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Research paper

Collaborative care regarding major depressed patients: A review of guidelines and current practices

Kris Van den Broeck [a,*], Roy Remmen [b], Marc Vanmeerbeek [c], Marianne Destoop [a,d], Geert Dom [a,d]

[a] Collaborative Antwerp Psychiatric Research Institute, University of Antwerp, Antwerp, Belgium
[b] General Practice, Department of Primary and Interdisciplinary Care, University of Antwerp, Antwerp, Belgium
[c] Département de Médecine Générale, University of Liège, Liège, Belgium
[d] Psychiatric Centre Brothers Alexianen, Boechout, Belgium

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ABSTRACT

Major Depressive Disorder (MDD) is a severe and common mental disorder. A growing body of evidence suggests that stepped and/or collaborative care treatment models have several advantages for severely depressed patients and caretakers. However, despite the availability of these treatment strategies and guidance initiatives, many depressive patients are solely treated by the general practitioner (GP), and collaborative care is not common. In this paper, we review a selected set of international guidelines to inventory the best strategies for GPs and secondary mental health care providers to collaborate when treating depressed patients. Additionally, we systematically searched the literature, listing potential ways of cooperation, and potentially supporting tools. We conclude that the prevailing guidelines only include few and rather vague directions regarding the cooperation between GPs and specialised mental health practitioners. Inspiring recent studies, however, suggest that relatively little efforts may result in effective collaborative care and a broader implementation of the guidelines in general.

1. Introduction and background

Major depressive disorder (MDD; American Psychiatric Association (2013)) is highly prevalent (Bromet et al., 2011), and its impact is large. For instance, MDD accounted for 3.8% of all disability adjusted life years (DALYs) in Europe in 2012 (World Health Organization, 2012). One aspect that causes MDD to retain its position in the list of leading causes of the global disease burden (Ferrari et al., 2013), is probably the treatment gap: in spite of the existence of effective treatment solutions, relatively few people receive optimal treatment.

Recent guidelines put forward collaborative (stepped) care models to effectively tackle depression (e.g., DGPPN (2012), NICE (2012) and Spijker et al. (2013)). According to 'collaborative care' (CC) models, treatment should be multi-professional, involving the general practitioner (GP) and at least one other health professional (e.g., nurse, psychologist, psychiatrist, etc.; Gunnet al. (2006)). CC models strongly emphasize the importance of collaboration and communication between all caretakers involved ('enhanced interprofessional communication'). They are particularly suited for complex and recurrent complaints, and ideally include a structured management plan and scheduled patient follow-up (Gunn et al., 2006). Although CC models strongly differ in intensity and complexity due to the ingredients that are incorporated (e.g., the presence and extensiveness of a structured management plan, whether or not there are explicit arrangements on interprofessional communication), CC has found to result in increased levels of therapy adherence (Thota et al., 2012) and better treatment outcomes compared to usual depression care, i.e., pharmacotherapy and/or cognitive behavioural interventions (Craven and Bland, 2006; Gilbody et al., 2012). CC has also found to result in both patients' (Thota et al., 2012) and caregivers' satisfaction (Byng et al., 2004). Finally, it is suggested that CC is a cost-effective strategy (e.g., Green et al. (2014) and Von Korff et al. (1998)) and practitioners may more efficiently use their discipline-specific skills (e.g., Katon, Von Korff, Lin, and Simon, 2001). A special kind of CC, is stepped care (SC), according to which depression should be treated differently according to the severity of the episode, whether or not it concerns a relapse, and in function of the responsiveness at the preset therapeutic strategy. These models generally involve regular monitoring of symptom severity and functional impairment, based on which treatment adjustments are made. They aim to provide the patient with the most (cost-)

* Correspondence to: Collaborative Antwerp Psychiatric Research Institute, University of Antwerp, Campus Drie Eiken, Universiteitsplein 1, D.R.323, B-2610 Wilrijk, Belgium.
E-mail address: kris.vandenbroeck@uantwerpen.be (K. Van den Broeck).

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effective, but least burdensome, and shortest treatment at every stage of the illness.

Notwithstanding these guidelines, it is estimated that only about half of the depressed patients in Europe get adequate treatment (Fernández et al., 2007). Many patients fail to seek help (e.g., Ohayon et al. (2000) and The ESEMeD/MHEDEA 2000 investigators et al. (2004), for a number of different reasons, e.g., stigma, ignorance about depression symptoms and care systems, or poor sense of self-efficacy (see Meltzer, Bebbington, Brugha, Farrell, Jenkins, and Lewis, 2000; Saver, Van-Nguyen, Keppel, and Doescher, 2007). Yet, although chances to consult a GP increase with the level of severity (Bebbington et al., 2000), only half of the depressed patients consulting a GP was found to be correctly diagnosed (Mitchell et al., 2009). Even those that are correctly diagnosed, do not always get adequate treatment in line with the guidelines. GPs may disregard the guidelines, because they feel that the guidelines are not fully applicable in real world situations where patients have co-morbid disorders, or because referral is complicated due to lack of available specialists (Lugtenberg et al., 2009; Smith et al., 2004). Also, patients may prefer to be cared for by their GP alone, perhaps because more specialised help makes them feel stigmatised (NICE, 2009). Finally, follow-up treatment, which is important to control the risk of relapse, may be suboptimal as antidepressants are often terminated prematurely, and less than 20% of the patients receive psychosocial follow-up (Melartin et al., 2005).

In sum, the literature identifies several issues impeding optimal care towards depressed patients. Apart from patients' reluctance to seek help, the bottlenecks are situated in the area of diagnosis and recognition, referral and guideline adherence, and follow-up. In this paper we aimed to inventory drivers for improved day-to-day collaboration between GPs and secondary mental health providers that are profitable in real world situations, in order to maximise the benefits for severely depressed patients and their caretakers. We therefore first reviewed the current guidelines on the treatment of depression for appropriate interactions between GPs and mental health professionals. Additionally – because guidelines actually run behind current practice – we have performed a semi-structured literature search, to update the evidence about directives on the collaboration between GPs and secondary mental health care practitioners. We will report on how collaboration should and could be organised during all phases of treatment, including those that precede the actual referral to and collaboration with a second level mental health professional (i.e. proper diagnosis and valid assessment of symptom severity and suicidal risk), as well as those that come after back-referral to the GP (follow-up, with special attention for relapse prevention). A good relationship between these practitioners has been shown to be advantageous in these treatment phases as well (e.g., Fredheim et al. (2011)).

