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Quality of clinical practice guidelines for inadequate response to first-line treatment for depression according to AGREE II checklist and comparison of recommendations: a systematic review

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ABSTRACT

Objective To assess similarities and differences in the recommended sequence of strategies among the most relevant clinical practice guidelines (CPGs) for the treatment of depression in adults with inadequate response to first-line treatment.

Data sources We performed a systematic review of the literature spanning January 2011 to August 2020 in Medline, Embase, Cochrane Library and 12 databases recognised as CPGs repositories. CPGs quality was assessed using the Appraisal of Guidelines for Research and Evaluation II (AGREE II).

Study selection The eligibility criteria were CPGs that described pharmacological recommendations for treating depression for individuals aged 18 years or older in outpatient care setting. We included CPGs considered of high-quality (≥80% in domain 3 of AGREE II) or recognised as clinically relevant.

Data extraction Two independent researchers extracted recommendations for patients who did not respond to first-line pharmacological treatment from the selected CPGs.

Results We included 46 CPGs and selected 8, of which 5 were considered high quality (≥80% in domain 3 of AGREE II) and 3 were recognised as clinically relevant. Three CPGs did not define inadequate response to treatment and 3 did not establish a clear sequence of strategies. The duration of treatment needed to determine that a patient had not responded was not explicit in 3 CPGs and was discordant in 5 CPGs. Most CPGs agree in reassessing the diagnosis, assessing the presence of comorbidities, adherence to treatment, and increase dosage as first steps. All CPGs recommend psychotherapy, switching antidepressants, and considering augmentation/combining antidepressants.

Conclusion Relevant CPGs present shortcomings in recommendations for non-responders to first-line antidepressant treatment including absence and divergencies in definition of inadequate response and sequence of recommended strategies. Overall, most relevant CPGs recommend reassessing the diagnosis, evaluate comorbidities, adherence to treatment, increase dosage of antidepressants, and psychotherapy as first steps.

PROSPERO registration number CRD42016043364.

Strengths and limitations of this study

- ► All included clinical practice guidelines (CPGs) were assessed for quality using the recognised tool 'Appraisal of Guidelines for Research and Evaluation II' in which a careful training of appraisers was conducted.
- ► The study was based on a comprehensive literature search about the pharmacological treatment of depression conducted in 15 databases using a sensitive strategy.
- ► The main comparison of management strategies was focused on the eight most relevant CPGs leading to a high-quality synopsis.
- ► The inclusion of three CPGs often used in clinical practice (from The Canadian Network for Mood and Anxiety Treatments; from the American Psychiatric Association; and from the US Department of Veterans Affairs, US Department of Defense) enabled a broader discussion of clinical questions mentioned in the CPGs.
- ► The main limitation was that the inclusion had been restricted to papers written in English, Portuguese or Spanish.

INTRODUCTION

Depression is a mental health problem with severe consequences for afflicted individuals. This mental disorder results in substantial professional, economic, social and personal losses owing to its incapacitating nature.[1] WHO[2] estimates that over 300 million people globally are affected by depression, which is the main contributor to 800,000 suicides

annually worldwide. Additionally, depression can cause critical social problems, as depressed individuals are less productive, resulting in additional costs to their employers and governments.[3]

The number of depressed persons has increased considerably.[4] This situation overburdens the healthcare system and generates a greater need for resource optimisation.[5] Thus, developing evidence-based interventions to achieve effective results is a pressing challenge in the mental health field.[6] Moreover, owing to the COVID-19 pandemic, an increase in mental illnesses is expected, perhaps persisting for several years. There will be an even greater need to optimise resources for dealing with this significant challenge.[7] A survey by the WHO[8] showed that the COVID-19 pandemic had suspended essential mental health services in about 93% of countries worldwide while the population increasingly needs mental healthcare.

Clinical practice guidelines (CPGs) are fundamental to optimise these mental health resources, which will be in greater demand with the increased incidence of depression.[9] These CPGs contain recommendations for optimising patient healthcare and have been developed by reviewing interventions and a cost–benefit analysis for each clinical health condition.[10] Hence, they enable the development of objective clinical decisions, help decrease clinical variability, educate patients and professionals on updated best practices and improve the cost-effectiveness of healthcare.[11]

Among the interventions proposed in the CPGs, evidence-based pharmacotherapy is one of the strategies used to treat depression.[12] However, a previous study demonstrated a lack of information regarding the best approaches when first-line pharmacological treatment for depression fails.[13] Considering that the response to first-line treatment is only moderate (40%–60%) and remission after antidepressant treatment is achieved in only a minority of patients (30%–45%), there is a need to investigate such gaps more thoroughly to improve CPGs.[14]

Additionally, there is a lack of clarity in the CPGs on clinical actions, and divergence among different approaches about the sequence of strategies for depressed individuals who presented an inadequate response to first-line treatment.[13] Thus, to improve clinical recommendations by mental health professionals and provide better healthcare to patients, in-depth evaluation of the CPGs recommendations for patients who do not respond adequately to initial pharmacological interventions is necessary.

Study aims

Here, we aimed to assess similarities and differences in the recommended sequence of strategies among the most relevant CPGs for the treatment of depression in adults who have shown an inadequate response to first-line treatment.

MATERIALS AND METHODS

A broad search was conducted to explore the methodological quality and transparency of CPGs for the pharmacological treatment of non-communicable diseases, including depression. We updated the search of a previous PROSPERO systematic review (CRD42016043364)[15] and conducted an analysis specifically assessing CPGs that can be used by health professionals for the pharmacological treatment of adults with depression in outpatient settings.

