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1. Introduction

The ROAMER project seeks to meet the essential need for a coordinated and comprehensive approach to the promotion and integration of research in mental health and well-being by means of an effective and widely accepted **Roadmap**. The roadmap is aimed at priority setting across Europe and the rest of the world, focusing on high quality scientific research and taking into account the priorities set out in the European Parliament Resolution, namely, “prevention, early detection, intervention and treatment of mental disorders”, and will establish infrastructure and capacity requirements for mental health and wellbeing research in Europe in the short, middle and long-term and as applicable across the life span.

In this context, it has been necessary to develop an accurate picture of the state-of-art of mental health research in Europe, both in general terms and with respect specifically to each track of mental disorder, mental health and wellbeing research (biomedical, psychological, social and economic aspects, public health and well-being) in order to find gaps and to define salient advances.

The current situation of mental health research in Europe was explored during the first phase of the project and defined by consensus in the deliverable D11.1 in terms of 1) mapping publications of the last 5 years in each field, 2) enumerating active research groups in each country, 3) listing the main advances achieved during the last 10 years and the gaps in knowledge, and 4) exploring the point of view of different type of Stakeholders.

Based on the State of the art analysis, groups of experts met in consecutive workshops to generate by consensus a list of gaps in knowledge and the advances needed to solve them in a time frame of 15 years for each area within mental health research.

The most important advances needed in each area have been described properly and justified according to several common criteria that will be used for the prioritization process later on. The criteria are defined below:

- **Efficacy/effectiveness:** Likelihood that the advance results in an effective intervention to diminish the appearance of a disorder or its consequences, or to solve a concrete problem.
- **Impact / deliverability / economic benefits in Europe:** Likelihood that the advance could be provided to the Europeans and impact on the society (i.e. to decrease disease burden, to improve the wellbeing, or to produce economic benefits).
- **Answerability/feasibility in Europe:** Likelihood that the advance can be achieved in Europe (lead to new knowledge, enabling development or planning of an intervention).
- **European research strength:** Relative competitiveness of Europe to other regions to achieve and implement the advance.

2. Objective of the report

The main goal of D11.2 is to show the list of gaps and advances needed in each area of knowledge within mental health research that have been defined by consensus in several workshops with experts that took place during the third phase of the project. The document also presents an accurate description of the most important advances needed (up to 20 items per area) and their justification according to common criteria. During the next phase, these advances needed will be prioritized by means of a general survey that will be widely distributed across Europe.

3. Areas of knowledge within mental health research

3.1. Analysis of geographic, clinical, multidisciplinary and life-course integration

3.1.1. Introduction to the area

The primary aim of WP2 is the integration of research with a focus on variation in geographical, clinical, multidisciplinary and life-course representation. The respective subareas of knowledge are briefly summarized below. Some of the subareas are primarily of interest with regard to the ROAMER process itself. Thus, integration of research from a **multidisciplinary perspective** and a **life course perspective** primarily refers to the activity in WP2 of inspecting the work of other WPs in order to make sure that these two subareas are well represented. Other subareas, however, are of interest as an outcome of ROAMER, rather than just referring to the process of ROAMER itself. Thus, the areas of **geographical distribution** and **clinical research** were the object of a preliminary analysis in terms of “state of the art”, gaps/needs, and priorities.

3.1.1.1. Definition of subareas

ROAMER outcome areas:

Analysis of the **geographical distribution** of mental health research in ROAMER focuses on the adequate representation of geographical areas in ROAMER. Analysis of the geographical distribution of mental health research in Europe focuses on variation occasioned by country-specific aspects. In order to examine this, a literature search was devised, using a specific strategy of “comparative literature section tracking” in order to analyse geographical variation/integration of mental health research.

Analysis of **clinical perspective** in ROAMER refers to adequate coverage of the range of mental disorders across the different WPs in ROAMER. Analysis of the clinical perspective in Europe refers to analysis of the area of mental health research in Europe with regard to diagnosis, treatment, course and outcome of mental disorders (the “what”), including methodological advances in the way this research is carried out (“the how”) and its place in relation to basic research (e.g. experimental medicine, translational approaches). A horizon scanning literature search was carried out and first discussed during the WP2 workshop.

ROAMER process areas:

Important disciplines that should be integrated in the ROAMER process, in order to provide a **multidisciplinary perspective**, include, amongst others, epidemiology, psychology, psychiatry, sociology, neuroscience, genetics, bioinformatics, biomedical sciences and user-perspectives.

In terms of **life-course integration**, WP2 will inspect processes in ROAMER with regard to representation of the whole life-span, ranging from child and adolescent to old age psychology and psychiatry.

3.1.2. Gaps in knowledge

3.1.2.1. Clinical and disorder-specific perspective

This subarea of knowledge of WP2 was the major focus during the first Scientific Workshop of WP2. The following challenges and research gaps (translating into needs and priorities) were identified in the expert-panel discussion:

- The need to bridge the gap between diagnoses of mental disorders and their underlying neuroscience.
- The need to overcome the problem of approximate replications, which neither confirm nor refute research findings, particularly in neurobiological research
- The need for different research paradigms to overcome the problem of ‘supernormal’ controls being compared to clinically heterogeneous cases. In particular, the need to conduct experimental medicine studies focusing on the synergistic pharmacological and non-pharmacological interventions.
- The need to rethink the concept of biomarkers, since categories of psychiatric disorders are extremely overlapping and interrelated and disorders tend to breed across categories almost as frequently as within (Dean et al., 2010)
- The need for symptom network approaches in line with the argumentation by Kendler and colleagues on psychiatric disorders relating to multiple causes, that give rise to underlying states which in turn give rise to symptoms, which again can influence each other (Kendler et al., 2011)
- The need to differentiate between nomothetic (staging) and idiographic (profiling) approaches to be able to distinguish between specific high risk perspectives from non-specific public health perspectives
- The need to systematically collect and prioritize backlog RCTs (a range of common questions that require answers but trials have not yet been conducted)
- The need for enhanced treatment research -> why does placebo work best when examining effect sizes?
- The need to implement within-person designs such as ABABAB designs (idiographic designs) in addition to efficacy and effectiveness trials (nomothetic approaches)
- The need to expand study periods beyond the period around illness onset in order to better research relapse prevention
- The need to implement the user perspective, focusing on user-relevant outcomes and taking into account user self-help approaches, user values and user research.
- The need to massively invest in self-management e-Health and m-Health approaches, as well as in virtual reality treatments.
- The need to invest in models of service delivery and service delivery research.

3.1.3. Advances needed and research priorities: Clinical Research Group

Based on the above literature and expert survey, the decision was taken in ROAMER (Dec. 19th, 2012) to initiate a cross-WP *Clinical Research Group* with members of the different work packages, in order to conduct a Delphi survey among a representative group of experts in Europe, and examine opinions as to advances needed and research priorities required, in relation to the gaps and needs identified in the WP2 expert survey and the WP2 Clinical Research Horizon Scanning Exercise.

The scope of clinical research in the ROAMER Clinical Research Group

Clinical research is of particular importance for mental disorders, particularly because of the low validity of animal models, and because of the sub-optimal definition and stratification of diseases. Testing diagnostic and treatment strategies in humans is therefore critical. The complexity of treatment strategies associating medicines, psychotherapy and medical devices also requires clinical trials supporting evidence-based medical practice. Specific methodological issues have to be addressed, including commonly agreed outcome measures. Clinical research on mental health therefore represents a highly multidisciplinary activity, and for this reason a cross-WP task force on clinical research was established in ROAMER. The objective of this task force is to define a strategy for clinical research in psychiatry in Europe, taking advantage of its patient population size and of its medical expertise, addressing three critical issues:

1. What are the scientific priorities?

- Disease areas, age, population, treatment intervention?

2. For each disease area, what are the priorities?

- Clinical research exploring the mechanisms of diseases,
- Clinical research aimed at improving the diagnostic strategies and the stratification of diseases
- Proof of concept clinical trials for innovative treatments
- Registration trials for new medicines or medical devices
- Investigator-driven trials assessing the efficacy, effectiveness and safety of authorised treatments, and exploring treatment combinations
- Interventional and non-interventional research assessing the efficacy and safety of treatments
- Clinical cohort studies, assessing course of symptoms, and functioning as control group for trials; analyzing rare events such as mortality, cross-cultural differences, and pharmacovigilance.

3. Methodological issues

- What randomisation procedures, blinding issues, placebos, preference study designs, can be used in intervention studies?
- How can cohort studies be used to nest RCTs? Are there alternatives for RCTs?

4. Which policies are needed to implement this strategy?

- a. In terms of research capacity and methodology
 - i. Structuring pan-European networks of investigation sites for each disease area
 - ii. Developing common standards and tools, including for Quality Assurance and monitoring
 - iii. Adoption of common outcome measures in line with the patients expectations
 - iv. Establishing common methodological principles, in particular regarding the issue of placebo use in randomised trials, the issue of blinding and comparator in non-pharmacological treatments.
 - v. Leading the search for alternatives of RCTs, e.g. within-person designs.
- b. In terms of funding for independent (multinational) clinical trials:
 - i. H2020, national funding, charity funding?
 - ii. Level of funding?
- c. In terms of legislation, particularly as regards
 - i. The low-risk category of clinical research
 - ii. The ethical aspects of informed consent in psychiatric patients

Clinical Research thus aims to address patient-related outcomes that are relevant for diagnosis, treatment and prognosis of patients with mental disorders. It includes development and validation of diagnostic methods and questionnaires in psychometric and validation studies that can be used by doctors or psychotherapists in order to establish diagnosis of a mental disorder and to propose a treatment for it. It involves development of new treatment interventions for mental disorders. It includes evaluation of efficacy and effectiveness of interventions in, for example, Randomized Clinical Trials, both proof of concept trials and pragmatic trials. Interventions can be pharmacological, brain-related (e.g. Deep Brain Stimulation, ECT), psychotherapeutic, technological (e-Health, m-Health), systemic, psychosocial in nature or a combination of several. The Cochrane Collaboration provides a clear methodology to establish such effectiveness of RCTs by a systematic review process. However, Clinical Research encompasses more than this methodology. It also encompasses establishment of risk profiles for patients that may lead to providing treatment specifically fit for specific patient groups, this way accounting for heterogeneity in syndromes such as e.g. subtypes in depression. Furthermore, Clinical Research has methods to include the patient perspective by the use of preference of patients in RCTs, and addresses adherence of doctors or therapists as well as patients to treatment

protocols as process or outcome measures. Outcomes of Clinical Research should be on specific mental symptom level, on treatment response, on remission of mental disorder, on occurrence of relapse in relapse prevention or long-term treatment in chronic conditions; but also on functioning, which is relevant in patients with comorbid physical disorders in terms of physical or general functioning, and in terms of work absenteeism in patients who are absent from work due to their mental disorder. Another important outcome is societal participation. Clinical Research should address diagnostic and treatment complexities in comorbidity by development of diagnostic and treatment algorithms designed to support medical decision making and it should take the patient perspective into account by use of Shared Decision Making methods.

Furthermore, large cohort studies are needed, namely clinical, broad disorder-based cohort studies. These are crucial to better understand the patients' needs from a "real world" perspective, which is necessary to supplement the information that may come from clinical trials and other studies in selected populations. They are also important from the perspective of analyzing rare events such as mortality, cross-cultural differences, and pharmacovigilance.

For specific information on gaps and advances needed in Clinical research, refer to **section 3.3 on 'Clinical research task force'**.

3.2. Structuring research capacity, infrastructures, capacity building & funding strategies

3.2.1. Introduction to the area

It is the task of work package 3 (WP3) to analyse the current landscape of resources in mental health research, and to establish which resources and measures are necessary in order to implement the advances set out by ROAMER. These research resources in mental health are represented by three areas of knowledge: First, research **capacity and infrastructure** entails all the research units, institutes, networks etc. necessary to perform research. It further includes the (technical) infrastructure that is instrumental in achieving the research work. Second, research **training and capacity building** refers to all activities contributing to the building of a workforce capable to perform the research tasks needed. Such activities include research master programs and PhDs as well as specific MD-PhD programs or targeted initiatives for capacity building in a given region. Third, **financial resources** have to be sufficient and can be provided amongst others by public, private, permanent grant-based funding sources.

All these areas are key for the advancement of mental health research in Europe, all the more so as recent data suggest that the resources allocated for this field in Europe (compared to other fields of health research) are inferior to those in the US (2% and 7% of total health research budget in France and the UK respectively vs. 16% in the US; Chevreur et al., 2012). This has to be addressed in order to ultimately improve mental health in Europe as set out by the 2005 EC Green Paper, the 2008 European Pact on Mental Health and Wellbeing and the European Parliament Resolution of 19 February 2009.

3.2.1.1. Definition of subareas

3.2.1.1.1. Research capacities and infrastructures

Concerning **research capacity and infrastructures**, the areas of interest include the different locations of research (universities, research institute, teaching hospital/industry/institution...), the facilities available for researchers in each of them and the workforce. A main issue is further the question of how non-mental health related infrastructures on European or national levels could be used for mental health research, or how they could serve as models for novel (infra)-structures to be set up.

The current issues faced by mental health research in terms of research capacities are the following: What is needed? What evidence needs to be generated for clinicians and for health policymakers? What are the existing infrastructures

relevant for mental health? What should be developed specifically for mental health? What is needed in terms of strategic partnerships? How to impact the development of national or EU infrastructures?

All these questions have to be asked while always keeping in mind the benefit to patients and their progressive empowerment.

Definitions and distinction of the terms “infrastructures” and “capacities” were elaborated, these two terms often being used as synonyms. It was pointed out that in European terminology infrastructures are the technical supports and facilities necessary for research. The term covers all the technical services provided, including e-infrastructures, databases, registries, surveys, cohorts, etc. Some experts raised the point that infrastructures should not mean only technical facilities but also protocols, procedures and common standards, especially in the particular field of psychiatry.

It has also been highlighted that infrastructures should be considered as working platforms where interdisciplinary and international research can be performed. This last idea has been pointed out as a gap in the current researchers’ perception.

Infrastructures can be distinguished from capacities that comprise the infrastructures but also contain other aspects like competences, training and organizations.

Capacities and infrastructures can be either centralized or not, as well as public or private: research units and public research centres, universities, non-for-profit centres, research foundations, etc. Their steering and coordination can be done by the central administration but this varies depending on countries. The need for a mapping of the existing mental health research infrastructures (not only RIs) in Europe and the way they are steered has been raised.

The EU generalized system of call for tenders has been questioned, mainly concerning the fact that it induces a waste of resources when several research groups answer a call but only one is accepted. Further, the subjects of the calls for tender were commented on as being too mainstream and thus not innovative enough. It has been acknowledged that more projects led by researchers should be supported. It has also been pointed out that competition-driven innovation may have reached its limits and that has to be coupled with a more cooperative approach, which is the purpose of the RIs. They are meant to help researchers fund consortiums and encourage them to answer to EU calls.

3.2.1.1.2. Capacity building and training in mental health research

Mental health research **capacity-building and training strategies** comprise training programs relevant to mental health research in Europe. The career path of researchers is an integral part of this area of knowledge, as it touches on the attractiveness of mental health research for young professionals and the issue of brain-drain.

Mental health research concerns psychiatry and psychology but also fundamental sciences, public health and social sciences. Further, capacity-building should not be considered as a topic associated merely with new EU member states but also to some “older” EU countries which have insufficient organization of mental health research training. Finally, training and capacity-building does not stop at graduation but includes continuous education and career development of established researchers.

The starting point of this area of knowledge is that training in (clinical) mental health does not necessarily include teaching on research methodology.

3.2.1.1.3. Funding strategies of mental health research

The **funding strategies** of mental health research concern three elements of the work-package research: first the total amount of funding available in Europe for this domain of research, either private or public, either permanent budgets or projects-based. The aim is to identify all the funds devoted to research in mental health at the EU level and within each European country. Questions concern the amounts coming from private or public sector, from the national, infra-national, international or EU level, and the funding mechanisms.

There is a vivid interest on the annual rate of return of mental health research investment. The possibility of measuring research impact has been seen as a valuable argument in order to convince policymakers that investments in mental research are worthwhile; generally, the idea that it is difficult to “claim for more money” without having clear scientific arguments about the relevance of research in mental health has been recurrent and unanimous during the discussion. In this context, it was agreed that indicators have to be found in order to evaluate the socio-economic impact of mental health research.

It worth remembering that in 2014 the “Year of the brain” will be organized by the EU and this event is meant to highlight the impacts and translations of mental health research.

It would be interesting to know which countries have a research budget dedicated to mental health as opposed to those where the distinction with other health research budgets is not made. In that context, it has been noted again that mental health research suffers from a lack of recognition which makes it difficult for mental health researchers to compete for funding with other research areas (e.g. cancer).

3.2.2. Gaps in knowledge

3.2.2.1. Research capacities and infrastructures:

Two general topics have dominated the discussions of the WP3 workshop participants: research networks and data sharing.

Research networks

Following the results of the ROAMER preliminary survey¹, the majority of the workshop experts agreed on the fact that there is need for more collaborative research. They recognized that networks, platforms and collaborative spaces are necessary for European researchers. However, arguments were made that networks can also be “*a harmless way to waste a lot of money*” and doubts were raised about the efficiency of such structures, suspected of being expensive and preventing innovation. Due to the high numbers of participants in networks, research would be reduced to the smallest common denominator and would, as a result, lack innovation. It has been added that researchers themselves should be able to contact each other and work together without the intervention of any supervision and without necessarily requiring funding. Finally, the aforementioned criticisms have been considered as avoidable mistakes rather than constitutive elements of networks. Several examples of successful networks (e.g. clinical trials networks in the UK) have been put forward in this context.

More generally, two main types of research networks have been identified. On the one hand, **scientific networks**: rather inexpensive, easily created and managed, they bring together scientists of different disciplines and nations on a common research field and allow them to discuss and elaborate projects together. They are dynamic and heterogeneous, and their mapping is difficult.

¹ At the question “What infrastructures are necessary to deliver [the main mental health research priorities] at a European level?” 66% called for more “network(s)” and/or “collaboration” (n = 44)

On the other hand, **investigation networks** allow small research units to mutualise their research tools (instead of buying expensive facilities which would be underused in each research unit). The investigation network allows an optimisation of the facilities (e.g. offices), equipment (e.g. MRI), databases or infrastructures (e.g. cohorts). It has been suggested to map them through the MERIL® project² and the ROAMER general survey.

To these two broad definitions, **e-networks** have been added identified as a need: networks that allow researchers to identify each other and facilitate contacts and exchanges. These can be virtual and general as ResearchGate®³, which has been mentioned, or more specialized for example in mental health. The e-networks contacts should also lead to real meetings and room for exchanges such as workshops or conferences where researchers can meet, which implicates an appropriate budget for such “networking activities”. Examples of dynamic researchers networking have been mentioned (in the UK and Canada) and it has been said that what is possible at a national level should be developed at the European level.

It emerged from discussions that “research networks” lack a clear definition and can be referred to via various kinds of infrastructures.

Discussions focused on the form that networks can take; participants have suggested the aims and characteristics of research networks which are as follows:

- to reach a critical size for research,
- to pass from individual to collective excellence,
- to allow different research groups to work together and to use the same tools,
- to allow researchers to contact and know each other,
- to insure the storage, sustainability and protection of databases,
- to avoid research overlaps and redundancies throughout Europe,
- to develop the use of common research languages, procedures and standards throughout Europe,
- to limit bias and increase the reproducibility of studies which in turn improves the quality, transparency and credibility of European research results,
- to balance the current competition-driven research field with more collaboration,
- to be researcher created and lead, and not an administrative top-down creation,
- to promote collaboration without dictating what should be researched,
- to be flexible enough to insure innovation,
- not to be “invasive” and hinder research performed outside the network,
- not to worsen the West/East gap but at the contrary participate to its closure,
- to have a limited administrative burden and be sufficiently independent from the institutions that “house” it.

Data sharing

Discussions on the sharing of research data have by and large reached consensus. The baseline was that every public funded research should provide open access and open (anonymised) data⁴. Indeed, the lack of continuity and sustainability of research results was perceived as a weakness and a waste of resources. At the European level, open access would necessitate a homogenisation of the language(s) used in the databases. Although support for the idea of open data and access was rather unanimous among the participants, discussions occurred on the form that they should take. Should it be a mandatory counterpart of any EU funding? Or should an incentive for the provider of the

² Mapping of the European Research Infrastructure Landscape - <http://www.esf.org/activities/science-policy/research-infrastructures/meril-mapping-of-the-european-research-infrastructure-landscape.html>

³ <http://www.researchgate.net/>

⁴ It was noted that the UK government is planning to make publicly funded research accessible free of charge to readers by 2014.

data be created? Open data refers to access and storage; it has therefore been underscored that data cannot be used without collaboration and proper methodology (e.g. for homogenization or standardization). Moreover it was noted that due to ethical questions not all databases can be completely open-access.

Concerning data sharing, the gap between clinical and research data has been identified: sometimes even within one hospital the data does not circulate sufficiently. A clear need for clinical data access and broadcast has been identified. The EU and RIs can be particularly useful for such data gathering, management and access, especially because raw data cannot be used if there is not a minimum of data management and quality control. Initiatives such as Euroreach⁵ have been mentioned as good examples of what is needed. The registries and databases in Europe could be mapped, detailed and provided by the EU. This was pointed out as being of great interest, since access to private and public data in the EU is a bottleneck for EU research.

3.2.2.2. Capacity-building and training in mental health research:

The need for multidisciplinary

It has been pointed out that mental health research covers such diverse areas of knowledge that it requires multidisciplinary and transversal approaches which should be enhanced in the current master's and PhDs devoted to mental health research and for the creation of new ones. In this context, more multidisciplinary training programs should be offered in Europe, with optional modules allowing students to develop their knowledge in the different fields encompassed by mental health research. This multidisciplinary was considered crucial for mental health research and necessary to allow mental researchers to communicate better. E-learning would be of great interest to answer that particular need.

Participants pointed out that training of mental health researchers is fragmented into numerous disciplines that are not fully defined (yet). For example, the question was raised as to what degree health promotion and prevention research should be part of mental health research training. It has further been deplored that the current scope of *European training programs* in research or clinical mental health is not sufficiently known. It was perceived as difficult to know how many disciplines are covered by the available courses. It was suggested that this level of access to the different areas of mental health research should be investigated and evaluated, and indicators of the quality of the programs should be developed. It was pointed out that a simple inventory, even if it is still needed, would not be sufficient.

Training researchers: who, how and how many?

It has been noted that it is currently difficult to know who is trained in mental health research. Discussions showed that there are important differences between countries regarding the contents of psychiatry, psychology and paramedical courses. In some countries the medical schools offer mandatory or dedicated research training, in others this is not the case, and the content of this research training differs considerably across Europe. These differences also concern the training of other mental health professionals (e.g., nurses). Participants raised the question of whether it could be the role of the EU to provide some guidance in order to harmonize this landscape. They also suggested that it would be of great benefit to develop European master's and PhDs involving several universities. Also, the role of E-learning was underscored in order to bridge training gaps.

Arguments were made that it is more and more difficult for mental health professionals to find time both for research and clinical practice. More generally the question has been raised whether or not physicians should continue to pursue a dual research and clinical practice career. It has, on the other hand, also been highlighted that the gap between clinical practice and research has to be reduced; implicating mental health professionals in research seems to be a meaningful way to facilitate the required knowledge transfer between practitioners and researchers. It has been underscored that it would not be relevant to give training on the methodology of research to each clinician. However, every European practitioner should have a consistent training in knowledge transfer and be able to understand and implement evidence-based medicine outcomes in their day-to-day practice.

⁵ Improved access to health care data through cross-country comparisons - <http://www.euroreach.net/>

There was a consensus regarding the fact that in order to enter into an academic career, a minimum of research training should have been mandatorily performed, which is not the case in all EU countries. Academic appointments should also be based on publications in European countries where it is not the case. This obligation would also contribute to reducing the differences in research training and performance between European psychiatrists.

There was further consensus concerning the fact that research training should be concentrated on the quality and excellence of the researchers more than on their quantity.

3.2.2.3. Funding strategies

Communication between funders and researchers

The majority of workshop participants put forward a lack of communication between the researchers' community and the EU Directorate general for research and innovation (DG research), in the sense that researchers are not sufficiently involved in the set-up process of calls. Some of the calls appear as not entirely relevant for the current state of the research and as not corresponding to mental health priorities, while other topics have not been covered by calls for long time. It has however been pointed out that in principle calls are created with researchers using a bottom-up methodology. According to many participants, however, there is a lack of communication and clarity about this process. Even if it is possible to raise to the attention of the DG research on some research topics, it is perceived as requiring too much time. Fast and flexible funding processes should be developed in order to perform some rapid research when necessary and relevant.

There was a general perception that research funding is decided by administrators and not enough by researchers, the latter not being competent for "lobbying" their cause. They should be more visible consulting processes or ways for researchers to voice their research questions and wishes.

The methodology of the calls has also been criticized on the basis that it is too time-consuming and expensive. Further, the evaluation and the mechanisms of funding control of the EU, although necessary, were perceived as too rigid. It is difficult to know exactly how a budget will be spent over three years; more flexibility should be introduced in the allocation of the money.

The instability of research careers

Due to the particular funding modalities, mainly through projects, concerns have been raised about the instability of a research career. After generally long studies, researchers are hired through repeated fixed-term contracts with few guarantees in term of salary and career. This job insecurity could be reduced by increasing the part of core funding in research, at the national and European levels.

ROAMER priorities

An important part of this discussion focused on the strategies that the ROAMER consortium should adopt in order to focus the attention of the DG research on mental health. It has been underscored that proportionally to the burden of mental health diseases, research in mental health is not sufficiently funded in comparison with other health fields. It would be particularly important and interesting to deepen the investigation on the payback of mental health research, especially in an economic crisis period. Also, the cost of mental health disorders seemed to be insufficiently taken into account by policymakers. It has been pointed out that details of Horizon 2020 were currently being discussed and the opportunity window was open, and ROAMER should therefore take advantage of that in order to inform funding allocation. More generally, it was pointed out that the combined expertise and outputs of the ROAMER consortium could be a means to continuously inform research priorities (even beyond the deliverables of the current project).

3.2.3. Advances needed and justification according common criteria

Below are the "advances needed" as drawn from the two WP3 workshops are presented. Note that these recommendations are currently being revised by the panel of experts and other ROAMER WPs, hence they might be modified in the near future.

Area of knowledge	Overarching goals	Advances needed
Resources and infrastructures	Optimise European research strengths.	<ol style="list-style-type: none"> 1. Create an infrastructure which maps the available databases of population, clinical and research data in mental health. 2. Promote mental health disease registries, mental health status surveys and the use of common indicators across countries. 3. Implement open access to publicly-funded mental health research publications. 4. Implement open access for publicly-funded mental health research data. 5. Increase visibility, access to and use of research infrastructures.
	Encourage collaborative and multidisciplinary projects so as to create the needed “critical mass”.	<ol style="list-style-type: none"> 6. Increase the number, quality and efficiency of international and interdisciplinary networks. 7. Develop knowledge exchange activities.
Training, capacity-building and career pathways	Develop access to mental health research training.	<ol style="list-style-type: none"> 8. Encourage and support the creation of European mental health research courses and share available training resources.
	Close the gap between clinical practice and research.	<ol style="list-style-type: none"> 9. Provide basic research training to every healthcare professional. 10. Condition academic careers on the development of research skills.
	Increase the attractiveness of mental health research.	<ol style="list-style-type: none"> 11. Improve the “employability” of researchers and bridge the academic and industrial sectors in order to offer variety and opportunities for research-oriented careers. 12. Incorporate and/or promote mental health research in related research training tracks (health promotion, prevention...).

Funding strategies	Promote innovative, competitive and excellent research.	<p>13. Increase transparency in the development of calls for proposals and involve more researchers in the setting of research priorities.</p> <p>14. Create faster and more flexible funding mechanisms, especially in the short term.</p> <p>15. Increase the proportion of core funding and/or develop long-term calls.</p>
	Improve efficiency of mental health research funding.	<p>16. Create specific funding dedicated to mental health research.</p>
	Improve the level of funding dedicated to mental health research.	<p>17. Increase the link between policymakers and researchers and foster evidence-based policies in mental health and well-being.</p>

3.2.3.1. Resources and Infrastructures

Goal 1: Optimise European research strengths.

1. Create an infrastructure which maps the available databases of population, clinical and research data in mental health.

- **Identified gaps addressed by the recommendation:** It seems that the available European research databases are neither sufficiently known nor used by researchers. This under-information and under-utilisation leads to duplication of efforts, waste of resources and loss of research opportunities. Moreover, the databases can be difficult to understand and use due to differences in standards and language.
- **Efficacy & impact:** In order to improve the accessibility and the (e-)sharing of European clinical and research data, it seems necessary to create a database of all available mental health databases in Europe, including clinical, routine, survey and research data.
- Providing harmonised information about these databases (including owner, objectives, types of variables, method and language), available in English, would facilitate their dissemination and usage in a way that matches their potential.
- This common tool would facilitate collaboration and the launch of single- and multi-national projects for the European research community. Moreover, by doing so, mental health would be more attractive for young researchers who are often interested in fields with solid research materials.
- **Answerability/feasibility in Europe:** The European network of Research Infrastructures (RIs; a leading example being the ESFRI roadmap⁶) is sufficiently developed so that an online database of health databases with free access for the research community could be established. Translation of the databases into English would further be needed in order to allow the actual use and analysis of the data across countries. Specific funding (cf. Recommendation n° 16) would be dedicated to the creation, maintenance and translations related to this database of mental health databases.

⁶ http://ec.europa.eu/research/infrastructures/index_en.cfm?pg=esfri-roadmap

- An FP7 project (**Euroreach**⁷) is currently attempting to improve the access to and use of European health care data. This project represents a pilot project for the present recommendation and illustrates its feasibility.
- **European research strength:** European countries have a high potential for data linkage (as illustrated by the experiences of the Nordic countries) and their routine data collection is among the best in the world. Their coordination and accessibility would transform this advantage into a long-term leading position for Europe.

2. Promote mental health disease registries, mental health status surveys and the use of common indicators across countries.

- **Identified gaps addressed by the recommendation:** In Europe, there is a lack of comparability among data designed to measure similar items; this is due to language differences but also to the way the data are collected, reported and classified.
- **Efficacy & impact:** The activity of an infrastructure in charge of mapping mental health databases (cf. Recommendation n°1) could be linked to the promotion of mental health registries and comparable indicators in order to increase the comparability of data across Europe.
- **Answerability & feasibility in Europe:** This recommendation would be feasible through the specific infrastructure described in Recommendation n° 1 but could also be the focus of a distinct research project. Again, the **Euroreach** project (cf. Recommendation n° 1) and existing working groups (e.g. at OECD and Eurostat) could provide models for carrying out such an initiative. Regardless of the solution chosen, dedicated funding for such initiatives in mental health research would be needed (cf. Recommendations n°16).