2. Methods

2.1. Guidelines

We searched for international guidelines published between 2005 and 2015 in Dutch, English, French, or German, using the databases Guidelines International Network and US National Guideline Clearinghouse. Fig. 1 summarizes our search strategy. Our search terms were combinations of 'primary care', 'primary care physician', 'family physician', 'general practitioner', 'family doctor', 'depression', and 'depressive disorder'. After excluding duplicates, guidelines that merely took into account mild to moderate depressive episodes, and guidelines that focused on depression in minors, we selected 16 documents. One guideline

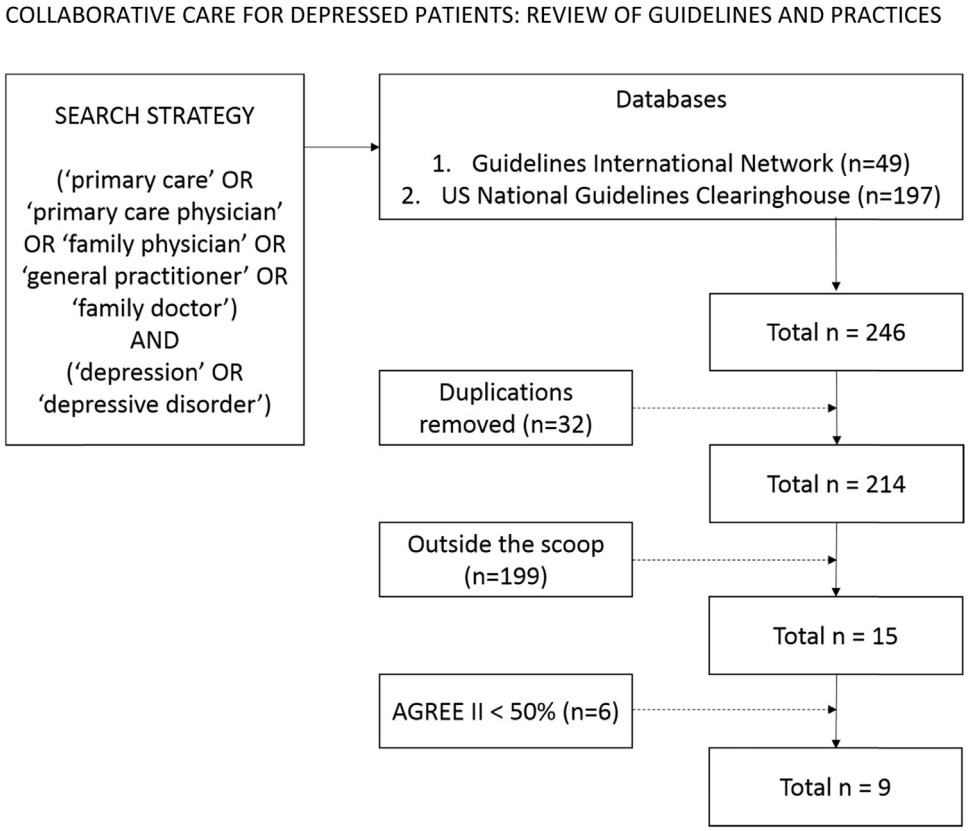

Fig. 1. Search strategy for the guidelines we selected.

Table 1
Selected guidelines, their origin, and their AGREE-II-scores.

Guidelines	Origin	AGREE score
American Psychiatric Association (2010)	USA	.55
DGPPN (2012)	Germany	.56
Heyrman et al. (2008)	Belgium, Flanders	.63
Kaiser Permanente (2014)	USA	.55
McDermott et al. (2010)	Australia	.77
Michigan University (2014)	USA	.53
NICE (2012)	United Kingdom	.94
Spijker et al. (2013)	The Netherlands	.86

was excluded because it did not mention anything about stepped care nor about collaboration amongst caretakers. The quality (e.g., rigour of development, clarity of presentation, editorial independence) of the remaining guidelines was further assessed in pairs of independent researchers (KVdB scored all guidelines; MD, GD, and RR all did one third) using the Appraisal Guidelines for Research and Education (AGREE) II instrument (Brouwers et al., 2010). Total score theoretically ranges from 0% (lowest possible quality) to 100% (highest possible quality). It expresses the mean overall quality that was agreed upon by two raters. Only those guidelines (n=8, see Table 1 for an overview) with total AGREE score >50% were further analysed.

2.2. PubMed search

To fit additional evidence about the topic under investigation we searched PubMed using the following terms: ("depression" or "depressive disorder") and ("general practitioner" or "family physician" or "primary care") and ("collaborative care" or "stepped care"), resulting in 417 publications (Fig. 2). Limiting the search to papers on adults (19+ years) that were published during the past 10 years, resulted in 177 papers. We were especially interested to find clear examples of how CC for MDD could be operationalised in a land as Belgium. Therefore, we further excluded review papers, papers that insufficiently described the studied treatment model or in which the treatment model did not match the definition of CC (or SC; e.g., a computer programme), papers that focused on

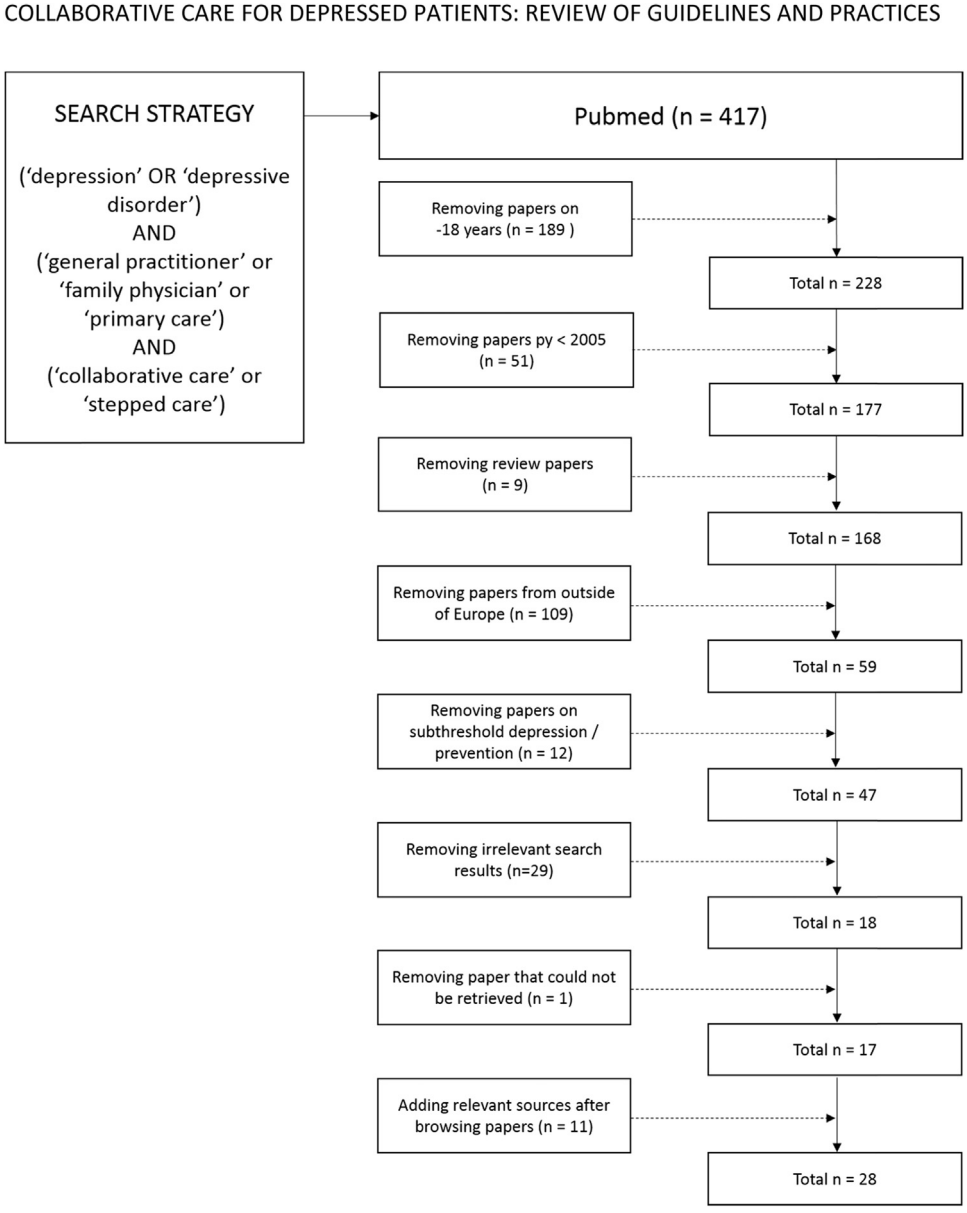

Fig. 2. Search strategy for the research papers in PubMed.

sub-threshold depression or prevention of depression, and papers describing projects outside Europe. One paper could not be retrieved. Browsing the selected papers and the (not included) review papers that were retrieved during the PubMed search, we added 11 relevant papers to our selection. The 28 selected papers, describing 16 different models (of which two are merely described in study protocols) of collaborative care, are summarized in Table 2.