We used the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument (https://www.agreetrust.org) to evaluate the quality of the CPGs identified in the research—a fundamental step of a systematic review. Additionally, the recommendations of high-quality CPGs or those most commonly used in clinical practice[16] were compared with a method applied in a previous study published by the authors.[13]

Identification of CPGs (Search data source)

A comprehensive search was conducted on PubMed, Embase and the Cochrane Library for CPGs published from 1 January 2011 to 22 August 2020 (online supplemental appendix 1). We consulted twelve databases traditionally recognised as CPGs repositories.[13 17 18] Mendeley software was used to conduct this search and remove duplicates. In December 2021, we searched the literature to update the included CPGs.

Eligibility criteria

Only CPGs that made pharmacological recommendations for treating depression in individuals aged 18 years or older were included. The following CPGs were excluded: those that did not have the full text available in Portuguese, English or Spanish; those that focused on psychotherapeutic treatment or neuromodulation; and those for specific populations, such as patients with cancer, multiple sclerosis, and pregnant or lactating women. CPGs for the treatment of bipolar depression only were also excluded. The latest versions of CPGs found on the original authors' websites were included. Two evaluators independently read the titles and abstracts of the retrieved articles and—if the content met the eligibility criteria—evaluated the full text. Discrepancies were resolved by one of the authors (GCHF-M), who acted as the third evaluator. The latest version of each CPG, and all related complementary documents, were sent to the evaluators for a quality assessment using the AGREE II. To be included, the CPGs should have a score ≥80% in domain 3 of AGREE II—considered of high-quality; or were among those most relevant in clinical practice either by being the most used ones,[16] or developed by an institution considered as a leader in developing CPGs.

Extraction of general data and CPGs quality evaluation

Previously validated forms[18] were used by two independent reviewers for data extraction. A third reviewer resolved the discrepancies. The following data were extracted: type of organisation that produced the CPG (government organisation or specialised society), country, method used to classify the evidence and the CPG development

method (whether done using adaptation methodology or other methods). Three independent researchers (FCG, IBS and ST) evaluated the CPGs using the six AGREE II domains. The AGREE II contains 23 items grouped into six domains and two global classifications (general evaluation items). Each AGREE II domain evaluates a different dimension of CPG quality[19]: scope and purpose (domain 1), stakeholder involvement (domain 2), rigour of development (domain 3), clarity of presentation (domain 4), applicability (domain 5) and editorial independence (domain 6). A Likert scale ranging from 1 to 7 was used to evaluate the 23 items. Each reviewer entered an evaluation into the AGREE II platform for each item. The calculation was made automatically on the platform for each quality domain.

Further, owing to the substantial heterogeneity of the general evaluation items, our protocol defined the items that would not be included in the analyses. We decided to primarily focus on domain 3. All evaluators underwent rigorous training on the AGREE II before using it to conduct the quality assessment (details of this training have been previously published).[18] When discrepancies of two or more score points were found, discussion about the assessment was conducted until a consensus was reached. The score was calculated individually for each domain.

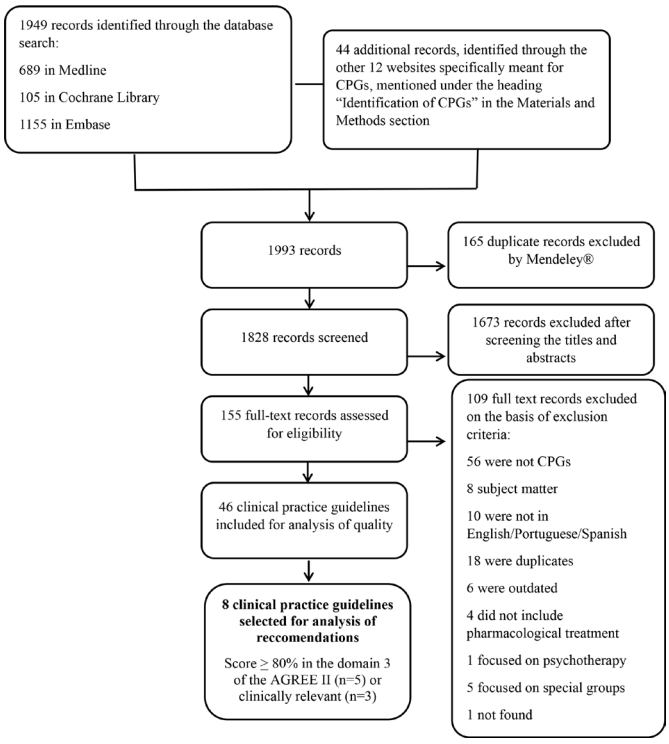

Figure 1 Flowchart of clinical practice guidelines selection. CPGs, clinical practice guidelines.

Comparison of recommendations

The recommendations of high-quality CPGs were compared. The inclusion criteria were: a score of 80% or above in domain 3 of AGREE II, CPGs that were most commonly used in clinical practice, and being developed by an important CPGs developer institution. Domain 3 (rigour of development) was used to classify a CPG as 'high-quality' since this is the most important item regarding the reliability of the recommendations.[20] Two independent researchers extracted all recommendations from the included CPGs. The final version of the comparative tables of recommendations were achieved after two rounds of discussion. The recommendations were grouped by the following main topics: terminology for responsiveness and recommended management strategies. The terminologies and sequences of the therapeutic strategies were compared between the CPGs and the strategies and terminologies that the CPGs had in common were synthesised in a third table.

Patient and public involvement

No patients were involved in this study.

