ROAMER

A Roadmap for Mental Health Research in Europe

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ROAMER: A road-map for mental health research in Europe

Coordination and Support Action

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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. The roadmap is vital for the EU future because mental health problems are known to have serious personal and economic consequences for both the individual and their families. This economic burden has an effect on EU competitiveness, economic growth and on jobs.

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.

At this stage, ROAMER has made great efforts to define, by consensus, the current situation 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 all types of Stakeholders. To this end, ROAMER has taken advantage of several techniques and activities such as the systematic literature mapping, survey consultations, and workshops with the most relevant European scientists in the field.

1.1   Scope of the ROAMER project

The scope of the ROAMER project has been defined by consensus in terms of geographic, diagnostic and life-span points of view during the first phase of the project.

Geographic dimension

From the geographic point of view, a decision to analyse all European countries was taken (i.e. EU-27 countries, EU Candidate countries and/or other European countries) either for research group and publication mapping, or research priority setting.

Furthermore, ROAMER aims to do an exhaustive study of mental health research funding in a given year. In order to have a more complete picture, this study will be performed as an individualised approach only for a subset of EU-countries (i.e. Spain, Germany, UK, Netherlands, France and Estonia), although general information on funding will also be collected from other European countries.

Diagnostic dimension

From the diagnostic point of view, ROAMER will cover mental health research either in general terms or with regard to any of those mental disorders described within the DSM-IV and the ICD-10, which are listed below:

- Schizophrenia and Non-affective Psychosis
- Bipolar Disorders
- Depressive Disorders
- Anxiety disorders
- Trauma- and Stress-Related Disorders
- Somatoform Disorders
- Somatic Symptom Disorders
- Dissociative Disorders
- Personality Disorders

- Elimination Disorders
- Substance Use and Addictive Disorders
- Autism and Other Neurodevelopmental Disorders
- Mental Retardation
- Eating Disorders
- Sexual Dysfunctions
- Disruptive, Impulse Control, and Conduct Disorders

The ROAMER consortium will try to avoid the duplication of efforts in those disorders that have already been the focus of study of other European roadmaps or similar initiatives (e.g. ALICE RAP for substance-abuse disorders; FUTURAGE for degenerative disorders).

Gender aspects

The ROAMER initiative will take gender differences into account.

Life-course dimension

The ROAMER initiative will adopt a life-course approach that is cognisant both of the trajectories of mental disorders across a person's life span, increasing severity and levels of comorbidity, and the mental health problems associated with different age groups. Therefore, all age groups will be taken into account (i.e., children, adolescents, adults and the elderly) although, again, the ROAMER consortium will take advantage of the results of similar initiatives that have focused their efforts on a specific age group (e.g. FUTURAGE has analysed aspects related to the elderly).

Ethnic groups

The ROAMER initiative will analyse mental health issues in all European populations and will not distinguish between ethnic groups.

2.   Objectives of the report

The main goal of the D11.1 [Report on the state of art in Mental Health and Wellbeing research in Europe] is to integrate the state-of-art review outcomes from all WPs into a single report on the current situation of European mental health and well-being research, including the review from Stakeholders and the Scientific Advisory Board and considering geographical, multidisciplinary, and life course perspectives.

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 summarised. Some 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 the project. Analysis of the geographical distribution of mental health research in Europe focuses on variation occasioned by country-specific aspects. To examine this, a literature search was devised using a specific "comparative literature section tracking" strategy 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 into the ROAMER process 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. Systematic literature mapping

3.1.2.1.   Geographical variation

The issue of geographical variation can be addressed to a degree through literature surveys. We devised a specific methodology, called "*comparative literature section tracking*" (CLST) in order to make quantitative and qualitative statements, as relevant for ROAMER, on the issue of geographical variation in mental health research. The CLST method was developed specifically to address the issue of geographical variation in mental health research. Firstly, different areas of mental health research were designed with "face value" primary interest and specialisation requiring specific group expertise. These were: Stigma Research, Epidemiological Research, Randomised Controlled Trials, Genetics/Neuroimaging Research and Research in the areas of Psycho-analysis/Psychotherapy. To examine country-specific variation in these areas, specific PUBMED search parameters were developed (Table 1). In addition, to contrast mental health PUBMED output in these areas with non-mental health somatic disorder output, a specific search parameter was developed for somatic disorder literature (Table 1).

Table 1. PUBMED search parameters used to define areas for the *comparative literature section tracking* exercise in ROAMER (example is given for UK).

Randomised controlled treatment trials	((RCT OR "randomised controlled trial" OR "randomized controlled trial") AND (psychiatry[ti/ab] OR "mental disorder" OR "mental illness" OR

	psychiatric[ti/ab] OR psychology[ti/ab] OR "depressive disorder" OR "depressive illness" OR "bipolar disorder" OR psychosis OR psychotic OR schizophr* OR anxiety OR anorexia OR Post-traumatic stress)) AND UK[ad]
Stigma research	((stigma OR stigmatization) AND (psychiatry[ti/ab] OR "mental disorder" OR "mental illness" OR psychiatric[ti/ab] OR psychology[ti/ab] OR "depressive disorder" OR "depressive illness" OR "bipolar disorder" OR psychosis OR psychotic OR schizophr* OR anxiety OR anorexia OR Post-traumatic stress)) AND UK[ad]
Epidemiology research	(("risk factor" OR "cohort study" OR epidemiology OR incidence OR prevalence) AND (psychiatry[ti/ab] OR "mental disorder" OR "mental illness" OR psychiatric[ti/ab] OR psychology[ti/ab] OR "depressive disorder" OR "depressive illness" OR "bipolar disorder" OR psychosis OR psychotic OR schizophr* OR anxiety OR anorexia OR Post-traumatic stress)) AND UK[ad]
Psychotherapy research	((psychoanalysis[ti/ab] OR psychotherapy[ti/ab] OR CBT[ti/ab] OR mindfulness[ti/ab] OR IPT[ti/ab] OR "interpersonal therapy" OR "cognitive-behavior therapy" OR "cognitive behavioural therapy") AND (psychiatry[ti/ab] OR "mental disorder" OR "mental illness" OR psychiatric[ti/ab] OR psychology[ti/ab] OR "depressive disorder" OR "depressive illness" OR "bipolar disorder" OR psychosis OR psychotic OR schizophr* OR anxiety OR anorexia OR Post-traumatic stress)) AND UK[ad]
Genetics/Neuroimaging research	((genetics OR (MRI OR fMRI OR sMRI OR PET OR neuroimaging[ti/ab] OR fMRS OR "resonance spectroscopy" OR SPET)) AND (psychiatry[ti/ab] OR "mental disorder" OR "mental illness" OR psychiatric[ti/ab] OR psychology[ti/ab] OR "depressive disorder" OR "depressive illness" OR "bipolar disorder" OR psychosis OR psychotic OR schizophr* OR anxiety OR anorexia OR Post-traumatic stress)) AND UK[ad]
Somatic non-psychiatric research	((cancer[MeSH Major Topic] OR cardiovascular[MeSH Major Topic] OR diabetes[MeSH Major Topic] OR hypertension[MeSH Major Topic] OR kidney[MeSH Major Topic] OR liver[MeSH Major Topic] or stomach[MeSH Major Topic] OR heart[MeSH Major Topic] OR pancreas[MeSH Major Topic] OR thyroid[MeSH Major Topic] OR spleen[MeSH Major Topic] OR pregnancy[MeSH Major Topic] OR bladder[MeSH Major Topic] OR arthritis[MeSH Major Topic] OR joint[MeSH Major Topic]) NOT (psychiatry OR "mental disorder" OR "mental illness" OR psychiatric OR psychology OR "depressive disorder" OR "depressive illness" OR "bipolar disorder" OR psychosis OR psychotic OR schizophr* OR anxiety OR anorexia OR Post-traumatic stress)) AND UK[ad]

The CLST exercise consists of conducting country-specific searches for each of the defined areas to graphically chart the output and compare the countries in rank order. The idea behind CLST is that since searches are defined identically, output can be compared across countries. Assumptions are that (i) PUBMED coverage of total research output for the different tracking areas is approximately similar for each country, (ii) search terms are not biased by country-specific idiosyncrasies. Given differences in country size and economic development and output was corrected for GDP. The raw data of the searches by area of research and by country can be found in Annex 3, and the analysis routines in Annex 4.

3.1.2.2. Correlations between areas of research in Europe

In the table 2 (below), the pattern of correlations is given for the different (GDP-corrected) areas of research. The lowest correlations were seen for Stigma with the other areas, and for Psychotherapy with Genetics/Neuroimaging. This suggests that there may not be a single underlying source of variation driving research, but rather that area-specific factors, for example for stigma and psychotherapy research, are also operating.

Table 2. Correlations between GDP-corrected output for different areas of research in European countries.

	Stigma	Epidemiology	RCT	Genetics/Imaging	Psychotherapy
Stigma	1.00				
Epidemiology	0.31	1.00			
RCT	0.51	0.84	1.00		
Genetics/Imaging	0.36	0.91	0.80	1.00	
Psychotherapy	0.35	0.81	0.85	0.66	1.00

3.1.2.3. GDP-corrected output per country

Results showed substantial variation between and within countries for the different areas of research, displayed in figures 1-5 below.
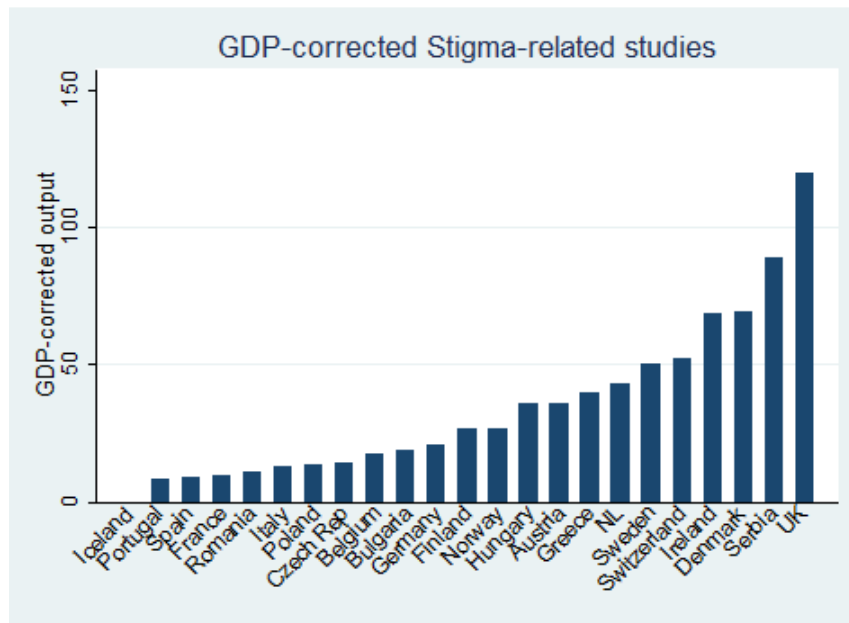
Figure 1. Variation in GDP-corrected Stigma-related research
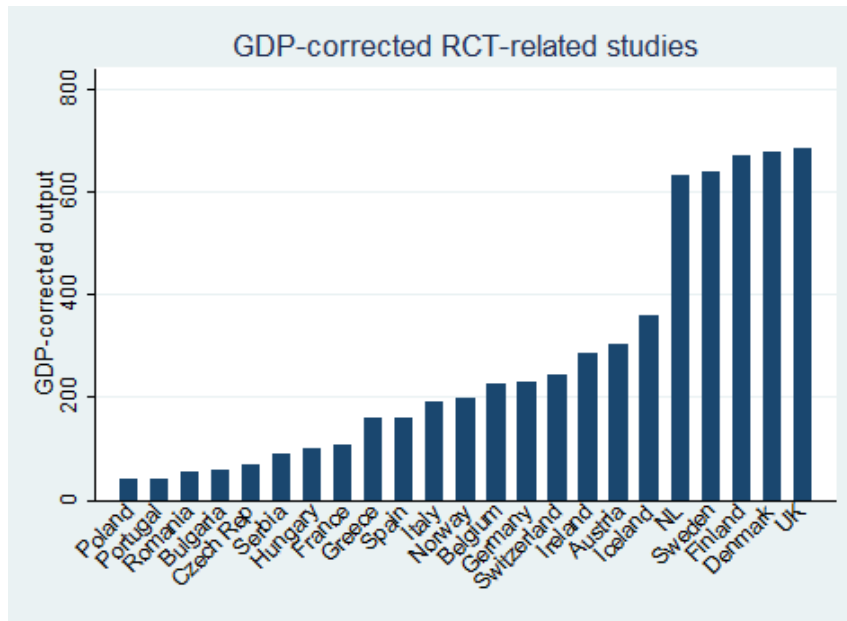
Figure 2. Variation in GDP-corrected RCT-related research
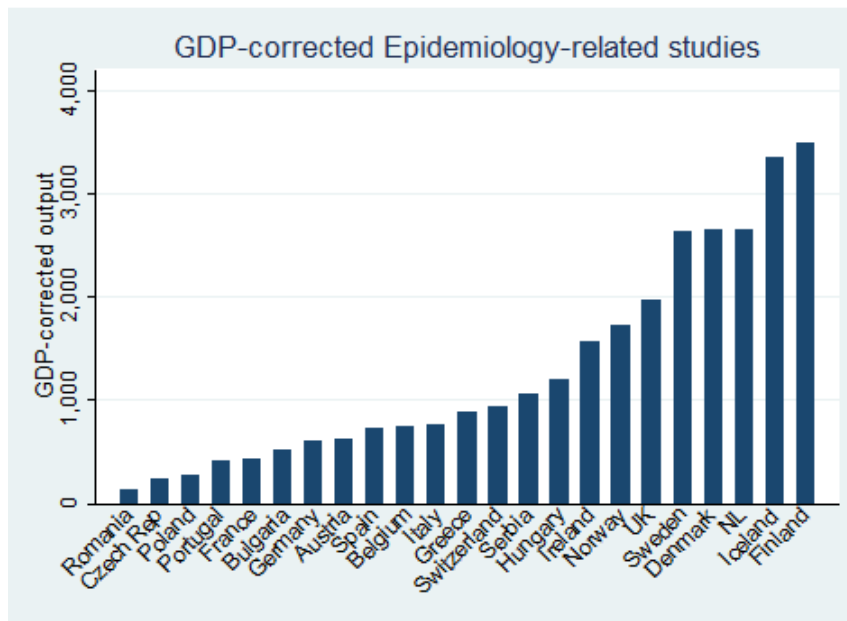
Figure 3. Variation in GDP-corrected Epidemiology-related research
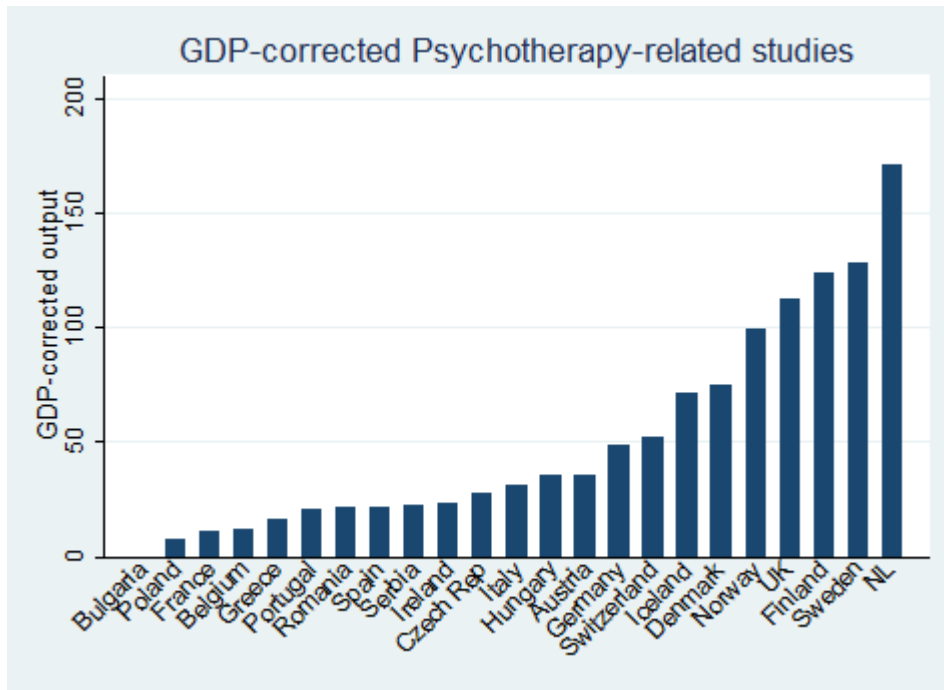
Figure 4.   Variation in GDP-corrected Psychotherapy-related research
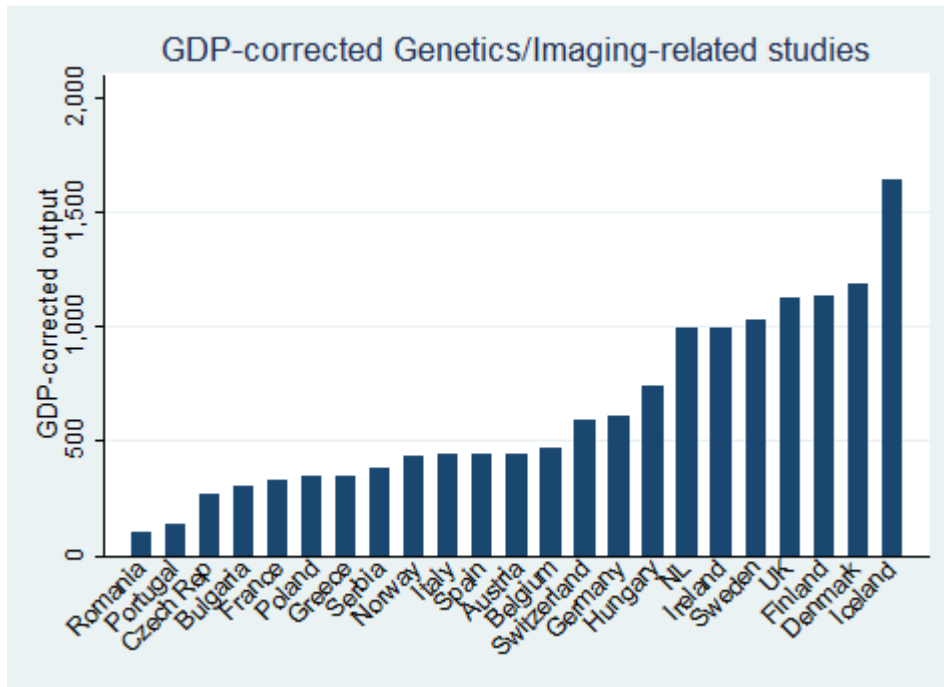
Figure 5.   Variation in GDP-corrected Genetics/Imaging-related research

Many findings illustrate within- and between-country variation as regards the areas that were tracked. For example, some countries, most notably the UK, are consistently among the countries producing the largest amount of research; if GDP is kept constant. Other countries are consistently among those with the lowest output. It is clear that some countries have substantial output despite having relatively low GDP's and, conversely, some countries have low output despite large GDP's. Also apparent is that there is considerable variation in rank order depending on the particular topic area. For example, Finland scores high on Epidemiology-related research, but low on Stigma-related research. This type of cross-topic variation indicates that country-specific factors operate in determining the type of research being conducted and therefore indicate that there is ample scope for cross-country complementary collaboration in mental health research, each country potentially providing specific expertise.

3.1.2.4. Somatic disorder research is more GDP-dependent than Mental Health research

In table 3, the proportion of between-country variance in research as a function of GDP is depicted. Compared to somatic research (90% variance explained by GDP), mental health is much less sensitive to GDP (56% variance explained by GDP). In fact, with the exception of the tracking area of Genetics/Imaging, all tracking areas explained variance <50%. In other words, the amount of research on somatic disorders carried out in a country is almost completely dependent on the country's GDP.

Table 3. Proportion of variance of Mental health and Somatic, non-mental health output explained by GDP

Tracking Area	Proportion variance explained by GDP
Stigma	27%
RCT	49%
Epidemiology	47%
Genetics/Imaging	73%
Psychotherapy	45%
Any mental health output (5 tracking areas combined)	56%
Somatic, non-mental health output	90%

The amount of mental health research in European countries, however, is not so much a function of GDP but of other, unknown factors. Only in the area of biological psychiatry, i.e. Genetics/Neuroimaging, does research funding follow GDP. The apparent conclusion is that in the area of mental health, available resources are not "automatically" allocated to research. Instead, idiosyncratic conditions appear to apply except when Mental Health research is attempting to relate mental disorders to genetic variation and brain structure/function.

3.1.2.5. Mental Health output as a proportion of Somatic Disorder output

To examine this issue further, we examined countries' Mental Health output as a proportion of Somatic, non-mental health output (as defined per the searches described in table 1). This again revealed an important pattern of variation, which was not associated with GDP (proportion of variance explained: 0%). The proportion of Mental Health output as a function of Somatic, non-mental health output varied from around 15% (Iceland) to around 2.5% (Czech Republic), a 6-fold difference (Fig. 6). Only the UK, Norway and Iceland have Mental Health research, as defined in Table 1, in excess of 10% of Somatic research, as defined in Table 1, whereas in France, Italy, Austria and Belgium this proportion does not exceed 5%. The statistic appears to have a clear "Scandinavian" component, these countries generally scoring higher in the proportion of Mental Health output as a function of somatic output.

Therefore, two issues are apparent. First, how much a country spends on Mental Health research is only weakly to moderately related to available resources, as compared to spending on somatic disorder research, except when research attempts to link mental disorder with biological dysfunction. Second, this discrepancy may become expressed in widespread, GDP-independent, variation in the proportion of Mental Health output as a function of Somatic disorder output. The Mental/Somatic index indicates that in some countries, non-biological Mental Health research is lagging behind, remaining relatively underfunded, while, in some countries, a more appropriate relation appears to exist in relation to GDP and Somatic research funding. The other apparent conclusion is that for Mental Health research to profit from GDP-proportional funding, a biological orientation may be required.
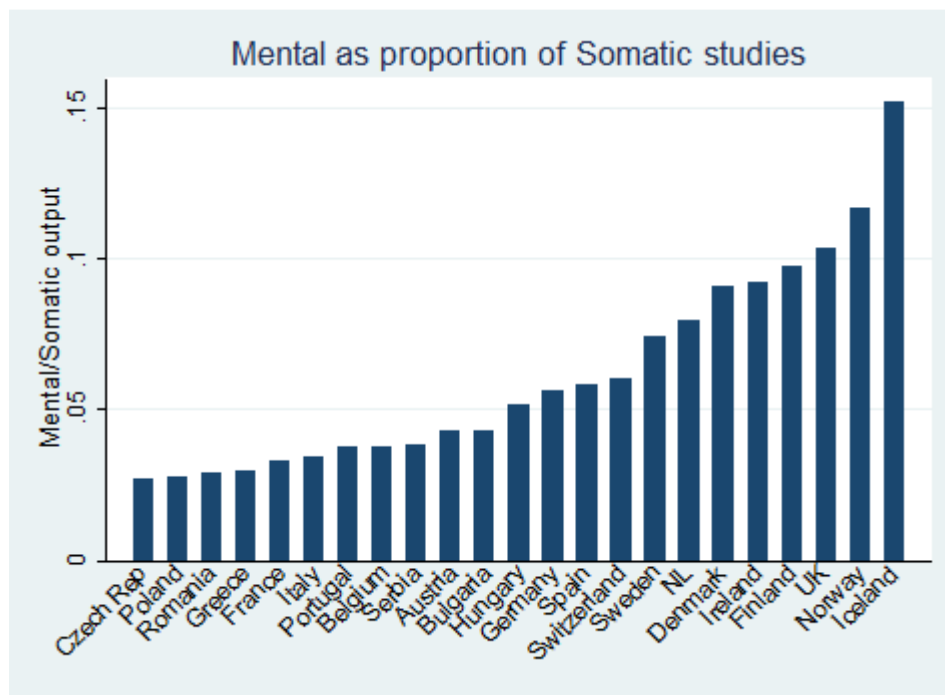
Figure 6. Mental Health output (5 tracking areas as per Table 1) as a proportion of Somatic, non-mental health output (Table 1)

3.1.3. State-of-the-art (main advances during the last 10 years)

The main advances during the last 10 years identified by WP2 experts are the following:

- Increased understanding of gene-environment interaction as well as epigenetic mechanisms in psychiatry
- Acknowledgment of effects of early (prenatal, perinatal, postnatal) environmental exposure and increased understanding of the trajectory of common mental disorder along the lifespan (from childhood through adolescence into adult life)
- Clinical trials (e.g. STARTD and CATIE)
- Advances in the dissemination of CBT
- New treatments, incl. drugs such as antidepressants and atypical neuroleptics but also psychological treatments such as online therapy
- Increased sophistication of neuroimaging techniques incl. techniques for data analysis
- Acknowledgment of early intervention in psychiatry
- Advances in the field of service user research, incl. research into non-traditional forms of service provision
- Development of large cohorts combining DNA-MRI-cognition-phenotype
- Development of international collaborative research networks

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 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** covers all the research units,

institutes, networks, and so on. necessary to perform research. It further includes the (technical) infrastructure that is instrumental in carrying out the research work. Second, research **training and capacity building** refers to all activities contributing to build a workforce capable of performing the research tasks needed. Such activities include research master programmes and PhDs as well as specific MD-PhD programmes 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 or grant-based funding sources.

All these areas are key for the advancement of mental health research in Europe, and 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 the total health research budget in FR and UK respectively vs. 16% in the US; Chevreul K. et al., 2012). This has to be addressed to ultimately improve mental health in Europe as set out in 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 institutes, teaching hospital/industry/institution …), the facilities available for researchers in each of them and the workforce. A further main issue is the question of how non-mental health related infrastructures at European or national level 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 influence the development of national or EU infrastructures?

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

Definitions and distinction of the terms "infrastructures" and "capacities" were agreed on, 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... 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 described as a gap in the current researchers' perception.

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

Capacities and infrastructures can be either centralised or not as well as public or private: research units and public research centres, universities, non-for-profit centres, research foundations... 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 generalised system of call for tenders has been questioned, mainly due to 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 programmes 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 members states but also with some "old" EU countries which have insufficient organisation of mental health research training. Finally, training and capacity building does not stop at graduation but includes continuous education and the 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 EU level and within each European country. Questions concern the amounts coming from the private or public sector, from the national, infra-national, international or EU level, and funding mechanisms.

There is a vivid interest in the annual rate of return of mental health research investment estimated in a recent report (Buxton M. et al, Health Economics Research Group, Office of Health Economics, RAND Europe. Medical Research: What recent report (available in Europe for this domain of research, in the UK. London: UK Evaluation Forum; 2008). The possibility of measuring research impact has been seen as a valuable argument to convince policy-makers that investments in mental research are worthwhile; generally, the idea that it is difficult to "ask for more money" without having clear scientific arguments about the relevance of research in mental health has been recurrent and consensual during the discussion. In this context, it was agreed that indicators have to be found to evaluate the socio-economic impact of mental health research.
It has been emphasised that in 2014 the "Year of the brain" will be organised by the EU. This event is meant to enhance the impact and translation 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 specific mental-health spending is not known. This is seen as further evidence 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.   Literature research

3.2.2.1. Objectives

After an initial screening yielding a very low number of articles (<100), systematic mapping, which is used for a very number of publications and which is carried out by Roamer's thematic WPs, did not seem meaningful. We therefore decided to carry out a traditional literature review.

Unlike other ROAMER work packages, WP3 does not cover a mental health discipline *per se* but rather a transversal set of facts, policies, administrative strategies and opinions. Therefore, the objectives of the literature review were to explore quantitative data, developments and opinions on the areas of knowledge covered.

The research questions of the systematic literature review were as follows:
- Have the funding, infrastructure and capacity building strategies of mental health research been scientifically explored?
- What are the scientist's views and aspirations for these issues?

3.2.2.2. Methods

The research was divided in three parts, according to the three areas of knowledge. The search base Pubmed was the only one explored systematically at this stage of the project.

We included articles published between January 1st, 2002 and September 31st, 2012.
We did not restrict the geographic area to Europe so as to maximise the input from the already scarce literature available.

The search process was as follows:
- Association of terms "*mental health research*" or "*psychiatric research*", both in all fields with "*infrastructure*" (titles or abstracts): 15 articles retrieved and 6 retained as relevant.

This research was extended to the association of *mental health research* and *infrastructure* which has permitted the finding of 3 more relevant articles among the 190 retrieved.

- Association of terms "*mental health research*" or "*psychiatric research*" (all fields) with "*financing*" (all fields): 16 articles retrieved, 4 articles retained as relevant.

- Association of terms "*mental health research*" or "*psychiatric research*" (all fields) with "*funding*" (all fields): 47 articles retrieved, 17 articles retained as relevant.

- Association of terms "*mental health research*" or "*psychiatric research*" (all fields) with "*capacity building*" (all fields): 3 articles retrieved, none of them was relevant.

- Association of terms "*mental health research*" or "*psychiatric research*" (all fields) with "*training*" (all fields): 163 results retrieved, 6 articles relevant.

In total, 419 articles were retrieved and 36 retained as relevant.

The pertinence of the articles was first evaluated according to their title, after this pre-selection the abstracts were read to keep only those papers focusing on mental health research itself: all the articles related to a particular disease, service, population or treatment were eliminated unless they included some elements about mental health research in general. The articles focusing on research in low and middle income countries were also eliminated as well as articles that did not focus on mental health research but rather on health research in general. Only the articles concerning mental health research infrastructures, funding strategies and capacity building in western countries or globally were kept. 4 doublets were deleted.

3.2.2.3. Results

The systematic literature review retained 32 articles relevant to the areas of knowledge represented according to the three different fields of investigation as follow:
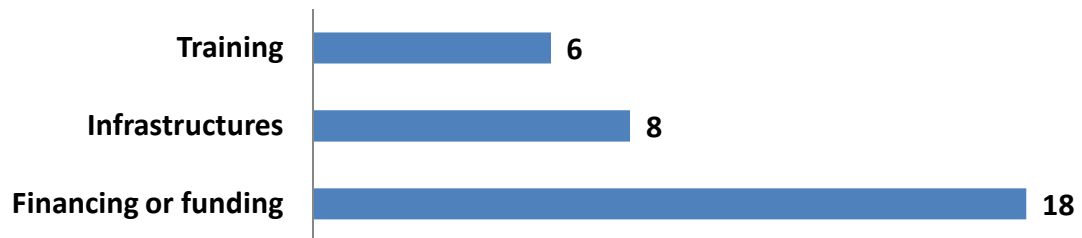
Figure 7.   Distribution of articles by area of knowledge

The papers came mostly from Anglo-Saxons countries as illustrated by the following pie chart (fig.8):
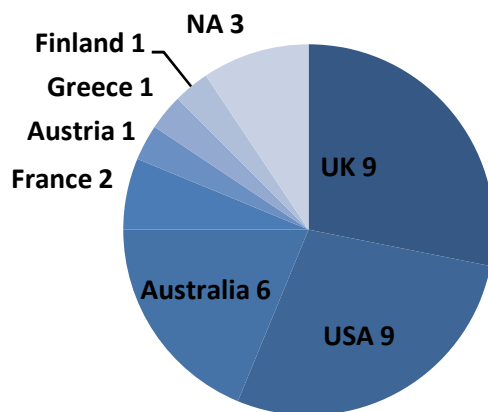
Figure 8.   Distribution of articles by country of origin

Just for Europe, one can see the quasi-monopoly of UK in the three areas discussed. On a global scale, EU countries are the lead contributors on those topics.

However, these results have to be put in perspective by the fact that at least 25% of these 32 articles can be considered as "comments" rather than "articles" and found more in editorials or letters to the editor. In the original articles, large parts are not based on qualitative or quantitative data. Several original articles explicitly represent the writers' opinions.

3.2.2.4.   Preliminary qualitative findings

The section below presents preliminary qualitative findings from the articles retained as relevant (N = 32). All references can be found in the appendix.

Several calls to increase mental health research funding (McCulloch 2009; Patel 2007; Kingdon 2006; Kingdon and Wykes, 2013) have been found, based on the underfunding in light of the burden of disease related to mental disorders. Figure 9 illustrates this.
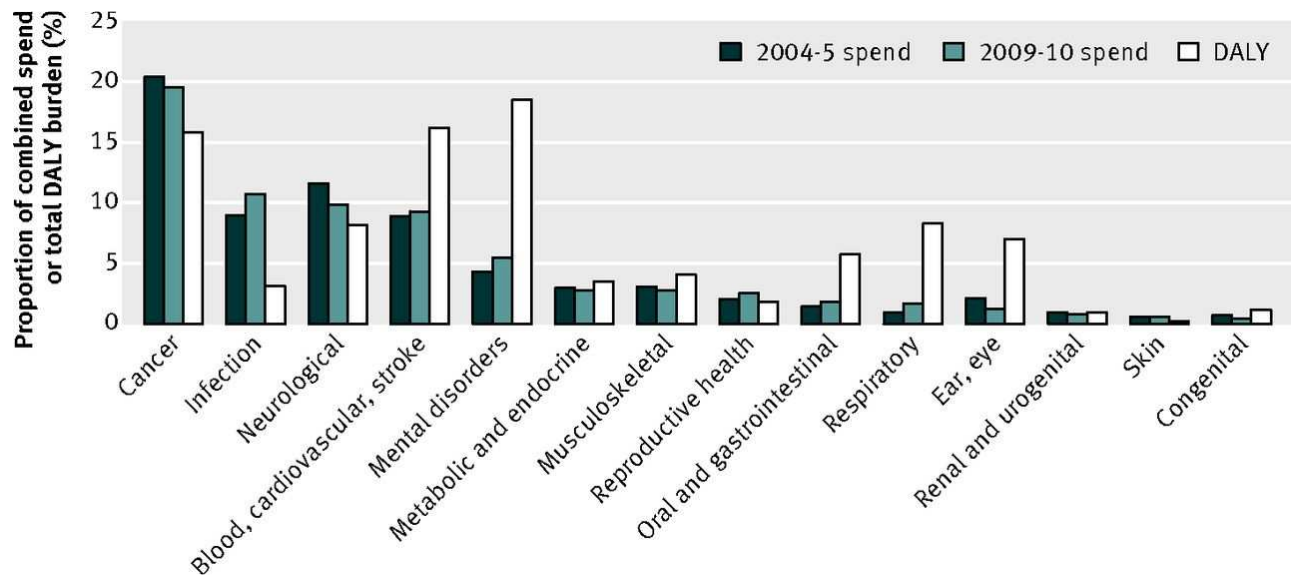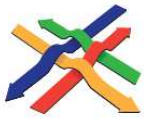
Figure 9. From David Kingdon and Til Wykes in BMJ (letters) "Increased funding needed for mental health research".

In the results of the literature search about infrastructures, several articles were analysed leading to calls for new infrastructures able to provide mental health research in specific fields: services (Bevilacqua et al., 1996), minorities (Yanagihara et al, 2009) or disasters (Pfefferbaum et al., 2010). Others called for a better user involvement in mental health research and the enhancement of partnership with carers and practitioners (Horsfall et al., 2011; Minogue et al., 2010). Two articles described new infrastructures or centres improving mental health research (Lizaola et al., 2011; Henry et al., 2011).

In the literature on mental health research funding, papers comparing mental health research funding with its burden of disease or with its expected impact have been found (Mitchell et al., 2009; Chevreul et al., 2012; Hickie et al., 2005). One of these is a comparison of funding strategies across France, the UK and the US (Chevreul et al., 2012). Two other articles explore different conflicts of interests existing in mental health research (Maj 2008; Henderson et al., 2003); others focus on the private (for profit or non-profit) funding and its impacts (Scott 2005; Kelly et al., 2006). Finally, two articles analyse mental health research history in a specific country or set of countries (Pylkkänen, 2012; Holzinger et al, 2004; Lewison et al., 2011).

In the 6 articles retained as relevant for capacity-building and training, two explore the link between training of carers and impact on research and/or stigma (Davies et al., 2002; Economou et al., 2012), two others offer a description and evaluation of summer school programmes (Hipolito et al., 2012) and community-based joint research (Alegría et al., 2011), and one explores the role of e-technology in mental health research (Cleary et al., 2008).

3.2.2.5.   Conclusion

Although publications in the field of WP3 are scarce, this literature review gave WP3 useful input on the problematic funding of mental health research, some tracks to explore capacity building mechanisms and infrastructure examples (involvement of services users in research; expert centres) as well as several arguments with relevance for policy-makers (e.g., rate of return on investment in mental health research).

3.2.3. State-of-the-art (main advances during the last 10 years)

This part will be supplemented by the results of our analysis of several databases, including the on-course®1 database listing biomedical training programmes in Europe; a CORDIS database with an inventory of projects funded by the EU research and innovation directorate and the list of European research infrastructures from which we hope to extract elements useful for mental health researchers.

3.2.3.1. Research capacities and infrastructures

- There is a split between research units and technical facilities; they are too "independent" from each other. Likewise, there is not enough collaboration and sharing of resources (databases, protocols...) between research units in Europe.
- The number of research networks remains limited, even though it is progressing.
- Biomarkers are increasingly researched but there is insufficient integration into clinical care
- Resources are not adequately used, databases or registries, for instance, should be exploited after the end of project
- There are not enough controlled trials in routine care
- No international fund is dedicated to mental health
- Mental health has taken its place in the FP7
- EU research, generally, is driven by competition rather than by collaboration

3.2.3.2. Capacity building and training in mental health research

An important limitation has been brought up: it is difficult to obtain information indicating which training programmes have actually been taken by researchers working in mental health. Similarly, it is not easy to follow the trajectory of students after graduation, the more so as there is currently no clear-cut career path after training programmes in mental health.

Inequalities exist between "new and old" member states of the EU (and non-EU members such as Serbia). The marginalisation of eastern European countries based on prejudices has been raised as well as the brain drain seeing numerous young researchers move from the Eastern European to Western research units. It has also been reported that health priorities differ between Eastern and Western Europe, with Estonia as example: its main health priorities are more centred on "survival" than mental health. At the same time, there is a perceived "enthusiasm" towards mental health research in certain Eastern countries.

In addition to this, it has been suggested that some countries are not large enough to have the appropriate means for building a dedicated programme in mental-health research training. These countries are therefore particularly dependent on initiatives at a European level.

- Inequalities between East and West create a brain drain which damages new member states and eastern countries. In addition, new member states can be affected by prejudices.
- Training programmes are numerous but their quality is not known and little information on the actual research training is available. Indicators to assess these points do not exist.
- Societal priorities differ across Europe and impact the respective agendas.
- Some countries do not have the critical size to create relevant training programmes in mental health research.

Preliminary list of research master programmes in France (N=37) and the UK (N=66) (see Annex I).

The European Medicines Research Training Network (EMTRAIN) is an initiative funded by both industries and RIs aiming to "establish a sustainable, pan-European platform for education and training (E&T) covering the whole life-cycle of medicines research, from basic science through clinical development to pharmacovigilance." EMTRAIN strives to bridge the academic and industry careers of scientists. The platform, among other things, provides a freely accessible online inventory of all biomedical postgraduate courses in Europe ("on-course") and proposes strategies to promote international mobility and inter-disciplinary culture.

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[1] http://www.on-course.eu/

3.2.3.3.   Funding strategies of mental health research

Focusing on the EU organisation of the research funding, "innovations cannot be prescribed" put forward one expert, even though researchers have to be aware of societal issues and priorities expressed by policy makers. The calls of the FP7 were estimated as being too specific and too "top-down"; it has been suggested that the researchers should be more able to propose projects themselves with less strict conditions.

- In the crisis context, national research funding decreases and within the EU, research has to compete with other EU priorities
- FP7 requirements are more and more difficult to meet
- Infrastructures and other outputs (e.g. databases) created by grant-based research are not always sustainable and/or accessible to the wider research community
- The share of core funding is too low which impedes project applications due to the lack of human resources

3.3.   Biomedical: Neurobiological, Pharmacological and Clinical Research

1.2.1. 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.

3.3.1.1.   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 though 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**

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

3.3.1.1.2.   Cognitive Systems

• Psychiatric disorders involve 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).

3.3.1.1.3.   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 generalised 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 calibrating and monitoring 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, which is usually chronic, is modulated by personality factors, self-esteem and the degree of optimism that helps in appreciating a sense of safety, social position and social support or combinations of these psychosocial contexts (Lazarus 2006, Taylor 2010).

3.3.1.1.4.   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 (Feinstein, 1970). 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.

3.3.1.1.5.   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.

3.3.1.1.6.   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 synchronisation of behaviours
- Self-other differentiation

Empathy is the capacity to recognise, 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 (see summary in Table 1, taken from Baird et al., 2011).
- Empathy is assumed to consist of three components: motor, emotional, and cognitive empathy (Blair, 2005).
  - o Motor empathy refers to automatically and unconsciously mirroring the facial expressions of another person, known as facial mimicry.
  - o Emotional empathy refers to the experience of emotions consistent with and in response to those of others.
  - o Cognitive empathy is the ability to rationally understand and recognise 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 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 synchronising emotions with other people facilitates emotion recognition, social interaction, as well as empathic functioning (Singer, 2006; Sonnby-Borgstrom, 2002; Stel and Kippenberg, 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 synchronisation and to facilitate emotion recognition (Hatfield et al., 2009; 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 OFC 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, 2003), 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 OFC (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.

