European Brain Council

13/12/2021

EBC Value of Treatment (VOT)

Terms of Reference

This document describes the modus operandi and key principles

for the launch and running of an EBC VOT case study

1) Background

The European Brain Council conceptualised in 2015 the Value of Treatment (VOT) research framework on the basis of the study on the cost and burden of brain disorders (2011)[1].

The VOT research methodology is a health economics and outcomes research. It provides evidence-based and cost-effective policy recommendations for the adoption of a more patient-centred and sustainable model of care for brain disorders.

The EBC VOT research framework aims to:

- Identify treatment gaps and causing factors* along the care pathway and propose solutions to address them.
- Assess health gains and socio-economic impacts resulting from the implementation of the proposed solutions (best practice healthcare interventions), in comparison with current care or no treatment.**
- Converge evidence to policy recommendations on how to improve the care pathway through a patient centered and sustainable model of care

*'treatment gaps' are not only within the provision of medicines, but also within health care systems and services. Causing factors / obstacles such as misdiagnosis, delayed treatment, delayed response to treatment, inadequate response to treatment, limited access to care due to country healthcare infrastructure or unaffordable access to care and pricing including therapies, reimbursement and social safety net cutbacks, non-adherence, etc.

** Both available and potential treatment options (medical and non-medical) can be explored.

2) Selection of therapeutic areas for the case studies – concept note

The VOT case studies cover all types of mental and neurological disorders. Topics are selected based on the assessment that they will benefit from the concept and objectives of the VOT methodology allowing to shed light on the particular and critical needs of patients through the analysis of the gaps in the patient pathway and demonstration of benefits of a proposed solution/ adequate treatment options.

[1] European Neuropsychopharmacology (2011) 21, 718–779

Topics are proposed by EBC member societies - scientific societies and patient organisations. They provide the mandate to EBC to start the project.

A concept note with a preliminary outline of the scope of the proposed study including required expertise (societies to be invited to contribute and identification of health economist and patient representatives) as well as budget estimate and funding sources is prepared by EBC in coordination with the society/experts proposing a new topic. The concept note is discussed and approved at an EBC General Assembly.

3) Governance of case studies

The EBC Board is the highest decision-making body for all case studies. It has sign off authority, validates and approves scopes and outcomes of studies.

A working group is established for each case study. It is composed of experts nominated[2] by EBC member societies and organisations, patient organisation representatives and industry partners. Industry representatives contribute in an advisory capacity (cf point 'support from industry').

The working group is responsible for the design and running of the case studies including the economic modelling. A health economist is part of the working group and can be proposed by an EBC member society involved. The health economist is involved from the onset of the study (phase 1: scope definition). EBC will be responsible for signing the contract with the subcontracted health economist in close collaboration with the working group. Case studies are analysed in collaboration with experts from the EBC's scientific societies in line with the research framework, applying empirical evidence from different European countries.

Preferably, the working group should not exceed 8-10 members: 1 leader (clinician), 1 secretary should be nominated. In addition: 1 industry representative, 1 patient representative, 1 health economist and other experts (eg. clinician, epidemiologist, etc.). A patient representative must be included in the working group.

All working group members are volunteers usually with no financial compensation for their contribution with the exception of the health economist who is subcontracted. On a case-by-case basis, this can be considered also for members of the working group for dedicated tasks such as the literature review.

Each working group has a leader responsible for the scientific coordination who works jointly with an EBC Project Manager in charge of the general coordination of the case study. Support from the EBC project Manager includes the following tasks, applicable on a case-by-case basis:

