

# DE DIMENSIONELE BENADERING VAN DEPRESSIE

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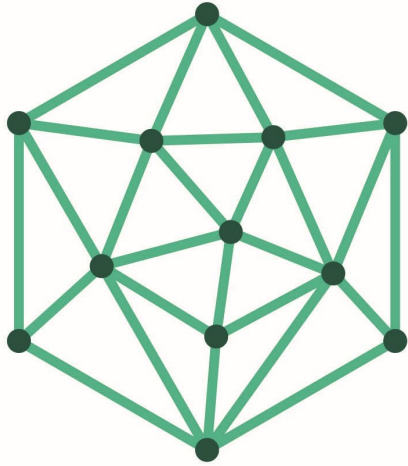
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## BACKGROUND

### MAJOR DEPRESSIVE DISORDER (MDD)

- Prevalence ~5%, Lifetime ~20% ♂:♀ = 1 : 2
- Recurrence rates of depressive episodes 50-80% in 5-10 yrs
- 15-20% persistent episodes  $\geq 2$  years
- Huge suffering in patients and relatives
- High costs: 1.8 billion Euro/year in NL
- Leading cause in 10% of disability pensions
  
- Heterogeneous: symptom-profiles and course of illness
- Treatments: psychotherapy and/or pharmacotherapy
- Trial and change, preference-based approach of treatment
- $\geq 35\%$  Difficult-to-Treat Depression (DtTD or TRD)
- MDD is a brain disease, but what is the 'substrate'





# Depression

## ECNP Meta Network

Andreas Reif & Brenda Penninx, chairs

## 4 WORKGROUPS of Depression Meta Network

### Workgroup 1.

Dissemination (e.g. Meta Network presentations/meetings, position paper on Unmet Needs in Depression Research & Treatment; educational outreach)

**Workgroup 2.** Charting EU-landscape in depression research: e.g. overview of EU-depression studies and large national trials/cohorts, creating a European Registry on Depression (Eu-ReD), analyzing needs, data collection & capture

**Workgroup 3.** Conceptualization of Depression (heterogeneity of depression, personalized medicine approaches, cross-disorder nature, preclinical evidence). Consensus or Delphi-paper that describes relevance and assessment tools.

**Workgroup 4.** Clinical trial harmonization (e.g. similar to/alike platform trials) and related interaction with industry.

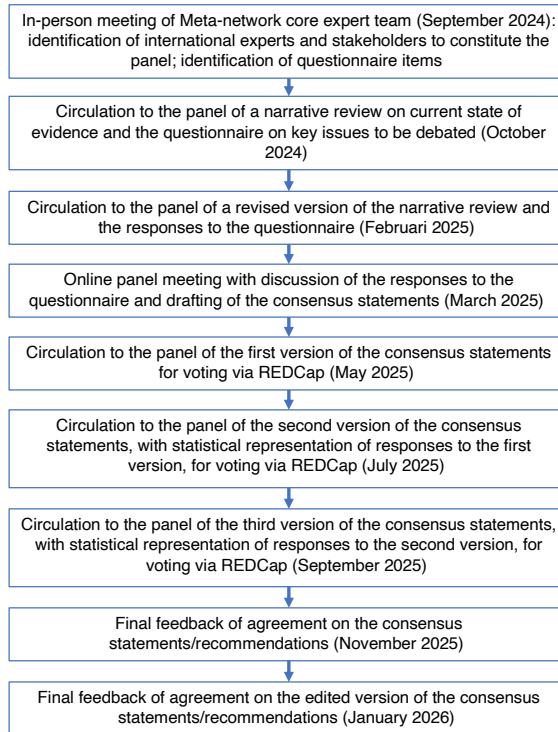
# WORKGROUP 3. CONCEPTUALIZATION OF DEPRESSION

## • Aim of Theme #3

Obtain consensus on internationally agreed, valid, co operationalisation of the concept of depression