3. Results

Each of the following paragraphs starts with an outline of the information coming from the guidelines, subsequently enriched by the studies retrieved in Pubmed.

3.1. Diagnosis and recognition

Information about diagnosis and diagnostic referral is retrieved from seven guidelines and eight models (12 papers), retrieved from our literature search. Guidelines generally do not recommend to screen patients for depression in primary care (Kaiser Permanente, 2014; Spijker et al., 2013), but the American guidelines suggest patients can be screened by GPs, obstetricians or physicians of other disciplines (APA, 2010). Exceptions can be made when staff-assisted care supports are in place (Kaiser Permanente, 2014), or when dealing with persons with high risk for depression in general hospitals or basic mental health services (Spijker et al., 2013). In many of the selected studies, however, it is clearly stated that the GP is responsible for diagnosing the depressive episode (Aragonès et al., 2007; 2008; 2014; Gensichen et al., 2009; Menchetti et al., 2013; Richards and Suckling, 2009; Seekles et al., 2009; 2011; van Straten et al., 2010; Watzke et al., 2014; Wernher et al., 2014). Sometimes, training on diagnosing depression was provided (e.g., Aragonès et al. (2007, 2008, 2014), Menchetti et al. (2013) and Watzke et al. (2014)).

Referral for diagnostic purposes to a specialist is required when the treating practitioner is not competent to perform mental health assessments (NICE, 2012), in case of doubt (McDermott et al., 2010; Michigan University, 2014; Spijker et al., 2013) or in case of suspected co-morbidities (Heyrman et al., 2008; McDermott et al., 2010; Spijker et al., 2013). The GP should be informed of the referral (NICE, 2012). Typically, specialised diagnostics can be performed by a psychiatrist, a psychotherapist, or a clinical psychologist (Spijker et al., 2013). In some of the retrieved studies, a psychiatrist was available for additional assessment (e.g., Menchetti et al. (2013)) or to discuss with in case of doubt (e.g., Aragonès et al. (2007, 2008, 2014), Oosterbaan et al. (2013) and Wernher et al. (2014)).

It should be noted that, in the light of the selected studies, patients suffering from co-morbid disorders and/or suicidal complaints were often excluded (in 25 of the 28 selected papers: Aragonès et al. (2007, 2008, 2014), Gensichen et al. (2009), Green et al. (2014), Huijbregts et al. (2013a, 2013b); IJff et al. (2007), Klug et al. (2008, 2010), McMahon et al. (2007), Mead et al. (2005), Oosterbaan et al. (2013), Richards et al. (2013), Seekles et al. (2009, 2011), Sharpe et al. (2014), van Straten et al. (2010), Walker et al. (2009, 2014), Walker and Sharpe (2009) and Wernher et al. (2014)).

3.2. Referral

Seven guidelines and eight models (16 papers) provide information about reasons for and arrangements about referral for treatment. The guidelines commonly cite the following reasons for referral to a specialist or a mental health service: (a) the patient is at risk for suicide (DGPPN, 2012; Heyrman et al., 2008; Kaiser Permanente, 2014; Michigan University, 2014; NICE, 2012); (b) the diagnosis is unclear, or the skills needed to assess depression severity or to treat the episode are lacking (DGPPN, 2012; McDermott et al., 2010; Michigan University, 2014); (c) the patient has a severe or chronic depression for which coordinated multiprofessional care is recommended (DGPPN, 2012; Kaiser Permanente, 2014; NICE, 2012); (d) somatic or mental co-morbid disorders are present (DGPPN, 2012; Michigan University, 2014); (e) response to treatment is insufficient (DGPPN, 2012; Heyrman et al., 2008; Kaiser Permanente, 2014; McDermott et al., 2010; Michigan University, 2014; NICE, 2012; Spijker et al., 2013). Also, relapse (Heyrman et al., 2008), or complex treatments (e.g., MAOI or ECT; Michigan University (2014)) may give rise to referral. This largely overlaps with the criteria for referral defined in the study protocols we retrieved: insufficient response to treatment (Richards and Suckling, 2009; Seekles et al., 2009, 2011; Sharpe et al., 2014; van Straten et al., 2010; Walker et al., 2009, 2014; Walker and Sharpe, 2009), depression severity levels (Oosterbaan et al., 2013; Seekles et al., 2009, 2011; van Straten et al., 2010; Watzke et al., 2014), co-morbidity (Huijbregts et al., 2013a, 2013b; IJff et al., 2007), emergencies (Sharpe et al., 2014; Walker et al., 2009, 2014; Walker and Sharpe, 2009), or patient preference (Watzke et al., 2014). Severely depressed patients who present significant risk of crises should be referred to home treatment teams to manage their crises (NICE, 2012) or to inpatient treatment (DGPPN, 2012).

Yet, guidelines differ regarding the referral strategies recommended for GPs. For instance, some guidelines recommend GPs to refer patients who do not respond to the first step of pharmacological treatment (Kaiser Permanente, 2014; Spijker et al., 2013), whereas according to the NICE guideline (2012) only patients should be referred for whom various (pharmacological) strategies and combination treatments showed insufficient. DGPPN guidelines (2012) merely suggest that a psychiatrist should be consulted in case of (interaction) problems with pharmacotherapy.

Although no concrete referral pathways are defined in the guidelines, it is suggested that these should be arranged beforehand (McDermott et al., 2010). Whereas the German guidelines (DGPPN, 2012) often use ‘co-treatment’ instead of referral, underlining the importance of collaboration between different practitioners, the Dutch guidelines stress the key role of the GP in recognizing the depression and referring the patient for the best treatment: “The GP should […] help the patient to actively seek a mental health specialist fitting the patient's problems and personality” (Spijker et al., 2013, p. 34). Additionally, accessibility of secondary care practitioners is an important condition for good referral (Spijker et al., 2013). This matches the protocol of Aragonès et al. (2007, 2008, 2014), by which GPs may only refer after discussing the case with a consulting psychiatrist. Another study used a web-based tool, allowing to check the availability of allied secondary care practitioners (Watzke et al., 2014).

The Flemish guidelines state that in some circumstances the GP may remain the main practitioner. However, a unique or collaborative (GP+psychiatrist) consultation may be helpful in these cases (Heyrman et al., 2008). Likewise, the guideline of Kaiser Permanente (2014) suggests that a psychiatrist may be consulted before prescribing tricyclic antidepressants (TCA) or venlafaxine to patients with (a history of) suicidal complaints.

3.3. Treatment

Treatment characteristics are discussed in detail by seven guidelines and all papers we selected. Most guidelines agree that treatment of severely depressed patients should consist of both pharmacological treatment and psychotherapy (DGPPN, 2012;

Table 2
Overview and summary of the studies (°=RCT) and study protocols (*) retrieved from Pubmed.