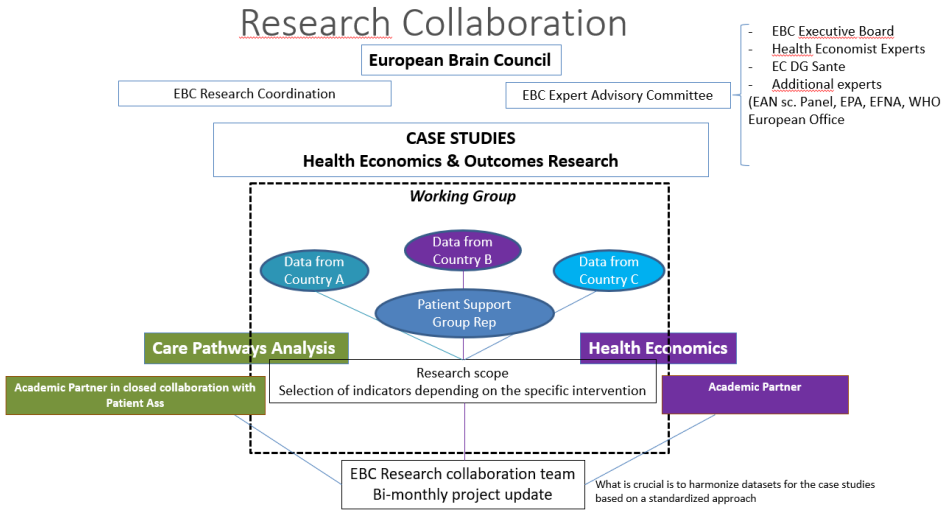
- provide insight to the research conducted by the working group and support for the understanding and implementation of the VOT methodology designed by EBC
- support the drafting of deliverables: concept note, scope document (phase 1), final EBC report with a synthesis of the results according to planned timelines
- contribute to the drafting of the research protocol and review the manuscript (proposing modifications, discussing the research data analysis and conducting literature review as appropriate); this contribution is being acknowledged (authorship).

[2] As expert nominated by the EBC member society or organisation, the expert contributes on behalf of the nominating society

- prepare and organise bi-monthly research updates and joint technical meetings with other case study groups when deemed useful at the time of presenting preliminary results from case studies
- design and implement the communication and advocacy plan in collaboration with group and EBC communication department
- draft contracts with subcontractors (e.g. health economist) to be signed by EBC Executive
- manage budget
- liaise with external experts and organisations working in the area of the study

Contributions from the experts and EBC will be acknowledged in the scientific publications and in the final policy papers. Authorship in the scientific publications will be discussed in the working group ideally at the start of the research phase (phase 2). In addition, EBC Executive Committee members are on an ad-hoc basis invited in contributing to the review of the scientific papers in neurology or in psychiatry, in such a case they are automatically included as co-authors.

The figure below illustrates the collaboration between all actors in the study.



4) Phases of studies and deliverables

Each working group will run its work through 3 phases: 1) scoping, 2) qualitative and quantitative research, 3) final results, publication and policy recommendations.

Phase 1: scope of the study/ deliverable: document outlining scope of the study (3-6 months)

The scope of the study describes the state of knowledge on the issue, the objectives and the policy/research area that will be addressed. A template (see Annex 1) is provided by EBC with the outline of the key components of the scope to facilitate the work under this phase.
These include:

a. The focus (specific disorder or focus if transversal issue)

b. The objectives: outline of the comparator and hypothesis: proposed solution to address key identified gaps in the patient pathway
c. The target patient population
d. Healthcare settings (e.g. Inpatient /outpatient interventions)
e. The segments of the patient journey (prevention/diagnostic/ treatment/rehabilitation, etc.)
f. European countries selected for case study analysis (min 3 known to have different healthcare systems /patterns)
g. Working group composition (including which patient group)
h. Economic partner for the economic evaluation
i. Journal for publication
j. Funders and budget breakdown (cf point 'funding')

The scope document/ completed template is validated by the EBC Board.

Phase 2: Research - Patient pathway analysis and economic evaluation (15 months)

Qualitative and quantitative research is undertaken for the purpose of defining the patient pathway and performing the economic evaluation.

