected impacts to be achieved by your idea, ensuring that they contribute to IHI general and relevant specific <u>objectives</u>, as described in the IHI SRIA:

Impacts are wider long-term effects on society (including the environment), the economy and science, enabled by the outcomes of R&I investments. Impacts generally occur sometime after the end of the project, e.g. successful implementation of digital solutions supporting people-centred care.

IHI general objectives: 1. contribute towards the creation of an EU-wide health research and innovation ecosystem that facilitates translation of scientific knowledge into innovations, notably by launching at least 30 large-scale, cross-sectoral projects, focussing on health innovations; 2. foster the development of safe, effective, people-centred and cost-effective innovations that respond to strategic unmet public health needs, by exhibiting, in at least 5 examples, the feasibility of integrating health care products or services, with demonstrated suitability for uptake by health care systems. The related projects should address the prevention, diagnosis, treatment and/or management of diseases affecting the EU population, including contribution to 'Europe's Beating Cancer Plan'; 3. drive cross-sectoral health innovation for a globally competitive European health industry and contribute to reaching the objectives of the new Industrial Strategy for Europe and the Pharmaceutical Strategy for Europe.

Developing innovative predictive enrichment strategies focusing for homogeneous subgroups of mental disorders is based on reinforced private-public collaboration towards:

- Discovery and validation of objective, quantifiable, targetable, robust, reproducible biomarkers ,with operational delivery stratification biomarkers using existing data or future data collection from longitudinal cohort studies or clinical trials data from Europe and beyond
- In silico selection, of mechanisms-based treatments to be tested in stratified homogeneous subgroups of patients
- Setting up European infrastructures to facilitate and support enrichment strategies in clinical trials based on the construction of a European Network of expert/excellence centers for mental disorders and on a robust data infrastructure allowing data sharing.
- Discussion with regulatory agencies, consumers to share the results
- Improvement of patient's prognosis and reduction of overall costs

4   Why should your idea become an IHI call topic?

Explain why collaboration through a cross-sectoral and multidisciplinary public private partnership is needed in particular:

Why does it require collaboration among several industry sectors (*e.g.* pharma, vaccines, biotech, medical devices, in vitro diagnostics, radiotherapy, medical imaging health ICT)?

Why does it require collaboration between private (industry) and public partners (*e.g.* academia, healthcare practitioners, patients, regulators)?

Developing objective, quantifiable biomarkers for enrichment strategies require public-private partnerships and patient-centric efforts. This can be achieved in Europe thanks to pre-existing databases (clinical trials, cohorts) as well as networks of academic/clinical centers specialised and organised in national and international networks, sharing similar assessments tools which can be used to discover and validate signatures using clinical and digital tools, blood based and brain imaging biomarkers for stratifying psychiatric disorders. This project will reinforce collaboration between scientists, industrials and patients on the discovery and validation of biomarkers. Regulators should also be included to discuss innovative diagnostic strategies, and clinical trials design, requirements to validate biomarkers for stratification or to be used as endpoints. Patient's associations are already associated with academic entities on the challenges of Precision Psychiatry, and they will be participating to the research and clinical designs.

Why is the contribution of industry needed to achieve the expected impacts?

Industry contribution is needed to develop enrichment biomarkers to identify subgroups of patients and appropriate endpoints for future clinical trials. This should increase study efficiency, produces larger effect sizes, and permits the use of a smaller study population

The industry is needed to develop blood-based biomarkers based on proteomics, metabolomics, cell-based assay, brain imaging, digital assessments and/or to explore biomarkers predicting efficacy in past clinical trials. By leveraging the combined strengths of academia, research institutions, and healthcare industry, this project can significantly accelerate the development of new diagnostic tools and personalized therapies for mental disorders. Both established enterprises and start-ups that focus on the fields of biomarker discovery, drug development or repurposing, will greatly benefit from this project.

Topic Idea to IHI - Reference Number: TI_001226

Are you submitting the idea:
☐ **in your personal capacity?**
☒ **on behalf of an organisation?**

Please select from the list below the type of stakeholders your organization represents: Large company (For-profit legal entity)

1 Title of your idea

Please provide a short title that accurately reflects the objective(s) of your idea:
INNOVATIVE ENRICHMENT STRATEGIES FOR MENTAL DISORDERS USING OBJECTIVE, QUANTIFIABLE PREDICTIVE BIOMARKERS FOR THERAPEUTIC INTERVENTIONS

2 Scope

Explain the specific challenges/problems to be addressed by your idea and how these affect relevant stakeholders, taking into account what is already known and/or available in the field:
Current therapeutic interventions for major psychiatric disorders only lead to remission in approximately one third of patients and partial remission in another third. This heterogeneity in treatment outcomes is thought to reflect the low accuracy of current categorical diagnostic frameworks. In addition, a large fraction of patients is not diagnosed or with delay, while clinical trials fail because of absence of objective endpoints to assess efficacy.

Developing predictive enrichment strategies will aid academia and industry to optimize future trial designs by guiding selection of the most appropriate patient population and outcome measures, using objective, measurable, quantifiable, valid biomarkers based on uni- or multi-modal patient-centered data such as cognitive batteries, blood-based omics, brain imaging, and electrophysiology, which can be used to predict treatment responses. By shifting away from the traditional one-size-fits-all approach, innovative enrichment strategies will enhance the signal-to-noise ratio of existing or new therapeutic strategies, and

The goal of this call would thus be to develop and validate robust, reproducible, sensitive to clinical changes, predictive biomarkers to be added to current diagnostic categories, possibly across psychiatric disorders, based on previously identified abnormalities. This can be done through re-analysis of existing cohorts or previous trial data, or through the development of new cohorts or RCTs in enriched or stratified populations. Examples include proteomics, pharmacogenomics to predict drug responses, electrophysiology to identify brain circuits, brain stimulation using brain imaging, immune dysfunctions targeting inflammation, metabolism, gut dysbiosis, mitochondria etc.

