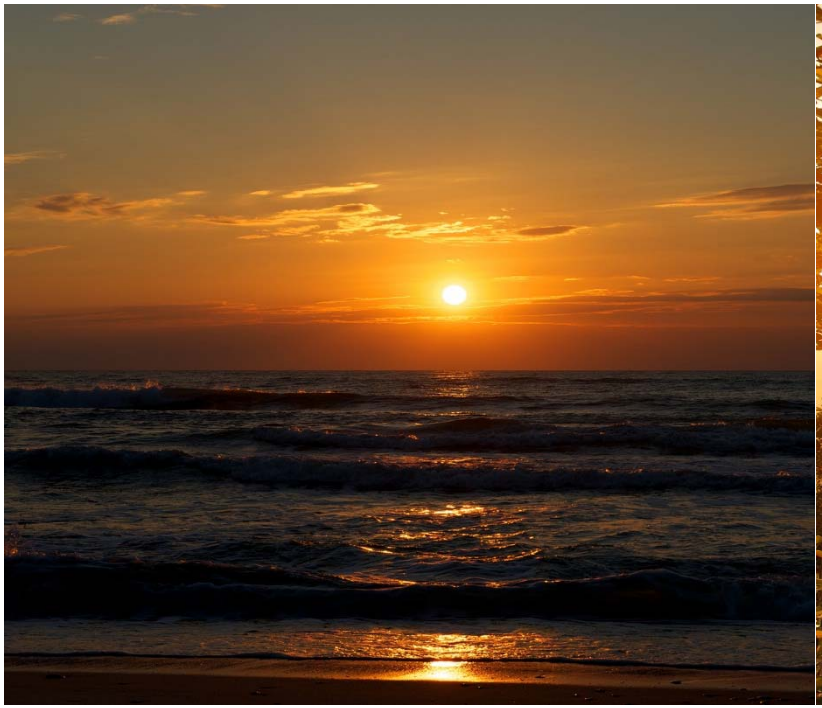
KCE REPORT 230Cs

Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

ABSTRACT

THE LONG-TERM EFFICACY OF PSYCHOTHERAPY, ALONE OR IN COMBINATION WITH ANTIDEPRESSANTS, IN THE TREATMENT OF ADULT MAJOR DEPRESSION



Belgian Health Care Knowledge Centre

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KCE REPORT 230Cs
GOOD CLINICAL PRACTICE

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COLOPHON

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Disclaimer:

- **The external experts were consulted about a (preliminary) version of the scientific report. Their comments were discussed during meetings. They did not co-author the scientific report and did not necessarily agree with its content.**
- **Subsequently, a (final) version was submitted to the validators. The validation of the report results from a consensus or a voting process between the validators. The validators did not co-author the scientific report and did not necessarily all three agree with its content.**
- **Finally, this report has been approved by common assent by the Executive Board.**
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FOREWORD

The essence of our identity, our creative talents, our intelligence, our willpower, our compassion… in short, everything that makes us human is packed into the 1.7 kg of soft tissue inside our skull. A few minor mishaps and we are no longer ourselves, or we simply are no more. That very large head of ours is terrifyingly vulnerable and we are often very powerless when we are “sick in our head” – our resilience is affected. The same applies to depression: our capacity for reason, our motivation – everything becomes black and it affects our resilience to make the correct decisions, including decisions about our treatment. Professional help is very welcome at times like this.

Depression is a common problem – between 4 and 10% of all individuals will experience it once in their lives. Use of anti-depressants is high in our country: nearly 50 million daily doses per year. Almost half of care home residents are thought to be treated with anti-depressants. Of course this does not mean that everyone being treated with anti-depressants is actually suffering from depression. However, it is clear that prescription of these medicines is now common practice.

The use of psychotherapy is not as clear. This is a relevant question at a time when clinical psychologists are being recognised as full healthcare professionals, as is the question regarding the role of psychotherapy in the treatment of depression. The official recognition as healthcare professionals does indeed pave the way to possible reimbursement. It is logical that the government asked the KCE (Belgian Health Care Knowledge Centre) about the approach that should be recommended in terms of a permanent favourable result.