1 - Care Pathway Analysis

Phase two starts with the patient pathway analysis. The patient pathway aims to understand how patients proceed through the care delivery system. It outlines the major gaps/constraints highlighting in particular those that will be addressed in the study. It includes:

1. Assessment of the treatment gaps in patient pathway (mapping) "issues": highlight of 3 to 5 gaps "barriers" to care, input from experts

2. Literature review of care pathways including existing guidelines and policies review.

3. Care pathways survey from both perspectives (clinician and patient*) are performed when needed surveying the target population in the target countries (using patient suggested outcomes measurement EQ5D, PROM and PREM)

4. Outline of the proposed solution to improve the current situation

2 – Economic Evaluation

The economic evaluation includes an analysis of:

- costs and burden of disease associated with the identified gap(s)

- socio-economic impact (costs and health benefits) of closing/reducing the gap via the proposed/identified solution (outcomes measure to capture eg. the reduction in morbidity, QALY gained, reduction of lost follow-up, reduction of unplanned hospital admission, …). Interventions are compared and a decision is

taken based on defined indicators on either conducting a cost-effectiveness analysis, a cost-consequences analysis or a cost-utility analysis.

Phase 3: Results/ Deliverables: scientific report, poster, manuscript for publication, final report with policy recommendations (6-9 months)

The results outline and generalise the findings from the case studies.

A stakeholder meeting is organised with preliminary findings during which experts and disciplines outside the working group are invited to provide feedback. Preliminary results can be communicated at relevant congresses as and when appropriate.

The working group is in charge of drafting the scientific report with results and description of the care pathway analysis and the economic modelling. The working group decides if there is one paper combining the care pathway analysis and the economic modelling or two separate papers.

In addition to the scientific paper, a poster is produced outlining results from the care pathway analysis and the economic evaluation. A template for the poster is provided by EBC (cf annex 2).

The working group is in charge of drafting the manuscript for the publication of the results in the most appropriate scientific journal. A template is provided by EBC for the manuscript (see annex 3). The care pathway analysis and the economic modelling can be published in one or two separate papers. The working group determines the authorship for the publication and the journal(s) in which it wants the manuscript to be published.

EBC is in charge of drafting a final report with the policy recommendations in close collaboration with the working group. A communication and advocacy plan is developed by EBC including activities to engage with EU policy makers (eg. event in the European Parliament, multistakeholder workshop).

5) Funding and timeframe of case studies

Possible funding sources must be indicated at the time of the submission to EBC of the concept note on the proposed topic.

A detailed breakdown of the cost estimates for the research phase (phase 2) and results phase (phase 3) must be included in the document outlining the proposed scope (phase 1) of the approved study topic.

The study can start when funding is secured. A threshold is fixed at 250.000 EUR to cover the three phases.

Studies are expected to run over a 2 ½ - 3 -year period. Longer timeframes can be foreseen when needed.

6) Industry support and acknowledgment

As per EBC rules on its collaboration with industry, industry can be a partner on a project basis including VOT case studies related to their area of interest. In this case, support, should be obtained from several partners ideally three and minimum two for each study.

Industry partners providing funding support may participate in project meetings as member of the working group and contribute with expertise and knowledge.

Industry representatives may also be included in the list of authors in the scientific publications resulting from the project.

Industry experts will be asked to notify EBC as to whether they would like to be included as a co-author in the care pathway analysis and the economic modelling scientific publications as well as the EBC final paper.

Industry support is acknowledged on the EBC VOT dedicated webpage. It is also acknowledged on study public deliverables (scientific report, poster, publication, final report with policy recommendations).

Authorship and acknowledgement on the various deliverables are openly discussed on a case-by-case basis in the working group with the working group leader having the final say.

Decision-making roles always remain with the experts nominated by EBC members and non-commercial partners involved.

ANNEX 1 – Template – Phase 1 – scope of the study

EBC Value of Treatment project

Methodology: Proposed template for working group discussion (Phase 1)

Case study:

Note:

As part of phase 1, this template will be discussed during a preliminary working group TC coordinated by EBC which will then be followed by a physical WG meeting at EBC.

- **Phase 1 - STEP1:** Please complete this template, once final it will be submitted to the EBC Board for validation.