3. Implement open access to publicly-funded mental health research publications.

- **Identified gaps addressed by the recommendation:** It is paradoxical that public money finances projects for which access to the published results requires payment of additional public money.
- **Efficacy & impact:** This recommendation aims to foster the diffusion of publicly-funded knowledge. Open-access is increasingly becoming a standard publication practice thereby making results available to a wider audience. Research funding entities and/or commissioners should establish this as an obligation for publicly-funded research to ensure that results are available to other research units.
- **Answerability/feasibility in Europe:** This has increasingly become the practice with respect to publicly-funded research in Canada and the US, and implementation of an open access requirement is planned for 2014 in the UK. Thus, the recommendation should be feasible for publicly-funded research in Europe. Penalties and random controls could be considered in order to enforce this rule.

4. Implement open access for publicly-funded mental health research data.

- **Identified gaps addressed by the recommendation:** Another identified gap is the waste of resources resulting from lack of access to data from publicly-funded research projects. Frequently, data collected by research projects are neither communicated nor accessible to the wider research community.
- **Efficacy & impact:** This recommendation aims to optimise the use of publicly-funded research data. This newly-available data would ultimately need to be structured and presented in an accessible format (e.g. a unique internet platform, the database of databases), within a dedicated infrastructure.
- **Answerability/feasibility in Europe:** The open data philosophy is making inroads in the scientific community, and it would be possible to condition public funding on open access to data unless these data are particularly sensible or not anonymised.
The US and UK governments have already implemented websites⁸ where national databases are available to their citizens. Likewise, a number of journals and websites offer the possibility of publishing anonymised datasets. Based on these examples, it seems feasible for the EU and national governments to condition funding to public access to data.

⁷ <http://www.euroreach.net>

⁸ <http://data-archive.ac.uk/> ; <http://www.data.gov/>

Goal 2: Encourage collaborative and multidisciplinary projects so as to create the “critical mass” necessary.

5. Increase visibility, access to and use of research infrastructures.

- **Identified gaps addressed by the recommendation:** It seems that the existence of European research infrastructures (RIs) and their accessibility rules and usability - such as imaging facilities or biobanks - are not always known among mental health researchers. This information gap leads to insufficient use of resources and lost research opportunities. Moreover, even when the RIs are known, they may be difficult for researchers to access, as the rules of accessibility are not homogeneous and sometimes not clearly communicated.
- **Efficacy & impact:** Even though Europe has an increasing network of research infrastructures, there is still a need to better communicate their presence so as to facilitate access by a maximum of users. In addition to this communication effort, financial and legal means should be provided to the RIs in order to allow them to increase their accessibility.
- **Answerability/feasibility in Europe:** Numerous and important generic RIs currently exist in Europe and are mapped by the current MERIL⁹ project. It is likely that complete information on infrastructures, their types and their accessibility rules (not yet on the MERIL website) will soon be available. This information will then need to be made available to the mental health research community.
- The recent European Research Infrastructure Consortium (ERIC) provides another example of tools promoting RIs: ERIC confers a specific legal status to infrastructures of European interest, thereby facilitating their extension to additional countries.
- **European research strengths:** The number of RIs in Europe is high, and via the ESFRI Roadmap the EU has expanded and streamlined them over the past ten years. Thus, Europe is in a favourable position due to the relative density of its scientific community, so that no research should be hindered by the distance between a research unit and the relevant RI(s).

6. Increase the number, quality and efficiency of international and interdisciplinary networks.

- **Identified gaps addressed by the recommendation:** Mental health research is particularly interdisciplinary, which leads to a need for more collaborative research work in Europe. This collaboration is further necessary in order to tackle regional disparities in terms of resources, access to data and funding.

Moreover, networks are perceived as a means by which competition in research can be replaced by collaboration, although existing networks have been described as creating an administrative burden.

- **Efficacy & impact:** European e-networks and investigative and scientific networks have been identified as key infrastructures to develop interdisciplinary and international research and as powerful tools for the mutualisation of research means.

They are further capable of ensuring the storage, sustainability and protection of open access databases, developing the use of common research languages, procedures and standards throughout Europe, limiting biases and increase the reproducibility of studies.

Moreover, networks can bring together scientists of different disciplines and nations in a common research field and allow them to discuss and elaborate projects together.

Such networks can be formal or informal but require a minimum level of funding which could be included in any funding proposal as “networking activities”. Networks should be inclusive in order to allow researchers from all geographic origins to close existing gaps.

- **Answerability/feasibility in Europe:** Important research projects in mental health require a minimum of financial and human resources in order to be competitive with the rest of the world. The critical mass can easily be reached at the European level.

Scientific networks should be more researcher-led, and funders should support the networking needs and activities of research units. Investigative networks can, on the other hand, be initiated by public bodies in

⁹ <http://portal.meril.eu>

order to provide services to national and European research units. These networks are Research Infrastructures as defined in the ESFRI roadmap¹⁰ and may be linked to it.

Attention should be given to not overburdening the management of networks and their accessibility with too heavy an administrative load. Furthermore, incentives and support could be given in order to develop the use of Information Technology (IT) in the networking activities.

- **European research strength:** The diversity and number of research units is clearly an added value for European research. Considering the quality and quantity of data collection and linkage in some countries of Europe, Europeans are in a position to be leaders in mental health research if the resources are mutualised. The network of RIs throughout Europe is growing, mental health researchers should voice their demands and infrastructures answering to their specific needs should be built.

7. Develop knowledge exchange activities.

- **Identified gaps addressed by the recommendation:** Virtual or physical spaces as well as some events dedicated to mental health topics are needed so that researchers may meet, have discussions and share contacts, ideas and concepts.
Apart from networks (cf. Recommendation n° 6), collaborative research should be fostered by informal meetings and exchanges among mental health researchers coming from different disciplines and countries.
- **Efficacy & impact:** A systematic knowledge exchange for mental health research in Europe would be a step towards reaching the “critical mass” necessary to attain a leading position in mental health research worldwide since this exchange would also create opportunities for new research projects.
- **Answerability/feasibility in Europe:** Knowledge exchange activities should be acknowledged as an integral and necessary part of mental health research to which research networks (cf. Recommendation n° 5) also contribute. Such small events where researchers can meet and develop ideas together could be initiated by public authorities, but they likely would be more efficient if they were initiated by the researchers themselves who would need funding. Therefore, a specific budget for “knowledge exchange activities” could be included in all funding, as a routine part of researchers’ activities. These types of activities could be virtual or physical and do not have to be formal.
- **European research strength:** European countries have sufficient researchers and available resources to create a critical mass if they are sufficiently linked.

3.2.3.2. Training, Capacity-Building and Career Pathways

Goal 3: Develop access to mental health research training.

8. Encourage and support the creation of European mental health research courses and share available training resources.

- **Identified gaps addressed by the recommendation:** Heterogeneity in research training in Europe may be perceived as a limit to mental health research collaboration.

Furthermore, for countries that do not have the critical size to support a specific training program for mental health research, programs with a European perspective are required for students from these countries. However, there are currently no European curricula for mental health research training.

- **Efficacy & impact:** Comparable research training among European researchers would facilitate exchanges and would likely improve overall research quality. To this end, specific mental health research master’s and PhDs could be created at the European level and organised by several universities. This could also address the specific training needs of clinicians by giving them the clinical and research skills necessary for the specificities of mental health research.

¹⁰ http://ec.europa.eu/research/infrastructures/index_en.cfm?pg=esfri-roadmap

Increasing the sharing of available training resources in research and further encouraging students' mobility (physically and virtually) would ensure access to research training in regions without their own capacities. This latter point is especially important in order to reduce the East-West gap in research training.

- **Answerability/feasibility in Europe and European research strength:** Europe has extensive experience in the mobility of students, with numerous European master's in a variety of domains. The EU and individual countries can provide incentives for the creation of European mental health master's and inter-university PhDs, guidance for the harmonisation of research training in medical schools and additional support for student mobility.

Efforts should be directed to increasing the possibility of e-learning and other distance training, based on existing pilots and experiences in other fields.

For example, CIBERSAM is currently launching a specific mental health research master¹¹, which could be an example for other initiatives.

Goal 4: Close the gap between clinical practice and research.

9. Provide basic research training to every healthcare professional.

- **Identified gaps addressed by the recommendation:** One of the main gaps identified is the current lack of coordination and exchange between clinical practice and research in mental health. There is also a lack of transversality in the training of psychiatrists and other mental health professionals, which is a handicap in such a multidisciplinary field.
- **Efficacy & impact:** In order to bridge the gap between research and clinical practice in mental health, it would be of great interest to transmit research basics to every health professional so that they understand the use of evidence in medicine and are equipped to implement research outcomes.

On the other hand, researchers need to be informed by clinicians about current interrogations and observations that could lead to research questions.

- **Answerability/feasibility in Europe:** This recommendation is of particular concern for professional associations and medical schools; the role of the EU and individual countries would be to provide leadership and recommendations in order to close the knowledge gap between clinical practice and research in mental health.

10. Condition academic careers on the development of research skills.

- **Identified gaps addressed by the recommendation:** In Europe, an individual's research record, training and teaching experience are not always the key determinants for appointments to senior academic positions.
- **Efficacy & impact:** In order to increase the competitiveness of European research, incentives should be created to increase the number of merit-based appointments i.e. focusing on the publications and/or the research training and skills of the candidate. These measures are also likely to increase the attractiveness for junior scientists of academic mental health research.
- **Answerability/feasibility in Europe:** Guidance could be provided on the EU and national levels. Moreover, better transparency regarding the criteria and processes of academic appointments would require little in terms of financial resources.

¹¹ http://www.ub.edu/web/ub/en/estudis/oferta_formativa/master_universitari/fitxa/R/M2806/index.html

Goal 5: Increase the attractiveness of mental health research.

11. Improve the “employability” of researchers and bridge the academic and industrial sectors in order to offer variety and opportunities for research-oriented careers.

- **Identified gaps addressed by the recommendation:** Due to the absence of clear career paths and the prevalence of short-term employment contracts, young trainees (in medical school or research training) may be discouraged from entering into an academic career in mental health research.
In particular, there is a gap between academic and industrial careers in some parts of Europe, compared to regions where researchers can easily pass from a private company to a public research unit with few difficulties (and vice versa).
- **Efficacy & impact:** The training of mental health researchers should include modules that foster their competencies not only in the public but also in the private sector. This would increase the exchange between private and public research as well as employability and research career opportunities, which would clearly improve the attractiveness of mental health research.
Moreover, the quality of research itself would be likely to be improved because cross-fertilisation could occur between ideas and concepts in private and public research.
Finally, several skills developed in the private sector could be useful in the public sector (e.g., project management, human resources management, public relations).
- **Answerability/feasibility in Europe:** Europe currently leads initiatives that bridge the academic and private sectors in the wider field of biomedicine. These experiences can provide concrete and applicable lessons that may be readily applied in the mental health field.
- **European research strength:** Europe has a well-trained research workforce as well as the training capacities needed to provide the appropriate incentives for the future generation of mental health researchers.

12. Incorporate and/or promote mental health research in related research training tracks (health promotion, prevention, etc.).

- **Identified gaps addressed by the recommendation:** The main share of mental health research training is currently taking place in courses related to psychiatry, psychology and neurosciences. However, mental health research is concerned with and requires a much wider range of disciplines.
- **Efficacy & impact:** In order to make the case for mental health research careers, efforts should be made to increase the awareness of future researchers of the implications of mental health research and to transmit the specific skills needed. To that end, mental health content should be incorporated into public health, epidemiology, health statistics and other related courses, given the disease burden represented by mental health disorders.
- **Feasibility and strength in Europe:** This recommendation is relevant both to institutions offering courses and to EU/national authorities. While the former may readily incorporate such a change in practice into their course designs, the latter may provide the appropriate guidance and harmonisation.

3.2.3.3. Funding Strategies

Goal 6: Promote innovative, competitive and excellent research.

13. Increase transparency in the development of calls for proposals and involve more researchers in the setting of research priorities.

- **Identified gaps addressed by the recommendation:** It appears that sometimes calls for proposals in mental health research do not respond to research needs and that their phrasing is ambiguous. This may be due to the absence or weak visibility of existing bottom-up and consultative mechanisms for the development of calls.

- **Efficacy & impact:** Researchers are the most informed of the state of research in their own domains, and they should be more involved in the selection of EU research topics, which would orientate the calls for proposals to the most innovative fields.
At the same time, exchanges among researchers and policymakers may be fruitful as policymakers are in a position to prioritise areas with particular importance for society.
In any case, the transparency of the development of calls for proposals must be improved, and the possibility to participate in this process should be actively communicated.
- **Answerability/feasibility in Europe:** Clarifying the means and consultative processes that allow researchers to voice their research priorities appears to be feasible at a limited cost (if any). In this context, the EU and many individual countries may draw upon a number of existing networks that can collectively and efficiently solicit participation in the setting of themes for calls for proposals.

14. Create faster and more flexible funding mechanisms, especially in the short term.

- **Identified gaps addressed by the recommendation:** It is difficult for mental health researchers to have access to rapid funding mechanisms. Moreover, with the grant application mechanism research units lose efficiency due to the time foregone for actual research.
- **Efficacy & impact:** Some dynamic fields of mental health research necessitate rapid investigation under specific circumstances; sufficiently reactive funding mechanisms should be developed in order to facilitate competitive research on these topics.
- **Answerability/feasibility in Europe:** Initiatives from researchers are difficult to fund at the European level, and thus the calls system may be balanced with more investigator-driven projects, such as those offered under the FP7 program “Ideas”.

15. Increase the proportion of core funding and/or develop long-term calls.

- **Identified gaps addressed by the recommendation:** The relative lack of core funding of mental health research has led to several gaps already mentioned: the instability of mental health researchers’ careers leading to a low attractiveness of the field and the lack of opportunities for researchers’ initiatives. In addition (and paradoxically), a low level of core funding impedes research units from responding to calls due to the lack of human resources necessary for the application processes.
Moreover, it is debatable whether having several research units compete for one project is efficient, given that eventually only one unit will obtain the grant while other competitors will have worked on the same subject for few if any outcomes.
- **Efficacy & impact:** Due to the dominance of project-based funding in European research, researchers are often faced with professional insecurity, which is a disincentive for pursuing research careers (especially compared to clinical practice). A shift towards longer projects and an increase in core funding would ameliorate this problem.
Calls for proposal also represent an administrative burden, such as the requirement of detailed budget predictions that may seem arbitrary. The necessary funding controls could be made more *a posteriori* and linked to a lighter administrative burden.
- **Answerability/feasibility in Europe:** With H2020, a window of opportunity is open for modifying funding procedures.
- **European research strength:** European research resources are numerous but need to be secured in order to ensure sustainability and quality.

Goal 7: Improve efficiency of mental health research funding.

16. Create specific funding dedicated to mental health research.

- **Identified gaps addressed by the recommendation:** There is a lack of resources dedicated to mental health research in Europe, and it appears that the proportion of investment in human and financial resources does not match the burden of mental disorders.

- **Efficacy & impact:** Dedicated mental health research funds would allow implementation of several of the recommendations made above (such as those listed in Part I), particularly the database of databases for mental health research (recommendation n° 1).
- **Answerability/feasibility in Europe:**
It seems worth considering the possibility of having an institution dedicated to funding and structuring European mental health research, similar to the NIMH¹² in the US.

Goal 8: Improve the level of funding dedicated to mental health research.

17. Increase the link between policymakers and researchers and foster evidence-based policies in mental health and well-being.

- **Identified gaps addressed by the recommendation:** There is a lack of dialogue between researchers and policymakers. This recommendation aims to tackle the gaps mentioned in the recommendations n° 13 and n° 16, i.e. the discrepancies between the needs for mental health research identified by researchers and the available calls and the discrepancy between the burden of mental disorders and the level of research investment.
- **Efficacy & impact:** It seems that European societies and decision makers are not fully aware of the importance of mental health and well-being research. Consultative entities should be created and expanded in order to transfer to decision makers the knowledge acquired about the mental health and well-being of the European population and the evidence on how to improve it. Likewise, researchers need to be better informed about the questions that are of particular interest to policymakers.
- Moreover, indicators to evaluate the potential benefit of mental health research, especially in terms of socio-economic impact, should be developed in order to 'make the case'. For instance, currently little is known about the return on investment in mental health research but early evidence has indicated a high rate of return¹³.
- **Feasibility and strength in Europe:** Europe has sufficiently developed research networks and administrative bodies that would allow the creation of effective consultative initiatives. Some new formats may need to be created in order to allow this exchange of knowledge between researchers and policymakers with the goal of supporting evidence-based policy.

3.3. Clinical research task force

3.3.1. Introduction to the area

Clinical Research aims to address patient related outcomes that are relevant for diagnosis and treatment of patients with mental disorders. It includes development and validation of diagnostic methods and questionnaires in psychometric and validation studies that can be used by clinicians or other healthcare professionals in order to establish diagnosis of a mental disorder and to delineate adequate treatment. It involves development of new treatment interventions for mental disorders. It includes evaluation of efficacy and effectiveness of interventions in, for example, Randomized Clinical Trials, including proof of concept trials, efficacy trials and pragmatic trials. Those interventions can be pharmacological, brain related (e.g. Deep Brain Stimulation), psychotherapeutic, systemic, psychosocial in nature, or a combination of several. The Cochrane Collaboration provides a clear methodology to establish such effectiveness of RCTs by a systematic review process. However, Clinical Research encompasses more than this methodology. It also encompasses establishment of risk profiles for patients that may lead to providing treatment specifically fit for specific patient groups, in this way accounting for heterogeneity in syndromes such as e.g. subtypes in depression. Furthermore, Clinical Research has methods to include the patient perspective by the use of patient preferences in RCTs and patient-related outcomes, and addresses adherence of doctors or therapists as well

¹² National Institute for Mental Health - <http://www.nimh.nih.gov>

¹³ Health Economics Research Group, Office of Health Economics, RAND Europe. Medical Research: What's it worth? Estimating the economic benefits from medical research in the UK. London: UK Evaluation Forum; 2008.

as patients to treatment protocols as process or outcome measures. Outcomes of Clinical Research can be on the specific mental symptom level, on treatment response, on remission of mental disorder, on occurrence of relapse in relapse prevention or long-term treatment in chronic conditions; but also on quality of life and functioning, which is relevant in patients with comorbid physical disorders in terms of physical or general functioning, and in terms of work absenteeism in patients who are absent from work due to their mental disorder. Another important outcome is societal participation. Clinical research should address diagnostic and treatment complexities in comorbidity by developing diagnostic and treatment algorithms designed to support medical decision making, and it should take the patient perspective into account by use of Shared Decision Making methods. Furthermore, large clinical cohort studies are needed, that is to say clinical disorder based cohort studies. These are crucial to better understand patients' needs from a "real world" perspective, which is necessary to supplement the information that may come from clinical trials and other sort of studies in selected populations. They are also important from the perspective of analyzing rare events such as mortality, cross-cultural differences, and pharmacovigilance.

3.3.2. Gaps in knowledge

This question resulted in a range of items (challenges) that could be categorized into twelve categories (themes) of challenges that survey participants evaluated as to be met in clinical research. The categories were formed by two independent post-doc researchers via qualitative analyses. These categories formed were, 'challenges with regard to...':

1. Understanding mental health related disorders
2. Diagnostics and assessment tools
3. Prevention approaches
4. Development of (novel) interventions/treatments
5. Evaluation of interventions (effects, effectiveness, cost-effectiveness etc.)
6. Outcomes
7. Understanding intervention processes and mechanisms
8. Overcoming stigma and social exclusion
9. Delivery of and access to mental health care
10. Translation, integration and dissemination of research findings and treatments
11. Conducting research
12. Facilitating research

Each of the categories captured several specific challenges. Duplicates were removed, and redundancies were cut by two independent researchers. The following section provides an overview of examples of challenges from each of the categories:

1. Specific challenges/goals regarding 'understanding mental health related disorders' are:
 - a) To intervene early
 - b) To gain more insight into the neurobiological base of brain disorders
 - c) To understand staging and subtyping of clinical trajectories
 - d) To assess comorbidity in severe mental disorders
 - e) To take into account protective factors
 - f) To acknowledge the developmental perspective
 - g) To identify environmental risk factors
 - h) To integrate biological research with epidemiological, psychological, and genetic research
 - i) To study specific populations such as children, adolescents and older people
2. Specific challenges/goals regarding 'diagnostics and assessment tools' are:

- a) To increase standardization of screening and/or specific diagnostic/scientific tools and to improve diagnostic precision
 - b) To foster adequate screening and early diagnosis of mental disorders
 - c) To foster adequate screening of developmental disorders
 - d) To foster the development of adequate screening tools for neurobiological rooted symptoms in psychiatric disorders
 - e) To foster the development of screening tools for comorbidity in psychiatric disorders
 - f) To establish risk profiles of patients in need of certain treatments
 - g) To develop of neuroimaging techniques and assess their relation to the diagnosis of mental illness
 - h) To identify biomarkers of main symptom dimensions for diagnosis and prognosis
3. Specific challenges/goals regarding ‘prevention approaches’ are:
- a) To develop and test primary prevention interventions for mental health disorders
 - b) To develop coping strategies (e.g. to deal with the economic crisis in Europe) in order to prevent the development of mental health disorders
 - c) To develop preventive educational programs
 - d) To identify risk factors (biological and psycho-social) for mental distress, for preventive purposes
 - e) To foster the use of personalized approaches in prevention
 - f) To prevent stigmatization and social exclusion of patients with mental health disorders
 - g) To increase secondary prevention tendencies aimed at reducing the duration of untreated illness
 - h) To increase the focus on children and adolescents (before onset of disease) for prevention purposes and assess the importance of early interventions (e.g. with regard to mood disorders)
4. Specific challenges/goals regarding ‘development of (novel) interventions/treatments’ are:
- a) To develop, assess and use e-Mental Health Tools
 - b) To increase the utilization of tailored approaches (personalized medicine)
 - c) To development of deep brain stimulation for treatment refractory psychiatric disorders
 - d) To develop more special treatments- pharmacological, psychological and somatic
 - e) To develop specific treatments in order to target comorbidity
 - f) To develop guidance tools that help the clinician to choose between various treatment modalities based on the type of psychiatric illness, stage/progression, previous outcomes, comorbidity and other factors
 - g) To increase attention for psycho-pharmacological approaches
 - h) To increase the development and evaluation of transcranial magnetic stimulation approaches
5. Specific challenges/goals regarding the ‘evaluation of interventions (effects, effectiveness, cost-effectiveness etc.)’ are:
- a) To increase the understanding of the effectiveness of complex interventions e.g. those that involve combinations of psychotherapy and pharmacotherapy
 - b) To assess barriers in the effectiveness of treatments (the interventions currently available for mental disorders are at least as effective as those available for other diseases, but the social context in which they are implemented is so unfavourable that their effectiveness is significantly reduced)
 - c) To gain insight into the efficacy and specificity of psychological interventions
 - d) To assess the cost-effectiveness of mental health related treatments
 - e) To assess the value of preventive approaches

- f) To assess the effectiveness of depot (IM) medication
 - g) Improve the outcome of treatments, since only a limited part of the disease burden of mental disorders can be taken away with current treatments.
6. Specific challenges/goals regarding 'outcomes' are:
- a) To standardize outcomes of psychological interventions
 - b) To identify outcome-related biomarkers
 - c) To increase the focus on reducing long-term chronicity
 - d) To predict which patients with schizophrenia or related disorder do not relapse and therefore do not need antipsychotic maintenance therapy
7. Specific challenges/goals regarding 'understanding intervention processes and mechanisms' are:
- a) To assess dose-response associations
 - b) To gain more insight into adherence and factors that facilitate adherence to treatments
 - c) To gain more insight into mediating factors
 - d) To identify factors that should always be taken into account in clinical trials
 - e) To assess the optimal intervention dose (duration of treatments)
8. Specific challenges/goals regarding 'overcoming stigma and social exclusion' are:
- a) To assess the level of stigmatization and social exclusion of persons with serious mental health problems and/or persons accessing care
 - b) To develop interventions to prevent and/or reduce stigmatization and social exclusion
 - c) To assess self-stigmatization and develop interventions for preventing and/or reducing self-stigmatization
9. Specific challenges/goals regarding the 'delivery of and access to mental health care' are:
- a) To improve provision of and access to effective services and evidence-based health care
 - b) To increase the focus on low social economic status groups in order to foster delivery and access
 - c) To develop patient-centred approaches based on experienced problems, difficulties and disabilities
10. Specific challenges/goals regarding the 'translation, integration and dissemination of research findings and treatments'
- a) To integrate mental health into general health care
 - b) To utilize more cross-disciplinary translational research approaches
 - c) To translate basic research into clinical science
 - d) To gain insight into dissemination processes
 - e) To develop pragmatic practice-based clinical research in real-world settings
11. Specific challenges/goals regarding 'conducting research' are:
- a) To collaborate more intensively with research groups across Europe
 - b) To standardize classification systems and measurements used in research (over countries and over time)
 - c) To conduct more research without financing by the pharmaceutical industry
 - d) To conduct more patient centred research, taking into account patient preferences

- e) To conduct more research focusing on specific clinical populations, high risk subjects, comorbid conditions
- f) To increase attention for differential effects of treatments in research (are certain treatments more effective in certain groups?)
- g) To utilize alternatives for randomized controlled trials
- h) To guarantee the inclusion of patients from both sexes and different age groups
- i) To develop an integrated psychosomatic model of mental health and psychiatric disorders
- j) To conduct large epidemiological studies
- k) To develop better staging and profiling tools in order to study different stages of the disease process
- l) To conduct multi-arm clinical trials designed to develop evidence-based guidelines for psychiatric treatments (including pharmacologic and non-pharmacologic intervention)
- m) To conduct more, longer-term naturalistic studies (clinical cohort studies)
- n) To gain more insight into pharmacological effectiveness in the “real world” beyond efficacy outcome measures
- o) To conduct more clinical drug trials in children and adolescents
- p) To conduct more research on alternatives to coercion
- q) To conduct interdisciplinary population-based research by biological, neurocognitive and behavioural scientists in order to identify their developmental and life-course determinants

12. Specific challenges/goals regarding ‘facilitating research’ are:

- a) To increase funding possibilities and invest in innovation
- b) To reduce regulatory barriers for conducting research in Europe (e.g. pharmacological research)
- c) To decrease the excessive administrative burden of research
- d) To develop common European guidelines for conducting research and harmonize clinical research in Europe
- e) To foster collaborations between clinicians (institutions) and researchers (university and other)
- f) To target the problem of the need to preserve confidentiality while also retaining the ability to study and report the individual case

These specific challenges will be included in the second round questionnaire by means of a close-ended questionnaire approach in which the mentioned challenges will be included as statements. The second round results will provide insight on the importance and prioritization of each of the challenges (in contrast to the first round results that asked for an individual’s perspective, but not how the proposed challenge is perceived by the whole group). Furthermore, the second round questionnaire will specify the disease areas for which the challenge is of importance as well as the strategies on how to meet the challenges (both items were also addressed in the first round questionnaire, but again this round did not assess the group’s perspective but only shows that at least one of the respondents perceives the challenge as relevant for a certain area).

Pre-defined gaps and advances

The first round questionnaire further included pre-defined gaps that were identified in the literature search and the expert survey that was conducted by WP2. These close-ended questions were included in order to guarantee that the respondents shared their opinions with regard to common gaps (as identified in WP2) in case these gaps would not come up in the open-ended questions. The respondents were asked to rate the importance of 23 pre-defined gaps and 9 methodological gaps. The table below gives an overview of the pre-defined gaps.

Pre-defined general and methodological gaps

General pre-defined gaps	Methodological gaps
<ol style="list-style-type: none"> 1. Improving diagnostic strategies and the stratification of diseases 2. Development and validation of diagnostic measures and questionnaires in psychometric and validation studies 3. Exploring the mechanisms of diseases 4. Role of comorbidity between mental disorders and somatic conditions for diagnoses, treatment decisions, treatment and patient-related outcomes 5. Development of new treatment interventions 6. Development of e-health, m-health, virtual reality, gaming methods for diagnostics and intervention 7. Evaluation of treatment effects 8. Development of efficient trial designs 9. Proof of concept clinical trials for innovative treatments 10. Registration trials for new medicines or medical devices 11. Improving interventions in terms of return-to-work, presenteeism/absenteeism 12. Determining the cost-effectiveness of interventions to increase rates of return-to-work, presenteeism, decrease rates of absenteeism 13. Investigator-driven trials assessing the efficacy, effectiveness and safety of authorized treatments, and exploring treatment combinations 14. Interventional and non-interventional research assessing the safety of treatments and treatment side effects 15. Analyzing psychovigilance 16. Clinical cohort studies, assessing course of symptoms and functioning as control group 17. Definition of patient related outcomes that are relevant for diagnosis and treatment of mental disorders 18. Identification of proxy outcome measures using behavioural, neuropsychological or neuroimaging tools 19. Definition of treatment related outcomes 20. Definition of social-economic treatment outcomes 21. Research on (protection of) rights of people with mental health problems, such as involuntary psychiatric treatment and inappropriate poly medication 22. Analyzing rare events such as mortality 23. Analyzing cross-cultural differences 	<ol style="list-style-type: none"> 1. Randomization procedures 2. Blinding issues 3. Placebos 4. Patient preferences by study designs 5. Psychotherapeutic intervention studies 6. Psychopharmacological intervention studies 7. Clinical cohort studies 8. Combining clinical cohort studies and RCTs 9. Other methodological issues

3.3.3. Advances needed in research and justification according to common criteria

The predefined gaps were followed by open questions on advances needed to overcome the gaps. Based on the priority ratings and the advances mentioned by the respondents a list of twenty advances was formed. Next table presents this list of advances.