Regardless of the contradictions between *believers* and *non-believers* – either in psychotherapy or in pills – there are currently a number of treatment strategies that can submit credentials: this appears to be the case primarily for a combination of psychotherapy and antidepressants. However, as with many scientific publications, the chorus here too is “*more study is needed*”. Preferably this should be research that does not focus only on the most commercially profitable ways of helping people to recover from depression. This research might need some government support.

Christian LÉONARD
Deputy general director

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General director

ABSTRACT

1 INTRODUCTION

Major depression is a common mental health disorder, characterized by the loss of interest or pleasure in ordinary things and experiences, low mood and a wide range of associated emotional, cognitive, physical and behavioral symptoms. The identification and diagnosis of major depression (which is also called 'clinical depression' or just 'depression') is based not only on the severity of symptoms but also on their persistence, the presence of other symptoms, and the degree of functional and social impairment.[1]

There is not a clear 'cut-off' between 'clinically significant' and 'normal' degrees of depression and it is best to consider the symptoms of depression as occurring on a continuum of severity; the greater the severity of depression, the greater the morbidity and adverse consequences.[2] When adding other aspects that need to be considered, including duration, stage of illness and treatment history, there are considerable problems in attempting to classify depression into categories.[1]

The aim of interventions for depression is to relieve symptoms, restore functions and, in long term, prevent relapse. Treatment continues to be hampered by resistance at the individual level to seek help and the failure, especially in primary care, to correctly identify those who are truly depressed. The most common interventions (treatments) for depression, are psychological and/or pharmacological treatments.

1.1 Incidence and prevalence

Mental diseases, in particular depression, are the first cause of disability in Belgium. Results from the health interview survey from the Scientific Institute of Public Health (WIV-ISP) in 2008 indicated a self-reported prevalence of depression of 9%, with 6% of the responders stating that they suffered from major depression during the past year. Among the responders who stated they had a depression, 88% received care from a health professional, 41% followed psychotherapy and 82% used antidepressant medications [3].

The Intego network is the first computerized network of general practitioners who voluntarily serve as a sentinel in Flanders. The network provides estimates on incidence and prevalence of all diseases registered in general practice in Flanders. The registration network includes approximately 55 practices spread across the Flanders region, representing 1.05% of all GPs working in Flanders.

Incidence rates for diseases are available on the Intego website, using International Classification of Primary Care, 2nd edition (ICPC2) codes per year and per age-group (http://www.intego.be/). For example, in 2008, there were 90 324 different patients seen in the 55 general practices. This is called the yearly contact group (YCG). Bartholomeeusen et al.[4] proposed a method to use the yearly contact group to estimate the entire practice population (estimated to be approximately twice the size of the yearly contact group). Based on this method, the average yearly incidence of depression was calculated to be 12.9 per 1000 persons per year (1.29% per year), during the time period 1994-2010 [5]. This incidence, however, is based on the primary health care classification ICPC-2 code classification system (and not on the likely more stringent DSM-IV classification), and therefore may be an overestimation of the actual incidence of major depressive disorder.

Additionally, Boffin et al. [6] reported on general practice-based data collected on all patients of >18 years who were diagnosed by their GP with a new episode of depression in Belgian sentinel general practices during 2008. Data on 1 739 persons were recorded by 172 sentinel general practices. Incidence rates for GP-diagnosed depression were estimated to be 719/100 000 for men and 1 440/100 000 for women. Of these patients, 31% were GP-diagnosed with a mild depression, 50% with a moderate depression and 19% with a severe depression. The criteria for the depression diagnosis was left to the judgement of the individual GP. Moreover, not all patients with a depression go to a GP for their problem.