RESULTS

We identified 1949 records in the database search—Medline (n=689), Cochrane Library (n=105), and Embase (n=1155), and 44 additional records through the other 12 specific websites for CPGs. After removing 165 duplicates, 1993 documents remained. From those, we included 46 CPGs[21–66] for quality assessment and selected eight of them for analysis of recommendation (figure 1). Online supplemental appendix 2 includes the reasons for including/excluding documents. Five CPGs that presented an AGREE II domain 3 score ≥80% were considered high-quality and selected. Two others (from The Canadian Network for Mood and Anxiety Treatments—CANMAT[21] and from the American Psychiatric Association—APA-Psychiatry[22]) were also selected based on their widespread acceptance[16] and an additional one (from the US Department of Veterans Affairs (VA), US Department of Defense (DoD)—VA/DoD CPG for the Management of Major Depressive Disorder)[23] for been considered by the National Academy of Medicine (US) as a leader in CPG development. The eight CPGs included with their scores in the AGREE II domain 3 were: Depresión en Personas de 15 Años y Más, from the Ministerio de Salud Chile, score=89%[24]; Guía de Práctica Clínica (GPC): Detección Temprana y Diagnóstico del Episodio Depresivo y Trastorno Depresivo Recurrente en Adultos: Atención Integral de los Adultos con Diagnóstico de Episodio Depresivo o Trastorno Depresivo Recurrente from the Ministerio de Salud Colombia, score=86%[25]; Depression in adults: recognition and management from the National Institute for Health and Care Excellence (NICE)—UK, score=84%[26]; Depression, Adults in Primary Care from Institute for Clinical Systems Improvement (ICSI) Healthcare Guideline—US, score=81%[27]; CPG for the Treatment of Depression across Three Age Cohorts from the American Psychological Association (APA-Psychology)—US, score=81%[28]; VA/DoD CPG for the Management of Major Depressive Disorder from

Table 1 CPGs identified for quality assessment and AGREE-II scores

CPG; author, year	AGREE II domain score (%)						Organisation	Location	Grading*	Development†
	1	2	3	4	5	6				
Ministerio de Salud (Chile), 2012[24]	83	76	89	94	57	17	Governmental	Chile	GRADE‡	New
Ministerio de Salud (Colombia), 2015[25]	100	85	86	100	96	92	Governmental	Colombia	GRADE	Adapted
NICE, 2018[26]	89	83	84	81	71	75	Governmental	England	GRADE	New
Trangle *et al*, 2016[27]	96	78	81	91	72	97	Consortium	US	GRADE	New
American Psychological Association–Depression Guideline Development Panel, 2019[28]	91	67	81	80	57	83	Specialty society	US	GRADE	New
VA/DoD, 2016[23]	93	76	78	94	38	58	Specialty society	US	GRADE	New
KPCMI, 2012[29]	83	63	76	93	46	58	Specialty society	US	GRADE	Adapted
Minsan Spain, 2014[30]	94	93	70	91	57	53	Governmental	Spain	Own method	New
RNAO, 2016[31]	72	74	69	80	76	86	Specialty society	Canada	Own method	New
Perez-Bryan *et al*, 2011[32]	70	44	69	80	50	69	Governmental	Spain	GRADE	New
Qaseem *et al*, 2016[33]	80	39	69	70	32	67	Specialty society	US	GRADE	New
Instituto Mexicano del Seguro Social, 2011[34]	87	46	69	83	14	67	Governmental	Mexico	Own method	Adapted
Instituto Mexicano del Seguro Social, 2015[35]	81	43	69	80	32	31	Governmental	Mexico	Several	Adapted
Instituto Mexicano del Seguro Social, 2016[36]	94	56	63	81	42	64	Governmental	Mexico	Several	New
Chua *et al*, 2012[37]	78	72	60	89	50	28	Governmental	Singapore	Own method	Adapted
Malhi *et al*, 2015[38]	74	63	58	78	24	67	Governmental	Australia	NA	New
Driot *et al*, 2017[39]	69	30	56	72	11	83	Independent authors	France	NA	New
Bauer *et al*, 2013[40]	61	54	54	83	32	75	Governmental	Several	Own method	New
Kennedy *et al*, 2016[21]	63	48	54	89	26	53	Specialty society	Canada	Own method	New
Dua *et al*, 2011[41]	69	74	50	74	29	75	Governmental	Several	GRADE	New
McIntyre *et al*, 2017[42]	87	56	48	83	32	69	Specialty society	US	Own method	New
Bauer *et al*, 2015[43]	69	48	47	61	28	75	Specialty society	Several	Own method	New
Malaysian Health Technology Assessment Section, 2019[44]	81	50	47	70	54	78	Governmental	Malaysia	SIGN adapted	New
Gelenberg *et al*, 2010[22]	48	43	46	83	44	42	Specialty society	US	Own method	New
Cleare *et al*, 2015[45]	67	57	40	69	13	58	Specialty society	England	Own method	New
Ruberto *et al*, 2020[46]	43	11	35	39	1	72	Independent	US	NA	New
BC Guidelines Canada, 2013[47]	85	37	35	85	39	42	Governmental	Canada	Own method	New
Giakoumatos *et al*, 2019[48]	61	19	33	83	26	75	Specialty society	US	NA	New
Bauer *et al*, 2017[49]	56	41	23	76	21	50	Specialty society	Several	Own method	New
Bennabi *et al*, 2019[50]	50	33	22	65	13	67	Specialty society	France	NA	New
Grobler, 2013[51]	50	48	19	67	13	19	Specialty society	South Africa	NA	New
Connolly *et al*, 2011[52]	63	17	17	52	13	72	Independent	US	NA	New
Wang *et al*, 2017[53]	56	13	17	43	6	58	Specialty society	Korea	NA	New
Park *et al*, 2019[54]	33	22	17	50	18	31	Independent	US	NA	New
Voineskos *et al*, 2020[55]	44	11	15	50	10	22	Independent authors	Canada	NA	New

