

Evaluating best practices for treating clinical depression in Europe

A review of the BMJ best practice guidelines



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Abstract

Introduction and background. Clinical depression contributes significantly to the burden of disease in the European region. Developing best practice guidelines for treating depression can aid clinicians in applying the best possible interventions and lowering the burden of disease caused by the disorder.

Methodology. The current study focused on how best practices for treating clinical depression are determined and defined in leading European best practice guidelines. Additionally it aimed to determine to what extent standardization of treatments, biological, social and psychological approaches and the concept of the therapeutic relationship are incorporated in leading best practice guidelines for depression. To answer these questions a literature review of the best practice guidelines on major depressive disorder of the British Medical Journal was conducted.

Results. The BMJ best practice guidelines on depression were established by conducting two systematic reviews; one systematic review incorporated 93 publications on different drug and physical treatments, while the other systematic review incorporated 67 publications on psychological treatments. Within each systematic review, these publications were categorized based on PICO-characteristics (patient, intervention, comparison and outcome) and assessed and graded by using a GRADE evaluation. The grading system allowed for the creation of a hierarchy of the effectiveness of various treatments and was translated into a best practice guideline. The BMJ best practice guidelines didn't enforce the use of rigid standardized treatments, but supplied clinicians with various options and freedom regarding the exact implementation of a recommended treatment. Furthermore, the BMJ best practice guidelines seemed to emphasize the biological components of clinical depression. The concept of the therapeutic relationship was not addressed.

Conclusion. Extensive systematic reviews which incorporate a large body of evidence seem the most important tool in establishing the BMJ best practice guidelines. The recommendations regarding the treatment of depression as proposed in the BMJ guidelines are not perfectly aligned with recommendations from other renowned organizations. The BMJ's emphasis on the medical model of disease might be disproportional, although a more thorough comparison with other guidelines would be needed to further elaborate on this claim.

1. Introduction

Major depressive disorder, also known as clinical depression or unipolar depression, is a mental disorder which is characterized by a persistent depressed mood and an inability to experience pleasure. Additional symptoms include significant weight loss or weight gain, a disrupted sleep pattern resulting in either a lack of sleep or excessive sleeping, fatigue and energy loss and difficulties concentrating. Patients experience inappropriate and excessive feelings of guilt and worthlessness and have recurrent thoughts of death which are often accompanied by suicidal ideations (American Psychiatric Association, 2013). The disorder leads to a loss of quality of life for the affected and their families, a loss of productivity for firms and an increased risk of unemployment for individuals. A depressive episode causes people to withdraw from family life, social life and work. Furthermore, there are well established links between depression and physical illness (Directorate General Health and Consumer Protection, 2004). Consequently, clinical depression has been acknowledged by the WHO as a severe illness and has been appointed disability weights that vary between 0.140 and 0.760, depending on the quantity of symptoms displayed by the patient (World Health Organization, 2004).

Major depressive disorder is a highly prevalent mental disorder in the European region. The WHO estimates that annually 7 % of the total European population is afflicted by the disorder, equaling roughly 50 million Europeans (World Health Organization, 2012a). Combining the characteristics of the disorder with such a high prevalence rate, one can imagine that the negative consequences for society are significant. In monetary terms, the direct costs for society include the utilization of health care services and health care provisions, while indirect costs are experienced in the form of absenteeism or productivity losses at work. A recent report calculated the financial losses due to employees dealing with depression to be 92 billion Euro annually for European workplaces (Evans-Lacko & Knap, 2014). When expressing the societal burden of depression in disability adjusted life years (DALY), one sees that 3.8 % of DALY's in the European region were attributable to unipolar depression in 2012 (World Health Organization, 2012b). The WHO predicts that by 2030 depressive disorders will be the leading cause of disease burden in the world (World Health Organization, 2011).

In the last decade mental health issues have gained a more prominent position on the European Commission's agenda. In 2008 the Commission established "the European Pact for Mental Health and Well-being", in which the prevention of depression has been determined to be one of five priorities in the field of mental health in Europe (European Commission, 2008). One can conclude that both the prevention and adequate treatment of major depressive disorder in a European context are of great importance in combatting the related disease burden.