In summary, mental disorders represent the principal global cause of handicap (WHO, 2020) and a large unmet clinical need. The proposed enrichment strategies will optimize future clinical trials,

thereby increasing interest among industry to (re-)enter the field and tackle these needs. The ultimate goal is to bring the right treatment to the right patient at the right time, achieving better health outcomes and reducing the personal, societal and economic burden of mental illnesses.

Please indicate which IHI specific objective(s) (SO), as described in the IHI Strategic Research and Innovation Agenda (SRIA), your idea addresses:

["SO1: contribute towards a better understanding of the determinants of health and priority disease areas"
"SO2: integrate fragmented health research and innovation efforts bringing together health industry sectors and other stakeholders, focusing on unmet public health needs, to enable the development of tools, data, platforms, technologies and processes for improved prediction, prevention, interception, diagnosis, treat- ment and management of diseases, meeting the needs of end-users"]

Please select the keywords that are most relevant to your idea:

["Mental health"
"Immune system diseases"
"Metabolic diseases"
"Prediction"
"Prevention"
"Paediatric"
"Diagnosis"
"Treatment"
"Disease management"
"Digital health"
"Health technology"
"Interception"]

In alignment with the IHI specific objective(s) selected above, specify the objectives of your idea:

Following the established principles of precision psychiatry, innovation should improve discovery and validation of enrichment biomarkers to development robust, reproducible and sensitive biomarkers to improve diagnosis and clinical trials. This should reduce individual suffering and economic cost. Mental disorders constitute five of the top ten causes of disability. It is estimated that over 27% of the general population will experience mental disorders inducing a total cost across Europe above 4% of GDP.

This project will

1. contribute to the creation of an EU-wide Brain and Mental Health research and innovation ecosystem that will facilitate translation of scientific knowledge into diagnostic and therapeutic innovations

2. foster the development of safe, effective, people-centred, cost-effective predictive enrichment strategies that respond to strategic unmet public health needs across psychiatric disorders.

3. drive cross-sectoral health innovation for a globally competitive European health industry

4. create mentorship and capacity development opportunities to facilitate sustainability and implementation

3   Expected <u>impacts</u> to be achieved by your idea

Briefly describe the expected impacts to be achieved by your idea, ensuring that they contribute to IHI general and relevant specific <u>objectives</u>, as described in the IHI SRIA:

Impacts are wider long-term effects on society (including the environment), the economy and science, enabled by the outcomes of R&I investments. Impacts generally occur sometime after the end of the project, e.g. successful implementation of digital solutions supporting people-centred care.

IHI general objectives: 1. contribute towards the creation of an EU-wide health research and innovation ecosystem that facilitates translation of scientific knowledge into innovations, notably by launching at least 30 large-scale, cross-sectoral projects, focussing on health innovations; 2. foster the development of safe, effective, people-centred and cost-effective innovations that respond to strategic unmet public health needs, by exhibiting, in at least 5 examples, the feasibility of integrating health care products or services, with demonstrated suitability for uptake by health care systems. The related projects should address the prevention, diagnosis, treatment and/or management of diseases affecting the EU population, including contribution to 'Europe's Beating Cancer Plan'; 3. drive cross-sectoral health innovation for a globally competitive European health industry and contribute to reaching the objectives of the new Industrial Strategy for Europe and the Pharmaceutical Strategy for Europe.

Developing innovative predictive enrichment strategies focusing for homogeneous subgroups of mental disorders is based on reinforced private-public collaboration towards

-        Discovery and validation of objective, quantifiable, targetable, robust, reproducible biomarkers ,with operational delivery stratification biomarkers using existing data or future data collection from longitudinal cohort studies or clinical trials data from Europe and beyond

-        In silico selection, of mechanisms-based treatments to be tested in stratified homogeneous subgroups of patients

-        Setting up European infrastructures to facilitate and support enrichment strategies in clinical trials based on the construction of a European Network of expert/excellence centers for mental disorders and on a robust data infrastructure allowing data sharing.

-        Discussion with regulatory agencies, consumers to share the results

-        Improvement of patient's prognosis and reduction of overall cost

4   Why should your idea become an IHI call topic?

Explain why collaboration through a cross-sectoral and multidisciplinary public private partnership is needed in particular:

Why does it require collaboration among several industry sectors (*e.g.* pharma, vaccines, biotech, medical devices, in vitro diagnostics, radiotherapy, medical imaging health ICT)?

Why does it require collaboration between private (industry) and public partners (*e.g.* academia, healthcare practitioners, patients, regulators)?

Developing objective, quantifiable biomarkers for enrichment strategies require public-private partnerships and patient-centric efforts. This can be achieved in Europe thanks to pre-existing databases (clinical trials, cohorts) as well as networks of academic/clinical centers specialised and organized in national and international networks, sharing similar assessments tools which can be used to discover and validate signatures using clinical and digital tools, blood based and brain imaging biomarkers for stratifying psychiatric disorders.

This project will reinforce collaboration between scientists, industrials and patients on the discovery and validation of biomarkers. Regulators should also be included to discuss innovative diagnostic strategies, and clinical trials design, requirements to validate biomarkers for stratification or to be used as endpoints.

Patient's associations are already associated with academic entities on the challenges of Precision Psychiatry, and they will be participating to the research and clinical designs.

Why is the contribution of industry needed to achieve the expected impacts?