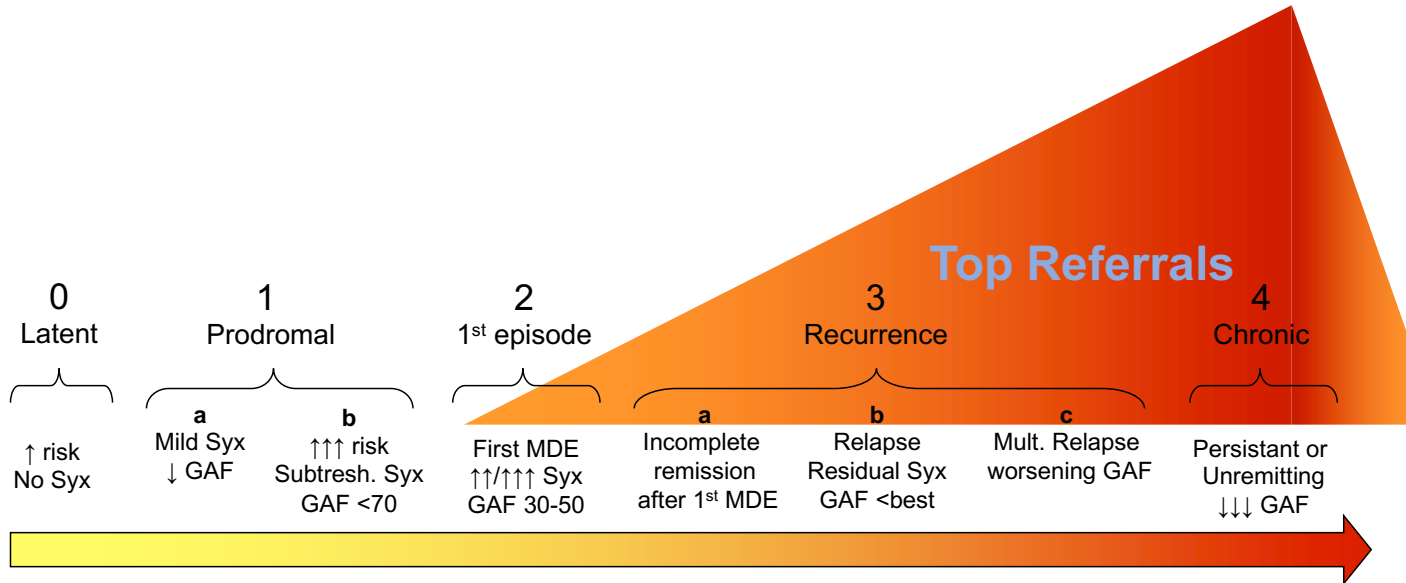
- Identify relevant depression dimensions
  - How to measure
  - (Possible) link to pre-clinical evidence/relevance of
  - Transdiagnostic translation
- DELPHI consensus approach
  - Protocol (preregistration)
  - Work group: Eric Ruhé, Aiste Lengvenyte, J Torino and Luca Sforzini
  - Preparation of 1<sup>st</sup> draft Narrative review

Figure 1



# HETEROGENEITY IN MAJOR DEPRESSIVE DISORDER (MDD)

- Different Symptom profiles
- The role/merit/disadvantage of Specifiers in DSM
- The course of illness



exist to qualify for major

33 patients with depression from (864 of 1030) of which were participants.

# 52 DIFFERENT MDD-SYMPTOMS IN 7 COMMON SCALES



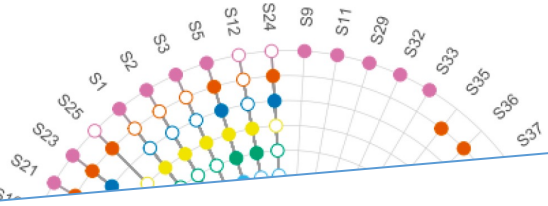
○ IDS   ● BDI   ● SDS   ● HRS   ● CESD   ● QIDS   ● MADRS

- 1 Early insomnia
- 2 Middle insomnia
- 3 Late insomnia
- 4 Hypersomnia
- 5 Sad mood
- 6 Anxious
- 7 Panic
- 8 Irritable
- 9 Mood reactivity
- 10 Diurnal variation
- 11 Grief
- 12 Appetite decrease
- 13 Appetite increase
- 14 Weight loss

- 52 disparate depression symptoms

This underscores the need for consensus  
 Patients -> Improvement  
 -> Understanding why

- Patients -> Symptoms -> Dimensions -> Neurobiology -> Targets
- all instruments



- 38 Crying
- 39 Lonely
- 40 Effort
- 41 Talked less
- 42 People are unfriendly
- 43 People disliked me
- 44 Feeling bothered
- 45 Feeling good
- 46 Feeling happy
- 47 Feeling needed
- 48 Life is full
- 49 Inner tension
- 50 Inability to feel
- 51 Hypochondriasis
- 52 Loss of insight

○ Scale contains compound symptom   ● Scale contains specific symptom

Fried et al., 2017

# DELPHI: PROTOCOL

An international conceptualization of Major Depressive Disorder: a Delphi method...