- **Phase 1 - STEP2:** based on this template, a study protocol will then be drafted that will be used for end publication (e.g. EAN Journal or any other peer reviewed scientific journal). Once final, it will also be submitted to the EBC Board for validation.

Outline and research questions - example:

Covering a range of mental and neurological disorders, the EBC Value of Treatment study aims to examine health gains and socio-economic impacts resulting from best practice healthcare interventions in comparison with current care, or – in some cases – in comparison with no treatment at all. Care pathways are mapped for each specific disorder along the whole care process from prevention, prodromal, early diagnosis to disease management in order to identify the major unmet needs and causes for treatment gaps (both those needing research and better evidence to inform treatment decisions and those needing better organization of services).

The following research questions are addressed to examine the best options for optimizing research and care for brain disorders:

■ What is the scale of current unmet needs in the pathology under study [xxxxxx] in Europe? What is the size of so-called "treatment gaps", not only within the provision of medicines, but also within health care systems and services? Considering obstacles such as misdiagnosis, delayed treatment, delayed response to treatment, inadequate response to treatment, suicide risk, limited access to care due to country healthcare infrastructure or unaffordable access to care and pricing including therapies, reimbursement and social safety net cutbacks… and non-adherence. What are the socio-economic benefits of targeting these gaps (e.g. avoidable costs…)? What have we learned from the "Patient Journey" or the patient care pathway analysis?

■ What is the added value of the Value of Treatment study? What are the new research developments in early intervention to improve [primary and secondary] prevention and treatment?

■ How can we ensure that evidence built from robust research can have an impact on policy? What are the priorities for policy making in the current context of health systems reforms (articulating their impact investment social return) while continuing in investing in health ("health is wealth") and legislation implementation? There is still no cure for most brain disorders; hence, it is necessary to focus on risk reduction, preclinical and early detection and diagnosis, timely intervention. Primary and secondary prevention strategies remain essential (available diagnostic tools for neurological disorders including biomarkers, and routine mental health screening). More research is needed to understand the causes but also the progression of brain disorders and to develop new treatments that do not only symptomatically improve the condition but may modify, i.e. slow down, or even stop their course.

PLEASE COMPLETE

BACKGROUND

STUDY TITLE:
ABSTRACT:
Background and objectives:
Discussion:
Key words:

WORKING GROUP COMPOSITION					
Name	**Surname**	**Affiliation***	**Capacity****	**Expertise*****	**Email Address**

***If applicable, please indicate the EBC organization/industry partner you belong to**
****** **1 leader, 1 secretary should be nominated. In addition 1 industry representative, 1 patient representative and experts can be included. Preferably, the working group should not exceed 8 members.**
******* **Clinician, health economist, epidemiologist, etc.**

HEALTH ECONOMIC EXPERTISE	
Do you have already health economic experts within the working group that can work on the economic evaluation (under the guidance of identified external academic institution)? **<u>If yes, please specify</u>** who they are and the type of involvement they would be willing to have in the economic analysis:	□ Yes □ No
If no, do you need support from an external academic institution in undertaking the economic evaluation? If you do not need support from an external academic institution, **<u>please specify</u>** who will be responsible for the economic evaluation:	□ Yes □ No

CARE MODELLING/CARE PATHWAY ANALYSIS

OBJECTIVE of this section is to identify some descriptors of the clinical intervention(s) addressed in the case study in relation to the care pathway services.

1 CARE PATHWAY SERVICES - it includes (please select more than one option where appropriate):		
Component		**Description (please indicate the following descriptors for each service: - Health care setting (for some suggestion see list note 1) - Population descriptors (for some suggestion see list note 2)**
Prevention	□	
Screening/Prodromal/Early Diagnosis	□	
Care and Treatment	□	
Rehabilitation	□	
End-stage Management/ suicide risk prevention	□	
Other	□	

Note 1, HEALTH CARE SETTING:

Primary Care; Community Care home and social care; Hospital: general hospital, psychiatric hospital, specialist care; Tertiary Care: Reference (academic) Networks or Excellence Centers at national and European level; Nursing Home; Pharmacies; Work, occupational health; Rehabilitation Disability and rehabilitation Centre

Note 2, POPULATION DESCRIPTORS:

General population, chronic patients, high-risk patients, high complexity patients, age and disease stage (mild moderate or severe), socially emarginated people.