List of advances established from the first wave survey by the Clinical research Task Force

Goal	Advances needed to reach the goal
New, safe and effective treatment interventions (pharmacological, brain related, psychotherapeutic, systemic, psychosocial, e-Health/m-Health approaches and virtual reality/gamification... or a combination of these)	<p>1. To increase research on new intervention approaches in order to gain more insight into their working mechanisms and to successfully develop effective new interventions. This research can/should specifically focus on:</p> <ul style="list-style-type: none"> - Exploring strategies in order to foster adherence to treatments/interventions - Exploring mediation factors - Exploring the role of these new treatments as an add-on intervention - Conducting more research in order to identify the best diagnostic measures for complexity (of the interventions) and treatment outcomes - Assessing differential treatment effects: are specific approaches more effective for specific subgroups? - Conducting more research on e-Health/m-Health approaches and assessing the level of human contact that is needed to motivate individuals towards sustained use of e-Health/m-Health based treatments - Conducting research that incorporates patient perspectives in treatment - Better trial design (see below)
To understand the mechanisms of diseases	<p>2. To conduct more research in order to reach a wider understanding of different mechanisms (e.g. psychological mechanisms, biological mechanisms, brain mechanisms, molecular mechanisms and environmental interactions) that may underlie diseases.</p> <p>3. To conduct longitudinal clinical cohort studies with nested RCTs.</p>
To evaluate treatment effects	<p>4. To conduct more research on different approaches to evaluate treatment effects, specifically more research is needed on:</p> <ul style="list-style-type: none"> - Standardization of psycho-therapeutic treatment studies - Equivalence trials - Side-effects of treatments - Alternative and/or non-randomised designs - Improved reliability and validity of outcome measures <p>5. To increase the involvement of health-care staff, among others in order stop non-effective treatments.</p>

<p>To perform proof of concept clinical trials for innovative treatments</p>	<p>6. To establish (European) research networks to coordinate and facilitate clinical research.</p> <p>7. To identify or develop standard definitions and guidelines to increase the understanding of the term 'proof of concept'.</p>
<p>To gain insight into the role of comorbidity between mental disorders and somatic conditions for diagnosis, treatment decisions, and treatment and patient-related outcomes</p>	<p>8. To develop research in order to better understand mechanisms of comorbidity and how to investigate and treat comorbidity (including diagnostic strategies).</p> <p>9. To increase research on intervention studies that target comorbidity.</p>
<p>To improve diagnostic strategies and the stratification of diseases</p>	<p>10. To define and validate stages for different diseases.</p> <p>11. To develop and validate new diagnostic approaches and to foster standardization of diagnostic tools.</p>
<p>To improve interventions in terms of return/to/work, presenteeism-absenteeism</p>	<p>12. To conduct more research on interventions that target work disability and return-to-work as the main outcomes.</p> <p>13. To identify or develop standard measures for return-to-work and related outcomes.</p>
<p>To determine the cost/effectiveness of interventions to increase rates of return to work, presenteeism, decreased rates of absenteeism</p>	<p>14. To foster the standard inclusion of cost-effectiveness assessments in studies on return-to-work interventions.</p>
<p>To overcome methodological gaps regarding the inclusion of patient preferences by study designs (specific gaps are for instance the lack of time for the explanation of the trials to patients, no consistency in the measurement of preferences, not sufficiently covered, etc.)</p>	<p>15. To develop or identify standard measures of preferences (thus: to reach more consistency in the measures of preference used)</p> <p>16. To develop designs for preference studies</p>
<p>To overcome methodological gaps regarding psychotherapeutic interventions studies (a specific gap is for instance that placebo studies are missing)</p>	<p>17. To explore what is the most likely accepted placebo in psychotherapeutic studies.</p> <p>18. To increase research on the process and outcomes of different psychotherapies, especially by conducting more RCTs in this field.</p>
<p>To overcome methodological gaps regarding psychopharmacological intervention studies (one of the specific gaps mentioned is that most pharmacological studies are funded by the pharmaceutical industry).</p>	<p>19. To work more closely with industry in a precompetitive environment to ensure high quality trial design, on an independent basis</p>
<p>Overall advance</p>	<p>20. To increase funding/financial investment in order to conduct more research (this advance is needed to reach each of the goals)</p>

Policy related advances

Finally, the first round of the Delphi study included statements on policy related advances that may be needed in order to close the gaps in clinical research. The table below presents the results and shows that effectively all policies are perceived as important in order to close the gaps and to facilitate adequate clinical research in the field of mental health and wellbeing.

Policies needed to close the gaps in clinical research in the field of mental health:

	I do not agree	half-half	I fully agree	Total	Average
Which policies are needed to meet the gaps in Clinical Research in Europe in terms of research capacity?	0	0	0	0	
Structuring pan-European networks of investigation sites for each disease area	13	27	47	87	2.39
Developing common standards and tools, including for Quality Assurance and monitoring	8	31	48	87	2.46
Adoption of common outcome measures in line with the patients expectations	10	25	52	87	2.18
Establishing common methodological principles, in particular regarding the issue of placebo use in randomised trials, the issue of blinding and comparator in non-pharmacological treatments	10	30	47	87	2.43
Which policies are needed to meet the gaps in Clinical Research in Europe in terms of funding for independent (multinational) clinical trials?	0	0	0	0	
Horizon 2020	3	14	70	87	2.77
National funding	2	24	61	87	2.68
Charity funding	9	41	37	87	2.32
Which policies are needed to meet the gaps in Clinical Research in Europe in terms of legislation, particularly as regards?	0	0	0	0	
The low-risk category of clinical research	12	43	32	87	2.23
Ethical aspects of informed consent in psychiatric patients	14	42	31	87	2.2
Total	81	277	425	783	2.44

Furthermore, although we were able to suggest advances based on the outcomes of this first wave of the Delphi survey, no indication could be provided of the following four dimensions of those advances yet:

- Efficacy/effectiveness
- Impact / deliverability / economic benefits in Europe
- Answerability/feasibility in Europe
- European research strength

3.4. Biomedical: Neurobiological, Pharmacological and Clinical Research

3.4.1. Introduction to the area

Work package 4 covers biomedical (neurobiological, pharmacological and clinical) mental health research. Its major aims include the creation of a roadmap to facilitate the translational use of neuroscientific findings to better treat and prevent mental disorders.

It is increasingly clear that core neurobiological dysfunctions operate both within and across diagnostic categories. Exclusively using current diagnostic criteria may be an impediment to improved aetiological understanding of dysfunctions, one possible consequence being pharmaceutical companies cutting resources devoted to psychiatric drug development. This is in the face of manifest unmet needs and thus is an urgent public health situation. There is increasing agreement that biomedical research into the aetiology and treatment of mental disorders needs to overcome such obstacles with new approaches and novel psychopharmacological targets with which to reduce the burden of mental disorders.

3.4.1.1. Definition of subareas

WP4 uses the NIMH Research Domain Criteria (RDoC, <http://www.nimh.nih.gov/research-funding/rdoc/nimh-research-domain-criteria-rdoc.shtml>) as a starting point for its organisation. The RDoCs aim to classify psychopathology using a set of constructs based on observable behaviour and neurobiological measures. The constructs are organised into five domains, which are in turn divided into 'Units of Analysis' such as genes, cells, circuits, behaviour etc. WP4 uses these domains as subareas, assigning a group of experts to each one. Details of the subdivisions and definitions of the domains proposed by the NIMH can be found through the link above. The intention is not to restrict WP4 experts to using identical definitions and constructs to those of the RDoC, rather to use them as an initial heuristic framework which may be adapted as necessary. In particular the RDoC are agnostic with regard to traditional diagnoses, but these will naturally be considered by WP4, along with developmental and environmental aspects not explicitly included in the RDoC matrix. The Expert Groups based on RDoC domains are completed by the addition of two further areas, Comorbidity and Pharmacological Treatments (including regulatory aspects), which are of great importance yet not directly encompassed by the RDoCs. The resulting WP4 Expert Groups are as follows:

- Positive and Negative Valence Systems
- Cognitive Systems
- Arousal and Regulatory Systems
- Comorbidity
- Pharmacological Treatments, including Regulatory Aspects
- Systems for Social Processes

3.4.1.1.1. Positive and Negative Valence Systems

- Positive and negative valence are evolutionarily essential states underlying two opposite behavioural tendencies: approach and withdrawal. These two opposite ancestral behaviours guide an organism to emission of the necessary responses to search for life-supporting events and to avoid harms. Thus they warrant survival and evolution (Alcaro and Panksepp, 2011).
- The RDoC divide negative and positive valence systems into several constructs. They include definitions which were used as starting points for this expert group. The full definitions may be found through the links below and are not reproduced in this interim report.

<http://www.nimh.nih.gov/research-funding/rdoc/positive-valence-systems-workshop-proceedings.shtml><http://www.nimh.nih.gov/research-funding/rdoc/negative-valence-systems-workshop-proceedings.shtml>

3.4.1.1.2. Cognitive Systems

- Psychiatric disorders implicate deficits in many cognitive systems, as well as their interface with affective (including motivational) and social processes.
- Cognitive systems may include processes of perception, attention, memory, learning, thinking and executive function (including decision-making, problem solving and planning).

3.4.1.1.3. Arousal and Regulatory Systems

- Arousal: a state of being conscious, awake and alert, which is required for information processing underlying all cognitive functions and emotional expressions. According to an operational definition (Pfaff et al. 2007), an animal or human with higher generalized arousal shows greater sensory alertness, enhanced mobility and is more reactive

emotionally. Arousal is crucial for motivating various behaviours including sexual activity, exercise, the anticipation of a reward, and coping with stressful experiences.

- Stress: a composite multidimensional construct in which three components interact:
 - the input, when a stimulus, the stressor, is perceived and appraised,
 - the processing of stressful information, and
 - the output, or stress response (Levine, 2005).
- The three components interact via complex self-regulating feedback loops with the goal to restore homeostasis through behavioural and physiological adaptations. Since adaptations imply dynamic changes in specific emotional and cognitive brain circuits requiring energy, a new science is emerging dedicated to calibrate and monitor these changes as indices of vulnerability and resilience. This is the science of allostasis and allostatic load (McEwen and Gianaros, 2011).
- Arousal does not necessarily cause a stress response, but the reaction to a stressor is always preceded and accompanied by arousal, particularly in cases of an adverse experience.
- The most arousing and stressful condition is a situation of uncertainty where there is no or ambiguous information, lack of control and poor prediction of upcoming events, but with a fearful anticipation of worry and other cognitive/emotional representations of inability to cope.
- The impact of such a stressor, that is usually chronic, is modulated by personality factors, self-esteem and the degree of optimism that help to appreciate a sense of safety, social position and social support or combinations of these psychosocial contexts (Lazarus 2006, Taylor 2010).

3.4.1.1.4. Comorbidity

The term 'comorbidity' was established by Feinstein (1970) to designate those cases in which a 'distinct additional clinical entity' occurred during the clinical course of a patient having an index disease. The concurrent presence of several pathological conditions in the form of comorbidity and multimorbidity is more a rule than an exception in all populations of patients.

3.4.1.1.5. Pharmacological Treatments, including Regulatory Aspects

-
- Includes compounds that affect mental functions (such as mood and cognition) and behaviour.
 - Clinical psychopharmacology examines those compounds that show efficacy in treating mental disorders.
 - Another approach: symptoms clusters and compounds as treatments for specific symptoms or groups of symptoms.

3.4.1.1.6. Systems for Social Processes

Starting point: Social processes should be understood as intra-individual, such as imitation, theory of mind (social cognition), social dominance, facial expression identification, attachment/separation fear, self-representation areas.

Possible processes for inclusion:

- Empathy
- Social approach-avoidance
- Sense of identity
- Personality traits
- Mindfulness
- Smell/odour
- Touch
- Body rhythms

- Eye contact, gaze
- Personality traits
- Deception, humour, smile
- Interpersonal sensitivity
- Interpersonal attraction
- Interpersonal synchronization of behaviours
- Self-other differentiation

Empathy is the capacity to recognize, understand and share the emotional states of others (Decety and Jackson, 2004; Decety and Moriguchi, 2007).

- Lack of empathy has been invoked as an explanatory mechanism in various forms of psychopathology, but foremost in autism spectrum disorders (ASD) and conduct disorder (CD). Usually, various forms of imitation and empathy can be differentiated that are likely to be underpinned by partially independent neural substrates. These forms include emotional and non-emotional, automatic, and voluntary imitation, as well as motor, cognitive, and emotional empathy (Baird et al., 2011).
- Empathy is assumed to consist of three components: motor, emotional, and cognitive empathy (Blair, 2005).
 - Motor empathy refers to automatically and unconsciously mirroring the facial expressions of another person, known as facial mimicry.
 - Emotional empathy refers to the experience of emotions consistent with and in response to those of others.
 - Cognitive empathy is the ability to rationally understand and recognize the emotional state, and take the perspective of other persons; so called Theory of Mind (ToM).
- The perception-action model posits that observation of emotions activates neural circuits responsible for generating the same emotion and thus activating the motor representation, i.e. motor empathy, and associated emotional autonomic responses. This is suggested to result in resonance with the emotional state of another person, i.e. emotional empathy, and facilitating emotion recognition, i.e. cognitive empathy (Preston and de Waal, 2002; see also Decety and Jackson, 2004; Decety and Moriguchi, 2007).
- Automatically mimicking and synchronizing emotions with other people facilitates emotion recognition, social interaction, as well as empathic functioning (Singer, 2006; Sonnby-Borgstrom, 2002; Stel and Knippenberg, 2008; Stel and Vonk, 2010).
- Emotional facial expressions trigger facial mimicry, even if expressions are observed unconsciously (Dimberg et al., 2000). Facial expressions are suggested to generate concordant changes in the autonomic nervous system (ANS), associated with feeling the corresponding emotion (Hess et al., 1992; Levenson et al., 1990; Sonnby-Borgstrom, 2002). Hence, facial mimicry is assumed to induce emotional synchronization and to facilitate emotion recognition (Decety and Jackson, 2004; Preston and de Waal, 2002; Stel and Knippenberg, 2008; van Baaren et al., 2009).

Theory of Mind (ToM) is a broader concept that refers to the ability to understand mental states, intentions, goals and beliefs, irrespective of the emotional state and relies on structures of the temporal lobe and the pre-frontal cortex. (Singer, 2006).

- Although empathy and ToM are often used as synonyms in the literature, these capacities represent different abilities that rely on different neuronal circuitry.
- Finally, the abilities to understand other people's thoughts and to share their affects display different ontogenetic trajectories reflecting the different developmental paths of their underlying neural structures.

- In particular, empathy develops much earlier than mentalising abilities, because the former relies on limbic structures which develop early in ontogeny, whereas the latter rely on lateral temporal lobe and pre-frontal structures which are among the last to fully mature.
- Human social skills require the ability to adapt and regulate instinctive reactions to emotional signals, in particular the communicative signals of threat or appeasement conveyed by emotional facial expressions (Ohman, 1986; Blair, 2003). In particular, the lateral orbitofrontal cortex and the adjacent ventrolateral prefrontal cortex are involved in the selection of actions that override automatic and motivationally (reward) driven response tendencies (Elliott et al., 2000; Passingham et al., 2000; Rushworth et al., 2007).
- Numerous studies have addressed the neural bases of perception of social emotional signals, in particular facial expression (Adolphs, 2002), detailing the crucial role of the amygdala and other limbic structures in the automatic processing of (negative) facial expressions (Adolphs, 2002; McClure et al., 2004; Strauss et al., 2005). The cerebral and cognitive mechanisms controlling the behaviour evoked by these perceptual processes, i.e. approach-avoidance tendencies, appear to be controlled by the lateral orbitofrontal cortex (Roelofs et al., 2009).
- The 'self' is a complex multidimensional construct deeply embedded and in many ways defined by our relations with the social world. Normal individuals preferentially recruit the middle cingulate cortex and ventromedial prefrontal cortex in response to self compared with other-referential processing.

3.4.2. Gaps in knowledge

1. ICD/DSM Classification and WP4

ICD/DSM are distant from biological mechanisms, hence WP4 has adopted an organisation by mechanism based on the RDoC. However we should not omit traditional diagnostic categories, as current healthcare systems and funding are based on them. We already relate many mechanisms to diagnoses in our position statements, and we can cite examples of these. We should not claim to be comprehensive as we do not have experts in every single diagnostic category.

Current diagnostic systems have limited utility for biological research because they are distant from biological mechanisms, yet there is a risk to being too negative about existing clinical diagnostic systems. They are real disorders which occur frequently and there is a risk that political understanding of this may be compromised. It is correct that we have doubts about the relationship between diagnosis and biology, and we can bear this in mind when doing research but it is not necessarily appropriate when approaching funding issues. Current diagnoses do have specificity: there is a huge difference between schizophrenia and depression and we would not treat them the same. However their validity is not good for genetic and biological investigations of mechanism. There are common intracellular pathways and genetic variants that can cause different mental disorders. An analogy is that a house and a bridge may both be made from bricks but that overall constructs are very different. A diagnosis contains a variety of different kinds of patient and is by definition a simplification. One suggestion is to define underlying mechanisms for big symptom clusters, then deal with diagnoses. From the point of view of epidemiology we try to explain variance. This depends on how we define endpoints. We may be able to get more valid definitions of these. This does not mean we do not know what traditional diagnoses such as depression and schizophrenia are, but we are trying to define endpoints with higher explanatory power.

It was suggested that WP4 should include specific coverage of each ICD/DSM domain and that our analysis should emphasise gaps by diagnosis. It was pointed out that WP5 plans to take a dual approach, using an RDoC-type approach but incorporating traditional ICD/DSM categories by including a statement making the link from these to the other material. It was felt that without this the output would lack substance. One concern is that WP4 does not have experts covering every diagnostic category and such a statement may end up being uneven. However WP5 reached a consensus that dealing with the 15 DSM domain areas is feasible. We might name some gaps that overarch mental disorders in general while others are more appropriate to certain disorders (e.g. the genetic architecture of bipolar depression is better delineated for bipolar depression than for unipolar depression; certain mechanisms are implicated in drug addiction that may or may not be involved in behavioural addictions). It was decided that WP4 will try to cover diagnostic categories pragmatically using experts covering the diagnostic spectrum. In our position papers

we already mention many dimensions that cut across different diagnoses. A strategy would be to cite examples from these, without claiming to be comprehensive.

2. Terminology: psychiatric ‘disorder’, ‘disease’, ‘disease entities’ or ‘illness’?

Some misunderstandings in biological mental health research stem from the incorrect idea that we are dealing with ‘diseases’. ‘Mental disorders’ is the only term used in ICD/DSM. ‘Mental and behavioural disorders’ is a WHO terminology that European countries have signed up to. It was suggested ‘disease’ implies a monogenic, pathogenic entity, however it was pointed out that is not the case in for example cancer and hypertension. It was decided to respect the convention of using the term ‘disorder’.

3. Terminology: ‘personalised medicine’

‘Personalised medicine’ was identified as an overarching theme in WP4, but scepticism was expressed about the usefulness of this term. It is used in a very variable way and we need to define what we mean by it. Personalised medicine could be taken to mean treatment based on mechanisms, but we usually do not have the mechanisms in psychiatry. When we talk about ‘personalised medicine’ we mean treatment of causal mechanisms.

4. Organisation of gaps and advances required

The overarching themes initially presented were:

1. Personalised medicine
2. Environment
3. Lifespan
4. Collaborative networks and infrastructure
5. Harmonisation of methods

After discussion this was edited to highlight the division into *discovery* and *execution*:

1. Discovery
 - a. Individual differences/intervention and translation
 - b. Environment
 - c. Lifespan
2. Execution
 - a. Collaborative networks and infrastructure
 - b. Harmonisation of methods

5. Translational gap

There is a huge gap between what we know in basic research and clinical application. This might be considered the ‘basic’ problem: the other gaps follow from it. It encompasses the gaps between different levels of analysis, for example ‘personality/clinical’, functional (including neural and neuroendocrine) and genotype.

For example there is huge investment in basic research in Systems for Social Processes, but it is difficult to incorporate this with current diagnostic systems. There is a huge gap in what is known in the basic science of the mediation between environment and disorders. One conceptual option is to have 3 different inputs with different levels of priority and put these into a 3D matrix. If we can identify dimensions for gaps and advances we may arrive at an ordering principle for the advances we are to produce. Lifespan, environment and personalised medicine are all related to each other, they overlap but each has their own identity. The question is what are the underlying mechanisms.

The translational gap is a huge problem, the ‘basic’ problem; the other gaps follow from it. Translation is already prioritised by the ROAMER criteria. A priority is to link basic research on human development and clinical issues. In clinical work practical solutions are sought whereas research is driven differently in that research develops from itself. There is a problem of little communication between disciplines.

The gaps we have identified may not be specific enough for a roadmap for research. However they do provide a framework. For example, do we not need to spend a lot on 'environmental' research, rather on the interactions between environment and mental disorder.

To organise our gaps and prioritise we might use a 3D matrix with individual differences, environment and lifespan. However it was pointed out that these axes are not independent or orthogonal, for example personalised medicine and environment interact.

The overarching themes identified fall into different categories: some are about methods, others apply to things we want to do for patients.

One possibility is to try a bottom-up approach. We should come up with about 10 things we think are priorities, for example the need for more relevant environmental measures: there are no reliable ways to measure family structure, synchronicity between mother and child, social structure e.g. in eating disorders. Parental age at conception has huge impact on mental disorders but is under-researched. If we do not measure such environmental factors then we cannot hope to study genetic associations. We need objective measures of normal developmental and to prioritise early diagnosis.

Collaborative networks are an important gap, especially with regard to Eastern European integration.

In personalised medicine there is a gap in the way science is translated into treatment. Individual differences, environment and lifespan come into play. The last two overarching themes are structural. We are not happy with the way we translate basic science into medicine and not happy with the way we integrate environment and lifespan. In the case of themes 4 and 5, we can gain from collaboration and harmonisation of methods.

Some gaps are clearly soluble given will and money. In the case of other gaps we do not know the correct approach yet.

There is a gap in tapping basic scientific knowledge in a clinical context. Examining how cells work is relatively easy, but integrating this up through the levels to circuits and how a human being functions is difficult.

A gap is understanding complexity. What is the overarching principle of diversity based on molecular mechanisms?

There is a need for neurobiological research on the population level (which is different from the patient level). This is needed to address the overall mental health of Europe. 'Population-targeted neurobiology'.

The distinction between clinical and functional phenotype and genotype

We need to measure different levels, 'mechanism' is too general. Three levels:

- Personality/clinical
- Functional (including neural and neuroendocrine) phenotype
- Genotype

The gap is in the integration of these levels.

6. European competitive advantage

Europe has advantages including excellent public data registries and isolated populations for study. Eastern and Central Europe are a particular resource that must be further developed.

Europe has many isolated populations which is an advantage over the US, e.g. the islands of Sweden. Also extensive public data registries, for example the ability to identify almost all individuals with schizophrenia. Research networks may be fuzzy, may need to focus a research network on a particular need e.g. schizophrenia. Aims in schizophrenia include prolonging life, addressing nicotine dependence, metabolic syndrome and others, to ultimately provide care as good as for patients with somatic disorders. Iceland is another example of a region highly competitive in research that should be looked to for collaboration.

Eastern and Central Europe must be included: they encompass a huge part of Europe. One task would be to list their strengths (e.g. large populations, large cohorts, appropriate centres). Eastern and Central Europe should be regarded as a resource that is not being used and developed as much as we would like. We should think in terms of comparative advantages, think of things they can do in those regions they cannot do easily elsewhere. We need to

point to research units where we can utilise comparative advantages. Eastern and Central Europe may have these, e.g. appropriate registers and populations. The point is to analyse to see which we have. This belongs to the execution part of the project.

7. Analysis of specific gaps

The first 3 gaps in Valences are general, they extend beyond valences.

<p>1.4 Characterisation of underlying mechanisms for shared and distinct symptoms of reward and punishment processing within and across disorders.</p>

<p>1.5 Identification of predictors and prognostic markers for risk, disease progression and therapy response.</p>

<p>1.6 Identification of treatment targets, both pharmacologic and psychotherapeutic, and delivery of prophylactic, or early intervention using therapies that target causal mechanisms of disease.</p>
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One approach would be to collapse biomarkers together from different gaps. Gaps may be too general, the real need is for studies with comprehensive characterisation of individuals along the RDoC. We could go through to RDoC applying these gaps to all of them. Studies could benefit from more precise characterisation of patients, this could be based on RDoC and not necessarily specific to reward and punishment. It is difficult to say what the gaps are without defining goals.

There is overlap between neurobiology and environment, for example the experience in Switzerland with different groups covering the two areas is that a general framework is important to avoid missing data.

We might define outcomes in a more general way, to identify 3 basic outcome dimensions on a population level:

1. Illness vs. health
2. Suffering vs. wellbeing (it is possible to be ill but feel well and vice-versa)
3. Low burden of disease vs. high burden of disease (cost-utility)

For example to reduce burden of disease in Europe one might try to reduce depression (because it contributes most to burden of disease); to reduce suffering and increase wellbeing one might consider psychosis the prime challenge; to increase health one would consider mental capital. These are only examples, the point is that criteria for long term research needs concepts such as health, wellbeing and economic assessment. The solution may be to start at the other end: to define gaps then look for goals.

8. Early intervention, prevention and research into transitional developmental stages

Focussing on ages 12-21 when most psychopathology begins may be the most effective way to reduce psychopathology on a population level. There is a need for translational research in transitional periods with particular emphasis on adolescence and old age.

We should focus on early intervention and prevention. It was pointed out that WP5 deals with this, they do not refer to it as 'prevention', but if one knows what markers to measure then one can make early targeted interventions.

We spend billions on quality of life, wellbeing etc., we sink 60% of research funding into depression, along with psychosis and bipolar disorder these swallow most research funding. Why not start earlier, with for example anxiety disorders in childhood, maternal issues and critical trajectories. Most psychopathology begins its expression between the ages of 12 and 21 yet a minority of funding goes into this age range.

We should consider goals in a population. A goal may be to start before birth or in kindergartens, this may be a better investment for health in Europe. Our knowledge about basic psychological and other dysfunctions relate to

mechanisms is under research. The endgame may be to see trajectories, see what is actually taking place in the 5 years of development where most mental disorders start.

From epidemiological data, dealing with the developmental age (12-21) may be the way to have a big impact on psychopathology on a population level. Criteria might include illness, economy, hotspots of development, should dealing with these be an aim?

The best return on money, to produce the most health and wellbeing, would be by investing in the stages from pregnancy to 10 years of age. One can deduce in all different directions from this statement, for example an aim from one agenda may be to do a gene-neuroimaging analysis in adolescents. But we should be careful about saying do this or that, given that there is a gap in terms of how many people with particular resources work in this field and how hard it is to get funding in this field. There are windows where the brain is susceptible. But perhaps not so much our knowledge of public health or epidemiology but more knowledge of aetiopathogenesis of disorders.

In child psychiatry clinical practice it is common to discuss how to prevent a child of say 5-7 years old from developing future mental disorders: one can already see the precursors of mental disorders in, for example, a child's temperament. It was acknowledged that while this issue is important and we must include it in WP4, we cannot simply recommend 'Europe must do child and adolescent mental health research'. There is a relative gap in developmentally sensitive targeted research on mechanisms that are relevant for explaining the basis of disorders: 80% of psychopathology manifests in adolescence.

There is a need for translational research in transitional periods with particular emphasis on adolescence and old age. (Though it was pointed out that birth is the biggest transition.)

The question was raised as to whether it is wise to focus on the young when the population is old and getting older. The reply made was that economically a healthy young population is needed to pay for the old population. But resources are also needed for the old.

We should broaden translation to preventive measures, to advise e.g. midwives, educators and politicians.

We should ask where the greatest discovery can be made in the near future, then longer term, in wellbeing and mental health. We might request programs that effect clear prevention strategies, for example by targeting transitional stages.

9. Environment

There is a need to better understand environmental factors, their experience and their effects on the mechanisms of mental disorders.

In many cases the biological mediators for environmental influences are unknown.

Possible advances:

To better understand...

...environmental effects on psychopathology and biological differences.

...environmental mechanisms of mental disorders and resilience.

...experience of environmental factors and their consequence on resilience.

...experience of environmental factors and their role in causing disorders.

Conceptual issues relating to environment:

'Toxic stress' in infancy and early childhood might be a concept useful as a crossing point for environmental and genetic (and other biological) mechanisms.

We might make definitions not based on input but on subjective experience and how an individual copes.

It was suggested that biomedical research does not 'know' what environment is. Psychology looks at role performance in work and neuropsychological performance domains. The problem is defining an input but not knowing how an individual reacts. Measuring and describing the environment is a problem that requires sophistication.

A useful concept may be the ‘exposome’: the entire spectrum of chemical stimulation outside and inside an individual.

One example raised was the difference between being fired individually or with everyone else in a factory (say, because of overseas investors pulling the plug). These have very different effects on the chance of becoming depressed. Europe has competitive infrastructure for researching such issues.

We might consider clusters not based on particular diagnoses but about the effects of environment on transitional stages in psychopathology.

10. Sex differences

There is a need to elucidate the mechanisms behind the effects of gender on mental disorders.

Another issue is sex differences, basic research is biased towards males. Gender is not listed in the analysis: this is needed. There is a mechanism behind the effects of gender and we need to determine what that is. An example question is why marriage is so good for men (halving the rate of depression) but bad for women (doubling the rate of depression). Gender is an issue for some disorders but not all.

11. How can we best add value to a coordinated European mental health research strategy?

Short term:

- identification and sharing of cohorts and clinical samples.
- data linkage
- recommendation of core sets of phenotypic data to maximize comparability of samples.

(these should be feasible and relatively uncstly)

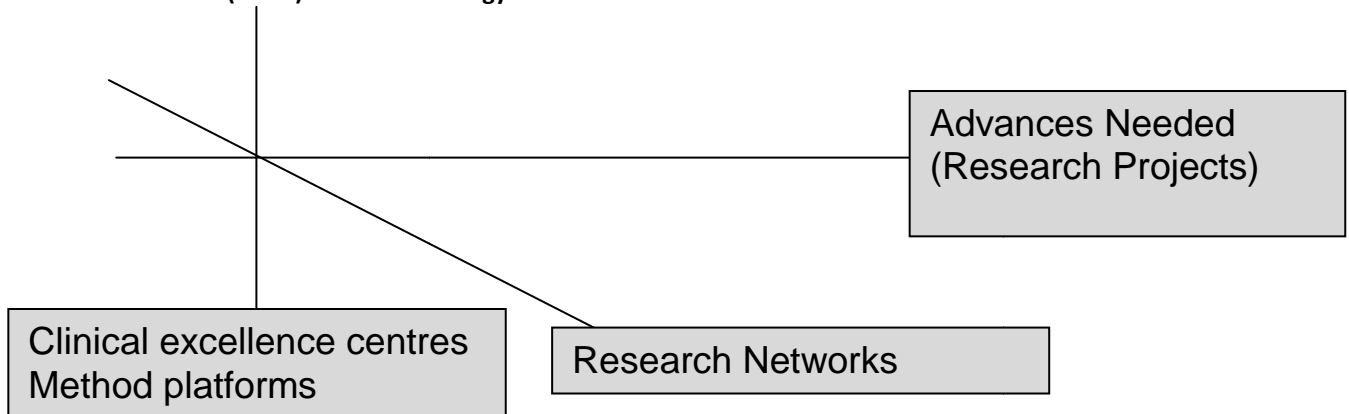
Medium term:

Improving infrastructure and sustainability in European mental health research by a dynamic and adaptive trans-European network of centres of excellence with specific competence and a sustained perspective.