3.3.2. Systematic literature mapping

3.3.2.1. Literature Search

Initially keywords were identified by surveying WP4 experts and making lists from draft expert position statements. When searched for simply in the title and abstracts of articles, the search results were poor in that they included a very large number of irrelevant articles while omitting very relevant ones. Part of the problem was explicitly identifying neurobiological keywords for a simple textual search: potentially this might include thousands of keywords identifying, for example, every neuro-molecule and brain structure. This problem was overcome by using the Medical Subject Headings (MeSH) of Pubmed. These provide keywords that have been intelligently attached to each article. Moreover, they are hierarchical. For example, by selecting the MeSH category 'macromolecular substances', all such catalogued molecules are included. Therefore, a WP4-specific search strategy was constructed by working through the hierarchy on the MeSH Browser (http://www.nlm.nih.gov/mesh/MBrowser.html) selecting keywords and overarching categories that correspond to WP4 concepts and keywords previously identified by experts. The resulting search syntax is in two halves, the first containing neurobiological domains and constructs and the second containing generic biomedical terms and different 'units of analysis' including various molecular categories and techniques such as imaging. The two halves were combined with an 'AND' to produce search results as relevant to WP4 as possible. This WP4 specific search was combined ('ANDed') with the generic ROAMER search terms for different mental disorder diagnoses and European countries. The search was limited to articles with abstracts published between 1/1/2007 and 31/12/2011. This produced 12,102 results.

3.3.2.2. WP4 Keywords

(("emotions"[MeSH Terms] OR "motivation"[MeSH Terms] OR "helplessness, learned"[MeSH Terms] OR "reinforcement (psychology)"[MeSH Terms] OR "satiation"[MeSH Terms] OR "punishment"[MeSH Terms] OR "motivation"[MeSH Terms] OR "anhedonia"[MeSH Terms] OR "cognition"[MeSH Terms] OR "attention"[MeSH Terms] OR "perception"[MeSH Terms] OR

"memory"[MeSH Terms] OR "language"[MeSH Terms] OR "executive function"[MeSH Terms] OR "social behaviour"[MeSH Terms] OR "theory of mind"[MeSH Terms] OR "empathy"[MeSH Terms] OR "facial expression"[MeSH Terms] OR "self concept"[MeSH Terms] OR "stress, psychological"[MeSH Terms] OR "stress, physiological"[MeSH Terms] OR "arousal"[MeSH Terms] OR "homeostasis"[MeSH Terms] OR "sleep"[MeSH Terms]))

AND

("medicine"[MeSH Terms] OR "biomedical research"[MeSH Terms] OR "neurosciences"[MeSH Terms] OR "genetics"[MeSH Terms] OR "molecular biology"[MeSH Terms] OR "Macromolecular Substances"[MeSH Terms] OR "Hormones, Hormone Substitutes, and Hormone Antagonists"[MeSH Terms] OR "Enzymes and Coenzymes"[MeSH Terms] OR "Carbohydrates"[MeSH Terms] OR "Lipids"[MeSH Terms] OR "Amino Acids, Peptides, and Proteins"[MeSH Terms] OR "Nucleic Acids, Nucleotides, and Nucleosides"[MeSH Terms] OR "Biological Factors"[MeSH Terms] OR "Biomedical and Dental Materials"[MeSH Terms] OR "Pharmaceutical Preparations"[MeSH Terms] OR "neurons"[MeSH Terms] OR "neuroglia"[MeSH Terms] OR "neuroimaging"[MeSH Terms] OR "physiology"[MeSH Terms] OR "Physiological Phenomena"[MeSH Terms] OR "behaviour"[MeSH Terms])

3.3.2.3.   Analysis

The 12,102 results randomly sampled down to 3,000 for further analysis. After manual removal of abstracts irrelevant to WP4, 1,760 remained. These were read and classified by study type and mental health content as per the ROAMER methodology. The abstracts and associated information (including MeSH keywords) were loaded into a database to facilitate analysis.

Abstracts by Mental Health Content
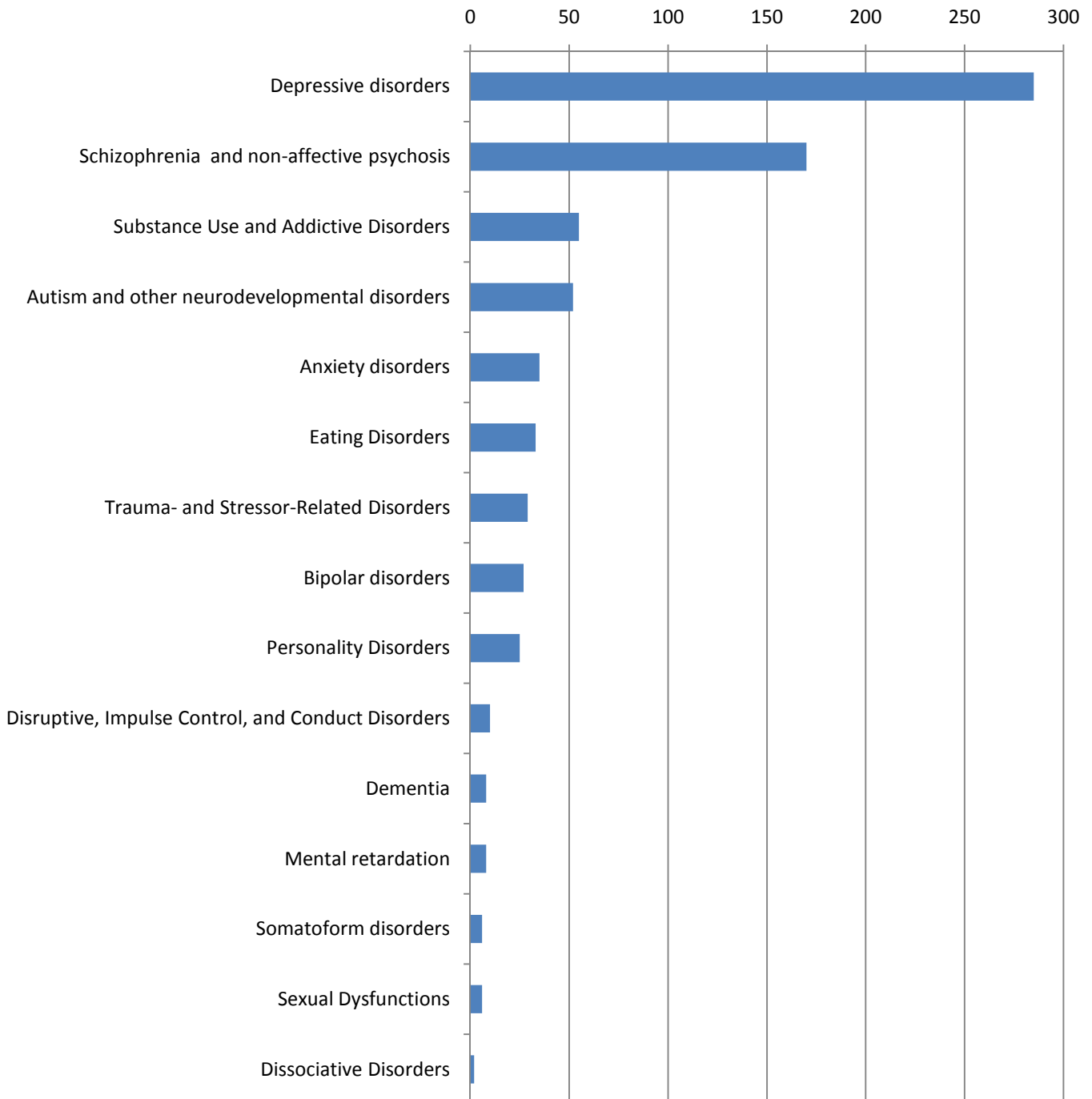
Figure 10. Distribution of articles by mental health content

A large number of abstracts in the WP4 mapping applied to several disorder categories, as they were about basic neurobiological processes. The 'more than one disorder' category contains 1,009 abstracts and has been excluded from this chart to maintain a useful scale.
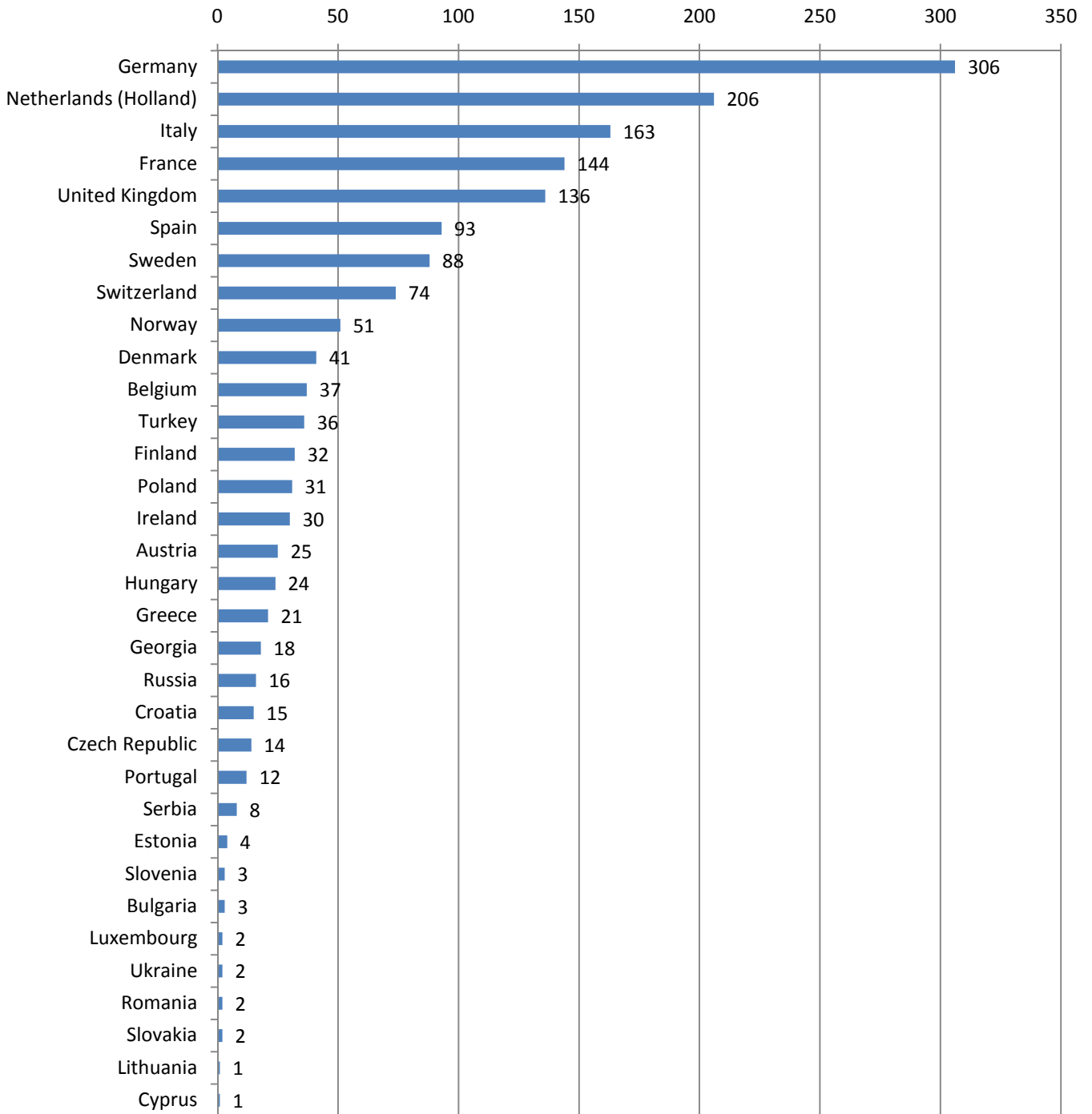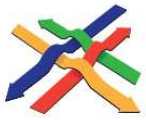
Figure 11. *Distribution of articles by country of the corresponding author*

Figure 12. First authors

Table 4. Articles by mental health content and country

Country	Total	Schizophrenia and non-affective psychosis	Bipolar disorders	Depressive disorders	Anxiety disorders	Trauma- and Stressor-Related Disorders	Somatoform disorders	Dementia	Dissociative Disorders	Personality Disorders	Substance Use and Addictive Disorders	Autism and other neurodevelopmental disorders	Mental retardation	Eating Disorders	Sexual Dysfunctions	Disruptive, Impulse Control, and Conduct Disorders	More than one disorder
	119	8	3	26		2				3	5	2	1	2	2	1	64
Austria	25	2		1	2						1			2			17
Belgium	37	3		10	1						1			1			21
Bulgaria	3			1													2
Croatia	15			4		1	1										9
Cyprus	1			1													
Czech Republic	14	2	1	4							1						6
Denmark	41	4		11	1		1				1						23
Estonia	4			1													3
Finland	32	5		6	1						2	2			1		15
France	144	16	5	31	6						5	7	1	2	1	1	69
Georgia	18	3		1	4	1					1						8
Germany	306	31	5	44	7	11	2	1		7	9	4	1	4		2	178
Greece	21	3		7						1							10
Hungary	24	5		7								1		1			10
Ireland	30	3	1	7							1						18
Italy	163	11	4	18	1	1		1		1	6	7	1	3			109
Lithuania	1																1
Luxembourg	2										1						1
Netherlands	206	10	1	32	3	6		2	1	3	2	11		4	1	1	129
Norway	51	9	1	12	1			1		1	3			1			22
Poland	31	3		1	1						1	1		1			23
Portugal	12	1		2	1						1						7
Romania	2	2															
Russia	16	1		3													12
Serbia	8	1														1	6

Slovakia	2																2
Slovenia	3														1		2
Spain	93	12	2	4	2					6	1		2			1	63
Sweden	88	5	1	24	2			1		4	4	4		2				41
Switzerland	74	8	1	9	1	2	1			2	1	1	2			2	44
Turkey	36	1	2	5					1	1				1			25
Ukraine	2																2
UK	136	21		13	1	5	1	2		2	3	11	2	7		1	67

Table 5. Number of repetitions of each keyword within the hits

TOP MeSH KEYWORDS	
Keyword	Count
Humans	1,441
Male	1,250
Female	1,092
Adult	840
Middle Aged	530
Animals	448
Adolescent	341
Young Adult	303
Aged	242
Questionnaires	239
Neuropsychological Tests	205
Rats	192
Child	174
Analysis of Variance	164
Psychiatric Status Rating Scales	160
Risk Factors	148
Mice	142
Schizophrenic Psychology	120
Time Factors	119
Social Behaviour	113
Severity of Illness Index	105
Comorbidity	101
Brain Mapping	100
Magnetic Resonance Imaging	100
Depression / psychology	99
Disease Models, Animal	97
Case-Control Studies	95
Cross-Sectional Studies	95
Stress, Psychological / psychology	93
Rats, Wistar	91
Follow-Up Studies	88

Aged, 80 and over	86
Anxiety / psychology	83
Treatment Outcome	82
Brain / physiopathology	81
Cognition / physiology	78
Genotype	77
Psychometrics	77
Dose-Response Relationship, Drug	75
Quality of Life	75
Emotions / physiology	72
Self Concept	72
Behaviour, Animal / drug effects	71
Sex Factors	71
Prospective Studies	69
Reward	69
Attention / physiology	64
Depression / epidemiology	64
Emotions	64
Age Factors	62
Diagnostic and Statistical Manual of Mental Disorders	62
Facial Expression	62
Antipsychotic Agents / therapeutic use	61
Schizophrenia / diagnosis	61
Adaptation, Psychological	60
Cognition	60
Brain / metabolism	59
Stress, Psychological / physiopathology	59
Reaction Time / physiology	58
Stress, Psychological / complications	58
Mice, Inbred C57BL	57
Schizophrenia / physiopathology	57
Cognition Disorders / diagnosis	55
Cohort Studies	55
Longitudinal Studies	54
Social Adjustment	54
Electroencephalography	53
Interpersonal Relations	53
Memory / physiology	53
Prevalence	53
Cues	52
Stress, Psychological / epidemiology	52
Affect	51
Depression / diagnosis	51
Health Status	51

Bipolar Disorder / psychology	50
Mental Disorders / psychology	50
Motivation	49
Pregnancy	49
Attention	48
Depressive Disorder / psychology	48
Psychomotor Performance / physiology	48
Stress, Psychological / metabolism	48
Anxiety / epidemiology	47
Anxiety / physiopathology	47
Cognition / drug effects	47
Life Change Events	47
Rats, Sprague-Dawley	47
Reproducibility of Results	47
Child, Preschool	46
Inhibition (Psychology)	46
Brain / physiology	45
Phenotype	45
Attention Deficit Disorder with Hyperactivity / psychology	44
Reference Values	44
Antidepressive Agents / therapeutic use	43
Cognition Disorders / psychology	43
Schizophrenia / drug therapy	43
Behaviour, Animal / physiology	42
Brain / drug effects	42
Double-Blind Method	42
Image Processing, Computer-Assisted	42
Reaction Time	42
Depression / etiology	41
Language	41
Mice, Knockout	41
Motor Activity / drug effects	41
Cognition Disorders / etiology	40
Photic Stimulation / methods	40
Anxiety Disorders / psychology	39
Memory / drug effects	39
Psychotic Disorders / psychology	39
Social Support	39
Alcoholism / psychology	38
Depressive Disorder, Major / psychology	38
Personality Inventory	38
Socioeconomic Factors	38
Maze Learning / drug effects	37
Psychiatric Status Rating Scales / statistics & numerical data	37

Regression Analysis	37
Social Environment	37
Stress, Psychological / etiology	37
Aggression / psychology	36
Depression / physiopathology	36
Magnetic Resonance Imaging / methods	36
Pattern Recognition, Visual / physiology	36
Photic Stimulation	36
Sex Characteristics	36
Exploratory Behaviour / physiology	35
Anxiety / etiology	34
Models, Psychological	34
Psychotic Disorders / diagnosis	34
Stress, Psychological	34
Anxiety / metabolism	33
Arousal / physiology	33
Behaviour, Animal	33
Body Mass Index	33
Genetic Predisposition to Disease	33
Mental Disorders / epidemiology	33
Anxiety Disorders / diagnosis	32
Statistics as Topic	32
Depressive Disorder / diagnosis	31
Hydrocortisone / metabolism	31
Oxygen / blood	31
Statistics, Nonparametric	31
Anxiety / genetics	30
Dopamine / metabolism	30
Hippocampus / metabolism	30
Memory, Short-Term / physiology	30
Mental Disorders / diagnosis	30
Retrospective Studies	30
Schizophrenia / genetics	30
Anxiety / diagnosis	29
Chronic Disease	29
Depression / complications	29
Predictive Value of Tests	29
Social Perception	29
Antipsychotic Agents / adverse effects	28
Anxiety / drug therapy	28
Attitude to Health	28
Bipolar Disorder / diagnosis	28
Cooperative Behaviour	28
Maze Learning / physiology	28

Quality of Life / psychology	28
Serotonin Plasma Membrane Transport Proteins / genetics	28
Stress, Psychological / genetics	28
Substance-Related Disorders / psychology	28
Visual Perception / physiology	28
Anxiety / complications	27
Autistic Disorder / psychology	27
Combined Modality Therapy	27
Electroencephalography / methods	27
Frontal Lobe / physiopathology	27
Prefrontal Cortex / physiopathology	27
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3.3.3. State-of-the-art (main advances during the last 10 years)

3.3.4.1.   Affective (Negative and Positive Valence) Systems

Circuits and physiology

- Neuroanatomical correlates of these responses consist of ancient neuronal structures including basal ganglia, the amygdaloid complex, the hypothalamus and other conserved areas of the brain.
- In humans and other primates, involvement of recent evolutionary neuronal structure which includes the neocortex also play a role in shaping approach and withdrawal responses thus suggesting that unique features may distinguish these species from others (Noonan et al 2012).
- Positive and negative valence states both guide a live organism to emission of goal oriented responses, in the first case to approach the reward in the second to avoid the threat (Everitt and Robbins 2005).
- To a large extent, these two opposite emotional states are regulated by the same neurotransmitter systems and that their fine tuning is responsible for approach and reward or withdrawal and aversion. Such a role has been described, for instance, for dopamine (DA), serotonin (5-HT), noradrenalin (NE) corticotropin releasing factor (CRF), orexin and others.

Positive valence - reward
- Olds and Milner (1953) showed that rats learn electrical self-stimulation when an electrode is placed in the lateral hypothalamus-medial forebrain bundle.
- Subsequent studies demonstrated that activation of the mesolimbic DAergic A10 pathway originating from the ventral tegmental area (VTA) and projecting to the nucleus accumbens (Nac) is key neurocircuitry in reward processing and positive salience attribution (Volkow et al 2008).
- Opioid system also implicated in the regulation of reward mechanisms and positive valence attribution. Activation of μ-opioid receptors in the Nac increases reward valence and stimulates reward consumption. On the other hand, stimulation of the μ-opioid receptors in the VTA decreases GABAergic inhibitory tone on VTA DA cells (Johnson and North 1992).
- Recent brain-imaging studies using PET ligands to monitor DAergic as well as μ-opioidergic activity in response to drugs of abuse have confirmed these preclinical findings (Heinz et al 2007; Volkow el al 1997).

Negative valence: Responses to acute threat (Fear)
- Neurocircuitry and physiology extensively studied in non-primate animals, especially rodents, and in non-human primates and in healthy humans.
- Experiments typically involve classic condition and extinction learning or use unconditioned threat stimuli. Neuroimaging methods that allow the study of function and structure of circuits in the living brain are increasingly used.
- The 'fear' circuitry consists of the amygdala, the hippocampus, the dorsomedial and ventromedial prefrontal cortex, the anterior cingulate cortex, the orbitofrontal cortex, the insular cortex, and a number of brain areas involved in initiating physiological and behavioural responses (Shin and Liberzon, 2010).
- These latter areas are the periaqueductal grey, ventral striatum, brainstem nuclei (autonomic nervous system) and hypothalamus (HPA-axis).
- A distinction can be made between the 'fast' or quick and dirty route and the slower, indirect one that allows regulation of the initial response by higher cortical areas.

Negative valence: Responses to potential harm (Anxiety)
- Anxiety circuitry has been less studied and characterised as compared to fear circuitry, especially in humans.

- Typically used paradigms are darkness in humans or light in rodents or slowly fluctuating indicators of potential risk, typically leading to an enhanced unspecific environmental threat monitoring.
- Work in rodents and non-human primates have shown this type of hypervigilant monitoring to be more dependent on involvement of the bed nucleus of the stria terminalis (BNST) and its reciprocal connections with the central nucleus of the amygdala.
- Recent neuroimaging studies have implicated the BNST, the insular cortex and lateral prefrontal cortex in anxiety in healthy humans (Somerville et al., 2010). Exaggerated responses in this circuitry correspond with higher trait anxiety.

Negative valence: Sustained threat circuitry
- The concept of sustained threat is applicable to subclinical and clinical forms of anxiety, but also to other stress-related states, probably including some depressive symptomatology.
- It is a more complex construct than the previous two, because of its broad definition (internal/external, weeks to months, actual or anticipated exposure, etc.).
- The sustained threat circuitry and physiology overlap with those of fear and anxiety, but also include frontostriatal circuitry and probably circuitry involved in, for instance, self-processing in humans (Shin and Liberzon, 2010).

Genes, molecules and cells

- While not many human genetic studies have examined the contribution of genetic variation to constructs related to positive or negative valence, animal studies have given strong evidence for the importance of specific genes and molecules in these constructs.
- This is especially true for constructs for which valid animal models are present, such as the constructs related to threat and reward with less evidence for constructs such as loss, for example.
- The advances in our understanding of the genetic underpinning of negative and positive valence have been made possible by an increasing number of molecular tools, allowing site- and timing-specific manipulations of specific genes as well as the study of human genetic polymorphisms in laboratory animals (Barr et al., 2003; Carola and Gross, 2012; Chen et al., 2006; Kaun et al., 2011; Muller and Holsboer, 2006; Soliman et al., 2010; Stewart et al., 2012).
- While main genetic effects are not consistently observed in human studies, a number of studies have shown significant interactions of stress with genetic variants on phenotypes related to both negative and positive valence.
- Environmental factors relevant for both positive and negative valence, such as early life stress, have been shown to have effects not only on specific genes, but on a large number of loci to possibly allow orchestrated changes across several systems. For example, McGowan et al., report that the epigenetic response to maternal care is coordinated in clusters across broad genomic areas and not restricted to single candidate genes (McGowan et al., 2011).
- Data emerge that miRNA can be stress sensitive and orchestrate gene expression changes in a number of important targets. Haramati et al., report that in the central amygdala, miR-34c is reactive to stress and one of the targets of this miRNA is the CRH receptor type 1, an important mediator of anxiety behaviour (Haramati et al., 2011).
- An important emerging concept, related to the molecular mechanisms of positive and negative valence is that inherited genetic variation in sites determining miRNA transcription, environment induced epigenetic changes or the effects of transcription factors could have broad effects on a number of downstream systems and targeting such master regulators may be promising preventive or therapeutic approaches.
- Non-hypothesis driven, genomic investigations, mostly within animal models, have identified diverse classes of genes and molecules involved in mediating both negative and positive valence.
- It thus became increasingly evident that in addition to neurotransmitter systems, other types of molecules are equally important including cell-cell adhesion molecules, cytoskeleton, synaptic molecules, transporters not only of neurotransmitters but also amino acids, neurosteroids, second messenger systems, transcription factors and others.

- This highlighted the importance of brain cells other than neurons for the neurobiological regulation of behaviour. These include astrocytes and microglia as well as modulatory influences of peripheral cells such as immune cells (Eroglu and Barres, 2010; Graeber, 2010; Miller et al., 2009).

Behaviour and clinical research

Positive Valence

- Major psychiatric disorders including addiction, depression and psychosis involve alterations of brain reward mechanisms. Each one of these is characterised by its own collection of etiological predisposing factors, physiopathological dysregulations and symptoms. However, they also share important common features. For instance, they all involve allostatic changes of the brain reward system that is shifted towards a hypohedonic state (Eshel and Roiser 2010; Koob and Le Moal 2007). High comorbidity between addiction and depression or psychosis has also been well documented (Nunes and Rounsaville 2006; Schuckit 2006).
- Both depressed and psychotic patients appear to be more prone to abuse addictive substances that, at least in part, are used to self-medicate against the negative affect associated with the primary disease.
- On the other hand, addiction is known to trigger psychotic episodes and exacerbate depression in some individuals. The intimate nature of this intricate disease interaction is unknown at present but alteration of brain reward mechanisms seems to play a pivotal role.
- On the physiological level, a striking difference between addictive drugs and natural reinforcers is that DA is always released in the shell portion of the Nac following administration of the former while a natural reinforcer appears to activate this nucleus only when experienced for the first time (Bassareo and Di Chiara 1997; 1999). Based on this finding it was proposed that drugs of abuse, through nonphysiological recruitment of the DAergic mechanisms usurp the brain reward system, leading to the development of addiction.
- On the other hand, it is also known that under some circumstances individuals can develop addictive-like behaviours also towards natural stimuli such as food or sex, which suggest that this "dopaminocentric" hypothesis of addiction is reductive (Lutten and Nestler 2009; Volkow et al 2012);

Negative valence

- Changes in fear/anxiety circuitry, frontostriatal circuitry, and physiology (i.e. HPA axis and autonomic nerve system) related to sustained threat have been typically studied in animal models and in anxious and depressive patients.
- The neurocircuitry of some of these clinical anxiety states has been relatively well studied, including posttraumatic stress disorder (PTSD) and obsessive compulsive disorder (OCD), but the 'common' anxiety disorders, i.e. panic disorder, social anxiety disorder and generalised anxiety disorder, in which fear/anxiety circuitry is believed to be the key circuitry involved, are understudied.
- In PTSD and OCD the fear/anxiety circuitry is involved, but other circuits are also clearly involved and are, especially in OCD (frontostriatal circuitry), probably even more relevant for the phenomenology (van den Heuvel et al., 2011).
- Meta-analyses and reviews of functional neuroimaging studies show the presence of a hyper-responsive amygdala (and insular) across the different anxiety disorders but findings in the other elements of the circuits vary with disorder and scan paradigm (Etkin and Wager, 2007).
- To date, there are no meta-analyses of structural studies across anxiety disorders available although structural abnormalities have been consistently found in some anxiety disorders (OCD, PTSD), but not in others.
- On the physiological level, abnormalities in HPA axis regulation have been demonstrated in anxiety disorders, most consistently for PTSD.

Major advances

- While most studies still rely on traditional diagnostic categories, some recent publications support the use of the proposed transnosographic, transdiagnostic approach in disorders related to positive and negative valence.

- For instance, a meta-analysis of more than 250 brain-imaging publications on a variety of mental disorders in children and adolescents (Mana et al. 2010) suggested that when various types of brain imaging techniques are collapsed in the meta-analysis, (i.e., functional and structural imaging reports are included) the disorders involving negative effects are characterised by reports of abnormalities in a limited number of regions.
- This analysis clustered three groups of mental disorders according to both structural and functional location of brain abnormalities:
  - affective disorders characterised by abnormalities of the frontal-limbic regions;
  - mental disorders with ''cognition deficits'' mainly related to posterior and anterior cortex abnormalities;
  - one disorder with marked motor deficits.
- In children and adolescents, the group of affective disorders encompassed major depression, bipolar and anxiety disorders (except OCD) with prominent abnormalities in the amygdala, bilateral cingulate cortex bilateral middle (vmPFC) and inferior frontal gyri, caudate nuclei and hypothalamus (Mana 2010).
- These findings from transnosological, transdiagnostic approaches in neuroimaging studies suggest that to investigate the neurobiological basis of psychiatric disorders, biological, biomarker and human genetic studies need to move away from diagnosis and symptom-based associations towards intermediate phenotypes that might better reflect these domains, including neuroimaging phenotypes (Loth et al. 2011).
- For example, adolescent drug use can be conceptualised as a behavioural manifestation of reward responsiveness. It was recently shown that specific brain networks contributing to impulsivity are associated with adolescent drug use behaviour, and a genetic variation in the norepinephrine transporter gene (Whelan et al. 2012).

3.3.4.2. Cognitive Systems

Major advances

- We have summarised some of the main themes for psychiatry arising from a cognitive neuroscience approach. This approach embraces advances in both methodology and theory: virtually all of the conceptual themes outlined above can be associated with such developments.
- One product of the approach will be the definition of more accurate psychiatric phenotypes. Another will be in the development of new treatments, whether cognitive, electrophysiological or pharmacological.
- An example of the general process would be initially establishing relationships between neural processing, behavioural performance and decision-making models. The fitting of a model would then allow identification of dysfunctional processes and, potentially, a suitable target for therapeutics.
- The application of the cognitive systems perspective will necessarily involve interfaces with other approaches, for instance with respect to affective systems, comorbidity and psychiatric genetics.
- We have not here to relate dysfunctions of specific neural systems to underlying molecular pathology and neurogenetics, but these will also be important goals.

Perceptual dysfunction and electrophysiological biomarkers

- Subtle perceptual deficits are present in many psychiatric disorders, notably including schizophrenia and autism, that may impinge on highly relevant capacities such as the perception (and eventually the production) of emotional pitch in spoken language.
- Dysfunctions are paralleled by specific abnormal patterns of electrical brain activity, namely attenuated or absent mismatch negative (MMN) potentials to auditory, and even visual, stimuli. These have been observed in a number of psychiatric and neurological disorders. They point to common dysfunction in NMDA-mediated neurotransmission and have the advantage of being possible to obtain even in the absence of patient cooperation.

- As well as MMN, studies on brain connectivity (see below) can be implemented via neurophysiological techniques.

Attention and neural networks of cognition

- Attentional deficits are often prominent in psychiatric patients, but attentional processes are diverse and mediated by a variety of neural networks.
- A recent major discovery has been that of the 'default system' (comprising several midline structures such as the medial prefrontal, and portions of the anterior and posterior cingulate cortex) which is deactivated during most cognitive tasks requiring external orientation to the world and generally activated during the resting state in fMRI tasks or during periods of passive reflection (Fair et al 2008).
- Discovery that complex interconnected and dynamic systems can be described and analyzed using a set of mathematical techniques termed 'graph theory' (Sporns et al., 2004).
- Brain graphs provide a relatively simple way of representing the human brain as a comprehensive map of neural connections, (the 'connectome').
- These network properties are being studied with a mixture of electrophysiological (EEG, MEG and transcranial magnetic stimulation) and functional imaging methods, thus setting the foundations for novel approaches to understand the brain 'at work' in health and disease.
- Applications so far have ranged from Alzheimer's disease and stroke to obsessive-compulsive disorder and schizophrenia, re-conceptualising some of these disorders as complex examples of 'disconnection syndromes'.

Working memory and cognitive training

- Varying definition between research areas.
- Knowledge about neural mechanisms has come from electrophysiological and neuropharmacological studies of nonhuman primates, specifying delay specific activity in prefrontal and parietal areas.
- Neural network models have successfully made biologically realistic models of reverberatory, re-entrant activity that maintains the activity of cue-specific neurons.
- Neurophysiological data are largely consistent with neuroimaging studies of sustained activity in humans.
- Overlap between 'top-down attention' and 'working memory' regarding both behavioural and neuroimaging findings and the relationships between certain aspects of attention and working memory need to be resolved.
- Promising translational findings from animal and human volunteer research indicate that it is possible to enhance working memory function acutely using pharmacological treatments such as D1 dopamine receptor agonists.
- Training can improve working memory capacity, which also translates to improvements of other executive functions relying on working memory and top-down attention (Jaeggi et al. 2008), as well as increased attentiveness in everyday life.
- This has implications for use as a remediating intervention for individuals where low working memory capacity is a limiting factor for academic performance or everyday life.
- Working memory training is the beginning of a new research field exploring the possibilities of enhancing other executive functions such as self-control with help of computerised training methods, possibly combined with neuroimaging and pharmacological treatment (Klingberg 2010).

Long term memory and plasticity

- Profound deficits in declarative memory are not only present in early Alzheimer's disease but also in schizophrenia, probably as a result of overlapping pathology within the medial temporal lobe, including the hippocampus.
- Stress can profoundly impact neuronal plasticity and neurogenesis within the hippocampus relevant to a range of affective disorders (Lupien et al 2009).

- Neuroscientific advances have characterised molecular mechanisms of plasticity relevant to memory consolidation and extinction that may be relevant to such disorders as pathological anxiety, post-traumatic stress disorder and addiction.
- Phenomenon of memory reconsolidation provides a basis for eliminating maladaptive plasticity of memory circuits (Milton and Everitt 2010).
- These advances have also motivated the development of a range of 'cognitive enhancing' drugs, often based on potentiating glutamate neurotransmission through the NMDA receptor.

Decision-making, learning and neurocomputation

- Reinforcement-related decision-making cognition broadly encompasses: how individuals learn the value of stimuli (e.g. associations with reward or punishment); how those stimulus values can influence choices and actions (both explicitly and implicitly); and how conflicts between different possible choices are resolved.
- In humans, paradigms have often been developed such that behaviours can be compared directly with those seen in experimental animal models of psychiatric disorders.
- The study of reinforcement-related decision-making has important implications for understanding cognitive performance in other domains, since tasks often feature elements that are intrinsically reinforcing (for example, performance feedback)
- Decision-making deficits in various forms have been found in virtually all psychiatric disorders, including depression and bipolar illness, addiction, attention deficit/hyperactivity disorder, obsessive-compulsive disorder and anti-social behaviour.
- Advances within the past decade include the use of formal computational approaches to analyse decision-making and the study of human behavioural phenomena identified in the field of economics ('neuroeconomics'; Glimcher et al. 2008).
- The neuroeconomics literature has focused on understanding why humans depart from rational, normative accounts of decision-making (such as expected utility theory) when performing value-based choice tasks. Examples include:
   - loss aversion (the tendency for losses to appear proportionately worse than gains are good);
   - risk aversion (the tendency to prefer certain outcomes to risky outcomes);
   - framing (the influence of the way that a decision is presented on choice);
   - temporal discounting (the preference for smaller, short-term outcomes than larger more temporally distant ones).
- More generally, there has been considerable expansion in the use of fMRI to understand the brain bases of decision-making in (mainly healthy) volunteers, largely replicating earlier animal-study literature, and also a great focus on investigating the role of chemical neurotransmitters in decision-making through both experimental psychopharmacology and naturally-occurring (e.g., genetic) variation.
- These investigations have confirmed important roles for the following brain regions (among others) in decision-making: striatum; orbitofrontal cortex; anterior cingulate; amygdala; pallidum; thalamus; and the midbrain dopaminergic and serotoninergic nuclei.
- Computational modelling approaches are attractive as they appeal more directly to mechanistic hypotheses and can sometimes be directly linked to putative neurophysiological processes. For example, reinforcement learning theory has highlighted the importance of prediction errors as teaching signals for learning and has related these to phasic firing of midbrain dopamine neurons (Schultz et al. 1997). This has triggered a wide range of investigations into psychiatric diseases, trying to understand maladaptive behaviour as a consequence of aberrant prediction error processing and learning (e.g. Murray et al. 2008).
- These approaches differ from previous attempts to correlate brain signal with clinical data in some important ways:
- First, explaining behavioural observations in terms of mathematical models of the underlying computations (e.g., by assessing learning rates and prediction error signals in different disorders, see Park et al. 2010) can dissect out a number of influences on behaviour that may be conflated together using traditional measures.
- Second, the systematic use of statistical model selection, which enables one to disambiguate between competing models (hypotheses) and select the model that generalises best (i.e., has the best trade-off

between accuracy and complexity) allows inference on 'hidden' quantities that are otherwise very difficult to measure (e.g. neuronal processes that underlie measured EEG, fMRI or behaviour).

- Third, recently developed Bayesian model selection procedures account for population heterogeneity, specifically the possibility that patients may solve problems differently and hence display alterations in brain signals that simply reflect alternative cognitive strategies and not biological differences (Stephan et al. 2009).

- The use of computational modelling will enable us to look at cognitive mechanisms and their behavioural and biological correlates in a manner that cuts across traditional disease entities (Heinz 2002; Robbins et al. 2012).

- Recent computational approaches to decision-making often take a Bayesian perspective (Behrens et al. 2007; Mathys et al. 2011; Frank & Badre 2012) which is beginning to be applied routinely in pharmacological (e.g., Passamonti et al. 2012) and clinical studies (Averbeck et al. 2011).

- Moreover, Bayesian model comparison is becoming a standard approach for computational analyses of decision-making, including reinforcement learning models (Shiner et al. 2012).

- Notably, Bayesian model selection can also be applied to assess which model (e.g., single SNP versus haplotype analysis) is most appropriate for explaining genotype x phenotype interactions (Puls et al., 2009).

Metacognition, executive function and social cognition

- Metacognition includes thinking about the thinking of others, where it is usually called mentalising or theory of mind (ToM). Metacognition is impaired in psychiatric disorders, in particular in schizophrenia and autism.
- Lack of insight, a particular aspect of metacognition, is one of the defining features of psychosis.
- The monitoring and control of cognition is also referred to as 'executive function' (EF).
- Several studies suggest that EF and ToM can be impaired independently of one another, but this is not always found, one problem being that EF is not a single entity.
- Recent developments in the study of ToM have revealed the existence of an implicit form (Biederman et al 2012).
- In autism there is evidence that implicit ToM is impaired, while the explicit form is intact, or at least can be acquired.
- Implicit ToM is closely linked to the other major theme in social cognition.
- This theme involves such phenomena as emotional contagion, mirroring of action and learning through observation of others. These phenomena underlie implicit ToM. Many tasks have been developed for the study of these aspects of social cognition and are being applied to the study of autism.
- Considerable advances have been made in computational modelling of mechanisms of top-down control.
- These are often described in terms of a Bayesian algorithm that optimally combines prior expectations (the top-down component) with new sensory evidence to determine perception and behaviour (Fletcher and Frith 2009).
- This approach has been most successful in relation to understanding the experience of action and delusions of control (Frith 2011). There is now much evidence for failure in the adaptation or updating of predictions (i.e., prior expectations), based on prediction errors, in schizophrenia.
- Theory in social cognition has been enriched by the cognitive neuroscience of social decision-making that has derived from the study of economic games (such as 'the Ultimatum game' (e.g. Sanfey et al 2008) or "The prisoner's dilemma").

3.3.4.3.   Arousal and Regulatory Systems

Spatial and chemical organisation

- Arousal and stress are distinct, but partial overlapping constructs. What distinguishes arousal and stress is their biological substrate.