Contribution of industry: Large companies that are members of the IHI industry partners (i.e. COCIR, EFPIA, EuropaBio, MedTech Europe, Vaccines Europe) contribute to the programme, primarily through 'in-kind' contributions (e.g. their researchers' time, laboratories, data, compounds). At least 45% of each project's total costs have to be in-kind contribution.

Industry contribution is needed to develop enrichment biomarkers to identify subgroups of patients and appropriate endpoints for future clinical trials. This should increase study efficiency, produces larger effect sizes, and permits the use of a smaller study population

The industry is needed to develop blood-based biomarkers based on proteomics, metabolomics, cell-based assay, brain imaging, digital assessments and/or to explore biomarkers predicting efficacy in past clinical trials.

By leveraging the combined strengths of academia, research institutions, and healthcare industry, this project can significantly accelerate the development of new diagnostic tools and personalized therapies for mental disorders. Both established enterprises and start-ups that focus on the fields of biomarker discovery, drug development or repurposing, will greatly benefit from this project.

Topic Idea to IHI - Reference Number: TI_001230

Are you submitting the idea:
☐ **in your personal capacity?**
☒ **on behalf of an organisation?**

Please indicate the name of the group organisation: Holmusk

Please select from the list below the type of stakeholders your organization represents: Small & medium enterprise (SME)

1   Title of your idea

Please provide a short title that accurately reflects the objective(s) of your idea:

INNOVATIVE ENRICHMENT STRATEGIES FOR MENTAL DISORDERS USING OBJECTIVE, QUANTIFIABLE, PREDICTIVE BIOMARKERS FOR THERAPEUTIC INTERVENTIONS

2   Scope

Explain the specific challenges/problems to be addressed by your idea and how these affect relevant stakeholders, taking into account what is already known and/or available in the field:
Current therapeutic interventions for major psychiatric disorders only lead to remission in approximately one third of patients and partial remission in another third. This heterogeneity in treatment outcomes is thought to reflect the low accuracy of current categorical diagnostic frameworks. In addition, a large fraction of patients are not diagnosed or with delay, while clinical trials fail because of absence of objective endpoints to asses efficacy.
Developing predictive enrichment strategies will aid academia and industry to optimise future trial designs by guiding selection of the most appropriate patient population and outcome measures, using objective, measurable, quantifiable, valid biomarkers based on uni- or multi-modal patient-centered data such as cognitive batteries, blood-based omics, brain imaging, electrophysiology,….which can be used to predict treatment responses. By shifting away from the traditional one-size-fits-all approach, innovative enrichment strategies will enhance the signal-to-noise ratio of existing or new therapeutic strategies, and
The goal of this call would thus be to develop and validate robust, reproducible, sensitive to clinical changes, predictive biomarkers to be added to current diagnostic categories, possibly across psychiatric disorders, based on previously identified abnormalities. This can be done through re-analysis of existing cohorts or previous trial data, or through the development of new cohorts or RCTs in enriched or stratified populations. Examples include pharmacogenomics to predict drug responses, electrophysiology to identify brain circuits, brain stimulation using brain imaging, immune dysfunctions targeting inflammation, metabolism, gut dysbiosis, mitochondria...
In summary, mental disorders represent the principal global cause of handicap (WHO, 2020) and a large unmet clinical need. The proposed enrichment strategies will optimise future clinical trials, thereby increasing interest among industry to (re-)enter the field and tackle these needs. The ultimate goal is to bring the right treatment to the right patient at the right time, achieving better health

outcomes and reducing the personal, societal and economic burden of mental illnesses.

Please indicate which IHI specific objective(s) (SO), as described in the IHI Strategic Research and Innovation Agenda (SRIA), your idea addresses:

["SO1: contribute towards a better understanding of the determinants of health and priority disease areas"
"SO2: integrate fragmented health research and innovation efforts bringing together health industry sectors and other stakeholders, focusing on unmet public health needs, to enable the development of tools, data, platforms, technologies and processes for improved prediction, prevention, interception, diagnosis, treat- ment and management of diseases, meeting the needs of end-users"
"SO5: enable the development of new and improved evaluation methodologies and models for a comprehensive assessment of the added value of innovative and integrated health care solutions"]

Please select the keywords that are most relevant to your idea:

["Mental health"
"Prediction"
"Detection"
"Diagnosis"
"Treatment"]

In alignment with the IHI specific objective(s) selected above, specify the objectives of your idea:

Following the established principles of precision psychiatry, innovation should improve discovery and validation of enrichment biomarkers to development robust, reproducible and sensitive biomarkers to improve diagnosis and clinical trials. This should reduce individual suffering and economic cost.
Mental disorders constitute five of the top ten causes of disability. It is estimated that over 27% of the general population will experience mental disorders inducing a total cost across Europe above 4% of GDP.
This project will
1. contribute to the creation of an EU-wide Brain and Mental Health research and innovation ecosystem that will facilitate translation of scientific knowledge into diagnostic and therapeutic innovations
2. foster the development of safe, effective, people-centred, cost-effective predictive enrichment strategies that respond to strategic unmet public health needs across psychiatric disorders.
3. drive cross-sectoral health innovation for a globally competitive European health industry
4. create mentorship and capacity development opportunities to facilitate sustainability and implementation

3   Expected impacts to be achieved by your idea

Briefly describe the expected impacts to be achieved by your idea, ensuring that they contribute to IHI general and relevant specific objectives, as described in the IHI SRIA:

Impacts are wider long-term effects on society (including the environment), the economy and science, enabled by the outcomes of R&I investments. Impacts generally occur sometime after the end of the project, e.g. successful implementation of digital solutions supporting people-centred care.

