Generating outcome domains for COS development: Method for a large and international patient and public participation. The PROCEED Study

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Developing a COS for Depression
Depression

• **A frequent and disabling disorder:**
  – Prevalence: around 6% *(Kessler 2013)*
  – Lifetime prevalence: 15-18% *(Bromet 2011)*
  – One of ten patients in primary care *(Malhi 2018)*
  – Fifth leading cause of Years Lived with Disabilities *(Vos, 2017)*
  – 4.2% (3.2,5.3) of the Global Burden of Diseases. *(Vos, 2017)*

• **Treatment options:**
  – Medication
  – Psychotherapy
  – Neurostimulation
Outcomes in trials

- **Multiple outcomes** *(Tyler 2011)*
- **Heterogeneity** *(Tyler 2011)*
  - 280 tools published *(Santor 2006)*

*FIGURE 3* Pie graphs showing the proportionate frequency of use of measures of depression. In total, some 70 different measures of depression were used in the past 10 years. However, only 6 measures were used with any frequency.
What is measured?

**Heterogeneity in assessment of domains:** 20% of studies did not operationalized mood with « sadness » or « depressed ».
Step 1
Define the scope of the COS

Step 2
Check whether a new COS is needed
Register the COS in the COMET database

Step 3
Develop a protocol for the development of the COS

Step 4
Determining outcome domains (OD)
1) Methodological systematic review
2) Fill gaps in knowledge with a qualitative study
3) Elicit views about important outcomes in a consensus process (Delphi Method)
4) Hold a face to face meeting to finalise the COS

Step 5
Determining outcome measurement instruments (OMI)
1) Identifying existing OMI or definitions for each outcome in the COS
2) Quality assess instruments and definitions
3) Use a consensus process to finalise the recommended OMI and definitions

Review and reupdate

Major depressive disorder
Adults (>18)

Registered december 2017

Ongoing writing of the paper

PROCEED

The COMET Handbook 1.0, Trials, 2017
PROCEED

Participative Research on Outcomes' and Core Expectations' Elicitation for Depression

http://clinicalepidemio.fr/depression/en/
• **Objective:**
  Identifying the diversity of expectations for the treatment of depression.

• **Method:**
  – Online international survey based on a few open-ended questions
  – Population:

<table>
<thead>
<tr>
<th>Patients</th>
<th>Carers</th>
<th>Clinicians</th>
</tr>
</thead>
<tbody>
<tr>
<td>➢ Over 18 years old</td>
<td>➢ Over 18 years</td>
<td>➢ A professional that deals with MDD during its occupation</td>
</tr>
<tr>
<td>➢ Report ongoing or previous episode of depression</td>
<td>➢ Report supporting a patient during an episode of depression</td>
<td></td>
</tr>
</tbody>
</table>
Exploratory qualitative study: Interviews with patients, clinicians, caregivers

Questionnaire development and testing

Questionnaire translation

Questionnaire administration:
• Self-administration through internet
• Interviewer-administration as a complement

Thematic analyses

Method

Pilot study

Questionnaire creation

Data collection

Analysis

1 month

1 month

4 months

3 months
Exploratory qualitative study

• Objective:
Determining open-ended questions for the online questionnaire that would bring back **accurate and rich responses**.

• Purposive sampling:
  – 9 Clinicians: profession, experience, workplace
  – 4 Carers: link to the patient
  – 6 Patients: age, gender, ongoing/previous depression, severity.
Open-ended questions for patients

• For all patients:
  – For you, what is the most difficult aspect of depression to live with or endure?
  – For you personally, what might improve or refine treatments for depression?

• For patients who consult/have consulted a healthcare practitioner:
  – What prompted you to seek out a healthcare professional?

• For patients who declared being no more suffering under depression:
  – What made you consider yourself as no longer depressed?
Open-ended questions for carers

• What do you consider to be the most difficult aspects to live with for your family member/friend with depression?

• What do you consider most important to address in a depressed person?

• What types of improvement do you expect from the treatment of depression for your family member/friend?
Open-ended questions for clinicians

- According to your experience, what do you consider to be the most difficult aspects to live with for your patients with depression?

- According to you, what aspects of their condition should be prioritized for depressed patients?

- Under which criteria do you consider a patient to be cured of his/her depression?

- In the case of rheumatoid arthritis, studies have for a long time used the number of painful and swollen joints to evaluate treatment efficacy. However it has been shown that patients expect a reduction in their level of fatigue. Ever since, fatigue has been measured in efficacy studies. According to you, which criteria would be essential to measure in treatment efficacy studies for depression?
Caring for depression: what matters to you?