- If novel sensory input is perceived, it produces an alarm reaction that is initially processed by the nucleus gigantocellularis of the brain stem causing generalised arousal by enhanced activity of ascending excitatory pathways (Csete and Doyle, 2004).
- Arousal has therefore an exclusive neural substrate that governs activation of the reticular activating system in the brain stem, the sympathetic nervous system and the neuroendocrine system.
- Arousal, caused by glutamate-enhanced excitability, is modulated by the classical neurotransmitter systems and by neuropeptides that induce behavioural and physiological activations characterised by increased attention, alertness and vigilance.
- Novel aversive signals are also evaluated by processing the novel information into the limbic-cortical circuitry. If the outcome of the appraisal process in these circuits is interpreted as a threat to integrity, the individual attempts to cope with the stressor by executing appropriate behaviours and by mobilizing energy and physiological responses that facilitate adaptation. Bodily influences are integrated in the central stress circuitry as well as signals of the immune, cardiovascular-kidney, gastro-intestinal and metabolic system affecting brain function either directly or via the nervus vagus. The stress information from body and brain converges with inputs from various neural networks such as the arousing brain stem neurons, notably the locus coeruleus, visceral and immune systems and from higher cortical regions, and feeds into relay stations: e.g., the emotional amygdala complex and the neuroendocrine hypothalamic paraventricular nucleus (PVN) (Herman et al. 2003).
- The amygdala generates emotionally loaded information, which is labelled in time, place and context while processed in, for instance, the hippocampal formation (Eichenbaum et al. 2007). In mutual feedback and feedforward loops the amygdala and hippocampus communicate with frontal brain regions, notably the prefrontal cortex, subregions of which are involved in specific higher cognitive functions, as well as mood, affect, emotional and stress regulation. All this information converges in the PVN, which organizes the autonomous and neuroendocrine responses to stressors, i.e., the sympathetic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis that ultimately feedback on the limbic and arousal circuitry. These regions organised in the limbic-cortical circuitry show during and in the aftermath of the stressful experience a profound functional and structural adaptation that is regulated by neural and hormonal factors in temporal fashion.

Temporal organisation

Arousal and stress regulatory systems operate in distinct temporal domains:

- Basal rhythmic and sleep / wake states
  - The parasympathetic nervous system is dominant in the resting state, at a time that the arousal and stress systems operate in a basal state of activity. The latter systems display circadian rhythms controlled by the circadian clock in the suprachiasmatic nucleus which is entrained by the diurnal light-dark cycle. Moreover, the HPA axis shows hourly ultradian pulses, particularly of cortisol. These cortisol pulses vary in amplitude over the circadian cycle (Lightman & Conway-Campbell, 2010) with highest amplitude at the circadian peak. The ultradian rhythm can vary in amplitude and frequency of the spikes depending on the psychological and physical condition of the individual.
  - It is thought that the pulsatile rhythm enables synchronisation and coordination of daily activities and sleep-related events. In the elderly, the organisation of the ultradian rhythm disappears and becomes de-organised which explains why old individuals may have compromised sleep and daily-activity patterns. Also, the ultradian and circadian rhythms provide a basis for the threshold and sensitivity of the stress system: the magnitude and nature of the behavioural and physiological stress response varies depending on the phase of the hourly cortisol pulse.

- Response to stressors
  - The stress-induced sympathetic and HPA-axis activity have two modes of operation that can be separated into distinct temporal domains: fast initial defence reactions which are then slowly dampened to prevent these initial reactions from overshooting and becoming damaging themselves

(Sapolsky et al. 2000; Joëls and Baram, 2009). Overall, the fast and slow domains of the stress reaction aim to defend the integrity of the organism and to restore homeostasis. While doing so, the systems operate in concert to facilitate coping with stress and to promote adaptation, and to store the experience in the memory in preparation for a future experience. Likewise, the systems coordinate allocation of energy required to meet the cost of coping with stress, the recovery process aimed to restore homeostasis and to promote storage of energy resources for future needs, collectively called allostasis. This process involves energy metabolism in the glial cell compartment, which produces energy substrates rather than storing them.

o How the HPA axis is activated by stressors is well documented. The stressor activates, through multiple innervating pathways, the PVN neuropeptide secreting cells that produce a cocktail of CRH, vasopressin, angiotensin II and other neuropeptides released in the portal vessel system to activate the corticotrophs in the synthesis of the pro-opiomelanocortin precursor (POMC) and the release of its cleavage products. Of these peptides, including the endorphins and melanocortins, ACTH stimulates the adrenal cortex in the secretion of the glucocorticoids cortisol and corticosterone. The glucocorticoids feed back precisely on the sensory-limbic-cortical circuits that have generated the initial reaction to the stressor by way of a closed feedback loop. This action, exerted by a single glucocorticoid, has enormous diversity, depending on time, context and site.

Chronic stress and vulnerability to psychiatric disorders

- If coping behaviour fails repeatedly, the reaction to the stressful situation is reinforced and adaptation occurs to the chronic stress condition. Selye indicated this adaptation as the 'resistance' phase that slowly develops over a period of weeks after the initial stress (alarm) reaction and which ultimately may culminate in the exhaustion phase characterised by breakdown of adaptation. McEwen calls the adaptation to stress 'allostasis' meaning that the brain has the capacity to maintain homeostasis through changes in brain (synaptic) structure and function, and behaviour. The cost of allostasis is termed 'allostatic load', a term that describes the individual's state during Selye's resistance phase, and which can be monitored and calibrated using an increasing number of biomarkers.

- In such a chronic stress condition profound changes take place in the stress system. Chronic stress produces, in basal state, desynchronisation of circadian cycles and sleep wake states, and evokes REM sleep abnormalities that accompany depression and other psychiatric disorders. An elevated sympathetic tone at inappropriate times and a flattened circadian and ultradian pattern of HPA axis activity caused by an enhanced magnitude of cortisol pulses at the circadian trough is then a characteristic feature of the stress system (Holsboer and Ising, 2011).

- The dynamics of the acute stress response in individuals with a history of chronic stress experience can be used as endocrine marker to monitor the allostatic load in the resistance phase. Under chronic stress, the activation of the HPA axis can be more profound and it may take a longer time to shut off the HPA axis responses to stressors. This more sluggish HPA axis pattern is due to enhanced CRH activity and the secretion of cortisol is excessive and prolonged, a phenomenon that is caused by resistance to the cortisol feedback action in the pituitary corticotrophs and hypothalamic CRH cells. The excessive and prolonged cortisol secretions are linked to emotional dysregulation and cognitive deorganisations rather than to depression per se. For several decades escape (either enhanced by CRH) from suppression by the synthetic glucocorticoid dexamethasone (the dexamethasone suppression test or the dexamethasone – CRH test) has already assisted in diagnosis of cortisol resistance at the pituitary level (Ising et al. 2005). In contrast, other adaptations after a single traumatic experience may occur that lead to low circulating cortisol levels because of hypersensitive feedback at the pituitary-hypothalamic level in the face of a very high sympathetic tone, as is the case for post-traumatic stress disorder (PTSD) (Yehuda and Seckl, 2011).

- While cortisol feedback potential may reveal the actual state or setpoint of the HPA axis regulation characterised by resistance or hypersensitivity, the rest of the body and brain is exposed to aberrant levels of the circulating hormone. Thus, in the case of elevated cortisol levels due to feedback resistance, immune function is suppressed, the bones are osteoporotic and a cardio-metabolic syndrome may develop that is hazardous for physical health and further aggravates changes taking place in the brain. Likewise, if too little cortisol is circulating to restrain sympathetic nervous activity and other stressful reactions, including pro-

inflammatory and pro-immune reactions, a condition evolves that is reminiscent to pro-inflammatory state in some age-related neurodegenerative disorders such as Alzheimer's disease.

- The functional and structural plasticity of limbic circuitry allows adaptation to either excessive or inadequate cortisol levels. In response to chronic stressors, the apical dendrites of neurons in the hippocampus CA3 region and areas of the prefrontal cortex atrophy (McEwen and Gianaros, 2011). At the same time, the dendritic organisation of neurons of the amygdala and orbitofrontal cortex become hypertrophic. Chronic stress also affects the fate and embedding of newborn neurons into the circuitry of the hippocampal dentate gyrus and discrete regions of the olfactory brain, a process that was shown to produce functional changes (Fitzsimmons et al. 2012). The organisation and function of the newly-built circuitry is therefore affected by stress, while other studies demonstrate enhanced neurogenesis after taking antidepressants. Yet, even though small circuit changes can have profound consequences, the function of neurogenesis in psychiatric disorders, if any, still needs to be elucidated.

Conclusion

- Genes and neuronal circuits do not act by themselves but need to be regulated by signals produced by environmental changes, and the mediators of the arousal and stress systems are extremely important for this purpose. Our position is that dysregulation of the arousal and stress mediators compromises resilience and enhances vulnerability to psychiatric disorders. Patterns of HPA axis hormones are commonly used as biomarkers in endophenotypes of psychiatric disorders both in the clinic and in animal models. It is recognised that the repair and normalisation of a dysregulated arousal and stress system is the key to causal treatment of psychiatric disorders. The identification of biomarkers in the action of the arousal and stress systems themselves is therefore an important objective in understanding the pathogenesis of stress-related psychiatric disorders.

General advances

Technical

- Understanding the significance of arousal and stress systems requires approaches that link changes in molecular signalling cascades with the plasticity of neural circuitry and behaviour. The tools of genetics and circuit analysis or a combination of these in imaging genetics have allowed, in recent years, an enormous advance in understanding the structural and functional plasticity of the brain (Akil et al., 2011). It is now feasible to examine in a rapid economic fashion the whole genome for responsive genes, to identify haplotypes, copy number variations and epigenetic profiles using the next generation sequencing technology and computational biology. Functional connectivity is examined in human and animal brains with powerful fMRI and diffusion tensor MRI revealing microscopic details about brain architecture, either in a normal or diseased state.
- In experimental animals, non-invasive optical methods are developed to turn on or off specific genes in discrete neural circuits. This optogenetic methodology is complemented by ligand-gated protein variants with customised binding sites that also can affect circuit activity. The generation of transgenic animals or lentiviral delivery of gene constructs is common practice. Electrophysiological approaches as well as multiphoton imaging and calcium imaging technology add to the study of circuit dynamics and synaptic plasticity.

Technical Application

Using these methods it becomes feasible to examine the circuits involved in the processing of arousing sensory information stemming from olfactory, auditory, gustatory, vestibular and visual inputs. The major ascending neurotransmitter pathways relaying and integrating sensory information into the arousal mode of the brain can also be monitored. These include the (nor)adrenergic, dopaminergic, serotonergic, cholinergic and histaminergic neurons that innervate specific brain regions involved in a variety of functions involved in emotional and cognitive processes, motivational aspects, executive operations and motor outputs. Then neuropeptides feed back, coordinate, synchronise and activate circuits underlying behavioural programmes. These neuropeptides include the opioids and

other melanocortins, vasopressin, oxytocin, orexins and a variety of other neuropeptide families capable of modulating and directing circuits underlying adaptation and energy allocation. On top of this, the 'classical' hormonal systems governed by metabolic, sex and stress hormones exert action that is capable of programming the brain during critical periods of development and operating as master-switches during behavioural adaptation, reproductive behaviour and energy metabolism.

Brain Organisation-the rich club

Using diffusion tensor imaging and a mathematical approach to profile complex networks in the brain, van den Heuvel and Sporns et al. (2011) discovered, using a top-down approach, that only a limited number of 'hubs' had wide control over the overall network organisation in the brain and called them the 'rich club'. These hubs include regions in the hippocampus, putamen and thalamus as well as the superior and parietal cortex and total about 12 hubs. They discovered that targeted attacks on these hubs had far greater impact on network efficiency than random attacks according to the mathematical model. Future studies might provide a clue to how stress and arousal affect these hubs in the connectome to provide clues on how these key regions might affect overall brain function. From the other end, using a bottom-up approach, computational models hold great promise as is highlighted in the Blue Brain project (Henry Markram) where, essentially, a brain is built from microscopic anatomy and modelled in a supercomputer to see what happens under certain conditions.

Conceptual advances

- Stress mediator signalling and susceptibility pathways

   o One major advance in understanding the arousal and stress system is the mechanistic underpinning of its regulations. The progress includes the identification of an increasing number of signalling cascades initiated from the actual receptor binding of the stress system mediators as well as their downstream non-genomic and genomic actions (Joëls and Baram, 2009). These signals operate in a complementary manner and in concert but each in their typical temporal, spatial and functional domains. It is now known that this cortisol action is mediated by two receptor systems, i.e., mineralocorticoid (MR) and glucocorticoid receptors that bind the hormone with differential affinity and that operate in a complementary fashion. The MR is important for threshold and sensitivity and, therefore, the onset of the stress reaction because activation of this receptor facilitates the appraisal processes of novel sensory information and cognitive flexibility. When the stress response develops, the rising cortisol levels activate the GR to terminate (dampen) the stress reaction and to promote recovery and storage of the experience in the memory; this favours behavioural adaptation (de Kloet et al. 2005).

   o Several hypotheses of psychiatric disorders have been developed based on dysregulations of the stress system. These hypotheses include the anxiogenic actions of CRH (Holsboer and Ising, 2011). Also, the glucocorticoid cascade hypothesis which states that the rising glucocorticoid levels due to chronic stress downregulate their glucocorticoid receptors (GR) leading to a vicious cycle that ultimately precipitates stress-related brain disorders (Sapolsky et al. 2000). We now know that in the limbic brain, the imbalance of MR and GR mediated actions is thought to enhance vulnerability (de Kloet et al. 2005). Such an imbalance may occur with genetic variants of the receptors or their co-regulators and chaperones such as the FKBP5 protein that were found to protect or enhance vulnerability, or due to epigenetic modification induced by environmental inputs.

   o The reactive alleles associated with emotional reactivity appear crucial for vulnerability and resilience to psychopathology of the programmed phenotype depending on adaptation to the environmental context the individual is facing in later life. A striking example is presented by the carriers of the short allele of the 5HT transporter which are more reactive to negative life experiences, but also to positive experiences, if compared with carriers of the long-allele (Lesch, 2007). Also BDNF variants have been associated with affective states (Pezawas et al. 2008), and recently MR variants were found to be associated with appraisal processes, dispositional optimism and protection against depression (Klok et al. 2005).

o Unbiased genomic approaches have identified susceptibility pathways linked to glutamatergic transmission and glucocorticoid actions. At the same time, candidate genes and their variants in the DA, NE and 5HT systems, as well as of neuropeptides and glucocorticoids, were identified as risk factors. Chronic stress and glucocorticoids downregulate BDNF in animal models of chronic stress and depression suggesting that this growth factor acts as a mediator of stress-induced changes in plasticity.

- Programming by (early) life experience and epigenetics.

  o A major advance is that an epigenetic mechanism is evolving that underlies programming of emotional and stress reactivity during critical times of brain development with lasting consequences over the life span. Epigenetic changes may involve DNA methylation, histone acetylation and phosphorylation, that in response to stress present also a novel candidate mechanism (Meaney 2010). The studies have demonstrated that stressful experiences during early life can remodel brain circuitry underlying emotional regulation. The outcome of early adversity can be modulated by maternal influences and frequently investigated models are animals that have experienced, as pups, reduced or fragmented maternal care. Such a period of early neglect enhances the pup's responsivity to adverse emotional experiences and was found to prematurely advance the development of emotional and fear circuitry involving cortisol and the locus coeruleus NE input (Sullivan and Holman, 2010).
  o An increasing number of studies highlight the impact of various contexts during early life, puberty and adulthood on the mechanism of resilience and vulnerability to psychiatric disorders. One hypothesis predicts that a mismatch between early life experiences and later life context enhances vulnerability to disease (Nederhof and Schmidt, 2012).

Conclusion

The adult brain shows plasticity in response to stressful experiences and we are beginning to understand its potential in terms of resilience and vulnerability to psychiatric disorders. During critical periods in development these mediators can modulate circuitry involved in regulation of emotional expressions and the stress response. Adaptations to the programmed emotional circuitry in later life may lead to resilience and vulnerability depending on environmental context and genetic background.

3.3.4.4. Comorbidity

General comments

- A recent review conducted as part of the World Psychiatric Association Action Plan 2008-2011 demonstrated 2-3 fold excess mortality in patients with severe mental disorders, compared with the general population.
- They found that the mortality gap was mainly due to physical illness and that this gap seems to have increased in recent decades, even in countries where the quality of the health care system is commonly recognised as being good (de Hert et al., 2011).
- Progress in understanding the human genome, and the increasing information about the role of epigenetic factors and mediators such as immunological and inflammatory factors in both mental and somatic disorders, indicates an opportunity for mental health research to focus on these common systemic elements of mental disorder pathology in the shaping of future new insights into the aetiology and pathophysiology of psychiatric disorders.

- Factors and theories used to explain comorbidity of mental disorders and somatic diseases include:
  o shared predispositions (genetic, temperamental and personality traits);
  o shared risk factors (stress, trauma, food intolerance, lifestyles, social support, negative emotions);

o shared mechanisms (coping, resilience or defence mechanisms, endocrine and immune disruption) (Jakovljević et al., 2010).

The anticipation is that a better understanding of psychiatric-somatic comorbidity in combination with increasingly advanced methods of neurobiological research will provide

- Descriptions of systemic clinical manifestations of psychiatric phenotypes.
- Sub (or even) endophenotypes for genetic research based on co-occurring somatic and psychiatric symptoms
- A better understanding of the biological patho-mechanisms of psychiatric disorders and somatic diseases
- Improved understanding of biological treatment mechanisms including their potential for harmful side-effects, and the detection of new targets for psychopharmacological treatment interventions.

The somatic comorbidity of schizophrenia and bipolar disorder

- It is commonly accepted that both schizophrenia and bipolar disorder patients have an increased risk of developing somatic diseases, and higher mortality rates in comparison with the general population (de Hert et al., 2011).
- A review including 15 original research articles on somatic co-morbidity in patients suffering from psychotic disorders concluded that these patients run a substantial risk of developing diabetes mellitus, metabolic syndrome, hypertension, cardiovascular diseases, lung diseases such as COPD, hypothyroidism and visual problems (Oud and Meyboom-de Jong, 2009).
- A recent population-based cohort study from Denmark investigating the impact of 19 severe chronic diseases on excess mortality due to diseases and medical conditions (natural death) in individuals with schizophrenia and bipolar disorder found that somatic diseases accounted for half of the excess mortality (Laursen et al 2011).
- Furthermore, almost all somatic, chronic disorders investigated in this study were more frequent in schizophrenia and bipolar disorder than in the general population.
- The only somatic disorders with a lower prevalence in psychotic patients were connective tissue diseases, mainly rheumatoid arthritis (with symptoms of musculoskeletal pain).
- According to a recent study comparing the prevalence of somatic comorbidity in a clinical sample of patients with bipolar disorder and schizophrenia, somatic comorbidity appears to be more frequent in bipolar disorder than in schizophrenia (67.1% vs. 50.6%). In this study, the three most prevalent somatic comorbidities in patients with bipolar disorders were cardiovascular (22.6%), endocrinological (22.6%), and gastrointestinal (16.4%) disorders while neurological (11.4%), gastrointestinal (10.9%) and endocrinological (9.3%) disorders were the most frequent in patients with schizophrenia (Oreški et al., 2012).
- Whereas rheumatoid arthritis is less prevalent in schizophrenia compared with the general population, this is not the case in bipolar disorder (Mors et al., 1999). Conversely, fibromyalgia is more prevalent in bipolar disorder but not in schizophrenia (Wilke et al, 2010). Some studies indicate cardiovascular disease is "truly" more prevalent in bipolar disorder, whereas in schizophrenia it is, most likely, secondary to atypical antipsychotic medications and smoking (Osby et al, 2001).

Physical health in patients with depressive disorders

- There is evidence that patients with affective disorders suffer from greater physical morbidity and mortality than the general population (Vieta & Colom, 2011). The mortality rate is approximately twice that of the general population with suicide mortality being up to 20 times higher (Osby et al., 2001). The relationship between affective disorders and physical illness is reciprocal: many chronic illnesses cause higher rates of depression and affective symptoms have been shown to be precursors of many chronic diseases and worsen their outcomes (Kupfer et al., 2012). People suffering from chronic illnesses are almost three times more likely to be depressed (Egede, 2007), and having two or more chronic illness increases the risk of being depressed up to seven times that of healthy subjects (3.2% vs 23%) (Moussavi et al., 2007). Moreover, depression is associated with a decrement in health significantly greater than that associated with other chronic diseases (Moussavi et al., 2007). This includes increasing illness-related morbidity and mortality, and

decrement in functional outcomes, such as disability and decline in health-related quality of life (Kupfer, 2012).

- Depression can also precede physical disease and act as a risk factor. It has been shown to act as a predictor of coronary heart disease (Kendler et al. 2009), stroke (Everson et al. 1998), obesity and metabolic syndrome (Luppino et al. 2010), diabetes (Campayo et al., 2010) colorectal cancer, back pain, irritable bowel syndrome, multiple sclerosis and infant stunting and death if depression occurs during pregnancy (Goldberg et al., 2010).
- The list of associations between affective disorders and physical illnesses is long and includes cardiovascular (e.g., hypertension, heart disease, stroke), metabolic and endocrinological (e.g., diabetes, metabolic syndrome), respiratory (e.g., asthma, chronic obstructive pulmonary disease) and gastrointestinal (e.g., peptic ulcer, liver disease, inflammatory bowel diseases) illnesses along with nephropathies, cancer, rheumatoid arthritis, migraine, HIV/AIDS, psoriasis, etc. (Moussavi et al., 2007; Krishnadas et al., 2012; Kupfer 2012; Leboyer et al., 2012).

The association between affective disorders and higher prevalence of physical morbidity and mortality can be explained partially considering health behaviours (e.g. smoking, physical inactivity, poor diet), psychosocial functioning and chronic medication exposure (Leboyer et al., 2012). However, this association remains significant after controlling for these confounding factors, which suggests additional and specific mechanisms (Leboyer et al., 2012).

Anxiety Disorders and physical Illness

- Comorbidity between anxiety disorders and physical illness is a limited but expanding area in scientific literature. Several studies relying on clinical or epidemiologic samples have shown higher rates of medical illnesses among patients with anxiety disorders compared with controls (Rogers et al., 1994). Clinical and community studies have also reported an association between physical illness and anxiety disorders as strong as or stronger than that with mood disorders (McWilliams, 2004).
- Studies examining associations with specific illnesses, such as thyroid disease, cancer, diabetes, cardiac disease, gastrointestinal disease, respiratory disease, and chronic pain, have found levels of anxiety disorders among patients seeking treatment for medical conditions to be higher than expected compared with the general population (Harter et al., 2003).
- Data on comorbidity, according to specific subtypes of anxiety and medical illness, reveal that the association is greater for panic disorder and generalised anxiety states than for phobias. Patients with panic disorder are more likely to have specific comorbid medical disorders such as angina, mitral valve prolapse, idiopathic cardiomyopathy, labile hypertension, respiratory illnesses, migraine headaches, peptic ulcer disease, diabetes mellitus, or thyroid disease (Rogers et al., 1994). With the publication of DSM-IV, individuals could receive a diagnosis of PTSD as a direct result of being traumatised by the experience of a life-threatening illness. This development has contributed to interest in the association between PTSD and physical illness. Among DSM-IV anxiety disorders, PTSD had the greatest number of significant associations with chronic physical disorders, including neurological, cardiovascular, gastrointestinal, metabolic/autoimmune, and bone or joint conditions (Sareen et al. 2005). Anxiety disorders are associated with physical illnesses, but the specific nature of these associations is largely unknown.

Alcohol use disorders and comorbid somatic disorders

- Clinical experience supports the evidence that somatic disorders are frequent in subjects with alcohol use disorders. However, depending on the sample investigated, the rates of somatic disorders as a consequence of chronic and pathological alcohol use vary. Further, since alcohol is widely distributed in the human body, several tissues and organ systems can be affected by the toxicity of alcohol. Most frequently investigated are alcohol-associated liver and pancreatic diseases, followed by malign tumours and disorders of the central and peripheral nervous system.
- Earlier epidemiological data of more than 10,000 inpatients from the U.S. demonstrated that more than 70% of the alcohol-dependent men and 73% of the women had a significant comorbid medical problem (Mendelsohn et al 1986). The most prevalent disorders among them were diseases of the liver, gallbladder

and pancreas; bronchitis; emphysema; and asthma. Hypertensive disease was found in 15% of the men and 7% of the women.

- Significant comorbidity was also detected in European samples. In alcohol-dependent subjects in inpatient detoxification treatment, a Polish study reported a rate of almost 44% of alcohol-related liver disease (Kroch et al 2004). Some 5.2% of the patients had pancreatitis and suffered from hepatitis B infection. Approximately 1/3 of the sample had diabetes and cardiovascular diseases. 55 patients (12.4%) had a history of severe head trauma, and 51 (11.3%) were treated for "multiorgan trauma". In addition, comorbidity of mental disorders was high. A total of 102 patients (23%) reported affective disorders, and in 92 (20.7%) personality disorders were diagnosed.

- These findings are paralleled by a study of German inpatients in an addiction treatment ward (Preuss et al 2012). In almost 500 subjects, equally high rates for alcohol-related liver (45%), stomach (19.3%) and pancreatic diseases (8.9%) were found. PNP and memory deficits were reported by 19% and 35% of the subjects, respectively.

- The individuals in this sample had a high rate of somatic illnesses before the onset of alcohol dependence. 13% reported arterial hypertension and 4-5% a liver or pancreatic disease that they already had before they started drinking frequently.

Taken together, rates of alcohol-related comorbid somatic disorders are high in subjects with alcohol-use disorders and range, dependent on setting and sample, between 30% to more than 70%. These somatic comorbidities include a wide range of diseases of the liver, pancreas, heart and the nervous system. However, the potential beneficial effect of treatment of comorbid somatic disorder on alcohol dependence treatment outcome, short- and long-term, is largely unknown.

Medication related somatic disorders

- Psychotropic drugs have been shown to compare favourably with medications used in other fields of medicine (Leucht et al., 2012). However, the optimal use of the psychotropics is often hampered by adverse effects, some of which can develop into treatment-emergent comorbid medical conditions. As opposed to psychopharmacology-associated acute medical reactions such as sudden cardiac death or malignant neuroleptic syndrome that are dramatic but rare, there are several delayed or chronic somatic disorders that are rather frequent. Examples include lithium-induced thyroid dysfunctions (Lazarus, 2009); valproate-associated hormonal dysregulations and the polycystic ovary syndrome (Hu et al., 2011); antipsychotic-induced weight gain, adverse metabolic influences (De Hert et al., 2009) hyperprolactinemia (Cookson et al., 2012) and movement disorders. The different somatic disorders are generally not restricted to one particular group of psychotropics. For example mood-stabilisers, antidepressants and antipsychotics all share propensities for inducing weight gain. This point is important as the concomitant use of several drugs is common in clinical practice, which increases the risk of additive or even potentiated adverse somatic effects.

- Metabolic drug effects have received particular attention in recent years as patients with severe mental disorders have a high degree of glucose and lipid regulation disturbances (Fleischhacker et al., 2008) believed to contribute significantly to a reduced life-expectancy of about 25 years compared to those in the general population (Tiihonen et al., 2009), and cardiovascular diseases account for the majority of these premature deaths (De Hert et al., 2009). Psychotropics, and antipsychotics in particular, are prone to adversely influence several of the components of metabolic health although the mechanisms are only partially understood.

- Differential propensities among antipsychotic drugs for inducing weight gain and other metabolic disturbances have been found in recent meta-analyses of clinical trials (Rummel-Kluge et al., 2010), with clozapine and olanzapine being the most prominent offenders.

- Although movement disorders have become much less of a clinical problem since the introduction of new generation antipsychotics, a certain risk of acute and tardive motor adverse effects remains. Of these, tardive dyskinesia is by far the most worrisome, as in contrast to acute dystonia, parkinsonism or akathisia, an appreciable percentage of tardive dyskinesia does not respond to treatment and may turn into a chronic comorbidity (Dayalu et al., 2008).

- Most of the adverse events exemplified above are relatively easy to either prevent or manage. A prerequisite to reduce the risk of psychotropic induced comorbidity therefore lies in the awareness of such side effects and the regular monitoring of a respective drug's safety and tolerability.

Conclusion

In summary, many physical disorders have been identified that are associated with severe mental health disorders and alcohol abuse, and medical disorders account for more than half of the excess mortality found in these patients. The increased somatic comorbidity is due to many factors such as side-effects of pharmacological treatment, unhealthy diet, and high levels of cigarette smoking, as well as inadequate medical treatment or provision of health care. However, a better understanding of comorbidity and multimorbidity also carries the potential of developing new insights into the biological underpinning of both psychiatric disorders and somatic diseases, and improving the treatment of these patients.

3.3.4.5.   Pharmacological Treatments, including Regulatory Aspects

Clinical psychopharmacology

- A corresponding treatment is selected after making a diagnosis based on observed behaviour and described symptoms, possibly with a view to tailoring the most probable side-effects to a patient's presentation (e.g., selecting a more sedating drug for a more agitated and anxious patient).
- Certain compounds are indicated for particular symptoms rather than diagnoses. For example, benzodiazepines are used for (short-term) treatment of anxiety and insomnia, in the context of many different diagnoses.
- Others are indicated for particular disorders, though frequently there is no one-to-one correspondence between disorder and drug response (e.g., the selective serotonin reuptake inhibitor (SSRI) antidepressants are effective in OCD as well as depression).
- Although developments in molecular biology and neuroimaging provide many candidate biomarkers which may be relevant to selecting treatment and predicting response, so far there are only a few circumstances in which biomarkers are clinically useful to the psychiatrist.

- Antidepressants
  - show efficacy relative to placebo in randomised controlled trials (RCTs) in both the acute and maintenance phases of depression. The size of this effect is larger in severe depression.
  - There is RCT evidence indicating that they reduce suicidal thoughts and behaviour, as well as epidemiological studies from a number of countries indicating reduced suicide rates with increased antidepressant prescription (Möller et al. 2012).
  - Indicated for conditions other than unipolar depression, including anxiety disorders, bipolar affective disorder (generally combined with a mood stabiliser) and neuropathic pain.
  - As well as increasing the activity of monoaminergic neurons, antidepressants have diverse effects on restoring neuronal plasticity and neurotransmission, including enhanced brain-derived neurotrophic factor (BDNF) expression and hippocampal neurogenesis (Baudry et al. 2011).

- Antipsychotics
  - show efficacy relative to placebo in RCTs in both the acute and maintenance phase of schizophrenia. They are also indicated in bipolar affective disorder and psychotic depression.
  - demonstrate strong effects in treating positive symptoms (hallucinations, delusions and thought disorder).
  - facilitate individuals with chronic mental illness to reside in the community rather than being institutionalised.

o the different side-effect profiles of the various antipsychotic drugs allow a degree of personalisation to a patient's specific presentation.

o as well as their effects at neurotransmitter receptors they induce molecular and structural changes, including protein phosphorylation, gene expression and neuroplasticity, which may be relevant to their therapeutic effects (Konradi and Heckers, 2001).

Drug development

- typically starts with the identification of ligands with a high affinity and selectivity for a molecular target associated with a neurotransmitter system thought to be involved in a disorder.
- Candidate compounds then screened in rodent behavioural assays.
- compounds demonstrating similar effects to a previously proven one may then be further developed as drugs of the same class.

Neurobiology

- functional neuroimaging has elucidated cerebral circuits underpinning mental processes disrupted in psychiatric disorders.
- the application of high-throughput genetic techniques has allowed genome-wide approaches to examine polymorphisms associated with psychopathology.
- The application of such techniques to traditional nosological entities such as schizophrenia has led to the discovery many associated genes of small effect. It is likely that such entities involve complex gene-gene and gene-environment interactions and, moreover, involve heterogeneous neurobiological processes and hence underlying genetics.
- current state of the art is exemplified by convergent approaches combining neuroimaging with genomics, clinical and neuropsychological testing and validation in relevant animal models. Such approaches probe multiple RDoC 'units of analysis' for each behaviour or psychopathology. Such a convergent approach harnesses the closer correspondence of genotype to brain function than to clinical diagnosis. It allows the investigation of the genetic and neurobiological underpinning of psychological traits and their value for predicting the development of mental disorders. Moreover, it has the potential to provide novel drug targets, particularly when coupled with a symptom cluster approach to psychopathology.

A translational approach based on symptom clusters

- This has the potential to inform more effective drug development as well as more personalised, effective treatment.
- Common factors, symptom clusters or endophenotypes can be discerned that are dysfunctional across different diagnostic categories.
- From knowledge of the biology of affect (negative and positive valence), arousal and regulatory systems, social processes and cognition, an alternative approach to drug discovery would therefore be to examine the neurobiology and pharmacology of the endophenotypes within these broad functional domains via translational neuroscience and experimental medicine.
- In essence, treatments might be developed for specific aspects of several diseases, rather than the unrealistic aim of finding a single treatment for complex multifactorial conditions. This also removes the equally unrealistic requirement for animal models to exhibit the full range of symptoms encompassed by ICD-10 diagnoses.
- The RDoC initiative provides a draft framework with which to classify psychopathology in terms of constructs that are more neurobiologically tractable than ICD-10 diagnoses.
- The abnormal must be understood in terms of anatomy, biochemistry, physiology and behaviour. In other words, the question is how genetics is expressed through these levels and interacts with the environment to produce phenotypes at the extremes of normally distributed characteristics.
- Animal models might be replaced by experimental manipulations such as
  o temporary pharmacological inactivation of certain brain regions ('circuits')

o local injection of pharmacologically specific agents to define the transmitter systems ('molecules')

o operating in those circuits an over and under-expression of genetic factors ('genes').

Biomarkers

- Definition: objectively measurable biological variables used as indicators of normal or abnormal biological processes.
- Typically, necessary steps in a cascade of changes which produces the symptoms of a disease.
- May be measured to predict disease events, prognosis or response to treatment.
- Some may be manipulated for therapeutic effect.
- Many biomarkers have the potential to be reverse translated, i.e., adapted from humans to animals. This allows more precise validation of animal models by ensuring they encompass precisely homologous aspects of disease aetiology, rather than simply an approximation of symptoms.
- Forward validation of novel biomarkers discovered in animals may lead to the discovery of entirely novel disease mechanisms.
- Biomarkers such as PET and SPECT receptor occupancy may be used to measure the engagement of a particular molecular target and inform dose selection as well as target validation.

Examples of the symptom cluster – biomarker approach

- Depression
  o Nutt et al. (2007) define different symptoms clusters within the depressions syndrome, symptoms of 'decreased positive affect', better treated with drugs that enhance noradrenergic and dopaminergic function, and symptoms of 'increased negative affect', which may be better treated with agents that have noradrenergic and serotonergic activity.
- Schizophrenia
  o symptom clusters include positive symptoms, negative symptoms and cognitive impairment.
  o Current antipsychotics are relatively ineffective for treating cognitive deficits which, to a varying degree, are a feature of many other psychiatric disorders.
  o Intense efforts are underway to develop new medications to address cognitive impairment, making use of new understanding at the molecular, cellular and circuit level. The cerebral circuits underlying cognitive function include loops between frontal lobes, basal ganglia and thalamus as well as structures underlying contextual memory and fear conditioning (hippocampal formation and amygdala) (Millan et al. 2012).
  o Biomarkers relevant to drug development include fMRI of defined brain regions to explore the actions of putative pro-cognitive agents and validate models. Other biomarkers include mismatch negativity (an EEG marker) and pre-pulse inhibition.
  o Behavioural characterisation of cognitive function requires batteries of tests measuring different cognitive domains, such as the CANTAB (Cambridge Neuropsychological Test Automated Battery).

This illustrates the approach of studying a complex construct at multiple unit of analysis including circuit, physiology and behaviour.

3.3.4.6. Systems for Social Processes

In progress

3.4.   Psychological Research and Treatments

3.4.1.   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 intervention 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), and 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 the 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 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 of understanding of behaviour change in the specific context of CBT**. In spite of high effectiveness and some progress in clinical psychology 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 EU countries, where and what kind of research and service delivery programmes 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:

- Reaching consensus on terminology and concepts. Consensus is currently lacking on 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 different countries.
- 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, evidenced-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.

3.4.1.1.   Definition of subareas

Initially, 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 aims 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 emerging findings on mental health. For the workpackage 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.

3.4.1.1.1.   The nature and definition of the term "psychological"

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

3.4.1.1.2.   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 intended 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, recognising though that doing so could be considered as an unduly restriction. It was nonetheless emphasised 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 due to their aetiology on one side and intervention on the other.

3.4.1.1.3.   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*: emphasising 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 put stronger emphasis on social systems perspectives.
- *Developmental pathway models:* It was emphasised that the development of functions and dysfunctions should be considered from a broader, novel, developmental and public health relevance approach that takes the traditional biomedical disease model as well as conventional

approaches of "personalised 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 emphasised.

- *Diagnostic and domain area perspective*: Similar to WP 4, 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 programme to investigate the basic and applied issues of what determines the human ability to change behaviour is of core relevance for treatment and prevention.

3.4.2. Systematic literature mapping

The primary research question underlying the systematic mapping was "What is the *status quo* of the research in Europe in the area of psychological research and treatment for mental health?" Secondary questions referred to the identification of the main topics, description of the nature of the evidence (i.e., disorder of interest, study designs, age groups), and mapping of the most important European research network and/or groups (countries) in which this research is done.

In WP5, the systematic literature mapping was originally intended to be based on two approaches, namely the common ROAMER methodology (searching PsycInfo, PubMed (Medline) and Web of Science) on the one hand, and on bibliometric analyses using InCites by Thomson Reuters (limited to Web of Science) on the other.

For both approaches, identification and extraction of work-package specific keywords (related to psychological research and treatment) was based on screening of the ERC Panel Structure and Keywords (consolidated version 7/11/06), NIH consensus documents from 2000 to 2012 as listed in web of science, Cochrane reviews (http://onlinelibrary.wiley.com/o/cochrane), subject categories of the Science Citation Index and the Social Science Citation Index, screening of MESH terms, and via expert suggestions.

Inclusion criteria across all databases were: articles published from 2007-01-01 to 2011-31-12, all languages, English abstract available.

The rationale behind the bilateral approach is to handle some of the challenges that arise from the ROAMER methodology in this work package such as a very large number of hits (PubMed Central N = 4,076, Web of Science N = 16,125 hits, PsycInfo N = 12,907 hits), which also include non-European authors, non-European source countries (such as the US), and difficulties of identifying and covering institutions due to multiple ways of abbreviating or denoting Universities. Hence, it appeared questionable whether the literature mapping according to the ROAMER methodology yields meaningful results; also, this approach was difficult to follow, given the extremely time-consuming but necessary screening of abstracts in spite of limited personal and financial resources of WP 5. Despite extensive personal efforts of WP 5 members and initiation of a collaboration with the Saxonian State and University Library Dresden (SLUB) at an early stage of phase 2 of the working process (February, 2012), bibliometric analyses via InCites by Thomson Reuters could not be realised as pricing was far beyond funding limits.

Table 6. Ranking of disorder categories by Web of Science, PsycInfo and PubMed Cental

	Web of Science (2012-08-27)		PsycInfo (2012-08-27)		PubMed Central (2012-08-28)	
total hits (N)	16125		12907		4076	
	1 affective disorders	13145	**1** affective disorders	6935	**1** schizophrenia and	747

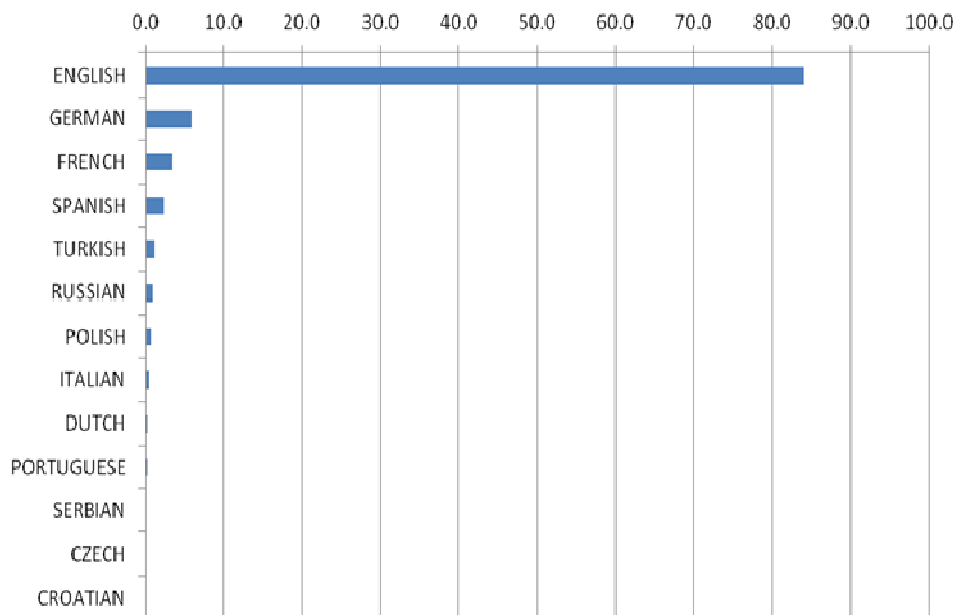| #			#			#		
							psychosis	
2	anxiety disorders	6051	**2**	disorders of childhood & adolescence	3581	**2**	affective disorders	590
3	disorders of childhood & adolescence	6041	**3**	anxiety disorders	3255	**3**	disorders of childhood & adolescence	550
4	schizophrenia and psychosis	4108	**4**	schizophrenia and psychosis	2874	**4**	anxiety disorders	325
5	substance use disorders	2656	**5**	substance use disorders	1660	**5**	substance use disorders	271
6	eating disorders	1206	**6**	eating disorders	673	**6**	somatoform disorders	229
7	somatoform disorders	850	**7**	somatoform disorders	397	**7**	eating disorders	41

As shown in Table 6, the number of hits ranges substantially across databases from 4,076 (PubMed Central) to 16,125 (Web of Science). Similarly, number of hits by disorder category and, accordingly, rank order for the top 3 positions varies by database despite identical keywords and search strings that were only adopted according the database specific requirements (i.e., search for TOPIC in Web of Science reflects search for Title or Abstract in PsycInfo). The differences may be attributable to differences in inclusion/exclusion criteria of the databases, mapping of psychology as the primary (PsycInfo) or secondary (Web of Science, PubMed Central) field of interest, journal coverage, indexing (Thesaurus) and update intervals. Web of Science was considered as the gold standard because of multidisciplinary coverage (spanning multiple academic disciplines such as the sciences, social sciences, arts, and humanities), and translation of original work into English title and abstract.