IHI general objectives: 1. contribute towards the creation of an EU-wide health research and innovation ecosystem that facilitates translation of scientific knowledge into innovations, notably by launching at least 30 large-scale, cross-sectoral projects, focussing on health innovations; 2. foster the development of safe, effective, people-centred and cost-effective innovations that respond to strategic unmet public health needs, by exhibiting, in at least 5 examples, the feasibility of integrating health care products or services, with demonstrated suitability for uptake by health care systems. The related projects should address the prevention, diagnosis, treatment and/or management of diseases affecting the EU population, including contribution to 'Europe's Beating Cancer Plan'; 3. drive cross-sectoral health innovation for a globally competitive European health industry and contribute to reaching the objectives of the new Industrial Strategy for Europe and the Pharmaceutical Strategy for Europe.

Developing innovative predictive enrichment strategies focusing for homogeneous subgroups of mental disorders is based on reinforced private-public collaboration towards
-        Discovery and validation of objective, quantifiable, targetable, robust, reproducible biomarkers ,with operational delivery stratification biomarkers using existing data or future data collection from longitudinal cohort studies or clinical trials data from Europe and beyond
-        In silico selection, of mechanisms-based treatments to be tested in stratified homogeneous subgroups of patients
-        Setting up European infrastructures to facilitate and support enrichment strategies in clinical trials based on the construction of a European Network of expert/excellence centers for mental disorders and on a robust data infrastructure allowing data sharing.
-        Discussion with regulatory agencies, consumers to share the results
-        Improvement of patient's prognosis and reduction of overall cost

4   Why should your idea become an IHI call topic?

Explain why collaboration through a cross-sectoral and multidisciplinary public private partnership is needed in particular:

Why does it require collaboration among several industry sectors (*e.g.* pharma, vaccines, biotech, medical devices, in vitro diagnostics, radiotherapy, medical imaging health ICT)?

Why does it require collaboration between private (industry) and public partners (*e.g.* academia, healthcare practitioners, patients, regulators)?

Developing objective, quantifiable biomarkers for enrichment strategies require public-private partnerships and patient-centric efforts. This can be achieved in Europe thanks to pre-existing small scale and fragmented databases (clinical trials, cohorts) as well as networks of academic/clinical centers specialised and organized in national and international networks, sharing similar assessments tools which can be used to discover and validate signatures using clinical and digital tools, blood based and brain imaging biomarkers for stratifying psychiatric disorders. This project will reinforce collaboration between scientists, industrials and patients on the discovery and validation of biomarkers. Regulators should also be included to discuss innovative diagnostic strategies, and clinical trials design, requirements to validate biomarkers for stratification or to be used as endpoints. Patient's associations are already associated with academic entities on the challenges of Precision Psychiatry, and they will be participating to the research and clinical designs.

Why is the contribution of industry needed to achieve the expected impacts?

Industry contribution is needed to develop enrichment biomarkers to guide characteristics of relevant subgroups of patients and appropriate endpoints for future clinical trials. This should increase study efficiency, produces larger effect sizes, and permits the use of a smaller study population

The industry is needed to develop blood-based biomarkers based on proteomics, metabolomics, cell-based assay, brain imaging, digital assessments and/or to explore biomarkers predicting efficacy in past clinical trials. By leveraging the combined strengths of academia, research institutions, and healthcare industry, this project can significantly accelerate the development of new diagnostic tools and personalized therapies for mental disorders. Both established enterprises and start-ups that focus on the fields of biomarker discovery, drug development or repurposing, will greatly benefit from this project.

Topic Idea to IHI - Reference Number: TI_001231

Are you submitting the idea:
☐ **in your personal capacity?**
☒ **on behalf of an organisation?**

Please indicate the name of the group organisation: Copenhagen Research Centre for Biological and Precision Psychiatry, Mental Health Centre Copenhagen

Please select from the list below the type of stakeholders your organization represents:
Research/higher or secondary education organisation (private or public)

1   Title of your idea

Please provide a short title that accurately reflects the objective(s) of your idea:
INNOVATIVE ENRICHMENT STRATEGIES FOR MENTAL DISORDERS USING OBJECTIVE, QUANTIFIABLE PREDICTIVE BIOMARKERS FOR THERAPEUTIC INTERVENTIONS

2   Scope

Explain the specific challenges/problems to be addressed by your idea and how these affect relevant stakeholders, taking into account what is already known and/or available in the field:
Current therapeutic interventions for major psychiatric disorders only lead to remission in approximately one third of patients and partial remission in another third. This heterogeneity in treatment outcomes is thought to reflect the low accuracy of current categorical diagnostic frameworks. In addition, a large fraction of patients are not diagnosed or with delay, while clinical trials fail because of absence of objective endpoints to asses efficacy.

Developing predictive enrichment strategies will aid academia and industry to optimise future trial designs by guiding selection of the most appropriate patient population and outcome measures, using objective, measurable, quantifiable, valid biomarkers based on uni- or multi-modal patient-centered data such as cognitive batteries, blood-based omics, brain imaging, and electrophysiology, which can be used to predict treatment responses. By shifting away from the traditional one-size-fits-all approach, innovative enrichment strategies will enhance the signal-to-noise ratio of existing or new therapeutic strategies.

The goal of this call would thus be to develop and validate robust, reproducible, sensitive to clinical changes, predictive biomarkers to be added to current diagnostic categories, possibly across psychiatric disorders, based on previously identified abnormalities. This can be done through re-analysis of existing cohorts or previous trial data, or through the development of new cohorts or RCTs in enriched or stratified populations. Examples include pharmacogenomics to predict drug responses, electrophysiology to identify brain circuits, brain stimulation using brain imaging, immune dysfunctions targeting inflammation, metabolism, gut dysbiosis, and mitochondria dysfunction.

In summary, mental disorders represent the principal global cause of handicap (WHO, 2020) and a large unmet clinical need. The proposed enrichment strategies will optimise future clinical trials, thereby increasing interest among industry to (re-)enter the field and tackle these needs.