Please choose the Care pathway service that you want to include in the economic Evaluation. The others that you have indicated will still be considered but on a qualitative level to build the integrated model of care.

ECONOMIC MODELLING

OBJECTIVE OF THE ECONOMIC MODELLING: To compare the socio-economic impact of different healthcare scenarios. Please define the scenarios you would like to include, see below:

1 APPROPRIATE TREATMENT(S) - they include (please select more than one option where appropriate):	
(a) Medical treatment(s) already available in practice	
If yes, please report here the three best practices you may want to value (please rank them in order of priority)	1: ……
	2:

Note: Considering the time and budget constraints we may decide to focus our attention on a limited number of interventions.	…… 3: ……
(b) Coordinated care services already available in practice	
If yes, please report here the three best practices you may want to value (please rank them in order of priority) **Note: Considering the time and budget constraints we may decide to focus our attention on a limited number of interventions.**	1: …… 2: …… 3: ……
(c) Hypothetical intervention(s) (not available in practice yet)	
If yes, please specify:	

2 COMPARATOR(S) - they include (please select more than one option where appropriate):		
Current care:	if current care is your comparator, please specify:	
Non treatment:	if non-treatment is your comparator, it would be defined as:	
	Missed (or delays in diagnosis)	□ Yes □ No
	Lack (or delays in treatment)	□ Yes □ No
	Inappropriate treatment	□ Yes □ No
	Non-adherence to treatment	□ Yes □ No
	Other, please specify:	□ Yes □ No

SUGGESTED OUTCOMES FOR THE ECONOMIC EVALUATION:	**For each outcome do you have access to data related to …**	**If you have data, please specify if you can access: Published evidence (PE); Secondary data (SD) – national registries, administrative data, surveys, RCTs, etc; Expert opinion (EO)**
Costs		
NHS - Tests, Hospitalisation, emergency services, medications, visits with specialists, GP visits, etc….. Would this be applicable for your case study? □ Yes □ No	**Interventions?** □ Yes □ No **Current care?** □ Yes □ No **Non-treatment?** □ Yes □ No	□ PE □ SD □ EO □ PE □ SD □ EO □ PE □ SD □ EO

Social Services - long-term care/nursing homes, etc ….. Would this be applicable for your case study? □ Yes □ No	**Interventions?** □ Yes □ No **Current care?** □ Yes □ No **Non-treatment?** □ Yes □ No	□ PE □ SD □ EO □ PE □ SD □ EO □ PE □ SD □ EO
Productivity at work Would this be applicable for your case study? □ Yes □ No	**Interventions?** □ Yes □ No **Current care?** □ Yes □ No **Non-treatment?** □ Yes □ No	□ PE □ SD □ EO □ PE □ SD □ EO □ PE □ SD □ EO