In determining what constitutes as adequate treatment for major depressive disorder, one could opt to establish best practice guidelines. Best practices are described by the Centre for Disease Control Best Practices Workgroup (2010) as a “continuum of practices that represent the ongoing application of knowledge about what is working to improve desired outcomes in a given context.” Levels of effectiveness and evidence of public health impact are taken into account in evaluating such best practices. An alternative way of formulating best practices is stating they represent a collection of “methods and techniques that have consistently shown results superior than those achieved with other means, and which are used as benchmarks to strive for. There is, however, no practice that is best for everyone or in every situation, and no best practice remains best for very long as people keep on finding better ways of doing things” (Krafft, 2014). When applying the concept of best practices to evaluate potential treatments for major depressive disorder, one could stumble upon some challenges and complexities however.

One possible complexity when aiming to establish best practice guidelines for treating clinical depression, is the diversity in both patient characteristics and etiology. Some experts in the field of clinical psychology and psychiatry argue that due to the heterogeneity in both the patient population and the underlying mechanisms causing the disorder, treatments should be tailored to the specific case characteristics of every individual patient (Derksen, 2012). This view possibly complicates the identification and application of best practices. On the other hand there are mental health experts who opt for developing and using standardized, predetermined and structured protocols for treating clinical depression without discriminating on patient characteristics. These experts have adopted a ‘one treatment fits all’ approach which builds on the notion that there are general core characteristics of the disorder present in all patients, and that these core characteristics can be targeted via interventions (Keijsers, van Minnen & Hoogduin, 2011).

A second complexity is the debate to what extent mental disorders, including depression, are rooted in either biological, psychological or sociological causes. The views and conceptions one upholds in this matter, generally have implications for the chosen path of treatment; pharmacotherapy is often suggested to address an alleged biological cause, psychotherapy to address a supposed psychological cause and a system intervention to address a presumed sociological cause. There are also theories that combine these viewpoints, such as the biopsychosocial model that states that psychological, social and biological factors all play an important role in human functioning in the context of disease and illness (Suls, Luger & Martin, 2010).

A very important factor of psychotherapeutic treatment success which might bring forth some issues as well when trying to implement it in best practice guidelines is the concept of the therapeutic relationship. These issues may lay in the notion that the therapeutic relationship is hard to define, even harder to grasp clinically, and difficult to

study empirically (Saeed, 2000). Still, attempts have been made to define and scrutinize the therapeutic relationship. The therapeutic relationship can be described as the relationship between a healthcare professional and a patient. This relationship interacts with treatment methods, patient characteristics, and practitioner qualities in determining effectiveness of treatment (Norcross & Lambert, n.d.). The therapeutic relationship is characterized and influenced by qualitative features of the therapist such as understanding, empathy, support, genuineness, equality, respect, self-awareness and clear boundary-setting (Dzjopa & Ahern, 2008). The therapeutic relationship is not a dichotomous entity, either bad or good, but a very delicate qualitative continuum. Polinghorne and Vernon (2000) identified a positive relationship between therapist and client as most crucial for producing successful outcomes in therapy. Aligned findings were done by Krupnick et al. (2006), who found the therapeutic relationship as experienced by the patient to be of significant importance for treatment outcomes in cases of clinical depression specifically.

When attempting to construct best practice guidelines for clinical depression treatments, it is important to be aware of the previously described concepts and challenges, and the diversity of theoretical frameworks that exist for mental disorders in general and clinical depression in particular. This brings us to the purpose and research aims of the current paper.

1.1 Purpose statement and research questions

The purpose statement of this literature study is to explore how best practices for treating major depressive disorder in Europe have been determined and defined in leading best practice guidelines. In order to provide a solid answer to the above statement, this paper aims to address the following research questions, the first one being the main question:

1. How are best practices for treating major depressive disorder in a European context defined and determined in contemporary best practice guidelines?
2. How do best practice guidelines for treating clinical depression deal with contradicting theories on the applicability of standardized treatments?
3. How do best practice guidelines for treating clinical depression deal with the different viewpoints on the etiology of depression and the question to what extent the disorder is rooted in psychological, sociological or biological factors?
4. Do best practice guidelines for the treatment of clinical depression elaborate on the role of the therapeutic relationship?