Authors, origin	Inclusion/exclusion	Main caretaker	Training	Diagnosis and monitoring	Treatment management	Consultation	Inter-professional communication	Supervision	Tools
Aragonès et al. (2007*, 2008*, 2014°) – Spanish adaptation of the INDI-model	PHQ-9 > 9 for > 1 month, and no anti-depres-sant in the previous 3 months. Exclusion: psychosis, bipolar disorder, alcohol or drugs dependency, pregnancy/breast feeding	GP, assisted by case managers (nurses in primary practice).	Eight-hour course based on the NICE guidelines to improve GPs' knowledge and skills in diagnosing depression, evaluating suicidal risk, clinical treatment, monitoring depression, and modifying therapy in accordance with a treatment algorithm + periodic updates. Eight-hour course for nurses on the clinical aspects of depression, antidepressant treatment, secondary effects, treatment adherence, warning signs in the evolution of depression, etc. + periodic updates.	Case manager monitors therapeutic adherence every visit, + PHQ	GP detects and diagnoses depressive episode. Case manager's visits will alternate GP's appointments. Case manager identifies anamnestic information relevant to individualised care for the patient and his family; provides health education and support on health care needs and resources. Case manager's visits are structured, supported by prints and videos. Frequency: one week after inclusion, and then monthly until remission in the acute phase; once every two/three months in the continuation and maintenance stage.	GPs and psychiatrists may consult each other by telephone or e-mail. Whenever patient care is shared, responsibility for the treatment and monitoring of the patient will be clearly established to prevent any gaps in the care provided. Referral is always preceded by cross-consultation.	The case manager informs the GP about therapeutic adherence, possible adverse effects, PHQ-monitoring.		Toolkit for Managing Depression in Primary Care, e.g., chapters on the detection and diagnosis of depression; use of PHQ-9 for diagnosis and monitoring of depression; risk of suicide; how to draft a therapeutic plan (incl. treatment algorithm and decision making regarding antidepressants); procedures for coordinating and liaising with the psychiatric services; information on secondary effects of antidepressants.
Chew-Graham et al. (2007°) - UK	Patients of 60 or above, with GDS > 4 and MMSE > 23.	Community psychiatric nurse		SCID axis I, HSCL-20, HAQ and the Burville physical illness scale at inclusion, and again every four weeks.	If excluded, patients were referred back to their GP for further treatment. The community psychiatric nurse gave the patient education about depression and advice about antidepressant medication. The nurse further supported a manualised facilitated self-help intervention (SHADE), and did signposting to other services, e.g., voluntary agencies. Over 12 weeks, 6 face to face contacts took place at the patient's home and 5 telephone contacts.	The community psychiatric nurse had regular access to advice from an old-age psychiatrist according to a defined protocol	The community psychiatric nurse sends a written report to the GP after each patient assessment. In between, the nurse liaised with the GP in person if changes in medication were required or if there were concerns about concordance or risk.	Every 4 weeks, the community psychiatric nurse reviewed the patients' progress with the old-age psychiatrist, or more frequently if necessary. The nurse had regular supervision with the author of SHADE.	SHADE (Mead et al., 2005).
Gensichen et al. (2009°) - Germany	PHQ > 9 and MDD confirmed by the GP's administration of DSM-IV and ICD-10 checklist, 18–80 years of age, access to private telephone. Exclusion:	Health care assistant	Health care assistants, making part of the private practice, got 18 h of interactive training, including information on depression, communication skills,	GP diagnosed depression and necessity to start with antidepressants. The health care assistant monitors depression symptoms and medication adherence	The health care assistant briefly contacts the patients twice a week in the first month, and once a month for the next 11 months by telephone. They encourage patients to follow self-management activities.		The health care assistants inform the GP using a structured report that stratifies the urgency of the contact by a robot scheme.		Structured form, used to facilitate communication between health care assistants and GPs.

Table 2 (*continued*)

Authors, origin	Inclusion/exclusion	Main caretaker	Training	Diagnosis and monitoring	Treatment management	Consultation	Inter-professional communication	Supervision	Tools
	pregnancy, severe alcohol or illicit drug use, acute suicidal ideation.		telephone monitoring, and behavioural activation. GPs are trained on evidence-based depression treatment guidelines (NHG, 2003)	using the Depression Monitoring List and a modified Morisky patient self report scale respectively, during phone calls.					
Huijbregts et al. (2013a°, 2013b°) and IJff et al. (2007*) – Dutch adaptation of the IMPACT model, The Netherlands	MDD according to MINI; PHQ > 9. Exclusion: high risk suicide, psychosis, dementia, drug or alcohol dependence, already getting mental health treatment	Care manager (not specified), supervised by the psychiatrist	GPs and care managers got training in the collaborative care model, including contracting and the antidepressant treatment algorithm, and the use of the web-based tracking system.	The PHQ was administered of all consulting patients by mail (screening), the MINI was administered by telephone. Care managers monitor the patients' progress and caregivers' adherence to the treatment protocol.	During the initial visit, the care manager informs the patient about MDD, and discusses all treatment options (problem solving, antidepressant medication; contracting). Together with the patient and the GP, a treatment plan is formulated. Patients get written instructions on self-help (e.g., behavioural activation, sleep-wake-rhythm). GPs' adherence to the protocol is supported by written instructions, phone calls, and reminders. Care managers provide 6–12 sessions (30–60 min) of problem solving treatment. When patients get in remission, a relapse prevention plan is made up. When patients do not progress or are unsatisfied with initial treatment, a new treatment plan is contracted. Treatment may be adapted every six weeks (stepped care).	The decision aid instructs to consult a psychiatrist in case of co-morbidity or non-adherence to the treatment protocol by the GP.	The care manager advises the GP following his consultation by the psychiatrist and when necessary. The GP discusses response and adverse effects to antidepressants with the care manager. The latter decides whether or not to step up the treatment (if necessary, after consulting a psychiatrist).	Care managers are supervised every six weeks by the psychiatrist, or in case of difficulties.	Web-based decision aid (what is the next treatment step? When to start or switch medication?), including a protocol for handling suicidality, whether referral is indicated due to limited expected progress, and a signal function to the consultant psychiatrist when a health care professional did not undertake the prescribed action.
Klug et al. (2008, 2010*) - Austria	> 63 years of age; MDD according to ICD-10; 21 < GAF < 60; independently living. Exclusion: symptoms of dementia; MMSE < 27; intention to move to a nursing home.	Team member			Patients have free access to regular Austrian care + geriatric home treatment (team of psychiatrist; psychologist; social worker-psychiatric nurse) that visit the patient once or twice every week (up to four times per week in case of crises), and kept regular telephone contacts with the patient. During each visit, the geriatric home carers talked about self-esteem, coping resources, and medication adherence; supported the individual practically to establish and maintain social networks; increased social and leisure activities; coped with tasks of daily living; supported carers; and provided crisis interventions when required – all according to an individually based care programme.		Team meetings		