Worldwide estimates of the incidence rates and prevalence of depression varies between studies and settings. It is suggested that the best estimate of the proportion of people, who are likely to experience a major depression at some point in their life lie between 4 and 10%.[7] Prevalence rates have consistently been found to be between 1.5 and 2.5 times higher in women than men.[7] Depression can occur at any age from early childhood to old age, and across all social classes. However, in a UK survey, described in the NICE guideline on depression from 2010, people with a depression were more likely to be aged between 35 and 54, be separated or divorced and living alone or as a lone parent. Socioeconomic factors such as unemployment or belonging to lower social classes and below were also found to be associated with a higher prevalence rate[1].

Diagnosis and classification of major depression. The diagnosis and classification of depression were considered out of scope. As a basis for discussion with the guideline development group (GDG), the current two major classification systems DSM-IV-TR and ICD-10 were used. However, all studies based on previous versions of the DSM classification system or on Feighner or Research Diagnostic Criteria were considered.

1.2 Course of the disease

The following information is extracted from the NICE guideline on depression from 2010.[1]

Depression used to be viewed as a time-limited disorder, lasting on average 4 to 6 months with complete recovery afterwards. However, it is now clear that incomplete recovery and relapse are common. A WHO study of mental disorders in 14 centres across the world found that 50% of patients still had a diagnosis of depression 1 year later and at least 10% had persistent or chronic depression. At least 50% of people, following their first episode of major depression, will go on to have at least one more episode and, after the second and third episodes, the risk of further relapse rises to 70 and 90%, respectively. People with early onset depression (at or before 20 years of age) and depression occurring in old age have a significantly increased vulnerability to relapse. Thus, while the outlook for a first episode is good, the outlook for recurrent episodes over the long term can be poor with many patients experiencing symptoms of depression over many years.

2 OBJECTIVES AND SCOPE OF THIS GUIDELINE

2.1 Background

According to a report from the Superior Health Council (Hoge Gezondheidsraad-Conseil Supérieur de la Santé) the prescription of antidepressants in Belgium has increased from 100 million daily defined doses (DDDs) in 1997 to 250 million DDDs in 2008.[8] Based on this report, the Belgian Ministry of Health created a scientific platform for psychopharmacology drugs in 2012, designed to provide advice regarding the use of psychopharmacology drugs or alternative treatment forms. This platform submitted the topic of "what is the place of psychotherapy in the treatment of major depression to the KCE.

2.2 Objectives

A clinical practice guideline (CPG) on major depression:

- Will assist clinicians, in collaboration with the individual patient, in making appropriate treatment choices for major depression
- Will provide scientific background for a possible future KCE project related to antidepressants and psychotherapy.

This guideline focuses on the role of psychotherapy in the treatment of adult major depression. The target population is the adult outpatient and inpatient with confirmed major depressive disorder (MDD). The definitions used and selection criteria are described in the methods section below.

2.3 Research questions

This CPG addresses the following clinical research questions:

1. What is the long-term efficacy of main psychotherapy interventions in the treatment of adults with major depression?
2. Is there a difference between the long-term efficacy of anti-depressive agents and psychotherapy in adults treated for major depression?
3. Is there an advantage in combining both treatments in adults with major depression in the long-term?

3 METHODS

A systematic literature search was conducted in the bibliographic databases including Medline (PubMed.com), PsycInfo, Embase and the Cochrane library from database inception to 19/6/2013. Systematic reviews as well as randomized controlled trials were considered for inclusion.

3.1 Selection criteria

3.1.1 Type of patients

Adult patients with MDD defined according to the DSM-5, DSM-IV, DSM-III-R, DSM-III, Feighner or Research Diagnostic Criteria were included. The MDD had to have been established through a diagnostic interview conducted by a third person and the study had to state explicitly that all included patients had MDD. Studies aimed at people who scored high on a self-report measure, but who were not examined by a clinical interview, were excluded, as were studies that included both patients with a major depressive disorder and patients with e.g. dysthymia or a minor depression, if outcomes were not reported separately for patients with a major depression. Studies in outpatients as well as in inpatients were included. Co-morbid general medical conditions (e.g. diabetes, migraine, cancer) or other psychiatric disorders were not used as an exclusion criteria.