An international conceptualization of Major Depressiv...

Metadata

OSF

The panel will anonymously rate their agreement with each of the individual statements on a [...] 9-point Likert scale (with the additional possibility of "no answer"). They will be given the opportunity to comment on, or suggest changes to the phrasing of the statements

- A mean score of agreement
- 1 to 3 'low agreement'
- 4 to 6 'moderate agreement'
- 7 to 9 'agreed upon substantially'

Consensus regarding a statement is reached when  $\geq 75\%$  of the panel votes in substantial agreement with a score of 7 to 9.

... and depression (2, 3). It will be performed and reported according to the Guidance on Conducting and Reporting DELphi studies (CREDES; Figure 1) (4, 5). The study and this protocol will be preregistered at the Open Science Foundation (<https://osf.io/jy68n/>).

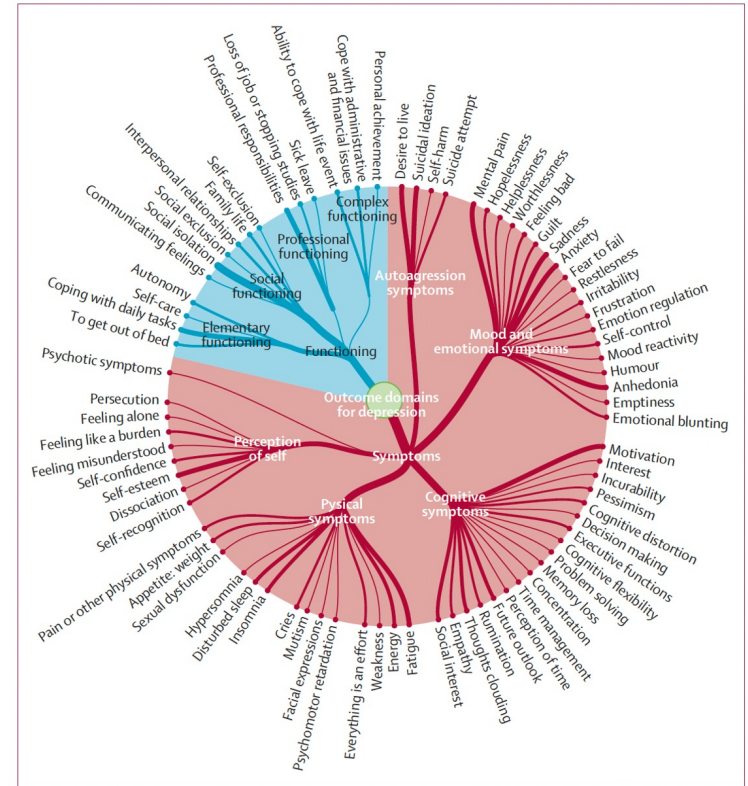


Resource type  
StudyRegistration  
Resource language  
English  
Date created  
September 19, 2024  
Date modified  
December 6, 2024

# NARRATIVE REVIEW

- We expect that answers in DELPHI will
  - For what purpose do we want dimensions
    - Clinical practice
    - Neurobiological insights
    - Clinical Trials
    - Patient-perspective
- Avoid DSM sub-categories (based on [van Tilburg et al. 2012, Fried 2020] and have no relevance for [Chevance et al. 2011])
- Chevance et al. 2020: Bottom up survey of the history of depression (n = 1912), inform healthcare professionals
  - 10 main categories; 80 dimensions
  - Add 1 additional main category (longitudinal)