Tasks might include:

- data acquisition and data analysis, including access to high throughput genotyping, creation of functional –omics and neuroimaging centres.
- repositories of methodological and procedural expertise (that otherwise tends to get lost between successive waves of national network funding).
- knowledge transfer within networks and to wider scientific community.
- partner for pharmaceutical industry.

12. Do we need an (infra-)structural strategy to achieve these advances?



13. Transnational collaboration: shared biobanks and databases

We should look at present biobanking initiatives such as the BBMRI (Biobanking and Biomolecular Resources Research Infrastructure) and make specific statements about what is needed to take these forward to study psychopathology.

It was acknowledged that shared databases and transnational biobanks would be valuable.

Problems:

- Most patients with mental health problems in Europe are not treated in centres of excellence. For many doctors the motivation to do the work in contributing would be unclear.
- There are issues of regional organisation. For example in Italy there is the issue of Ministry of Health vs. National Universities. The result is that patients with certain disorders from provincial areas may not be included in research programs leading to a biased sample of about 5% of the population.
- Biobanks may miss samples from patients treated by general practitioners rather than specialist centres. Hence there is a need for transnational biobanks mandated from a political level.
- There are different data protection laws across Europe, different political attitudes and different interests involved.
- The stigma of mental disorder is one reason we do not have registers like those existing for somatic disorders.

We should look at present biobanking initiatives such as the BBMRI (Biobanking and Biomolecular Resources Research Infrastructure) and make specific statements about what is needed to take these forward to study psychopathology

14. Encouraging innovative research

There is a need for programs and funding to encourage research that is not 'more of the same', including funding for proof-of-concept pilot studies with lower probability of success.

Published research tends to be repetitive: there are small areas where there is disagreement or where no-one has done research. How can we stimulate innovation and creativity, to encourage unconventional research? Reviewers may be more critical of unconventional research. In the US foundations provide specific funding for studies with high risk and low probability of success, which if successful can then apply for conventional grants. These are not large grants but are sufficient for proof-of-concept pilot studies.

3.4.3. Advances needed in research and justification according to the common criteria

Based on the expert statements as well as the above described consensus we developed the following recommendations:

3.4.3.1. Advances relevant to discovery

1. **Functional characterisation of neurobehavioral mechanisms across the life span.**

While the mechanism of action of single molecules or some specific chains of molecular events important for psychopathology have been elucidated, our understanding of how the many different types of molecules act in a concerted way is insufficient. One of the challenges in the coming years will be to explore the systemic context of such molecules on different cell types, investigate their relation to our current molecular understanding of the neural underpinnings of behaviour, and assess their function across the life span. Meeting this challenge will require harnessing the emerging methods of systems biology to model how molecular interactions and cellular networks contribute to form a self-organising ordered system with vulnerability and resilience to mental disorders.

Efficacy/effectiveness: Models of mental disorders that implicate a single molecular perturbation (e.g. the 'dopamine hypothesis' of schizophrenia) were useful in the development of the prototypical psychiatric drugs but they are insufficient as a basis for developing new treatments. Modelling how different molecules and cells act in

concert will provide novel therapeutic targets prompting the development of treatments with greater efficacy and effectiveness.

Impact / deliverability / economic benefits in Europe: The economic benefits will be reaped from treating mental disorders earlier through understanding the systemic organisation of vulnerability and resilience, thereby reducing disability and unemployment.

Answerability/feasibility in Europe: Further collaborative networks will be required (see below), but there are no ethical barriers to doing such studies.

European research strength: Europe has centres of excellence in the different disciplines required to study such concerted mechanisms and relatively universal healthcare allows for large cohorts for their study across the lifespan. Europe has other advantages, for example isolated populations for study such as on the islands of Sweden.

2. Identifying behavioural patterns defined by neurobehavioral mechanisms and relating those to current diagnostic criteria.

Psychiatric disorders are increasingly regarded as diseases of the brain as opposed to diseases of the mind; they are alterations in neurobiological brain circuits that are influenced by genetic and environmental factors. Nonetheless, diagnostic classifications are still largely based on clinical observation and symptom reports by patients, rather than biological evidence. Consequently, treatment is aimed at merely reducing and managing observable symptoms. This inability to target the causes of disease results in suboptimal response rates and adverse effects of medication: for example, 30-40% of patients with depression do not respond to appropriate drug/therapy treatment and approximately a third of those with schizophrenia do not respond to standard treatments. Understanding the real biological causes of psychiatric disorders would therefore help to improve diagnostics, treatment efficiency and reduce adverse side effects.

Efficacy/effectiveness: More effective treatment will require not only medications developed on the basis of biological mechanism but relating such mechanisms to practical diagnostic systems.

Impact / deliverability / economic benefits in Europe: Personalised treatment (treatment of mechanisms) is required to move part the current impasse of treatment resistance. Taking schizophrenia as an example, at present 80% of patients are unemployed.

Answerability/feasibility in Europe: Europe provides a diverse population with near universal healthcare, allowing field trials in large cohorts of relationships between neurobiological mechanisms and observed symptoms.

European research strength: In terms of relating neurobiological mechanisms to clinical diagnoses, Europe carries the advantages of the open development process of ICD-11 and expertise in translational research.

3. Identifying reliable biomarkers to predict and measure risk of mental disorders, their progression and response to treatment.

There is a need for reliable biomarkers that can be used to stratify patients based on risk, prognosis and predicted treatment response. Biomarkers may be based on knowledge of the biological mechanisms of mental disorders and forward translation from animal models. Certain mechanisms are implicated across mental disorders. Repeated exposure to stress may result in psychopathology or conversely may mobilise health protective psychosocial resources.

Better insight into these mechanisms of vulnerability and resilience may help to identify genes and epigenetic modifications influencing critical pathways that may serve to stratify patients by risk. Reward and punishment mechanisms are implicated across disorders including anxiety and mood disorders as well as substance and behavioural addictions, and thus similarly have great potential for yielding pertinent biomarkers. Cognitive impairment is a feature of many mental disorders and is frequently inadequately addressed by current methods of assessment and treatment. Future research should include the development of neurocomputational models that will provide a foundation for the use of human electrophysiological responses as markers of cognitive impairment.

Efficacy/effectiveness: Stratified treatment of mental disorders will require pertinent biomarkers. The current practice of classifying patients into traditional diagnostic categories and delivering treatments that were developed based on their similarity to the prototypical psychiatric drugs in animal models has left a manifest efficacy gap.

Impact / deliverability / economic benefits in Europe: Stratification of patients using biomarkers will bring about more intelligently focussed use of healthcare resources.

Answerability/feasibility in Europe: Large scale studies examining putative biomarkers have been shown to be feasible in Europe, typically employing multi-centre consortia.

European research strength: Europe combines diverse and accessible populations with translational expertise in -omics, animal models, neuroimaging and neuropsychology, all of which domains have the potential to yield pertinent biomarkers.

4. *Understanding risk and resilience for mental disorders across the life span by investigating gene x environment interactions and gene x environment correlations (the genetic influences on environmental exposure) and their mediation through epigenetic and transcriptional mechanisms.*

The majority of mental disorders are a product of nature and nurture. Variations in vulnerability among individuals within and between populations arise as a function of interactions among genetic and environmental, including psychological and social factors that vary over the course of a lifetime. Therefore, there is a need to investigate the contribution of these factors to age-related resilience or vulnerability to mental disorder and wellbeing in different environments and populations across Europe. This is required to better understand the relation of individual vulnerability/resilience in adverse conditions as well as the consequences of a nurturing environment on mental health. Such studies will require massive data sets if current crude environmental measures are used due to the modest effect sizes associated with single genes; development of better and more relevant environmental measures are sorely needed. On the other hand, as more and more genes are identified to be associated, use of genetic risk scores and genome-wide scores will bring much more power to such studies, permitting analyses in sample of reasonable size (i.e. from a single study rather than combined over multiple studies).

Efficacy/effectiveness: Treatments that target gene x environment interactions have the potential to afford strategies for early intervention and prevention of mental disorders.

Impact / deliverability / economic benefits in Europe: Such treatments will reap economic benefits by treating disorders earlier, when the burden of disease has not fully developed.

Answerability/feasibility in Europe: Multicentre studies measuring genotype and environment have been feasible in Europe and there have not been ethical impediments to such studies. The identification of more associated genes, the use of genetic risk scores and genome-wide scores will in any case allow smaller, more feasible studies.

European research strength: Europe encompasses diverse socio-economic and other environmental factors. At the same time, there are already Europe-wide biobanking initiatives that could be harnessed to gather the required data.

5. *Investigation of the exposome.*

The Exposome is a measure of the effects of life-long environmental exposures on health. One of the most ubiquitous chemical exposures is ingestion of ethanol and smoking of tobacco. It is known that these compounds have different effects during pregnancy (e.g. fetal alcohol syndrome spectrum and low-birth weight among smokers). In addition, lasting effects on brain development have been reported that are still poorly understood. While there is good documentation in rodent models, the lasting effects of alcohol and tobacco have been poorly investigated in the human. In general little is known about the effects of several chemical/medications/drugs over the life-course. It is therefore necessary to investigate the effect of these toxins on the exposome and its implications for transgenerational transmission, and its possible modulation by genetic and epigenetic factors. Ultimately, the same neuroplasticity that engenders vulnerability to toxins also provides the potential for focussed interventions during transitional periods.

Efficacy/effectiveness: The exposome encompasses environmental exposures of great importance in psychiatric and somatic morbidity and mortality. There interventions based on such understanding have a high chance of reducing these.

Impact / deliverability / economic benefits in Europe: Such exposures carry a large and diverse set of public health and economic burdens. Understanding the mechanisms of such exposures will allow treatments that reduce them.

Answerability/feasibility in Europe: Multicentre studies measuring aspects of the exposome along with genetic and epigenetic characterisation have been feasible and ethically approved in Europe.

European research strength: Europe encompasses populations with diverse patterns of chemical and other exposures. Due to high level of healthcare provision it is relatively easy to recruit large cohorts of individuals and examine epigenetics, genetics and neuroplasticity across the lifespan.

6. *How does early life experience affect health over the lifespan?*

To address this question it is crucial to understand how early experiences can program perinatally and during puberty emotional and stress regulations for life. This requires insight in epigenetic and epistatic mechanisms that can change brain plasticity towards a vulnerable phenotype, which may become expressed under specific circumstances in later life and result in chronification. Unresolved is why some individuals progressively fail to cope with adverse early life experiences and accumulate risks for mental disorder, while others gain strength even from seemingly abusive early life adversity as if such conditions prepare for life ahead. In addition to human studies, humanized animal models are needed that test the mismatch or the cumulative stress hypothesis. Such models depend on modulations of gene-environment interaction in a living organism which will benefit enormously from technological advances in imaging, gene modification and cell biological technology. In fact, we are witnessing a constant renewal of technology to address in these models the same questions: who is at risk, and how do we prevent and cure disorders; how can the quality of life, particularly of the elderly, be improved.

Efficacy/effectiveness: Understanding the mechanisms of adverse early life experience and subsequent trajectories will permit more effective treatments on the basis that treatments will be more targeted to those at most risk and delivered earlier in the natural history of a disorder.

Impact / deliverability / economic benefits in Europe: This advance is central to treating mental disorders earlier and ultimately preventing them and their economic and public health burden.

Answerability/feasibility in Europe: Long-term birth cohort studies have been shown to be feasible in Europe.

European research strength: Europe's healthcare infrastructure coupled with centres of excellence in genetics and epigenetics and diverse populations create an excellent environment to study the effects of early life experience over the lifespan.

7. *What are the mechanisms underlying failures in social processes and how can interventions best be developed?*

Failures in the brain systems for social processes are core to a large number of mental disorders, though because they contribute only modestly to differentiation between ICD categories they often go undiagnosed. While the behavioural phenomena of such failures have been described, there is a need for developmental studies that chart these and describe their neurobiological bases, as well as integration of information from different approaches into unitary paradigms. Examples of areas for further research include imitation, a primary means by which children learn new skills; whether failures in imitation (e.g. in autism) result from an abnormal mirror neuron system or from this system not being fed appropriate information due to direct gaze deficits remains to be established. Another example is interpersonal touch, the neural aspects of which have only recently begun to be addressed by demonstrating different patterns of brain activation in response to more perceptual versus more social touch. The role of oxytocin in the mechanisms underlying interpersonal touch suggest it may be investigated for its potential as a therapeutic agent in disorders characterised by fear, reduced trust and social avoidance. This is an example of a potential new treatment based on knowledge of biological mechanisms. It also raises ethical questions how to deal with new drugs that affect moral emotions.

Efficacy/effectiveness: Treatments targeting failures in systems for social processes have the potential for broad efficacy due to the pervasive nature of such failures across psychiatric disorders.

Impact / deliverability / economic benefits in Europe: Failures in social processes carry a heavy burden for the individual as well as society yet are not well covered by the current diagnostic system in spite of several obvious clinical phenomena (e.g. shyness vs. unsocial personality traits; callous/unemotional vs. reactive/impulsive aggressive behaviour; lonely mass murderers (c.f. Anders Behring Breivik, Oklahoma bomber, Tim Kretschmer – the German school killer). Thus there is great scope for delivering benefits in terms of reduced morbidity, mortality and economic burden.

Answerability/feasibility in Europe: Social processes have been well charted over development at the behavioural level. What remains is to describe their neurobiological underpinnings. This will require a combination of developmental and environmental studies with integrative approaches which will provide the new knowledge with which to formulate research and clinical questions.

European research strength: Europe has centres of excellence in the range of disciplines required to realise the integration of development and environmental studies, and cohorts that may be followed across developmental stages.

8. Investigating psychiatric disorders and physical health.

Brain-body interactions on the one hand reflect the impact of the environment on mental and physical health, and on the other hand the devastating influence of physical diseases on higher brain functions underlying emotion and cognition. It is therefore important to (a) understand how environmental circumstances such as physical or psychological deprivation can promote brain system dysregulations leading to disorders and likewise to elucidate the brain mechanisms of the beneficial effects of factors such as lifestyle, exercise and cognitive therapy; (b) understand how stress and other environmental mediators not only communicate neural information that aggravates cardio-metabolic-inflammatory disease conditions but also how these disease conditions can affect mental health, in interactions where hormonal and autonomic synergism are increasingly implicated.

Efficacy/effectiveness: Such investigations will prompt more effective treatments of somatic and psychiatric disorders, and moreover a holistic, personalised approach to treating an individual based on their somatic, mental and environmental factors.

Impact / deliverability / economic benefits in Europe: Understanding the interactions between psychiatric disorders and physical health will have a positive impact on the leading causes of mortality in Europe (e.g. cardiovascular disease) as well as chronic, disabling mental disorders.

Answerability/feasibility in Europe: A great deal is already known about the hormonal and autonomic mechanisms implicated, what remains is precise integration of the diverse mechanisms that mediate mental and somatic health.

European research strength: Europe has centres of excellence that span mental and somatic health, which encompass expertise in studying hormonal, autonomic and other systems and which deliver healthcare to the entirety of their catchment population, allowing the recruitment of appropriate cohorts.

9. Investigating allostatic load in relation to comorbidity.

There is an overarching need to better understand the causal relation between comorbid diseases. Allostatic load refers to the “cost of chronic exposure to fluctuating or heightened neural or neuroendocrine response resulting from repeated or chronic environmental challenge that an individual reacts to as being particularly stressful”. Allostatic load provides a theory of comorbidity that spans levels of research, for example: at the population level it provides an explanatory framework for epidemiological associations between mental disorders and between mental disorder and somatic diseases such as cardiovascular disease, diabetes and cancer; at the levels of circuit and physiology it implicates perturbations in the HPA axis and monoamine systems in the comorbidity of mood disorders and functional illnesses; at the molecular level it implicates mechanisms including oxidative and nitrosative stress, mitochondrial dysfunction and inflammation. Research should focus on further clarifying the mechanisms of allostatic load, including its epigenetic, inflammatory and neuroendocrine aspects. These mechanisms will provide novel treatment targets for mental disorders as well as their somatic comorbidities. These are urgently needed to address the increasing mortality gap between psychiatric patients and the general population.

Efficacy/effectiveness: Future treatment strategies that target allostatic load have the potential for effectiveness across different mental disorders and across mental and somatic disorders.

Impact / deliverability / economic benefits in Europe: Treatments that modulate allostatic load have the potential to address the most burdensome mental and somatic disorders in Europe (chronic mental disorders, cardiovascular disease, cancer).

Answerability/feasibility in Europe: Specific mechanisms are already implicated, and it will be feasible and ethical to employ these in developing new treatments.

European research strength: Europe has research strengths spanning the required levels of research, for example public health and epidemiology, neuroimaging and physiology, molecular biology and genetics.

10. Development of more valid animal models for behavioural and pharmacological studies.

These may be based on translated biomarkers of disease processes reverse translated from humans. Increased knowledge of the underlying biology of mental disorders will allow models based on mechanism. These will have greater construct validity than previous models based on superficial resemblance to human psychopathology (face validity) and response to compounds of known efficacy. More valid animal models will allow earlier 'go / no go' decisions to be made about candidate compounds, reducing the attrition cited as a reason for withdrawal of pharmaceutical companies from neuroscience research. Moreover such models will facilitate the development of truly novel drug mechanisms, as opposed to simply improving the tolerability and toxicity of the prototypical psychiatric drugs. While rodent models have dominated drug development, there is need for a cross-species approach including non-mammalian models as appropriate for different biological domains. The ideal would be models that recapitulate gene-environment interactions and model disease development so as to produce treatments that target transitional periods, rather than approximating ultimate symptoms in affected humans.

Efficacy/effectiveness: Pharmaceutical companies have been pulling out of psychiatric drug development. In great part this is due to attrition: for every compound that reaches market approximately ten others fail. The most common reason for failure is not toxicity but lack of efficacy. The efficacy gap is due in part to the limited validity of animal models for drug development.

Impact / deliverability / economic benefits in Europe: There are clear unmet needs in terms of treatment resistant disorders and inadequately addressed aspects of disorders (e.g. negative symptoms in schizophrenia). These carry heavy economic burdens (e.g. 80% unemployment in individuals with schizophrenia).

Answerability/feasibility in Europe: There are already multicentre, translational studies taking place in Europe involving translation between humans and animal models.

European research strength: Europe has research strengths spanning the required levels of research, for example neuropsychological testing, animal work and neuroimaging.

3.4.3.2. Advances relevant to infrastructure

11. Establishing centres of excellence and research networks.

The challenges associated with elucidating the neuroscientific basis of psychiatric disorders are too great to be tackled by one institution alone. The scope of the challenges requires a coordinated approach within and across disciplines. For example, it requires standardised instruments, both psychometric and neurobiological (Neuroimaging), dedicated centres for data acquisition including access to high throughput -omics and neuroimaging centres, behavioural studies and pharmacological studies, as well as biostatistical and bioinformatic analysis. While there are already efforts at a European level to address some of the infrastructural issues on a general biomedical level, there is a lack of coordination in the mental health sector linking centres of scientific excellence with infrastructural projects, and creating infrastructure responding to the specific needs of mental health research. Research networks would combine expertise in relevant areas from molecular biology and genetics to the methodology of cognitive neuroscience for improved definitions of disease endophenotypes and assessment of new therapeutics. These groups would also combine clinical neuroscientists (to enable experimental medicine studies) with basic neuroscientists, including those working with experimental models and

cognitive neuroscience. Collaborative networks will increasingly be needed for investigating the large populations required to investigate psychiatric disorders, in order to resolve the difficulties posed by their heterogeneity.

Efficacy/effectiveness: Collaborative networks are required both to provide a translational approach involving different disciplines and to study large diverse cohorts, to ultimately elucidate the mechanisms of mental disorders and provide more effective treatments.

Impact / deliverability / economic benefits in Europe: The lack of coordination across Europe with regard to mental health research opens an opportunity to pool complementary resources into networks of excellence, stimulating translational medicine for mental disorders.

Answerability/feasibility in Europe: Multicentre consortia have been shown to be feasible across Europe, without insurmountable ethical issues.

European research strength: Europe has centres of excellence across the translational spectrum: what is required is the coordination of centres with complementary expertise to study large cohorts and unravel the heterogeneity of mental disorder.

12. Sustained, renewable research funding for large European initiatives.

Current EU-funding provides unprecedented opportunity for large scale collaboration among European research teams. The awarded projects often require a significant investment in the establishment of methods and infrastructure. Often the most informative data are acquired towards the end or after funding for the project has expired. In order to avoid incomplete data analysis and maximal benefit from methods and infrastructure development a competitive renewal of projects after the initial funding period is highly desirable.

Efficacy/effectiveness: More complete and informative data will prompt greater understanding of neurobiological mechanisms and more effective treatments.

Impact / deliverability / economic benefits in Europe: The benefits will be through more complete data sets and less wastage of resources from incomplete analysis.

Answerability/feasibility in Europe: Such competitively renewable funding is feasible and ethical in extracting the maximum value from funded projects.

European research strength: EU funding has the potential to provide the sustained, renewable funding to extract maximum benefit from projects.

13. Developing a comprehensive capacity building programme.

Capacity building across Europe is an important factor for a biomedical research strategy. It can be achieved through: (a) agile funding schemes targeting high-risk and high-impact pilot studies, aimed at testing creative hypotheses with great heuristic potential. (b) funding schemes targeting specifically interdisciplinary research, aimed at bringing together investigators with very different backgrounds and integrating them into problem-centred networks; (c) long training programs for young investigators, to be spent in another centre belonging to the same EU-funded consortium; (d) shorter exchange programs/sabbaticals for established investigators, to foster scientific and technological updating, as well as interdisciplinary cross-pollination within EU-funded consortia; (e) stimulation packages for the development of new technological poles for scientific investigation in countries with below-average participation in European funding programs; (f) contribution to national programmes providing incentives for scientists to return to their home countries.

Efficacy/effectiveness: There is potential for truly novel and more effective treatments to be developed on the basis of creative hypotheses about the mechanisms of mental disorders. Developing more effective treatments requires a translational, multidisciplinary approach.

Impact / deliverability / economic benefits in Europe: The costs of such high-risk and high-impact pilot studies, exchange and stimulation packages need not be great and the benefits in terms of discovery and cross-pollination of expertise would be great.

Answerability/feasibility in Europe: Agile funding schemes for high-risk and high-impact pilot studies already exist in the US; the funding they supply is modest, enough for proof-of-concept. Such schemes would be feasible

in Europe. There is already exchange of expertise between EU countries. It is entirely feasible to develop this into a more organised programme.

European research strength: Europe has investigators with diverse backgrounds and expertise. This strength would be maximised by the programmes described here.

14. *Public private collaborations.*

The convergent translational approach described here requires a range of expertise and capabilities that lies beyond any single commercial or academic organisation. It requires cooperation that is incompatible with the traditional closed and secretive approach to drug development. Thus there is a need for further public-private projects such as the European Innovative Medicines Initiative (IMI). Such projects will harmonise complementary expertise and pool resources. They will allow the use of common assays and models between basic research and drug development, facilitating forward and reverse translation and reinvigorating neuropsychiatric drug development by reducing attrition and prompting development of novel therapeutic mechanisms.

Efficacy/effectiveness: Developing more effective treatments requires a more collaborative approach, in that the public and private sectors have different and complementary resources.

Impact / deliverability / economic benefits in Europe: The benefits stem both from more effective treatments reducing the burden of disease and establishing Europe as a more attractive location for pharmaceutical research and development.

Answerability/feasibility in Europe: The European Innovative Medicines Initiative has already shown the feasibility of such an approach.

European research strength: Europe has immense research strengths in both public and private sectors. These will be maximised then they can complement each other's resources and expertise.

3.5. Psychological Research and Treatments

3.5.1. Introduction to the area

Psychological treatments and interventions comprise a large group of methods and approaches to address the needs of patients and groups of patients with mental disorders or mental health problems, as well as their networks of support (e.g. partner and family) as it applies to prevention, treatment and rehabilitation. Psychological treatments and interventions range from highly sophisticated psychotherapy delivered by specialised psychotherapists, to the application of specific behavioural techniques as part of a broader treatment plan (e.g. psychoeducation or motivational interviewing). The effectiveness of strictly psychological treatments is well-established by randomised clinical trials of variants of Cognitive Behavioural Therapy (CBT) in the areas of anxiety, depressive, somatoform and stress-related disorders (e.g. PTSD), the eating disorders and personality disorders, where such methods are typically regarded as first-line treatments. They are also established as core elements in the treatment of substance use disorders and most childhood and adolescent neurodevelopmental disorders and conditions (e.g. ADHD). For the group of psychodynamic and psychoanalytic methods similar strong evidence is lacking. However, at this moment there are several fundamental barriers to progress in the area of psychological treatments:

- There is a general **lack of understanding about the basic mechanisms of behaviour, the moderators or mediators of (behavioural) interventions**. There is a limited understanding of the mechanisms of behaviour initiation, maintenance and change and their critical trajectories and determinants. We do not know whether mechanisms governing these aspects of behaviour change are the same, or different, and whether, for example, individual variation (genetic, or in capacities such as "self-regulation") play a role.
- There is also a fundamental **lack in understanding behaviour change in the specific context of CBT**. In spite of high effectiveness and some progresses in clinical psychological research, little is known about the

mechanism of action of established methods of CBT. What are the neural and neurobiological changes associated with CBT induced change? What is the role of individual (e.g. genetic or experiential) differences?

- There is a **fundamental lack of knowledge about the situation of research on psychological treatments and interventions in Europe**. In fact – and despite some coordinated EU-efforts in this domain - there is even a profound lack of knowledge about the degree to which psychological treatments are applied in the EU countries, where and what kind of research and service delivery programs are in place and how they are integrated into the wider network of mental health care infrastructure. As a result of this situation, Europe lacks even the most basic prerequisites for an evidence-based mental health research policy.

To promote research and to integrate findings in the area of Psychological Research and Treatments, the following coordination strategies are reasonable:

- Developing a consensus about terminology and concepts. Consensus is currently missing about the way to define psychological and psychosocial treatments and to translate this into a typology of interventions and service delivery modes and associated strategies in the current and future mental health system.
- Collecting existing data on psychological and psychosocial treatments in Europe, their spectrum and delivery formats, taking into account the perspectives of countries and places.
- Developing a map of existing research centres and programmes involved in psychotherapy research as well as more broadly psychological and psychosocial interventions, including basic research issues in all countries.
- Developing a methodology to identify gaps between science, evidence-based psychological methods and their application and delivery in routine care. A methodology aiming to successfully identify gaps between science and practice must be able to make distinctions by country, diagnostic domain, age group and so on.
- Integration: knowledge and insight gathered in the four preceding steps need to be unified, updated and processed in an integrated database – from which consultations processes and consensus can be developed.

3.5.1.1. Definition of subareas

Initially, and in order to cluster the broad field of psychological research and treatment, the ROAMER Research Domain Criteria (ROAMER domains, ROAMER RDoC) were drafted, which follow an initiative of the NIMH Research Domain Criteria (RDoC) project that is aimed to develop new ways of classifying disorders based on dimensions of observable behaviours and brain functions. Acknowledging the developmental stage and ongoing working processes at the NIH/NIMH, the RDoC system has been modified for ROAMER by the addition of environment as a unit of analysis and developmental stage as a third axis.

The same principle can be applied to the other RDoC domains by substituting the appropriate constructs. The matrix can be used as a guiding framework, with experts deciding which combinations of construct, unit of analysis and developmental stage are most relevant. Thereby, ROAMER RDoCs serve as a heuristic framework within a dimensional, agnostic and unit-based approach to picture the state of the art as well as new emerging findings on mental health. For work package 5, the RDoC domains Cognitive Systems and Systems for Social Processes, as well as the additional subareas of Psychological Interventions and Pharmacological Treatment and Comorbidity, were chosen.

3.5.1.1.1. The nature and definition of the term “psychological”

The work group converged on the opinion to define psychological as the theory, knowledge and methods of the Psychological Sciences that covers – depending on country – the Cognitive and Affective Neurosciences as well as the traditionally defined areas of Experimental Psychology, Developmental, and Social Psychology within the traditional psychological approaches of multi-trait and multi-method perspectives, functional analyses, etc.

3.5.1.1.2. Psychotherapy

Consistent with conventions in Clinical Psychology and Psychotherapy, Psychotherapy was defined and restricted as clinically relevant, empirically supported psychological (in contrast to pharmacological or somatically induced) behavioural (cognitive-affective, motor, social) interventions of any type (in groups, in individuals) that are based on the application of basic psychological knowledge to change “behaviour” and “disorders” by psychological means (typically communication, exercises, etc). There was some agreement that we should use the term CBT for these interventions, recognizing though that politically that doing so could be considered as an undue restriction. It was nonetheless emphasized that this work package does deal – in parallel to WP4 – with understanding the basic psychological (as opposed to biomedical, molecular) mechanisms for disorders and clinical relevant behavioural syndromes that are relevant for their aetiology on one side and intervention on the other.

3.5.1.1.3. Conceptual models

The following conceptual models were discussed and agreed upon:

- *Basic psychological models of relevance for understanding normal and abnormal cognition, affect and behaviour:* emphasizing a cognitive systems perspective and in particular cognitive factors of higher order (decision making, memory, impulsivity, motivation etc.). These approaches fit well with the RDoC domain approaches in WP4.
- It was also felt that exclusive emphasis on cognition and emotion / affect might be inappropriate. Current models should additionally adopt stronger emphasis on social systems perspectives.
- *Developmental pathway models:* It was emphasized that the development of functions and dysfunctions should be considered from a broader novel developmental and public health relevant approach that supplements the traditional biomedical disease model as well as conventional approaches of “personalized medicine” beyond the traditional heuristic vulnerability-stress models for mental disorders.
- The need to review *novel psychological paradigms* beyond traditional learning models and the learned helplessness model for example, and prevailing simple heuristical models was emphasized
- *Diagnostic and domain area perspective:* Similar to WP4 a combined traditional diagnostic approach and a facet-oriented domain approach by functions and elements on the basis of the NIMH criteria was adopted as the working model, despite recognition of the limitations and restrictions of this approach (i.e. lack of development).
- *Adopting a Science of Behavioural Change - perspective:* This perspective was adopted following discussion of background material. It was felt that a coordinated and concerted program to investigate the basic and applied issues of what determines the human ability for changing behaviour is of core relevance for treatment and prevention.

3.5.2. Gaps in knowledge

The experts identified a number of gaps and advances needed most of which are of significant effectiveness, impact and feasibility to add to European research strength. However, in order to appropriately rank the suggestions from various research domains, relevant overarching criteria which are intrinsic to mental health research, and in particular psychological research and treatments, are essential. While it is necessary to identify gaps and advances which characterise (1) areas of discovery, it is equally important to establish (2) the structural (and infrastructural) gaps and advances needed to achieve the discovery goals.