3.1.2 Types of interventions

Psychotherapy was defined as an intervention in which verbal communication between a therapist and a patient is the core element, or in which a psychological treatment is contained in book format (bibliotherapy) or electronic format (internet-based treatment) that the patient works through more or less independently, but with some kind of personal support from a therapist (guided by telephone, e-mail, or otherwise).[9] Types of psychotherapy that have been identified as main type of psychotherapy in an expert taxonomy of psychotherapy for depression were examined.[9] Here, psychotherapy was classified into seven different types: interpersonal therapy, behavioural activation, cognitive-behavioural therapy, problem solving therapy, social skills training, psychodynamic therapy, and supportive counselling. The operational definitions of each type of therapy are given in the scientific report. Marital/couple therapy was excluded by the present review because it involves the partners of depressed patients in the

therapeutic intervention and has the relationship of the couples as a primary focus, rather than the depression.

3.1.3 Types of comparators

The selected comparators were:

- Research question 1: usual care, waiting list, no treatment (no pharmacotherapy), placebo pill, placebo treatment. Light therapy or other types of psychotherapy, not defined as a main type of psychotherapy, were not considered eligible as a comparator.
- Research question 2: pharmacotherapy (antidepressants)
- Research question 3: main psychotherapy intervention or antidepressants alone

3.1.4 Outcomes

The primary outcome was treatment response. Treatment response was defined as every positive outcome achieved, such as whether a patient met criteria for remission or was free from relapse or recurrence. A sustained response was defined as a treatment response that was continued during and after maintenance treatment. Other outcomes were condition-related outcomes (depression rating scales such as the Hamilton Depression Rating Scale, Beck Depression Inventory), quality of life, work-related outcomes, and safety/tolerability.

Note that only studies in which outcomes were assessed at six months or longer after randomization were considered for inclusion. This cut off was chosen because remission is defined as the absence of a depressive disorder three months after the end of therapy, and because it was assumed that most psychotherapies will last around three months. A longer cut off did not seem feasible as few studies have a longer follow up period.

When available outcomes were extracted at six months, one year, two years, three years and beyond.

4 RESULTS

4.1 Main psychotherapy interventions only vs. no treatment

- There is limited evidence that psychotherapy results in a better acute phase treatment response compared to no treatment, at 6 months or longer after the start of treatment, in adults with MDD (low level of evidence).
- There is limited evidence that psychotherapy results in a better acute phase treatment response compared to no treatment, at 1 year or longer after the start of treatment, in adults with MDD (very low level of evidence).
- There is limited evidence that psychotherapy results in a better quality of life compared to no treatment, at 6 months or longer and at 1 year or longer after the start of treatment, in adults with MDD (very low level of evidence).
- It is plausible that maintenance treatment with psychotherapy results in a better sustained response compared to no treatment at 6 months or longer and at 2 year or longer after the start of maintenance treatment, in adult patients who had had MDD and who responded to acute phase treatment (moderate level of evidence).

4.2 Main psychotherapy interventions only vs. antidepressants

- There is limited evidence that psychotherapy results in a better acute phase treatment response compared to antidepressant medication (ADM) (without continuation), at 6 months and at 1 year or longer after the start of treatment, in adults with MDD (very low level of evidence).
- There is limited evidence that psychotherapy results in an equal response to treatment, compared to ADM (continuation), at 6 months and at 1 year or longer after the start of treatment, in adults with MDD (very low level of evidence).
- It is plausible that maintenance treatment with psychotherapy results in an equally sustained response, compared to maintenance treatment with ADM at 8 months or longer after the start of maintenance treatment, in adults who had MDD and who responded to acute phase treatment with either psychotherapy or ADM (high level of evidence).
- There is limited evidence that maintenance treatment with psychotherapy results in an equally sustained response, compared to maintenance treatment with ADM, at 2 years or longer after the start of maintenance treatment, in adults who had MDD and responded to acute phase treatment with either psychotherapy or ADM (low level of evidence).