- Affective disorders yielded the most hits in two out of three databases, and somatoform and eating disorders the least across all databases. The most striking difference in **rank order of diagnostic categories** between the databases is the position of anxiety disorders, affective disorders, psychosis/schizophrenia and disorders of childhood and adolescence.
- About ¼ (PsycInfo) to ½ (Web of Science) of the records in the field of psychological research and treatment were dedicated to disorders in **childhood and adolescence**. This contrasts with recent reports suggesting that studies on children / adolescents are under-represented despite the rising needs in child and adolescent psychology/psychiatry (Costello et al., 2005; Kieling et al., 2011). Similarly, this can be expected for studies in the elderly (see sections 3.5.2, 3.6.2, and 3.7.2).

records by TOP 10 authors

Author	Records
VAN OS J	65
DE GRAAF R	59
CUIJPERS P	55
VERHULST FC	53
KIVIMAKI M	52
PETERMANN F	52
HARO JM	49
MOLLER HJ	48
VIETA E	46
LONNQVIST J	45
BEEKMAN ATF	40
ARANGO C	38
ORMEL J	38
WITTCHEN HU	38
HOFMAN A	36

records (%) by language

Language	%
ENGLISH	
GERMAN	
FRENCH	
SPANISH	
TURKISH	
RUSSIAN	
POLISH	
ITALIAN	
DUTCH	
PORTUGUESE	
SERBIAN	
CZECH	
CROATIAN	

records by Top 10 countries (affiliations)

records (%) by year of publication

Figure 13. Records from Web of Science by author, language, country and publication year (A-D, respectively)

- On visual inspection, the number of **publications by year** does not indicate notable tendencies or patterns. The overall rate appeared to slightly increase in 2011 relative to previous years. When considered separately by diagnostic categories, a similar picture is observed, with marginally increasing record rates for affective, child and substance use disorders in 2011 (Figure 14).

records (%) by year and diagnostic category
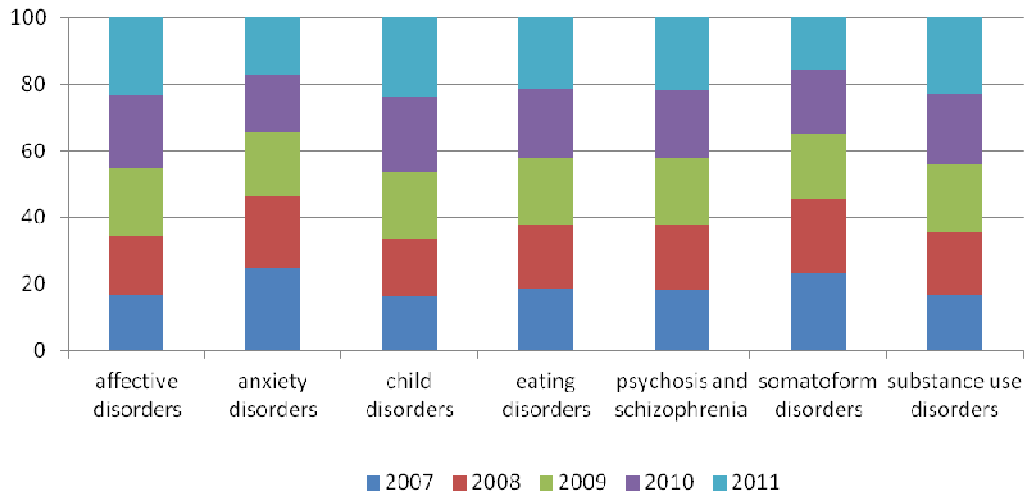
Figure 14. Publication rate by year and diagnostic category

- Further, the official **language for publications** in the field is English, followed by German and French. Native publications, particularly of Eastern Europe, are scarce, and thus, are also less likely to be heard about and to have an impact on the scientific community that is dominated by research(ers) from the UK, Germany, and the Netherlands.

records by Top 20 funding agencies
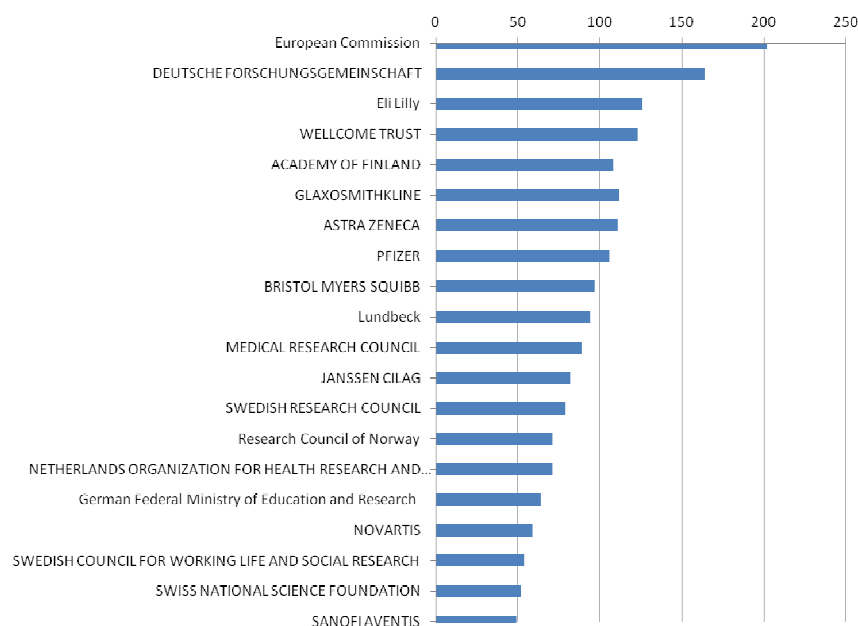
Figure 15. Records from Web of Science by Funding agencies

<u>Note:</u> European Commission incl European Union, EU, European Community, European Science Foundation

Deutsche Forschungsgemeinschaft incl Deutsche Forschungsgemeinschaft DFG, German Research Foundation, German Research Foundation DFG, DFG

Eli Lilly incl Lilly, Eli Lilly and Company

Glaxosmithkline incl GSK

Astra Zenca incl ASTRAZENECA

Pfizer incl Pfizer Foundation

Brystol Myers Squibb incl BMS

Lundbeck incl Lundbeck Foundation

Research Council of Norway incl Norwegian Research Council

Netherlands Organisation for Health Research and... incl NETHERLANDS ORGANISATION FOR HEALTH RESEARCH AND DEVELOPMENT, ZONMW, NETHERLANDS ORGANISATION FOR HEALTH RESEARCH AND DEVELOPMENT ZONMW

German Federal Ministry of Education and Research incl Federal Ministry of Education and Research, German Federal Ministry of Education and Research BMBF, German Federal Ministry for Education and Research BMBF, BMBF

- The role of funding agencies is difficult to evaluate reliably, because it cannot be determined whether the funding is related to the particular study (meeting inclusion criteria for the bibliometric analyses) or to the first or last author of the particular study (i.e., authors list grants as part of their conflict of interest statements). Also, different names for the same funding agencies (see note in Figure 15) may lead to underestimations of funding sources. Thus, in these analyses, institutions with the same title but different abbreviations, as well as institutions with full and abbreviated titles were lumped together. However, numbers (Figure 15) only refer to record counts and do not necessarily reflect the amount of money invested by these companies and institutions in research. Numbers may tentatively reflect the amount of original studies that may be funded.

- From that, 200/16,125 studies (1.2%) were based on EU-funding but the amount of funding from pharmaceutical companies (Ely Lilly, Glaxosmithkline, Astra, Pfizer, Brystol Myers Squibb, Lundbeck, Janssen, Novartis, Sanofi) exceeds this rate (836/16,125; 5.2%). Among the top 20 funding agencies, nine institutions are national agencies for which, usually, only researchers of the respective country can apply. When considering the list of authors and countries, one can easily see that records for authors or countries do not map onto records for funding despite the UK (England), Germany and the Netherlands holding the first positions.

- Despite the high publication output of Western and Central European countries, this may not necessarily reflect or correlate with a wide mental health care provision.

records by source titles

Figure 16. Records from Web of Science by Journals (source titles)

- Inspection of source titles (Figure 16) suggests that the majority of research is published in low to medium impact (ISE highly cited Impact factor) journals, which are very often allocated to the field of psychiatry. These findings may be attributable to the search strategies used for bibliometric analyses (i.e., using disorder categories) but also reflect the fact that research on psychology, and psychological treatments in general, is well documented in the field of psychiatry (Figure 17) though psychiatrists usually cite references from their own field (psychiatry) and less often from the field of psychology (Haslam and Lusher, 2011).
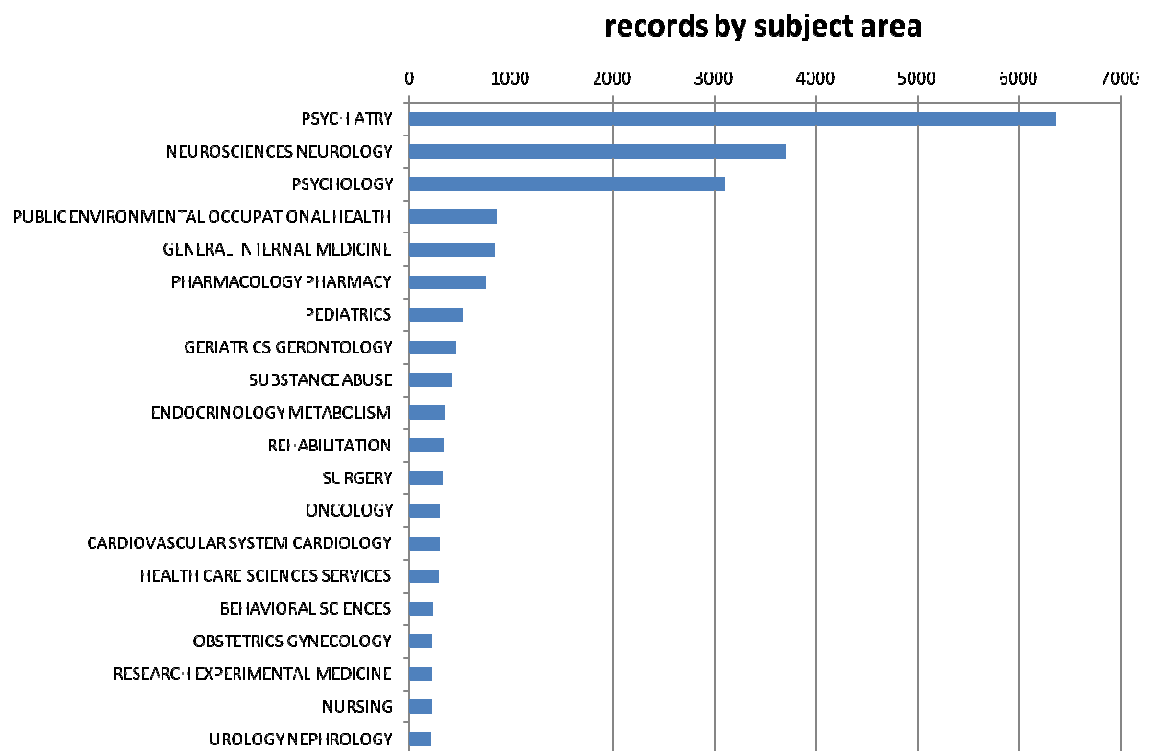
records by subject area

Figure 17. Records from Web of Science by subject areas

- Interestingly, though search strings were specified for the field of psychology, psychology itself only ranks #3 on the list of subject areas (Web of Science) after Psychiatry and the Neurosciences; which is concordant with bibliometric reports (Haslam and Lusher, 2011) indicating that these disciplines may collaborate and publish together, with psychology often referencing the other fields, but not vice versa.

3.4.3. State-of-the-art (main advances during the last 10 years)

The aim of the first scientific workshop was to map advances in the field during the last ten years, to identify gaps in current knowledge and to identify putative research topics in future mental health research in Europe. In preparation for the workshop, experts were asked to respond to a 10-question survey. Responses were collected and presented again at the workshop to clarify statements, to further map the current state of research and identify the main gaps in current knowledge. A summary of statements was then sent to experts via e-mail for final edits.

Putative research topics, and priorities of research will be developed in more detail in the second scientific workshop.

Successful efforts have been made in regard to mental health and mental disorders, the science of behaviour change, and in the fields of maintenance of mental health and treatment of mental disorders.

The WP5 has commissioned the following state of the art position papers.

0. Mental health and mental disorder research (introduction)
1. Arousal and stress: A Roadmap towards rational treatment of psychiatric disorders
Arousal and stress systems are crucial for resilience and health but if these systems are dysregulated the

vulnerability to psychiatric disorders is enhanced. In recent years, it is better understood how the mediators of these systems can change their action from protective to harmful. In addition to these novel insights into the action mechanism, it is also recognised that vulnerability and resilience are adaptations to the outcome of (adverse) experiences at critical times during brain development and maturation. At the root of this notion are newly discovered mechanisms explaining the interaction of experience-related factors with genetic and environmental inputs that underlie emotional expression and cognitive function for better and for worse. Here, a roadmap is presented that identifies major advances and gaps in our current knowledge and that highlights possible causal treatment strategies directed towards preventing the precipitation of psychiatric disorders or promoting mechanisms of resilience present in the diseased brain.

2. Negative and positive valence

Positive and negative valence are evolutionarily essential states underlying two opposing behavioural tendencies: approach and withdrawal. These two opposing ancestral behaviours guide an organism to emission of the necessary responses to search for life-supporting events and to avoid harm. Thus, they help with survival and evolution (Alcaro and Panksepp, 2011). Approach and withdrawal are also referred to as reward and punishment are highly conserved states common to vertebrates, reptile birds, amphibians and probably to other simpler species like invertebrates (Huber et al 2011; O'Connell and Hofmann 2011). Given the fundamental importance of reward and punishment-related behaviour, it is unsurprising that maladaptive forms of these traits are a pervasive component of psychopathology, most often associated with anxiety and mood disorders as well as substance and behavioural addictions.

3. Cognitive systems

A new approach to psychiatry in terms of neurocognitive systems is proposed which encompasses processes of perception, attention, working memory, long-term memory, executive functioning, decision-making, metacognition and social cognition. Critical techniques and conceptual approaches include sophisticated human neurophysiology, 'brain training', functional connectivity and neural network analysis, neurocomputation, mechanisms of neural plasticity and animal models. New psychological theory will reinvigorate neuroimaging approaches in all modalities and neuropsychopharmacological investigations. These approaches will enable the identification of biomarkers (or neurocognitive endophenotypes) to provide alternative, dimensional descriptions of neuropsychiatric endophenotypes. Such endophenotypes will allow more accurate mapping of genetics with neuropsychiatric phenotypes, the use of 'purer' (more homogeneous) populations for clinical trials, and the identification of vulnerabilities, and hence the possibility of early detection and early interventions or treatments for disorders such as schizophrenia and depression. Following a review of the current status of research in the field ('State of the Art') and recent advances ('Major Advances'), we identify specific issues in each of the main domains surveyed, as well as gaps and needs for future advances in this research area. The main problems posed in the European context are the need for collaborative research (i) to help compensate for the withdrawal of many pharmaceutical companies from the field and also (ii) to provide multi-disciplinary investigations in suitably large populations of patients with the major neuropsychiatric disorders to allow definitive phenotypic descriptions and the effective application of genomics.

4. Social processes

Human beings are an incredibly social species and, along with eusocial insects, engage in the largest cooperative living groups in the planet's history. Twin and family studies suggest that uniquely human characteristics such as empathy, altruism, sense of equity, love, and trust, are partially hardwired. The leap from twin studies to identifying specific genes engaging the social brain has occurred in the past decade, aided by deep insights accumulated about social behavior in lower mammals (Ebstein et al., 2010). Meanwhile, the neurobiological underpinnings of well-known psychosocial influences, such as interpersonal interactions with emotionally relevant Figures, are also beginning to be understood. Systems for Social Processes (SSP) refer to the intraindividual neurobiological and psychological systems and functions that 1) develop both prenatally and postnatally throughout the life of an individual, 2) prepare and set up individuals for social interaction and, 3) are directly relevant to support and promote development of mental health and well-being and causal understanding, clinical assessment, treatment and prevention of mental impairment. A clear theoretical delineation of SSP from systems of emotion, cognition and language is hardly possible and has to be done pragmatically. The social brain is the cortical and subcortical network of regions that underlies SSP. Its regions include ventral and medial prefrontal cortex, superior temporal gyrus, fusiform gyrus (FG), cingulate gyrus and amygdala, which are specialised to process social information such as the face, gaze, biological motion, human action, goal-directedness, theory of mind and empathy. Deficits in SSP, either alone or in interaction with cognitive, affective, and motor systems, are implicated in many psychiatric disorders

ranging from neurodevelopmental disorders such as autism, conduct disorder and schizophrenia, through anxiety and affective disorders to personality disorders.

5. Pharmacological Treatments

Since the development of effective treatments for mental disorders 60 years ago, further drug development has concentrated on animal models validated using drugs of known efficacy or relying on resemblance between animal behaviours and human psychiatric symptoms. These approaches have succeeded in improving the tolerability of the prototypical psychiatric drugs. However, recent years have been characterised by a paucity of novel drug treatments and reduced investment in their development, in spite of manifest unmet clinical needs. As we will point out, another promising approach is to consider compounds as treatments for specific symptoms or groups of symptoms ('symptom clusters'). When coupled with translational neuroscience (based on endophenotypes and intermediate phenotypes) such an approach has the potential to improve the discovery and validation of novel drug targets as well as providing biomarkers to stratify patients and conduct personalised psychiatry. The effective use of such strategies will require increased private-public collaboration and new regulatory frameworks. Here, we summarise some of these issues, point out gaps in current approaches and strategies required to address these. The issues are illustrated using the treatment of schizophrenia and depression as examples.

6. Dysfunctions of cognitive control and decision-making as transdiagnostic core mechanisms in mental disorders

Maladaptive decision-making and impaired volitional control over one's actions, thoughts, or emotions are core characteristics of many mental disorders such as addiction, eating disorders, depression, and anxiety disorders, which incur immense personal and societal costs (Wittchen, et al., 2011). Elucidating the underlying psychological and neurobiological processes and pathways of these disorders is a precondition for theory-based improvement of prevention and intervention, as well as for moving from symptom-based classifications towards disorder models based on underlying mechanisms (Maia & Frank, 2011; Morris & Cuthbert, 2012). Although, in the past two decades, substantial progress has been made in research on the neurocognitive basis of decision-making and cognitive control, to date this research has had relatively limited impact on mainstream theorising and classification of mental disorders.

7. Science of behavioural change – reinventing psychotherapy?

In progress

8. Psychological Models and Paradigms of Mental Disorders – Recent Evolution, Current Developments and Future Challenges

Psychological models of mental disorders guide research into factors that provoke and maintain mental disorders and interventions that reduce them by offering insight into formal, efficient and final explanations for disordered behaviour. In recent years, psychological models of specific mental disorder have been supplemented by transdiagnostic approaches. This development runs parallel to a general emphasis on a dimensional perspective of psychopathology. We anticipate that psychological interventions for mental disorders will increasingly target specific cognitive dysfunctions rather than symptom-based approaches to the treatment of mental disorders. We further argue that a dimensional perspective on mental disorders will necessitate the development of psychological paradigms that instantiate "weak" rather than "strong" situations and will require a multi-faceted assessment of the external validity of psychological paradigms for mental disorders. In terms of interventions, exciting progress is to be expected from psychopharmacological interventions that build on a further integration of an understanding of mental disorders based on translational research.

9. Psychotherapy in children and adolescents

Up to one third of children and adolescents develop mental health problems during their developmental years and a significant proportion of these youth are referred for psychological treatment. The purpose of the present "bird's eye" overview is to provide a picture of the current status of psychotherapy research in children and adolescents, thereby highlighting various directions for future studies: (a) an improvement of treatment outcome research by examining mediators, moderators, and effectiveness in everyday clinical practice of currently available 'evidence-based' psychotherapies; (2) the development of new and/or improved psychotherapeutic interventions on the basis of developmental psychopathology research; and (3) developmental neuroscience research to uncover aberrant brain processes in youth with mental health problems and to investigate their correction by means of psychotherapy. This research should have the ultimate goal of providing more effective psychological interventions to youth suffering from behavioural and emotional disorders.

10. E-health and innovation of mental health care

In order to contribute better to a reduction of the disease burden of mental disorders, psychotherapy research has to move from a narrow clinical focus on individual patients to more public health strategies and simpler, more cost-

effective treatments that can be applied. One important option is to focus on Internet-based treatments and e-mental health tools (e.g., to support "on time" clinical decision-making to prevent treatment failure or relapse). European researchers are dominant in this area and are at the frontline of new developments, but the US and Australia are getting stronger rapidly. In this field, three broad research areas can be distinguished: research on how to apply the knowledge in mental health care that Internet-based treatments are efficacious; further development of existing Internet-based treatments; and the use of technological innovations, such as a move to the mobile phone, serious gaming, and the use of Avatars. All this will lead us to more information, not only about the common and specific effects of psychological treatments, but also about the question of how much therapy for whom in which setting is necessary.

11. Comorbidity of mental and somatic disorders (includes conceptual issues, emerging clinical trends and perspectives in mental disorder comorbidity, and comorbidity of mental and somatic conditions)
In progress
12. Critical aspects in structuring resources in the EU
The reintegration of former "Eastern European" countries into the European Union is in progress. When planning investment, administrative measures and activities which may improve mental health in Europe, the differences within Europe, including geographical, financial and organisational differences should be taken into consideration. There is a tradition in mental health research in "Eastern Europe" with an available educated workforce. A significant new investment is in progress in Prague, and strong basic neuroscience is present in some centres. However, effects of stigma surrounding mental disorders heavily affect decision-making, provision of national funds, disinvestment and instability of research structures. With the communication revolution, fast-emerging technologies can bring researchers from various European regions together in a highly efficient, inexpensive and mutually beneficial way. There is, however, a notable risk in that a substantial portion of the talent and research capacity of the "New Union" will link up and integrate into external (non-European, e.g., North-American and Asian) research hubs.
13. Epilog
in progress

3.4.3.1.   Mental health and mental disorders

There was general agreement about the substantial progress made in the Psychological Sciences as well as some major gaps and possible future issues. Some of these elements discussed converge with conclusions made in the draft chapter of WP4. There was also substantial agreement about definitions, core constructs and deficits. Consensus highlights are, at this point:

- Growing understanding of multiple developmental pathways in psychological and neurobiological terms and methods leading to mental disorders
- Advances in the understanding of how family and molecular genetic factors as well as socio-environmental factors act as vulnerability factors
- Growing synergies between psychological and neurobiological approaches to understand the dynamic and plastic nature of mental disorders
- Emphasis on continuity, and discontinuity, between optimal (normal) and non-optimal (psychological) functioning psychopathology
- Improved models of normal, abnormal and clinically relevant fear and anxiety and improved understanding of related disorders incl. cognitive, neural, and behavioural underpinnings via psychological paradigms in combination with genetic fMRI (fear circuitry disorders)
- Improved knowledge of the mechanisms of action of cognitive-behavioural treatment approaches such as exposure techniques. New perspective on prevention and targeted early prevention for anxiety, substance use disorders and depression
- The assumption that health and illness are two independent dimensions allows study of the interaction between them, and not only to measure them but also to address both illness and health specifically (Linden 2012). There are probably many forms of health.
- The development and tests of models and treatments for personality disorders, somatoform and sexual disorders, psychosis

- The revitalisation of epidemiology in schizophrenia or "psychotic experiences"; for example, the range of prevalence rates observed in Scandinavian register studies pointed to the role of social environment factors (taking into account that many studies refer to "psychotic experiences" rather than to schizophrenia, which are a quite common experience in the population)
- Models for fear, anxiety and phobia lead to understanding of related disorders including cognitive, neural, and behavioural underpinnings; vice versa, successful treatment approaches such as exposure techniques fed this knowledge
- Convincing evidence that depression and suicidality can be prevented (up to population-based levels)
- The use of psychological theories to understand and treat mental health problems, to guide research, to delineate treatment; nonetheless, substrates can still be biological
- The understanding of the putative difference between a biomedical approach (looking for substrates) and - more genuine - psychological approach (looking for functions)
- The growing understanding that there is a continuity, not discontinuity, between optimal (normal) and non-optimal (psychopathological) functioning and that psychological functions must be the basis of understanding psychological dysfunction (pathology), which implies that we must change to a multi-dimensional system of diagnosing and abandon the present categorical system

3.4.3.2. The science of behaviour and behaviour change

Efforts have been made in regard to

- the understanding of different functions in infant communication and their development
- Improved understanding of processes involved in emotional memory change (usually in fear)
- Increasing research on mediators, moderators and mechanisms of change
- the use of neuroimaging techniques to examine biomedical vs. psychological models of behaviour
- establishment of different paradigms and perspectives

3.4.3.3. The maintenance of mental health and the field of treatment of mental disorders

Efforts have been made in regard to

- the standardisation of treatment concepts and guidelines for specific disorders
- the development and establishment of cognitive-behavioural therapies which has led to an evidence-based attitude to psychotherapy in general
- the shift from paradigms like psychoanalysis, family or systematic (psychotherapeutic orientations)
- the finding of non-differences between different psychotherapeutic orientations may be due to patient variables (fast- vs. slow- vs. non-responders); this may also apply to psychopharmacology and other fields
- research on outcomes management and feedback into clinical practice and process research
- research on process variables (courses of treatment/continuity) combined with adherence/compliance issues
- the development of online supported treatments and examination of the role of new technologies such as smart phones, web applications, ecological momentary assessments for designing interventions to change behaviour
- Launch of several initiatives in recent years
    o WHO mental health GAP Action Programme Intervention Guide to support the implementation of treatment for mental, neurological, and substance-use disorders in primary care health settings (2010)
    o Grand Challenges of Mental Health initiative to support a new generation of research (Collins et al., 2011)

3.5.   Social and economic issues

3.5.1. 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, stigmatising 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 designed that 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.

3.5.1.1.   Definition of subareas

Work package six 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 the impact of both mental illness and positive mental health.

Research topics which will be investigated by work package six including:
- 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.

3.5.2. Systematic literature mapping

The overall objective of the systematic mapping exercise is to map the current state of the art of social and economic issues for mental health and well-being in Europe. For this review, we performed two separate searches, one specific to social exclusion and one specific to economics. Data for each research topic were analysed separately, but overlapping studies were discussed and we maintained consistency of search methods and inclusion / exclusion study criteria across both research topics. Below, we discuss the objectives, methods used, search strategy and initial findings for each of the systematic mapping exercises.

3.5.2.1. Research questions

Primary research questions:
- Where (i.e., which countries and European centres) is research on social exclusion in relation to mental health and well-being being performed?
- Where (i.e., which countries and European centres) is research on economics in relation to mental health and well-being being performed?

Secondary questions:
- What is the nature of the research on social exclusion in relation to mental health and well-being in Europe (i.e., methodology, type of disorder, age groups)
- What is the nature of the research on economics in relation to mental health and well-being in Europe (i.e., methodology, type of disorder, age groups)
- What are the main research topics in relation to research on social exclusion and mental health and well-being in Europe?
- What are the main research topics in relation to research on economics and mental health and well-being in Europe?

3.5.2.2. Research methods

Medline and PsycINFO databases were searched using the ROAMER search terms for mental illness and well-being (in the title or abstract) and search terms for social exclusion and / or economics (in the title or abstract) (See annex II for search terms used). The social exclusion search terms were based on Challenges in Multidisciplinary Systematic Reviewing: A Study on Social Exclusion and Mental Health Policy which covered the years 1948-2003 (Curran et al., 2007). We focused on subsequent years (2007-2012) and also modified the search terms based on feedback from the Roamer workshop expert participants. The ROAMER search terms for countries were not used as this did not appear to be a valid way of identifying geographic region when piloting the initial search strategies. Thus, inclusion / exclusion of geographic region associated with the article was performed for each individual article.

3.5.2.3.1. Inclusion / exclusion criteria

Studies had to be published in peer-reviewed journals between 2007 and 2012 and include an English language abstract. The paper had to be an empirical paper (and/or methods advancement paper in the case of economic research) and include an abstract. Review papers were excluded. The research must have been performed in a European Union country (including EU-27 countries, EU Candidate and Accession countries and countries in the European Economic Area) or the first author or corresponding author must be based at an EU institution. With regard

to study outcomes, articles were included if one or more of the primary outcomes was related to mental illness, well-being or social exclusion. Articles which simply performed an evaluation of psychological or pharmacological treatments were noted but excluded from detailed analysis unless the treatments included a social care component or measured an outcome related to social exclusion (e.g., related to stigma, human rights or an outcome which was closely related to social exclusion such as social relations, social functioning or employment). Articles which investigated outcomes solely in relation to e.g., clinical symptoms or continuity of care were excluded, although studies recording the costs and or resource use associated with poor mental health were included in the economic review.

3.5.2.3.2.   Selection of studies

Two reviewers independently considered whether each abstract met the inclusion criteria. Full papers would also be examined subsequently to ensure that each paper met the inclusion criteria, with disparities in inclusion decisions being resolved through discussion. Reviewers did not contribute to inclusion decisions regarding studies in which they were involved.

For the literature mapping reviews for both social exclusion and economics, two authors independently screened the initial 200 articles (10%). Agreement for study exclusion between the two authors was 93% and 85% respectively, thus the remaining 1,800 articles were divided between the reviewers. Reference Manager (Social Exclusion) and Endnote (Economics) were used to store all selected studies and export relevant information into an excel database.

3.5.2.3.   Results

3.5.2.3.1.   Results of Social exclusion literature mapping

The search on September 4, 2012 resulted in 11,078 articles from Medline and 16,047 articles from PsycINFO. When duplicates were removed, this resulted in 20,122 references. These references were supplemented by recent systematic reviews of research related to social exclusion and mental health (Clement et al., 2011; Weiss, 2008). Of the total references, 2,000 were randomly selected for review and data extraction. 1,680 articles (84%) were excluded and 320 (17%) were included.

Reasons for exclusion included:

- The paper was not published in a peer-reviewed journal: 0.1%
- The paper did not include an English language abstract: 0%
- The paper was not an empirical paper: 6.3%
- The paper did not include an abstract: 0.9%
- The paper was a review paper: 7.4%
- The research was not performed in a European Union country or the first author or corresponding author was not based at an EU institution: 72.8%
- Primary study outcome was not related to mental illness, well-being or social exclusion or the study simply performed an evaluation of psychological or pharmacological treatments: 11.1 %

3.5.2.3.1.1.   Geographic region

To answer the primary research question: Where (i.e., which countries and European centres) is research on social exclusion in relation to mental health and well-being performed, articles were categorised both by geographic region of the corresponding author and research setting. Specifically, each included reference was coded based on the city and country in which the corresponding author was based. Additionally, articles were categorised by the type of centre (i.e., hospital, university, research centre or other) and the name of the centre in which the research took place. Finally, the country(s) in which the research took place was also categorised.

The majority of studies took place in the United Kingdom (16%), followed by the Netherlands, Norway, Spain (8%), Sweden and Turkey (7%). About 8% of published studies included a sample outside of Europe. The distribution of countries in which the corresponding author resided closely mirrored those of where the research took place (See Figure 18) with the United Kingdom (21%), Netherlands (9%), Spain (8%), Norway, Sweden and Turkey (7%) holding the additional top six places. Studies were dispersed across cities, but most research was associated with large capital cities with the top 6 cities being: London (1.5%), Oslo (0.7%), Helsinki (0.6%), Barcelona and Madrid (0.5%). In terms of research centres, most research relating to social exclusion and stigma took place in a university setting (66%). Nineteen, fourteen and two percent of research took place in a research centre, hospital or other type of setting, respectively.
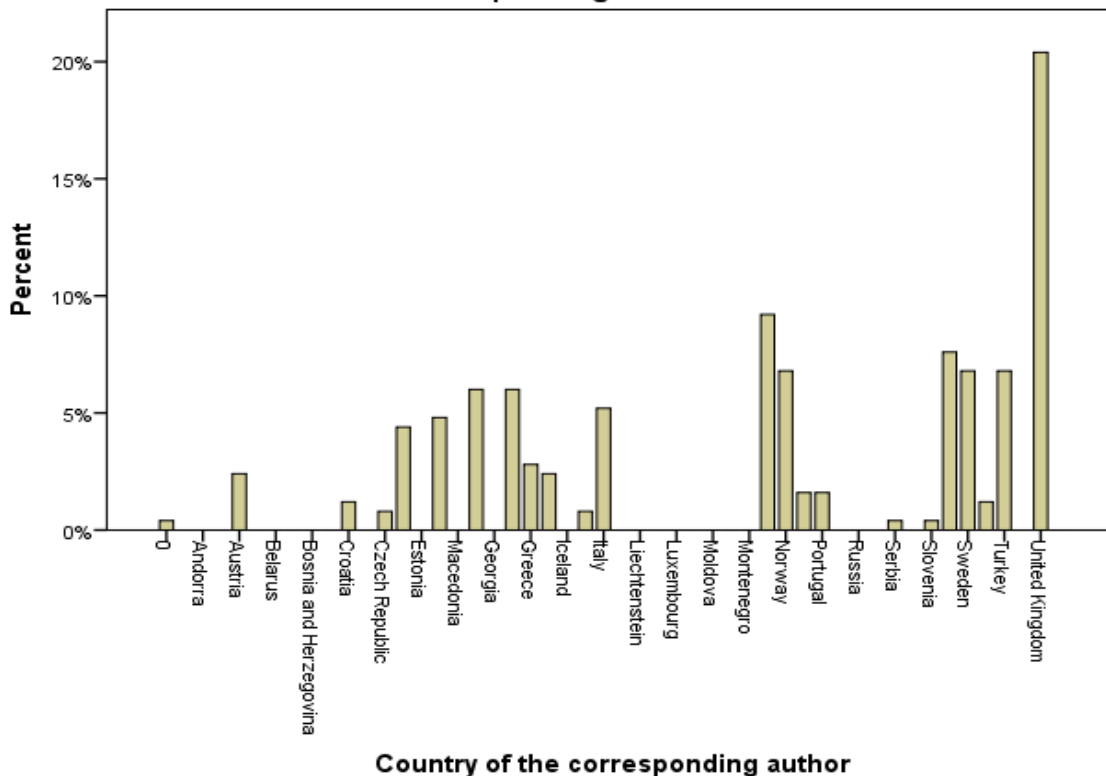

Figure 18.   Distribution of published stigma and social exclusion articles by country of corresponding author

3.5.2.3.1.2.   Type and nature of research performed

To answer the secondary research questions: (i) What is the nature of the research on social exclusion in relation to mental health and well-being in Europe (i.e., methodology, type of disorder, age groups) and (ii) What are the main research topics in relation to research on social exclusion and mental health and well-being in Europe, we characterised the study sample and type of research. In terms of sociodemographic characteristics, we investigated representation of gender and age groups in the included studies. The majority of studies were performed among adults (55%) and included unspecified (57%) or both genders 36%. Further information on the distribution of gender and age of study participants is included in tables 7 and 8. In terms of clinical or mental-health related characteristics, most studies focused on depressive disorders (13%), unspecified mental illness (12%), common mental disorders (11%), schizophrenia (10%) or comorbid mental health problems (10%). Other disorders represented less than 5% of published papers (See Table 9). In terms of the type or nature of research published, most studies focused on: detection, screening or diagnosis (41%), underpinning research (26%), evaluation of treatments and interventions (12%), health and social care research (12%), while other types of research represented less than 5% of studies (See Table 10).

Table 7. Distribution of gender of study participants for studies on social exclusion in relation to mental illness and well-being

Gender	Percent
Male only	2%
Female only	5%
Both genders	36%
Unspecified	57%

Table 8. Distribution of age of study participants for studies on social exclusion in relation to mental illness and well-being

Age	Percent
Children	4%
Adolescents	6%
Children and adolescents	1%
Adults	55%

Elderly	7%
More than one age group	21%
Unspecified	21%

Table 9. Distribution of mental health characteristics of study participants for studies on social exclusion in relation to mental illness and well-being

Type of mental health problem	Percent
Anxiety	3%
Autism and neurodevelopmental disorders	2%
Bipolar	2%
Common mental disorders	11%
Depressive disorders	13%
Dementia	3%
Dissociative disorders	
Disruptive, impulse control and conduct disorders	2%
Eating disorder	2%
Mental retardation	1%
Mental capacity	1%
Personality disorders	1%
Schizophrenia and non-affective psychosis	10%
Sexual dysfunctions	0.5%
Somatic symptom disorders	1%
Substance abuse and addictive disorders	4%
Trauma and stress related disorders	3%
More than one disorder/comorbidity	15%
Other or unspecified	22%

Table 10. Distribution of study type* categories specific to studies on social exclusion in relation to mental illness and well-being

Type of study	Percent
Underpinning research	26%
Aetiology	2%
Prevention of Disease and Conditions, and Promotion of Well-Being	5%
Detection, Screening and Diagnosis	41%
Development of Treatments and Therapeutic Interventions	3%
Evaluation of Treatments and Therapeutic Interventions	12%
Management of Diseases and Conditions	<1%
Health and Social Care Services Research	12%

*Based on the Health Research Classification System of the UK Clinical Research Collaboration, 2009

3.5.2.3.2. Results of Economics literature mapping

The search performed in October, 2012 resulted in 10,098 articles from Medline and 7,845 articles from PsycINFO. These references were supplemented by recent systematic reviews of research related to economics of mental health and hand searches of some key journals. The research results reported here concern only papers identified from the Medline review. Of the Medline reference, 2,000 were randomly selected for review and data extraction. 1,810 articles (91%) were excluded and 190 (9%) were included.

3.5.2.3.2.1. Geographic region

As with the review on social exclusion, we recorded the geographic region of the corresponding author and research setting. Specifically, each included reference was coded based on the city and country in which the corresponding author was based. Additionally, articles were categorised by the type of centre (i.e., hospital, university, research centre or other) and the name of the centre in which the research took place. Finally, the country(s) in which the research took place was also categorised.

The majority of studies had corresponding authors based in the United Kingdom (44%), followed by the Netherlands and Sweden (each 9%), Spain (7%), Germany (6%), France (4%) and Ireland, Denmark and Finland (each 3%). (See

Figure 19). In terms of countries covered, several studies covered multiple countries, including one that covered all countries in the EU. Several studies were conducted by European authors but were focused on countries outside our area of study, including one covering many of the excluded countries of the former Yugoslavia. Other studies looked at the US, and a number at Asian and Sub-Saharan, African countries.