**Figure 1.** Eighty outcome dimensions related to symptoms and functioning clustered in 10 main categories

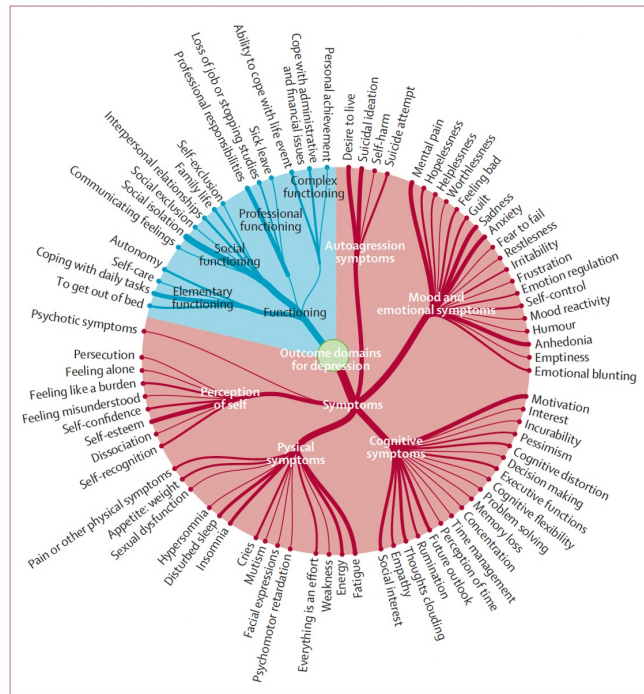


In red symptoms related to depression, in blue functional outcomes related to depression. From Chevance et al. *Lancet Psychiatry*<sup>10</sup>

# THEREFORE PROPOSAL OF 11 MAIN CATEGORIES

- Mood & Emotion
  - Cognition
  - Physical
  - Self-perception
  - Psychotic symptoms
  - Autoagression
  - Elementary functioning
  - Social functioning
  - Professional functioning
  - Complex functioning
- } Combined as 'Functioning'
- Longitudinal course
  - More additional categories?

**Figure 1.** Eighty outcome dimensions related to symptoms and functioning clustered in 10 main categories



In red symptoms related to depression, in blue functional outcomes related to depression. From Chevance et al. *Lancet Psychiatry*<sup>10</sup>

# ARE THERE MORE THAN 11 PROPOSED MAIN CATEGORIES OF DIMENSIONS RELEVANT FOR DEPRESSION?

- Longitudinal course
- Personality Traits
- Preexisting and co-occurring psychiatric conditions
- Physical illness
- Family history
- Early environmental exposures
- Recent environmental stress
- Protective factors / resilience
- Dysfunctional cognitive schemas
- Socioeconomic status



# WHO ARE RELEVANT STAKEHOLDERS IMPORTANT TO INCLUDE IN THE DELPHI PANEL?

- Which areas of expertise/backgrounds?
    - Academic / Researcher
    - Clinician – Psychiatrist
    - Clinician - Psychologist/Psychotherapist
    - Industry
    - Regulatory Body
    - Patient Advocate / Representative
- GAMIAN

# NEXT STEPS

## 1. Purposive Sampling

- Academic / Researcher
- Clinician – Psychiatrist
- Clinician - Psychologist/Psychotherapist
- Industry
- Regulatory Body
- Patient Advocate / Representative
  
- Neurobiological insights
- Clinical trials



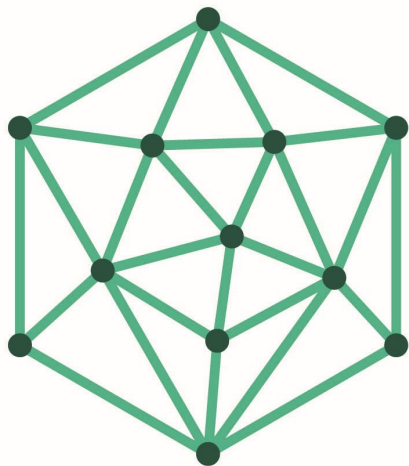
## 2. Next iteration

- Combine certain dimensions based on comments?
- Ask to re-rate ‘almost consensus’

## 3. Instruments for quantification

- For dimensions with consensus

# QUESTIONS AND DISCUSSION



## Depression ECNP Meta Network

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Depression  
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