McMahon et al. (2007 – pilot study) UK	Depressive illness according to ICD-10, MINI and HRSD17 > 13; having anti-depressants for at least 8 weeks. Exclusion: 65+, personality disorder, organic brain disorder, substance dependency, pregnancy, learning disability, secondary mental health care involvement	Graduate primary mental health worker	Case managers received 2 days of training delivered by two consultant psychiatrists.	At baseline, at 12 and at 24 weeks, depression severity was measured using different measures.	Treatment as usual by GP+case management from a graduate primary mental health worker. GPs prescribed an antidepressant in line with the NICE guidelines. Case management consisted of 6 contacts over 16 weeks (week 1, 4, and 16) and over the telephone (weeks 2, 6, and 10). Appropriate and minimal supportive counselling was provided. They operated according to a written protocol.	Case managers could consult two specialist registrars by telephone as and when required.	At weeks 4 and 10, the case manager could recommend an increase in medication dosage to the GP.	Weekly supervision for the case manager was available from two specialist registrars in psychiatry.	
Mead et al. (2005°) (SHADE) - UK	18+, at least 3 months on a waiting list for psychotherapy or councelling, and still BDI > 14 (and/or anxiety symptoms). Exclusion: active suicidal thoughts or plans, involved with other statuary specialist mental health services.	Assistant psychologist (graduate level)	Case managers received three days of training on therapeutic skills, knowledge of interventions and how to guide patients using the self-help manual.	BDI and other measures on daily functioning at baseline + at 3 months. Monitoring of patients' self-reported use of the manual and a 8-item questionnaire of their relationship with the assistant psychologist.	Guided self-help by (a) a written self-help manual (information and exercises based on CBT, exposure, problem solving, cognitive restructuring and lifestyle strategies); and (b) up to 4 (weekly) one-to-one sessions (15–30 min) with an assistant psychologist			Assistant psychologists were supervised by 'clinical supervisors' (no further information).	Self-help manual, especially developed for this trial
Menchetti et al. (2013°) - Italy	Broad spectrum	GP	GPs received a 2-day training on depression, instruments for diagnosis and monitoring, first-line treatment choice, follow-up visits		Stepped care protocol based on NICE-guidelines	A psychiatrist was available for assessment, start-up of pharmacological treatment and brief psychological interventions	Patient-specific written or verbal feedback between GP and psychiatrist	The GP received supervision by the psychiatrist every two months	
Oosterbaan et al. (2013°) – The Netherlands	Unipolar major and minor depressive disorder, dysthymia, or one of the stress-related adjustment disorders+anxiety. Exclusion: substance dependence, dementia, psychosis, bipolar disorder, current treatment with psychotropic drugs, CBT or IPT.	GP	GPs received one educational session by a psychiatrist to clarify the medication algorithm and to advise on enhancing medication adherence.	A (research) psychologist administers the MINI to inventory depression severity and the degree of functional impairment (MINI).	Severely depressed patients were immediately referred to the outpatient department of the specialised mental health service and got CBT+antidepressants (=step 2). In case of psychotic features, suicidal ideation, or when the patient's family was overly strained, patients were referred to a (day care) clinic. First-step intervention was a 3.5 month self-help course with guidance of the psychiatric nurse (5 45-min sessions), including workbook, psycho-education and cognitive and behavioural exercises. Moderately severely depressed patients were additionally offered antidepressant medication (clear algorithms)	Caretakers had the opportunity to directly consult a psychiatrist		Psychiatric nurses received group supervision every two weeks by an experienced behavioural therapist for feedback and adherence to the manual.	Manual of treatment algorithms, including interventions and treatment decisions for all caretakers.
			Psychiatric nurses participated in a 2-day training in basic CBT strategies.	The psychiatric nurse monitors depression severity using the CGI-S					

Table 2 (*continued*)

Authors, origin	Inclusion/exclusion	Main caretaker	Training	Diagnosis and monitoring	Treatment management	Consultation	Inter-professional communication	Supervision	Tools
				at 4 months. Patients scoring mildly severe or worse are referred to step 2.					
Richards et al. (2013°) and Green et al. (2014°) - UK	ICD-10 diagnosis of depression. Exlcusion: suicidality, psychosis, type I or II bipolar disorder, drug or alcohol abuse as a primary diagnosis, involved in specialised mental health treatment	Care manager, employed in primary care and supervised by mental health specialists (clinical psychologist, psychiatrist, academic GP with special interest in mental health, or a senior nurse psychotherapist), having UK mental health qualifications	Care managers received a 5-day training in collaborative care.	Care managers measure symptoms (HADS) during every contact.	GPs followed the NICE-guidelines when prescribing antidepressant drugs. Care managers have 1 30-40 min face-to-face contact, followed by 5-11 15-20min telephone contacts in 14 weeks. They advise participants on drug adherence, and provide brief psychotherapy (behavioural activation) and relapse prevention (i.e., individualised recovery plans, alert symptoms), all according to the clinical protocol that was made up in advance.		Care managers inform GPs on drug adherence or tolerance problems. Care managers provide regular updates and patient management advice (at least monthly or more often if indicated).	Care managers were weekly supervised by specialist professionals in mental health. Every patient was talked about at least monthly.	A computerised system (www.pcmis.co.uk) automatically alerted supervisors and care managers of the need to discuss (not-responding) patients.
Richards and Suckling (2009 – Phase IV prospective cohort study) - UK	Patients with depressive and/or anxiety symptoms, as diagnosed by the GP	Mental health worker		Each time the patient and the case manager meet, the PHQ-9 and GAD-7 are administered.	Treatment is based on the first face-to-face assessment by the case manager. Low intensity treatment included a CBT-based guided 'Recovery Programme' (Lovell & Richards, 2008) for depression. Web-based CBT programmes were offered as well. Workers gave information about the (unwanted) effects of medication, and monitored adherence. In case low-intensity treatment had no effect, or in case of severe problems, patients were referred to high-intensity CBT (max. 8 sessions). All further contacts were by phone, although face-to-face appointments or referral to other care takers were possible as well. During the contacts, patients were supported in the followed therapy.			Case managers received weekly supervision by the high-intensity CBT therapist, and each patient is discussed once every four weeks.	A computerised system (www.pcmis.co.uk) automatically alerted supervisors and care managers of the need to discuss (not-responding) patients.
Seekles et al. (2009*, 2011°); van Straten et al. (2010*) – The Netherlands	MDD, dysthymia, panic disorder, social phobia, generalised anxiety disorder, minor depression or minor anxiety disorder. Exclusion: psychotic complaints, bipolar disorder, involved in	Psychiatric nurse	Psychiatric nurses got 2 days of training on problem solving.	Screening and re-screening after 4 weeks. Diagnosis with CIDI. Then every 8 weeks symptom count and daily functioning. Researchers suggest that this could be done by the GP.	In case of severe complaints, patients are directly referred to specialised mental health care. Otherwise, treatment starts with four weeks of watchful waiting. When no progression is made, patients are referred to 'guided self-help', i.e., based on problem solving treatment ('Alles onder controle'). The care manager motivates the patient and		Care managers are responsible to set up an appointment with the GP in case of referral for pharmacotherapy, or with a mental health care specialist in case specialised mental health	Psychiatric nurses received weekly group supervision.	