4.3 Main psychotherapy interventions combined with antidepressants vs. main psychotherapy intervention or antidepressants only

- There is limited evidence that combined psychotherapy with ADM results in an equal acute phase treatment response compared to psychotherapy at 6 months and at 1 year or longer after the start of treatment, in adults with MDD (very low level of evidence).
- There is limited evidence that combining psychotherapy with ADM results in a better acute phase treatment response compared to ADM alone, at 6 months or longer after the start of treatment, in adults with MDD (low level of evidence).
- There is limited evidence that combined psychotherapy with ADM results in a better acute phase treatment response compared to ADM alone, at 1 year or longer after the start of treatment, in adults with MDD (very low level of evidence).
- There is limited evidence that maintenance treatment with combined psychotherapy and ADM results in a better sustained response compared to maintenance psychotherapy alone, at 6 months and at 1 year or longer after the start of treatment, in adults who had had MDD and who responded to acute phase treatment (low level of evidence).
- There is limited evidence that maintenance treatment with combined psychotherapy and ADM results in a better sustained response compared to maintenance with ADM alone, at 6 months or longer after the start of treatment, in adults who had had MDD and who responded to acute phase treatment (low level of evidence).
- It is plausible that maintenance treatment with combined psychotherapy and ADM results in a better sustained response compared to maintenance with ADM alone, at 1 year or longer after the start of treatment, in adults who had had MDD and who responded to acute phase treatment (moderate level of evidence).

4.4 Formulation of recommendations

Based on the retrieved evidence, a first draft of recommendations was prepared by a small working group (KCE experts and GDG president). This first draft was circulated to the guideline development group two weeks prior to the face-to-face meetings (December 10th, 2013 and May 9th, 2014). Recommendations were changed if important new evidence supported this change. A second set of recommendations was then prepared and once more circulated to the guideline development group for final approval.

The strength of each recommendation was assigned using the GRADE system (Table 1 and 2). The strength of recommendations depends on a balance between all desirable and all undesirable effects of an intervention (i.e., net clinical benefit), quality of available evidence, values and preferences of the patients, and estimated cost (resource utilization).

It was decided to supplement the literature searches with a specific search for patient preferences. If relevant, information from this search was included in “Other considerations” during the recommendation and GRADEing process.

The recommendations prepared by the GDG were submitted to key representatives of the relevant stakeholders, who also acted as external reviewers of the draft guideline. They rated the three recommendations with a score ranging from 1 (‘completely disagree’) to 5 (‘completely agree’) and discussed them at a face-to-face meeting (the ‘stakeholder meeting’).

Finally, prior to its publication, the guideline was reviewed by 2 external assessors and, additionally, underwent a CEBAM validation with 3 validators using the AGREE II checklist. The validation of the report is the result of a consensus or voting process between the CEBAM validators.

Declarations of interest were formally recorded.

Table 1 – Levels of evidence according to GRADE [$]

Quality level	Definition	Methodological Quality of Supporting Evidence
High	We are very confident that the true effect lies close to that of the estimate of the effect	RCTs without important limitations or overwhelming evidence from observational studies
Moderate	We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies
Low	Our confidence in the effect estimated is limited: the true effect may be substantially different from the estimate of the effect	RCTs with important limitations or observational studies or case series
Very low	We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect	

[$] *Balshem H, Helfand M, Schunemann HJ, Oxman AD, Kunz R, Brozek J, et al. GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol. 2011;64(4):401-6.*

Table 2 – Strength of recommendations according to GRADE [$]

Grade	Definition
Strong	The desirable effects of an intervention clearly outweigh the undesirable effects *(the intervention is to be put into practice),* or the undesirable effects of an intervention clearly outweigh the desirable effects *(the intervention is not to be put into practice).*
Weak	The desirable effects of an intervention probably outweigh the undesirable effects *(the intervention probably is to be put into practice),* or the undesirable effects of an intervention probably outweigh the desirable effects *(the intervention probably is not to be put into practice).*