Continued

Table 1 Continued

CPG; author, year	AGREE II domain score (%) 1	2	3	4	5	6	Organisation	Location	Grading*	Development†
Voineskos *et al*, 2018[56]	54	39	15	65	8	42	Independent	US	NA	New
Piotrowski *et al*, 2017[57]	54	26	15	72	25	50	Specialty society	Poland	NA	New
Bayes *et al*, 2019[58]	46	22	14	48	7	33	Independent authors	Australia	NA	New
Malhi *et al*, 2013[59]	44	20	13	63	17	39	Governmental	Australia	NA	New
Mulsant *et al*, 2014[60]	50	28	13	61	8	36	Governmental	Canada	NA	New
Avasthi *et al*, 2018[61]	70	24	12	80	36	0	Independent authors	India	NA	New
Möller *et al*, 2012[62]	28	15	12	11	10	33	Governmental	Several	NA	New
Busch *et al*, 2012[63]	46	11	10	65	15	17	Independent authors	US	NA	New
Taylor, 2014[64]	41	7	8	57	8	33	Independent authors	US	NA	New
Sánchez *et al*, 2019[65]	54	24	6	61	8	33	Independent authors	Spanish	NA	New
Gautam *et al*, 2017[66]	39	20	6	57	15	0	Independent authors	India	NA	New

*Grading of evidence system.
†Method of clinical practice guideline development.
‡Modified version of GRADE.
AGREE II, Appraisal of Guidelines for Research & Evaluation II; APA-Psychology, American Psychological Association; BC, British Columbia; CPG, Clinical Practice Guideline; IMSS, Instituto Mexicano del Seguro Social; KPCMI, Kaiser Permanente Care Management Institute; MH, Ministry of Health; MS, Ministerio de Salud (Ministry of Health); NA, not available; NICE, National Institute for Health and Care Excellence; RNAO, Registered Nurses' Association of Ontario; SIGN, Scottish Intercollegiate Guidelines Network; VA/DoD, US Department of Veterans Affairs (VA).

the US Department of VA, US DoD, score=78%[23]; Clinical guidelines for the management of adults with major depressive disorder from the CANMAT 2016—from Canada, score=54%[21]; Practice Guideline for the Treatment of Patients with Major Depressive Disorder from the APA, Third Edition (APA-Psychiatry) —from US, score=46%.[22]

Table 1 describes the characteristics of all the 46 CPGs identified for quality assessment. There is considerable quality variation among CPGs. For instance, the AGREE's domain 3 median value is 46.5% ranging from 6% to 89%. Table 2 presents a detailed description of the management strategies proposed by the most relevant CPGs concerning inadequate response to first-line treatment.

Terminology for responsiveness to the first line treatment and clear definition of terminology varied among CPGs. We found the terms remission,[23–28] response,[23 25 27 28] partial response,[21 23 27] no response,[21] inadequate response[21] and refractory or resistant to treatment[24 25] (table 2). Among the eight most relevant CPGs, four (50%) used the terms but did not present a clear definition of them[22 23 26 28] (table 2). Three (37.5%) CPGs also did not establish the length of treatment time needed to declare an inadequate response.[23 24 28]

Most CPGs recommended as first steps to assess treatment adherence, reassess diagnosis and/or evaluate comorbidities (6/8, 75%). The majority of CPGs emphasised the importance of adjusting antidepressant dose (7/8, 87.5%) in cases where patients do not respond to first-line treatment. However, only the NICE[26] and CANMAT[21] CPGs establish the time that should be waited specifically for increasing the dose; CANMAT: 2–4 weeks and NICE: 3–4 weeks. Adding psychotherapy was recommended by seven (87.5%) CPGs; three (37.5%) recommended neurostimulation and four (50%) switching from antidepressants to non-pharmacological treatment. Other recommendations, although less frequently mentioned, were to assess the occurrence of side effects (3/8, 37.5%; the APA-Psychiatry guideline[22] specify that replacing the drug should be considered), check substance abuse (3/8, 37.5%), increase the frequency of appointments (2/8, 25%), try previous treatments (1/8, 12.5%) and consider longer periods for improvement evaluation (1/8, 12.5%) (table 3). All CPGs included the recommendation of switching antidepressants and adding other medicines. Some CPGs used the term combination for the use of two antidepressants and augmentation for adding another type of medicine to an antidepression while others did not make such distinction. The APA-Psychology[28] included the possibility of adding another antidepressant but did not include the possibility of adding other medicines. Six CPGs recommended switching to another antidepressant before combining or augmentation strategies.[21 23 24 26–28] Regarding combining and augmentation, only the MS Chile guideline[24] stablished a sequency between them, recommending first augmentation and then combination. Most CPGs are congruent with the inclusion of antipsychotics, lithium and T3 as augmentation strategies to antidepressant treatment.