The distribution of single country studies very closely resembled those of the corresponding authors.
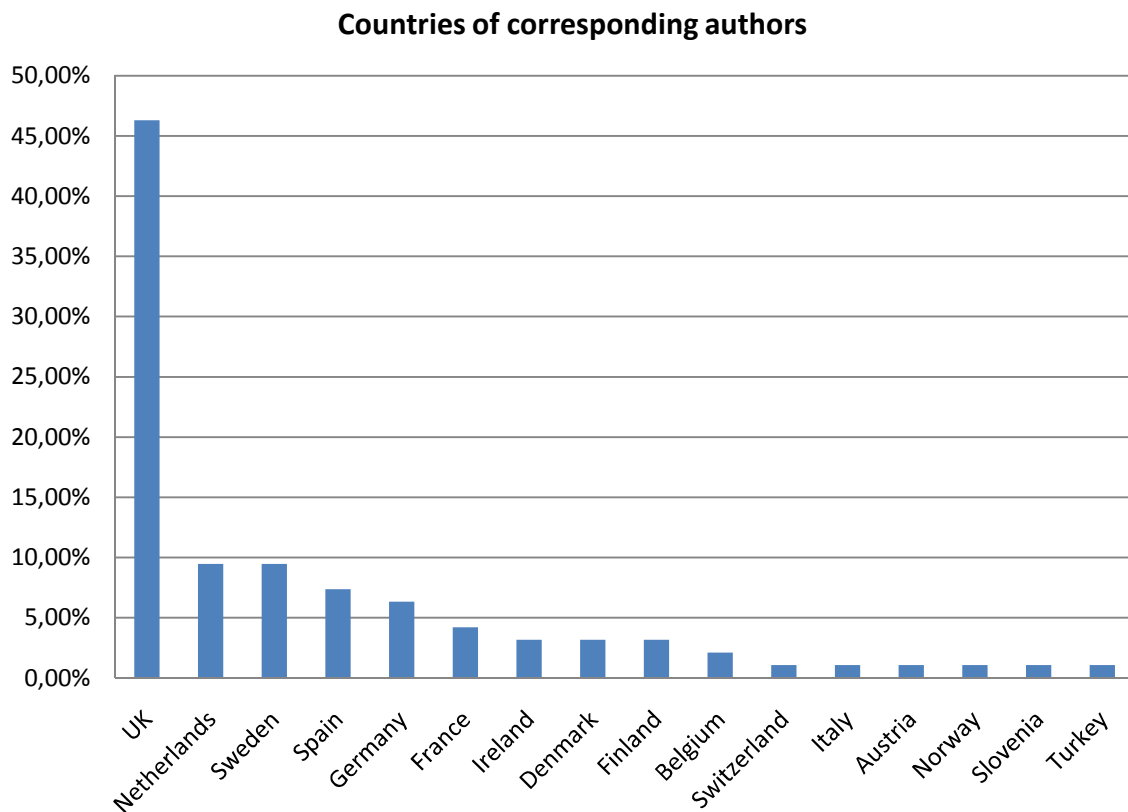
Figure 19. Countries of corresponding authors of economic studies

We also looked at the breakdown of cities and research centres where economic analysis was coordinated. There was a significant concentration of work in the UK in a small number of centres in England, predominantly based in London.

3.5.2.3.2.2.   Type and nature of research performed

In terms of types of research centres Figure 20 shows a breakdown by types of institution by corresponding author. Almost half of all papers were produced in university setting medical departments, with a further 18% led by health economics or health management units in universities. 9% were produced within university departments of psychology and 8% led by specialist consultancy firms.

Figure 20. Type of institution of corresponding author

As with the research on social exclusion, we also sought to answer initial secondary research questions on the type of research currently being conducted in terms o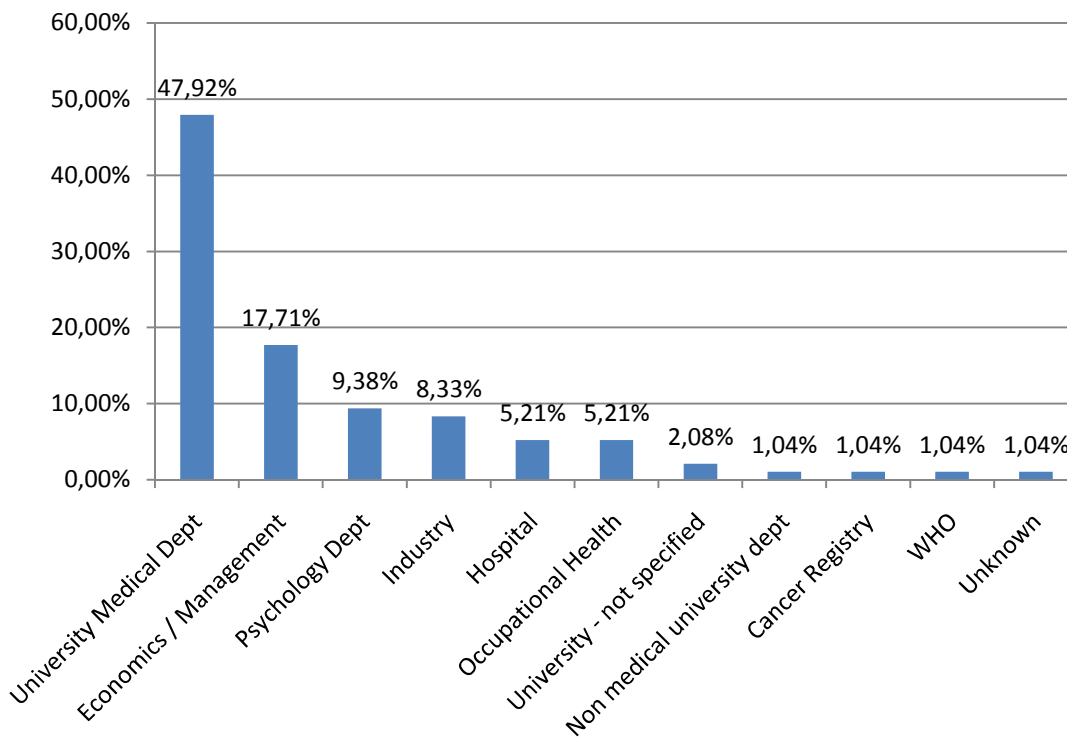f methodologies, mental health problems and age groups, as well as key research topics. The majority of studies did not specify an age range in their abstracts, while 12% had a focus on children and/or adolescents; 18% on people of working age and 12% on older people. Very few studies were gender specific in this mapping sample with just 2% focused solely on men or women.

Table 11 provides information on the broad clinical or mental-health related characteristics of the economic studies. Most studies focused on depression (26%), anxiety (14%), schizophrenia and non-affective psychoses (15%), and dementia (8%). 11% of studies focused on economic aspects of co-morbid physical and mental health problems. 19% of studies did not specify the mental health problem examined while 3% focused on psychological health and wellbeing.

Table 11. Distribution of mental health characteristics of study participants for studies on economics, mental health problems and well-being

Type of mental health problem	Percent
Anxiety	14%
Autism and neurodevelopmental disorders	2%
Bipolar	2%
Common mental disorders	1%

Depressive disorders	26%
Dementia	8%
Dissociative disorders	
Disruptive, impulse control and conduct disorders	7%
Eating disorder	2%
Learning disabilities	1%
Phobias	3%
Personality disorders	3%
Schizophrenia and non-affective psychosis	15%
Sexual dysfunctions	
Somatic symptom disorders	
Substance abuse and addictive disorders	4%
Stress and burnout	3%
Trauma and stress related disorders	2%
More than one disorder/comorbidity	
Psychological health and wellbeing	3%
Other or unspecified	19%
Physical health problem co-morbidity	11%

Looking now at trends in economic analysis performed, Figure 21 provides a breakdown of the main methodologies used. All types of economic evaluation synthesising cost and outcome data dominate studies, although there is only limited information within abstracts to determine which specific type of economic evaluation method has been used. Studies looking at the costs of poor mental health account for one quarter of all studies, while 20% of studies identified in the sample look at the impact of financial shocks and/or economic recession on mental health. We were also able to identify a small number of studies that look specifically at the economic impact of social exclusion and or stigma, as well as the cost effectiveness of measures to tackle this issue. Approximately one third of all economic evaluations identified made use of a modelling approach to determining cost effectiveness of interventions, with remaining studies linked to empirical studies. 23% of all studies were linked to randomised controlled trials. We also included study protocols in our analysis in our sample for 2012; they now account for 11% of all studies found. We also looked at the settings in which mental health issues were being examined; where settings were specified, community and primary care settings were most commonly mentioned (26%) with 6% of studies set in workplaces and 4% in schools. 10% of studies were concerned with the economic evaluation of pharmaceuticals.
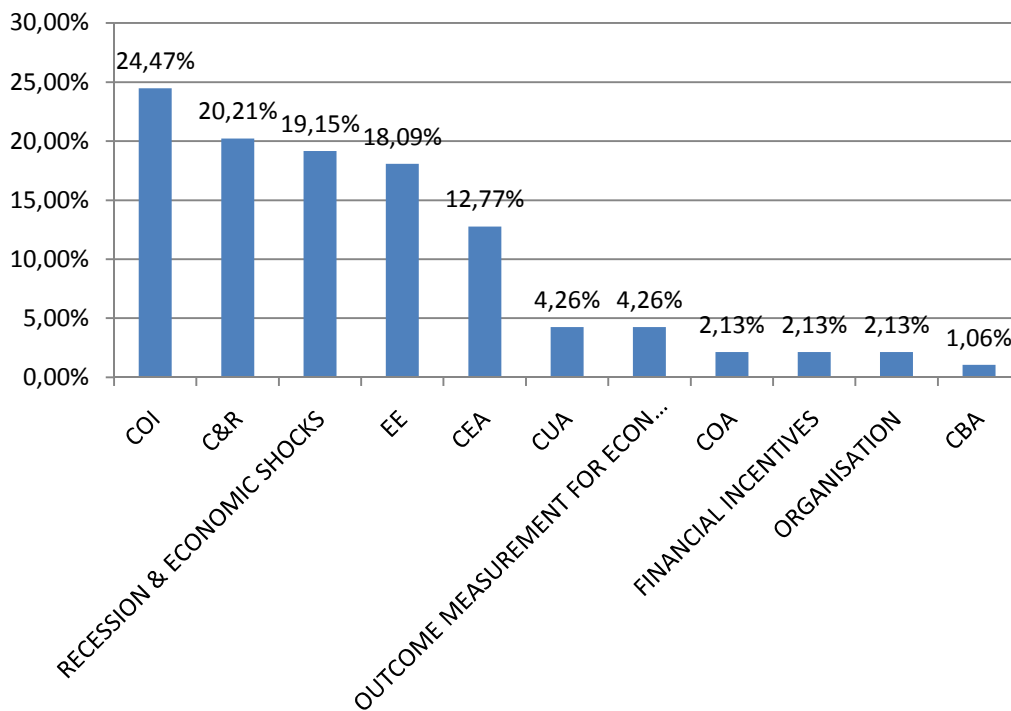
Figure 21. Breakdown of types of economic study conducted

3.5.3. State-of-the-art (main advances during the last 10 years)

In this section we highlight some of the conclusions that were drawn out of our first expert workshop. We summarise these separately for the two themes of this work-package.

3.5.3.1. Social exclusion and stigma

Advances			
Users' involvement	*Paradigm shifts*	*Definition and measurement*	*Practice and intervention*
- Stigmatised persons are now considered as subjects, and must take an active role in fighting stigma - User involvement in anti-stigma research - User/survivor-controlled research	- Mental health problems have been treated as health problems in recent years - Stigma research is connected to suicide prevention, primary care and public health research -Development of disability rights and gender perspective Shift of paradigm in	- Improvement in diversity of the definition of "stigma" and recognition of the overlap in concepts - Recognition that stigma and mental illness are dynamic and accounting for this in models and theories of stigma - Better understanding of the different paradigms of stigma and rejection of the invalid paradigms	-Importance of working with small groups of similar people (focused work) and of social contact -Effectiveness of anti-stigma campaigns and possible improvements -Stigma is now on the research agenda -Interventions (like suicide prevention) can help to reduce stigma -Evidence-based

disability research (individual shortcoming to collective shortcoming, research on individual budgets)	- Social stigma and social exclusion have many facets and affect every area in which an individual functions - Stigma has changed in the past years (more focus on relationships, drugs side-effects) - Distinction between self-stigma, anticipated discrimination - A lot of attention in research has been devoted to recovery - Development of a number of surveys on stigma and attitudes to mental health - Relation between stigma and suicide - Connection between social exclusion, stigmatisation and human rights - Improved understanding of the full picture of social exclusion (intergenerational transmission, importance of early intervention)	practices in IPS and ACT – focus on quality of life -Development of early intervention teams -Policy makers have linked stigma with other aspects of health (e.g., health inequalities) -Development and use of internet and social media -Difference between expressed attitudes and realised behaviours -Stigma in the areas of work and employment (importance of supported employment)

3.5.3.2. The role and use of economics in mental-health related research.

A summary of the wide ranging discussion and key points that were raised during the first scientific workshop with respect to economics are included below. These points have been loosely separated into issues around evaluation and analysis; methodological developments and implementation.

3.5.3.2.1. Evaluations and analysis

Economic evaluations in the area of mental health continue to grow and they have moved beyond analysis solely of pharmaceutical therapies.

One key advance in **some EU countries has been in producing estimates of the economic impacts of poor mental health in childhood and across the life course**. The UK and the Netherlands in particular have been at the forefront of much of this work. It was highlighted that this analysis has been broad, increasingly looking at impacts beyond the health system, such as in schools, workplaces and in the criminal justice system. All of this analysis has been helped by the availability of longitudinal cohort datasets.

More generally, the last decade has seen the **emergence of economic studies looking at the economic benefits of prevention of mental health problems** and, more recently, **an interest in the economics of wellbeing**, or what was coined by one participant as '**mental fitness'**. Among prevention strategies, the effectiveness of screening for mental health problems is an important question. There is no international professional consensus that general screening for depression proves effective (WHO, EU) but there is enough evidence that some countries produced national recommendations on screening for depression although only as a supportive measure in holistic management (UK, US). We know already that a lot of resources are used for screening of depression in primary care (i.e., PHQ and other questionnaires), but we do not know about the effects or side-effects of these screenings – whether this has its place in a stepped care approach or not and whether it proves to be efficient.

There is also an **increasing interest in, and emergence of, literature on the short, mid- and long-term economic benefits of early interventions for the treatment and prevention of mental health problems**, particularly focused on children and young adults. Again, this analysis has gone beyond health outcomes to look at impacts in employment, housing and physical health.

There is emerging **economic literature on investment in some psychological interventions**. Economic analysis has looked at their role not just in treating poor mental health, but also in promoting better mental fitness.

An emerging area where evaluation is underway concerns **e-health, m-health and other technological innovations** that may be a complement or alternative to face-to-face services. Economic circumstances have increased interest in funders in this area and some economic analyses have been built into funding for trials. These interventions potentially may be a cost effective way of engaging with hard-to-reach populations. Examples to tackle some of the high levels of absenteeism and withdrawal from the labour force include economic evaluations of new on-line approaches to preventing burnout, stress and anxiety disorders. Other examples includes studies looking at the role these types of interventions can play in protecting the mental health of people living with physical health problems.

There is also an **emerging economic evidence base now on the consequences of poor mental health in workplaces** from different perspectives: public purse, employee and employer.
The beginnings of the emergence of **studies looking at different aspects of co-morbidity between mental and physical health.**

3.5.3.2.2.   Methodological developments

Developments in the use of **modelling techniques, alongside data from clinical trials, in some countries** to estimate the mid- to long-term consequences of investment in mental health.

Development **of techniques to estimate the costs of resources for mental health and the costs of scaling up interventions** – with reference made to recent work on this topic for countries outside Europe at the World Health Organisation in Geneva. It was also noted that there have been developments in our understanding of how to look at the **socio-economic determinants of equality and inequity in mental health**, e.g., the recent work of Wilkinson and Pickett. There is also ongoing methodological work to **develop more appropriate mental health outcome measures** for use in economic analysis, e.g., for children and adolescents, but also with respect to adult mental health problems.

3.5.3.2.3.   Implementation developments

Use at regional and national policy-making level in some EU countries of economic arguments to support the case for investing resources in mental health. Some economic arguments have been particularly powerful and have **resonated** with policy makers, e.g., on promoting the mental health and wellbeing of children and young people.

Inclusion of economic arguments in discussions and strategy documents at EU level on mental health. Moreover, at a global level, economic arguments are also being advanced to invest in more resources in mental health.

Clear indications in some EU counties **that further economic evidence is being demanded to inform the decision-making process**. This is part of a formal health technology assessment process in a few countries, e.g., NICE in England where economic analysis of treatments, prevention and promotion actions have been undertaken to inform national guidelines.

3.6. Public health research

3.6.1. 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 needed 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 to 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 is 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 smart, sustainable and inclusive growth in the EU. Particular focus will be on how public health research can address the situation of 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 WP 7 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.

3.6.1.1. Definition of subareas

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

3.6.1.1.1. 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 of the workforce, novel health technologies, as well as the relationship 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 population 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 the use of novel and alternative approaches to psychiatric phenotypes. Crucial building blocks in epidemiological research will be common European mental health surveys and improved co-ordinated use of existing national health registers.

3.6.1.1.2. 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 of the workforce, novel health technologies, as well as relationship between users and professional carers and issues around governance and accountability.

3.6.1.1.3. 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.

3.6.1.1.4. 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.

3.6.1.1.5. 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 successful policies will be provided.

3.6.2. Systematic literature mapping

3.6.2.1.   Objectives

The overall objective was to review the current state of public health research in Europe regarding mental health and well-being, covering five research areas; epidemiology, health services research, promotion, prevention and policy analysis.

The research questions were as follows:

Primary research question:
1. What public health research on mental health and well-being is currently conducted in Europe within the five selected research areas?

Secondary research questions:
2. What kind of research is conducted (i.e., study design and research methodology)?
3. Where and by whom is this research being conducted (i.e., European research networks and groups)?
4. Are there any research gaps in these five research areas?

3.6.2.2.   Methods

The reviewing technique used for this review is systematic mapping (Clapton et al., 2009). Systematic mapping is a transparent technique for describing research literature on a broad topic. The overall aim with the technique is to create a broad overview of any research field to provide knowledge of the current situation, as well as guidelines and suggestions for future actions and development.

Types of studies and research

- Only research conducted in Europe was considered in this review.
- The included research should have a public health perspective (as defined by the *SPHERE* Project (Strengthening Public Health Research in Europe; Clarke et al., 2007).
- The included studies should primarily target mental health or mental disorders. Studies targeting mental health aspects of physical conditions (such as psychological distress associated with chronic physical illness) were included in the review if the mental health aspects are the main focus of the study in question.
- Only research conducted within the time period 2007-present (May, 2012) was included in the systematic mapping.

Electronic searches

Study identification from electronic databases included the following:

1. CINAHL
2. Health Management
3. Medline
4. PsycINFO
5. Social Services Abstracts

These databases were together regarded as most suitable for mapping the public mental health research area due to the many scientific disciplines that they represent.

No language restrictions were applied within the limitations of the search tools.

Search strategies

Structure of the search strategies used:

- Search terms for mental health and mental well-being, mental ill-health and mental disorders
- Search terms for public health research
- Search terms for Europe

The search strategies were individually designed for each applied database. Detailed search profiles can be found in annex III.

Data collection

The references retrieved from the search strategies described above were all processed in a specially designed software programme designed to automatically categorise and code the data based on the reference information generated from the databases (e.g., title and keywords of publication, author information, abstract). Ten per cent of the retrieved data will also be manually coded by an independent researcher in order to measure the accuracy of the automatic coding.

Data extraction and management

The retrieved publications were screened and data extracted and categorised by targeting the following:

1. First author/corresponding author of the publication
2. Country of the corresponding author
3. City of the corresponding author
4. Affiliation of the corresponding author (research centre)
5. Year of publication
6. Journal of publication
7. Title of publication
8. Keywords of publication
9. Public mental health research area (which of the five research areas?)
10. Country of study sample
11. Age group of study sample
12. Gender of study sample
13. Measurements of mental health (mental health content)

3.6.2.3. Results from the systematic mapping

The data material retrieved from the electronic searches (Figure 22) was preliminary analysed by using a software programme especially designed for the systematic mapping of WP 7. The programme automatically extracted the identified publications as described above and categorised them according to the five research areas to enable comparisons within the data material. Below, a few Figures are presented and discussed to provide an overview of the findings from the systematic mapping.
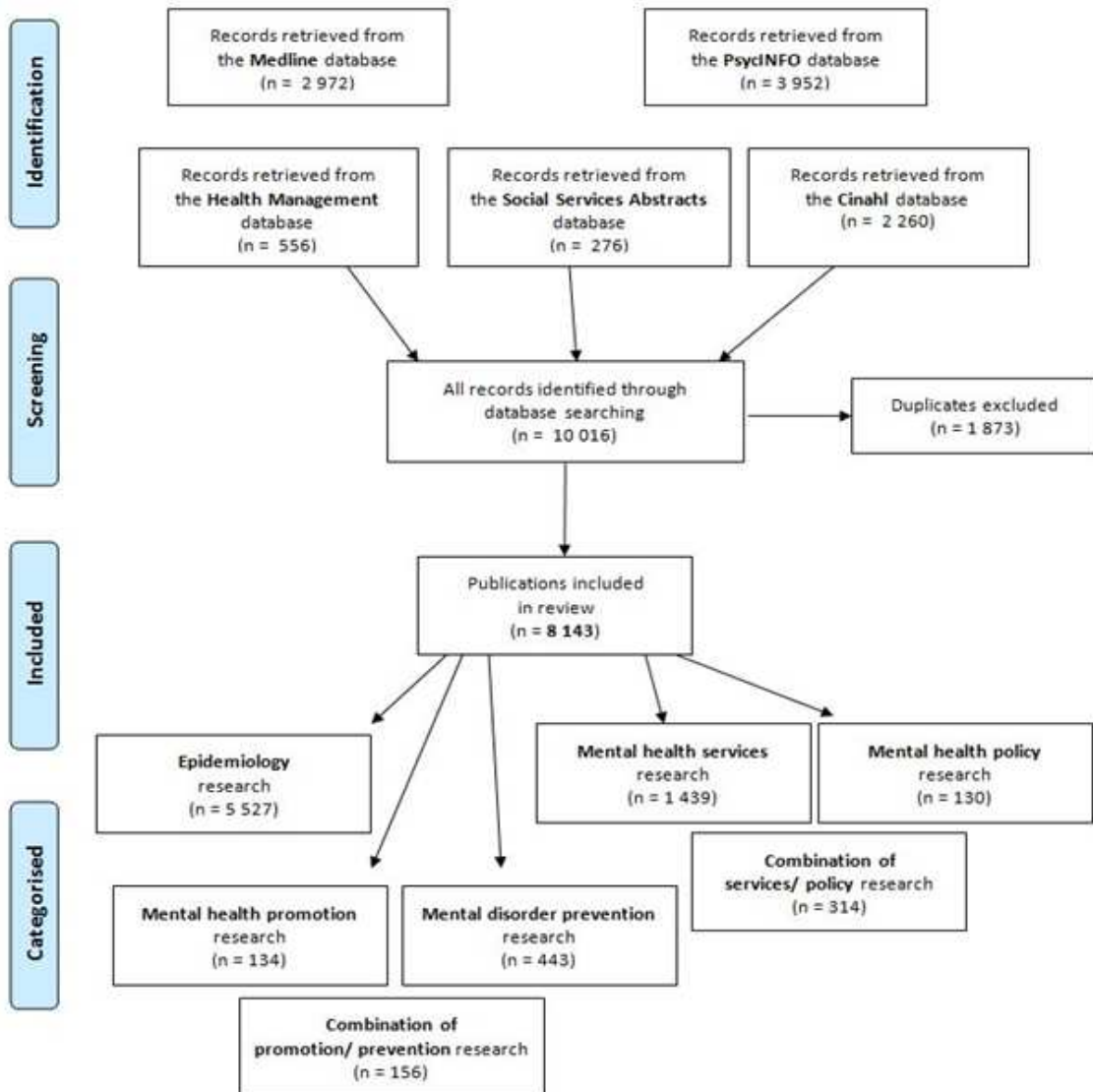
Figure 22. Flow chart of the identified and screened records obtained from the electronic searches.

The searches in the five literature databases provided 10,016 records in total. After exclusion of duplicates the number of identified records for automatic screening and categorising were reduced to 8,143. Most of these could be automatically categorised into one of the five research areas (n = 7,643). 500 references were manually coded into one of the five research areas or into the categories of combining promotion and prevention or mental health services and policy research.

According to the automatic coding conducted by the software programme used, epidemiology research dominated the data material (5,527 records), followed by mental health services research (1,439 records). 443 records were coded into the mental disorder prevention category, while 134 and 130 records were defined as mental health promotion and mental health policy research, respectively. The category encompassing research that focuses on both promotion and prevention in the mental health field consists of 156 references, while the combination of mental health services and policy research contains 314 references. The distribution of the publications according to research area was stable over the five-year time period (Figure 23).

Based on the distribution of records according to research areas, it is evident that European public mental health research focuses on occurrence and distribution of mental disorders and service provision. Such research is often based on the medical paradigm. In comparison, rather few records were found in the field of mental health promotion, which is often set in a positive mental health framework. However, the share of mental health promotion research seems to be increasing over time (Fig. 23).
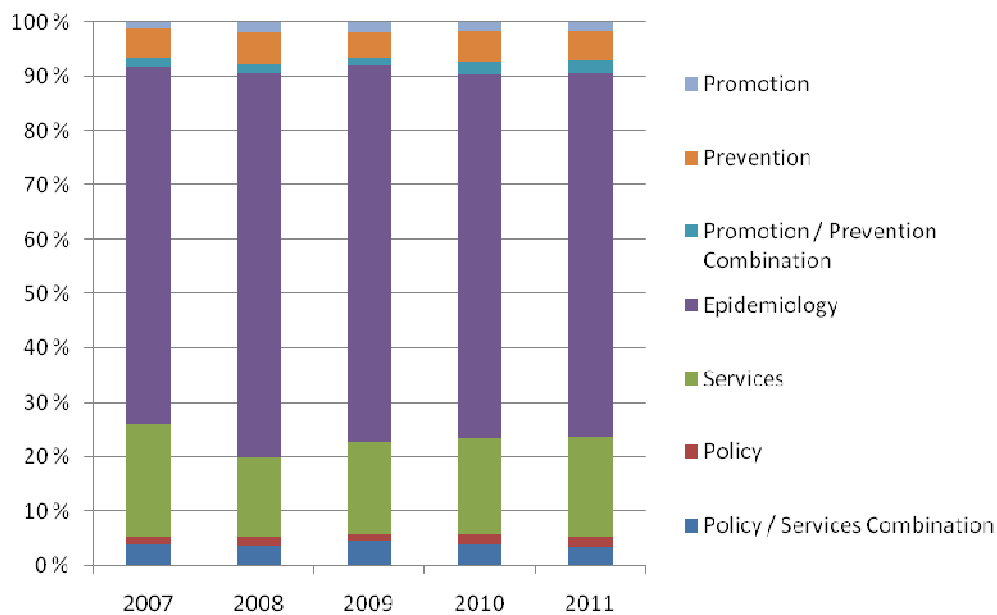

Figure 23.   The distribution of publications by the five research areas during the time period of 2007 to 2011.

All retrieved records were also coded by the targeted age group. The alternatives were: Children and adolescents, adults, older adults, more than one defined age group, and age group unspecified. The analysis found that a majority of the research conducted focused on children and adolescents (approx. 25 %), while publications targeting older people were clearly under-represented (7 %). However, it should also be noted that nearly half of the screened records were not possible to categorise into one of the specific age-group categories, but targeted a general population with various age groups represented. This might also explain the small amount of studies that could be categorised as specifically targeting adults in our material, as working-age adults often are the majority in many of the studies targeting unspecified age groups. On the other hand, it is noteworthy that although older adults represent 17% of the European population, they are the target group in less than 10 % of the records screened in our material.

Looking at the targeted age groups within the five public mental health research areas (Figure 24), it was found that the youngest age groups were frequently represented across the different areas. Children and adolescents were the focus to a large extent within mental health promotion and mental health disorder prevention research especially, reflecting the need for early preventive measures. On the other hand, the categories of unspecified or mixed age groups were dominant within mental health services and policy research.
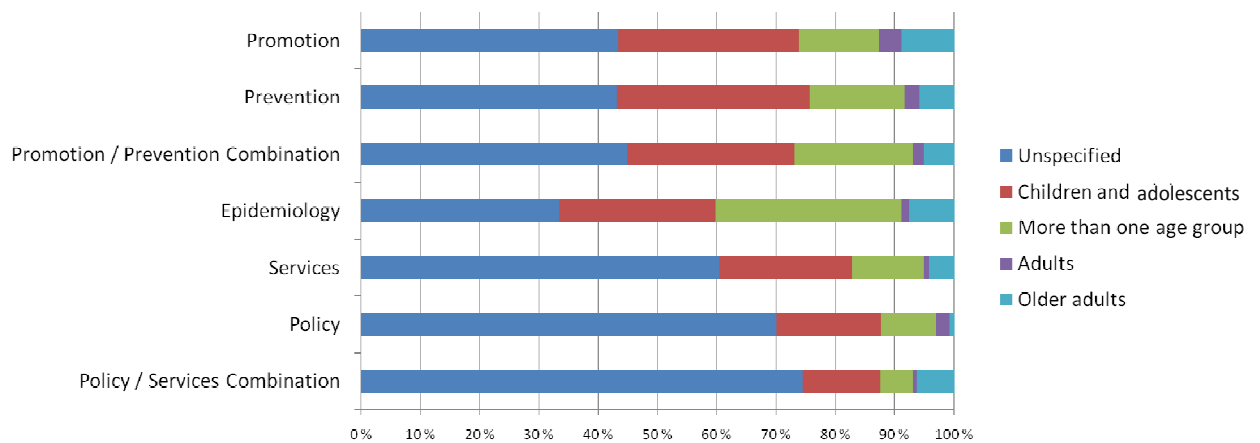
Figure 24. Age groups targeted in public mental health research in Europe by public health research area (2007-2012).

Public health research is, by definition, targeting the population at large. It is thus not surprising that specific terms and diagnoses of mental health disorders were not focused on (Figure 25). Instead, general mental health status or other specific determinants of mental health or mental ill-health were used to a great extent in the studies considered, such as various measures of distress, satisfaction or quality of life.
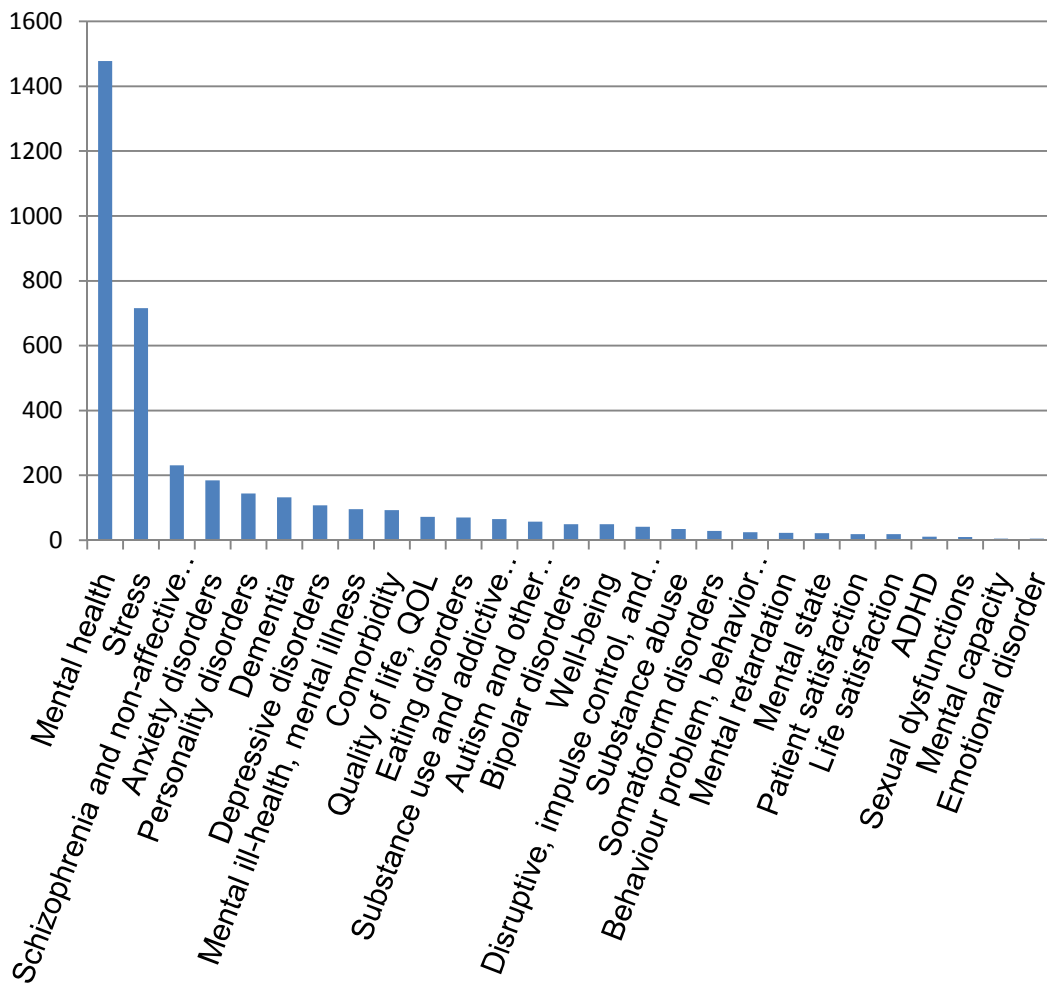
Figure 25. Measurements of mental health used in the screened publications.

Besides looking at the distribution of records according to publication year and age groups within the five public mental health research areas, the distribution of research by European country was also studied in the preliminary analyses. Out of 8,143 records that were retrieved from the five databases searched, 3,752 records could be automatically assigned to a specific European country, if based on the affiliation of the first author. When looking at country sample, 4,495 records could be allocated to one or several specific European countries. The number of publications from each European country was summarised and then weighted by the population size of each considered country to obtain an index indicating the proportion of publications for each country for the five-year time period (Figure 26). When taking the population size into account in the analyses, it was found that the Nordic countries were ranked highly compared to other European countries, looking at the number of research publications. Ireland, the Netherlands and the United Kingdom were also high on the list. Based on the analyses, public mental health research is a currently a matter primarily of the affluent Northwest Europe, and major efforts will be needed to support and promote public mental health research in Southern and Eastern Europe.
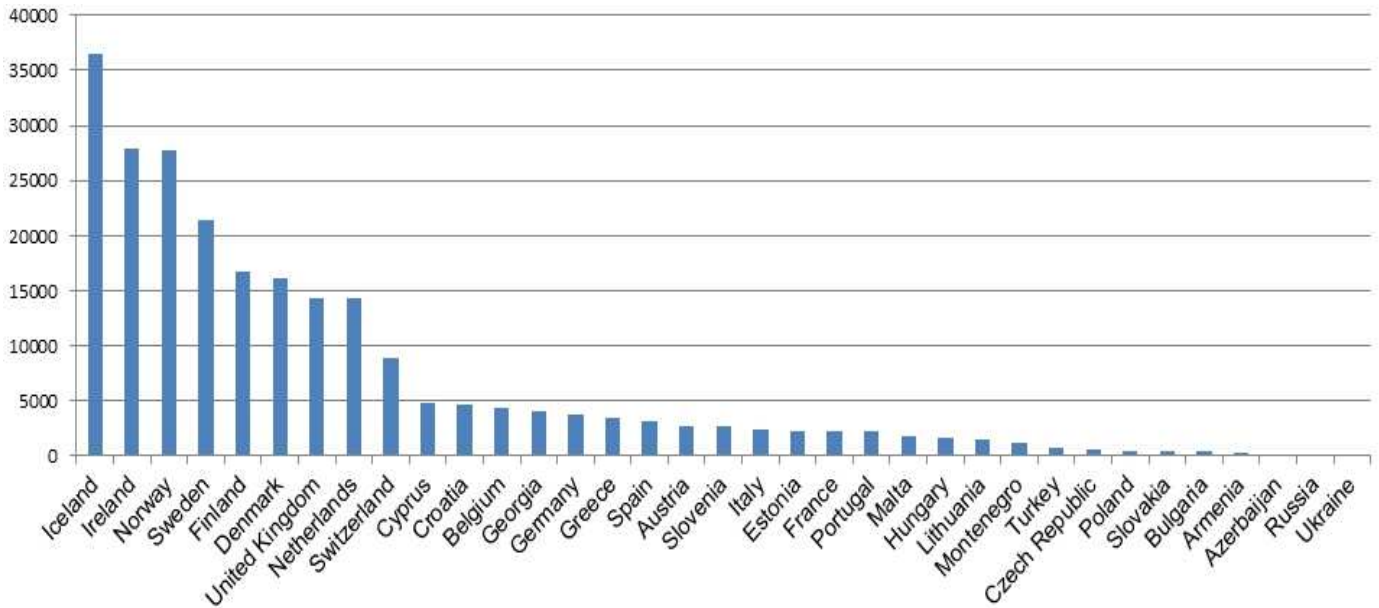
Figure 26. ***Distribution of public mental health publications by European country, weighted by population size (based on first author affiliation).***

In addition to listing the most active European countries within the public mental health research field, the active research institutes were also mapped looking at the number of published publications retrieved from any of the five literature databases for the studied time period (Figure 27). This data was retrieved with the help of the software programme that automatically screens the first author affiliation, in addition to the abstract and listed keywords, of each publication.
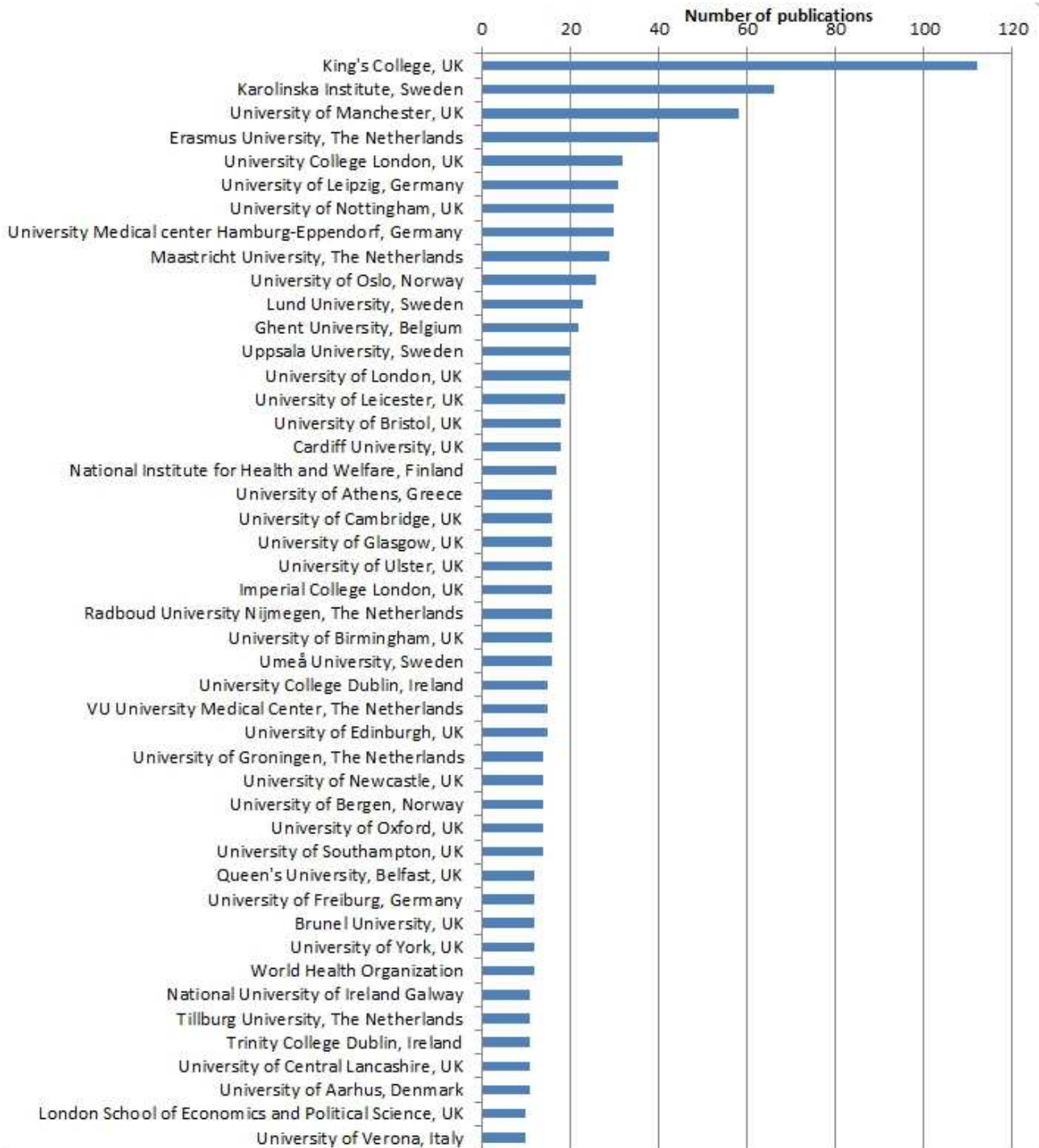
Figure 27. The most active European research centres/institutes in public mental health research (2007-2012).