SUGGESTED OUTCOMES FOR THE ECONOMIC EVALUATION:	**For each outcome do you have access to data related to … (to be detailed per country by the working group)**	**If you have data, please specify if you can access:** Published evidence (PE); Secondary data (SD) – national registries, administrative data, surveys, RCTs, etc; Expert opinion (EO)
Effectiveness		
Mortality Would this outcome be applicable for your case study? □ Yes □ No	**Interventions,** □ Yes □ No **Current care,** □ Yes □ No **Non-treatment,** □ Yes □ No	□ PE □ SD □ EO □ PE □ SD □ EO □ PE □ SD □ EO
Disability Would this be applicable for your case study? □ Yes □ No	**Interventions,** □ Yes □ No **Current care,** □ Yes □ No **Non-treatment,** □ Yes □ No	□ PE □ SD □ EO □ PE □ SD □ EO □ PE □ SD □ EO
Comorbidities - Presence of, their socio economic burden Would this be applicable for your case study? □ Yes □ No	**Interventions,** □ Yes □ No **Current care,** □ Yes □ No **Non-treatment,** □ Yes □ No	□ PE □ SD □ EO □ PE □ SD □ EO □ PE □ SD □ EO
If yes which comorbidities would you like to consider? Please specify 2-3 max:		
Quality of life (eg Eq5D) Would this be applicable for your case study? □ Yes □ No	**Interventions,** □ Yes □ No **Current care,** □ Yes □ No **Non-treatment,** □ Yes □ No	□ PE □ SD □ EO □ PE □ SD □ EO □ PE □ SD □ EO
Other, please specify:	**Interventions,** □ Yes □ No **Current care,** □ Yes □ No **Non-treatment,** □ Yes □ No	□ PE □ SD □ EO □ PE □ SD □ EO □ PE □ SD □ EO

Other, please specify:	**Interventions,** □ Yes □ No **Current care,** □ Yes □ No **Non-treatment,** □ Yes □ No	□ PE □ SD □ EO □ PE □ SD □ EO □ PE □ SD □ EO
Other, please specify:	**Interventions,** □ Yes □ No **Current care,** □ Yes □ No **Non-treatment,** □ Yes □ No	□ PE □ SD □ EO □ PE □ SD □ EO □ PE □ SD □ EO
COUNTRY SETTINGS		
Which country settings you would like to consider in the evaluation? Please specify the countries you have data on and rank them according to priority. Note: Considering the time and budget constraints we may decide to focus our attention on a limited number of country settings. You may want to consider country settings where coordinate care is already implemented in current practice vs. countries where is yet to be introduced/recently introduced.		
1-	2-	3-
4-	More:	

Care pathways for people with major depressive disorder

Rebecca Strawbridge, Roland Zahn, Jonas Eberhard, Danuta Wasserman, Ulrich Hegerl, Paolo Brambilla, Judit Balazs, Jose Caldas-de-Almeida, Paul McCrone, Andrea Ulrichsen, Spyridon Baltzis, Vladmir Carli, Ana Antunes, Giandomenico Schiena, Claudia Hastedt, Erkan Tetik, Vinciane Quoidbach, Patrice Boyer, Allan H Young

MDD working group lead Professor Allan Young *Affiliation* Centre for Affective Disorders, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, U

Background

Major depressive disorder (MDD) is now considered the leading cause of disability worldwide (WHO, 2017) in part due to its high prevalence (which exceeds 300 million) and often enduring nature. The high rates of recurrence, chronicity and treatment-resistance indicate that MDD is treated suboptimally despite a multitude of effective interventions and well-regarded best-practice treatment guidelines MDD's burden also stems from the widespread, common comorbidities with other physical and mental health conditions Many individuals are not receiving treatment at any one time and it is known that both duration of untreated illness and the number of ineffective treatments trialled are risk factors for poorer long-term outcomes. Together, these phenomena demonstrate a need for improved management of MDD. To achieve this, we need to understand the nature and extent of 'gaps' in care pathways

This project aimed to:

1) Identify the current 'treatment gaps' and patient needs along the care pathway, and determine the extent of these gaps (i.e. discrepancy between best- and current-practice).
2) Propose policy recommendation on how to improve the care pathway (i.e. minimise treatment gaps).

Methods

1. **Care pathway analysis (objective 1):**
   - The project working group agreed upon a set of relevant treatment gaps, *a priori*, based on the current gold standard 'stepped care' MDD management guidelines (e.g. NICE).
   - Data was gathered from a variety of sources pertaining to each treatment gap in each country - UK, Sweden, Germany, Italy, Portugal and Hungary – and was synthesised
2. **Consensus recommendations to optimise care pathways (objective 2):**
   - Based on the care pathway analysis, a modified-Delphi approach was undertaken for attaining expert consensus on proposed recommendations (Hidalgo-Mazzei et al. 2019).
   - A set of 35 possible recommendations was developed by a core group based on our previous results A panel of 15 experts across European countries [including mood disorders specialists, GP's, psychiatrists people with lived experience of depression (non-clinicians)] rated their views across three survey rounds New items were introduced or modified where suggested by panel members .
   - Recommendations accepted where >80% agreement of item being 'essential' or 'important'.