DISCUSSION

Although there are many modalities to treat depression, pharmacotherapy remains the most common first-line strategy.[12] However, clinical remission after treatment with first-line antidepressants is usually only

Table 2 Strategies for inadequate response to first-line treatment of depression according to the most relevant CPGs

CPG; author, year	Terminology for responsiveness	Recommended strategies
Ministerio de Salud (Chile), 2012[24]	Refractory or resistant to treatment: no appropriate response to pharmacotherapy under usual dosage or when there is poor or inadequate response to one or more treatments. Remission: absence of signs and symptoms for 2 months	1. Reevaluation of the diagnosis 2. Adjusting dosage 3. Switching to a different antidepressant 4. Augmentation with a second medication (lithium, liothyronine or second antidepressant) 5. Combining antidepressants
Ministerio de Salud (Colombia), 2015[25]	Refractory or resistant to treatment: absence of substantial remission of depressive symptoms or no improvement of social functioning with trial of pharmacotherapy at adequate duration and dosage. Remission: the patient responds to treatment in the initial or acute phase (within 12 weeks) and does not present further relapses in the continuation and follow-up phase. Response: defined as a 50% decrease in the score on a symptom scale depressives	Reevaluate adherence diagnosis and adverse events, adjusting dosage, add psychotherapy, switching to a different antidepressant, combining antidepressants, augmentation with a second medication (lithium or thyroid hormone)
NICE, 2018[26]	Inadequate response: no clear definition is presented. Remission: complete relief of symptoms	1. Check adherence and adverse events 2. Increase the frequency of appointments and monitor results 3. Consider reintroducing previous treatments (increase the dose) 4. Consider switching to an alternative antidepressant 5. Combining medications or augmentation 6. Combined psychological and drug treatment
Trangle *et al*, 2016[27]	Partial response: 25%–50% reduction in symptoms Response: >50% reduction in symptom Remission: devoid of symptoms.	1. Reassessment of patient/family engagement and adherence 2. Optimise antidepressant dose 3. Switching to a different antidepressant 4. Adding, switching or substituting treatment modality 5. Adding cognitive psychotherapy or adding another medication (buspirone or bupropion) 6. Reevaluating the diagnosis and the possibility of a bipolar diagnosis 7. Check comorbidities and/or substance abuse (inclusion referral to specialised care) 8. Augmentation therapy: augmentation with lithium, antipsychotics or triiodothyronine (T3) and combination of antidepressants adding bupropion or buspirone, mirtazapine +SSRI, TCA+SSRI 9. Other strategies such as electroconvulsive therapy and hospitalisation
APA-Psychology, 2019[28]	Partial response and no response: no clear definition is presented. Remission: no longer having symptoms Response: reduction in depressive symptoms	1. Switch from antidepressant medication alone to cognitive therapy alone 2. Switch from antidepressant medication alone to another antidepressant medication 3. Add psychotherapy (interpersonal psychotherapy, cognitive-behavioural therapy, or psychodynamic therapy) 4. Augment with another antidepressant medication (do not include augment with other medicines)
VA/DoD, 2016[23]	Partial response:<50% improvement in symptoms Response: improvement >50% PHQ scores Remission: PHQ score <4 for at least 1 month No response: no clear definition is presented.	Reevaluation of the diagnosis, comorbidities and adherence, adjusting dosage, augmentation of drugs, switching to another monotherapy (medication or psychotherapy), augmentation with a second medication including antidepressant, antipsychotic, lithium, T3 or psychotherapy.

Continued

Table 2 Continued

CPG; author, year	Terminology for responsiveness	Recommended strategies
Kennedy *et al*, 2016[21] (CANMAT)	Partial response: 25%–49% reduction in symptom scores. No response: <25% reduction in symptom scores. Inadequate response: partial response and no response	1. Optimise antidepressant by increasing dose. 2. Consider adjunctive use of psychological and neurostimulation treatments. 3. Switch to an antidepressant with superior efficacy. 4. Add an adjunctive medication, either combination with other antidepressant or augmentation with other medication (eg, triiodothyronine). 5. Consider switch to a second-line or third-line antidepressant. 6. Consider longer evaluation periods for improvement. 7. Increase dose if not at maximal doses. 8. Consider a chronic disease management approach, with less emphasis on symptom remission and more emphasis on improvement in functioning and quality of life.
Gelenberg *et al*, 2010[22] (APA-Psychiatry)	No response and partial response: no clear definition is presented.	During initial weeks—assess adherence, consider increasing medication dosage, and increase intensity of psychotherapy. For severe cases consider electroconvulsive therapy. At 4–8 weeks—Switch to a different antidepressant, change to or augmentation with psychotherapy, augmentation therapy with other antidepressant or other medicine, or electroconvulsive therapy.

AGREE II, Appraisal of Guidelines for Research and Evaluation II; APA-Psychiatry, American Psychiatric Association; APA-Psychology, American Psychological Association; CANMAT, Canadian Network for Mood and Anxiety Treatments; CPG, Clinical Practice Guideline; ICSI, Institute for Clinical Systems Improvement; MS, Ministerio de Salud; NA, not available; NICE, National Institute for Health and Care Excellence; PHQ, Patient Health Questionnaire; SSRI, Serotonin Selective Reuptake Inhibitor; TCA, Tricyclic Antidepressants; VA/DoD, US Department of Veterans Affairs (VA).

achieved in a minority of patients.[14 67] Thus, in this review we compared the recommendations from the eight (five with AGREE II domain 3 score ≥80% and three most used/relevant in clinical practice) most relevant CPGs for the management of depression in adults who have shown an inadequate response to first-line antidepressant treatment.

Most CPGs agree on the need to reassess the diagnosis, assess the presence of comorbidities, assess adherence to treatment, adjust antidepressant dosage and add psychotherapy as the first steps for those not responding to first-line antidepressant treatment. However, our findings revealed important flaws in recommendations including not presenting a standardised definition of an adequate/inadequate/partial response; not establishing the length of treatment time needed to declare an inadequate/partial response/non-response; all CPGs include the possibility of switching the antidepressant, augmentation with other medicines and combination of antidepressants, but three CPGs do not recommend a clear sequence among them.