3.6.3. State-of-the-art (main advances during the last 10 years)

3.6.3.1.   Mental health promotion research

- Mental health promotion has been included in the broader health agenda. There is wider acknowledgement of the concept of mental health promotion, which is linked to the development of the concept of positive mental health. For example, promotion probably would not have been an area in the ROAMER project 10 years ago.
- Greater understanding of collective as well as individual aspects of mental health promotion. We know more about collective aspects such as the impact of environment and indirect factors like social inequalities, housing and transport. There is a greater amount of research conducted with intersectoral approaches. The development of mental health impact assessment tools has become an important way of assessing the effect of policies, interventions and environments. Advances in individual aspects of mental health promotion include the concept of positive psychology, and mindfulness.
- Research methodology has advanced by the development of frameworks for analysing data, for example structural equation modelling, more qualitative participatory approaches, and use of complex studies and interventions. We know that there is a need for more sophisticated approaches to research, as standard randomised controlled trials are difficult to apply and are probably inappropriate in many real-world situations with on-going organic changes.
- The evidence-base for mental health promotion has been brought together internationally by systematic reviews.
- The nature of well-being is being disentangled, and there is a broader theoretical understanding of what mental health promotion is. Central thoughts are the focus on the positive, and the connectedness of social, physical and mental aspects of health: you cannot affect one without influencing the others.
- More determinants and mediators of mental health have been identified. Mental health is, in complex ways, affected by environments and contexts on various levels including socio-economic factors.
- There is a greater number and wider use of measures of positive mental health, instead of measuring health by negative outcomes, for instance, coping skills, and quality-of-life scales.
- Mental health promotion research has advanced especially regarding promotion in the early years of life. There is more knowledge of promotion in pre-school and school settings, the effects of supporting parenting, and development of the infant brain.
- An emerging evidence-base on cost-effectiveness shows that investing in mental health promotion pays off and has multiple benefits.
- There is more funding for research than 10 years ago, even though it still is limited.
- There is an awareness of the importance of the psychosocial environment in the workplace.

3.6.3.2.   Mental disorder prevention research

- There is a wider acceptance and recognition of the importance of prevention in mental disorders, especially in affective disorders. An example of recognition is the European Union's green paper towards a strategy on mental health for the union (2005) and European Mental Health Pact (2008).
- There is more evidence for the importance of the postnatal period for the mental health in mother and child, e.g., consequences of the mother's depression on the cognitive development of the baby.
- The multi-factorial concept of mental health is acknowledged to a greater extent; biological, psychological and socio-economic factors, as well as vulnerability, is important for research on prevention of mental disorders
- The importance of developmental factors; we have found how important it is to start the prevention in childhood and adolescence, since prevention is most effective if done as early as possible, for example in school settings.

- Findings on the association between lifestyle factors, risk behaviour and mental health open new areas of prevention.
- Considerable evidence is available for the effectiveness of community-based, multi-level interventions targeting primary care providers, gate keepers, general populations, and patients with their relatives concerning the reduction of suicidal acts.
- Evidence for targeted or indicated prevention of depression is available. There has been progress in finding out how to best find the high-risk groups and deliver interventions. There is recognition that the same is needed for schizophrenia, psychosis and other mental disorders.
- Preventive work among older adults in Alzheimer's disease and related disorders.
- Recognition of common risk factors for mental disorders and possibilities for broad spectrum impact. By acting on common risk factors instead of trying to prevent specific disorders you get impact not only on mental health, but also employability, educational achievement, social adjustment, etc.
- We have more knowledge about the links between prevention and neurodevelopment

3.6.3.3. Epidemiology research

- There are increased possibilities for conducting register-based and register-linkage studies, enabling sophisticated methods for causality research within mental health epidemiology. Related to this, there have been considerable technical advances that facilitate epidemiology research using multiple data sources.
- Nation-wide surveys have provided much information on the prevalence and impact of mental disorders, common pathways for mental health problems, environmental interactions, and also on more subtle phenomena like well-being.
- Improved knowledge and understanding of childhood adversity and factors affecting mental health in early childhood has been gained.
- Increased knowledge has been gained in the important role of human interaction for mental health, e.g., the impact of social exclusion and of stigmatised attitudes towards mental health problems.
- Studies on risk and protective factors of mental health by looking at mental processes or traits have led to increased knowledge.
- Birth cohort studies have increasingly been undertaken, which has enhanced the knowledge in important mental health factors across the lifespan and the causes of common diseases and mortality.
- There is increased knowledge of the comorbidity within mental disorders, e.g., in the association between mental and physical disorders.
- Advances have been made in research on the effects of psychosocial interventions for mental health promotion and disorder prevention. Research on the cost-effectiveness of interventions has also been developed and emphasised.
- There are increased collaboration between genetic and environmental research due to the acknowledgement of interaction effects between genetics and environment.
- Valid mental health indicators have been acknowledged that can be used for monitoring the mental health status on a population level. Measurement instruments that, for example, indicate burden of disease/loss of productivity and quality of life (e.g. DALYs and QoL) have been developed and increasingly used.
- Better understanding of child mental health. We have a more robust understanding of child mental health epidemiology, needs, disorders, aetiology and underlined mechanisms that cause and maintain child mental health disorders. We know more about infant development and development processes in early years, including findings from neuroscience.
- We have a better understanding of ecological models used for understanding the complexity of child mental health and problems. We are now, to a greater extent, differentiating levels and complexity of child mental health needs, understanding the variability within diagnoses, and that individuals with the same disorders may have different trajectories. There is also an increased understanding in services of the importance of early identification and recognition of mental disorders in adulthood.

3.6.3.4. Mental health services research

- Mental health is increasingly considered a key component of overall health. Functional brain imaging has led to a paradigm shift by making the 'mental' more 'real' to biomedicine, there is a greater understanding that the physical and mental are intertwined.
- Development of new models of cost effective health care, such as collaborative care. Integrating care for medical and mental health problems has many benefits.
- Development of generic ways of evaluating the outcomes of interventions (QALYs) that allows the benefits of interventions to be compared across 'mental' and 'physical' illnesses. This allows us to decide where to best spend money to improve the health of the population. The concept of quality of life has also been developed. An example of the utilisation of these to concepts is that quality of life can be improved more cost effectively by psychological interventions than medical interventions in cancer patients.
- There has been a vast improvement in methodological rigour of mental health services research with emphasis on theory-led research and conceptual frameworks, e.g., the UK Medical Research Council's complex interventions guidance for the development and evaluation of complex interventions.
- The development of "survivor-controlled research". These are projects that are shifting participator methodologies to the extreme, and have the potential to lead to a new theoretical model, analogous to the social model of disability.
- Human rights of psychiatric patients came onto the research agenda, in parallel to the UN Convention on Rights of People with Disabilities.
- The user-perspective has become more prominent through evaluative methodologies such as User Focus Monitoring and involvement of user organisations in planning of mental health care and research. Interventions have been developed that take into account the burden on the family as a factor affecting the outcome of treatment.
- An increasing number of evidence-based treatments, outcome studies and more approval in general health services.
- Development and evaluation of measurements and instruments to be used in research. For example fidelity measures to be used in the development and implementation of evidence based treatments. These measures allow us to examine to what extent the service is doing what seems to be wise to do.
- Migrant mental health research came onto the agenda. There is a lot of intra-European as well as intercontinental migration, and there are initiatives to make mental health care more culture-sensitive.
- Record linkage of routinely collected service utilisation data enables research methods that supplement the ones currently used, e.g., longitudinal studies using register-based data.
- Instruments have been developed for assessment of how well psychiatric institutions comply with human rights (e.g., ITHACA).
- Mental health services research is still on the agenda, as a counter point to the biological paradigm.
- The European perspective has been highlighted, allowing us to compare the national perspective on problems in service provision to the European perspective. This has also to do with increasing involvement of Eastern European countries. More cross-country comparisons are being made, as well as studies on developing countries' role in affecting Europe in different ways, e.g., through migration.
- More mixed-method studies. Qualitative methods, including user perspectives, are more accepted and used.
- E-health and e-mental health is more in focus, with a lot of research and literature produced.
- There is a rapid development and testing of manualised interventions, and research evidence from clinical outcome and progress monitoring. There is a drive to broaden the base of knowledge of child mental health and intervention skills, to share the skills with non-mental health practitioners and for the development of community-level interventions
- We are better at differentiating user-perspective, with greater seriousness paid to the views of children and younger people as opposed to only the views of adults or parents.
- Progress has been made in some areas of healthcare but not in others, e.g., treatment process, moderators of care and outcomes.
- There is awareness and discussions about intervention implementation; why do we not use some of the interventions that have been developed?

- Better understanding of the relevance and importance of stigma and discrimination. We know that it effects both use of and processes in mental health services. Also, staff attitudes are being examined.
- More knowledge of the health economics of service delivery and cost-benefit.

3.6.3.5. Mental health policy research

- There has been exchange of experience of the paradigm shift in provision of mental health services: move from hospitals to community care, integration of mental health and general health, increasing role of primary care, collaborative care, and stepped care.
- There is increasing acknowledgement of the importance of human rights, including rights of people with disabilities (as reflected by the UN Convention on Rights of People with Disabilities), and of the importance of user empowerment.
- There is increasing knowledge of how poorly mental health services perform and the proportion of untreated cases
- Treatment delivery has evolved towards individualised treatment based on the recovery concept. This has been accompanied by a shift in power from professionals to patients and emerging concepts of self-help, peer support and e-treatment.
- There is trend toward evidence-inspired politics and increased recognition that policies, services, and priority setting should be evidence-based.
- There has been development in measurement and research of outcomes of mental health care, including measurement of quality of care.
- The view on mental health has been broadened to include mental health promotion and prevention of mental disorders, which is increasingly implemented (without knowing the causes) as cross-sectoral collaboration.
- Improved information of mental health and mental disorders has become available, such as the WHO calculations of burden of diseases, the European Union mental health surveys, European Study of the Epidemiology of Mental Disorders (ESEMED), and the European and World Value Surveys.
- There is increased awareness of the interconnectedness between mental and other policies as well as mental health in a global context.
- There is increased acceptance of the importance of macro-economic policy for mental health.
- Mental health has successfully been placed on the international health and social agenda. Examples are EU investment in mental health research and the WHO European strategy for mental health.
- Increasing evidence for possibilities of preventing depression has emerged.
- There has been an increase in health economics knowledge.
- Advances in employment policies have been introduced, such as graded sick-leave and supported employment.
- Research has demonstrated the role of families, early interventions, primary care, and assertive community treatment (ACT).

3.7. Well-being research

3.7.1. Introduction to the area

Well-being reflects individual's 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 conceptualisations 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-realisation, 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 individual's 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 in a longer life-time, the effect on mental health manifests in 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 and 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 with 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 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 has an impact on 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 have an impact on the various components of subjective well-being, and also how well-being affects 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 Organisation (2011) defines mental health as: "a state of well-being in which every individual realises 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 into 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.

3.7.1.1.   Definition of subareas

3.7.1.1.1.   Theoretical models of well-being

There are two basic traditions in the study of well-being, that arising from social sciences and that from health-related sciences. In order to refine measurement approaches, the first requirement is a clear conceptualisation 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.

3.7.1.1.2.   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.

3.7.1.1.3.   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.

3.7.1.1.4.   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 to prevent their mental disorders and support their well-being. This will benefit also the well-being of patients.

3.7.2. Systematic literature mapping

3.7.2.1. Objective

A mapping of the main publications in peer-reviewed journals for well-being and mental health research was performed.

The research questions were as follows:

- Main research question:

    - *What is the current state of research in the area of mental health and well-being in Europe?*

- Secondary research questions:

    - *What is the nature of the evidence (type of studies, samples used, etc.)?*

    - *What countries did this research?*

    - *What are the main topics?*

3.7.2.2. Method

The reviewing technique used for this review is systematic mapping. Methodology based on the protocol described in Curran et al. (2007) for the systematic multidisciplinary reviewing of the literature was followed.

The inclusion criteria were:

- Academic peer-reviewed papers.
- Published during the previous five years (2007-2011).
- In English language.
- Corresponding author from any of the European countries (EU-27, EU Candidates or other European countries). If the corresponding author was not specified, the reference author was considered the first one.
- Research set in any of the European countries.
- Only publications including an abstract.

The search was performed in the following databases:

Pubmed: search performed on 26th March, 2012.

PsycINFO: search performed on 28th March, 2012.

Structure of the search strategies:

- Search terms for mental health, mental ill-health and mental disorders.

- Search terms for well-being.

- Search terms for Europe.

The search strategies were individually designed for each database.

Each paper was coded as either included or excluded, with a secondary code reporting the reason for rejection. A total of 10% of the papers were reviewed by two independent researchers. The percentage of agreement was 85.65%. Kappa was 0.715 (95% CI = 0.625, 0.804).

3.7.2.3.   Data extraction and management

The retrieved publications were screened and data extracted and categorised by targeting the following:

1.   Reference author of the publication
2.   Country of the reference author
3.   City of the reference author
4.   Research centre of the reference author
5.   Publication year
6.   Journal of publication
7.   Title of publication
8.   Keywords of publication
9.   Research area
10.   Country of study sample
11.   Age group of study sample
12.   Gender of study sample
13.   Measurements of mental health (mental health content)
14.   Measurements of well-being

3.7.2.4.   Results

The searches in both literature databases provided 2,928 records in total. After exclusion of duplicates, the number of identified records for screening and categorising was reduced to 2,295. Figure 28 shows a flow chart with the number of papers identified in each of the electronic searches and the number of articles included and excluded after reviewing the abstracts.
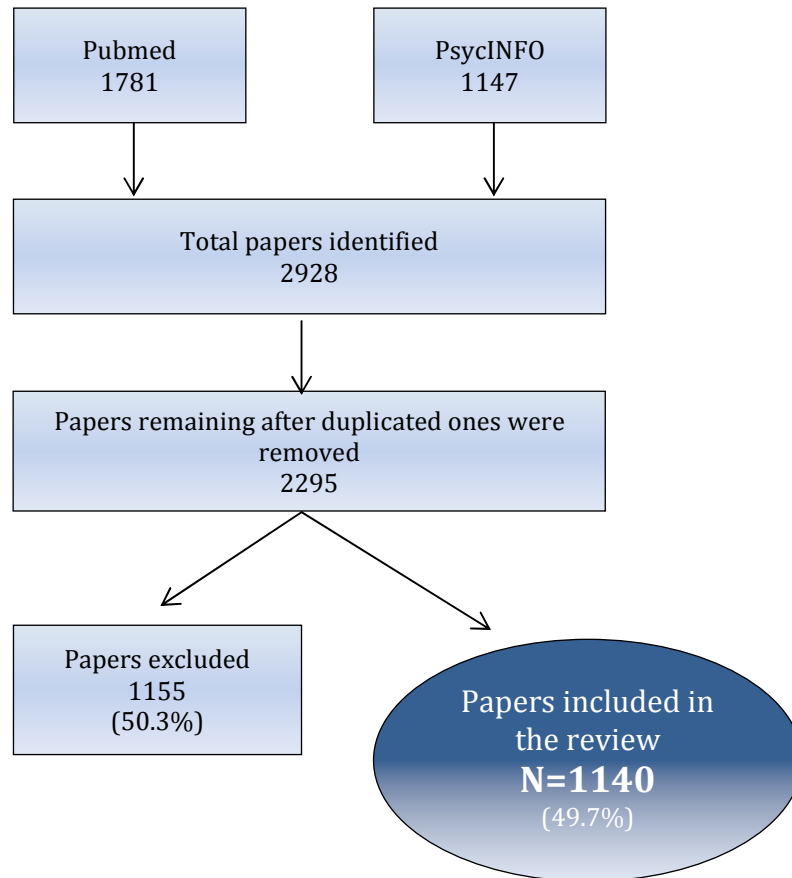
Figure 28. Flow chart of the identified articles obtained from the electronic searches.

The reasons for excluding the papers were:

- No mental health or well-being content (65.4%)

- Reference author from outside Europe (23.1%)

- Not published between 2007 and 2011 (6.1%)

- No European sample (1.9%)

- Not an academic, peer-reviewed paper (0.1%)

- More than one reason (3.4%)

As can be seen in the following Figures, more than half of the studies were performed in the United Kingdom, Germany and The Netherlands. When adjusted by population size of each country, the leading countries are the Nordic countries and The Netherlands. Eastern European countries have performed little research in the area.
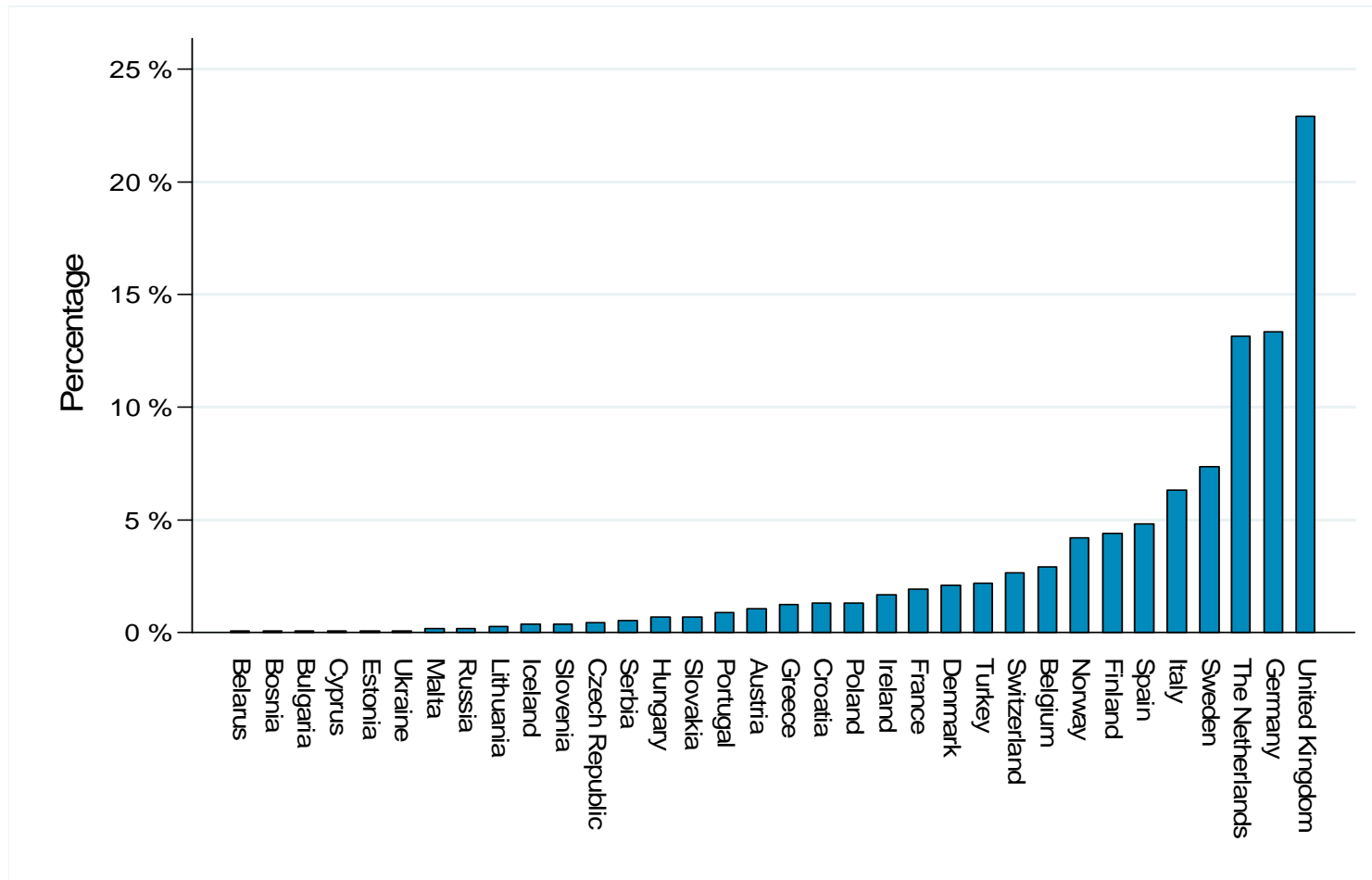
Figure 29. Country of the reference author
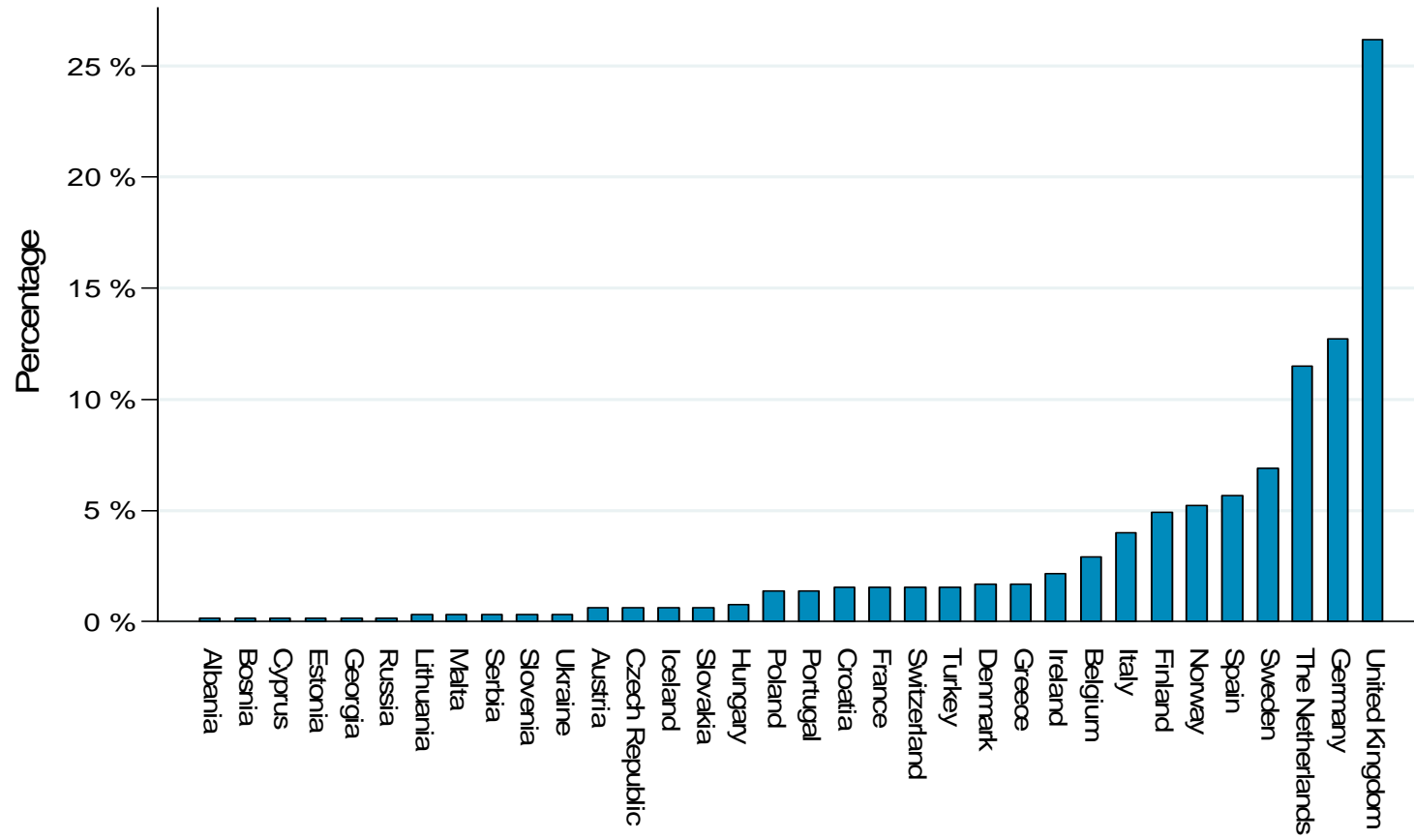
Figure 30. Country of the sample
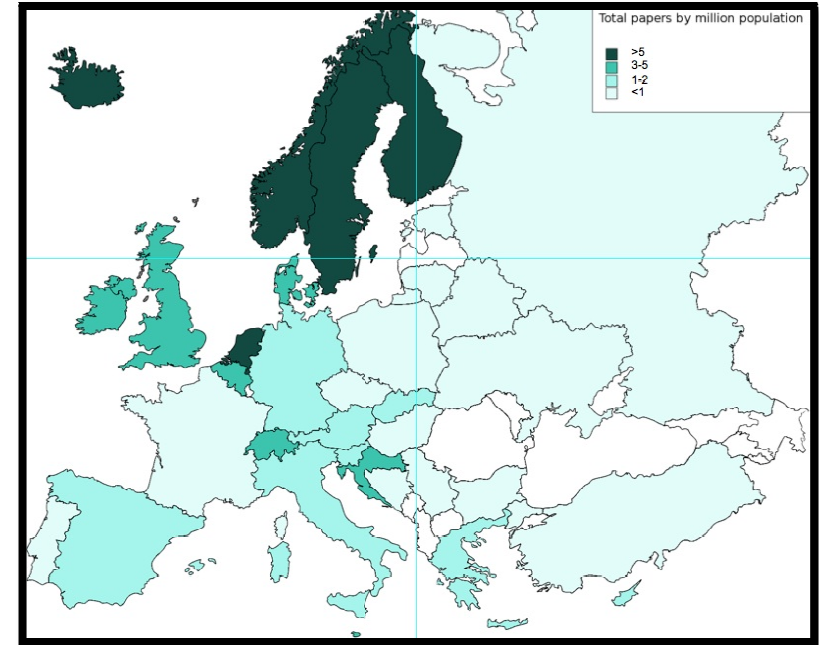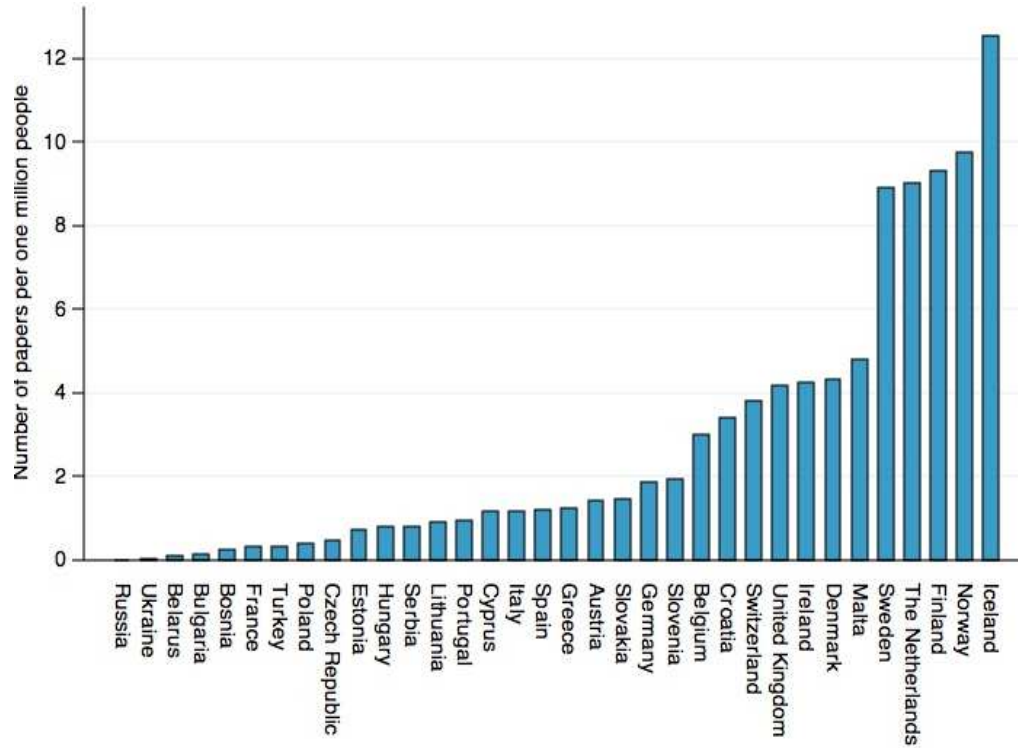
Figure 31. Country of the reference author (adjusted by the population of each country)
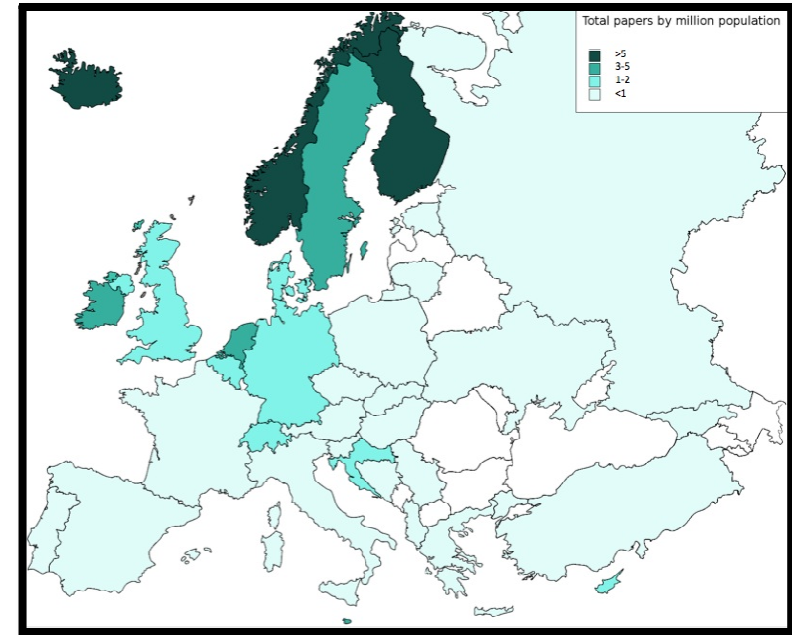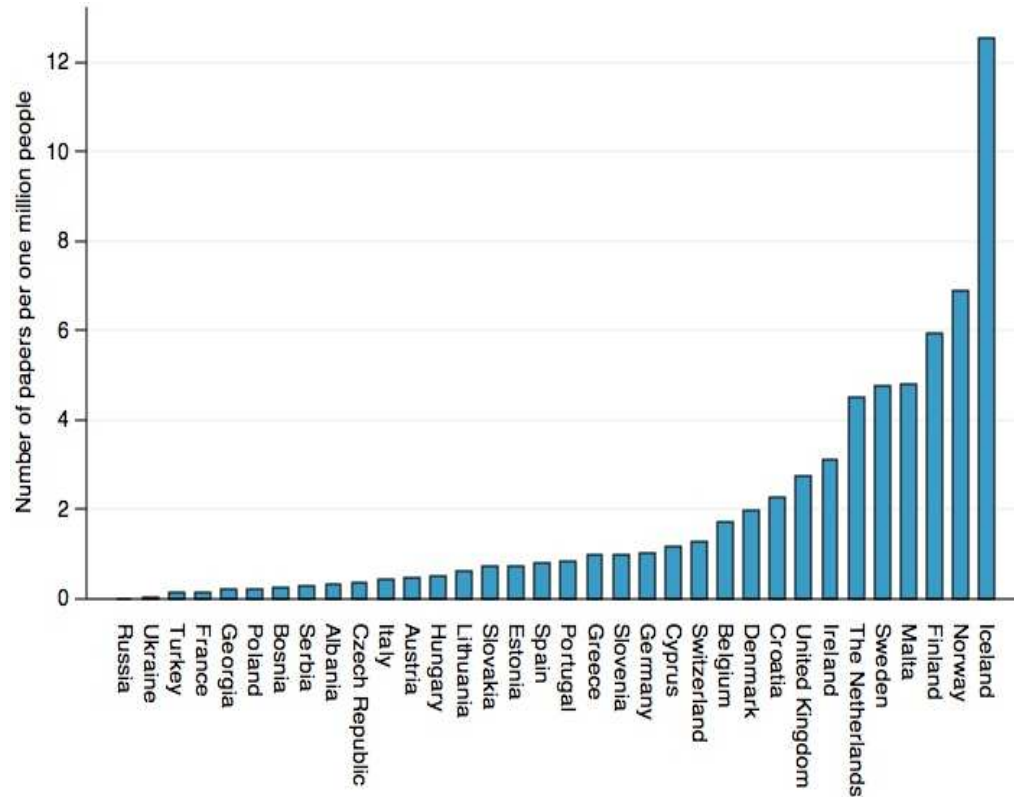
Figure 32. Country of the sample (adjusted by the population of each country)

As shown in Figure 33, the research was carried out mostly in universities, followed by research centres.

5.27 %
9.62 %
11.07 %
74.04 %

| Hospital | University | Research Centre | Other |
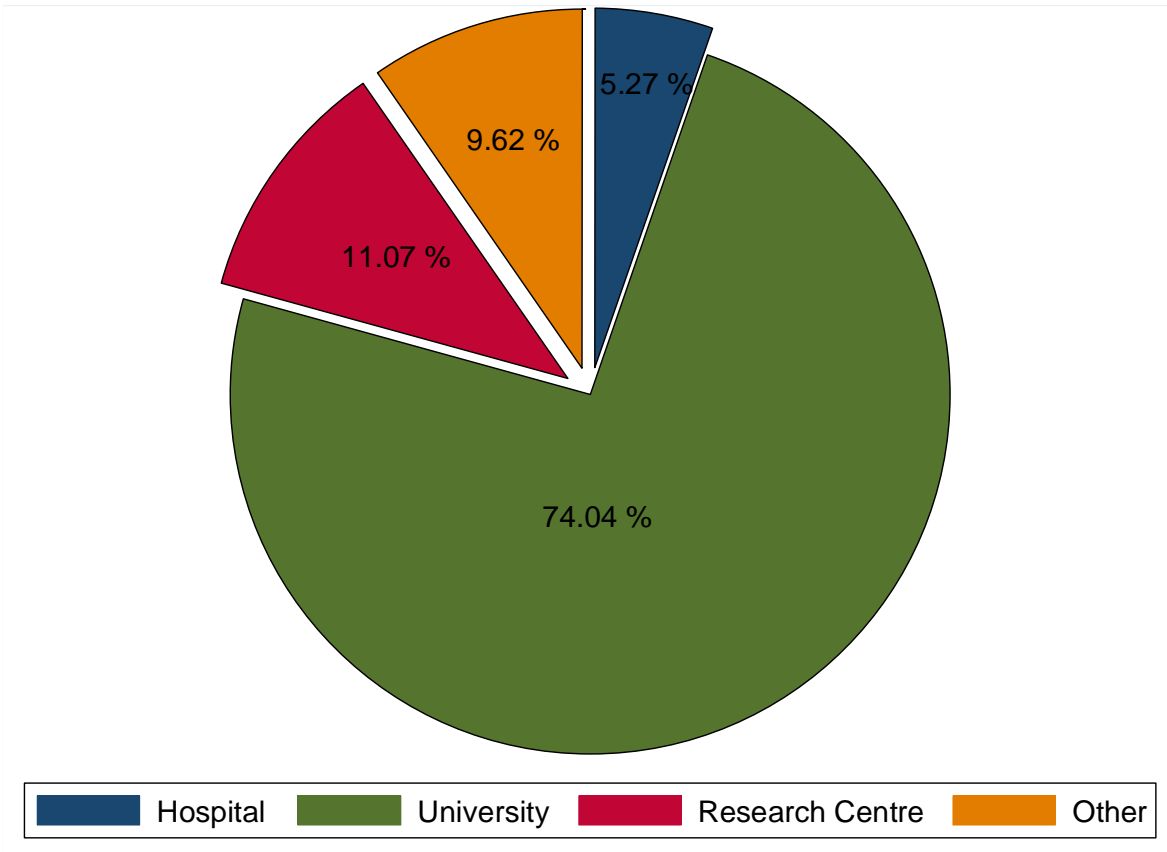
Figure 33. Institution of the reference author

Figure 24 shows the number of papers published each year. As can be seen, the number of articles in the area of mental health and well-being has increased each year.
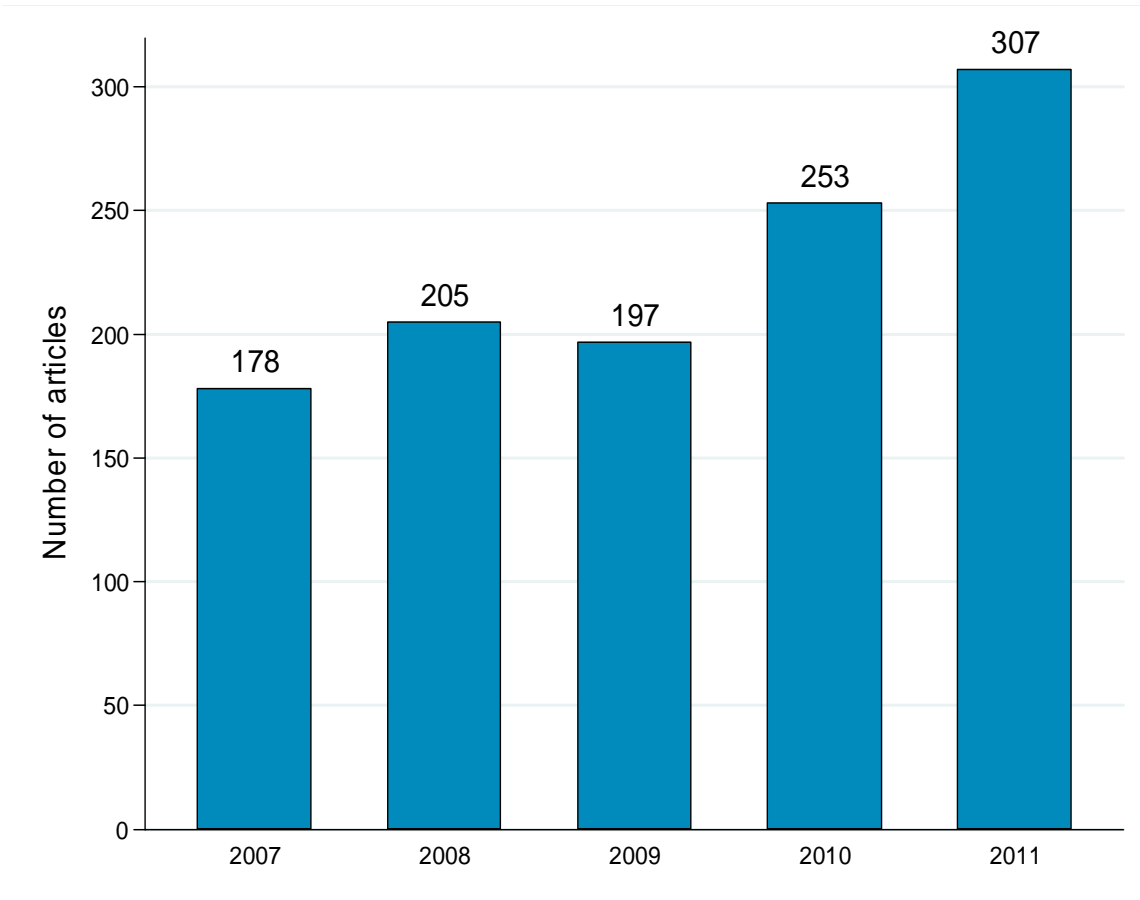
Figure 34. Publication year

As shown in Figure 23, nearly half of the studies were epidemiological studies, the rest of the articles were categorised as clinical trials, experimental studies and systematic reviews or meta-analyses.
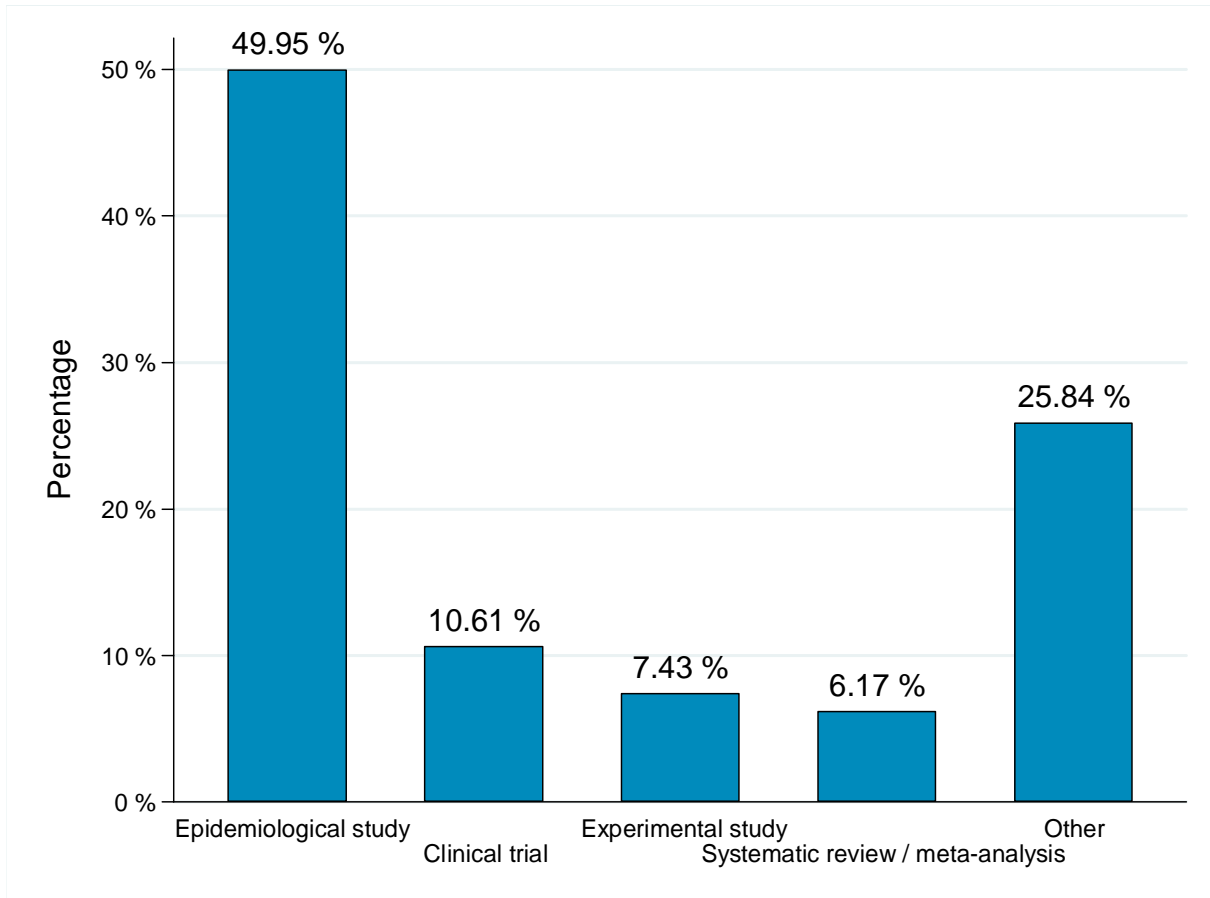
Figure 35. Type of study