Quotations from project communications

"Primary care should have also employed psychologist, social workers and link with psychosocial rehabilitation units and institutions supporting employmen seekers" [Psychiatrist, Sweden]

"We're 10,000 GPs short in England … We need as much help as we can get to deliver a caring, effective service." [GP, UK]

"I feel that physicians MUST be able to allocate the time that is really needed for thorough evaluation of the patient and careful integrated therapy plan (pharmacological + psychological) prescription" [Person with lived experience, Italy]

"Increases in access to secondary care for those who are suffering from depression is very important – rejection to access these services can really be damaging to the patient" [Person with lived experience, UK]

Treatment Gaps / Unmet Needs

Current care pathways (split by treatment gap) averaged across data sources and countries

1: Rate of depression detection: ~ **50% episodes**

2: Delays to detection or treatment of depression ~ **1-5 years**

3: Rates of treatment: ~ **25-50% of patients. Low rates particularly of psychological therapy**

4: Follow-up after treatment initiation ~ **30-65% of patients seen < 3 months**

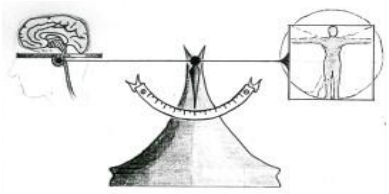
5: Access to secondary (psychiatric) services: ~ **5-25% of patients**

6: Access to specialist mood disorders services: **Limited/no data**

Recommendations

Consensus reached on 28 recommendations to optimise care pathways

1. **To enhance depression detection (pathway entry):** improved information provision to patients, increased service availability (GP appointment number, flexibility, duration), integrate self-management e-mental health tools with healthcare practice.
2. **To improve treatment provision:** The right treatment to each patient (via e.g. decision-support tools, information provision to patients and encourage patient preference), prescribing support tools (integrated with electronic health records & facilitate shared-care provision between types of staff), increased provision of various psychological therapies, help for patient stime off from work/education
3. **Continuity of follow-up after treatment:** Optimise self-management tools & feedback to clinicians, automatic appointment scheduling & reminders, increased service provision, standardised assessment of symptoms and side effects, screen for risk factors to indicate if more (or less) follow up needed.
4. **Access to specialist care:** Enhanced training programs for clinicians to obtain specialism, clear and more lenient criteria for accepting psychiatric referrals (for those not responding to initial treatments), increased resources to services, integrating specialists into primary care, systems for transition into and out of specialist services – *applies to both secondary and tertiary care.*



Conclusions

There are substantial and concerning treatment gaps in depression care across Europe, from the proportion of people not entering care pathways to those stagnating in primary care with impairing and persistent illness A wide range of recommendations can be made to enhance care throughout the pathway.

Acknowledgements : We are most grateful to the European Brain Council (EBC) for managing this project and for grants from Ingelheim Boerhinger and Johnson & Johnson. This work is also supported by the National Institute for Health Research (NIHR) Maudsley Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London. The views expressed are those of the authors and not necessarily those of the NIHR or the Department of Health and Social Care.

WHO: World Health Organisation, 2017. Depression fact sheet. http://www.who.int/news-room/fact-sheets/detail/depression
National Institute for Clinical Excellence (NICE). 2009 Depression: the treatment and management of depression in adults (update). Vol. 90.
Hidalgo-Mazzei et al. 2019 Treatment-resistant and multi-therapy-resistant criteria for bipolar depression: consensus definition. Br J Psychiatry. 214(1):27-35.