Convergencies among CPGs

Considering the first steps for inadequate response to first-line antidepressant treatment, reassessing the diagnosis is almost always one of the first steps. CPGs recommend the investigation of bipolarity, personality disorders and the presence of comorbidities. Assessing the adherence to treatment is also frequently included among the first steps. Some CPGs are constructed based on other CPGs and their recommendations are identical in various aspects. In this regard, the Colombian guideline[25] place the assessment of adherence as the first step for patients with an inadequate response to treatment as does its font CPG, the NICE.[26] Increase of dose, another frequent recommendation curiously does not have consistent support by literature. It has been suggested that an increase in the dosage of most antidepressants may be effective for some patients, partially determined by individual differences in metabolising enzymes, but not for others.[26] All CPGs include the possibilities of switching and adding another medicine, and most of them recommended switching to another antidepressant before combining or augmentation strategies (table 2). Another convergence by most CPGs is the inclusion of antipsychotics, lithium and T3 as augmentation strategies to antidepressant tretament.[21–23 25–27] Adding psychotherapy to the antidepressant treatment is recommended by all, except the MS Chile guideline.[24] This strategy may decrease treatment abandonment, improve adherence to pharmacotherapy and increase the effectiveness of treatment.[68 69]

Divergencies and Shortcomings of CPGs

Among the shortcoming of CPGs, this review shows a high heterogeneity in quality of the rigour of development (domain 3 of AGREE II). A difficult finding to explain. The Diagnostic and Statistical Manual of Mental

Table 3 Summary of used definitions and strategies for inadequate response to first-line treatment among most relevant CPGs

Items	Author of the CPG							
	MS Chile, 2012[24]	MS Colombia, 2015[25]	Nice, 2018[26]	Trangle *et al*, 2016 (ICSI)[27]	VA/DoD, 2016[23]	APA-Psychology, 2019[28]	Kennedy *et al*, 2016 (CANMAT)[21]	Gelenberg *et al*, 2010 (APA-Psychiatry)[22]
Clear treatment response definition								
No response							✔	
Inadequate response							✔	
Remission	✔	✔	✔	✔	✔	✔		
Response		✔		✔	✔	✔		
Partial response				✔	✔		✔	
Refractory or resistant	✔	✔						
Length of treatment time needed to declare an inadequate response (weeks)	–	3	4	6	–	–	2–4	4–8
Time that should elapse before increasing the dose	–	–	3–4	–	–	–	2–4	–
Management of inadequate response or resistant depression								
Switching antidepressants	✔	✔	✔	✔	✔	✔	✔	✔
Consider augmentation/combining drugs	✔	✔	✔	✔	✔	✔	✔*	✔*
Dosage adjustment	✔	✔	✔	✔	✔		✔	✔
Add psychotherapy to pharmacotherapy		✔	✔	✔	✔	✔	✔	✔
Assess adherence to treatment		✔	✔	✔	✔		✔*	✔
Reassess diagnosis	✔	✔	✔*	✔	✔		✔*	
Evaluate comorbidities	✔*	✔*		✔	✔		✔*	✔*
Switch from antidepressants to NPT				✔	✔	✔		✔
Consider neurostimulation				✔			✔	✔
Check occurrence of side effects		✔	✔		✔			
Consider substance abuse		✔*		✔			✔*	
Increase appointments			✔					✔
Consider longer periods for improvement							✔	
Try previous treatments			✔					

*Not listed in the recommendations section but mentioned in the clinical practice guideline.
APA-Psychiatry, American Psychiatric Association; APA-Psychology, American Psychological Association; CANMAT, Canadian Network for Mood and Anxiety Treatments; CPG, Clinical Practice Guideline; ICSI, Institute for Clinical Systems Improvement; MS, Ministerio de Salud; NICE, National Institute for Health and Care Excellence; NPT, non-pharmacological treatment; VA/DoD, US Department of Veterans Affairs (VA).

Disorders V (DSM V) replaced DSM IV in 2013, and the diagnostic criteria for depressive disorder have been updated. Such change could impact on case identification and estimative of depression prevalence. However, diagnostic criteria are not covered by AGREE II checklist and differences in quality among CPGs might have not been influenced by that change in DSM version. CPGs were from different years, and the APA-Psychiatry, published in 2010, the oldest included, received the worst score on quality of rigour in development. It is possible that for the APA-Psychiatry and other CPGs the absence of a more recently updated version could have contributed to their low appraisal by AGREE II.

Of concern, standardised definition of an inadequate/adequate/partial response is not clear in 3 CPGs. This is a problematic point considering that we selected most relevant CPGs.[12] The absence of a clear definition of such a central aspect limits the applicability of the recommendations, increasing the risk of a more severe course of depression and, potentially, suicide.[70] MacQueen *et al*,[12] using the AGREE II, also found a lack of definition for inadequate response to antidepressant treatment in their review of 21 CPGs for treatment of depression published between 1980 and 2015.

For patients with inadequate or partial response, all CPGs include the possibilities of switching and adding another medicine. Although all CPGs recommend switching antidepressants for an inadequate antidepressant response, there is little scientific evidence supporting this approach.[71] Five CPGs recommend switching to another antidepressant before combining or augmentation strategies.[21 24 26–28] However, most CPGs do not specify whether switching should be made within the same or to a different antidepressant class. Here, we have a specific difference in the CANMAT guideline,[21] their recommendation is first switch to a more efficacious antidepressant, then to combination or augmentation and then switch to a second-line or third-line antidepressant. CPGs are not consensual regarding the use of the terms combination and augmentation. The concept of augmentation to denominate the addition of a non-antidepressant medicine to the antidepressant and the term combination to designate the use of two antidepressants are not adopted by all CPGs.[26] The CANMAT[21] guideline, uses the term 'adjunctive treatment' to denominate combination for two antidepressants or augmentation with other medicine; the APA-Psychology use the denomination 'augment' to the use of two antidepressant. Also, the APA-Psychology guideline[28] suggests the possibility of the use of two antidepressants but does not include the possibility of augmentation with other medicines. Most CPGs do not give the reader a clue of which could be tried first, augmentation or combination, only the ICSI CPG[27] establishes a sequency, recommending that drug combination should be first and then augmentation.