Please indicate which IHI specific objective(s) (SO), as described in the IHI Strategic Research and Innovation Agenda (SRIA), your idea addresses:

["SO1: contribute towards a better understanding of the determinants of health and priority disease areas"
"SO2: integrate fragmented health research and innovation efforts bringing together health industry sectors and other stakeholders, focusing on unmet public health needs, to enable the development of tools, data, platforms, technologies and processes for improved prediction, prevention, interception, diagnosis, treat- ment and management of diseases, meeting the needs of end-users"]

Please select the keywords that are most relevant to your idea:
["Immune system diseases"
"Mental health"
"Prediction"
"Prevention"
"Detection"
"Diagnosis"
"Treatment"
"Disease management"
"Digital health"
"Health technology"]

In alignment with the IHI specific objective(s) selected above, specify the objectives of your idea:

Following the established principles of precision psychiatry, innovation should improve discovery and validation of enrichment biomarkers to development robust, reproducible and sensitive biomarkers to improve diagnosis and clinical trials. This should reduce individual suffering and economic cost. Mental disorders constitute five of the top ten causes of disability. It is estimated that over 27% of the general population will experience mental disorders inducing a total cost across Europe above 4% of GDP.

This project will
1. contribute to the creation of an EU-wide Brain and Mental Health research and innovation ecosystem that will facilitate translation of scientific knowledge into diagnostic and therapeutic innovations
2. foster the development of safe, effective, people-centred, cost-effective predictive enrichment strategies that respond to strategic unmet public health needs across psychiatric disorders.
3. drive cross-sectoral health innovation for a globally competitive European health industry
4. create mentorship and capacity development opportunities to facilitate sustainability and implementation

3 Expected impacts to be achieved by your idea

Briefly describe the expected impacts to be achieved by your idea, ensuring that they contribute to IHI general and relevant specific objectives, as described in the IHI SRIA:

Impacts are wider long-term effects on society (including the environment), the economy and science, enabled by the outcomes of R&I investments. Impacts generally occur sometime after the end of the project, e.g. successful implementation of digital solutions supporting people-centred care.

IHI general objectives: 1. contribute towards the creation of an EU-wide health research and innovation ecosystem that facilitates translation of scientific knowledge into innovations, notably by launching at least 30 large-scale, cross-sectoral projects, focussing on health innovations; 2. foster the development of safe, effective, people-centred and cost-effective innovations that respond to strategic unmet public health needs, by exhibiting, in at least 5 examples, the feasibility of integrating health care products or services, with demonstrated suitability for uptake by health care systems. The related projects should address the prevention, diagnosis, treatment and/or management of diseases affecting the EU population, including contribution to 'Europe's Beating Cancer Plan'; 3. drive cross-sectoral health innovation for a globally competitive European health industry and contribute to reaching the objectives of the new Industrial Strategy for Europe and the Pharmaceutical Strategy for Europe.

Developing innovative predictive enrichment strategies focusing for homogeneous subgroups of mental disorders is based on reinforced private-public collaboration towards:
- 	Discovery and validation of objective, quantifiable, targetable, robust, reproducible biomarkers ,with operational delivery stratification biomarkers using existing data or future data collection from longitudinal cohort studies or clinical trials data from Europe and beyond
- 	In silico selection, of mechanisms-based treatments to be tested in stratified homogeneous subgroups of patients
- 	Setting up European infrastructures to facilitate and support enrichment strategies in clinical trials based on the construction of a European Network of expert/excellence centers for mental disorders and on a robust data infrastructure allowing data sharing.
- 	Discussion with regulatory agencies, consumers to share the results
- 	Improvement of patient's prognosis and reduction of overall cost

4 Why should your idea become an IHI call topic?

Explain why collaboration through a cross-sectoral and multidisciplinary public private partnership is needed in particular:

**Why does it require collaboration among several industry sectors
(*e.g.* pharma, vaccines, biotech, medical devices, in vitro diagnostics, radiotherapy, medical imaging health ICT)?**

**Why does it require collaboration between private (industry) and public partners
(*e.g.* academia, healthcare practitioners, patients, regulators)?**

Developing objective, quantifiable biomarkers for enrichment strategies require public-private partnerships and patient-centric efforts. This can be achieved in Europe thanks to pre-existing databases (clinical trials, cohorts) as well as networks of academic/clinical centers specialised and organized in national and international networks, sharing similar assessments tools which can be used to discover and validate signatures using clinical and digital tools, blood based and brain imaging biomarkers for stratifying psychiatric disorders. This project will reinforce collaboration between scientists, industrials and patients on the discovery and validation of biomarkers. Regulators should also be included to discuss innovative diagnostic strategies, and clinical trials design, requirements to validate biomarkers for stratification or to be used as endpoints. Patient's associations are already associated with academic entities on the challenges of Precision Psychiatry, and they will be participating to the research and clinical designs.

Why is the contribution of industry needed to achieve the expected impacts?

Industry contribution is needed to develop enrichment biomarkers to identify subgroups of patients and appropriate endpoints for future clinical trials. This should increase study efficiency, produces larger effect sizes, and permits the use of a smaller study population

The industry is needed to develop blood-based biomarkers based on proteomics, metabolomics, cell-based assay, brain imaging, digital assessments and/or to explore biomarkers predicting efficacy in past clinical trials. By leveraging the combined strengths of academia, research institutions, and healthcare industry, this project can significantly accelerate the development of new diagnostic tools and personalized therapies for mental disorders. Both established enterprises and start-ups that focus on the fields of biomarker discovery, drug development or repurposing, will greatly benefit from this project.