2. Methods

The first step in attempting to meet the research aims of the current paper, was to identify leading and renowned examples of guidelines, in which evidence on the

effectiveness and applicability of diverse treatment practices for depression had been assessed, integrated and finally translated into a best practice framework. These guidelines could take the form of a website, report, governmental program or scientific publication. The aim of these guidelines should be to incorporate a comprehensive body of evidence on various approaches for depression in a European context in assessing what possibly constitutes as best practice, with the goal of informing clinical professionals in their decision making process regarding the application of treatments for major depressive disorder.

In order to identify such guidelines for best practices on clinical depression, we first scrutinized the database of the 'Consumers Health and Food Executive Agency' of the European Commission (CHAFEA) and the 'CRD databases of the Centre of Reviews and Dissemination' of York University. An initial publication search was done within these databases combining the search terms "best practice" and "depression". From the 73.539 publications in the CRD-database, 10 publications met our search criteria. From the 663 research proposals in the CHAFEA-database, 0 publications or projects matched our search criteria, leading to a readjustment of our search criteria for this specific database. An additional search was done in the CHAFEA-database using the search term 'depression', supplying us with 10 publications. The identified publications of both the CHAFEA-database and the CRD-databases were then thoroughly examined in terms of specific exclusion criteria. Excluded were publications that focused on prevention or screening rather than treatment, publications focusing on depression in the context of specific comorbidity, publications with a deliberate narrow scope regarding interventions (e.g. focusing just on system-level interventions) and publications lacking a clinical practice approach. After applying these exclusion criteria 1 publication from the CHAFEA-database and 1 study from CRD-database remained. These publications were then assessed in terms of how well they met the research purpose of the current paper and to what extent they reflected a representative best practice model in a European context. Unfortunately both publications were eventually determined to be inadequate for the purposes of the current study. The 'mental health and well-being' project retrieved via the CHAFEA-database (Joint action on mental health and well-being, 2012) had promising research aims, but hadn't been finalized yet and provided insufficient accessible information in its current state to be useful for the current study. The publication obtained via the CRD-database was from the National Collaborating Centre for Mental Health (2005) in Britain. More thorough inspection of the contents made clear this publication was potentially too outdated for the scope of the current research.

Our search strategy was then altered and we chose to perform a generic Google search, using the search term "best practice guidelines major depressive disorder Europe". The first search hit linked to the American Psychiatric Association's website on practice guidelines, from which the specific practice guideline for the treatment of patients with

major depressive disorder was retrieved (American Psychiatric Association, 2010). The American Psychiatric Association (APA) warned on their website that most guidelines were more than 5 years old and may not represent current knowledge and practice. The depression guideline was the only exception, having been updated in 2010. Their guideline on depression was deemed appropriate for the aims of the current research in most aspects. The American Psychiatric Association is a renowned authority in the field of mental health, both in the United States and in some European countries, including the Netherlands, where an official diagnosis based on the DSM-IV (American Psychiatric Association, 1994) is a compulsory requirement in order to get reimbursement for the psychotherapeutic treatment of any mental disorder. Still, the differences in health care values and accessibility of health care facilities between the United States and most (Western) European countries were reason to continue the search for a more European oriented best practice guideline on clinical depression.

The second search hit from the generic Google search we performed, linked to the best practice information platform of the British Medical Journal (BMJ). This website aimed to provide healthcare professionals with the latest relevant information on prevention, diagnosis, treatment and prognosis of various health hazards, diseases and disorders. The platform used recent evidence-based research and expert opinions to provide guidelines (About BMJ Best Practice, 2014). After thorough assessment of the content, the best practice guidelines for depression of the British Medical Journal were deemed appropriate for the aims of the current research paper. Regarding depression, the BMJ Best Practice portal thoroughly discriminated between different forms of depression based on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (American Psychiatric Association, 2013). We evaluated their section devoted to major depressive disorders in adults (MacKinnon, 2014). By examining the information provided in this best practice section, we then proceeded with answering our research questions.

3. Results

In order to provide a clear overview of our findings, we clustered the results in the following subsections. The subsections 3.1, 3.2, 3.3 and 3.4 respectively correspond with research questions 1 , 2, 3 and 4 as stated in the purpose statement.