[$] *Guyatt GH, Oxman AD, Kunz R, Falck-Ytter Y, Vist GE, Liberati A, et al. Going from evidence to recommendations.[Erratum appears in BMJ. 2008 Jun 21;336(7658): doi:10.1136/bmj.a402]. BMJ. 2008;336(7652):1049-51.*

5 CLINICAL RECOMMENDATIONS

The details of the evidence used to formulate the recommendations below are available in the scientific report and its supplements. The recommendations below are based on the conclusions from the scientific evidence and do not follow the sequence of the chapters in the scientific report. The comparison of different types of psychotherapy was considered out of project scope, however, the vast majority of studies found (approximately 90% of the studies) were on cognitive behavioral therapy (please see section on Quality of the Evidence).

5.1 Psychotherapy alone, or in combination with antidepressants

Recommendations	Strength of Recommendation	Level of Evidence
Psychotherapy* combined with anti-depressant medication is the preferred treatment option for patients with a major depression both in the acute phase and the continuation phase.	Weak	Very Low
If a patient with a major depression does not want combined treatment (i.e. if the patient prefers to start with only one type of treatment) psychotherapy* could be a first choice, because psychotherapy* is at least as effective as antidepressants in the short term and superior to antidepressants in the long-term. This recommendation might not apply to patients with a severe major depressive disorder having psychotic symptoms.	Weak	Very Low
Antidepressant medication only should be avoided as a treatment option for major depression in the symptomatic phase, because the combination of psychotherapy* and antidepressants has superior effect in the long-term.	Strong	Moderate

The effect is currently only sufficiently studied for **cognitive behavioural therapy (CBT)*

Considerations linking evidence to recommendations.

Factor	Comment
Balance between clinical benefits and harms	In preparation of the final GDG meeting draft recommendations were prepared by KCE researchers and circulated to the GDG group in advance. Each of the three recommendations were discussed, and each GDG member were given time to comment on the recommendation as it was stated, and to suggest changes to the wording of the recommendation. The recommendations are a result of agreement within the GDG group (no formal consensus method utilized). Regarding the first recommendation the GDG collectively endorsed, that this recommendation should state that combined therapy is preferred over anti-depressant medication alone, because of its proven superior effect in the long-term. The GDG made this a weak recommendation based on low level of evidence on combination therapy, because the evidence that adding psychotherapy to ADM is superior to ADM but that the evidence that adding ADM to psychotherapy is beneficial is much weaker or non-existent. However, one group member argued that it should be specified that this had not been proven for all psychotherapies, and that the effect currently only sufficiently is studied for CBT. Another group member did not agree with