Regarding the area of study, as shown in Figure 36, more than two thirds of the studies are about detection, screening and diagnosis, 18.33% are evaluation of treatments and therapeutic interventions, and the rest of the articles focus on health and social care services research, followed by aetiology.
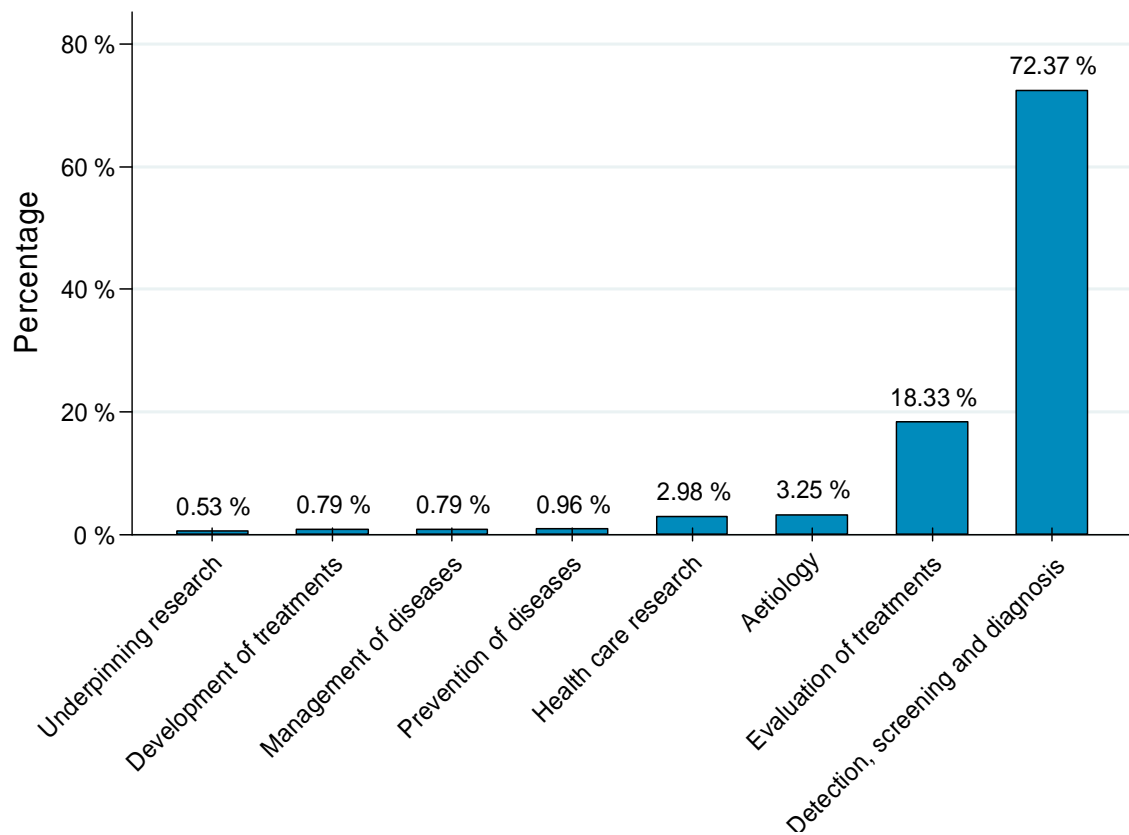
Figure 36. Area of study

Looking at the definitions and measurements of mental health, it could be concluded that more than half of the well-being studies analyse mental health in general. The studies that focus on specific disorders are mainly concerned with: depression, schizophrenia, substance abuse and eating disorders.
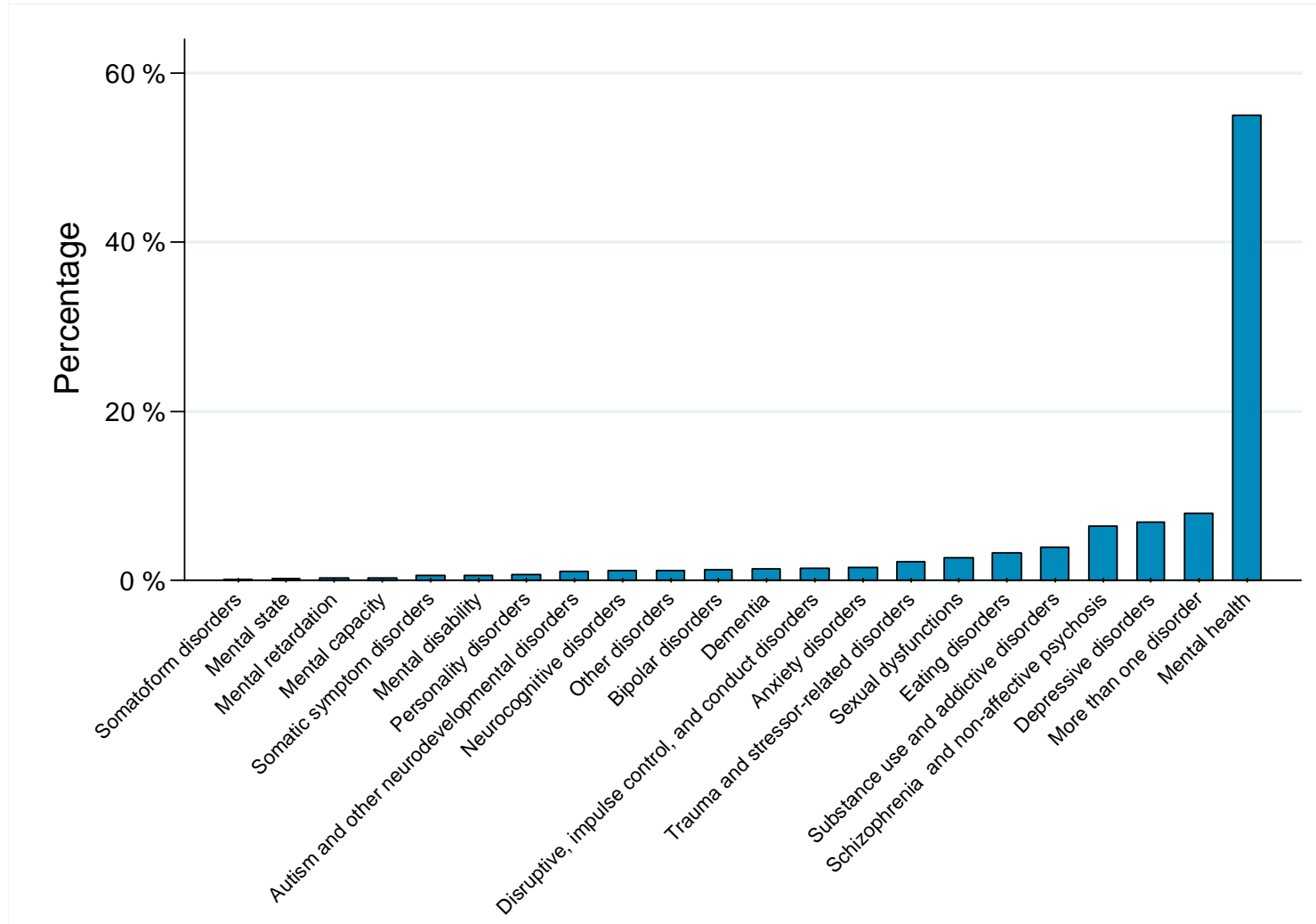
Figure 37.   Mental health content

A total of 51.32% of the studies analysed factors associated with well-being, whereas 19.39% of the studies evaluated well-being in people with mental disorders. The rest of the papers published were categorised in the areas of promotion of well-being, evaluation of well-being, well-being of carers, theoretical models of well-being, and relationships between mental health and well-being.
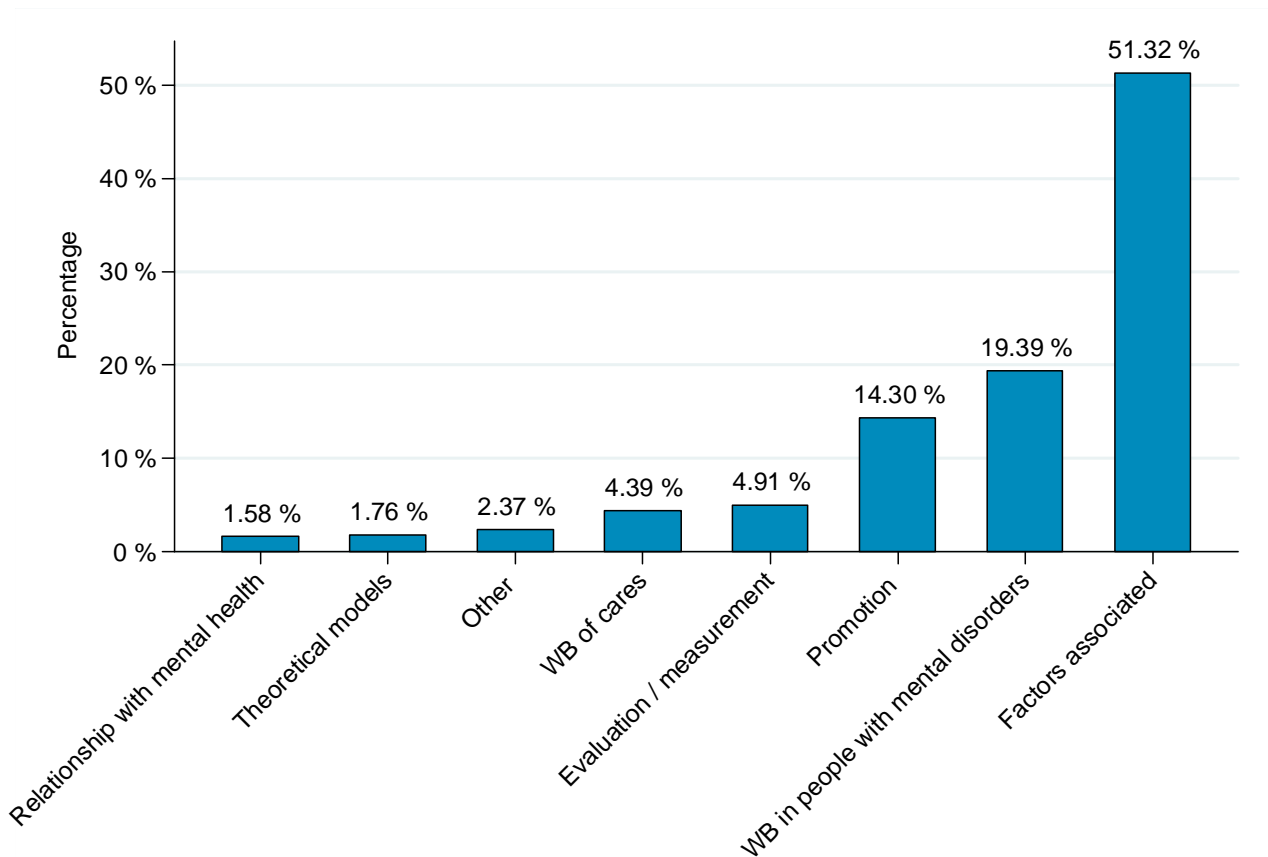
Figure 38. Well-being area

Figure 39 shows that more than half of the studies are about well-being in general, followed by studies about quality of life, positive and negative effect, satisfaction, and happiness.
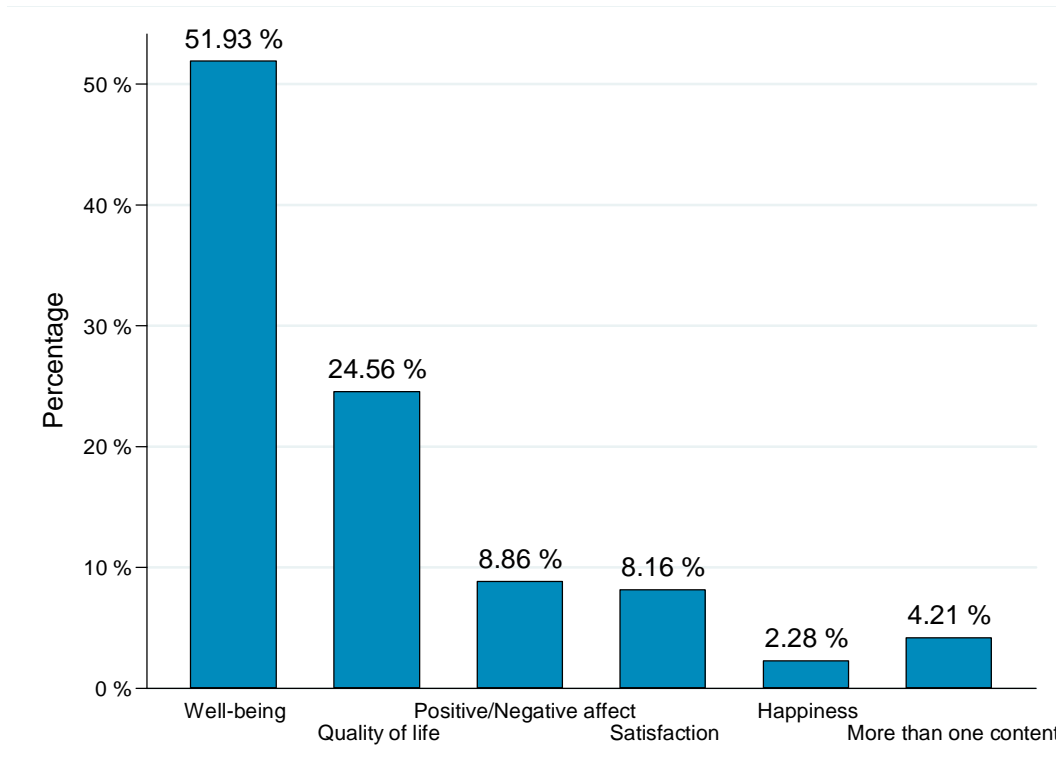
Figure 39. Well-being content

Regarding the age group of the sample, it was found that the majority of the research conducted focused on adults (48.1%) followed by children and adolescents (14.47%), whereas the elderly seemed to be understudied. However, it should also be noted that 40% of the screened records were not possible to categorise into one of the age group categories, since this information was not specified in the abstract.
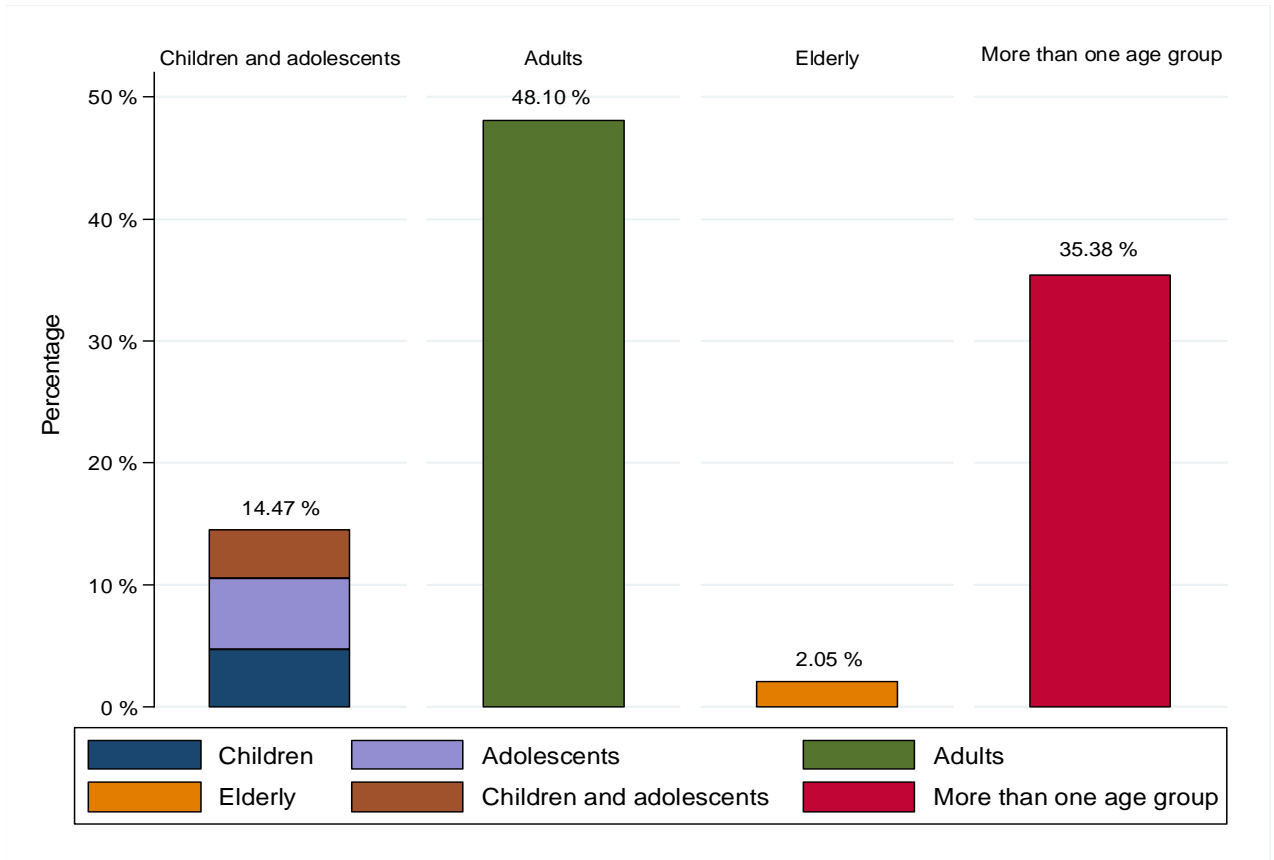
Figure 40. Age group of the sample

3.7.3. State-of-the-art (main advances of the last 10 years)

The aim of the first scientific workshop was to map advances in the field during the last ten years, to identify gaps in current knowledge and set priorities in future public mental health research in Europe. Experts were instructed to focus mainly on the first two topics and to start to set priorities only if they had the time to do so, since this topic will be developed in more detail in the second scientific workshop.

The discussions provided the views and knowledge of the experts in the field. This process, in conjunction with the systematic mapping of literature and survey consultations of researchers, provided good potential to map the current state of research and main gaps in current knowledge.

3.7.3.1. Theoretical models of well-being

- Integration of basic psychological knowledge into well-being research.
- Emerging consensus on the definition of subjective well-being.
- New terms, such as emotional intelligence, and new insights related to terms such as resilience.
- The International Classification of Functioning, Disability and Health (ICF) (World Health Organisation, 2001).
- Awareness of the fact that focusing on negative emotions is insufficient. Recognition of positive emotions.
- Positive psychology has broadened its interest from the individual level to the societal and organisational level.
- The Person-centred Integrative Diagnosis (PID) model (Mezzich et al., 2010) and the patient-reported outcomes approach. Broader understanding of recovery beyond symptom improvement.
- Contribution of healthy ageing and active ageing.
- Research on well-being has become more interdisciplinary, there is more interaction between different fields.
- Increased interest in well-being in children.
- Development of a better understanding of the concept of well-being as it relates to young people by The Good Childhood Inquiry in the United Kingdom (The children's society, 2012).

3.7.3.2. Evaluation of well-being

- Evaluation of well-being
  - The Warwick-Edinburgh Mental Well-being Scale (WEMWBS) (Tennant et al., 2007).
  - Advance in measurement strategies-honing in on remembered aspects and experienced aspects of well-being.
  - Implementation of new psychometric methods.
  - Improved and more rigorous measurement of well-being carried out by the National Accounts of Well-being (Michaelson et al., 2009).
  - Development of research methods such as web-based studies.

- Availability of data
  - Increases in the amount of data available from studies such as the Gallup World Poll (Diener et al., 2010) and the European Social Survey (Georgellis et al., 2009).
  - Measurement of well-being at a cross-national level.
  - Insistence on cohort studies to allow for longitudinal research in many European countries.
- Political implications
  - Political legitimation of well-being, inclusion of well-being on government agendas.

- o Impact of research on policy design: The New Economics Foundation (NEF). Social determinants of well-being. Relationship between employment policies and well-being.
  - o Growing interest among international organisations in incorporating well-being measures (e.g., OECD, UNICEF).
- Reports
  - o Foresight Report on Mental Capital and Wellbeing (Foresight Mental Capital and Wellbeing Project, 2008).
  - o The Mental Health Promotion Report by the World Health Organisation (2005).
  - o The Scottish Work on Mental Wellbeing Indicators (Taulbut et al., 2009).
  - o The European Community Health Indicators Monitoring (ECHIM) (2008).
  - o Declarations and calls for action at European level related to well-being and mental health, i.e., Mental and physical health: a call to action.
  - o European Quality of Life Survey (Eurofond, 2010).
  - o World Happiness Report (2012).

3.7.3.3. Relationships between mental health and well-being

- Evidence on relationships between health and well-being
  - o Growing literature on the relationship between hedonic and eudaimonic well-being features and physiological parameters (e.g., cortisol, fibrinogen).
  - o Studies relating eudaimonic well-being and hedonic well-being with biological correlates, such as plasma triglycerides and lung function (Steptoe et al., 2012).
  - o Studies that show the longitudinal effect of well-being on health outcomes and mortality.

- Interventions to promote well-being
  - o Development of theoretically based models of health promotion, e.g., well-being in the workplace, at schools, in cities. Advances in interventions regarding work and stress.
  - o Development of interventions to improve well-being, specifically mindfulness.
  - o Cost-effectiveness analysis of interventions to improve well-being.
  - o Effective web-based interventions to promote well-being (The Netherlands, All Your Life).
  - o Implementation of more psychological and psychosocial interventions beyond pharmacological interventions. More ambitious interventions, multiphase, implementation of new methodologies.
- Evidence on the determinants of well-being
  - o Increasing evidence of the role of early childhood and prenatal factors as determinants of well-being.
  - o Ecological studies demonstrating the relationships between population well-being and social capital.

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

- Approach to lifestyles and health behaviour in groups of people with mental illnesses.
- Recognition of the importance of listening to patients, realising that patients have different opinions about quality of life and tolerability of drug treatments.
- Incorporation into the clinical trials of subjective evaluations of the patients as an outcome variable.
- The perspective of the clinician is changing: long-term outcomes beyond the symptoms. The focus of the interventions is broader.
- Evaluation of the interventions.
- Incorporation of the stakeholders in ROAMER project.
- Increasing access to interventions.

- Epidemiological and population studies have identified people with mental disorders as having the lowest levels of well-being.
- Recognition that there is a need to include patients and families in the design of the studies. Patient-defined outcome measures for intervention studies.
- Emphasis on functional outcomes in research, especially in patients with severe mental illness.

4.   Stakeholders

4.1. First survey consultation

4.1.1. Methodology

The survey has been conducted with 108 associations/organisations active in the mental health field in individual European Union countries (please see the complete list of associations in Annex IV). These included 31 associations of psychiatrists, 32 associations of other mental health professionals, 23 organisations of users or carers, and 22 associations of psychiatric trainees. All these associations/organisations have provided their collective feedback (not the responses of individual officers). The associations of psychiatrists that responded represented 91.2% of those contacted (31 out of 34). The associations of other mental health professionals that responded represented 61.5% of those contacted (32 out of 52). The organisations of users or carers that responded represented 52.3% of those contacted (23 out of 44). The associations of psychiatric trainees that responded represented 91.7% of those contacted (22 out of 24).

4.1.2. Results

3.7.4.1.   Priorities for mental health research

Table 12. Priorities for mental health research in Europe selected by the associations/organisations (%)

Priorities	Total sample (N=104)[a]	Psychiatrists (N=31)	Other mental health professionals (N=30)	Users/carers (N=23)	Trainees (N=20)
New medications for mental disorders **	**32.0**	**46.7**	10.0	26.1	**50.0**
New psychological interventions for mental disorders *	23.3	10.0	**30.0**	**39.1**	15.0
Increasing access to available treatments	26.2	**40.0**	**30.0**	17.4	10.0
Improving adherence to available treatments	11.7	23.3	3.3	13.0	5.0
Quality of mental health services	**43.7**	**53.3**	**43.3**	**43.5**	30.0
Early detection and management of mental disorders	**52.4**	**53.3**	**60.0**	34.8	**60.0**
Resilience and mental health	10.7	10.0	16.7	13.0	0
Stigma and discrimination	29.1	26.7	20.0	**39.1**	**35.0**
Rehabilitation and social inclusion	**32.0**	23.3	**33.3**	**39.1**	**35.0**
Relationships between mental and physical health	18.4	20.0	16.7	21.7	15.0
Mental health and well-being in the general population	15.5	6.7	**30.0**	13.0	10.0
Genetic risk/protective factors for mental disorders	7.8	13.3	3.3	4.3	10.0
Environmental risk/protective factors for mental disorders	17.5	16.7	26.7	4.3	20.0
Prevention of mental disorders	**40.8**	**36.7**	**53.3**	30.4	**45.0**
Neuroimaging of mental disorders ***	9.7	3.3	3.3	0	**40.0**
Molecular bases of mental disorders	9.7	13.3	6.7	0	20.0
Animal models of mental disorders	1.0	3.3	0	0	0
Cognitive dysfunction in mental disorders and its neural bases*	6.8	0	10.0	0	20.0
Social and economic impact of mental disorders	16.5	20.0	23.3	8.7	10.0
Clinical characterisation of mental disorders *	8.7	20.0	0	4.3	10.0
Users' perception of illness and treatment impact *	15.5	6.7	10.0	34.8	15.0
Suicide prevention	18.4	20.0	16.7	17.4	20.0
Health and well-being of carers **	14.6	6.7	10.0	**39.1**	5.0
Epidemiology of mental disorders	12.6	13.3	10.0	17.4	10.0
Mental health consequences of trauma	1.9	3.3	3.3	0	0
Culture and mental health	1.9	0	6.7	0	0

Bold prints identify the top 5 priorities for each group. Significant differences among groups: *p<0.05; **p<0.01; ***p<0.0001.
[a] Four associations/organisations did not complete the section of the questionnaire identifying the 5 priorities for research.

Table 13. Top 5 priorities for mental health research in Europe according to groups of associations or organisations (%)

Priorities	Total sample (N=104)
Early detection and management of mental disorders	52.4
Quality of mental health services	43.7
Prevention of mental disorders	40.8
New medications for mental disorders	32.0
Rehabilitation and social inclusion	32.0

Priorities	Psychiatrists (N=31)
Quality of mental health services	53.3
Early detection and management of mental disorders	53.3
New medications for mental disorders	46.7
Increasing access to available treatments	40.0
Prevention of mental disorders	36.7

Priorities	Other mental health professionals (N=30)
Early detection and management of mental disorders	60.0
Prevention of mental disorders	53.3
Quality of mental health services	43.3
Rehabilitation and social inclusion	33.3
New psychological interventions for mental disorders	30.0
Increasing access to available treatments	30.0
Mental health and well-being in the general population	30.0

Priorities	Users/carers (N=23)
Quality of mental health services	43.5
New psychological interventions for mental disorders	39.1
Stigma and discrimination	39.1
Rehabilitation and social inclusion	39.1
Health and well-being of carers	39.1

Priorities	Trainees (N=20)
Early detection and management of mental disorders	60.0
New medications for mental disorders	50.0
Prevention of mental disorders	45.0
Neuroimaging of mental disorders	40.0
Stigma and discrimination	35.0
Rehabilitation and social inclusion	35.0

"Other" priorities for mental health research identified by respondents (one mention each): e-health, deontological issues and mental health, etiology, perspectives of users, health promotion and prevention of geriatric disease, Internet treatment, making recovery a reality for all, neural basis of psychiatric disorders and of pharmacological drugs, occupational psychiatry, psychiatric emergencies, spiritual and social determinants of mental health, research of psychiatric holocaust, pastoral medicine, child and adolescent psychiatry, relationship between screening and psychiatric care, financial crisis and mental health/suicides, psychotherapy process research, differential indications of psychotherapies.

3.7.4.2. Importance of the various research areas

Table 14. Importance of the research areas as rated by the associations/organisations (mean, SD)

Importance	Total sample (N=107)[a]	Psychiatrists (N=30)	Other mental health professionals (N=32)	Users/carers (N=23)	Trainees (N=22)
New medications for mental disorders	3.9 (1.2)	4.3 (1.0)	3.5 (1.3)	3.8 (1.3)	3.9 (0.9)
New psychological interventions for mental disorders **	4.1 (0.9)	3.8 (0.8)	4.2 (0.8)	**4.6 (0.7)**	3.8 (1.1)
Increasing access to available treatments *	4.2 (0.9)	**4.5 (0.7)**	**4.3 (0.8)**	4.1 (1.1)	3.9 (0.9)
Improving adherence to available treatments	3.9 (1.0)	4.2 (0.9)	3.7 (0.8)	3.6 (1.3)	4.0 (0.8)
Quality of mental health services *	**4.5 (0.7)**	**4.6 (0.7)**	**4.5 (0.6)**	**4.8 (0.4)**	4.1 (8.9)
Early detection and management of mental disorders	**4.4 (1.0)**	**4.5 (0.6)**	**4.4 (0.7)**	4.0 (1.6)	**4.5 (0.7)**
Resilience and mental health	3.6 (1.1)	3.7 (1.0)	3.8 (1.0)	3.8 (1.4)	3.1 (1.1)
Stigma and discrimination	4.2 (0.9)	4.2 (1.0)	4.0 (0.8)	**4.5 (0.9)**	**4.2 (0.8)**
Rehabilitation and social inclusion	**4.4 (0.9)**	4.3 (0.8)	**4.3 (0.9)**	**4.6 (1.1)**	**4.3 (0.9)**
Relationships between mental and physical health	4.2 (0.8)	4.4 (0.7)	4.1 (0.9)	**4.5 (0.7)**	4.0 (1.0)
Mental health and well-being in the general population	4.0 (1.2)	4.1 (0.9)	**4.3 (1.1)**	4.0 (1.5)	3.6 (1.1)
Genetic risk/protective factors for mental disorders	3.4 (1.1)	3.6 (1.1)	3.3 (1.0)	3.3 (1.3)	3.1 (0.9)
Environmental risk/protective factors for mental disorders	4.0 (1.0)	4.0 (1.0)	4.1 (0.8)	4.1 (1.0)	3.7 (1.0)
Prevention of mental disorders	**4.3 (1.0)**	**4.5 (0.7)**	**4.4 (0.8)**	4.1 (1.5)	**4.2 (0.9)**
Neuroimaging of mental disorders	3.3 (1.2)	3.5 (1.1)	3.1 (1.1)	2.9 (1.5)	3.8 (1.1)
Molecular bases of mental disorders	3.2 (1.2)	3.5 (1.1)	3.0 (1.2)	2.9 (1.5)	3.7 (0.9)
Animal models of mental disorders	2.6 (1.4)	2.8 (1.4)	2.3 (1.3)	2.3 (1.7)	2.9 (1.1)
Cognitive dysfunction in mental disorders and its neural bases	3.7 (1.1)	3.7 (0.9)	3.6 (1.1)	3.6 (1.4)	3.9 (1.0)
Social and economic impact of mental disorders	4.2 (0.9)	4.1 (1.0)	4.2 (0.8)	**4.5 (1.0)**	3.9 (0.8)
Clinical characterisation of mental disorders ****	3.7 (1.2)	4.3 (0.8)	3.4 (1.0)	3.1 (1.7)	4.1 (0.7)
Users' perception of illness and treatment impact *	4.1 (1.0)	4.0 (0.9)	4.1 (0.9)	**4.5 (1.2)**	3.9 (0.9)
Suicide prevention	**4.5 (0.8)**	**4.6 (0.7)**	**4.4 (0.7)**	4.4 (1.2)	**4.5 (0.7)**
Health and well-being of carers ***	4.0 (1.0)	3.8 (1.1)	4.1 (0.9)	**4.6 (0.8)**	3.4 (1.1)
Epidemiology of mental disorders	3.8 (1.0)	3.9 (0.8)	3.8 (1.1)	3.8 (1.1)	3.6 (0.8)
Mental health consequences of trauma	3.6 (1.0)	3.7 (0.9)	3.7 (0.7)	3.4 (1.5)	3.6 (0.8)
Culture and mental health	3.5 (1.0)	3.4 (0.9)	3.5 (1.0)	3.9 (1.2)	3.2 (1.1)

Bold prints identify the 5 areas with the highest mean scores. Significant differences among groups: *p<0.05; **p<0.01; ***p<0.001; ****p<0.0001.

a One association did not complete the section of the questionnaire evaluating the research areas in terms of importance.

Table 15. Top 5 research areas in terms of importance according to the groups of associations/organisations (mean, SD)

Importance	Total sample (N=107)
Suicide prevention	4.5 (0.8)
Quality of mental health services	4.5 (0.7)
Early detection and management of mental disorders	4.4 (1.0)
Rehabilitation and social inclusion	4.4 (0.9)
Prevention of mental disorders	4.3 (1.0)

Importance	Psychiatrists (N=30)
Quality of mental health services	4.6 (0.7)
Suicide prevention	4.6 (0.7)
Increasing access to available treatments	4.5 (0.7)
Prevention of mental disorders	4.5 (0.7)
Early detection and management of mental disorders	4.5 (0.6)

Importance	Other mental health professionals (N=32)
Quality of mental health services	4.5 (0.6)
Prevention of mental disorders	4.4 (0.8)
Early detection and management of mental disorders	4.4 (0.7)
Suicide prevention	4.4 (0.7)
Mental health and well-being in the general population	4.3 (1.1)
Rehabilitation and social inclusion	4.3 (0.9)
Increasing access to available treatments	4.3 (0.8)

Importance	Users/carers (N=23)
Quality of mental health services	4.8 (0.4)
Rehabilitation and social inclusion	4.6 (1.1)
Health and well-being of carers	4.6 (0.8)
New psychological interventions for mental disorders	4.6 (0.7)
Users' perception of illness and treatment impact	4.5 (1.2)
Social and economic impact of mental disorders	4.5 (1.0)
Stigma and discrimination	4.5 (0.9)
Relationships between mental and physical health	4.5 (0.7)

Importance	Trainees (N=22)
Early detection and management of mental disorders	4.5 (0.7)
Suicide prevention	4.5 (0.7)
Rehabilitation and social inclusion	4.3 (0.9)
Prevention of mental disorders	4.2 (0.9)
Stigma and discrimination	4.2 (0.8)

3.7.4.3.   Level of development of the various research areas in their countries

Table 16. Level of development of research areas in their countries as rated by the associations/organisation (Mean, SD)

Level of development	Total sample (N=106)[a]	Psychiatrists (N=31)	Other mental health professionals (N=32)	Users/carers (N=21)	Trainees (N=22)
New medications for mental disorders	**3.0 (1.2)**	2.7 (1.2)	**3.4 (1.1)**	**2.8 (1.4)**	**3.1 (1.1)**
New psychological interventions for mental disorders	2.7 (1.2)	**2.9 (1.1)**	**2.9 (1.2)**	2.2 (1.3)	2.4 (1.1)
Increasing access to available treatments	**2.8 (1.1)**	2.8 (1.2)	2.6 (1.1)	**2.8 (1.1)**	3.0 (0.8)
Improving adherence to available treatments	2.7 (0.9)	2.7 (1.1)	2.6 (1.0)	**2.6 (0.7)**	2.6 (0.8)
Quality of mental health services	**2.8 (1.0)**	**3.0 (1.1)**	2.7 (0.9)	2.4 (1.0)	**3.1 (0.9)**
Early detection and management of mental disorders	**2.8 (1.1)**	**2.9 (1.1)**	2.6 (0.9)	2.6 (1.3)	**3.1 (1.1)**
Resilience and mental health	2.3 (1.1)	2.4 (1.2)	2.5 (0.9)	1.7 (1.1)	2.2 (1.0)
Stigma and discrimination	2.6 (1.1)	2.5 (1.2)	2.6 (1.0)	**2.6 (1.1)**	2.9 (0.9)
Rehabilitation and social inclusion	2.6 (1.1)	2.7 (1.1)	2.7 (0.9)	2.2 (1.3)	2.9 (0.9)
Relationships between mental and physical health	**2.8 (1.0)**	2.8 (1.0)	**2.9 (0.9)**	2.5 (1.1)	2.6 (1.0)
Mental health and well-being in the general population	2.5 (1.1)	2.5 (1.1)	2.8 (1.0)	2.0 (1.3)	2.4 (1.1)
Genetic risk/protective factors for mental disorders	2.5 (1.3)	2.5 (1.3)	2.8 (1.2)	2.2 (1.2)	2.2 (1.3)
Environmental risk/protective factors for mental disorders	2.3 (1.2)	2.6 (1.2)	2.5 (1.1)	1.8 (1.1)	2.2 (1.2)
Prevention of mental disorders	2.3 (1.1)	2.4 (1.1)	2.5 (1.1)	1.7 (1.2)	2.4 (0.9)
Neuroimaging of mental disorders	2.6 (1.4)	2.5 (1.4)	2.8 (1.4)	1.9 (1.2)	2.9 (1.4)
Molecular bases of mental disorders	2.3 (1.3)	2.0 (1.2)	2.6 (1.5)	1.7 (1.1)	2.6 (1.1)
Animal models of mental disorders	1.8 (1.4)	2.0 (1.4)	1.9 (1.5)	0.7 (0.8)	2.1 (1.3)
Cognitive dysfunction in mental disorders and its neural bases	2.7 (1.1)	2.7 (1.1)	**2.9 (1.0)**	2.2 (1.3)	2.9 (1.1)
Social and economic impact of mental disorders	2.4 (1.1)	2.4 (1.3)	2.5 (1.0)	2.2 (1.1)	2.3 (1.1)
Clinical characterisation of mental disorders	**3.3 (1.0)**	**3.3 (1.1)**	**3.2 (1.1)**	**3.3 (1.3)**	**3.4 (0.9)**
Users' perception of illness and treatment impact	2.5 (1.0)	2.6 (1.1)	2.4 (1.2)	2.2 (1.0)	2.7 (0.7)
Suicide prevention	**3.0 (1.3)**	**3.2 (1.1)**	**3.0 (1.2)**	2.2 (1.4)	**3.4 (1.2)**
Health and well-being of carers	2.2 (1.0)	2.3 (1.1)	2.2 (1.0)	2.0 (1.0)	2.1 (1.1)
Epidemiology of mental disorders	2.7 (1.4)	2.5 (1.5)	2.2 (1.4)	2.5 (1.6)	2.9 (1.0)
Mental health consequences of trauma	2.5 (1.1)	2.3 (1.1)	2.7 (1.2)	2.1 (1.1)	2.7 (1.0)
Culture and mental health	2.0 (1.2)	2.1 (1.4)	1.8 (0.9)	2.1 (1.0)	1.9 (1.3)

Bold prints identify the 5 areas with the highest level of development.
a Two organisations did not complete the section of the questionnaire evaluating the research areas in terms of development in their countries

Table 17. Top 5 research areas in terms of development in their countries according to the groups of associations/organisations (mean, SD)

Level of development	Total sample (N=106)
Clinical characterisation of mental disorders	3.3 (1.0)
Suicide prevention	3.0 (1.3)
New medications for mental disorders	3.0 (1.2)
Increasing access to available treatments	2.8 (1.1)
Early detection and management of mental disorders	2.8 (1.1)
Quality of mental health services	2.8 (1.0)
Relationships between mental and physical health	2.8 (1.0)