During the meeting, the following issues were discussed:

(1) To determine the areas most relevant for discovery, assessment of psychopathological burden across the lifespan (as well as in various environmental conditions) is a useful indicator. Here it is important to note that the main

psychopathological burden across the lifespan occurs in transitional periods, namely during transition from childhood to adulthood. In fact, 80% of the lifetime psychopathological burden can be detected during adolescence. Transition from adulthood to old age is another period of increased incidence of psychopathology. Therefore, research focusing on transitional periods should have high priority. In addition, most mental disorders are the result of an interaction of individual biology and environmental factors.

Identification and characterisation of environmental factors conferring risk and resilience for mental disorders and their interaction/correlation with psychological and biological mechanisms is thus also of high priority.

Hence, preliminary areas of discovery in the field of psychological research and treatments are:

(a) Theory and models, (b) approaches and paradigms, (c) methods & assessments, (d) technologies & tools for interventions, (e) applications to clinical and non-clinical groups.

(f) In addition, a “translational gap” has emerged which calls for the application of scientific and methodical advances in psychological research and treatments to better understand human behaviour and develop diagnostics and interventions that target specific pathological processes across mental disorders. Research aiming at decreasing this “translational gap” should be prioritized.

(2) The structural and infrastructural advances needed to achieve the discovery goals on a European scale include the creation of transnational collaborative structures and infrastructures which take into account the competitive advantages of different European regions, collaboration with existing institutions, European research infrastructure projects, national cohorts etc., as well as capacity building across Europe. The scope of the effort to establish structural and infrastructural advances is considerable and includes the establishment of dedicated centres for data acquisition and data analysis, as well as research networks. Together dedicated centres and networks may contribute to developing and supporting a research infrastructure to maximally benefit from Europe’s unique universal access to healthcare and its cultural diversity which allows differentiated analysis of environmental and cultural influences. In addition to reducing the personal and public burden of mental disorders, a thus evolved research infrastructure might be an important partner for pharmaceutical industry and strengthen European competitiveness and advantage of location.

List of gaps:

1. What could be understood by the term “behaviour” – does it include behaviour of/mechanisms within cells?, i.e. software-hardware-boundaries (analogy).
2. Similarly: what are mental/psychiatric disorders?
3. Is there an unmet public health interest in behavioural genetics?
 - The common genetic factors for example for depressive disorders, dysthymia and personality disorders or across personality disorders on a molecular level question our current diagnostic classification of disorders on the one hand.
 - On the other hand, the lack of relevant genetic markers or mechanism related to particular (personality) disorders points to further putative interactions on the behavioural and/or other genetic level. PDX, specificity probably more on behavioural (x genetic) level.
 - Are we yet in the position to evaluate the impact of this knowledge on the understanding of mental disorders, their prevention or treatment in the future?
4. There are probably different mechanisms of action for the onset, course, maintenance and change of human behaviour which are to date still poorly understood.
5. What causes shift of vulnerability? – also applies to other disorders.
6. In regard to behaviour change, we do not know yet what dose of which intervention fits for whom. What motivates people to change their behaviour? (“to shove somebody” vs. “full intervention” vs. incentives)
7. How to overcome barriers to treatment for the mentally ill (access to treatment, knowledge about treatment)
8. We do not know yet effective community psychological strategies for mental health promotion and mental disorder prevention.

9. "There is a gap between rising public health needs in child and adolescent psychiatry/psychology (...) and its marginal scientific contribution to the worldwide scientific community in relation to other medical fields or subjects with similar public health impact but rather high publication activity"
10. There is no broader behavioural science platform that covers basic research and translation into clinical research and practice; findings are often communicated in peer-reviewed journals, to which the majority of the population has neither access, nor the capacity for high-level, fine-grained analyses. Also, translation of findings from basic research into clinical research and finally into clinical practice rarely exists.

3.5.3. Advances needed in research and justification according common criteria

In order to fill the gaps listed above, advances are needed regarding our general understanding of mental health and mental disorders, improving treatment for mental disorders, understanding behaviour and behaviour change, the translation of research findings into policy decisions.

During the 2nd scientific workshop and also in preceding position statements the experts identified a number of gaps and advances needed, most of which are of significant effectiveness, impact and feasibility to add to European research strength. However, in order to appropriately rank the suggestions from various research domains, relevant overarching criteria which are intrinsic to mental health research, and in particular psychological research and treatments, are essential. While it is necessary to identify gaps and advances which characterise (1) areas of discovery, it is equally important to establish (2) the structural (and infrastructural) gaps and advances needed to achieve the discovery goals. Finally, a list of 25 goals and related advances needed was delineated.

Advances needed in Psychological Research and Treatments in Europe for the next 15 years.

General issues of psychological research relevant for mental health		
1	Promotion of basic psychological research aiming to identify the basic mechanism involved in the initiation and maintenance of behaviour relevant for health	Stronger emphasis and integration of research of basic psychological functions (i.e. attention), processes (i.e. learning) and cognitive factors of higher order (decision making, memory, impulsivity, motivation etc.), including their neurobiological underpinnings, relevant for healthy functioning and mental health.
2	Promotion of psychological (behavioural) research regarding change of health-related behaviour	Identification of how such psychological factors and mechanisms (including gene-environment interactions) influence health-related behaviours, their initiation, maintenance as well as change (spontaneous-natural and induced change). Focus should be laid upon determinants for critical trajectories from normal (adaptive) to abnormal/clinical dysfunctional patterns and their dynamic interactions (i.e. stress).
3	Adopting a stringent developmental perspective over the life span	There is a strong need of improved developmentally sensitive models and approaches that allow integration of findings regarding normal and abnormal functioning within a developmental perspective. Such research should cover the whole lifespan but in particular childhood and adolescence as the core high risk period for onset of mental disorders. There is a need to specify how vulnerabilities and stress influence critical developmental trajectories to poor health and specific mental disorders.
4	Identification of core moderators, mediators and mechanisms involved in behaviour change	Particularly pronounced research gaps were identified with regard to the mechanisms, moderators and mediators involved in behaviour change in general and within the specific context of psychological interventions and treatments (i.e. CBT) in particular. Core questions are: What are the neural and neurobiological changes associated with effective CBT? What is the role of individual (e.g. genetic or experiential) differences?

5	<p>Overcoming translational barriers (Translation of basic psychological research into application and dissemination)</p>	<p>Development of translational models on at least four levels:</p> <ul style="list-style-type: none"> • improved aetio-pathogenetic research that incorporates systematically social-environmental context and determinants as well as the neural underpinnings of mental disorders, • improved broader (multi-level) assessment procedures targeting the core aetiopathogenic processes, rather than psychopathological features (as specified in imperfect diagnostic classificatory rules). • coupling of clinical efficacy/effectiveness randomized trials with mechanistic research to better identify the core active ingredients and core mechanisms of treatments. • derivation of psychological intervention modules for prevention and treatment that target dysfunctional developmental processes • improved models of dissemination and transfer to routine care, that take into account the needs of clinicians and patients.
<p>Example: Functions and Dysfunctions of cognitive control as core mechanisms in mental disorders</p>		
6	<p><i>Cause or consequence?</i></p>	<p>There is a strong need to identify whether impairments of decision-making and cognitive control are consequences (by-products) of mental disorders, or antecedent vulnerability or even causal factors. This requires prospective-longitudinal designs, validating developmentally sensitive behavioural tasks to assess and functionally decompose decision-making and cognitive control, the establishment of latent-variable models of cognitive control and the incorporation of measures of behavioural, cognitive, and neural phenotypes.</p>
7	<p><i>Identifying of commonalities and differences across disorders</i></p>	<p>There is a strong need to examine core questions like: Are dysfunctions of decision-making and cognitive control reflecting shared neurocognitive mechanisms across mental disorders? Are different components of cognitive control (e.g., response inhibition, set shifting, goal maintenance) specifically impaired in different disorders and what are commonalities and differences in such patterns across disorders? How do multiple learning and valuations systems cooperate or compete in determining value signals and choice behaviour, and which variables moderate and modulate these interactions?</p>
8	<p><i>Competence or performance?</i></p>	<p>Do dysfunctions of decision-making and cognitive control in mental disorders reflect impaired competence (e.g. impaired inhibitory control ability) or performance deficits (e.g. insufficient recruitment of otherwise intact control resources)?</p>
9	<p><i>Motivational vs. volitional deficits? Under- vs. over-control?</i></p>	<p>Which phenotypical features of mental disorders (e.g. drug abuse, avoidance in anxiety disorders) reflect <i>motivational</i> deficits (e.g. maladaptive or biased decision-making due to overly high delay discounting), and which reflect deficits in <i>volitional</i> control processes (e.g. impaired response inhibition) despite otherwise intact reasoning and decision-making capabilities? Which mechanisms are involved in impaired or insufficient control, and excessive or chronic <i>over-control</i>? Does “over-control” (e.g. continuous suppression of emotional or reward processes; intrusive thoughts; rebound effects; alienation from basic needs) have other (detrimental) effects as compared to under-control?</p>

10	Identifying the role of dysfunctional control parameter settings	<p>Are there systematic relations between specific phenotypical features of mental disorders and dysfunctional settings of meta-control parameters? Are dysfunctional control parameter settings shaped by genetic variation, learning history, and acute stress? A closer integration of computational models and psychopathology provides an avenue towards explanations of how phenotypical expressions of mental disorders emerge from nonlinear interactions among underlying neurocognitive mechanisms, dysfunctional meta-control parameter settings, and aberrant systems interactions on different levels of analysis. Computational models generate novel hypotheses about common mediating mechanisms across disorders.</p>
The need for a comprehensive Behavioural Science program		
11	Conceptualization of mental disorders as the outcome of maladaptive developmental processes on various levels	<p>There is a major need for reconceptualising the concept of mental disorders by:</p> <ul style="list-style-type: none"> • Elucidating the “normative” (adaptive) expressions of psychological functions and processes, their neurobiological, molecular and genetic substrates, and their interaction by developmental stage in well-defined “normal” populations with theory-driven, tailored task paradigms. • Modelling pathways and system interactions both at a structural (e.g. latent trait and growth; reduction of complexity, “higher order constructs”) and a “mechanistic” level (e.g. circuitry processes, computational neuroscience). • Validating, challenging and improving the derived models by basic science experiments (e.g. cells, animal models) to derive improved models for further testing (e.g. systems biology). • Incorporating individual and contextual factors to determine how functions, processes and circuitries are developmentally influenced by learning, plasticity, emotional traits, and stress. • Applying the derived models in defined risk cohorts to examine how, why, when and where system components are affected and prospectively associated with increased risk for onset. • Testing when, how and to which degree these dysfunctions can be altered by interventions
Advancing Psychotherapy and Evidence-Based Psychological Interventions		
12	Why does CBT work?	<p>Adopting improved principles and heuristics in evaluation evidence-based psychological interventions</p> <p>Exploiting basic experimental research to characterise commonalities and differences across disorders and optimize core active ingredients of cognitive-behavioural treatments (CBT): Core high priority issues are:</p> <ul style="list-style-type: none"> • Which factors and mechanisms are diagnosis-specific and which are shared or common factors that apply to a wider scope of clinical problems and diagnoses? • What are the core moderators and mediators of change in patients treated by CBT?

13	What is the role of individual variation?	<p>Are there specific endo-phenotypes that allow optimization of the choice and allocation of interventions to specific patient characteristics? This involves:</p> <ul style="list-style-type: none"> • Using multiple levels of assessment to improve response prediction, such as using (epi-) genetics, neuroimaging, experimental psychobiological, objective behavioural measures (virtual reality EMA, actography, mobility), bio- and social-behavioural markers • Testing putative endo-phenotypes and respective neurobiological, psychological and behavioural markers that could more reliably guide clinicians' treatment choice and improve the prediction of treatment outcome • Identifying individual patient constellations associated with non- or partial response • Identifying the role of concomitant and prior appropriate or inappropriate treatment (i.e. What type and pattern of medication has an impact? See also 16) • Reduction of exclusion rules in RCTs to include typical patterns of comorbidity in order to provide guidance as to what targets and procedures should be chosen in comorbid patients. • Identifying the needs of neglected, or particularly vulnerable patient groups and incorporating matching treatment components.
14	Overcoming the gap between science-based and evidence-based psychotherapy in research and its application in clinical routine settings	<p>The continued and seemingly widening gap requires addressing a range of issues:</p> <ul style="list-style-type: none"> • Understanding how variations in usual care practices impact patient outcomes • Employing RCT templates to address questions about real world service implementation and conduct explicit effectiveness and transfer trials • Examining the impact of patient and provider preferences • Integrating constructs of organisational culture and climate into services and intervention research • Designing culturally and socially adapted interventions • Exploring how technology-based intervention and e-monitoring might increase adherence to state-of-the-art methods • Increase the "ecological validity" and clinical utility of CBT programs by avoiding overly selective inclusion criteria and diagnostic fragmentation • Examine to what degree therapist adherence to treatment protocols plays a role and when, what type of individual modification might be allowed (i.e. comorbid conditions, or life events during treatment) without threatening the integrity of treatment.
Psychological Models and Paradigms of Mental Disorders from a Cognitive Perspective		
15	Focus on the dimensional nature	<ul style="list-style-type: none"> • To acknowledge the gradual or dimensional nature underlying clinical phenomena may supplement existing psychiatric classification systems, and moreover, point to the relative role of biological, psychological and particularly social-environmental variables and their dynamic interplay for understanding behaviour. A facet-oriented, dimensional multi-level domain approach by functions and elements of behaviour is needed.

16	Linking psychological and psychopharmacological research for intervention	<ul style="list-style-type: none"> To understand how pharmacological processes can affect specific psychological functions, e.g., memory processes, will likely allow for much more targeted, interactive interventions, in which pharmacological agents are specifically used to impact a psychological process that is more or less causally implicated in mental disorder
17	Increasing external validity of psychological models for mental disorders	<ul style="list-style-type: none"> Validity testing may be an integral and explicit part of a continuous research program – more than is current practice in experimental psychopathology research. Examining the mechanisms, moderators and mediators underlying the (experimental) model likely has an impact on the construct validity of the model and/or the theory of the disorder (or behaviour of interest) itself.
Psychotherapy research in children and adolescents		
18	Improvement of treatment outcome in children and adolescents	<p>Psychological interventions in children and adolescents imply a number of technical, procedural and ethical challenges that are relevant for improving outcomes. There is also a need to understand why a substantial proportion does not respond to evidence-based treatments. Research priorities are:</p> <ul style="list-style-type: none"> Identifying relevant and potentially developmentally specific mediating and moderating variables of evidence-based psychotherapies for youths with mental disorders Investigating the efficacy of psychotherapies in difficult-to-treat populations (e.g. mentally retarded youth, children and adolescents with autism spectrum disorders); Evaluating the effectiveness of evidence-based psychotherapies for youths and parents who seek help in everyday clinical practice; Exploring the additional value of motivational techniques and strategies to increase the efficacy of psychotherapy for youths with mental disorders and their parents. <p><i>New insights of ongoing developmental psychopathology research should be employed:</i></p> <ul style="list-style-type: none"> To further improve the efficacy of already effective psychotherapeutic interventions; To develop new psychological interventions targeting newly discovered vulnerability and protective factors of childhood psychopathology; To develop more developmentally sensitive and appropriate treatment programs.
10	Exploiting developmental psychological and developmental neuroscience research	<p>We know little about the aberrant processes underlying psychopathology in children and adolescents and in what way they can be changed by means of psychological interventions and psychotherapy in particular.</p> <p>There is a need to implement knowledge and expertise derived from developmental neuroscience research in order to</p> <ul style="list-style-type: none"> establish the links between childhood psychopathology and aberrant processes in the developing brain explore whether and to what extent these processes can be corrected and modified by means of psychotherapy

E-health and innovation of mental health care		
20	How can evidence-based e-health and innovative treatments be applied in routine (mental) health care settings?	<ul style="list-style-type: none"> • Testing the value of Internet-based treatments as automated versions of standard psychological treatments in specialized mental health care, in “indicated” prevention and for use in primary care settings in particular • Examine the role of dosage and intensity of internet-based interventions on outcome • Examine acceptability (patients) as well as the immediate and long-term health-economic benefits. • Examine their value for relapse prevention and cost-benefits • Explore their use in targeted preventive trials, such as occupational and school settings.
21	Further development of improvement of internet-based treatments	<ul style="list-style-type: none"> • Are self-guided Internet-based treatments as effective as guided treatments? • Research about the logistical organisation of Internet-based treatments, i.e. how many treatment sessions are needed, who can deliver the treatments, how many treatment sessions are needed, and what the best intensity is. • Examine the role of internet-based treatments for bipolar disorders, psychotic and other understudied mental disorders. • What are the benefits of Internet-based treatments in terms of cost-effectiveness ratios?
22	Incorporating technological innovations	<ul style="list-style-type: none"> • Improving outcome measurement by implementing new forms of technology-assisted clinical tools (e.g. virtual reality applications or minimal contact therapies) and by supplementing the traditional treatment modalities with psychometric feedback tools • Testing ‘real time’ psychometric feedback over the course of treatment (supported by modern software tools as well as data entry systems like touch screens) to adapt dosage and intensity of treatment to patients complexity and problem profile in order to promote better outcomes. • Examine the value of combining Ecological Momentary Assessment tools (i.e. sensors in the mobile phone (accelerometer, GPS, audio, contact with other phones) with personal information from the user (where are you, what are you doing, how is your mood, how did you sleep), to examine mental health problems in real time, actual assessment during day-to-day life, • Examine the value of telepsychiatry using television sets and allowing the provision of face-to-face treatments and support from a distance (without travelling) and the development of Avatars: together with the improved possibilities to recognize emotions through webcams, it may be possible to develop Avatars which can replace human contact more and more. • Virtual reality applications for mental disorders.

Critical Issues in the Evaluation of Comorbidity of Mental Disorders and Future Research Needs		
23	Agreeing on standards of comorbidity research	<p>The lack of consensus about methodological standards in comorbidity research hampers progress and requires agreement on methodological standards on various levels</p> <p>Further needs are the development of clinical and research methods for the assessment and evaluation of comorbidity within mental disorders as well as with regard to relationships to somatic diseases and social functioning/disability:</p> <ul style="list-style-type: none"> • Use of innovative approaches like clinimetrics
24	Treatment implications of comorbidity	<ul style="list-style-type: none"> • Examination of the clinical implications of comorbidity with regard to treatment effects, side effects, clinicians judgement and patient preferences within appropriate clinical trial designs • Examinations of moderators including developmental and social-cultural factors and the incorporation of patients perspective
25	Identification of factors underlying co- and multimorbidity	<ul style="list-style-type: none"> • There is a need to extend aetipathogenic research on single disorders to typical comorbid constellations (see above)

3.6. Social and economic issues

3.6.1. Introduction to the area

Within the ROAMER project, work package 6 has a particular focus on social exclusion, stigma and the economics of mental health. These issues are associated with substantial public health significance for Europe, especially in the face of the current economic recession. Social exclusion of people with mental illness is damaging to individuals with mental illness and is associated with substantial societal burden. Low levels of knowledge, stigmatizing attitudes and discriminatory behaviours are associated with lower rates of help-seeking and under-treatment. Evidence of the economic impact of social exclusion is limited; however, growing evidence demonstrates the substantial financial impact of mental illness across multiple sectors including employment, housing, education and health care. Information on the costs associated with mental illness and well-being are essential to inform policy and practice decisions so that effective strategies can be made to achieve best value for money using available resources.

In recent years, European networks focused on social and economic issues in relation to mental illness and well-being have formed to facilitate research in these areas across Europe including the Mental Health: European Economic Network (MHEEN); Mental Health Economics European Network, Anti-Stigma Programme European Network (ASPEN) the European Network for Mental Health Evaluation (ENMESH) and REFINEMENT (Research on Financing and Quality of Mental Health Care in Europe).

The results below correspond to the initial findings in relation to social and economic issues for mental health in Europe, including what is known about the economic costs and social consequences of stigma and discrimination, as well as economic impacts of co-morbid physical and mental health problems. This interim report is based on the findings from the first work package meeting, initial surveys with experts and systematic mapping and sampling of the literature.

3.6.1.1. Definition of subareas

Work package 6 is divided into two broad themes with overlapping content, i.e. social and economic aspects in relation to mental health and well-being. Importantly, we will investigate the social and economic impact of mental illness across a range of sectors (i.e. not only focusing on medical care), including: employment, housing, education,

social care, criminal justice and health care. We also plan to investigate impact of both mental illness and positive mental health.

Research topics which will be investigated by work package six include:

- Mental, health and social care financing systems
- Economic evaluation and economic modelling
- Socio-economic impact of social inclusion, exclusion and discrimination
- Information on the cost-effectiveness of interventions to tackle/prevent stigma, social exclusion and discrimination
- Understanding of the economics of co-morbidity (multiple mental disorders / somatic health problems)
- Gaps in economics of some disorders
- Social determinants of mental health
- Social welfare systems and impact on mental health – housing, employment, education to work, older people
- Non-traditional interventions – e.g. debt/finance management
- The impact of economic shocks on mental health

3.6.2. Gaps in knowledge

3.6.2.1. Main gaps in the current knowledge in relation to social exclusion and stigma

<i>Knowledge gaps</i>	<i>Translation and implementation gaps</i>
<ul style="list-style-type: none"> - Stigma is difficult to grasp (inc. implicit measures of stigma) - What is social exclusion? What is social withdrawal? What is due to side effects of medication? Negative symptoms (social withdrawal) as representation of social exclusion and despair - How should we speak about stigma? - Physical health care and physical health outcomes (better understanding of the co-existence of mental and physical problems and their implications) - More research is needed on social inclusion (inc. access to treatment) - Multi-morbidity - What is the connection among poverty, exclusion and stigma? Do poor and excluded people feel more stigmatized than more privileged? - What are the criteria for wellbeing and what is evaluation of effective mental health promotion strategies? - What positive stereotypes do we have about those suffering from mental illness? Is it relevant to explore the positive outcomes of suffering from a mental illness? Could it help in reducing the perceived legitimacy of stigma among the mentally ill, and foster solidarity among them? 	<ul style="list-style-type: none"> - Dominance of social psychology in stigma research, more could be done on interventions and there could be more application of theories and models to guide research - Need more research on interventions (e.g. contact, what kind of contact? costs) - Stigma research lacks theoretical grounding - Exclusion from treatment (Supply-side problems? Demand-side problem?) - Does seeking help in different settings (e.g. primary care, e-mental health) reduce the impact of labelling? - How do we counteract the fact that mental illness is highly under reported when trying to assess or estimate the impact of stigma? What can we learn about implications for effective policymaking and financing?

3.6.2.2. Main gaps in the current knowledge in relation to economics

Again a wide ranging discussion on gaps in knowledge also unfolded and the main points that came up in discussion are collated below.

- There remains a lack of capacity and indeed a lack of demand for economic analysis to complement effectiveness analysis in many countries. This is not just in eastern European countries – one example of significant funding on early intervention research was cited from the EU-15, but it was noted that no economic analysis was commissioned. Economics is not mainstreamed into health research in some countries.
- While it was noted that the use of economic evaluation in health policy and other decision making is growing, this takes a long time to embed.
- Costing studies and economic evaluations are hampered in many parts of Europe by a lack of survey, epidemiological and registry data. Moreover more needs to be done to improve the comparability of data across countries and to standardise (or at least make more transparent) the methods used for economic evaluation and analysis.
- There are therefore still are many gaps in what is known about the costs of poor mental health across different European countries. It is difficult to make cross-country comparisons in costing studies often because of a lack of transparency in cost of illness methodologies.
- Not been enough attention paid to the ethics of mental health economics. There is a need for more on what happens with the results of health economic research. Have there been any controversial decisions to deny access to an intervention as a result of economic analysis?
- Data issues also mean that there is little information on the long term impacts of poor mental health across the life course in many European countries, although millennium cohort studies will provide future opportunities for research.
- There is a lack of comparative outcome measures that can be used as part of economic analysis, particularly for children and young people. For instance, there is little data in the OECD health database on these issues for some countries.
- There remains a reliance on relatively easy to obtain indicators, such as readmission rates and suicide rates, which are of limited used in benchmarking the performance of mental health systems. This includes limited use of important non-health indicators such as rates of employment, housing and education status.
- There has been little comparative research on the performance, including technical and allocative efficiency, of mental health systems in Europe. This stands in contrast to performance assessment of other aspects of health care systems.
- In terms of areas for economic analysis it was noted that there has been very limited research on the cost effectiveness of interventions to tackle stigma and discrimination, as well as on the potential cost effectiveness of some potential approaches to promote and protect mental health such as mindfulness and meditation. In the same way another gap cited is the limited research that has been conducted on the economic costs and benefits of the recovery model.
- There is also a need to work on positive wellbeing measures, with a lack of consensus on outcome indicators for positive mental health for use in economic analysis, which it makes it more difficult to make the case for investing in mental health promotion.
- Limited amounts of information are available about resource allocation and funding of mental health in some parts of Europe.
- There is also limited information on the unit costs of resources for mental health in some countries.
- There is sometimes a lack of contextualisation of the results of economic analysis when transferring study findings between different regions/countries in Europe.

- There is limited contact between other branches of economics and health economics, which implies that we may not be learning as much as we could from economics, for instance in respect of current research in the field of behavioural economics
- The focus of mental health economic research is still dominated by the psycho-medical model. More use could be made of economic approaches in helping to learn about what increases the risks of poor mental health and why people present to the health services with mental health problems.

3.6.3. Advances needed in research and justification according to the common criteria

3.6.3.1. List of social inclusion advances needed

Top three priorities

1. **Research on access to and continuity of employment (including effective procedures and practices related to disclosure when applying for a job, absenteeism and presenteeism), especially for people with long-term illness and disability.**
2. **We need effective interventions against public stigma supported by rigorous empirical research on: (i) who should be targeted; (ii) how interventions work; (iii) by whom; (iv) when; (v) evaluated by whom and how and (vi) their cost-effectiveness.**
3. **We need to revisit psychopathology and associated concepts and to consider to what extent some symptoms may be secondary to stigmatizations, possibly leading to reclassification of some symptoms.**

Additional priorities

4. Improved physical health care and physical health outcomes (access to physical healthcare and assessment, treatment and outcomes of physical health conditions and reductions in secondary effects of medications and treatments).
5. We need to increase research on service user (and carer)-oriented involvement in treatment choice through use of shared decision making and provision of evidence-based information.
6. We need more thorough research and randomised controlled trials in different populations on what kinds of interventions successfully reduce self-stigma and increase empowerment in which populations.
7. We need a better understanding of the determinants, processes, costs and consequences of stigma and multiple stigma (including mediators and moderators) and to investigate the early impact of stigma and discrimination and the relevance for timing of interventions and/or early intervention.
8. We need more research to better understand the relationship between stigma and symptoms, and facilitate appropriate care pathways.
9. Research into the identification and development of support systems for family members and carers of people with mental health problems.

Example. More work is needed on the methods of measuring and valuing informal care and looking at the cost effectiveness of interventions to support carers. Most work has focused on providing support for people with dementia and not other groups.
10. Impact of mental illness on social life, social functioning and personal relationships.

3.6.3.2. List of economic advances needed

Top three priorities

1. There is scope generally for increasing and improving the quality of country specific economic evaluation of interventions to protect and promote mental health and treatments and support for people living with mental health problems. This includes improving information on the unit cost of resources for mental health.
2. We need to further develop methods to calculate the budgetary and economic implications of task shifting, changing responsibilities for the delivery of care.

Example. There is a need for work on developing methods to better estimate the economic impacts of co-morbid physical and mental health problems, as well as the cost effectiveness of interventions to prevent/alleviate co-morbidity and to consider this as a task shifting issue.

3. There is a need for more economic evaluation of different combinations of interventions, e.g. different combinations of psychological and pharmacological therapies or stepped care, as well as new modes of services delivery, for instance making use of the internet. In respect of internet based delivery there is scope for collection of data online on a routine basis for use in evaluation.

Additional priorities

4. More research is needed on accurately capturing quality of life as well as developing positive mental wellbeing (including potential proxies like happiness) for use in economic evaluation. Measurement should take into account the appropriateness of measures for population sub-groups such as young children and those with cognitive problems.
5. More information is needed on the efficiency/performance of mental health systems in Europe for health and non-health indicators such as employment, housing and education.
6. What are the most cost-effective ways of financing, regulating, organizing and providing services to promote and protect mental health systems across Europe? This includes information on their funding, differences in resource allocation and reimbursement mechanisms, including the use of activity and reward mechanisms and governance/regulatory structures.
7. Timely research is needed on different aspects of the impact of current and past economic shocks (e.g. booms, recessions) on mental health and wellbeing. Do they lead to any positive impacts on mental health and wellbeing as well as negative impacts? What factors cushion individuals from the most adverse impacts of crises?
8. We need to draw more on mainstream economics to look at the economics of mental health, for instance, using the theories and mechanisms from behavioural economics and psychology to advance research around behaviour change and including motivation and incentives. One example would be to look at the potential for influence in individual behaviour to strengthen mental resilience another might be to motivate individuals to engage with appropriate series when needed or challenge procrastination.

3.7. Public health research

3.7.1. Introduction to the area

Within the ROAMER project, mental health research is understood as something distinct from mental disorder research. Public mental health research focuses on population level distribution and determinants of mental health, the relationship between health and mental or physical disorder and on finding means of sustaining and improving mental health on a population level. From the public health perspective it is thus important that the society and its citizens have the prerequisites for maintaining and enhancing mental health and mental well-being, instead of focusing merely on reducing the prevalence and severity of mental disorders.

Mental well-being encompasses the subjective perspective of the individual's mental health status. Mental well-being is a dynamic state in which the individual is able to develop their potential, work productively and build strong and positive relationships with other people. An individual without disorders can experience varying degrees of health, depending on whether he or she can realise his or her own abilities, cope with the normal stressors of life and be able to make a contribution to his or her community (Cooper et al., 2009; WHO 2001).

The coordination activities in this area, in preparation for an integrated roadmap for mental health research in the public health field, focus on research needs in mental health epidemiology, mental health services research, prevention research in mental health, mental health promotion research and mental health policy analysis. The roadmap will provide a coordinated research action plan outlining the research needed to establish an evidence base for national mental health policies and an EU mental health strategy.

The research priorities chosen will contribute with building blocks for a smart, sustainable and inclusive growth in the EU. Particular focus will be on how public health research can address the situation of under- and poor treatment for mental disorders and our general lack of knowledge about how service provision for mental disorders, as well as mental health promotion, is organised in European countries.

The definition of public health research used within WP7 is as follows:

Public mental health aims to develop mental health and mentally healthy societies. Public mental health research is research concerned with population mental health.