Help us to improve research on the treatments of depression!

We invite you to participate in PROCEED, an international scientific survey with the goal of identifying your expectations for treatments of depression.

You are eligible if:
- you are over 18 years old AND
- you suffered or are currently suffering from an episode of depression OR
- you are an informal caregiver, that is to say a family member or a friend of someone who has suffered or is suffering from depression OR
- you are a healthcare practitioner working with depressed patients (for instance: psychiatrist, psychologist, nurse, general practitioner/family doctor, etc)

PROCEED is a participative research project involving patients at each step of the research process: please answer the anonymous questionnaire and share it with others.

The more participants will be included, the more we will be able to make things change in the improvement of treatment for depression...

To make your voice count, we invite you to answer ONCE the APPROPRIATE questionnaire below. It will take less than 10 minutes.

Your participation in this study is voluntary. Participation will not impact your medical care. You can choose to cease your participation at any moment without justification. At the end of the questionnaire you will have the possibility to give your e-mail address if you want to be aware of the results of the study AND/OR to be recontacted in order to participate to the following steps of the study. Your e-mail will be stored in one database unlinked with the database with your responses to the questionnaire in order to preserve its anonymity. Data are anonymous and stored on a non shared secure server of a private host. IP address is not tracked. Data will be used only by researchers of the team to answer the questions of the PROCEED study. The results of the study will be published in a scientific journal and communicated via scientific conferences. Astrid Chevance is the Principal Investigator of the study. She is a PhD student in Public Health at the Paris-Descartes University working in the METHODS team of the Center for research in epidemiology and statistics. The protocol of the study has been approved by the the CEEIRB (IRB00003388) on the 15th of May 2018 (Paris, France). We declared the study to the French Data Protection Authority (CNIL).

Please complete only one questionnaire.

Download the participant note

Patient
I accept to participate as a patient
Start

Family or friend
I accept to participate as family or friend of a depressed person
Start

Healthcare professional
I accept to participate as a healthcare professional
Start

3183 participants have shared their expectations with us. Would you like to share yours?
Thank you!

http://clinicalepidemio.fr/depression/en/
## Recruitment

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➢ Report supporting a patient during an episode of depression | ➢ A professional that deals with MDD during its occupation |

### Online recruitment:

- Articles in general and specialized media websites
- Advert on websites of patient or professional associations
- E-mail to professionals
- Share and advert on social networks
Thematic Analyses

Exploratory code
- Code
- Code
- Code
- Code

Coding themes
- Theme
- Theme
- Theme

Mapping themes
- Category
  - Theme
  - Theme

Collaborative decision
- Map of the expectations of patients, clinicians, and caregivers

Validation

Two independent investigators (at least one out of the lab)

Investigators and participants
DESCRIPTION OF THE POPULATION
(french speaking)
Patients (n =1479)

• Socio-demographical-characteristics:
  – **Women**: 74%
  – **Age**: 23 % <30 years, 25%[30-49], 3%>50
  – **Residency**: 25 countries (88% France)

• Experience of depression:
  – **Currently depressed**: 55%
  – **Severity** (PHQ-9): 15% without depression, 17% light, 21% mild, 23% mildly severe, 22% severe.
  – **History of suicidal attempt**: 32.5%

• Treatment:
  – 66% consulted a **psychiatrist**
  – 5.3% consulted only their **GP**
  – 70% are/have been once under **antidepressant medication**
  – 57% are/have been one under **psychotherapy**
Carers (n=402)

- Socio-demographical characteristics:
  - **Women**: 70%
  - **Mean age**: 46 (18)
  - **Residency**: 17 countries (80% France)
  - **Income**: 74% declared having sufficient income
  - **Employment status**: 49% employed, 22% retired

- Experience of depression:
  - **Personal history of depression**: 52%
  - **Lived with the depressed person**: 40%
  - **Relationship with the depressed person**: 15% were taking care of their husband, 12% of their mother, 11% of a friend.
Clinicians (n=392)

• Socio-demographical characteristics:
  – **Women**: 54%
  – **Mean age**: 38.7 (12.4)
  – **Practice**: 16 countries (89% France)
  – **Profession**: 57% psychiatrist, 13% psychologist, 8% nurses, 6% GP

• Experience of depression:
  – **Personal history of depression**: 26%
  – **Relative with an history of depression**: 56%
Thematic analysis
Theme analysis of the French data