Level of development	Psychiatrists (N=31)
Clinical characterisation of mental disorders	3.3 (1.1)
Suicide prevention	3.2 (1.1)
Quality of mental health services	3.0 (1.1)
New psychological interventions for mental disorders	2.9 (1.1)
Early detection and management of mental disorders	2.9 (1.1)

Level of development	Other mental health professionals (N=32)
New medications for mental disorders	3.4 (1.1)
Clinical characterisation of mental disorders	3.2 (1.1)
Suicide prevention	3.0 (1.2)
New psychological interventions for mental disorders	2.9 (1.2)
Cognitive dysfunction in mental disorders and its neural bases	2.9 (1.0)
Relationships between mental and physical health	2.9 (0.9)

Level of development	Users/carers (N=21)
Clinical characterisation of mental disorders	3.3 (1.3)
New medications for mental disorders	2.8 (1.4)
Increasing access to available treatments	2.8 (1.1)
Stigma and discrimination	2.6 (1.1)
Improving adherence to available treatments	2.6 (0.7)

Level of development	Trainees (N=22)
Suicide prevention	3.4 (1.2)
Clinical characterisation of mental disorders	3.4 (0.9)
New medications for mental disorders	3.1 (1.1)
Early detection and management of mental disorders	3.1 (1.1)
Quality of mental health services	3.1 (0.9)

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6.   Annexes

Annex I. Annex I. Mental health research training offer in France and the UK

Keywords (France):
1. Master recherche
2. Doctorat
3. Thèse
4. Santé mentale
5. Psychologie
6. Psychiatrie
7. Neurosciences
8. Psychopathologie
9. Psychologie cognitive
10. Neuropsychologie

Websites:
Réseau national des psychologues (France) : http://www.wmaker.net/reseaupsycho.fr/Masters-professionnels-et-masters-de-recherche-en-psychologie_a875.html
Portail des métiers en sciences cognitives (France) :
http://www.metiers-sciences-cognitives.fr/formation.php
Écoles doctorales (France) : http://appliweb.dgri.education.fr/annuaire/ListeEntite.jsp?entite=ed&sd=9&prov=ListeSd
Formations de niveau master et au-delà (UK) : http://www.findamasters.com/search/CourseDetails.aspx?CID=7279

France

Research masters

1. Université Aix en Provence : Neuropsychologie
2. Université Angers : Psychologie cognitive
3. Université Besançon : Psychologie humaine et psychopathologie
4. Université Caen : Psychologie normale et pathologie des processus cognitifs
5. Université Caen : Neuropsychologie
6. Université Chambéry : Neuropsychologie
7. Université Chambéry : Psychologie expérimentale, cognitive et sociale
8. Université Dijon : Analyse des fonctionnements cognitifs - approche de psychologie et psychologie sociale
9. Université Grenoble 2 : Sciences Cognitives
10. Université Grenoble 2 : Psychologie expérimentale, cognitive et sociale
11. Université Lyon 2 : Psychologie et psychopathologie cliniques
12. Université Lyon 2 : Psychologie cognitive
13. Université Lyon 2 : sciences cognitives
14. Université Montpellier 2 : Psychologie: acquisition et gestion des connaissances
15. Université Nancy 2 : psychologie de la communication, de la cognition et des représentations de soi
16. Université Nantes : Psychologie, Cognition, Communication
17. Université Paris 5 : Psychopathologie et psychologie clinique - perspectives anthropologique, cognitive et psychanalytique
18. Université Paris 5 : Psychologie cognitive : étude de l'enfant et de l'adulte

19. Université paris 7 : Médecine scientifique, psychopathologie et psychanalyse
20. Université paris 7 : Psychopathologie clinique et expérimentale
21. Université paris 7 : Psychoses et états-limites
22. Université paris 8 : Psychologie des processus cognitifs
23. Université paris 8 : Psychologie clinique et psychopathologie - interactions et processus d'influence
24. Université paris 8 : Psychanalyse, concepts et clinique
25. Université paris 10 : Psychologie Comportements, processus cognitifs et affectifs
26. Université paris 13 : Psychopathologie et psychanalyse (approches cliniques, sociale et culturelle)
27. Université Poitiers : psychologie de la Cognition : Acquisitions, Représentations, Communication
28. Université Rennes 2 : Psychologie, cognition et communication
29. Université rennes 2 : Sciences humaines option psychopathologie
30. Université Rouen : Psychologie et cerveau (spécialité caennaise ; resp. : H. Platel)
    Université Rouen : Fonctionnement et dysfonctionnement cognitifs (spécialité rouennaise ; resp. A. Vom Hofe)
    Université Rouen : Développement, régulation émotionnelle, praxies (spécialité rouennaise ; resp. D. Mellier)
    Université Rouen : Langage et communication (spécialité caennaise ; resp. J. Vivier)
    Université Rouen : Violences, traumatismes et société (spécialité rouennaise ; resp. JL Viaux)
31. Université Strasbourg : Psychologie humaine et psychopathologie Subjectivité, liens familiaux, langage et culture
32. Université Strasbourg : Psychologie expérimentale et clinique Du normal au pathologique
33. Université Toulouse 2 : psychopathologie
34. Université Toulouse 2 : neuropsychologie
35. Université Toulouse 2 : psychologie des processus cognitifs
36. Université Toulouse 2 : Neurosciences, Comportement, Cognition
37. Université Tours : Cognition, développement : comportement et cerveau

PhD (clinical psychology, psychology and social psychology) inventoried by the National Education website

1. ED 356 cognition, langage, éducation (Aix Marseille)
2. ED 476 neurosciences et cognition (Lyon 1)
3. ED 485 sciences de l'éducation, information et communication, psychologie (Lyon 2)
4. ED 504 cognition, éducation et interactions (Nantes)
5. ED 261 cognition, comportements et conduites humaines (paris 5)
6. ED 158 cerveau, cognition, interaction (paris 6)
7. ED 450 recherche en psychanalyse (paris 7)
8. ED 224 cognition, langage, interaction (paris 8)
9. ED 527 cognition, comportement, langage (Poitiers)
10. ED 326 comportement, langage, éducation, socialisation, cognition (Toulouse 2)
11. ED 472 ED de l'école pratique des hautes études (EPHE Paris)
12. ED 238 sciences humaines sociales (Amiens)
13. ED 216 ingénierie pour la santé, la cognition, l'environnement (Grenoble 1)
14. ED 454 sciences de l'homme, du politique, du territoire (Grenoble 2)
15. ED 473 sciences de l'homme et de la société (Lille 3)
16. ED 484 Lettres, langues, linguistiques, arts (Lyon 2)
17. ED 420 santé publique paris 11 – paris 5 (Paris 11)
18. ED 493 Erasme (Paris 13)
19. ED 507 ED sciences humaines et sociales (Rennes 2)
20. ED 154 sciences de la vie et de la santé (Bordeaux 2)
21. ED 414 sciences de la vie et de la santé (Strasbourg)

United Kingdom:

Results from the website findamasters (http://www.findamasters.com/)

Search = « psychology & psychiatry » < « UK » < « research only »

1. Liverpool john Moores University: psychology higher degrees
2. Middlesex University: applied psychology (MSc)
3. Newcastle University : MPhil Neuroscience, MPhil Psychology
4. University of Buckingham: MSc/MPhil/DPhil Psychology
5. University of Essex: MAD psychoanalytic studies
6. University of Essex: MSD sports and exercise psychology
7. University of Glamorgan: MSc Psychology by research.

Search = « psychology & psychiatry » < « UK » < « any » : 641 results

Sample:
1. Aston U : (MSc) work psychology & business, in health psychology, psychology of health & illness
2. Bangor U (school of psychology) : (MSc) in applied behavioural analysis, in foundations of clinical psychology, in foundations of clinical neuropsychology, in psychological research, in mindfulness based approaches
3. Birkbeck, U of London (dpt of psychological sciences) : (MSc/MA) psychological research methods, educational neuroscience, cognitive neuroscience and neuropsychology
4. […]

With the title "research" or qualified as « MRes »:

1. Aberdeen University, college of life sciences & medicine: MRes psychology
2. Aston University, school of life and health sciences: MRes in cognitive neurosciences
3. Bangor University, school of psychology: MSc in psychological research / PhD
4. Bangor University, school of psychology: MRes psychology
5. Birkbeck, university of London, dpt of psychological sciences: psychological research methods MSc
6. City University London, school of social sciences: MSc research methods and psychology
7. Goldsmiths, university of London, dpt of psychology: MSc research methods in psychology
8. Keele University, faculty of natural sciences: MSc in clinical psychological research
9. King's college London, institute of psychiatry: MSc forensic mental health research
10. King's college London, institute of psychiatry: MSc mental health service and population research
11. King's college London, institute of psychiatry: MSc psychiatric research
12. Lancaster University, psychology department: MSc in psychological research methods
13. Liverpool john Moores University, faculty of health and applied social sciences: MA counseling and psychotherapy, a research based programme
14. Manchester metropolitan university, faculty of health, psychology & social care: MSc psychology (by research)
15. Northumbria University, school of life sciences: MRes psychology
16. Nottingham Trent University, school of social sciences: MSc/MRes psychological research methods
17. Plymouth University, faculty of sciences and technology, psychological research methods
18. Swansea University, faculty of health: MSc research methods in psychology
19. University College London, division of psychology and language sciences: MSc research methods in psychology
20. University college London, division of psychology and language sciences: MSc social cognition: research and application
21. University College London, research dpt of mental health sciences: MSc psychiatric research
22. University of Bath, dpt of psychology: MRes psychology
23. University of Bristol, faculty of sciences: MSc in research methods in psychology

24. University of Birmingham, school of psychology: MRes brain imaging and cognitive neurosciences
25. University of Birmingham, school of psychology: MRes clinical psychology
26. University of Birmingham, school of psychology: cognition and neuroscience MRes
27. University of Birmingham, school of psychology: MRes cognitive neuropsychology and rehabilitation
28. University of Birmingham, school of psychology: MRes psychology
29. University of Dundee, school of psychology: MSc in psychological research methods
30. University of Essex, dpt of psychology: MSc research methods in psychology
31. University of Exeter, college of life and environmental sciences: MSc in psychological research methods
32. University of Glamorgan, faculty of business and society: MSc psychology by research
33. University of Glasgow, college of sciences and engineering: MSc research and methods of psychological science
34. University of Hertfordshire, school of psychology: MSc research methods in cognitive neuropsychology
35. University of Hertfordshire, school of psychology: MSc research methods in psychology
36. University of Kent, school of psychology: MSc in research methods in psychology
37. University of Leicester, school of psychology: MSc in psychological research methods
38. University of Manchester, school of psychological sciences: MRes psychology
39. University of Nottingham, institute of work, health & organisations : MSc psychological research methods
40. University of reading, school of psychology and clinical language sciences : MSc in research methods in psychology
41. University of Roehampton, dpt of psychology: MSc applied psychological research
42. University of Southampton, dpt of psychology: MSc research methods
43. University of Stirling, school of natural sciences: MSc psychological research methods
44. University of Stirling, school of natural sciences: MSc psychological research methods: child development
45. University of Stirling, school of natural sciences: MSc psychological research methods: evolution and behavior
46. University of Stirling, school of natural sciences: MSc psychological research methods: measuring perception
47. University of Stirling, school of natural sciences: MSc psychological research methods: psychology of faces
48. University of surrey, faculty of arts and human sciences: MSc research methods in psychology
49. University of Sussex, school of psychology: MRes in psychological methods
50. University of the west of England, Bristol, dpt of psychology: MSc research methods in psychology
51. University of Westminster, school of social sciences humanities and languages: MSc research methods for psychological practice
52. University of Winchester, faculty of humanities and social sciences: MSc psychological research methods
53. University of York, dpt of psychology: MRes in psychology
54. Anglia Ruskin University, faculty of science and technology: MSc research methods in psychology
55. Kingston University, school of social science: development psychology MRes
56. Kingston University, school of social science: psychology MRes
57. Loughborough University, dpt of human sciences: MRes psychology
58. Open University, faculty of social sciences and psychology: MSc in psychological research methods
59. University of Edinburgh, dpt of psychology: MSc psychological research methods
60. University of Edinburgh, dpt of psychology: MSc by research psychology
61. University of Greenwich, dpt of psychology and counseling: MSc by research psychology
62. University of Greenwich, dpt of psychology and counseling: MSc research methods in psychology
63. University of Liverpool, school of psychology: MSc research methods in psychology
64. University of St Andrews, school of psychology: MRes in psychology
65. University of Strathclyde, dpt of psychology: MRes in research methods in psychology
66. University of Warwick, dpt of psychology: MSc in research methods in psychology

Annex II. Annex II. Systematic mapping terms for social and economic aspects

Social exclusion search terms (title or abstract)

(Social exclusion OR socially excluded OR social isolation OR socially isolated OR social rejection OR socially rejected OR (social adj3 disadvantage) OR (social adj3 disadvantages) OR (social adj3 disadvantaged) OR social alienation OR (socially inactive) OR (social adj3 inactivity) OR (social adj3 inactive) OR (social adj3 inaction) OR social outcast OR underclass OR social distance OR social hierarchy OR anomie OR vulnerable populations OR underprivileged OR Social inclusion OR socially included OR social capital OR social cohesion OR Social engagement OR socially engaged OR social involvement OR socially involved OR Social participation OR social cohesion OR social capital OR Social environment OR social insurance OR social protection OR social security OR social support OR social welfare OR social wellbeing OR social well-being OR support networks OR welfare benefit OR welfare rights OR minimum income OR minimum wage Social adjustment OR social interaction OR social interactions OR social justice OR social networks OR social adaptation OR Interpersonal relations OR social interaction OR social responsibility OR Social responsibilities OR right to treatment OR Inequity OR disparity OR disparities OR unfair treatment OR differential treatment OR social discrimination OR prejudice OR Social characteristics OR shame OR stigma OR stigmatise OR stigmatizing OR stigmatization OR stigmatization OR social perception OR stereotype OR stereotyping OR
Barriers or barrier OR social class OR right to treatment OR social segregation OR
Community participation OR community support OR community networks OR community
mental health services OR (Neighbourhood AND support) OR (neighborhood support) OR
(Friends AND support) OR friendship OR Family life OR family relations OR family relationships OR family relationship OR partner OR communication OR family support OR Marriage OR divorce OR marital status OR Civil rights OR human rights OR basic rights OR
Rights AND (freedom OR move OR movement) OR food OR starvation OR starving OR
Hunger OR Political rights OR vote OR voting OR voice OR voicing OR politically active OR politically inactive OR politically engaged OR political engagement OR autonomy OR
Patient rights OR (rights AND health) OR (rights AND physical health) OR (rights AND
somatic health) OR (rights AND healthcare) OR standard of care OR living will OR poor
healthcare OR professional patient relationship OR right to treatment OR
Data protection OR access to information OR informed consent OR community networks
OR confidentiality OR (Patient adj3 access adj3 medical records) OR
Consent to treatment OR forced treatment OR cruel treatment OR inhuman treatment OR
inhumane treatment OR degrading treatment OR Involuntary admission OR involuntary interventions OR involuntary treatment OR (involuntary AND medication) OR coercion OR coerce OR threat OR threaten OR refuse to treatment OR treatment refusal OR
Maltreatment OR maltreat OR persecution OR persecute OR punishment OR punish Rights AND (child bearing OR pregnant OR pregnancy OR parenting OR abortion) OR
unwanted pregnancy OR Access AND (social services OR public services OR mental health services OR public facilities) OR   Socioeconomic factors OR economically inactive OR (gap adj3 income) OR (socioeconomic adj3 inequalities) OR (socioeconomic adj3 inequality) OR (social adj3 inequalities) OR (social adj3 inequality) OR Low income OR (income adj3 inequality) OR (income adj3 inequalities) OR (poor adj3 community) OR (poor adj3 family) OR (poor adj3 families) OR (poor adj3 household) OR (poor adj3 households) OR (poor adj3 neighbourhood) OR (poor adj3 neighborhood) OR poor adj3 community OR (poor adj3 income) OR (poor adj3 money) OR deprivation OR deprive OR low earning OR poverty OR low wage OR low wages OR (Practice adj3 monitor) OR (quality adj3 care) OR (quality adj3 services) OR (complain and services) OR treatment guidelines OR admission principles OR
Poor housing OR residence characteristics OR (poor AND accommodation AND standard)
OR (rights adj3 ownership) OR (rights adj3 assets) OR (poor housing) OR (poor
adj3 shelter) OR housing conditions OR living conditions OR rights adj3 treatment OR
Homeless or homelessness OR (Access AND education) OR job and training OR (rights adj3 education) OR basic skill OR basic skills OR continuing education OR education OR poor education OR qualification OR illiteracy OR adult education OR educational status OR educational achievement OR special education OR Labour market OR labor market OR employment OR labour force OR labor force OR workforce OR employment OR employed

Unemployed OR unemployment OR Occupations OR (Job AND flexibility) OR (flexible AND job) OR (work AND voluntary) OR paid job OR paid work OR working conditions OR lonel*)

Mental illness and mental health and well-being search terms (title or abstract)

(("drug abuse" OR "drug addict" OR "drug addicts" OR "drug addiction" OR "drug addicted" OR "drug dependent*" OR "drug dependence*" OR "drug withdrawal" OR "drug abuse") OR ("addictive disease*" OR "addictive disorder*") OR ("alcoholic patient*" OR "alcoholic subject*" OR alcoholism OR "alcohol dependent*" OR "alcohol dependence*" OR "fetal alcohol*" OR "prenatal alcohol*" OR "chronic ethanol*" OR "chronic* alcohol*" OR "alcohol withdrawal" OR "ethanol withdrawal") OR ("caffeine dependent*" OR "caffeine dependence" OR "caffeine addiction" OR (caffeine AND addict*) OR "caffeine withdrawal") OR (((cocaine OR heroin OR cannabis OR mdma OR ecstasy OR morphine*) AND (abuse OR depend* OR dependent* OR dependence* OR addict* OR addicts OR addicted OR addiction* OR withdrawal)) OR methadone) OR (addiction OR addictive OR "substance abuse" OR "withdrawal syndrome" OR psychoactive*) OR ((schizophrenia OR schizophrenic) OR Schizotyp* OR ((Delusional OR paranoid) AND disorder*) OR hallucination* OR Psychotic OR Schizoaffective OR psychosis) OR (((manic OR bipolar OR mood) AND disorder*) OR (depressive AND (disorder* OR episode*)) OR "depressive symptom*" OR hypomania OR mania* OR ((major OR psychotic OR disorder*) AND depression) OR "suicide attempt*" OR suicidal* OR cyclothymia OR Dysthymia) OR (((anxiety OR panic OR "Obsessive-compulsive" OR adjustment OR conversion OR dissociative OR Somatoform OR Somatization OR neurotic) AND disorder*) OR ("hypochondriasis*" OR "body dysmorphic disorder*" OR "pain disorder*") OR agoraphobia OR "social phobia*" OR "Post-traumatic stress" OR "stress disorder*") OR ("Eating disorder*" OR "Anorexia nervosa" OR "Bulimia nervosa" OR "sleep disturbance" OR (sexual AND (disorder* OR dysfunction)) OR ((postnatal OR postpartum) AND depression) OR ((antidepressant* OR laxative* OR analgesic* OR psychotropic* OR vitamin* OR steroids OR hormone*) AND abuse)) OR (((insomnia OR sleepiness OR "sleep disturbance") NOT (apnea OR "side effect*" OR parkinson* OR alzheimer OR neurodegenerat* OR cancer OR obesity OR obese*)) OR (hypersomnia NOT narcolepsy) OR ((sleep OR night) AND terror*) OR nightmare*) OR ((disorder* AND (personality OR identity OR impulse* OR impulsive* OR impulsivity)) OR asocial OR antisocial OR psychopathic OR anxious OR narcissi* OR "Pathological gambling" OR pyromania* OR Trichotillomania OR Psychosexual OR ("Munchhausen syndrome")) OR ("Pervasive developmental disorder*" OR autism OR autistic* OR "Rett* syndrome" OR "Asperger* syndrome") OR (((Hyperkinetic OR Conduct OR Emotional OR tic) AND disorder*) OR (anxiety AND (separation OR phobic OR social)) OR (hyperactivity AND (disorder* OR syndrome)) OR "Tourette syndrome" OR " Tourette's syndrome") OR ((Mental AND (disorder* OR illness OR health)) OR "psychological distress" OR "psychiatric disorder ") OR (Nervousness OR "nervous tension" OR Irritability) OR anorexia OR (neurosis OR neuroses OR psychoses) OR (("mental confusion*") OR ("mental disability*") OR ("mental capacity*") OR ((psychiatric OR mental) AND (comorbidity OR comorbid)) OR psychiatry OR psychology))

Economic Medline Search Strategy

PubMed/ Medline
1. Mental Disorders/
2. Mental Fatigue/
3. Mentally Ill/
4. Psychological Stress/
5. Mental Health/
6. Personal Satisfaction
7. Happiness/
8. 1-7/OR
9. Suicide/
10. Assisted Suicide/
11. 9 NOT 10
12. 8 OR 11

13. Mental Disorder$.ti,ab
14. Mental Illness.ti,ab
15. Mental Disease.ti,ab
16. Mentally Ill.ti,ab
17. Psychological problem$.Ti,ab
18. Psychiatric Disorder$.ti,ab
19. Psychosocial Health.ti,ab
20. Psychosocial Problems.ti,ab
21. Psychosocial Wellbeing.ti,ab
22. Emotional Health.ti,ab
23. Emotional Distress,ti,ab
24. Depressi*.ti,ab
25. Anxiety.ti,ab
26. Schizophreni*.ti,ab
27. Bipolar Disorder.ti,ab
28. Psychotic Disorder.ti,ab
29. Psychosis.ti,ab
30. Psychiatr*.ti,ab
31. Mental Health.ti,ab
32. Mental Wellbeing.ti,ab
33. Psychological Health.ti,ab
34. Psychological Wellbeing.ti,ab
35. Pyschological Distress.ti,ab
36. Emotional Wellbeing.ti,ab
37. 13-36/OR
38. 37 OR 12
39. Economics/
40. Economic*.ti,ab
41. Cost*.ti,ab
42. 39-41/AND
43. Limit / Publication Date 1/01/2007 –

Limit / English language abstract only

Annex III.   Annex III.

Annex III - 1.   Search strategy for the ProQuest databases

The searches were conducted May 5th 2012 using the following search strategy:

#	Search terms	Results Health Management	Results Social Services Abstracts
1	AB("mental health" or "mental dis*" or "problem behav*" or "behav* problem*" or psychiatric or psychological or psychosocial or "mental well*" or "psychological well*" or "emotional well*")	14 757	8 180
2	AB(epidemiol* or prevalence* or incidence* or occurrence* or comorbid* or aetiolog* or population-based or "population study" or "population survey" or "population representative" or "general population")	37 159	4 783
3	AB("public health" or "public polic*" or "health polic*" or "welfare polic*" or "policy program*")	13 721	2 002
4	AB("health promotion" or "mental health promotion" or promotion or "health intervention" or "national health program*" or "health impact")	4 452	788
5	AB(prevention or "disorder prevention" or "primary prevention" or "secondary prevention" or "tertiary prevention" or "early intervention")	13 112	3 644
6	AB("health service*" or "health service* delivery" or "health service* access" or "health care delivery" or "health service* organi*" or "health service* need*" or "health service* demand*"or "health advocac*" or "health education")	7 748	1 488
7	AB("European Union" or Europe* or "EU-27" or "European country" or "European countries" or Austria or Belgium or Bulgaria or Cyprus or "Czech Republic" or Denmark or Estonia or Finland or France or Germany or Greece or Hungary or Ireland or Italy or Latvia or Lithuania or Luxembourg or Malta or Netherlands or Holland or Poland or Portugal or Romania or Slovak* or Slovenia or Spain or Sweden or "United Kingdom" or England or Wales or Scotland or "Great Britain" or Croatia or "Former Yugoslav Republic of Macedonia" or Macedonia or Iceland or Montenegro or Turkey or Albania or Andorra or Armenia or Azerbaijan or Belarus or "Bosnia and Herzegovina" or Bosnia or Georgia or Liechtenstein or Moldova or Monaco or Norway or Russia or "San Marino" or Serbia or Switzerland or Ukraine or (Vatican AND (City or State)) or European* or Austrian* or Belgian* or Bulgarian* or Cypriot* or Czech* or Danish* or Estonian* or Finnish* or French* or German* or Greek* or Hungarian* or Irish* or Italian* or Latvian* or Lithuanian* or Luxembourg* or Maltese* or Dutch* or Hollander* or Netherlander* or Polish* or Portuguese* or Romanian* or Slovak* or Slovenian* or Spanish* or Swedish* or English* or Scottish* or Britannic* or British* or Welsh* or Croatian* or Macedonian* or Icelandic* or Turkish* or Albanese* or Andorran* or Armenian* or Azerbaijani* or Belarusian* or Bosnian* or Georgian* or Liechtenstein or Moldavian* or Monaco or Nordic* or Norwegian* or Russian* or Serbian* or Swiss* or Ukrainian* or Vatican*)	80 791	10 907
8	#2 OR #3 OR #4 OR #5 OR #6	68 656	10 592
9	#1 AND #7 AND #8	**556**	**276**

Additional limits - Date: From January 01 2007 to 31 May 2012.

Annex III - 2.   Search strategy for the Cinahl database

The search was conducted May 5th 2012 using the following search strategy:

#	Search terms	Results
S1	TI ((mental* or "mental dis*" or "problem behav*" or "behav* problem*" or psychiatric or psychological or stress or distress or psychosocial* or "mental well*" or "psychological well*" or "emotional well*" or happiness or "life satisfaction")) OR SU ((mental or psychiatric or psychological or Self-Injurious Behavior))	68305
S2	TI, AB, MH (epidemiol* or prevalence* or incidence or comorbid* or co-morbid* or occurrence or aetiolog* or population-based or "population study" or "population survey" or "population representative" or "general population")	81283
S3	TI, AB, MH ("public policy" or "health polic*" or "public health" or "welfare polic" or "government program*" or "government policy" or "policy program*" or "policy guideline*" or "health advocac*" or "community development" or "national health program*")	44908
S4	TI, AB, MH ("health promotion" or "mental health promotion" or promotion or "health impact" or "early intervention")	18918
S5	TI ((prevention or preventive)) OR AB ((prevention or preventive)) OR MH ((prevention or "disorder prevention" or "preventive health care"))	32137
S6	TI, AB, MH ("health service*" or "health services delivery" or "health care delivery" or "health services need*" or "health services demand*" or "health services access" or "health service organi*" or "health education" or "patient satisfaction")	36008
S7	S2 or S3 or S4 or S5 or S6	181880
S8	AB, TI (("European Union" OR Europe* OR "EU-27" OR "European country" OR "European countries") OR (Austria OR Belgium OR Bulgaria OR Cyprus OR "Czech Republic" OR Denmark OR Estonia OR Finland OR France OR Germany OR Greece OR Hungary OR Ireland OR Italy OR Latvia OR Lithuania OR Luxembourg OR Malta OR Netherlands OR Holland OR Poland OR Portugal OR Romania OR Slovak* OR Slovenia OR Spain OR Sweden OR "United Kingdom" OR England OR Wales OR Scotland OR "Great Britain") OR (Croatia OR "Former Yugoslav Republic of Macedonia" OR Macedonia OR Iceland OR Montenegro OR Turkey) OR Albania OR Andorra OR Armenia OR Azerbaijan OR Belarus OR "Bosnia and Herzegovina" OR Bosnia OR Georgia OR Liechtenstein OR Moldova OR Monaco OR Norway OR Russia OR "San Marino" OR Serbia OR Switzerland OR Ukraine OR (Vatican AND (City OR State)) OR (European* OR Austrian* OR Belgian* OR Bulgarian* OR Cypriot* OR Czech* OR Danish* OR Estonian* OR Finish* OR French* OR German* OR Greek* OR Hungarian* OR Irish* OR Italian* OR Latvian* OR Lithuanian* OR Luxembourg* OR Maltese* OR Dutch* OR Hollander* OR Netherlander* OR Polish* OR Portuguese* OR Romanian* OR Slovak* OR Slovenian* OR Spanish* OR Swedish* OR English* OR Scottish* OR Britannic* OR British* OR Welsh* OR Croatian* OR Macedonian* OR Icelandic* OR Turkish* OR Albanese* OR Andorran* OR Armenian* OR Azerbaijani* OR Belarusian* OR Bosnian* OR Georgian* OR Liechtenstein OR Moldavian* OR Monaco OR Nordic* OR Norwegian* OR Russian* OR Serbian* OR Swiss* OR Ukrainian* OR Vatican*))	65477
S9	S1 and S7	17247
S10	(S1 and S7) and (S8 and S9)	**2260**

(Limiters - Published Date from: 20070101-20120531)

Annex III - 3.   Search strategy for the Medline database

The search was conducted May 5th 2012 using the following search strategy:

#	Search terms	Results
1	exp mental disorders/ or mental fatigue/ or mentally ill/ or *stress, psychological/	892 714
2	exp mental health/ or personal satisfaction/ or happiness/	28 805
3	1 or 2	913 259
4	("mental disorder*" or "mental illness" or "mentally ill" or "mental disease" or "psychological problem*" or "psychiatric disorder*" or "psychosocial problem*" or "emotional health" or "psychiatric distress" or psychiatr* or "mental health problem*").ti.	91 249
5	("mental wellbeing" or "mental health" or "psychological wellbeing" or "emotional wellbeing").ti.	27 416
6	4 or 5	115 901
7	3 and 6	74 773
8	exp Europe/	1 010 994
9	European Union/	10 502
10	exp Scandinavia/	114 376
11	(europe* or scandinavia* or "nordic countries").ti,ab.	162 459
12	or/8-11	1 109 696
13	epidemiology/ or prevalence/ or ep.fs.	1 063 164
14	exp *Health Services Research/ or *Health Services/ut or *"Health Services Needs and Demand"/ or *Delivery of Health Care/	70 122
15	exp *Health Promotion/ or exp *Tertiary Prevention/ or exp *Secondary Prevention/ or exp *Primary Prevention/	70 674
16	exp Public Policy/ or exp Health Policy/ or exp *Public Health/	1 155 160
17	(epidemiol* or prevalence or incidence or occurrence or comorbid* or co-morbid* or "population-based" or "population based" or "population survey*" or "population stud*").ti.	269 291
18	((promoti* and preventi*) or "early intervent*").ti.	2 807
19	("health polic*" or "health care policy" or "public policy" or "welfare policy" or "government* polic*" or "policy program*" or "public health" or "national health program*" or "community development" or "health advocac*" or "health education").ti.	50 275
20	or/13-19	2 177433
21	7 and 12 and 20	5 744
22	(news or comment or editorial or letter or interview or historical article).pt.	1 600 624
23	21 not 22	5 316
24	limit 23 to yr="2007 -Current"	**1 572**

In addition to this search with a narrow approach, a broader search was conducted to complement the first Medline search, using the following search strategy:

#	Searches	Results
1	*mental disorders/ or *mental fatigue/ or *mentally ill/ or *stress, psychological/ or *anxiety/	152253
2	*mental health/ or *happiness/ or *"personal satisfaction"/	15697
3	("mental wellbeing" or "mental health" or "psychological wellbeing" or "emotional wellbeing").ti.	28059
4	or/1-3	180675
5	exp Europe/	1028809
6	European Union/	10774
7	exp Scandinavia/	116152
8	(europe* or scandinavia* or "nordic countries").ti.	49125
9	or/5-8	1049871
10	*epidemiology/ or *prevalence/	9494
11	exp *Health Services Research/ or *Health Services/ut or *"Health Services Needs and Demand"/ or *Delivery of Health Care/	71729
12	exp *Health Promotion/ or exp *Tertiary Prevention/ or exp *Secondary Prevention/ or exp *Primary Prevention/	72499
13	exp *Public Policy/ or exp *Health Policy/ or exp *Public health/	1146450
14	(epidemiol* or "population-based" or "population based" or "population survey*" or "population stud*").ti.	104906
15	("health polic*" or "health care policy" or "public policy" or "welfare policy" or "government* polic*" or "policy program*" or "public health").ti.	43069
16	or/10-15	1322721
17	4 and 9 and 16	4039
18	(news or comment or editorial or letter or interview or historical article).pt.	1627849
19	17 not 18	3688
20	limit 19 to ed=20070101-20120531	1400

After removing duplicates from these searches, the total number of retrieved publications from Medline was 2 972.

Annex III - 4.   Search strategy for the PsychINFO database

The search was conducted May 5th 2012 using the following search strategy:

#	Search terms	Results
# 1	TI (mental* or "mental dis*" or "problem behav*" or "behav* problem*" or psychiatr* or psychological or stress or distress or psychosocial* or "mental well*" or "psychological well*" or "emotional well*" or happiness or "life satisfaction") OR KW (mental* or "mental dis*" or "problem behav*" or "behav* problem*" or psychiatr* or psychological or stress or distress or psychosocial* or "mental well*" or "psychological well*" or "emotional well*" or happiness or "life satisfaction")	88 863
# 2	TI, KW AND AB (epidemiol* or prevalence* or incidence or comorbid* or co-morbid* or occurrence or aetiolog* or population-based or "population study" or "population survey" or "population representative" or "general population")	20 516
# 3	TI, KW AND AB ("public policy" or "health polic*" or "public health" or "welfare polic" or "government program*" or "government policy" or "policy program*" or "policy guideline*" or "health advocac*" or "community development" or "national health program*")	5 526
# 4	TI, KW AND AB ("health promotion" or "mental health promotion" or promotion or "health impact" or "early intervention")	3 853
# 5	TI, KW AND AB (prevention or preventive or "disorder prevention" or "preventive health care" or "primary prevent*" or "secondary prevent*" or "tertiary prevent*")	10 417
# 6	TI, KW AND AB ("health service*" or "health services delivery" or "health care delivery" or "health services need*" or "health services demand*" or "health services access" or "health service organi*" or "health education" or "patient satisfaction")	5 552
# 7	AB, TI("European Union" OR Europe* OR "EU-27" OR "European country" OR "European countries") OR (Austria OR Belgium OR Bulgaria OR Cyprus OR "Czech Republic" OR Denmark OR Estonia OR Finland OR France OR Germany OR Greece OR Hungary OR Ireland OR Italy OR Latvia OR Lithuania OR Luxembourg OR Malta OR Netherlands OR Holland OR Poland OR Portugal OR Romania OR Slovak* OR Slovenia OR Spain OR Sweden OR "United Kingdom" OR England OR Wales OR Scotland OR "Great Britain") OR (Croatia OR "Former Yugoslav Republic of Macedonia" OR Macedonia OR Iceland OR Montenegro OR Turkey) OR Albania OR Andorra OR Armenia OR Azerbaijan OR Belarus OR "Bosnia and Herzegovina" OR Bosnia OR Georgia OR Liechtenstein OR Moldova OR Monaco OR Norway OR Russia OR "San Marino" OR Serbia OR Switzerland OR Ukraine OR (Vatican AND (City OR State)) OR (European* OR Austrian* OR Belgian* OR Bulgarian* OR Cypriot* OR Czech* OR Danish* OR Estonian* OR Finnish* OR French* OR German* OR Greek* OR Hungarian* OR Irish* OR Italian* OR Latvian* OR Lithuanian* OR Luxembourg* OR Maltese* OR Dutch* OR Hollander* OR Netherlander* OR Polish* OR Portuguese* OR Romanian* OR Slovak* OR Slovenian* OR Spanish* OR Swedish* OR English* OR Scottish* OR Britannic* OR British* OR Welsh* OR Croatian* OR Macedonian* OR Icelandic* OR Turkish* OR Albanese* OR Andorran* OR Armenian* OR Azerbaijani* OR Belarusian* OR Bosnian* OR Georgian* OR Liechtenstein OR Moldavian* OR Monaco OR Nordic* OR Norwegian* OR Russian* OR Serbian* OR Swiss* OR Ukrainian* OR Vatican*	305 639
# 8	#2 OR #3 OR #4 OR #5 OR #6	43 095
# 9	#1 AND #7 AND #8	**3 952**

Limiters - Published Date from: 20070101-20120531.

Annex IV. Professional associations and organizations of users/carers participating in the ROAMER Stakeholder's survey

Austria

- Austrian Association for Psychiatry and Psychotherapy
- Austrian Psychological Society
- Pro Mente Oesterreich – Austrian Federation for Mental Health
- Hilfe für Angehörige und Freunde psychisch Erkrankter
- Psychiatric Trainees' Section of the Austrian Association of Psychiatry and Psychotherapy

Belgium

- Society of Flemish Neurologists and Psychiatrists
- Belgian Association for Psychological Sciences
- Flemish Mental Health Association (VVGG)
- Vlaamse Vereniging Assistenten Psychiatrie

Bulgaria

- Bulgarian Psychiatric Association

Cyprus

- Cyprus Psychiatric Association
- Cyprus Advocacy Group for the Mentally Ill (KIPRO.DI.PS.A)

Czech Republic

- Czech Psychiatric Association
- Czech-Moravian Psychological Society
- Union of Psychologists Associations in the Czech Republic
- KOLUMBUS
- Section of Young Psychiatrists of the Czech Psychiatric Association

Denmark

- Danish Psychiatric Association
- Danish Psychological Association

Estonia

- Estonian Psychiatric Association
- Estonian Psychologists' Association

- Estonian Patient Advocacy Association (EPAA)
- Young Psychiatrists' Section of the Estonian Psychiatric Association

Finland

- Finnish Psychiatric Association
- Finnish Psychological Society
- Finnish Psychological Association
- Finnish Association for Mental Health
- National Family Association Promoting Mental Health in Finland (FINFAMI)
- Young Psychiatrists' Section of the Finnish Psychiatric Association

France

- French Association of Psychiatry
- French Psychiatric Information Society
- French Association of Psychiatrists in Private Practice
- Medical Psychological Society
- Ligue Française pour la Santé Mentale
- Advocacy France
- Association Française Federative des Etudiants en Psychiatrie

Germany

- German Association for Psychiatry and Psychotherapy
- German Psychological Association
- Bundespsychotherapeutenkammer
- Wissenschaftlicher Beirat Psychotherapie
- Young Psychiatrists' Section of the German Association for Psychiatry and Psychotherapy

Greece

- Hellenic Psychiatric Association
- Hellenic Society of Neurology and Psychiatry
- Hellenic Psychological Society
- Pan-Hellenic Association of Families for Mental Health
- Society for the Rights and Responsibilities of Psychiatric Patients
- Hellenic Association of Psychiatric Trainees

Hungary

- Hungarian Psychiatric Association
- Hungarian Psychological Association
- Pszichiatriai Erdekvedelmi Forum
- Young Psychiatrists' Section of the Hungarian Psychiatric Association

Ireland

- Psychological Society of Ireland
- SHINE – Supporting people affected by mental ill health
- Impero (Irish Mental Patients' Educational and Representative Organization)
- Trainee Committee, College of Psychiatry of Ireland

Italy

- Italian Psychiatric Association
- Italian Psychological Society
- Italian Society of Psychopathology
- UNASAM
- IDEA
- Early Career Psychiatrists' Committee of the Italian Psychiatric Association

Latvia

- Latvian Psychiatric Association
- SKALBES
- Young Psychiatrists' Section of the Latvian Psychiatric Association

Lithuania

- Lithuanian Psychiatric Association
- Lithuanian Psychological Association
- Club13&Co
- Young Psychiatrists' Section of the Lithuanian Psychiatric Association

Luxembourg

- Luxembourguese Society of Psychiatry, Neurology and Psychotherapy

Malta

- Maltese Association of Specialists in Psychiatry
- Maltese Psychological Association
- Malta Mental Health Association
- ANTIDE
- Young Psychiatrists' Section of the Maltese Psychiatric Association

Netherlands

- Netherlands Psychiatric Association
- ANOIKSIS
- Netherlands Psychiatric Trainees Association

Poland

- Polish Psychiatric Association
- Coalition for Mental Health, Poland
- INTEGRATION
- Division of Psychiatric Training, Polish Psychiatric Association

Portugal

- Portuguese Society of Psychiatry and Mental Health
- Portuguese Association for Mental Health
- Associaçao Portuguesa de Internos de Psiquiatria

Romania

- Romanian Association of Psychiatry and Psychotherapy
- Romanian Association of Community Psychiatry
- Romanian League for Mental Health
- ALIAT ONG
- Romanian Association of Residents in Psychiatry

Slovak Republic

- Slovak Psychiatric Association
- Slovak League for Mental Health

Slovenia

- Psychiatric Association of Slovenia
- Slovenian Psychological Association
- Slovenian Association for Mental Health
- HUMANA
- Psychiatric Trainees, Psychiatric Association of Slovenia

Spain

- Spanish Society of Psychiatry
- Spanish Association of Neuropsychiatry
- Young Psychiatrists' Section of the Spanish Psychiatric Association

Sweden

- Swedish Psychiatric Association
- National Coalition for Mental Health (NSPH)
- Swedish Association of Psychiatric Trainees

UK

- Royal College of Psychiatrists
- British Psychological Society
- RETHINK
- Hafal
- PENUMBRA
- Trainees' Section of the Royal College of Psychiatrists