Factor	Comment
	this specification, and as a result decided to have her name removed from the list of authors. Since the rest of the group agreed with this specification an asterisk* was added to the word “psychotherapy” with an explanation stated below. Regarding the second recommendation the GDG, based on the available evidence found, collectively agreed that, if a patient with a major depression does not want combined treatment (i.e. if the patient prefers to start with only one type of treatment) psychotherapy could be a first choice, because psychotherapy is at least as effective as antidepressants in the short term and superior to antidepressants in the long-term. Regarding the third recommendation the GDG argued that antidepressants alone should be avoided as a treatment option in the symptomatic phase. This is because the evidence that adding psychotherapy to ADM is superior to ADM but that the evidence that adding ADM to psychotherapy is beneficial is much weaker or non-existent. Therefore the GDG felt that a supplementary recommendation to avoid ADM monotherapy was useful and justified and that the evidence was sufficient to classify it as moderate. Additionally, the GDG argued that this recommendation should be stated strongly because some patients who are offered combination treatment continue medication treatment but discontinue psychotherapy and that this leads to a high risk of relapse. It was a general comment to all recommendations that it is a shortcoming of this review that no mentioning is made with respect to severity of the depression, and that the recommendations likely could have had more clinical relevance had this distinction been made. Side-effects of anti-depressants are diverse and depend on the type of anti-depressant used. Although there are statistics in Belgium on general consumption of different types of antidepressants, it is unclear what the consumption pattern is for major depression, as a large proportion of the anti-depressants may be prescribed for minor or misdiagnosed depression. Side-effects of antidepressants are partly reflected in decreased compliance in the RCTs; this is only evident on the condition that the results are analysed on an intention to treat basis. Side-effects of psychotherapies have hardly been examined systematically. It is suggested that psychotherapies potentially could result in deterioration in some depressed patients, and that some psychotherapies could increase the risk for other mental disorders (for example psychotic decompensation in depressed patients with personality disorders), and, furthermore, increase the risk of suicide. Unfortunately, these issues are hardly ever examined in psychotherapy trials, and whether such negative effects really occur cannot be verified empirically. As deterioration is partly accounted for in the effect measure this is unlikely to alter the balance benefit harm.
Quality of evidence	The evidence ranged from Very Low to Moderate. Based on discussions on the assigned level of evidence in the GRADE tables, the GDG argued that population indirectness was present because a number of the RCTs mixed patients with a first episode of depression with patients with a recurrent episode. Consequently, the level of evidence was lowered from Low to Very Low in the recommendations affected (first and second recommendation). However, in the third recommendation it should be noted that we did not downgrade all the studies for indirectness. The maintenance studies mainly included patients with a recurrent depression (usually patients with a third

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	or more episode) and it was agreed that it was not appropriate to downgrade, even though we do not have information on the severity of depression for this group either. It was discussed whether to further lower the quality (for indirectness) based on the fact that pregnant women were excluded from studies, but it was decided not to do so because this is a general issue with the design of RCTs. The vast majority of studies found were on cognitive behavioural therapy (CBT) and it was decided to clarify in the recommendations (as a footnote) that the effect currently only has been sufficiently studies for CBT. Additionally, a subgroup analysis on the CBT studies alone was added to the appendices. It was not feasible to do subgroup analyses on other types of psychotherapy due to an insufficient number of studies. The GDG agreed that the advice given in the second recommendation, that if a patient with a major depression does not want combined treatment, psychotherapy* only could be a first choice might not apply to patients with a severe major depression having psychotic symptoms (ICD-10 code F.32.3). These patients should, according to the GDG, first and foremost receive pharmacological management for their psychotic symptoms. In order to avoid that the patients were treated with psychotherapy as monotherapy, this consideration was consequently added to the second recommendation. Additionally, the GDG considered that patients in acute danger of suicide should not start a new treatment with psychotherapy, and should remain in hospital until the acute phase is over. None of the included studies examined this particular patient population. It was not deemed necessary to explicitly state this consideration in the recommendations. Although it is unclear if the antidepressants in the studies and those used in Belgium are the same, there is no compelling evidence that one antidepressant is more effective than the other, so this form of indirectness was not taken into account.
Costs (resource allocation)	The GDG argued that it is difficult to make recommendations without a cost-effectiveness analysis.
Patients values and preferences	The evidence supporting a direct relationship between patient preferences and outcome was very limited and not sufficiently strong to generate influence when the GDG formulated the recommendations. Although recent literature suggest that patients generally tend to prefer psychological treatment to anti-depressant the clinical benefits of psychotherapy in the long-term were the determinant factor for the formulation of recommendation # 2. From the literature review on patient preferences, there is no evidence to support a recommendation on routine variation in treatment strategy based on for example age, sex or race.

6 IMPLEMENTATION AND UPDATING OF THE GUIDELINE

6.1 Stakeholder involvement

In order to assess the agreement with the recommendations and the anticipated facilitators and barriers to implementation of the recommendations, we conducted a survey amongst the stakeholders and afterwards met with the stakeholders at a face-to-face meeting (5 June 2014) to further discuss and elaborate on these matters. Amongst the stakeholders included were the patient organization “Psytoyens”.

The result of the survey showed that a very high proportion of the stakeholders agreed with the recommendations (16/18, 14/18 and 16/18 for the three recommendations, respectively).