3.1 Defining and determining best practices

The BMJ best practice platform established its guidelines for treating clinical depression with a structured approach. In the following subsections the different steps of this structured approach will be elucidated.

3.1.1 Identifying the need for a best practice guideline

The first step was simply acknowledging the need and added value of a best practice guideline for major depressive disorder. The BMJ best practice portal stated that it aimed to cover all the most clinically important topics when developing best practice guidelines. Although it didn't elaborate on when or how a topic constitutes as clinically important, it did state that the process of determining these clinically important topics was done by consulting various health care professionals, contributors, editors, subscribers and peer reviewers of the British Medical Journal. Through this process, major depressive disorder was determined to be one of these clinically important topics.

3.1.2 Gathering evidence

An in-house team of medical information specialists of the BMJ regularly searches key global electronic databases, such as Medline and the Cochrane library, to extract systematic reviews, randomized controlled trials and occasionally observational studies on clinically relevant topics. These publications are then incorporated in extensive systematic reviews and published via the BMJ Clinical Evidence platform. Regarding treatment options in major depressive disorder in adults, the BMJ Clinical Evidence Platform performed two systematic reviews. For the first systematic review, covering the topic of drug and physical treatments for clinical depression, 93 publications (mainly systematic reviews and RCTs) were incorporated in the analysis. The second systematic review from BMJ Clinical Evidence focused on psychological treatments and care pathways in clinical depression, and 67 publications were incorporated. Also here it concerned mainly RCTs and systematic reviews.

3.1.3 Evaluating evidence

For each systematic review on the BMJ Clinical Evidence portal, the incorporated publications were categorized in terms of patient, intervention, comparison and outcome characteristics (PICO). Subsequently these publications were assessed and graded in terms of quality of evidence. This was done via a so called GRADE evaluation; a systematic and explicit approach to making judgments about quality with the aim of linking evidence-quality evaluations to clinical recommendations (GRADE Working Group, 2014). Quality was determined for aspects such as the type of study, the methodological soundness, generalizability of research results, consistency and effect size. In the grading system, RCTs and systematic reviews started out with a score of 4, for they were viewed as the strongest type of evidence. Observational studies were very rarely used in the BMJ Clinical Evidence systematic reviews, but when they were incorporated they were appointed a starting score of 2. Points were then deducted when publications contained flaws with regard to methodology (up to 3 points could be deducted here), generalizability or

consistency (1 point could be deducted, but 1 point could also be added when specific criteria were met). Publications establishing large effect sizes could gain an additional point as well. After deducting and adding all points, each publication was assigned a final numerical score, which was translated into one of four possible GRADE scores, judging the evidence to be of very low, low, moderate or high quality. This process can be visualized in a GRADE table (see Appendix 1, table 1). In such a table, studies which are similar in study design, outcome and comparison characteristics are assessed collectively.

3.1.4 Integrating evidence

By using the GRADE system, expected treatment effectiveness could be directly deduced from the assigned grades; the higher the grade, the greater the strength of recommendation for this intervention in a clinical setting. Depending on the intended goal of the intervention and specific disease or patient characteristics, different treatment recommendations could be provided. After all, the most effective intervention for immediate symptom reduction might not necessarily be the most effective intervention to establish relapse prevention. Similarly, the severity of the depressive symptoms might influence what intervention is recommended. Illustrating this for the systematic review on drug and physical treatments for clinical depression, clinical recommendations were provided relating to the effectiveness and safety of tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs), continuing prescription antidepressants, venlafaxine, electroshock therapy, lithium supplementation, pindolol supplementation and usage of St John's wort. In a similar manner, recommendations for psychotherapeutic interventions were given after grading the evidence from the systematic review on psychological treatments. The recommendations regarding course of treatment were categorized based on the presence and severity of symptoms and distinguished between three different levels of severity. Table 2, 3 and 4 in Appendix 1 illustrate on what case characteristics the different best practice recommendations were based and the recommended path of treatment for each category. The tables provide us with a treatment hierarchy. In the actual best practice guidelines of the BMJ there was additional nuancing of the selected treatments. For instance, for the recommendation of using a 'second- or third-generation antidepressant' in high acuity cases, an oversight was subsequently provided with 13 different antidepressants, their way of usage and recommended dosage.