In ROAMER, public mental health research thus encompasses research to describe collective experience, occurrence, distribution and trajectories of positive mental health, mental health problems and their determinants; research on mental health promotion and prevention of mental disorders; as well as research on mental health system policies and governance; service delivery; and organisation of mental health services.

3.7.1.1. Definition of subareas

Public health covers a broad range of disciplines which will be considered in the roadmap:

3.7.1.1.1. Epidemiology

Epidemiology research in the public mental health field maps the distribution of mental health determinants and the disease burden of mental health disorders at the population level. Key topics in mental health services research relate to service delivery, mental health workforce, novel health technologies, as well as relationships between users and professional carers and issues around governance and accountability.

The roadmap for epidemiological research will outline steps to cover gaps in our knowledge on prevalence of risk factors, protective factors and mental disorders in Europe, thus laying the ground for evidence-based planning of health care delivery. Actions to bridge the gaps in knowledge about mental health in work life, disadvantaged groups, children, older adults and migrant populations will enable targeted actions to address mental health problems in population groups. Research on the epidemiology of mental health in socioeconomic groups will pave the way for actions to promote mental health equity in Europe. The roadmap for epidemiological research will strongly take into consideration the need for data collection beyond that which is dependent on the current psychiatric diagnostic systems, such as research on positive mental health and subjective well-being determinants, and strongly encourage use of novel and alternative approaches to psychiatric phenotypes. Crucial building blocks in epidemiological research will be common European mental health surveys and improved coordinated use of existing national health registers.

3.7.1.1.2. Mental health services

Efforts to enrich EU information about disease burden need to be accompanied by comprehensive assessment of the quality of psychiatric services, identifying the regional and cultural differences in Europe. In other words, mapping of the disease burden must be supplemented by mapping of mental health care services (and their quality) in order to

provide the information basis to agree evidence-based standards of care and inform policies for consistent service provision and future health professionals' training. Key topics in mental health services research relate to service delivery, mental health workforce, novel health technologies, as well as relationships between users and professional carers, and issues around governance and accountability.

3.7.1.1.3. Prevention of mental disorders

Prevention research issues are linked to development of prevention strategies and actions, assessment of prevention efficacy and effectiveness, as well as issues regarding adaptability and transferability of preventive interventions. The roadmap will focus on prevention research with policy relevance, to provide decision makers with a sound evidence base for decisions regarding prevention of mental disorders and suicide.

3.7.1.1.4. Promotion of mental health

Mental health promotion research focuses on the entire lifespan in all settings for mental health promotion: home, school, communities and services. Close links are made to health psychology, social, psychiatric, educational and economic research, encompassing different ontological and epistemological approaches to mental health promotion research.

3.7.1.1.5. Policy analysis

Policy analysis research provides evidence on effectiveness, feasibility and acceptability of mental health policies. It will dissect processes and ideologies behind policies. Crucial success components will be identified and key strategies to implement successful policies will be provided.

3.7.2. Gaps in knowledge

3.7.2.1. Gaps in mental health promotion research

1. We have yet to arrive at a consensus of what mental health promotion means. A suggestion of what promotion is in relation to prevention is that prevention focuses on negative aspects, preventing problems, and risk reduction, while promotion focuses on the positive, is strength based and prevents as a side effect. A question of debate is whether promotion can be seen as primary prevention.
2. Research on the public's awareness and understanding of mental health. This is related to stigma and discrimination.
3. We need to get mental health (promotion) more prominent in all contexts and all societal levels. Inclusion in the policy agenda would help mental health promotion to become more intersectoral.
4. There is a need to develop and direct mental health research (including mental health promotion interventions), to take into account wider socio-economic and cultural factors due to societal changes. Considering an event such as an economic crisis - and how it affects social cohesion in individual countries and on a European level, and its impact on mental health - is an area of future research.
5. Development and evaluations of complex, long-term interventions, working on many levels and with input from many different scientific disciplines.
6. Development and validation of macro-level mental health promotion interventions, and improved skills in implementing them.

7. Understanding of the cultural context of mental health research could be improved. A large proportion of research comes from a small number of countries. However, the meaning of well-being, mental health and a mentally healthy society differs somewhat between cultures.
8. There is still a lack of appropriate measures for positive mental health, including protective factors and determinants. Advances have been made in this area, but we need more measures regarding such things as resilience and emotional wellbeing, adjusted for different age groups and gender.
9. There is an underdevelopment in the systematic implementation of interventions, dissemination of findings across cultures and settings, and translational research from evidence to practice and practice to evidence
10. Mental health promotion research is very scattered. There is a lack of common terminology and definitions of outcomes. We need to find a “home” for mental health promotion, as it does not quite seem to fit either in health promotion or mental health research.
11. We should reduce the artificial separation of mental health and physical health, both in research and in policies. Research capacity and training need to be expanded in order to bridge these areas. Research needs to be a hybrid of many things; today there are public health researchers that are not comfortable with mental health, and there are mental health researchers that are not comfortable with going beyond an individual paradigm.
12. Application of complexity theories is needed on the grounds that everything is connected. This calls for the use of different research methods, such as mixed methods and participatory approaches.
13. There is a need for improvement in the introduction of new programs to the public. This means development of implementation strategies in different cultural settings, in particular in outreach to more deprived communities, as it can be difficult to reach these groups that sometimes are in the greatest need of help.
14. More research on the links between mental health, alcohol and substance abuse, dieting, and other life style factors.
15. Research on ways of re-modelling the brain in adulthood. We know about the plasticity of the infant brain and how its development can make us more or less resilient in adulthood. We need approaches to remodel the brain in adulthood.
16. More research on the effects of supporting parenting and the most effective ways of delivering support, especially for parents with mental illness or addiction problems.
17. More research on older people, considering the demographical change.
18. Funding is still very limited, which in part is because of the prevailing problem-focused (disease-focused) paradigm. More research showing the potential of mental health to impact physical health could perhaps improve the situation.
19. Participatory research should be further developed.

3.7.2.2. Gaps in mental disorder prevention research

1. We need better markers, including biomarkers, for identifying groups of individuals for targeted intervention strategies.
2. Development of specific interventions for specific target groups, instead of general prevention aimed at the population.
3. We need innovative measures to reach those who suffer from social exclusion.
4. Reliable tools to evaluate suicidal risks across the life span should be developed.
5. We should make better use of e-mental health approaches for prevention of mental illness.
6. Research on prevention of work-related mental health problems.
7. More knowledge on how to prevent sickness leaves and loss of productivity due to mental illness.

8. Implementation research on preventive interventions, adapted for age groups. We have many good interventions that are not yet properly implemented in routine use.
9. Better understanding of neurobiology behind acquired vulnerability for certain disorders, for example how to avoid PTSD.
10. Consequences of media use in children and adolescents on neurobiology, cognition and emotional functioning.
11. To understand side effects of psycho-therapy, such as suicidality, and how to prevent them.
12. In psycho-therapy interventions, control groups are not possible to blind, making it difficult to measure effectiveness of psycho-therapy.
13. Research on the associations between fathers' mental health and mental health problems among children.
14. Early interventions targeting early childhood, as it is most effective to prevent ill-health in early stages of development.
15. Research on the effect of mental disorders and use of psychopharmacs during pregnancy and their long-term impact on maternal and offspring health.
16. There is a lack of research on the effect and cost-effectiveness of screening programs and preventive interventions for postnatal depression.
17. More knowledge is needed on the causes for fear of delivery and its risk factors, through national-wide cohort and register studies.
18. Development of statistical models to evaluate complex long-term interventions.

3.7.2.3. Gaps in mental health epidemiology research

1. There is a lack of adequate evaluation of interventions for enhancing mental health and preventing mental health problems. Further, dissemination and implementation of research are lacking.
2. There is a lack of comprehensive study approaches using multidimensional study designs and measures to capture the prevalence and impact of various mental health indicators. In addition, there is a need for increased research on trends and comparisons due to the lack of comparison and longitudinal studies using common methodologies.
3. Even though there is increased knowledge on mental health and related determinants in children and adolescents, there are still gaps in our understanding of mental health problems in the early years.
4. Research on inequalities in mental health and on the effects of socio-economic crises on mental health is limited.
5. There is a need to conduct research on various addiction problems using a wider scope than addictions related to substance abuse.
6. There is incomplete research on genetic influence on mental disorders (i.e. genetic risk factors) and little research on neurocognitive deficits after or connected with mental disorders.
7. There is a need to further investigate the aetiological association between physical and mental health in order to understand the comorbidities that are so common for mental health problems.
8. There is a need to acknowledge the new ways of communicating and interacting through technical advances (i.e. social media), which should be studied in research.
9. Studies are needed on effectiveness of integrated treatments, combining approaches to treating physical and mental comorbidities.
10. There is a need for research on the application and development of dynamic models that take account that what we are investigating is not stable, but dynamic.
11. There is a need for implementation studies that take into account and adapt interventions to the individual's developmental stage, disease process and context.

3.7.2.4. Gaps in mental health services research

1. There is an underrepresentation of research with a health-focus, as opposed to illness-focus. This includes research into understanding of and interventions to improve recovery and well-being at an individual level, as well as interventions on a societal level aimed at improving resilience and well-being.
2. Social determinants of mental health in Eastern Europe. A research area in need of special attention is the implementation of community based services, specifically with focus on recovery and user-led research, and policy research.
3. We need a research focus on mental health stigma and the barriers for participation in the work market and in social life. Research is also needed on how stigma influences service use, which may have to do with how the services are provided and organised.
4. Methods of delivering mental health care that are more integrated with physical care. A way to achieve this is by training non-mental-health staff to deliver mental health care.
5. We need to address the lack of knowledge of routine treatments' outcomes and their effectiveness. To achieve this we need more adequate outcome measurements. Mental health research cannot just count deaths, as some medical sciences do.
6. We need to regain a comprehensive bio-psychosocial approach and not simply a 'biological' or 'psychological' one. So far there has been too much enthusiasm for reductionist genetics, while the concept of quality of life has not been taken up and utilized to its full extent.
7. The role of psychiatric drugs in suicides needs to be further explored. This is motivated e.g. by a study that found that 80% of victims of suicides had psychiatric drugs in their body.
8. There is a need for comprehensive statistical data on suicides (suicide registers).
9. Forced community treatment and other coercive measures need research that is independent from service providers. There is a need to open the research area of mental health services to other professional groups than those who are currently conducting research.
10. We need more systematic reviews where research designs and outcomes are investigated from user-perspective.
11. More research on effective interventions that are not dependent on health care professionals, e.g. peer-support and alternatives to conventional psychiatric treatment.
12. More implementation research on the effect of evidence-based treatments and on how to ensure effective adoption and sustained implementation in the daily work of health professionals. Further research is needed to investigate if the effectiveness of interventions differs between e.g. different population groups or phases of a disease.
13. We need to try and evaluate a system where the patient is more engaged in the decision-making regarding their treatment, and recovery is viewed with a personal recovery focus.
14. We need to question our disease concepts, for example in relation to stigma. Brain imaging does not necessarily reduce stigma, it has been shown that it can have the opposite effect.
15. We need to use more caution when using randomised controlled trials, as they are ideal designs that do not translate well to reality. An example is polypharmacy, where the interactions that may occur when using several drugs at once are seldom examined. Alternatives to RCTs need to be explored and developed, e.g. growth-curve analysis.
16. There is a need for a holistic approach in studies of mental health services that takes into account factors such as accommodation, occupation, family life, social relationships, etc. Randomised controlled trials have become a gold standard that picks one single intervention in one single circumstance, as if the surrounding sectors have no influence.

17. Interdependence of other societal sectors, such as economics and welfare systems, and their impact of mental health service use and provision are neglected. We need to consider cultural determinants in service use and provision.
18. Other fields and disciplines, such as sociology, anthropology, complimentary medicine, economy, psychology and biology among others, should be consulted in mental health services research.
19. There is a lack of theoretical frameworks, for example organisational theory, in our research and reasoning.
20. There are various mental health service providers on different levels, with different cultures involved in how to look at mental health. We need research on how to develop systematic and well-integrated ways to deliver services for those with mental health problems.
21. We need to address the lack of knowledge of routine treatments' outcomes and their effectiveness.
22. We need to develop more user-friendly interventions, so people really accept them.
23. We need more utilization of the vast amount of information that can be found in registers.
24. We need to study the financing mechanisms of the provided services and the effect of these payment mechanisms on the quality of care. If certain actions by the service providers give them an economic advantage, it is probable that these actions will be taken, possibly at the expense of high quality care.
25. We need to know more about how to properly install evidence-based interventions in order to improve children's outcomes. We should look at differentiated responses instead of just mean effects, as variation can be more interesting than means. For whom does an intervention work well, and for whom less well?
26. Human moderators and processes of care and care delivery should be further investigated.
27. There has been a focus on treating individuals; we need to regain sight of social and economic interventions on a larger scale.
28. More research on evidence-based talking therapies. The research could be more culturally diverse, as the little evidence available is from Western and Northern Europe.
29. We need to investigate the level of discrimination within health services on the account of mental illness alone.
30. What is the feasibility for decentralization of services in Eastern Europe? The situation is quite different from what it was in Western Europe when the shift started there.
31. The efficacy of mental health services should be measured with new outcome variables, such as satisfaction with treatment, quality of life and social inclusion, not only rates of hospitalisations and relapses.
32. Clinicians need to know how and when interventions should be applied, e.g. should it be applied in the acute phase, for chronically ill patients, different age groups...?
33. We should do research on patients' pathways to mental health care. Look at low threshold primary contact points with mental health service, e.g. pharmacies and alternative medicine.
34. We need to realise that constant re-organisation of services is ineffective.
35. We need to realise that health and well-being is not best achieved through leaving health care to market forces.

3.7.2.5. Gaps in mental health policy research

1. In general, research in public mental health lacks critical mass due to inadequate volume of researcher training and capacity building, resulting in an imbalance between medical research and public mental health research. Dedicated journals are lacking.
2. There is a general lack of European research on interaction between research and policy, including qualitative research.
3. There is a need for much more policy implementation research, especially research analysing the barriers of implementation.

4. We need more evidence for child mental health policies and mental health policy for older people.
5. The investment in research on participation in mental health systems, social inclusion and human rights in the mental health setting needs to be scaled up.
6. We urgently need evidence for organising mental health systems in times of economic crisis with fewer resources to spend.
7. We need to collaborate across countries to develop mental health policy research capacity and foster a European critical mass in mental health policy research.
8. We need empirical research on the impact of various mental health care funding systems and effective reimbursement policies.
9. We need information on fidelity of interventions when scaled up.
10. We need evidence on the impact of empowerment on patient and system outcomes.
11. There is a lack of research on recovery and ability outcomes of mental health systems.
12. There is a lack of recognition of diversity across European mental health systems. Especially, there is a lack of research relevant for the low and middle income countries.
13. In general, there is a lack of evaluation of implemented policies.
14. In evaluation research, there is a lack of bottom-up approach.
15. There is a lack of research on new technologies, including e-health and m-health.
16. There is a lack of visionary and ambitious “man-on-the-moon” projects, e.g. zero suicide mortality.
17. We need more testing of priority setting based on evidence.
18. We need more knowledge of mental health literacy in the general population and population subgroups.
19. The links to other policy fields, such as nutrition and exercise, need to be included in future research.
20. We lack data on the effects and effectiveness of mental health screening.
21. We need to develop methodologies and measurements for large scale evaluation of public mental interventions, avoiding experimental settings.
22. Research on co-morbidity issues is scarce.
23. We need more research on new modes of service delivery, such as e-mental health.

3.7.3. Advances needed in research per subarea

3.7.3.1. Advances needed in the field of mental health promotion research

1. The concept of positive mental health should be well-defined, including the theoretical aspects and dimensions that we want to measure and influence. Well-established scales for measuring various aspects of positive mental health will be developed.
2. A better integration of quantitative and qualitative research depending on the research questions, in order to capture the complexity of mental health.
3. We should better understand the cultural elements and differences that are relevant in the field of mental health promotion and this would promote the general status of mental health promotion in European countries.

4. More high-quality interventions should be developed and evaluated in Europe. Now there is an overrepresentation of U.S. research, which is adapted to European settings. To make sure interventions fit European needs, a greater portion of interventions should be developed in Europe.
5. Methods for delivering mental health promotion to hard-to-reach disadvantaged groups.
6. Methods for stronger participation of subjects, including children, in all research.
7. More long-term cohort studies on well-being and protective factors. This is important for the understanding of well-being and how to best promote it.
8. More long-term outcomes from studies of complex interventions.
9. Applied research on natural experiments. Policy decisions regarding schools, workplaces, communities, are regularly made, but they are not systematically evaluated.
10. More research on ways of remodelling the adult brain, how to enhance resilience and coping skills in adulthood.
11. Stronger measurement of well-being, improved robustness of indicators and long-term monitoring of the population.
12. Studies on economic impact of lack of mental well-being. This would be a good argument for increased use of interventions as well as more research.
13. Further studies on the role of genetics in mental well-being, partly to counteract arguments emphasising the role of genetics; to show that environmental factors (that can be changed) are important.
14. Use of new technology for mental health promotion, such as different e-health approaches. An advantage of e-health from a research point of view is that it is easy to do randomised controlled studies of different interventions.
15. Work-force education by initiating more master's and Ph.D. programs in mental health promotion.
16. There are three paradigm shifts that could advance the field. First of all, an increased valuing of the positive instead of the negative. Secondly, a greater understanding of connectedness, both regarding mental and physical health, and the connections between the individual and the collective. Thirdly, an embracing of new ideas e.g. influences from eastern thinking.
17. More research supporting the reduction of stigma of mental disorders. Stigma can be seen as an indicator of lack of mental well-being in the rest of the population, which leads to the conclusion that the best way to reduce stigma is to raise mental well-being in rest of population.
18. Mental health promotion research should have a high-level status, and the value of mental health should be clear at all levels of society. We can reach this by emphasizing the societal relevance of mental health promotion, and by being able to show that mental health promotion also promotes ability to cope with everyday life and improved economic productivity of society. This would enable separate research programs to be established to fund mental health promotion research.
19. There is a need to strengthen the theory base for mental health promotion research, otherwise the research will stagnate.

3.7.3.2. Advances needed in the field of mental disorder prevention research

1. Randomized controlled trials of preventive interventions targeted at specific groups identified on the basis of risk or other markers including biomarkers.
2. Identification of the active components of the interventions that are currently known to be effective.
3. Development and validation of an evaluation tool for suicidal risks based on an interdisciplinary biological, psychological and social approach.
4. Evaluation of electronic tools for prevention and treatment of mental ill-health.

5. More evidence based knowledge on effective interventions and cost effectiveness for preventing and screening for postnatal depression.
6. More knowledge on the causes on fear of delivery based on nation-wide cohort and register studies.
7. Risk assessment of suicidality and other side effects of psycho-therapy and how to prevent them.
8. Longitudinal studies in children and adolescents on the effects of internet and mobile media use on neurobiology, cognition and emotion.
9. Optimizing sleep as a preventive measure concerning depression and other mental disorders in high risk groups.
10. Development of new intermediate outcome measures for intervention studies, as the long-term outcomes are difficult to measure within the time frame of many projects.

3.7.3.3. Advances needed in the field of mental health epidemiology research

1. There is a need for internationally comparable data based on common methodologies and for integrated databases enabling more comprehensive studies.
2. Knowledge in developmental processes or traits in children and adolescents. We need to increase our understanding of mental health and mental health problems, resilience and protective factors in the early years (among children and adolescents). This will facilitate the implementation of mental health promotion and early interventions targeting these age groups.
3. Evaluation of (medical and psychosocial) interventions looking at effectiveness in several dimensions and costs in various contexts are needed.
4. Expanded knowledge in and acknowledgement of economic and social determinants of mental health and marginalization are needed.
5. More research on comorbidities within mental health problems. This is especially important for the comorbidities between mental disorders, substance abuse, and physical disorders. We need to describe and increase our knowledge in how to handle multidimensional problems of alcohol abuse and other problems with addiction. In addition, we need to know more about complications, coincidence and causal associations.
6. Increased understanding of the interpersonal relationships in the postmodern society (including virtual realities and online social networks) is needed.
7. Increased research on neurocognitive deficits in mental disorders across the life span is needed.
8. There is a need for large-scale studies on the genetic and environmental influences on mental development and health in order to capture the complexity of mental health and its determinants across the lifespan.

3.7.3.4. Advances needed in the field of mental health services research

1. We need better understanding of how to optimise child mental health and have a clearer idea of how mental health services can best contribute alongside population and community social and economic actions.
2. Clinicians should be able to be confident in the value and impact of the care they provide, there is a need for compelling evidence.
3. We need a better knowledge of the frameworks on organisational, managerial and clinician levels that achieve effective care.
4. We need to realise that constant re-organisation of services is ineffective.
5. We need to realise that health and well-being are not best achieved through leaving the health care to market forces.
6. There should be a list of all effective interventions produced from research.
7. The patient should be involved in choosing treatment, monitoring outcomes and if needed, in choosing new paths of treatment.

8. We need a meta-perspective in this field of research, we should focus more on variance than on means, e.g. if you try to match therapist - method - patient, there are many variables and not necessarily one best way.
9. Mental health care provision should be more aware of its crucial role in society, and must be more self-confident in how it can contribute.
10. We need to be able to communicate with politicians and decision makers, and collaborate in the field of mental health services on various levels and contexts, e.g. by pentologue models, inviting users, their relatives, professionals, the public and decision makers to the discussion.
11. Researchers, together with users, relatives and clinicians, should be able to develop services that use good measures to monitor treatments, because it is useful and beneficial for everybody. The researchers would get valid data from the real situation where treatment is happening.
12. The narrow area of mental health services (research) should not exist; instead it should be a part of overall health services (research), as a gain to the whole, not a loss to mental health.
13. Taking part in research should be an accepted and routine part of the use of mental health services, as is currently the case in e.g. cancer services.
14. Mental health research should not be dominated by the biomedical model.
15. Experiential knowledge should become a legitimate source of knowledge and acquire a role in conceptualizing services.
16. Survivor controlled studies should be funded.
17. Scientific publications (not just abstracts) should be available to everyone (open access for databases).
18. Values and aspirations of mental health workers should become topics of research.

3.7.3.5. Advances needed in the field of mental health policy research

1. Any research strategy should reflect strategic priorities of mental health policies, such as the forthcoming WHO European mental health strategy.
2. Research on policies to ensure equal opportunities for everyone to realize mental wellbeing is needed. This would include research on maximising society's mental capital.
3. Research on protection of human rights of people with mental disorders.
4. Research on policies to provide safe, accessible and affordable mental health services in the community.
5. Research on delivery of respectful and effective treatment and on promotion of shared decision making.
6. Prioritise according to burden of disease.
7. Prioritise disorders that we know can be prevented rather than what we want to prevent.
8. Prioritise health promotion instead of illness prevention (learn from prevention of physical disorders).
9. Prioritise cost-effective interventions.
10. Prioritise general rather than targeted interventions.
11. Prioritise arenas outside of health care.
12. Strongly prioritise first years of life.
13. Prioritise reduction of level of mental distress in the population rather than reduction of number of people affected.
14. Perform research that is sensitive to the economic and cultural context.

3.7.4. Priorities for research and justification according common criteria

All statements included in the five lists of advances needed (presented in Chapter 3.7.3) were collapsed into one list of public mental health research priorities as suggested by the involved experts. Further, the list of research priorities has been developed based on the discussions held in the second scientific workshop meeting and on the results from conducted web-based surveys as part of a Delphi process. Consensus has been obtained by using the Delphi technique (Slocum, 2005; Hsu and Sandford, 2007), a process where a series of questionnaires is sent out to the experts for their comments. Also, in order to be able to organise the listed statements in order of importance, the involved experts have been asked to rank each statement on a scale from 1 to 6 and to motivate their preferences.

All scores and comments provided by the experts have been considered in the revision work.

In total, nearly 60 experts have been engaged in the work by providing their input along the process. The current version of the priority list, still subject to the final revisions, can be found below.

Overview of the public mental health research priorities

Goal	Research challenges
<p>Goal A: To identify causes, risk, protective and salutogenic factors and processes for mental health across the lifespan</p>	<p>3. To strengthen the understanding of the cultural factors (i.e. ethnicity, religion and value systems, and nationality), relevant for public mental health</p> <p>4. To perform and sustain long-term prospective cohort studies to investigate the determinants of mental health and well-being and to study risk and protective factors for mental disorders and suicidal behaviour</p> <p>12. To strengthen research across the lifespan and with regard to sensitive time windows of human development, including developmental and environmental salutogenic factors pertinent to public mental health</p> <p>13. To strengthen research on the influence of families, public policies and services on mental health throughout the life course of children and adolescents</p> <p>15. To strengthen the understanding of the links between physical and mental ill-health, and on their implications for services</p>
<p>Goal B: To advance the implementation of effective public mental health interventions</p>	<p>6. To develop systematic evaluations utilising natural experiments</p> <p>8. To identify or develop intermediate outcome measures which are predictive of long-term outcomes and can be used as proxy measures in intervention studies where long-term outcomes are difficult to measure</p> <p>11. To strengthen research on implementation, dissemination and sustainability of mental health promotion, mental disorder prevention and service delivery interventions</p> <p>14. To develop appropriate participatory approaches for</p>

			<p>evaluation of complex public mental health interventions</p> <p>16. To strengthen research on new approaches and technology for mental health promotion, disease prevention and mental health service delivery</p> <p>18. To strengthen research on the efficiency and quality of mental health systems and community-oriented interventions</p> <p>20. To strengthen research on the frameworks to achieve effective mental health care on organizational, managerial and clinical levels</p>		
<p>Goal C: To increase equity and to reduce disparities in mental health</p>			<p>5. To strengthen research on mental health of disadvantaged groups, marginalised populations and populations at risk</p> <p>17. To strengthen research on mental health promotion in all policies</p> <p>19. To strengthen research on the protection of rights of people with mental health problems</p>		
<p><i>Summary principles</i></p>	<p>1. Positive mental health and well-being and protective factors should be increasingly addressed in public mental health research</p>	<p>2. Public mental health research should build on interdisciplinary perspectives in order to understand the complexity of mental health</p>	<p>7. The theory base for public mental health research should be strengthened, including definitions and validity of concepts</p>	<p>9. Robust and standardised measures and typologies for public mental health research and validation of existing measures should be developed across Europe</p>	<p>10. Quantitative and qualitative research should be used in combination when relevant for capturing the complexity of public mental health and for enhanced understanding</p>

3.7.4.1. General research priorities

1. Positive mental health and well-being and protective factors should be increasingly addressed in public mental health research

- **Efficacy/effectiveness:** It is important to integrate the perspectives of mental health resources and protective or resilience factors in public mental health research in order to gain full understanding of population mental health. Mental well-being is under-researched, although early evidence suggests effectiveness in protecting against mental and physical illness and increasing both longevity and healthy life years, as well as productivity.
- **Impact / deliverability / economic benefits in Europe:** An emphasis on positive mental health reduces stigma and makes mental health a matter for everybody. Mental well-being is closely connected to healthy life years and productivity of Europeans. Some policies and programmes to improve mental wellbeing are being implemented in European countries showing positive outcomes and economic benefit. There is great need for more research, development and evaluation to enhance impact and deliverability of these programmes.
- **Answerability/feasibility in Europe:** Many of the leading centres in positive mental health and well-being research are located in the EU. Europe is thus well equipped for development of concepts and to answer the

questions about the role of positive mental health in preventing mental health problems and promoting well-being – Which are among the most important and unresolved issues in public mental health research.

Existing national mental well-being surveys (e.g. in England, Iceland and Scotland) form a starting point for pan-European measurement and monitoring of mental well-being.

- **European research strength:** The positive mental health perspective has largely been conceptualised in Europe, and many of the leading centres in positive mental health and well-being research are located in Europe.

- **Illustrative research questions:**

How do we strengthen mental health / well-being?

Which are the genetic, environmental, developmental and cultural determinants of positive mental health?

What is the relationship between mental disorders and mental well-being?

Do universal interventions, aimed at strengthening positive mental health, contribute to reduced incidence of common mental disorder (e.g. depression, anxiety disorders, eating disorders)?

What are the links between positive mental health and working ability / retirement age?

2. Public mental health research should build on interdisciplinary perspectives in order to understand the complexity of mental health

- **Efficacy/effectiveness:** In this context, we consider efficacy as utility of public mental health research in yielding relevant outcomes for public mental health.

All health research – including mental health research – should be dominated by multiple perspectives to understand the complexity of health. For that purpose even the comprehensive biopsychosocial model needs to be extended. Public mental health research needs to involve all potential aspects (including cultural, economic, spiritual and relational aspects) and stakeholders in order to adopt a more holistic view. Inclusion of new perspectives will strengthen innovativeness of European public mental health research.

- **Impact / deliverability / economic benefits in Europe:** Health at a population level – i.e. public health – is to a large degree influenced by how we organise our society and our economy. A broadened scientific scope will contribute to better public mental health actions and improve mental health of Europeans. New models, interpretations and concepts of mental health can underpin new approaches to promotion, prevention, care and rehabilitation.

- **Answerability/feasibility in Europe:** Cross-disciplinary public health research programmes and mental health research programmes exist in many European countries, building a base for inclusion of multiple perspectives. The European values and EU fundamental rights provide a basis for an inclusive approach to public mental health research. Further, it is not enough to show that public health initiatives work, we need to know the contexts in which they work and the balance between costs and benefits.

- **European research strength:** In Europe, there is a strong tradition of questioning biological reductionism and psychiatric positivism. The need to reform medically oriented public mental health is widely accepted in Europe, and the user-defined recovery concept has gained widespread acceptance.

- **Illustrative research questions:**

Can different perspectives of spirituality and/or different cultural values contribute to European mental health?

What are the links between macroeconomics and population mental health (e.g. suicides)?

Can new findings in political sciences (e.g. theory and practice of politics, analyses of political systems) contribute to our understanding of quality of mental health systems?

Can lessons learned from ethnographics and anthropology reduce mental health disparities?

How can additional perspectives be used in a systematic way to extend the biopsychosocial model to understand complex mental health issues?

What do semantic analyses and data mining techniques in large health datasets tell us about the determinants of mental health and well-being?

3. To strengthen the understanding of the cultural factors (i.e. ethnicity, religion and value systems, and nationality) relevant for public mental health

- **Efficacy/effectiveness:** Validity and relevance of mental health research will be strengthened by taking better consideration of the intercontinental as well as intra-European cultural aspects (e.g. ethnicity, religion and other value systems, and nationality) of mental health. This is relevant in order to assess transferability of the evidence base for mental health policies and practice between countries.

- **Impact / deliverability / economic benefits in Europe:** Understanding the cultural factors, such as peoples' beliefs, attitudes and values, is crucial for transferability, adaption and reinvention of public mental health policies and interventions. It is increasingly important for individual countries to have the capacity to provide culturally sensitive societies and understand the impact of diverse cultures on mental health promotion and prevention initiatives.