Other relevant point of variations is whether the CPGs recommend a class of antidepressant or specific drugs. For example, the CANMAT[21] guideline brings specific antidepressants and other specific drugs to be used as adjunctive medicine, drugs that are not recommended and also describes the criteria for the physician to decide on the drug substitution and adjunctive treatment, including the patients' preference.[21] On the other hand, other CPGs as the APA-Psychiatry guideline[22] did not mention specific antidepressants in detail in its recommendations. It should be considered that discrepancies of choices of particular strategies or medications found in our review may be governed by local contracting, availability or cost issues besides evidence-to-decision frameworks as it is recommended.[10]

Although most CPGs are congruent with the inclusion of antipsychotics, lithium and T3 as augmentation strategies to antidepressant treatment they usually do not establish the sequency among them.[21–23 25–27]

Shortcomings and strengths of our review

Our review has some limitations to be considered. It only included papers written in English, Portuguese or Spanish. CPGs' recommendations were usually described in a specific section, but in some CPGs', recommendations are also found throughout the text making it difficult to ensure that we could capture all of them. To minimise this problem, we included the content of the recommendation's section and also conducted a comprehensive search in the CPGs for additional recommendations. Another limitation to be considered is the questionable quality of evidence of primary efficacy studies for various therapeutic approaches, thus, weakness and disagreement among CPGs may at least in part reflect that condition. Last, we focus in some aspects, but the list of disagreements among the CPGs is long and there might be important points that we did not discuss here.

Strength points in this review are the use of the AGREE II to select CPGs with high quality; the inclusion of three extra CPGs among the most relevant in clinical practice[21 22] and the selection and extraction of the data performed by two independent researchers. Additionally, convergencies and divergencies among CPGs identified in our study may offer an opportunity to practitioners review their practice and help institutions in the development and adaptation of a CPG for treatment of depression.

Final considerations

It is relevant to point out that discrepancies among CPGs have led health professionals to be hesitant in applying CPGs in clinical practice.[72] Improvement in quality will help healthcare professionals in the implementation of CPGs.[73] Acceptancy by clinicians is the key for CPGs[74] effective implementation and achievement of optimal patient care. Healthcare professionals have a limited time to read a reliable literature and CPGs are essential for decision making, our study shows topics that could be reviewed and improved.[72 75]

CONCLUSION

In conclusion, most CPGs for the treatment of depression converge in including checking adherence to treatment, reassessing diagnosis, evaluating comorbidities, changing antidepressant dosage an including psychotherapy as first steps for non-responsive to first line antidepressant patients. Switching antidepressants, augmentation/combining medicines are also included strategies. However, some limitations are also present in most relevant CPGs for treatment of depression. The CPGs for the treatment of depression present differences in specific recommendations for non-responsive patients, mainly in their recommended sequence of strategies. Additionally, some do not present a standardised definition of adequate/partial/inadequate response and differ with respect to the duration of treatment needed to declare that a patient did not respond to the treatment. Our opinion is that these topics deserve further consideration in future CPGs.

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Appendix 1. Systematic search strategies

Medline (PubMed website)

(((“Guideline”[Publication Type] OR Guideline as Topic”[Mesh] OR ‘Practice Guideline”[Publication Type] OR ‘Health Planes Guidelines’[Mesh]) OR ‘Clinical Protocols’[Mesh])) OR (‘Consensus Development Conference, NIH” [Publication Type] OR (‘Consensus Development Conference, NIH” [Publication Type] OR (‘Consensus”[Mesh]))) OR Standard of Care[Mesh] “ Guideline” Publication Type] OR ‘Guideline as Topic’[Mesh] OR ‘Practice Guideline”[Publication Type] OR ‘Health Planes Guidelines’[Mesh]) OR ‘Clinical Protocols’[Mesh])) OR (‘Consensus Development Conference, NIH” [Publication Type] OR (‘Consensus Development Conference, NIH” [Publication Type] OR (‘Consensus”[Mesh]))) OR Standard of Care[Mesh]))) AND ((Depressive Disorder [Mesh] AND Depressive Disorder, Major [Mesh] OR Depressive Disorders OR disorder, Depressive OR Disorders, Depressive OR Neurosis, Depressives OR Depressive Neuroses OR Depressive Neurosis OR Neuroses, Depressive OR Depressions, Endogenous OR Endogenous Depression OR Endogenous Depressions OR Depressive Syndrome OR Depressive Syndromes OR Syndrome, Depressive OR Syndromes, Depressive OR depression, Neurotic OR Depressions, Neurotic OR Neurotic depression OR Neurotic Depressions OR Melhancholia OR Melancholias OR Unipolar Depression OR Depression, Unipolar OR Depressions, Unipolar OR Unipolar Depressions)))

Cochrane

# 1	MeSH descriptor: [Guideline] explode all trees
# 2	MeSH descriptor: [Consensus] explode all trees
# 3	MeSH descriptor: [Clinical Protocols] explode all trees
# 4	#1 OR #2 OR #3
# 5	MeSH descriptor: [Depression] explode all trees
# 6	#4 AND #5