ANNEX 3 – template publication manuscript – phase 3

VOT2 JOINT SCIENTIFIC PUBLICATIONS - TEMPLATE FOR Case Study Full Article Publication (Lead: WG Leaders and Academic Partners)

- European Journal of Neurology (EJN) guidelines for submission for Original Papers (https://onlinelibrary.wiley.com/page/journal/14681331/homepage/ForAuthors.html)

Max. 3,500 words for original papers and max. 250 words for abstract. Six figures or tables are allowed for original articles and eight figures or tables are allowed for reviews. Additional figures may be submitted as supplementary material for publication online only at the discretion of the editor. This supplementary material must be clearly labelled as supplementary on the title page and in citations throughout the manuscript and must be uploaded as a separate file type.

- European Psychiatry guidelines for submission https://www.cambridge.org/core/journals/european-psychiatry/information/instructions-contributors

Research Articles: Abstract no longer than 250 words, structured as follows: Background, Methods, Results, Conclusion. Main text should not exceed 3,500 words, with the following structure: Introduction, Methods, Results, Discussion. There is no limit on the number of figures, tables, or references.

- One paper combining the care pathway analysis and the economic modelling or 2 separate papers: this will need to be specified by each Working Group (WG).
- In addition, possibility to publish in other specialist journals. This will need to be specified by each Working Group (WG).
- All publications will need to be referred (journal w/ citations).
- Authorship: to be determined by each Group.

INTRODUCTION	
- **Disease description**: - definition and prevalence - symptoms and prognosis	
- **Socio economic impact**: - functional and social disability - associated costs (direct and indirect if available)	
- **Statement of the challenge**: e.g. there is an optimal treatment (e.g. good model of coordinated care/transition or continuity of care, best practice in terms of disease management, multidisciplinary specialist centre/specialist care service, early intervention,…) but it is not sufficiently delivered/available	
- **Study objectives:** - Identify the current treatment gaps and patient needs along the care pathway and analyse the underlying causes & Identify/propose solutions addressing the treatment gaps (“Care Pathway Analysis”) - Evaluate the costs and burden associated with the treatment gaps and the socio-economic of closing/reducing them by applying the solutions identified/proposed (“Health Economics Study”) - Propose policy recommendation on how to improve the care pathway	
METHODS (COMBINED APPROACH)	
1 - CARE PATHWAY ANALYSIS incl. survey, statistical analysis 1. Assessment of treatment gaps (mapping) “issues” among the sites involved: identification of 3 to 5 treatment gaps “barriers” to care, input from experts 2. Literature review of treatment/care pathways including existing guidelines and policies review.	

3. Care pathways survey from both perspectives (clinician and patient*) [*targeted age group(s)], level of severity, and considering selected countries – Indicators development [Patient suggested outcomes measurement EQ5D, PROM and PREM]	
2 – ECONOMIC EVALUATION - costs and burden of disease associated with the treatment gaps - socio-economic impact (costs and health benefits) of closing/reducing the treatment gap via the proposed/identified solution - outcomes measure to capture e.g. the reduction in morbidity, QALY gained, reduction of lost follow-up, reduction of unplanned hospital admission, …	
RESULTS	
1 - CARE PATHWAY ANALYSIS incl. survey data analysis and statistics analysis - Treatment gaps and patient needs along the current care pathway - Identified/Proposed solutions addressing treatment gaps and patient unmet needs In this section, the main treatment gaps and patient needs are discussed together with the underlying factors in contrast to the identified proposed solution to overcome them.	
2 - ECONOMIC EVALUATION - Costs and burden (e.g. QALY) associated with the treatment gaps - Socio economic impact (costs and health benefits) of the closing/reducing the treatment gap via the proposed solution identified. Economic modelling	
3 - POLICY RECOMMENDATIONS - Proposed policy recommendations on how to improve the care pathway	
DISCUSSION	
- Relation to other relevant studies. Results must be discussed in relation to other similar studies if such studies are available.	
- Limitations. Study limitations must be discussed.	
- Main Findings and Policy implications. The report should include a discussion of the policy implications of the results and limitations.	
REFERENCE	MAX 20 - 25
Supplementary Materials	