6.1.1 Facilitators and barriers

The main facilitators and barriers for implementation of the recommendation identified by the stakeholder (in the survey and the face-to-face meeting) are grouped by domain in the table below:

Domain	Facilitators	Barriers
Importance of primary care	• General practitioners (GPs) are key persons in diagnosing and treating depression, can facilitate access to psychotherapy and medication, can help ensure good follow-up	• Diagnosis might not be accurate • The access to psychotherapy is limited, might favour prescription of medication in primary care • Role of nurses in primary care is not clearly defined
Change resistance (patients and providers)	• Public information/public campaigns • Recognition and reimbursement of psychotherapy • Involvement of patients' associations	• "Habits of physicians" • Perception that psychotherapy requires too much time • Pressure from pharmaceutical industry
Human resources	• Recognition and reimbursement of psychotherapy • Clearer definition of the role of a clinical psychologist in treatment of depression • Increase number of cognitive behavioural therapists	• Lack of well trained professionals • Lack of skilled psychiatrists in affective disorders • Lack of well-trained physicians (incl. GPs) • Some psychotherapists have inadequate training and/or lack of experience to deal with depressed patients • Lack of training in 'good clinical practice guidelines' in Universities and in continuous medical education
Organisation/ Collaboration	• Development of networks for specialised professionals • Creation of excellence centres for diagnosis/treatment of severe/difficult affective disorders (including treatment resistant depression)	• Current lack of sound collaboration between professionals including GPs and psychotherapists • Financial barriers due to lack of reimbursement for psychotherapy • Complex health system in terms of communication

6.2 Dissemination and Implementation

This guideline is intended to be used by the concerned professional associations: general practitioners, psychiatrists, association of psychiatric nurses, organizations of psychotherapists/psychologists. In order to facilitate this process all members of the guideline development group and the stakeholder group will receive the final documents, and the synthesis with the aim to be disseminated within their respective associations. Additionally, the scientific synthesis is being transformed by a communication specialist into a text that should be easily understandable by clinicians, including those clinicians who might be less familiar with EBM. Furthermore, the publication on EBMPracticeNet will likely facilitate the access to all clinicians potentially interested.

The following aspects may, according to KCE, hamper the implementation of the recommendations:

- The scope of the guideline, and in particular the fact that the guideline does not cover diagnostic. It is well known that a number of patients are labelled as having a major depression without fulfilling the criteria (false positives) and therefore receive a treatment they do not need. On the other hand, a number of truly depressed patients do not receive a depression diagnosis and consequently might not receive the treatment they actually need;
- Although a law regarding the recognition and regulation of psychotherapy in Belgium was published in may 2014 and should take effect in september 2016, it is unclear how and when it will be implemented and to what degree it will provide the necessary guarantees concerning quality and protection of the patient in the field, as the concrete modalities for implementation still need to be determined. A Federal Council for psychotherapy will be established that should advice on these issues. Consequently, there are for the moment no qualifications needed for a person to call himself a psychotherapist, and the quality of the psychotherapy is not guaranteed.
- A major barrier for implementation of this guideline is the fact that for major depression, psychotherapy is currently not reimbursed in Belgium.

6.3 Monitoring the quality of care

Monitoring the quality of care cannot be performed by an analysis of administrative databases as psychotherapy is not registered for the moment in Belgium.

Instead specific surveys are needed by researchers or scientific societies in order to assess whether if the recommendations are followed, and in particular whether patients use psychotherapy for the treatment of depression and when they do which type of psychotherapy they use, the duration of the treatment and whether this is used in combination with antidepressants.

6.4 Guideline update

The KCE processes foresee that the relevance of an update would be yearly assessed for each published guideline by the authors. Decisions are made on the basis of new scientific publications on a specific topic (e.g. Cochrane reviews, RCTs on medications or interventions). This appraisal leads to a decision on whether to update or not a guideline or specific parts of it to ensure the recommendations stay in line with the latest scientific developments.

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