Topic Idea to IHI - Reference Number: TI_001232

Are you submitting the idea:
☐ **in your personal capacity?**
☒ **on behalf of an organisation?**

Please indicate the name of the group organisation: Istituto Superiore di Sanità

Please select from the list below the type of stakeholders your organization represents:
Research/higher or secondary education organisation (private or public)

1   Title of your idea

Please provide a short title that accurately reflects the objective(s) of your idea:
INNOVATIVE ENRICHMENT STRATEGIES FOR MENTAL DISORDERS USING OBJECTIVE, QUANTIFIABLE PREDICTIVE BIOMARKERS FOR THERAPEUTIC INTERVENTIONS

2   Scope

Explain the specific challenges/problems to be addressed by your idea and how these affect relevant stakeholders, taking into account what is already known and/or available in the field:
Current therapeutic interventions for major psychiatric disorders achieve remission in only about one-third of patients, with another third experiencing partial remission. This variability in treatment outcomes highlights the inadequacies of existing categorical diagnostic frameworks. Additionally, a significant portion of patients remain undiagnosed or receive delayed diagnoses, while clinical trials often fail due to the lack of objective endpoints to assess efficacy.

Developing predictive enrichment strategies is crucial for academia and industry to optimize future trial designs. By guiding the selection of the most appropriate patient populations and outcome measures, these strategies can utilize objective, measurable, and valid biomarkers derived from uni- or multi-modal patient-centered data. Such data can include cognitive batteries, blood-based omics, brain imaging, and electrophysiology, which can be used to predict treatment responses. Moving away from the traditional one-size-fits-all approach, innovative enrichment strategies will enhance the signal-to-noise ratio of both existing and new therapeutic interventions.

The goal of this initiative is to develop and validate robust, reproducible, and sensitive predictive biomarkers that can be integrated into current diagnostic categories, potentially across various psychiatric disorders. This can be achieved by re-analyzing existing cohort or trial data, or by developing new cohorts or randomized controlled trials (RCTs) in enriched or stratified populations. Examples of such approaches include pharmacogenomics for predicting drug responses, electrophysiology for identifying brain circuits, brain stimulation guided by imaging, and targeting immune dysfunctions related to inflammation, metabolism, gut dysbiosis, and mitochondrial function.

In summary, mental disorders are the leading cause of disability globally (WHO, 2020), presenting a substantial unmet clinical need. The proposed enrichment strategies aim to optimize future clinical

trials, thereby increasing industry interest in addressing these needs. Ultimately, the goal is to deliver the right treatment to the right patient at the right time, improving health outcomes and reducing the personal, societal, and economic burdens of mental illnesses.

Please indicate which IHI specific objective(s) (SO), as described in the IHI Strategic Research and Innovation Agenda (SRIA), your idea addresses:

["SO1: contribute towards a better understanding of the determinants of health and priority disease areas"
"SO2: integrate fragmented health research and innovation efforts bringing together health industry sectors and other stakeholders, focusing on unmet public health needs, to enable the development of tools, data, platforms, technologies and processes for improved prediction, prevention, interception, diagnosis, treat- ment and management of diseases, meeting the needs of end-users"]

Please select the keywords that are most relevant to your idea:

["Mental health"
"Immune system diseases"
"Metabolic diseases"
"Prediction"
"Prevention"
"Diagnosis"
"Treatment"
"Disease management"
"Digital health"
"Health technology"]

In alignment with the IHI specific objective(s) selected above, specify the objectives of your idea:

Adhering to the principles of precision psychiatry, innovation should focus on enhancing the discovery and validation of enrichment biomarkers. This will lead to the development of robust, reproducible, and sensitive biomarkers, improving diagnosis and clinical trials, ultimately reducing individual suffering and economic costs. Mental disorders are among the top causes of disability, with over 27% of the population experiencing such conditions, leading to a total cost exceeding 4% of Europe's GDP.

This project aims to:

1. Establish an EU-wide Brain and Mental Health research and innovation ecosystem, facilitating the translation of scientific knowledge into diagnostic and therapeutic advancements.
2. Promote the development of safe, effective, and cost-efficient predictive enrichment strategies that address critical public health needs across psychiatric disorders.
3. Propel cross-sectoral health innovation, enhancing the global competitiveness of the European health industry.
4. Create mentorship and capacity-building opportunities to ensure the sustainability and implementation of these innovations.

3 Expected impacts to be achieved by your idea

Briefly describe the expected impacts to be achieved by your idea, ensuring that they contribute to IHI general and relevant specific objectives, as described in the IHI SRIA:

Impacts are wider long-term effects on society (including the environment), the economy and science, enabled by the outcomes of R&I investments. Impacts generally occur sometime after the end of the project, e.g. successful implementation of digital solutions supporting people-centred care.

IHI general objectives: 1. contribute towards the creation of an EU-wide health research and innovation ecosystem that facilitates translation of scientific knowledge into innovations, notably by launching at least 30 large-scale, cross-sectoral projects, focussing on health innovations; 2. foster the development of safe, effective, people-centred and cost-effective innovations that respond to strategic unmet public health needs, by exhibiting, in at least 5 examples, the feasibility of integrating health care products or services, with demonstrated suitability for uptake by health care systems. The related projects should address the prevention, diagnosis, treatment and/or management of diseases affecting the EU population, including contribution to 'Europe's Beating Cancer Plan'; 3. drive cross-sectoral health innovation for a globally competitive European health industry and contribute to reaching the objectives of the new Industrial Strategy for Europe and the Pharmaceutical Strategy for Europe.

Developing innovative predictive enrichment strategies for homogeneous subgroups of mental disorders involves strengthened public-private collaboration. Key focus areas include:

- Discovery and validation of biomarkers: Identifying robust, quantifiable, and reproducible biomarkers using current or future data from longitudinal cohort studies or clinical trials from Europe and beyond. This includes operational delivery stratification biomarkers.