	current treatment for psychological problems, prominent suicidal ideation, severe alcohol problems, not motivated for treatment.			A more detailed diagnostic interview is recommended when pharmacotherapy or referral for longer-term face-to-face therapy is indicated, to determine why the former interventions were not useful.	helps him to understand the techniques explained at the website and hand-out, +/− 15 min per week by phone or email. When no progression is made, people are referred to face-to-face problem solving therapy (Mynors-Wallis protocol; by care manager; 5–7 sessions of 30–45 min). If no progression is made, the care manager discusses referral for pharmacotherapy and/or specialised mental health care with the patient.		care is indicated.		
van der Weele et al. (2011°; 2012°) – The Netherlands (PROMODE study)	> 74 year of age. Exclusion: involved in current treatment for depression, a diagnosis for dementia or MMSE < 19, loss of partner or child in the preceding 3 months, life expectancy < 4 months.	GP/community psychiatric nurse	Psychiatric research nurses are trained to evaluate depression.	Screening with the GDS, MADRS and MINI by psychiatric research nurses. Re-evaluation after 6 months with the MADRS.	Patients are referred by the GP to the community mental health centre. Treatment starts with individual counselling, inventorying treatment needs and motivation during one or two home visits by a community psychiatric nurse. Next, patients are enrolled in a coping with depression course (based on CBT, 10 weekly group meetings or individually at their home, if needed), given by trained mental health professional. Finally, patients are referred back to the GP to discuss further treatment.				The coping with depression course was adapted from Lewinsohn et al. (1984).
Walker, Cassidy et al. (2009*); Walker, Hansen et al. (2014°); Sharpe et al. (2014°); Walker and Sharpe (2009*) – Scotland, UK	Depressed patients with (lung) cancer, with predicted survival > 3 months. Exclusion: chronic episode, need for urgent psychiatric care or having current mental help, cerebral metastases, cognitive impairment, psychosis, bipolar disorder, obsessive-compulsive disorder, substance abuse or dependence	Cancer nurses.	Cancer nurses get a 3 month training, including how to deliver psychological interventions to patients who are physically deteriorating and dying.	Diagnosis by HADS and SCID. The cancer nurses monitor patients' progress (PHQ-9) during each structured session, and afterwards by telephone once a month during 4 months.	The cancer nurse establishes a therapeutic relationship with the patient. In maximum 10 structured sessions (30–45 min) over 4 months, the nurse provides information about depression and its treatment, delivers brief evidence-based problem solving therapy and behavioural activation.	Psychiatrists provide direct consultations to patients who are not progressing or in case of emergencies.	Psychiatrists advise GPs about prescription behaviour/adjustment. Nurses coordinate depression care by liaising with all relevant health professionals.	Psychiatrists supervise global treatment. They supervise nurses on a weekly basis, using video recordings of the sessions the nurses had with the patients.	PHQ-9 depression scores are put into a graph, which is used during supervision.
Watzke et al. (2014*) - Germany	MDD as primary diagnosis	GP for watchful waiting, bibliotherapy or internet-based self-help programs; psychotherapist for telephone-based psychotherapy or regular psychotherapy; psychiatrist or GP for pharmacotherapy	All caretakers get training regarding the German National Clinical Practice Guidelines for unipolar depression (2009) and about stepped care. GPs got personal training, reviewing the diagnostic routines in everyday routine practice. Psychotherapists who offer telephone-	The GP is responsible for the diagnosis, as well as determination of depression type and severity. Depression is systematically monitored by the main caregiver according to a frequency that was decided to in the network.	Stepped care as mentioned in the German National Clinical Practice Guideline for unipolar depression (2009). Depression severity and patient preference (shared decision making) determine treatment choice: watchful waiting, bibliotherapy or internet-based self-help program, (protocol-based) telephone-based psychotherapy, psychotherapy, pharmacotherapy, psychotherapy + pharmacotherapy (ambulatory or residential care)		A network was installed, consisting of all relevant care providers involved in the treatment of depressive patient. The caretakers gathered four times a year.	Psychotherapists who offer telephone-based psychotherapy receive weekly supervision.	www.deprexis.com was used as online self-help intervention. Information exchange about available treatment capacity in secondary care was facilitated using a specifically developed online tool. Every time outcome is

Table 2 (*continued*)

Authors, origin	Inclusion/exclusion	Main caretaker	Training	Diagnosis and monitoring	Treatment management	Consultation	Inter-professional communication	Supervision	Tools
			based treatment receive special training.						monitored, care providers fill out a checklist assessing treatment-related information. This may facilitate decisions regarding further treatment (continuation, stepping up or down, determination).
Wernher et al. (2014*) (German-IMPACT)	> 60 year of age, 9 < PHQ < 15 in the scope of a diagnosed (recurrent) depressive episode or dysthymia (ICD-10). Exclusion: alcohol or drug abuse, severe cognitive impairment (dementia), bipolar disorder, psychotic disorder or severe behavioural symptoms, obsessive-compulsive disorder, suicidal ideation, involved in a non-pharmacological (or combined) depression treatment by a specialist.	E.g., trained psychiatric nurse, supervised by a mental health specialist (psychiatrist or psychotherapist)	Care managers receive comprehensive training on the IMPACT concept and intervention techniques. Regular meetings with the trainers ensure the continuous high standard of the intervention.	The GP performs diagnosis (and inclusion screening).	The GP introduces the care manager to the patient. The care manager explains the treatment model and introduces the patient workbook and the activity journal. Additionally, an individual intervention plan is made up. 30min telephone sessions are held every week up to 12 months. Besides symptoms monitoring, the call includes an interview on GP visits, medication effects and adherence, experiences with behavioural activation, and further therapeutic aims and techniques. GPs are encouraged to follow the guidelines, including prescription of antidepressants.The mental health specialist only rarely has patient contact.	GPs are able to contact the supervising mental health specialist at any time for consultation.	The care manager informs the GP regularly on the patients' status.	The care managers are supervised by the mental health specialist on a regular basis.	GermanIMPACT stepped care algorithm (see paper), a detailed intervention manual.
			All caretakers are educated and instructed in how to deal with emergencies, e.g. suicidal ideation.				The mental health specialist regularly discusses cases with the care manager. GP and mental health specialist meet regularly to discuss every patient's status. Every eight weeks, the need for treatment changes is carefully evaluated.		
				Symptom severity is regularly measured by the care manager by phone (PHQ). Treatment evaluation is done every eight weeks by the GP and the mental health specialist according to a stepped-care algorithm. The patient's preferences are taken into account as well.					

Treatment may be continued or adapted as a result of this evaluation, according to the stepped care algorithm.

BDI=Beck Depression Inventory; CBT=Cognitive Behavioural Therapy; CIDI=Composite International Diagnostic Interview; DSM-IV=Diagnostic and Statistical Manual of mental disorder, 4th edition; GAF=Global assessment of functioning; GDS=Geriatric Depression Scale; GP=General practitioner; HADS=Hospital Depression and Anxiety Scale; HAQ=Health Assessment Questionnaire; HRSD17=Hamilton Rating Scale for Depression, 17 items; HSCL=Hopkins Symptom Checklist; ICD=International Classification of Diseases and related health problems; IPT=Interpersonal Therapy; MADRS=Montgomery-Åsberg Depression Rating Scale; MDD=Major depressive disorder; MINI=Mini International Neuropsychiatric Interview; MMSE=Mini Mental State Examination; NHG=Nederlands Huisartsengenootschap [Dutch Council of GPs]; PHQ=Patient Health Questionnaire; SCID=Structured Clinical Interview for DSM-IV disorders.

Heyrman et al., 2008; NICE, 2012; Spijker et al., 2013). Communication among clinicians (including those who are providing treatment for general medical conditions) is essential in this phase, as it may improve vigilance against relapse, side effects, and risk to self or others (American Psychiatric Association, 2010). Continuous and coordinated care is important as well, because of the risk of depressed episodes becoming chronic (DGPPN, 2012). All kinds of caregivers may be involved (DGPPN, 2012), depending on severity of the episode, the suicide risk, the patient's resilience and his context (Heyrman et al., 2008).