- **Answerability/feasibility in Europe:** The cultural diversity of Europe and its migrant population creates a rich starting point for conceptual and empirical studies on the role of culture for mental health.

- **European research strength:** Some research of culturally sensitive mental health services, including trans-cultural psychiatry, is already based in the EU. Several Pan-European research projects have been implemented in this area. Research can build on existing European research networks, such as the COST network for migrant health research.

- **Illustrative research questions:**

What are the culture-specific and different understandings of mental health?

What are the trans-cultural aspects of mental well-being?

What are the protective and mental health risk factors in minority groups and subcultures?

3.7.4.2. Methodological priorities

4. To perform and sustain long-term prospective cohort studies to investigate the determinants of mental health and well-being and to study risk and protective factors for mental disorders and suicidal behaviour

- **Efficacy/effectiveness:** Mental health is built in life-long processes. Long-term observational studies, as well as long-term outcomes of experimental studies, provide invaluable information about the distribution of mental health as well as determinants of mental health and mental disorders and their stability over time.

- **Impact / deliverability / economic benefits in Europe:** Mental disorders are leading causes of burden of disease and productivity loss. Mental well-being improves productivity and reduces health care costs. Long-term studies are needed to understand long term courses of mental well-being and mental illness. This is necessary in order to develop health policies and priorities. Linkage with European biobank data derived from genomics, proteomics and metabolomics provides unique possibilities to study biological as well as environmental determinants of mental health.

- **Answerability/feasibility in Europe:** Universal health and welfare structures in EU countries make long-term cross-country studies quite feasible in Europe as opposed to, for example, in the US. Existing longitudinal administrative health care registers provide rich opportunities for additional data in many EU countries.

- **European research strength:** Several existing national or regional cohort studies in the field of mental health provide unique research skills and databases for long-term cohort research. In northern Europe, well-developed health registers and unique identification codes provide unique and cost-effective opportunities for register-based long-term cohort studies, both within and across countries. The experience to conduct these cohort-studies exists in Europe.

- **Illustrative research questions:**

What are the determinants of mental health in a life course perspective in different geographical contexts?

How can we better use the existing register and biobank data?

What are the interaction effects between individual and societal factors in the processes leading to population mental health?

What is the comparative effectiveness of population-level risk factor-based targeted vs. universal prevention of mental disorders?

5. To strengthen research on mental health of disadvantaged groups, marginalised populations and populations at risk

- **Efficacy/effectiveness/advantage:** Disadvantaged groups (e.g. minority groups, people living in poverty, institutionalized individuals) have low levels of mental well-being and high levels of mental health problems, but are often excluded from or do not participate in research. A solid research basis is needed to reduce social inequalities in mental health and to promote inclusion of lesser heard groups in mental health research. It has been shown that non-responders in population studies may often be those with most problems. Representative sampling will improve external validity of research, and highlight the needs, solutions and outcomes among disadvantaged groups. For the sake of representativeness, it is important to reduce failure to include non-participation and drop outs of socially excluded groups in mental health research. The knowledge and research gap regarding the mental health of disadvantaged groups can be addressed only by participation of socially excluded groups.

- **Impact / deliverability / economic benefits in Europe:** The burden and costs of mental health problems are disproportionally distributed in Europe. Improving mental health in population subgroups with the worst mental health status will result in the greatest individual health gains. Emerging evidence indicates that interventions which promote social inclusion and mental health literacy can lead to mental health gains.

- **Answerability/feasibility in Europe:** European social policy aims at social cohesion and inclusion. Being at the heart of European values, there is both a need and a willingness to pursue this track of research. Existing fundamental rights and anti-discrimination research provides an existing support for improving mental health of disadvantaged groups.

- **European research strength:** A number of European countries have good population and health registers. There is a European commitment to public health systems and reduction of social inequalities in health.

- **Illustrative research questions:**

How can the determinants of mental health, mental health problems, and mental health literacy best be addressed in disadvantaged groups?

Which measures are effective in reducing social inequalities in mental health?

How to increase research participation of marginalized groups by culturally sensitive methods?

How to best improve uptake of mental health promotion and preventive interventions in disadvantaged and minority populations?

How to best address mental health needs of transnational groups with high cross-border mobility, such as Roma people?

Which are the positive factors that contribute to mental health for migrant populations?

6. To develop systematic evaluations utilising natural experiments

- **Efficacy/effectiveness:** Natural experiments are for example shifts in policy regarding e.g. families, schools, workplaces or communities. Currently rigorous evaluation of natural experiments is scarce, which leads to policy decisions frequently being based on uncertain assumptions. Better evaluation of policy actions and other natural experiments as well as effective knowledge translation is essential for building evidence-based policy.

- **Impact / deliverability / economic benefits in Europe:** High quality evaluation research will inform and guide policy and health decision-makers to improve policies, including allocation of scarce public health resources effectively. This will make public mental health policy more transparent and accountable.
- **Answerability/feasibility in Europe:** European countries are experiencing shifts in public policies which form natural experiments that provide unique research opportunities. Diversity of European public policies provides a rich soil for comparative policy evaluation research, involving two or more European countries.
- **European research strength:** European countries have stronger public health policies than many other countries, thus offering a wealth of natural experiments. Inter-country variation in Europe creates unique opportunities for comparative and transferable policy evaluations.
- **Illustrative research questions:**

What reforms within the mental health sector, or other reforms affecting population mental health (e.g. education, legal and tax systems, substance use policies, changes in infant and family care), have been implemented in European countries and how do their mental health impacts differ?

Which are the best financing mechanisms for mental health services?

Do restrictive alcohol policies protect children from abuse, neglect and other mental health risks?

What is the mental health impact of restrictions in alcohol availability?

What is the mental health impact of alternative allocations of austerity measures, based on comparisons between European countries?

Does legislation restricting access to firearms reduce violence (e.g. school shootings) and suicides?

How can complex models be designed to enable valid evaluations of natural experiments?

Which preventive interventions should be used for developing mental health policies in European countries?

Which are the most effective public policies in reducing mental health inequity?

7. The theory base for public mental health research should be strengthened, including definitions and validity of concepts

- **Efficacy/effectiveness:** It is important to conduct research that clarifies and validates the concepts underpinning public mental health research. Conceptual clarity is a cornerstone of successful research. Improved conceptual clarity is important because today much public mental health research is partly inconclusive and non-comparable with other research in the field due to simplistic or unclear concepts, which are neither linked to empirical data nor to theoretical considerations. The concepts of mental health, psychological well-being and mental ill health and their relation to functions and capacities need to be defined in a cross-disciplinary approach.
- **Impact / deliverability / economic benefits in Europe:** Theoretical contention and clarity about competing arguments about generative mechanisms on the one hand (explaining causal processes) and meanings attached to psychological difference in society on the other (interpreting professional and lay knowledge) as well as solid empirical data form the basis for successful mental health research. It is in the interest of all Europeans that mental health concepts are based on sound pre-empirical and empirical research, instead of being dictated by commercial or professional conflicts of interest.
- **Answerability/feasibility in Europe:** Further research in this field will lead us to a better European convergence of concepts and harmonisation of measurements, which will form a common base for European public mental health research.
- **European research strength:** Europe has a strong tradition of theoretical research regarding concepts and meanings of mental health in many disciplines, such as sociology, anthropology, psychiatry and psychology. Europe is not yet fully committed to US-based DSM mental disorder classification system, which provides opportunities for exploring alternative conceptual systems.

- **Illustrative research questions:**

What is the difference between mental health and mental ill-health?

Is current measurement of mental well-being valid and comprehensive enough?

How is mental well-being of children best measured?

What are the definitions and concepts of mental well-being in different cultures and languages in Europe?

Are there differences between the pre-existing assumptions and definitions of mental health in the research community and the public?

What is the range of lay and professional concepts of mental health, and what is the understanding behind them?

Which concepts would underpin a mentally healthy society?

8. To identify or develop intermediate outcome measures which are predictive of long-term outcomes and can be used as proxy measures in intervention studies where long-term outcomes are difficult to measure

- **Efficacy/effectiveness:** Intermediate outcomes, appropriately assessed, are vitally important to good quality evaluation research. Identification of intermediate outcomes requires studies, for example on mediation processes.

- **Impact / deliverability / economic benefits in Europe:** Use of intermediate outcomes increases feasibility and facilitates achieving research results within a shorter time frame. Significantly, use of valid intermediate outcome measures will improve cost-effectiveness of intervention studies. Identification of possible intermediate outcomes is especially important when final outcomes are rare, like suicide. Development and validation of an evaluation tool for suicidal risks based on an interdisciplinary biological, psychological and social approach is an important task.

- **Answerability/feasibility in Europe:** The longitudinal studies, health registers and biobanks based in Europe provide the data necessary for such studies which are cost-effective.

- **European research strength:** Europe has high scientific capacities in measure development.

- **Illustrative research questions:**

Which childhood outcomes predict good mental health in adulthood?

Does reduction in self-reported hopelessness predict reduction in suicide mortality?

9. Robust and standardised measures and typologies for public mental health research and validation of existing measures should be developed across Europe

- **Efficacy/effectiveness:** Valid research relies on valid measurements. A suite of reliable measures of positive mental health and wellbeing, as well as indicators of key protective factors, need to be developed and validated. Likewise, valid typologies for mental health interventions and services are needed for cross-national comparative studies.

- **Impact / deliverability / economic benefits in Europe:** Formulation of robust and standardized measures of interventions and services as well as mental health and its determinants and consequences will be a major step forward for public mental health research. Good measures are necessary in order to monitor the impact of policies and programmes and allow comparison across countries.

- **Answerability/Feasibility in Europe:** Further research in this field will lead us to European harmonisation of measurements, which will form a common base for European public mental health research.

- **European research strength:** Several theoretically well-founded measurement tools have been developed in Europe and field tested across European countries.

- **Illustrative research questions:**

How can important mental health concepts (e.g. sense of identity, sense of mastery, social support, family dynamics, resilience or coping) be adequately measured across European countries?

How can mental health interventions and services best be classified?

Can equally valid measurements be achieved more economically using shorter versions of existing measurement instruments?

Are mental health measurements valid across European countries and cultures?

10. Quantitative and qualitative research should be used in combination when relevant for capturing the complexity of public mental health and for enhanced understanding

- **Efficacy/effectiveness:** Prudent use of a mixed methods approach in public mental health research will support achievement of research results which are generalizable and feasible in public health practice. This is especially true for a better understanding of aspects such as processes, salience, acceptability and appropriateness, for example in the context of implementation studies on process of delivery.
- **Impact / deliverability / economic benefits in Europe:** More comprehensive research methods will produce research results with higher relevance for the community context. This will support more rational decisions by public health policymakers.
- **Feasibility in Europe:/European research strength:** There is a long European tradition of diverse research approaches (British empiricism, German hermeneutics and French post structuralism) and today several strong research groups in both qualitative and quantitative fields of research exist.
- **Illustrative research questions:**

How to best integrate quantitative and qualitative research methods in public mental health research?

How do different cultural concepts of mental ill health affect prevalence and incidence rates?

Why do people drop out of mental health promotion or preventive interventions?

How can qualitative results be integrated in a systematic way with quantitative results in defining evidence based practice?

Which are the obstacles for uptake and scaling up of public mental health interventions?

3.7.4.3. Research Topic priorities

11. To strengthen research on implementation, dissemination and sustainability of mental health promotion, mental disorder prevention and service delivery interventions

- **Efficacy/effectiveness:** It is important to study the uptake and implementation of new interventions developed by researchers and also why some interventions disseminate widely but many other effective ones do not.
- **Impact / deliverability / economic benefits in Europe:** Translational and implementation research are critical priority research areas in relation to both mental health promotion and prevention interventions. The facilitators and barriers in moving from knowledge to doing need to be identified. There is a need for innovative implementation, including holistic approaches, empowerment-based strategies and use of virtual social network implementation support.
- **Answerability/feasibility in Europe:** Strong public policies and well-organised public services in Europe form an excellent ground for universal promotion and prevention actions, as well as for identifying those in need of selective or indicated interventions. The European community mental health tradition forms a basis for implementation research focusing on mobilisation of community assets and avoiding unnecessary and possibly harmful medicalization of mental health challenges.
- **European research strength:** There is a growing body of evidence on the effectiveness of mental health promotion and mental disorder prevention interventions that have potential to be further developed and implemented in Europe.
- **Illustrative research questions:**

How can practitioners implement new interventions developed by researchers in public mental health?

How can effective interventions be widely disseminated?

How can implemented new interventions be sustained over a longer period of time?

How can implementation best be supported by new technology and social media?

What are the barriers to successful implementation among health care professionals?

Which factors are sufficient to promote mental health throughout childhood, adolescence and adult age?

12. To strengthen research across the lifespan and with regard to sensitive time windows of human development, including developmental and environmental salutogenic factors pertinent to public mental health

- **Efficacy/effectiveness:** In order to promote mental health and to prevent mental health problems, more knowledge about risk and protective factors and processes as well as developmental trajectories is needed. It is crucial to disentangle the effects of environment and genes on population mental health and resilience. In order to supplement existing knowledge, research should include age groups which are underrepresented so far.

- **Impact / deliverability / economic benefits in Europe:** Understanding the environmental prerequisites for mental health and well-being in all ages, including intra-uterine and family environment as well as parenting, is important in order to find ways of improving mental health and reducing the burden of mental health problems.

- **Answerability/feasibility in Europe:** The high level of health informatics in Europe, as well as strengths in cohort and parenting studies, builds the ground for longitudinal studies across the life-span.

- **European research strength:** Several existing long-term studies in Europe with data on genes, early environment and mental health outcome create a promising starting point.

- **Illustrative research questions:**

How is population mental health development impacted by community factors (e.g. schools, built environment) across the lifespan?

Why do age-specific suicide risks differ among males and females?

Do male and female coping strategies differ?

13. To strengthen research on the influence of families, public policies and services on mental health throughout the life course of children and adolescents

- **Efficacy/effectiveness:** It is important to understand how to optimise child and adolescent mental health and how health and social services can best contribute alongside population and community social and economic actions. Mental health in younger ages is important, not least because it is crucial for life-long development of mental health and strongly predicts mental health in adulthood. Public policies promoting parenthood and parenting and ensuring safe and non-abusive family life are proven to be effective and are urgently needed. Health and social services, day care and schools can promote mental health and prevent mental health problems.

- **Impact / deliverability / economic benefits in Europe:** Effective implementation of relevant promotion and prevention interventions by public services supports mental health of children and adolescents. Interventions targeting the early years and parents have potential to have long term effects and are thus also cost-effective.

- **Answerability/feasibility in Europe:** During pregnancy and early years of life parents and children utilise health services more frequently than in other life stages. This provides a good platform for implementing effective mental health promotion and mental disorder prevention. There is universal coverage of such services in many European countries.

- **European research strength:** Strong tradition in child and adolescent psychiatry and a diversified social care system. Strong research tradition on parenting.

- **Illustrative research questions:**

How to train primary care practitioners (e.g. GPs, midwives, nurses, psychologists, social workers) in effectively providing infant mental health promotion for parents and young families?

How to improve mental health promotion and social exclusion prevention in schools?

How to effectively bridge the gap between child health services and adult health services during the vulnerable phase of adolescence?

What are the effects of intense use of new media in early age and adolescents on later emotional and cognitive competence?

Can a system of mental health indicators for families, child care centres, schools, work places and old people's homes, respectively, on an organisational level contribute to enhancing public mental health?

How to improve maternal mental health in pregnancy and the postpartum period by universally applied programs of psycho-education?

How to improve mother-child relations in infancy by parent training programs?

How to improve mental health in preschool age by parenting programs?

14. To develop appropriate participatory approaches for evaluation of complex public mental health interventions

Research on complex or multimodal interventions should address efficacy and effectiveness but also the interaction of the parts of the intervention, including mediators and moderators, and their contribution to the whole.

Particularly important are:

- Research on the relationships between professionals/practitioners/lay workers and patient/participants/public.
- Research on public and target group engagement and empowerment in complex interventions.
- Research on best methods to enhance active participation of target groups, also children, in research.

- **Efficacy/effectiveness:** Population-level mental health interventions need to build on individual and community assets. Research on how to best mobilise these assets by public engagement and participation of target groups is the important next step in the evaluation and implementation research of public mental health interventions, regardless of whether the field is mental health promotion, prevention of mental health problems, delivery of mental health care or policy actions. This is the focal area of research to build effective interventions.

- **Impact / deliverability / economic benefits in Europe:** Identification of active components and/or combination of components will enable development of more precise and economical public mental health interventions.

- **Answerability/feasibility in Europe:** Public mental health interventions are contextual, and it is essential that research on intervention components is performed within the established welfare models of Europe.

- **European research strength:** Existing European research creates the necessary empirical base for studies on the components.

- **Illustrative research questions:**

Which are the most effective ways of engaging deprived communities in mental health promotion?

How can individual and community assets best be taken into account in public mental health programmes?

Which are the most effective means for implementing mental health promotion in schools?

What are the links between working conditions, social capital at work, individual resilience and productivity?

How can children, young people and older people best be involved in research?

How can mental health promotion interventions best support active ageing?

15. To strengthen the understanding of the links between physical and mental ill-health, and on their implications for services

- **Efficacy/effectiveness:** There is a high level of co-morbidity between physical diseases and mental disorders, including substance use problems. Physical and mental co-morbidity is linked to worse outcomes, lower access to care and high mortality rates. There is a lack of sensitivity in the mental health system to the complex needs of people with co-morbid problems, and a lack of evidence-based integrative care models. Effective models for organising care of people with complex needs will improve outcomes of people with co-morbid health problems. Research needs to identify, describe and raise awareness about disadvantaged groups with multiple health and social problems.
- **Impact / deliverability / economic benefits in Europe:** Establishment of integrative health, sensitive to the context and needs of people with co-morbid conditions, as well as integration of physical and mental health promotion will improve health outcomes and productivity of Europeans.
- **Answerability/feasibility in Europe:** In spite of generally acknowledged need for integration, Europe is still dominated by isolated service systems, creating a need for research that will support integrated care.
- **European research strength:** In Europe, epidemiological research on occurrence of mental and physical disorders is of high quality, as well as mental health service research. This creates a fertile ground for addressing research issues that link epidemiology with mental health services.
- **Illustrative research questions:**

What is the role of payment systems in promoting integrated systems?

Does increased physical activity in childhood reduce the incidence of depression in adult life?

What is the impact of childhood trauma on physical and psychiatric morbidity?

Does mental health promotion lead to a somatically healthier population and reduced mortality from non-communicable diseases?

Are psychosocial factors (e.g. sense of identity, meaning, mastery, belonging and affiliation, social support, social network) that protect against mental dysfunction also protective against non-communicable diseases?

16. To strengthen research on new approaches and technology for mental health promotion, disease prevention and mental health service delivery

- **Efficacy/effectiveness:** The ways people interact and services are provided is changing, with social media, virtual realities and e-health supplementing traditional social networks and health services. Organisation of e-health services can provide improved access to and compliance with mental health care. Promising new e-health approaches are being developed in the field of mental health promotion and prevention, and carry a potential for reaching large populations in a cost-effective way. However, we still largely lack evaluation research, dissemination research and research on the public mental health implications of these emerging new technologies. An interesting empirical challenge is whether the positive impact of social support and networks in traditional relations on mental health will be displaced by social media and what the balance sheet will be of positive and negative outcomes.
- **Impact / deliverability / economic benefits in Europe:** E-mental health has the potential for a major impact on the mental health of Europeans. It may be possible to substitute more expensive face-to-face interventions with cost-effective e-mental health applications. E-mental health interventions have the potential to become successful commercial products. It is also important to get more insight into the mental health impact of increasing use of internet and mobile media use.
- **Answerability/feasibility in Europe:** Europe is a well-developed information society, with a high level of computer literacy and an abundance of innovative enterprises in the e-health field. The potential for Internet as a cost-effective tool to enable both social contacts and accessibility of various services and interventions is broad. Simultaneously, there is an evident risk of social exclusion and other inequalities if for example the older generations are not given the support they need in order to be introduced to these e-resources. This is a challenge that should be given attention and priority.
- **European research strength:** Some of the leading centres in e-mental health research are located in Europe. By joining forces a critical mass could be achieved.

- **Illustrative research questions:**

Which mobile applications are effective in supporting a mentally healthy lifestyle?

Are e-mental health modes more effective in suicide prevention than traditional phone help lines?

Can mental health promotion interventions be embedded in electronic games in order to reach young people?

Can social isolation be reduced by new communication forms?

Are cross-border e-mental health services effective in providing services in the users' own languages?

What are the harms and benefits of the new technologies on mental health, including virtual realities and online social networks?

How to reach non-users of new technology in postmodern society to promote, prevent or protect their mental health?

17. To strengthen research on mental health promotion in all policies

- **Efficacy/effectiveness:** Research on policies to ensure equal opportunities for everyone to realize mental well-being has high policy relevance. Across Europe there are huge inequalities in mental health between population groups. It is important to develop policies that enable equal prerequisites across Europe for mental health and mental well-being. This includes defining society's mental capital and other community determinants of mental well-being. Reducing mental health inequalities is linked to poverty reduction, family and parenting support and universal access to mental health promotion in schools.

- **Impact / deliverability / economic benefits in Europe:** There are major mental health inequalities in Europe, both between countries and between socio-economic groups within countries. Research that moves beyond identifying inequalities to translating these into effective policy interventions is needed to bring the field forward.

- **Answerability/feasibility in Europe:** Strong European values of equity provide support to this research area, as well as cross-sector strategies of mental health promotion supported by the EU.

- **European research strength:** Europe is strong in research on socio-economic determinants of health, has registers that enable linkage of health data and socio-economic data on the individual level, and there is a growing awareness of the need for action to reduce health inequalities.

- **Illustrative research questions:**

What are the barriers to mental health development and well-being?

How do mental health inequalities develop?

What are the barriers and facilitators for getting mental health on non-health policy agendas?

Which are the most effective policy measures to reduce mental health inequity?

Is there a correlation between pension age and general mental health in society?

How do initiatives for extended labour-market inclusion affect mental health in older adults?

18. To strengthen research on the efficiency and quality of mental health systems and community-oriented interventions

- **Efficacy/effectiveness:** Mental health services are highly needed but high-quality intervention research on governance, funding mechanisms, organisation and delivery of mental health care is scarce. Randomized controlled trials are needed, but also other research designs should be promoted and developed to evaluate and develop service provision. Research is needed on mental health services programmes which have a potential for major public health impact, such as deinstitutionalisation programmes, universal promotion and prevention programmes, primary care capacity building programmes and programmes that improve access to mental health services. Also targeted interventions for mental health risk groups, identified on the basis of social or socio-economic risk or other markers, may translate into major effectiveness in these specific risk populations.

- **Impact / deliverability / economic benefits in Europe:** Effective mental health services result in lower mortality rates, higher longevity, less medical expense and fewer medical adverse events. Improving

efficiency of mental health systems will increase system affordability and accessibility. Removing barriers in access to mental health and establishing universal access are key objectives. Effective mental health services interventions, which improve mental health and reduce mental health-related morbidity, will have a major impact on the health of Europeans.

- **Answerability/feasibility in Europe:** The European mental health systems face common challenges in the need to shift resources upstream, to improve access and integration. The mental health systems in Europe are highly developed but fragmented, and thus there is both a need and a potential for research on integrated service provision models.

- **European research strength:** There are European research groups within this field (e.g. ENMESH) and their work can be built upon and further developed.

- **Illustrative research questions:**

How can community interventions be linked with primary care and special mental health care interventions (including liaison and consultations, collaborative care and general health care and mental health care)?

Does prevention of depression among pregnant women protect against later mental dysfunction (e.g. depression) among children? What are the cost benefits?

Which public mental health interventions have the best cost-benefit balance for whom, in what situation and at what stages (i.e. universal or targeted interventions; pre-natal, infant, early childhood, adolescence vs. adulthood)?

How can complex research design in mental health services research increase our understanding of the balance and interaction between community mental health services and inpatient mental health care?

19. To strengthen research on the protection of rights of people with mental health problems

- **Efficacy/effectiveness:** Universal fundamental rights of Europeans must include people with mental health problems on equal grounds, as well as the special rights laid out in the UN Convention on Rights of People with Disabilities. Involuntary psychiatric treatment and physical restraint and seclusion need special consideration.

- **Impact / deliverability / economic benefits in Europe:** Research on discrimination and protection of rights of people affected by mental health problems and their family members is needed in order to avoid discrimination and protect fundamental rights. Such research will contribute to the removal of stigma surrounding mental health problems, and will advance greater public awareness and participation in mental health promotion and prevention strategies. Mental health legislation across Europe varies and plays a crucial role. Promoting rights of people with mental health problems will support social inclusion and respect for fundamental rights of all Europeans.

- **Answerability/feasibility in Europe:** Respect for fundamental rights is a core value in the EU.

- **European research strength:** Cross-European research networks on mental health legislation exist.

- **Illustrative research questions:**

How to develop innovative strategies to reduce or prevent coercive measures in involuntary treatment for people with mental health problems?

Why do we see coercive services and legislation as socially progressive in principle?

20. To strengthen research on the frameworks to achieve effective mental health care on organizational, managerial and clinical levels

- **Efficacy/effectiveness:** Research evidence is increasingly utilised in the organisation and management of mental health policy and care. However, the evidence is traditionally focused on clinical decision making and research designed to support evidence-based policy-making in the public mental health field – focusing on the organizational and managerial concepts as well as financial mechanisms for funding of service provision is warranted.

- **Impact / deliverability / economic benefits in Europe:** Ineffective mental health systems, management models and financing mechanisms burden both the individuals in need of mental health care and society. Costs of ineffective health care systems are significant and these can be reduced by developing effective, evidence-based models to be applied at both clinical and policy levels for organisation and management of mental health care.

- **Answerability/feasibility in Europe:** The European mental health systems face common challenges in the need to shift resources upstream, to improve access and integration. The mental health systems in Europe are highly developed but fragmented, and thus there is both a need and a potential for research on integrated service provision models.

- **European research strength:** There are well-established European research networks in this area and their work can be built upon and further developed.

- **Illustrative research questions:**

Which models of organization and management are most effective in mental health care?

How can conceptual models be used in the application of research evidence to policy and practice?

Which funding mechanisms support upstream promotion and prevention actions best?

3.8. Well-being research

3.8.1. Introduction to the area

Well-being reflects individuals' perception and evaluation of their own lives in terms of their affective states and psychological and social functioning (Keyes & Lopez, 2001). There are many different conceptualizations of well-being, those which understand well-being as an evaluative or affective state and those which conceptualise well-being as referring to one's psychological make-up, being equipped to deal adequately with adversity. Furthermore, some scientists distinguish between hedonic well-being (moods and feelings) and eudaimonic well-being, which is more concerned with factors such as self-realization, social contribution and meaningfulness.

Recently, well-being measures have been adopted by population surveys and country governments as a way to assess societal progress. The report of the Commission on the Measurement of Economic Performance and Social Progress (Stiglitz et al., 2009) has pointed out that governments and population surveys should measure individuals' well-being as a way of assessing societal progress, rather than relying entirely on standard economic indicators.

Subjective well-being fosters good health, both physical and mental. The effect on physical health appears most clearly as a longer life-time, the effect on mental health manifests as less morbidity and faster recovery. Though we know the beneficial effects of well-being, the evidence definitively linking well-being to specific health and economic outcomes at the population level is limited. We also know little about the mechanisms and pathways through which particular kinds of subjective well-being impact on health outcomes, and of the modifiable factors in individuals or societies that might be useful intervention targets. From both a policy and a health perspective, well-being at any stage in life is an important outcome in and of itself, but it is also strongly related to long-term health outcomes. Well-being research, in short, is urgently needed for evidence based mental health care in Europe.

Despite these advances, however, the field of well-being research lacks a consensus on important questions of measurement and cross-national comparability. What is needed for a roadmap of this important research is to:

1. Identify obstacles to accurate measurement at both the individual and population levels and develop a research strategy to overcome them.
2. Identify barriers and obstacles to incorporating well-being measures into intervention studies.

3. Understand the mechanisms and pathways through which aspects of subjective well-being impact health outcomes.
4. Identify modifiable factors in individuals or societies that are potential targets for intervention, enhancing the potential policy impact of this emerging field.

The main goal of a coordinated and integrated research roadmap for well-being in Europe is to identify ways to increase our understanding—from both an individual and a population perspective—of how health (physical and mental) status or other relevant life circumstances impact the various components of subjective well-being, and also how well-being impacts health. This will include an exploration of the relationship between well-being and specific mental disorders. To do so will require an interdisciplinary approach with experts on behavioural, social, biomedical and bio-behavioural sciences.

For policymakers, well-being is an emergent social and political priority in Europe. Many countries are now trying to devise ways of measuring well-being in addition to tracking economic growth. The Commission on the Measurement of Economic Performance and Social Progress was created to identify the limits of gross domestic product as an indicator of economic performance and social progress. According to the report's authors, "the time is ripe for our measurement system to shift emphasis from measuring economic production to measuring people's well-being. And measures of well-being should be put in a context of sustainability" (Stiglitz et al., 2009) (page 12). Along the same lines, the *World Happiness Report* (2012) states that: "In addition to specific measures of economic, social, and environmental performance, governments should begin the systematic measurement of happiness itself, in both its affective and evaluative dimensions" (page 8).

Well-being is especially relevant in the field of mental health. The World Health Organization (2011) defines mental health as: "a state of well-being in which every individual realizes his or her own potential, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to her or his community." From a health perspective, the concept and measure of well-being goes beyond the concept of health considered as the mere presence or absence of illness or disability. Well-being also incorporates the impact of positive health and functioning, which has typically received little attention in health sciences. From both a policy and a health perspective, well-being at any stage in life is an important outcome in and of itself and a strong health predictor.

The focus of the present work package is on the relationship between well-being and mental health, not on more general aspects of well-being, and it covers the entire life-span.

The work package was divided in four sub-areas:

- Theoretical models of well-being:
- Evaluation of well-being:
- Relationship between mental health and well-being:
- Well-being in people with mental disorders and carers

Below is a detailed definition of each sub-area.

3.8.1.1. Definition of subareas

3.8.1.1.1. Theoretical models of well-being

There are two basic traditions in the study of well-being, that arising from social sciences and that from the health-related sciences. In order to refine measurement approaches, the first requirement is a clear conceptualization of subjective well-being, its components, its determinants and its separation from other quantities of interest, such as health. There is a need to ask people what well-being means for them, and not focus solely on an expert theoretical

standpoint. In other words, the measurement approach should be closely aligned with the intuitive notion of subjective well-being.