- In silico selection of treatments: Choosing mechanism-based treatments for testing in stratified, homogeneous patient subgroups.

- Establishing European infrastructures: Creating a network of expert/excellence centers for mental disorders, along with a robust data infrastructure to facilitate data sharing and support enrichment strategies in clinical trials.

- Engaging with regulatory agencies and consumers: Sharing results with regulatory bodies and the public.

- Enhancing patient prognosis and reducing costs: Improving patient outcomes and lowering overall healthcare costs.

These efforts aim to create a comprehensive approach to the treatment and management of mental disorders through collaborative innovation and infrastructure development.

4 Why should your idea become an IHI call topic?

Explain why collaboration through a cross-sectoral and multidisciplinary public private partnership is needed in particular:

Why does it require collaboration among several industry sectors (*e.g.* pharma, vaccines, biotech, medical devices, in vitro diagnostics, radiotherapy, medical imaging health ICT)?

Why does it require collaboration between private (industry) and public partners (*e.g.* academia, healthcare practitioners, patients, regulators)?

Developing objective, quantifiable biomarkers for enrichment strategies requires public-private partnerships and patient-centric efforts. Europe is well-positioned for this due to its existing clinical trial and cohort databases, as well as networks of academic and clinical centers. These centers are specialized and organized in national and international networks, using similar assessment tools to discover and validate signatures through clinical and digital methods, blood-based markers, and brain imaging for stratifying psychiatric disorders. This project aims to strengthen collaboration between scientists, industry professionals, and patients in the discovery and validation of biomarkers. It is

crucial to involve regulators to discuss innovative diagnostic strategies, clinical trial designs, and requirements for biomarker validation for stratification or as endpoints. Patient associations, already working with academic entities on the challenges of Precision Psychiatry, will actively participate in research and clinical design efforts.

Why is the contribution of industry needed to achieve the expected impacts?

Contribution of industry: Large companies that are members of the IHI industry partners (i.e. COCIR, EFPIA, EuropaBio, MedTech Europe, Vaccines Europe) contribute to the programme, primarily through 'in-kind' contributions (e.g. their researchers' time, laboratories, data, compounds). At least 45% of each project's total costs have to be in-kind contribution.

Industry collaboration is essential to develop enrichment biomarkers for identifying patient subgroups and determining appropriate endpoints for future clinical trials. This approach will enhance study efficiency, yield larger effect sizes, and allow for smaller study populations.

Developing blood-based biomarkers through proteomics, metabolomics, cell-based assays, brain imaging, and digital assessments, as well as exploring biomarkers predicting efficacy from past trials, is crucial. By harnessing the combined expertise of academia, research institutions, and the healthcare industry, this project can significantly accelerate the development of new diagnostic tools and personalized therapies for mental disorders. Both established companies and startups focused on biomarker discovery, drug development, or repurposing will greatly benefit from this initiative.

Topic Idea to IHI - Reference Number: TI_001233

Are you submitting the idea:
☐ in your personal capacity?
☒ **on behalf of an organisation?**

  Please select from the list below the type of stakeholders your organization represents:
   Healthcare professional organisation/healthcare provider

1   Title of your idea

Please provide a short title that accurately reflects the objective(s) of your idea:
INNOVATIVE ENRICHMENT STRATEGIES FOR MENTAL DISORDERS USING OBJECTIVE,
    QUANTIFIABLE PREDICTIVE BIOMARKERS FOR THERAPEUTIC INTERVENTIONS

2   Scope

Explain the specific challenges/problems to be addressed by your idea and how these affect relevant stakeholders, taking into account what is already known and/or available in the field:
Current therapeutic interventions for major psychiatric disorders only lead to remission in approximately one third of patients and partial remission in another third. This heterogeneity in treatment outcomes is thought to reflect the low accuracy of current categorical diagnostic frameworks. In addition, a large fraction of patients are not diagnosed or with delay, while clinical trials fail because of absence of objective endpoints to asses efficacy.
Developing predictive enrichment strategies will aid academia and industry to optimise future trial designs by guiding selection of the most appropriate patient population and outcome measures, using objective, measurable, quantifiable, valid biomarkers based on uni- or multi-modal patient-centered data such as cognitive batteries, blood-based omics, brain imaging, electrophysiology,….which can be used to predict treatment responses. By shifting away from the traditional one-size-fits-all approach, innovative enrichment strategies will enhance the signal-to-noise ratio of existing or new therapeutic strategies, and
The goal of this call would thus be to develop and validate robust, reproducible, sensitive to clinical changes, predictive biomarkers to be added to current diagnostic categories, possibly across psychiatric disorders, based on previously identified abnormalities. This can be done through re-analysis of existing cohorts or previous trial data, or through the development of new cohorts or RCTs in enriched or stratified populations. Examples include pharmacogenomics to predict drug responses, electrophysiology to identify brain circuits, brain stimulation using brain imaging, immune dysfunctions targeting inflammation, metabolism, gut dysbiosis, mitochondria...
In summary, mental disorders represent the principal global cause of handicap (WHO, 2020) and a large unmet clinical need. The proposed enrichment strategies will optimise future clinical trials, thereby increasing interest among industry to (re-)enter the field and tackle these needs. The ultimate goal is to bring the right treatment to the right patient at the right time, achieving better health outcomes and reducing the personal, societal and economic burden of mental illnesses.