To conclude, by conducting a systematic review on different interventions with a specific intervention aim in mind, and after grading the publications incorporated in that systematic review, the authors of the BMJ Best Practice guidelines were able to establish a hierarchy in the effectiveness of several medical and physical treatments and eventually the identification of what constitutes as best practice. In the same manner psychological

treatments for major depressive disorder were evaluated and translated into best practice recommendations.

3.2 The applicability of standardized treatments in best practice

The research question regarding this topic was: "how do best practice guidelines for treating clinical depression deal with contradicting theories on the applicability of standardized treatments?" The answer is that in case of the BMJ guidelines, such theories were not considered when assessing the body of evidence. The best practice guidelines were based on effectiveness outcomes of a wide array of treatments retrieved via systematic reviews. These effectiveness outcomes were what mattered, and not the hypothesized theoretical frameworks behind certain treatments. It's safe to say the BMJ best practice guidelines didn't represent a 'one treatment fits all'-approach. As described before, treatment recommendations were tailored toward certain case characteristics. The recommendations on psychotherapeutic interventions revolved around the application of specific psychotherapeutic approaches, such as cognitive behavioral therapy (CBT). Recommendations for the duration of treatment and frequency of therapy sessions were also provided. However, solely stating that CBT is the recommended approach, leaves therapists with a lot of room to apply CBT in a way they see fit. The best practice guidelines didn't elaborate on a specific CBT protocol to be adhered to.

3.3 Psychological, social and biological determinants of depression

The BMJ best practice guidelines devoted a small section to the etiology of depression, mentioning the hypothesized contribution of social and biological variables. Noticeable was the emphasis on the chemical and hormonal imbalance affiliated with depression, both in the etiology section and in the treatment recommendations. Even in cases where a combination of antidepressants and psychotherapy was the recommended course of action, the recommendations concerning the pharmaceutical treatment seemed more specific and extensive than the recommendations concerning psychotherapy. This also implied an emphasis on the biological determinants of depression. We conclude that in the BMJ best practice guidelines on depression, there was an extensive amount of information on biological determinants and pharmaceutical interventions, complemented by a smaller, but still sufficient and substantial amount of information on psychological determinants and psychotherapeutic interventions. Social determinants for depression seemed to be given no specific consideration.

3.4 Elaborating on the role of the therapeutic relationship

The BMJ best practice guidelines for depression made no mention of the concepts of the therapeutic relationship or therapeutic alliance. There was a section in which links

to other relevant major clinical guidelines on the diagnosis and treatment of depression were provided. These guidelines were developed by governments, medical organizations or medical societies, and in some guidelines there was explicit mention of the therapeutic relationship. Still, simply providing a link to another guideline was deemed insufficient in order to say the BMJ addresses the concept of the therapeutic relationship.

4. Discussion

The current study describes the process of determining best practices in treating clinical depression, and the way these best practices are subsequently incorporated in best practice guidelines. This is done by scrutinizing the BMJ best practice study on clinical depression, for it represents a renowned best practice guideline in a European context. Additionally the current study elaborates on the way and extent to which standardization of treatments, biological, social and psychological approaches and the concept of the therapeutic relationship are incorporated in leading best practice guidelines for depression.

Our findings have given rise to the notion that the BMJ guidelines may somewhat favor the medical model of depression and emphasize the usage of antidepressants in treating the disorder. This might be partly due to the medical origin and philosophy of the British Medical Journal. Closer inspection of the background of the four main authors and contributors of the BMJ guidelines on depression confirms that all have a background in medicine. A quick glance at the treatment recommendations for depression from the WHO (2012c), shows a greater emphasis on psychosocial support and greater reticence in initiating pharmacological treatment compared to the BMJ guidelines. These discrepancies between the best practice recommendations of the WHO and the BMJ suggest we have to be reticent when trying to generalize the findings of the current study. Although the aim of the current paper was to identify how best practices are generally defined and determined in guidelines for clinical depression, our findings may just apply to the BMJ best practice guidelines. To counter this shortcoming of the current study, future research could strive to compare and incorporate the best practice guidelines from numerous renowned organizations, while focusing on the same research questions we aimed to answer in the current study. Such a study could additionally provide more insights on if and how the backgrounds of the contributors of a guideline influence the recommendations.