Evidence supporting CC is recent and limited, and further research is necessary to unravel the relative importance of its components (e.g., NICE (2012) and Spijker et al. (2013)). Nevertheless, the selected guidelines have proposed different strategies to ensure coordination and collaboration – as pieces of advice, rather than evidence-based recommendations. Firstly, teams working with severely depressed patients are advised to develop comprehensive multidisciplinary care plans in collaboration with the patient (NICE, 2012), including plans for the management of crises or relapse (American Psychiatric Association, 2010), and agreements regarding symptom monitoring (Spijker et al., 2013). Indeed, recent studies on collaborative care models often include treatment plans that are tailored to the patient's complaints (Green et al., 2014; Huijbregts et al., 2013a, 2013b; IJff et al., 2007; Klug et al., 2008, 2010; Richards et al., 2013). Some models include pre-defined contact moments (Aragonès et al., 2007, 2008, 2014; Chew-Graham et al., 2007; Green et al., 2014; McMahon et al., 2007; Mead et al., 2005; Richards et al., 2013; Sharpe et al., 2014; Walker et al., 2009; Walker et al., 2014; Walker and Sharpe, 2009; Wernher et al., 2014). Additionally, sharing the plan with the patient, his GP, and other relevant people involved in the patient's care (NICE, 2012; Spijker et al., 2013), and having a case manager coordinating the care (NICE, 2012) will result in more collaboration. The American guidelines suggest that the psychiatrist may be the optimal coordinator of care (American Psychiatric Association, 2010), whereas according to the German guidelines this is part of the central role of the GP, in particular when also somatic specialists are involved (DGPPN, 2012). In our selection of research papers, programmes strongly differ regarding the indicated case managers. In some studies, care is coordinated by the GP (Aragonès et al., 2007, 2008, 2014; Menchetti et al., 2013; Oosterbaan et al., 2013; van der Weele et al., 2011, 2012; Watzke et al., 2014), although researchers sometimes gave these tasks to counsellors (Green et al., 2014; Richards et al., 2013), ((community) psychiatric) nurses Chew-Graham et al. (2007), Green et al. (2014), Richards et al. (2013), Seekles et al. (2009, 2011), van der Weele et al. (2011, 2012), van Straten et al. (2010) and Wernher et al. (2014)), psychological well-being practitioners (Green et al., 2014; Richards et al., 2013), (graduate primary) mental health workers (Gensichen et al., 2009; McMahon et al., 2007; Mead et al., 2005; Richards and Suckling, 2009), psychotherapists (Watzke et al., 2014), or psychiatrists (Watzke et al., 2014). In the protocol of Walker and colleagues (Sharpe et al., 2014; Walker et al., 2009; Walker et al., 2014; Walker and Sharpe, 2009), designed for patients with cancer and depression, cancer nurses took the role of main caretakers.

Secondly, collaboration is thought to be encouraged when the roles and responsibilities of all caretakers that are involved are clearly defined (American Psychiatric Association, 2010; NICE, 2012), and when they receive regular high-quality supervision to evaluate and reflect upon the treatment strategies (NICE, 2012). Indeed, some programmes include regular supervision for the main caretaker (Chew-Graham et al., 2007; Green et al., 2014; Huijbregts et al., 2013a, 2013b; IJff et al., 2007; McMahon et al., 2007; Mead et al., 2005; Menchetti et al., 2013; Oosterbaan et al., 2013; Richards and Suckling, 2009; Richards et al., 2013; Seekles et al., 2009, 2011; Sharpe et al., 2014; van Straten et al., 2010;

Walker et al., 2009, 2014; Walker and Sharpe, 2009; Watzke et al., 2014; Wernher et al., 2014), whereas others hold regular discussions by different practitioners of patients' progress or treatment adherence (Chew-Graham et al., 2007; Green et al., 2014; Huijbregts et al., 2013a, 2013b; IJff et al., 2007; Klug et al., 2008, 2010; Menchetti et al., 2013; Richards and Suckling, 2009; Richards et al., 2013; Watzke et al., 2014; Wernher et al., 2014). In other programmes (e.g., Aragonès et al. (2007, 2008, 2014), McMahon et al. (2007) and Oosterbaan et al. (2013)), first level practitioners and psychiatrists had the opportunity to consult each other, but no structural moments were defined. In the protocol of Walker and colleagues (Sharpe et al., 2014; Walker et al., 2009; Walker et al., 2014; Walker and Sharpe, 2009), the nurse is responsible for transmitting all necessary information to the psychiatrist and the GP, without them having contact per se.

Thirdly, collaboration and coordination of care are believed to improve when all treating clinicians have sufficient contact with the patient and each other, when relevant information is available to guide treatment decisions, and when treatments are synchronized (American Psychiatric Association, 2010). Treatment should be function of regular monitoring of treatment results (DGPPN, 2012; Michigan University, 2014). The programmes we found indeed regulatory monitored treatment outcomes by a set of predefined measures (Aragonès et al., 2007, 2008, 2014; Chew-Graham et al., 2007; Gensichen et al., 2009; Green et al., 2014; Huijbregts et al., 2013a, 2013b; IJff et al., 2007; McMahon et al., 2007; Mead et al., 2005; Oosterbaan et al., 2013; Richards and Suckling, 2009; Richards et al., 2013; Sharpe et al., 2014; van der Weele et al., 2011, 2012; Walker et al., 2009, 2014; Walker and Sharpe, 2009), of course partly in the light of the research questions underlying the studies.

Finally, CC will profit from practitioners that pay attention to continuity of care, over all levels of care (Spijker et al., 2013). Therefore, they are advised to initiate contact with patients who discontinue treatment (Spijker et al., 2013), and to discuss confidentiality issues when making up the treatment plan (McDermott et al., 2010). Likewise, the guidelines repeatedly advise GPs to establish good collaborative relationships with local specialists, so that a secure access to specialists is ensured when needed (DGPPN, 2012; McDermott et al., 2010). In practice, telephone contacts are sometimes used to encourage continuation of treatment or to support patients during treatment (Gensichen et al., 2009; Green et al., 2014; Klug et al., 2008, 2010; McMahon et al., 2007; Richards and Suckling, 2009; Richards et al., 2013; Seekles et al., 2009, 2011; van Straten et al., 2010).

Strikingly, and contrasting the studied guidelines, recent programmes on collaborative care used tools or websites, supporting treatment. Whereas some tools are meant to educate or train the patient (Richards and Suckling, 2009; Watzke et al., 2014), others solely serve the practitioners. Practitioners' tools may be helpful in making decisions regarding the next steps in treatment (Huijbregts et al., 2013a, 2013b; IJff et al., 2007; Watzke et al., 2014), to facilitate communication amongst practitioners (Gensichen et al., 2009), or to alarm the involved practitioners of problems during treatment (Green et al., 2014; Huijbregts et al., 2013a, 2013b; IJff et al., 2007; Richards and Suckling, 2009; Richards et al., 2013). One programme installed reminders for the GPs, in order to let them stick to the treatment protocol (Huijbregts et al., 2013a, 2013b; IJff et al., 2007). Oosterbaan et al., (2013) gave their psychiatric nurses feedback on protocol adherence. Sometimes, supportive written information on different aspects of treatment was provided to the GPs (Aragonès et al., 2007, 2008, 2014; Huijbregts et al., 2013a; IJff et al., 2007; Oosterbaan et al., 2013; Wernher et al., 2014). McDermott et al. (2010) suggest treatment for Australian patients may be impeded because of lack of secondary care therapists. They suggest to install a 24 h hotline providing specialised advice supporting other caretakers to facilitate treatment.