Please indicate which IHI specific objective(s) (SO), as described in the IHI Strategic Research and Innovation Agenda (SRIA), your idea addresses:

["SO1: contribute towards a better understanding of the determinants of health and priority disease areas"
"SO2: integrate fragmented health research and innovation efforts bringing together health industry sectors and other stakeholders, focusing on unmet public health needs, to enable the development of tools, data, platforms, technologies and processes for improved prediction, prevention, interception, diagnosis, treat- ment and management of diseases, meeting the needs of end-users"]

Please select the keywords that are most relevant to your idea:
["Immune system diseases"
"Metabolic diseases"
"Mental health"
"Prediction"
"Prevention"
"Diagnosis"
"Treatment"
"Disease management"
"Digital health"
"Health technology"]

In alignment with the IHI specific objective(s) selected above, specify the objectives of your idea:

Following the established principles of precision psychiatry, innovation should improve discovery and validation of enrichment biomarkers to development robust, reproducible and sensitive biomarkers to improve diagnosis and clinical trials. This should reduce individual suffering and economic cost.
Mental disorders constitute five of the top ten causes of disability. It is estimated that over 27% of the general population will experience mental disorders inducing a total cost across Europe above 4% of GDP.
This project will
1. contribute to the creation of an EU-wide Brain and Mental Health research and innovation ecosystem that will facilitate translation of scientific knowledge into diagnostic and therapeutic innovations
2. foster the development of safe, effective, people-centred, cost-effective predictive enrichment strategies that respond to strategic unmet public health needs across psychiatric disorders.
3. drive cross-sectoral health innovation for a globally competitive European health industry
4. create mentorship and capacity development opportunities to facilitate sustainability and implementation

3   Expected <u>impacts</u> to be achieved by your idea

Briefly describe the expected impacts to be achieved by your idea, ensuring that they contribute to IHI general and relevant specific <u>objectives</u>, as described in the IHI SRIA:

Impacts are wider long-term effects on society (including the environment), the economy and science, enabled by the outcomes of R&I investments. Impacts generally occur sometime after the end of the project, e.g. successful implementation of digital solutions supporting people-centred care.

IHI general objectives: 1. contribute towards the creation of an EU-wide health research and innovation ecosystem that facilitates translation of scientific knowledge into innovations, notably by launching at least 30 large-scale, cross-sectoral projects, focussing on health innovations; 2. foster the development of safe, effective, people-centred and cost-effective innovations that respond to strategic unmet public health needs, by exhibiting, in at least 5 examples, the feasibility of integrating health care products or services, with demonstrated suitability for uptake by health care systems. The related projects should address the prevention, diagnosis, treatment and/or management of diseases affecting the EU population, including contribution to 'Europe's Beating Cancer Plan'; 3. drive cross-sectoral health innovation for a globally competitive European health industry and contribute to reaching the objectives of the new Industrial Strategy for Europe and the Pharmaceutical Strategy for Europe.

Developing innovative predictive enrichment strategies focusing for homogeneous subgroups of mental disorders is based on reinforced private-public collaboration towards

-        Discovery and validation of objective, quantifiable, targetable, robust, reproducible biomarkers ,with operational delivery stratification biomarkers using existing data or future data collection from longitudinal cohort studies or clinical trials data from Europe and beyond
-        In silico selection, of mechanisms-based treatments to be tested in stratified homogeneous subgroups of patients
-        Setting up European infrastructures to facilitate and support enrichment strategies in clinical trials based on the construction of a European Network of expert/excellence centers for mental disorders and on a robust data infrastructure allowing data sharing.
-        Discussion with regulatory agencies, consumers to share the results
-        Improvement of patient's prognosis and reduction of overall cost

4   Why should your idea become an IHI call topic?

Explain why collaboration through a cross-sectoral and multidisciplinary public private partnership is needed in particular:

**Why does it require collaboration among several industry sectors
(*e.g.* pharma, vaccines, biotech, medical devices, in vitro diagnostics, radiotherapy, medical imaging health ICT)?**

**Why does it require collaboration between private (industry) and public partners
(*e.g.* academia, healthcare practitioners, patients, regulators)?**

Developing objective, quantifiable biomarkers for enrichment strategies require public-private partnerships and patient-centric efforts. This can be achieved in Europe thanks to pre-existing databases (clinical trials, cohorts) as well as networks of academic/clinical centers specialised and organized in national and international networks, sharing similar assessments tools which can be used to discover and validate signatures using clinical and digital tools, blood based and brain imaging biomarkers for stratifying psychiatric disorders. This project will reinforce collaboration between scientists, industrials and patients on the discovery and validation of biomarkers. Regulators should also be included to discuss innovative diagnostic strategies, and clinical trials design, requirements to validate biomarkers for stratification or to be used as endpoints. Patient's associations are already associated with academic entities on the challenges of Precision Psychiatry, and they will be participating to the research and clinical designs.

Why is the contribution of industry needed to achieve the expected impacts?

Contribution of industry: Large companies that are members of the IHI industry partners (i.e. COCIR, EFPIA, EuropaBio, MedTech Europe, Vaccines Europe) contribute to the programme, primarily through 'in-kind' contributions (e.g. their researchers' time, laboratories, data, compounds). At least 45% of each project's total costs have to be in-kind contribution.

Industry contribution is needed to develop enrichment biomarkers to identify subgroups of patients and appropriate endpoints for future clinical trials. This should increase study efficiency, produces larger effect sizes, and permits the use of a smaller study population

The industry is needed to develop blood-based biomarkers based on proteomics, metabolomics, cell-based assay, brain imaging, digital assessments and/or to explore biomarkers predicting efficacy in past clinical trials. By leveraging the combined strengths of academia, research institutions, and healthcare industry, this project can significantly accelerate the development of new diagnostic tools and personalized therapies for mental disorders. Both established enterprises and start-ups that focus on the fields of biomarker discovery, drug development or repurposing, will greatly benefit from this project.