The finding that the treatment recommendations for best practices may differ depending on the specific guideline one consults, does yield some importance for clinical practice. Clinicians who consult a specific best practice guideline, should be aware that the recommendations on what constitutes as best practice may not be supported by other guidelines. This also implies that best practice guidelines should merely complement a clinician's expertise, skill, common sense and knowledge in determining what course of treatment to initiate for treating a particular disorder or disease. Possessing these

characteristics seems essential when one touches upon the complex domain of mental disorders and one has to deal with people's experiences, cognitions, behaviors and emotions.

Regarding the implementation of the therapeutic relationship in a best practice guideline on depression, some might argue that the therapeutic relationship is not part of the treatment itself, but merely acts as a moderator in establishing treatment success. Referring once more to the importance of a clinician's skill and knowledge, we can hopefully assume that someone applying a (psycho-)therapeutic intervention, had sufficient training in doing so and is aware of the importance of the therapeutic alliance. Still, as opposed to the British Medical Journal, the American Psychiatric Association does make explicit mention of the therapeutic relationship and its importance in its best practice guideline (American Psychiatric Association, 2010). As discussed in the methodology section of this paper, this APA guideline was assessed in terms of suitability for being the subject of the current paper as well, hence why we are able to elaborate to some extent on its contents. In this regard there seems to be no absolute consensus on what exactly has to be implemented in a best practice guideline.

Another interesting aim for possible future research could be to determine if and how the country characteristics of the different European member states influence what constitutes as best practice. It has already been determined that there are significant differences in treatment practices for clinical depression within Europe (Willsher, Oltermann, Infante & Hamilos, 2013). The question then arises to what extent these treatment practices are aligned with evidence based best practices and how applicable international best practice guidelines are on a national level.

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Appendix 1 Tables

Table 1. An example of part of a GRADE table for publications on treating clinical depression on the BMJ Clinical Evidence platform

Number of studies (participants)	Outcome	Comparison	Type of evidence	Quality (methodology)	Consistency	Directness (generalizability)	Effect size	GRADE	Comment
3 RCTs (161)	Symptom severity	CBT v placebo	4	-1	0	-1	0	Low	Quality point deducted for incomplete reporting of results. Directness point deducted for uncertainty about generalizability of results.
1 Systematic review	Symptom severity	CBT vs no treatment	4	0	0	-1	0	Moderate	Directness point deducted for uncertainty about generalizability of results

Table 2. Treatment recommendations from the BMJ best practice guideline for a clinical depression with high acuity case characteristics

Case characteristics	Treatment Line	Treatment
High acuity: psychotic, suicidal, severe psychomotor retardation impeding activities of daily living, catatonia, or severe agitation	1st	hospitalisation + psychiatric referral ± ECT
	Plus (treatment recommended for all patients)	second- or third-generation antidepressant
	Adjunct (treatment recommended for some patients)	benzodiazepine ± antipsychotic

Table 3. Treatment recommendations from the BMJ best practice guideline for a clinical depression with moderate acuity case characteristics

Case characteristics	Treatment Line	Treatment
Moderate acuity: severe symptoms, significant impairment but no psychotic symptoms, suicidal ideation, or severe psychomotor retardation or agitation	1st	second- or third-generation antidepressant
	Plus (treatment recommended for all patients)	psychotherapy
	Adjunct (treatment recommended for some patients)	benzodiazepine ± antipsychotic
	2nd	switch to tricyclic antidepressant or combination therapy
	Plus (treatment recommended for all patients)	psychotherapy
	3rd	monoamine oxidase inhibitor (MAOI)
	Plus	psychotherapy
	4th	ECT

Table 4. Treatment recommendations from the BMJ best practice guideline for a clinical depression with low acuity case characteristics

Case characteristics	Treatment Line	Treatment
Low acuity: low to moderate severity symptoms, partial impairment, no psychotic symptoms, suicidal ideation, or psychomotor retardation or agitation	1st	second- or third-generation antidepressant
	Plus (treatment recommended for all patients)	psychotherapy
	1st	supportive interventions
	2nd	switch to tricyclic antidepressant or combination therapy
	3rd	St. John's wort