3.8.1.1.2. Evaluation of well-being

There are two approaches: Remembered well-being (i.e. overall evaluation/satisfaction, specific components), and experienced well-being (i.e. positive and negative effect, interest). Attention must also be paid to the various facets of well-being: emotional well-being, psychological well-being and social well-being. There is a need for a toolkit that can then be used to fit this purpose. Ideally, a measurement strategy for well-being would have a modular approach. The development of the measurement approach and the instruments should be simultaneously cross-cultural (not written in English and then translated), conceptually valid across the life-span, and have robust psychometric properties.

3.8.1.1.3. Relationships between mental health and well-being

There is a need for clear definitions of both mental health and well-being, as well as a clarification of their putative connections. One position is to consider mental health and well-being as two independent concepts, with optimal mental functioning as the core reflection of mental health. Well-being could be regarded as something different from mental health, both being umbrella terms (that still lack clear definition). Other theories find that any definition that claims that mental health and well-being are different is artificial. According to George Vaillant (2003), one of the main dimensions of mental health is subjective well-being indicated by life satisfaction and happiness.

3.8.1.1.4. Well-being in people with mental disorders and carers

In order to measure well-being from the patient's perspective, subjective assessments are needed. However, carers and other health care users should also be included. Caring affects people in many significant ways: financially, socially, and emotionally. Caring will also affect how important life choices involving jobs and even careers are made. Carers have the lowest collective well-being of any group (Cummins et al., 2007), lower than the unemployed, those living alone, and those on low incomes. Thus, this group should be addressed in order to prevent their mental disorders and support their well-being. This will also benefit the well-being of patients.

3.8.2. Gaps in knowledge

- Theoretical models and definitions:
 - Absence of a consensus on a construct of subjective well-being that is suitable for research.
 - Lack of an overview of what has been done in well-being research. Lack of harmonization of data.
 - Need of a map of existing theories, need to know which of these theories link to instruments, since not all the instruments link to theories.
- Evaluation:
 - Lack of normative data of subjective well-being from European countries across the life span and for specific groups.
 - Lack of studies on well-being with a longitudinal framework.
 - Meta-analyses of the existing normative and longitudinal data that already exist.
 - Further validation for existing well-being instruments.
 - Determinants of subjective well-being (such as resilience) in different populations. Research on life style.
 - Instruments to assess well-being in patients.

- Applications:
 - Added value, strengthening the case for well-being and well-being research.
 - Determining the best ways of translating knowledge gained from subjective well-being research into policies and tracking the impact over time.
 - Investigation on how the existing policies have an impact on well-being in the different countries.
- Interventions to protect and improve well-being
 - Evidence-based interventions to improve well-being in the general population and in specific vulnerable groups.
 - Determining the sustainability of the interventions.
 - Implementation and dissemination of the findings from intervention studies to promote well-being.
 - Generating the knowledge to scale up the interventions for well-being, and how to evaluate the scalability of the interventions.
 - Assessing whether population level well-being interventions impact mental health outcomes.
 - Research on targeted interventions to improve well-being in people with mental disorders, specific for specific populations (age groups, gender, ethnicity, culture, diagnosis) and carers.
- Well-being in people with mental disorders
 - Knowledge on patients' empowerment and its relationship to subjective well-being.
 - There is a need to understand the differences between good mental health and well-being. Is it possible to have good quality of life even if you have a mental illness?
 - Relationship between level of well-being and level of psychopathology.
 - How to improve the well-being of individual patients (personalized interventions).
- Evidence of relationships between health and well-being
 - Effects of well-being in the prevention and recovery of mental disorders.
 - Investigating the relevance of biomarkers and gene-environment interactions, in order to test whether the relationships are the same among people with mental illness. Biomarker research and imaging (fMRI).
- Well-being in carers
 - The impact of the stigma of being a carer on well-being. The extent to which carer-perceived stigma influences well-being.
 - Testing interventions that will improve the well-being of carers. Generic and specific interventions.
- Health services delivery
 - Effect of the national health care system on well-being, taking into account differences in the health care systems throughout Europe.

3.8.3. Advances needed in research and justification according common criteria

Goal	Challenges
Consensus on conceptual issues and measurement	1. To reach a consensus on the constructs for subjective well-being that are useful for mental health research.
	2. Increase knowledge on the relationship between the level of subjective well-being and psychopathology.
Identify antecedents and consequences of well-being	3. Collect normative data of subjective well-being from European countries across the life span and for specific groups.
	4. Maximize the use of new and existing longitudinal datasets regarding the relationships between mental health and subjective well-being.
	5. Establish evidence on biological, psychological, sociological and life-style determinants of subjective well-being, as well as on the socio-economic consequences and equity impacts of the interaction between mental health and subjective well-being.
	6. Use of economic techniques to support analyses of the benefits of improved subjective well-being and scope for looking at whether there are additional benefits from a reduction in mental health problems in the future as a result of better subjective well-being now.
	7. Establish a 'findings archive' on subjective well-being and mental health.
Advance the implementation of well-being interventions	8. Establish evidence on the impact of the differences of the organization and delivery of national health care systems on well-being of patients with mental disorders and carers.
	9. Increase evidence of population well-being interventions impacting mental health outcomes.
	10. Establish evidence on the impact and cost-effectiveness of clinical interventions to improve, protect and promote subjective well-being.
	11. Develop the mechanisms to best translate research results on subjective well-being to mental health care delivery and policies.
	12. Increase knowledge on patients' empowerment and its relationship to subjective well-being.
	13. Check and broaden evidence on the effects of subjective well-being on prevention of mental illness and recovery.
	14. Establish evidence on the impact on subjective well-being of informal caring for persons with mental disorders and on potentially effective interventions.

1. To reach a consensus on the constructs for subjective well-being that are useful for mental health research.

The full research and clinical impact of the notion of subjective well-being requires first of all that we overcome the current Babel. The research community must agree on a classification of kinds of subjective well-being and on the differences of these constructs with notions of mental health. This consensus can build on a map of existing conceptualisations, linked to measurement instruments. An agreed upon classification of concepts and related measures will open the door to the establishment of a 'findings archive' in which the available research findings are sorted by subject matter and become available for synthetic analysis. A firm conceptual foundation, moreover, will increase the effectiveness of subjective well-being as a clinical outcome for mental health interventions.

Illustrative research questions:

- What is the comparative validity of current concepts of subjective well-being?
- To what extent can current valid concepts of subjective well-being be harmonized?

- What are the best procedures for enabling effective harmonization of current valid concepts of subjective well-being?
- To what extent can findings be cross-culturally compared?
- Do special groups need special measures, or special modules?
- What relationships exist between subjective well-being and (the absence of) mental health problems?
- Which differences and similarities exist between various groups within a diverse population (in terms of sex/gender, ethnicity, SES etc.) regarding content, level and predictors of subjective well-being?
- Do different rater perspectives (the individual him/herself, relatives, staff, researcher) agree?
- How is the notion of subjective well-being different from (or similar to) concepts such as quality of life, life satisfaction, happiness, meaningfulness etc.?
- Which reliable and valid measurement instruments do exist already and what is known about their mutual relationships?
- When well-being is approached as a multidimensional construct, which dimensions are core dimensions of well-being and which dimensions should be treated as factors influencing well-being?
- How can cultural variations in lay conceptions on well-being be included in research on well-being across countries?
- What is the difference between subjective enjoyment of life (life satisfaction) and perceived meaning in life? Do these things necessarily go together? Which is most predictive of mental health?
- Is there a difference between cognitive evaluation of life and affective experience? Which is most predictive of mental health?
- How could an open-access bank of measures of subjective well-being be created, with data on their research properties and usability for researchers?

2. Increase knowledge on the relationship between the level of subjective well-being and psychopathology.

A targeted research priority involves the relationship between subjective well-being and the levels of psychopathology associated with different disorders at different stages. A findings archive would be an invaluable resource to identify gaps in our understanding of the association between levels of subjective well-being and different levels of psychopathology. From this starting point, more focused research questions, relying on different expertise across European mental health research centres, could target research to specific disorders and stages of disorder in order to more effectively increase our clinical knowledge in this important domain.

Illustrative research questions:

- Is subjective well-being simply the converse of psycho-pathological symptoms?
- Does subjective well-being vary between diagnostic groupings, even when controlling for levels of symptomatology and psychosocial functioning (GAF)?
- What are the mutual relations between well-being and mental health problems over time?
- Do existing treatments for psychopathology result in increases in well-being?
- Which kinds of subjective well-being are part of the mental-health syndrome and which are not? e.g. Can a happy person be mentally ill?
- In what conditions does unhappiness result in psychopathology?
- What ways of coping with unhappiness strengthen mental health?
- Does mental health education result in better coping with unhappiness?

3. Collect normative data of subjective well-being from European countries across the life span and for specific groups.

Relying on findings archives and other tools, both existing and those that can feasibly be developed, it will be possible to develop standards of comparison based on stratified information and from this to select appropriate reference points. Once gaps in these normative data have been identified and categorised by country and age-related population groups, the next step would be to develop and conduct population surveys designed to complete the normative data. The end result would be a truly life span understanding of the trajectories of subjective well-being associated with mental health problems, which would greatly enhance intervention strategies. In Europe, there are several research centres with expertise in the required survey methodologies, and this research would further extend the European research experience and worldwide reputation in this area.

Illustrative research questions:

- How does subjective well-being vary between European countries?
- How does European subjective well-being vary by key demographic variables including age, gender, social class and ethnicity?
- The developmental perspective: how do pregnancy and early childhood experiences contribute to later subjective well-being?
- How do physical disability and chronic somatic diseases impact on subjective well-being?
- Which developmental trajectories of well-being can be found from childhood and adolescence to early, middle and late adulthood?
- How happy was the average citizen in each European country around the year 2010?
- Which sub-groups in the population deviated significantly from the national average?
- Was the lag in happiness of people with mental problems similar in all European nations?

4. Maximize the use of new and existing longitudinal datasets regarding the relationships between mental health and subjective well-being.

We need longitudinal data for establishing the causal links between well-being and mental health. Since the effects will differ across subgroups, we need large panels. Several large-scale panel studies are already available in Europe and most of these involve measures of both subjective well-being and mental health. A first step is to locate and harvest this existing information. A next step is to add measures in future waves of ongoing panel studies. This approach is not only feasible but is a cost-effective and highly efficient use of existing research funding. Several centres across Europe are well positioned to take the lead in the development of suitably powerful longitudinal datasets, and developing this existing research capacity across Europe will have a direct impact on the clinical and public health usefulness of these data.

Illustrative research questions:

- What methods/techniques are needed to ensure location and harvesting of existing European datasets on subjective well-being?
- Which differences and similarities exist between various groups within a diverse population (in terms of sex/gender, ethnicity, SES etc.) regarding content, level and predictors of subjective well-being across the life span?
- How can subjective well-being predict future mental health?
- How do well-being and mental health problems mutually influence each other over time?
- What follow-up data do we need, which do we have already, which not?

- Does the effect of subjective well-being on mental health differ across subgroups? In which groups is the effect most pronounced?
- How long does the effect of subjective well-being on mental health last?

5. Establish evidence on biological, psychological, sociological and life-style determinants of subjective well-being, as well as on the socio-economic consequences and equity impacts of the interaction between mental health and subjective well-being.

Identifying the determinants of subjective well-being is essential to make effective interventions feasible. Depending on the nature of the determinant, the research strategy will differ: biomarker and epigenetic effect identification for biological determinants, instrument development and application for psychological determinants (e.g. the role of resilience), and large-scale surveys for life-style (e.g. work-life balance) and broader social determinants. The relevant expertise for all these methodologies is well-represented in Europe and further research targeting well-being determinants can greatly strengthen the European global position in this area. Moreover, existing research, although fragmentary, points strongly to the differential impact on subjective well-being of socio-economic factors on those with and those without mental health problems. With an appropriate sampling design – including cohorts from different age groups and responding to different economic, social and cultural differences – it would be possible to form the basis for a multi-centre study to address this central question across Europe.

Illustrative research questions:

- What biological, psychological and social factors are important in determining variation in subjective well-being across Europe?
- Unravelling the relations and the directions of the relationships between genetic, psychological, social and lifestyle factors and subjective well-being. What influences what? Possible third factors that have an impact on both determinants and subjective well-being?
- Room for the developmental perspective: which early childhood experiences impact on subjective well-being?
- How does well-being impact on health and functioning across the lifespan?
- What are the determinants of post-traumatic growth?
- How much activity is optimal for happiness? Does that optimum differ across the family life cycle?
- To what extent is the stress of an active life-style compensated by positive effects on happiness?
- What is the effect of later retirement on average happiness and mental health among elderly people? What kind of people benefit from the rising retirement age? What kind of people lose?

6. Use of economic techniques to support analyses of the benefits of improved subjective well-being and scope for looking at whether there are additional benefits from a reduction in mental health problems in the future as a result of better subjective well-being now.

Longitudinal studies are needed in order to show whether the interventions to improve well-being have an impact on the health (both physical and mental) of the population, and lead to a reduction in health care expenditure, improvements in the labour market and economic benefits for society. Europe is already developing and implementing interventions to improve the well-being of the population, but the benefits of these interventions need to be evaluated. The use of economic techniques can help inform policymakers of the benefits of improving the subjective well-being of the population.

Illustrative research questions:

- What are the benefits of improving the subjective well-being of the population?

- Will an improvement of subjective well-being at the population level lead to a reduction in mental health problems?

7. Establish a ‘findings archive’ on subjective well-being and mental health.

There is already considerable research on the relation between subjective well-being and mental health, but the results are not yet available in an organized body of knowledge. There are several reasons for this. One is the conceptual Babel. A second reason is that research reports are published in different languages and different research traditions across which there is little communication. A third reason is that even the technical jargon used is not identical and the measures used are incomparable. The fourth and most important reason is that scientific bodies invest in primary research rather than in synthesis of available findings. As a result the heap of research findings is growing by the day, but understanding is not, since we see typically only the findings at the top of the heap. This problem can be tackled with a ‘findings archive’ such as the World Database of Happiness (<http://worlddatabaseofhappiness.eur.nl>). Such an archive will not only capitalize on past research but will also increase the yields of new research.

Illustrative questions:

- How can we organize that all the findings available in European countries are entered?
- How can we organize that periodical state-of-the-art papers are made?
- How should the software of the World Database of Happiness be adapted for this particular purpose?

8. Establish evidence on the impact of the differences of the organization and delivery of national health care systems on well-being of patients with mental disorders and carers.

At the policy level, and to meet the demographic and economic challenges that Europe will face in the future, it will be necessary to explore innovations in the organization and delivery of health care. This exercise will be forced on Europe inevitably by events, but policymakers will need models to consider, and evidence on which to base their suggested health system innovations. A typology of health care delivery systems, across Europe and elsewhere and targeted investigations into, for example, the relative benefits of community care versus inpatient care, will be helpful research contributions. But it is essential that mental health, and the issues associated with problems in mental health, not be overlooked as these debates are conducted. What is needed, in particular, are instruments that can reliably measure not only satisfaction with the health care system, but the impact of health care encounters on subjective well-being of persons with mental health needs. These same instruments would also be useful to determine the relationship between social investments in mental health services and the general well-being of the population, in order to support additional policy innovations.

Illustrative research questions:

- How can impact of health care system on subjective well-being be reliably measured?
- What elements of health care systems (e.g. primary care focus yes/no, free at point of access yes/no) have most effect (positive and negative) on subjective well-being of patients with mental health problems?
- What elements of health care encounters (e.g. ease of access, role and attitude of reception staff, attitude and actions of health professional during clinical encounter) have most effect (positive and negative) on subjective well-being of patients with mental health problems?
- What kinds of mental patients live happier in an institutional context?
- Is time-sampling of happiness practicable among mental patients? If so, does that inform us about the effects of different kinds of care?
- Are mental patients happier in nations where mental health care is integrated in the wider health care system or does specialization yield greater happiness for these people?

9. Increase evidence of population well-being interventions impacting mental health outcomes.

For similar reasons as noted above, it is essential to increase Europe's evidence base regarding the impact, and cost-effectiveness, of public health interventions designed to improve subjective well-being and the impact of doing so on mental health outcomes. This research provides the important link between recent European endeavours to use subjective well-being as a general population indicator of policy effectiveness, and the urgent work that is required to investigate effective public health promotion measures targeting mental health. In this case as well, retrospective research on past public health interventions would be the most feasible start, but this research needs to be enhanced with more prospective investigations.

Illustrative research questions:

- What is the strength of current evidence for effectiveness and cost-effectiveness of interventions at the population level to enhance subjective well-being for people with mental health problems in Europe?
- What are the gaps in existing evidence, and hence what new studies are needed?
- What was the effect on average happiness of the cuts in welfare spending in European nations since the 1980s? Can that explain the rising use of mental health care?
- Did increased spending on mental-health care add to average happiness in Europe?
- Does greater spending on mental health care result in greater happiness and better mental health? How about absolute spending and spending relative to somatic health care?
- Which existing well-being interventions have been successful in impacting mental health outcomes?

10. Establish evidence on the impact and cost-effectiveness of clinical interventions to improve, protect and promote subjective well-being.

Using existing experience, it would be possible to design and perform randomized controlled trials on subjective well-being interventions, or carry out meta-analyses of such interventions, in order to empirically substantiate the impact of these interventions on the subjective well-being of mental health patients. Cost-effectiveness analyses can then be performed, suitable to the nature of the intervention. This important research provides a crucial input into policy decisions, and there is certainly European expertise in this area that can be channelled to research targeting subjective well-being interventions. Meta-analysis requires first of all that the available data are presented in a comparable way in a findings archive.

Illustrative research questions:

- What is the strength of current evidence for effectiveness and cost-effectiveness of interventions at the individual level to enhance subjective well-being for people with mental health problems in Europe?
- What are the gaps in existing evidence, and hence what new trials are needed?
- How can resilience be fostered in children and older people?
- How can post-traumatic growth be promoted?
- How can new technologies, e.g. e-health and m-health, be used to enhance and maintain the effects of well-being interventions?
- There is a need for more insights in the processes involved in well-being interventions: How and for whom do well-being interventions work best?
- What is the long-term effect of 'happiness lessons' in school on life-satisfaction and mental health?
- Which 'happiness trainings' are effective among what kinds of people?
- Does the use of happiness tracking websites (such as the HappinessIndicator.com) add to happiness and mental health?
- What kinds of interventions have been done to improve subjective well-being? How were the results measured? What was found among patients, the general population, parents, children, adolescents?

11. Develop the mechanisms to best translate research results on subjective well-being to mental health care delivery and policies.

Techniques of knowledge translation and evidence-based policy development are essential tools for moving research into the domain of practice, both at the micro clinical level, and the macro policy levels. Research about these techniques is greatly needed, especially as it related to getting research about subjective well-being into practice across the mental health sector. European researchers are well-versed in both the need for knowledge translation and its methodologies, although most of this research has been directed to biomedical results. There is an urgent need, however, to extend Europe's expertise in this area to the translation of results on the interaction between subjective well-being and mental health to practice. This requires experimental studies on a much larger scale than performed up to now.

Illustrative research questions:

- How can health promoting and rehabilitation-oriented interventions be developed to promote subjective well-being in the general population and in vulnerable groups?
- What are the best strategies for implementing subjective well-being interventions and policies?
- What are the barriers and facilitators to translation of the best evidence on interventions to improve subjective well-being into policy and practice? How can Normalization Process Theory (<http://www.normalizationprocess.org/>) and other toolkits help us understand the dynamics of implementing, embedding and integrating new interventions?
- To what extent can interventions be implemented outside the context of the health care system, but rather at schools, workplaces, etc.?
- How can different stakeholders (governments, nongovernmental organisations, researchers, practitioners, clients) best be represented in the translation from research to practice?
- Which technological innovations, e.g. e-health, can help to implement well-being policies for a broad public?
- Do we need particular mechanisms for this subject or are professionals sufficiently attended by the mass media?
- Is this subject adequately covered in professional education? Is the available information on the relation between happiness and mental health assessable on professional websites?

12. Increase knowledge on patients' empowerment and its relationship to subjective well-being.

One of the prominent issues addressed by patients' groups and recent international statements of the human rights of persons with disabilities and health problems is the central importance of preserving and promoting autonomy, both within and outside of the health sector. Europe is a leader in the area of mental health human rights, and research building on this expertise on the psychological determinants of empowerment and related notions such as locus of control and autonomy, and in particular the linkages between these factors and subjective well-being, is a key European priority. The impact of such research would be felt, not merely in increasing participation in and compliance with mental health interventions, but also in the development of mental health policies designed to further patient autonomy.

Illustrative research questions:

- Which kind of interventions aimed at enhancing patient empowerment lead to improved subjective well-being?
- How can patients be involved as stakeholders in the development of well-being interventions?
- Do well-being interventions increase patient empowerment?
- What kinds of patients benefit from autonomy? What kinds of patients rather need guidance?
- What degree of guidance is optimal for what kind of patients? How well does practice meet the optimum in European nations?

- How can the political lobby for mental health care be strengthened?

13. Check and broaden evidence on the effects of subjective well-being on prevention of mental illness and recovery.

Following considerable speculation on this issue, there is some empirical evidence for causal effects of subjective well-being on both prevention of mental health problems, and recovery from these problems. These effects should next be replicated in long-term follow-up studies that analyse the entire life span. Application requires that we know in which subgroups these effects are most pronounced. The impact of this research would be profound, both clinically and from a public health perspective, since it would not only increase our scientific knowledge of the effect of subjective well-being on mental health, but it would also assist in the development of suitable interventions, whether these be generic public health interventions, or targeted clinical interventions.

Illustrative research questions:

- To what extent can mental disorders be prevented by interventions targeted at enhancing subjective well-being?
- To what extent is it necessary to attune such interventions to specific groups (sex/gender, ethnicity, SES)?
- What is the role of subjective well-being in recovery-oriented mental health care?
- Do happy mental patients recover faster? If so, among which kind of patients is this effect most pronounced?
- Is the incidence of mental disorders lower in European nations where average happiness is highest?

14. Establish evidence on the impact on subjective well-being of informal caring for persons with mental disorders and on potentially effective interventions.

Evidence of demographic and economic changes across Europe make it clear that more and more reliance will be put on informal care, typically women family members. The available research suggests that care-giving involves a considerable loss in happiness. Still not all care givers get unhappy and there is as yet little view on the reasons for that difference. Extensive European research on caretaker socio-economic burden has typically ignored this issue. In the future, however, European social services will be required to promote subjective well-being and prevent mental health problems in this important population of informal caregivers, and it will be essential to base these policy initiatives on sound evidence.

Illustrative research questions:

- How can subjective well-being in informal carers best be enhanced or maintained?
- What support practices are effective in sustaining subjective well-being among informal carers?
- What are the possibilities for a systems approach (e.g. family systems) in well-being interventions?
- How often does caring for family members with a mental disorder involve a loss in happiness? What is the total loss in 'happy life years'?
- In which conditions is that loss of happiness most pronounced? Which of these conditions can be influenced by social policy?
- Do carer-support-groups help?
- Which existing interventions improve the mental and physical health of the carers?

4. Bibliographical references

- Adolphs R. Recognizing emotion from facial expressions: psychological and neurological mechanisms. *Behav Cogn Neurosci Rev.* 2002 Mar;1(1):21-62. Review.
- Adolphs R. Neural systems for recognizing emotion. *Curr Opin Neurobiol.* 2002 Apr;12(2):169-77. Review.
- Alcaro, A., Panksepp, J. Huber R., 2011. D-amphetamine stimulates unconditioned exploration/approach behaviors in crayfish: towards a conserved evolutionary explanation of ancestral drug reward. *Psychopharm.* 99(1), 75-80
- Baird AD, Scheffer IE, Wilson SJ. Mirror neuron system involvement in empathy: a critical look at the evidence. *Soc Neurosci.* 2011;6(4):327-35
- Blair RJ. Facial expressions, their communicatory functions and neuro-cognitive substrates. *Philos Trans R Soc Lond B Biol Sci.* 2003 Mar 29;358(1431):561-72. Review.
- Blair RJ. Responding to the emotions of others: dissociating forms of empathy through the study of typical and psychiatric populations. *Conscious Cogn.* 2005 Dec;14(4):698-718.
- Chevreur K, McDaid D, Farmer CM, Prigent A, Park A-L, Leboyer M, et al. Public and nonprofit funding for research on mental disorders in france, the united kingdom, and the united states. *J Clin Psychiatry.* 2012 Aug;73(7):e906-912.
- Cooper C.L., Field J., Goswami U., Jenkins R. & Sahakian B. (2009). *Mental Capital and Wellbeing.* Oxford: Wiley-Blackwell.
- Cummins, R. A., Hughes, J., Tomy, A., Gibson, A., Woerner, J., & Lai, L. (2007). *The Well-being of Australians - Carer Health and Well-being* Geelong: Deakin University.
- Dean K, Stevens H, Mortensen PB, Murray RM, Walsh E, Pedersen CB. Full spectrum of psychiatric outcomes among offspring with parental history of mental disorder. *Arch Gen Psychiatry.* 2010 Aug;67(8):822-9.
- Decety J, Jackson PL. The functional architecture of human empathy. *Behav Cogn Neurosci Rev.* 2004 Jun;3(2):71-100
- Decety J, Moriguchi Y. The empathic brain and its dysfunction in psychiatric populations: implications for intervention across different clinical conditions. *Biopsychosoc Med.* 2007 Nov 16;1:22
- Dimberg U, Thunberg M, Elmehed K. Unconscious facial reactions to emotional facial expressions. *Psychol Sci.* 2000 Jan;11(1):86-9.
- Elliott R, Dolan RJ, Frith CD. Dissociable functions in the medial and lateral orbitofrontal cortex: evidence from human neuroimaging studies. *Cereb Cortex.* 2000 Mar;10(3):308-17. Review.
- Feinstein AR. Pre-therapeutic classification of co-morbidity in chronic disease. *Journal Chronic Disease,* 1970; 23(7):455-468.
- Hess U, Kappas A, McHugo GJ, Lanzetta JT, Kleck RE. The facilitative effect of facial expression on the self-generation of emotion. *Int J Psychophysiol.* 1992 May;12(3):251-65.
- Hsu C-C. & Sandford B.A. (2007). The Delphi technique. *Making sense of consensus. Practical Assessment, Research & Evaluation;* 12: 1-8.
- Kendler, K.S., P. Zachar, and C. Craver, What kinds of things are psychiatric disorders? *Psychological Medicine,* 2011. 41(6): p. 1143-1150.
- Lazarus RS (2006). Emotions and interpersonal relationships: toward a person-centered conceptualization of emotions and coping. *Journal of Personality,* 74, 9-46.
- Levenson RW, Ekman P, Friesen WV. Voluntary facial action generates emotion-specific autonomic nervous system activity. *Psychophysiology.* 1990 Jul;27(4):363-84
- Levine S (2005). Developmental determinants of sensitivity and resistance to stress. *Psychoneuroendocrinology,* 30, 939-94.

- McClure EB, Monk CS, Nelson EE, Zarahn E, Leibenluft E, Bilder RM, Charney DS, Ernst M, Pine DS. A developmental examination of gender differences in brain engagement during evaluation of threat. *Biol Psychiatry*. 2004 Jun 1;55(11):1047-55.
- McEwen BS and Gianaros PJ (2011) Stress- and Allostasis-induced brain plasticity. *Annu Rev Med* 62, 5.1-5.15.
- Ohman A. Face the beast and fear the face: animal and social fears as prototypes for evolutionary analyses of emotion. *Psychophysiology*. 1986 Mar;23(2):123-45.
- Passingham RE, Toni I, Rushworth MF. Specialisation within the prefrontal cortex: the ventral prefrontal cortex and associative learning. *Exp Brain Res*. 2000 Jul;133(1):103-13. Review.
- Pfaff DW, Martin EM, Ribeiro AC (2007) Relations between mechanisms of CNS arousal and mechanisms of stress. *Stress*, 10, 316-325.
- Preston SD, de Waal FB. Empathy: Its ultimate and proximate bases. *Behav Brain Sci*. 2002 Feb;25(1):1-20; discussion 20-71.
- Roelofs K, Minelli A, Mars RB, van Peer J, Toni I. On the neural control of social emotional behaviour. *Soc Cogn Affect Neurosci*. 2009 Mar;4(1):50-8.
- Rushworth MF, Behrens TE, Rudebeck PH, Walton ME. Contrasting roles for cingulate and orbitofrontal cortex in decisions and social behaviour. *Trends Cogn Sci*. 2007 Apr;11(4):168-76.
- Singer T. The neuronal basis and ontogeny of empathy and mind reading: review of literature and implications for future research. *Neurosci Biobehav Rev*. 2006;30(6):855-63.
- Slocum N. (2005). Method: Delphi. In: Steyaer S. & Lisoir H. (Eds.). Participatory methods toolkit. A practitioner's manual. Available online: <http://www.samenlevingentechnologie.be/ists/en/pdf/projects/toolkitdelphi.pdf>
- Sonnby-Borgström M. Automatic mimicry reactions as related to differences in emotional empathy. *Scand J Psychol*. 2002 Dec;43(5):433-43.
- Stel M, van Knippenberg A. The role of facial mimicry in the recognition of affect. *Psychol Sci*. 2008 Oct;19(10):984-5.
- Stel M, Vonk R. Mimicry in social interaction: benefits for mimickers, mimicked, and their interaction. *Br J Psychol*. 2010 May;101(Pt 2):311-23.
- Stiglitz, J. E., Sen, A., & Fitoussi, J. P. (2009). Report by the Commission on the Measurement of Economic Performance and Social Progress.
- Strauss MM, Makris N, Aharon I, Vangel MG, Goodman J, Kennedy DN, Gasic GP, Breiter HC. fMRI of sensitization to angry faces. *Neuroimage*. 2005 Jun;26(2):389-413.
- Taylor SE (2010) Mechanisms linking early life stress to adult health outcomes. *Proc Natl Acad Sci (USA)* 107, 8507-8512.
- Vaillant, G. E. (2003). Mental health. *Am J Psychiatry*, 160, 1373-1384.
- van Baaren R, Janssen L, Chartrand TL, Dijksterhuis A. Where is the love? The social aspects of mimicry. *Philos Trans R Soc Lond B Biol Sci*. 2009 Aug 27;364(1528):2381-9. doi: 10.1098/rstb.2009.0057.
- WHO. (2001). Strengthening mental health promotion. Fact sheet, No. 220. Geneva: World Health Organization.
- World Happiness Report. Commissioned for the United Nations Conference on Happiness on April 2nd, 2012 (mandated by the General Assembly of the United Nations). Edited by: John F. Helliwell, Richard Layard and Jeff Sachs. New York: The Earth Institute, Columbia University.
- World Health Organization (2001). International Classification of Functioning, Disability and Health: ICF. Geneva: World Health Organization.
- World Health Organization (2011). Mental health: a state of well-being. http://www.who.int/features/factfiles/mental_health/en/index.html [On-line].