3.4. Follow-up: back-referral and relapse prevention

Five guidelines and one model discuss the follow-up phase. It is recommended to continue (pharmacological + psychological) treatment for severely depressed patients in order to prevent relapse (NICE, 2012; Spijker et al., 2013). Home treatment and crisis resolution may be added for depressed people who might benefit from early discharge from the hospital after a period of inpatient care (DGPPN, 2012; NICE, 2012).

Although it is emphasised that good coordination of care is important in this phase (DGPPN, 2012; Spijker et al., 2013), and that the criteria for the initiation of (maintenance) therapy should be clear for all practitioners involved (DGPPN, 2012), none of guidelines clearly mentions who is responsible for the management of treatment in this phase, or when responsibilities shift from one caretaker to another. The guideline of Kaiser Permanente (2014) only mentions that it is important in case of back-referral that practitioners are accessible for each other. Furthermore, it is suggested that GPs may consult specialists to develop relapse prevention psychotherapy (DGPPN, 2012), or when medication reduction is difficult or when long-term treatment is expected (Heyrman et al., 2008). Finally, taking into account the principles of 'stepped care', a relapse might be considered a signal to initiate a more intense treatment schedule, with active involvement of more specialists or more specialized help (Heyrman et al., 2008).

Likewise, the treatment programmes that were subject to research only limitedly mention follow-up interventions. In fact, only the protocol of Huijbregts et al. (2013a, 2013b) and IJff et al. (2007) explicitly states that a relapse prevention plan is made up once the patients gets into remission. Follow-up frequency then declines.

4. Discussion

In this review we aimed to clarify how and when caretakers ideally work together when treating severely depressed patients and to identify the present best evidence of collaborative care (CC) programmes. After screening on quality and content, we selected eight guidelines and 26 original research articles. Most guidelines underline the importance of good communication and collaboration amongst caretakers during all the phases of the treatment process. Yet, overall, although CC is mentioned in all selected guidelines, this form of treatment organisation is surprisingly underdeveloped within most guidelines. Only few concrete, practical directives on the organisation and maintenance of CC are included (e.g., what are criteria for referring a patient to his GP?). The additional literature search in Pubmed revealed some concrete and inspiring set-ups (e.g., the use of case managers who keep an eye on treatment progress and adherence, or the use of technology), which may add to a broader implementation of the guidelines. Yet, nor the guidelines, nor the selected studies in the Pubmed literature search included satisfying information about *how* practitioners could work together after acute treatment (back-referral, follow-up, relapse prevention).

Our findings suggest that guidelines only limitedly provide guidance on the practicalities of CC programmes, therefore insufficiently supporting practitioners in setting up a regional CC programme. We reason that this may impede the development of such programmes. Various reasons may underlie the lack of directives regarding the development of CC in the guidelines. First, as demonstrated by the papers we retrieved from Pubmed, CC may be operationalized in many different ways, and many models have

proven to be efficient. Second, in many studies we investigated, severely disordered/acute suicidal patients were excluded. These patients often were referred for specialised therapy, without the involvement of the GP. Within the scope of the selected studies, no guidance regarding interdisciplinary collaboration for these patients was included. It may be the case that the evidence today supporting CC for severely depressed patients seems insufficiently strong to get it incorporated into the guidelines. Third, studies are inconclusive about the so-called 'active ingredients' – those aspects of the programmes that are responsible for an improved effectiveness compared to treatment as usual – of these programmes. Some suggest that case management is essential (Gensichen et al., 2006; Williams et al., 2007), or the presence of psychotherapy (Coventry et al., 2014), but others did not succeed in identifying active ingredients (Bower et al., 2006; Suter et al., 2009). Finally, the development of these programmes also depends on local policies and authorities, which may strongly differ from one region to another (and also impedes generalizability of findings across studies).

An important difference between the guidelines and the research papers, concerns the operationalization of the case manager. Whereas some important guidelines (American Psychiatric Association, 2010; DGPPN, 2012; NICE, 2012) strongly recommend that care should be coordinated by a psychiatrist (American Psychiatric Association, 2010) or a GP (DGPPN, 2012), we noticed that in the reviewed research programmes case managers are often graduate mental health workers (who work under the supervision of the GP or the psychiatrist). This perhaps reflects the need of daily practice to efficiently organise the care, given the large demand of patients and the limited supply of caregivers. Alternatively, this discrepancy reflects the relatively large input of medical associations in the construction of the guidelines.

Although both guidelines and papers repeatedly stress that practitioners should invest in networking and interdisciplinary communication, little is said about what exactly should be communicated. Noteworthy in this regard is the French 'guideline on referral paths between GPs and psychiatrists regarding initial consultations of adult patients with mental problems' (Collège Nationale pour la Qualité des Soins en Psychiatrie (CNQS), 2010). This guideline was selected by our initial search, but AGREE scores were rather low and the authors themselves confirmed that their literature search is of poor evidence. Nevertheless, this guideline basically lists the essential elements of (a) a GP's referral letter to a psychiatrist; and (b) of a psychiatrist's answer after the first consultation, directed to the GP. The authors emphasize that GP's should clearly express their expectations towards the psychiatrist regarding the questions they have on behalf of the patient's problems and the role they would like to play in future treatment. Psychiatrists then, should propose a treatment plan, which involves the GP. Furthermore, Collège Nationale pour la Qualité des Soins en Psychiatrie (CNQS) (2010) argues that referral, guideline adherence and treatment adherence would largely benefit from clear definitions of practitioners' mutual roles and interactions. Similar recommendations can be found in the work of Van Audenhove et al. (2007). Essentially, all practitioners involved should communicate to each other those bits of information that allow the receiver to carry out the responsibilities included in one's role description.

Of course, our findings are not without limitations. It should be noted that we only included those guidelines with mean overall quality ratings $>50\%$ on the AGREE scale. Additionally, financing systems have an important impact on the formation of care. Although we specifically selected European studies focusing on CC, it is known that financing systems across Europe strongly differ.

In sum, we conclude that many problems remain in the organization and implementation of treatment for patients with MDD. Indeed, adherence to guidelines for the treatment of MDD is low. Though specifically the more severe patients seek help, only few get the treatment they need. Problems arise in the detection of depression, in referral and back-referral. Collaboration amongst caretakers could be useful in overcoming these difficulties, but the implementation of CC is impeded by local policies, ambiguity about its active ingredients, the broad variety of efficient phenotypes, and insufficient research concerning the strengths and weaknesses of CC for severely depressed patients. We think the implementation of CC may benefit from clear directives regarding role descriptions and communication rules ('what' and 'when', rather than 'to whom'), and from structural support, in order to consolidate the efforts undertaken to set up a collaboration network. Yet, our findings suggest that, although few concrete directives are available, relatively little interventions, such as indicated case managers and technological support, could largely promote the daily collaboration between practitioners regarding the treatment of depression, thereby probably also improving guideline adherence, treatment outcome, and patient and caretaker satisfaction.

Contributors

KVdB was responsible for the study set up, the searches, analyses and the different drafts of the paper. All other authors equally contributed in thinking about the format of the study and of the format of the papers. In addition, RR, GD, and MD each reviewed one third of the selected guidelines and filled out the AGREE instrument as second rater, besides KVdB.

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