**Coders:**
- 2 psychiatrists, master degree in social science
- Background: Psychoanalysis and Marketing, CBT and Sociology
- Mother language

**Coding:**
- Order of coding: clinicians, carers, patients
- Codebook made of verbatims
- Double coding for 300 individuals of each group (900 individuals and 3100 responses).
- Measurement of data saturation *(Tran et al. 2017)*
- Single coding (1100 patients, 100 clinicians) with a random control on 10%
- Consensus on 95.6% of the code

*Braun, Clarke 2006*
Example of themes

- Irritability
- Mental pain
- Self-esteem
- Attention trouble
- Memory loss
- Lack of energy
- Tailored medication dose
- Loss of emotion
- Quality of sleep
- 24/24, 7/7 available care
- Loneliness
- Help for choosing between psychotherapies
- Anger
Verbatims: the example of Mental Pain

• **Patients:**
  – Moral suffering made my daily life unbearable. I had to endure physical pain in my life but I consider them insignificant in comparison to depression.
  – The worst is the unexplainable pain that I’m feeling. I’m suffering so much that I can’t speak anymore.
  – I am suffering psychologically. It is so unbearable that it leads you to wish that everything could stop. You start to think that death could be less painful.
  – When depression is severe, mental pain turns into physical pain
  – The worst is how my children look at me when I am overwhelmed by suffering.
  – Depression is a psychological torture.
  – An extreme pain that is really difficult to understand by our relatives (it can’t hurt because it is NOT physical)
  – No-one can imagine what depressed people are experiencing deep inside: the pain and others lack of belief about the pain.

• **Carers:**
  – Psychological distress
  – Mental pain
  – The psychological suffering is a torture for him
  – Inside suffering
  – Suffering of her own thoughts without being able to share it

• **Clinicians:**
  – Mental pain
  – Inside pain
  – Inside suffering
  – Psychological pain
Discussion

- **Recruitment:**
  - **Fast:** 4 months
  - **Low cost:** home made website
  - **High number of participants:** 2273 french speaking, 522 other language
  - **Diversity of participants:**
    - **International** (3 languages, around 30 countries from 4 continents)
    - All pre-specified categories beside elderly patients (>65).

- **Quality of the data:**
  - Rich responses
  - Accurate
  - Comprehensive
Further analysis

- Analysing the data in English and German
- Merging the themes in one language
- Mapping the themes in categories

<table>
<thead>
<tr>
<th>10.20.2018</th>
<th>Patients</th>
<th>Healthcare professionals</th>
<th>Informal caregivers</th>
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</thead>
<tbody>
<tr>
<td>English-speaking</td>
<td>175</td>
<td>51</td>
<td>15</td>
</tr>
<tr>
<td>German-speaking</td>
<td>116</td>
<td>152</td>
<td>13</td>
</tr>
</tbody>
</table>
A COS for DEPRESSION

Who we are:

International scientific advisory board:

**Pr Andrea CIPRIANI**
NIHR Research Professor at the Department of Psychiatry, University of Oxford and Honorary Consultant Psychiatrist at the NHS Foundation Trust in Oxford (Great Britain)

**Pr Gerhard GARTLEHNER**
Professeur de Santé Publique, directeur du département d'épidémiologie clinique et de médecine fondée sur les preuves à la Donau-Universität de Krems, en Autriche. Il est aussi directeur adjoint de l'Institut international de recherche Triangle du Centre de médecine fondée sur les preuves de l'université de Caroline du Nord (USA)

**Pr Pim Cuijpers**
Professor of Public Health and Headchief of the Department for Evidence based Medicine and clinical Epidemiology at the Donau-University of Krems (Austria). He is also joint director of the Research Triangle Institute International at the University of North Carolina Evidence-based Practice Center (USA).

**Dr Evan MAYO-WILSON**
Assistant Scientist at the Epidemiology department of the Bloomberg Scholl of Public Health at the Johns Hopkins University of Baltimore (USA).

**Eiko FRIED**
Assistant Professor at Leiden University working on the measurement and modeling of mental illness

**Mrs Suzanne T., patient representative**

Pilot team:

**Astrid Chevance**
PhD student. principal investigator. METHODS team.

**Dr. Viet-Thi Tran**
Researcher, supervisor of the PhD. METHODS team.

**Pr. Philippe Rayaud**
Director of the CRESS and the METHODS team. supervisor of the PhD.

http://clinicalepidemio.fr/depression/en/

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