Embase

((practice guideline/mj OR ‘consensus development’/exp/mj OR ‘clinical protocol’/mj AND (‘depression’/exp) AND (2011:py OR 2012:py OR 2013:py OR 2014:py OR 2015:py OR 2016:py AND [embase]/lim)

Appendix 2. Reasons for excluding clinical practice guideline (CPG)

Reference of the excluded CPG	Reasons for exclusion
Institute for Clinical Systems Improvement. Adult Depression in Primary Care. Bloomington, MN: ICSI; 2016.	Duplicate
Austin M-P, Highet N, The Expert Working Group. Mental Health Care in the Perinatal Period: Australian Clinical Practice Guideline. Melbourne, Australia: Centre of Perinatal Excellence; 2017.	Duplicate
Grinspun, D, Bajnok I, Rey M. Delirium, Dementia, and Depression in Older Adults: Assessment and Care. Toronto, Canada: Registered Nurses' Association of Ontario; 2016.	Duplicate
National Guideline Clearinghouse. Delirium, Dementia, and Depression in Older Adults: Assessment and Care. Rockville, MD: Agency for Healthcare Research and Quality (AHRQ); 2016. Available from: https://www.guideline.gov. Accessed January 19, 2017.	Duplicate
National Institute for Health and Care Excellence. Depression in Adults: Recognition and Management. 2009. Available from: https://www.nice.org.uk/gui dance/cg90/evidence. Accessed June 30, 2017.	Duplicate
Boltz M (Ed.). Evidence-based Geriatric Nursing Protocols for Best Practice. New York, NY: Springer; 2012.	Duplicate
Depression. University of Michigan Health System. NGC:008672.	Duplicate
Álvarez Ariza M, Atienza Merino G, Ávila González MJ, et al. GPC sobre el Manejo de la Depresión en el Adulto. Madrid, Spain: Ministerio de Sanidad, Servicios Sociales e Igualdad; 2014.	Duplicate
National Guideline Clearinghouse. Depression (Singapore). Rockville, MD: Agency for Healthcare Research and Quality (AHRQ); 2012. Available from https://www.guideline.gov/summaries/summary/39324. Accessed October 19, 2016.	Duplicate
Austin M-P, Highet N, The Expert Working Group. Mental Health Care in the Perinatal Period: Australian Clinical Practice Guideline. Melbourne, Australia: Centre of Perinatal Excellence; 2017.	Duplicate

McDermott B, Baigent M, Chanen A, et al. Clinical Practice Guidelines: Depression in Adolescents and Young Adults. Melbourne, Australia: Agency for Healthcare Research and Quality; 2010.	Duplicate
Michigan Quality Improvement Consortium Guideline. Primary Care Diagnosis and Management of Adults with Depression. Detroit, MI: MQIC; 2018. Available from: http://mqic.org/guidelines.htm. Accessed October 19, 2016.	Duplicate
National Institute for Health and Clinical Excellence. Depression in Children and Young People: Identification and Management in Primary, Community and Secondary Care. Leicester, UK: British Psychological Society; 2005.	Duplicate
Michigan Quality Improvement Consortium Guideline. Primary Care Diagnosis and Management of Adults with Depression. Detroit, MI: MQIC; 2018. Available from: http://mqic.org/guidelines.htm. Accessed October 19, 2016.	Duplicate
Connolly KR, Thase ME. If at first you don't succeed: a review of the evidence for antidepressant augmentation, combination and switching strategies. Drugs 2011;71(1):43-64. doi:10.2165/11587620-000000000-00000.	Duplicate
National Institute for Health and Care Excellence. Common Mental Health Disorders. Identification and Pathways to Care. London, UK: NICE; 2011.	Without pharmacological treatment
Grinspun, D, Bajnok I, Rey M. Delirium, Dementia, and Depression in Older Adults: Assessment and Care. Toronto, Canada: Registered Nurses' Association of Ontario; 2016.	Duplicate
Joffres M, Jaramillo A, Dickinson J, et al. Recommendations on screening for depression in adults. CMAJ 2013;185(9):775-82. doi:10.1503/cmaj.130403.	Without pharmacological treatment
Boltz M (Ed.). Evidence-based Geriatric Nursing Protocols for Best Practice. New York, NY: Springer; 2012.	Duplicate
Patten SB. Updated CANMAT guidelines for treatment of major depressive disorder. Can J Psychiatry 2016; 61(9):504-5. doi:10.1177/0706743716660034.	Without pharmacological treatment
Rush AJ, Aaronson ST, Demyttenaere K. Difficult-to-treat depression: a clinical and research roadmap for when remission is elusive. Aust N Z J Psychiatry 2019;53(2):109-18. doi:10.1177/0004867418808585.	Without pharmacological treatment
Frye MA. Clinical practice: bipolar disorder--a focus on depression. N Engl J Med 2011;364(1):51-9.	Focused on special groups

Malhi GS, Bassett D, Boyce P, et al. Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders. Aust N Z J Psychiatry 2015;49(12):1087-206. doi:10.1177/0004867415617657.	Duplicate
Andersen BL, DeRubeis RJ, Berman BS, et al. Screening, assessment, and care of anxiety and depressive symptoms in adults with cancer: an American Society of Clinical Oncology guideline adaptation. J Clin Oncol 2014;32(15):1605-19. doi:10.1200/JCO.2013.52.4611.	Subject matter
American Medical Directors Association. Guideline Summary: Depression in the Long Term Care Setting. Columbia, MD: AMDA; 2011.	Subject matter
Joffres M, Jaramillo A, Dickinson J, et al. Recommendations on screening for depression in adults. CMAJ 2013;185(9):775-82. doi:10.1503/cmaj.130403.	Subject matter
Li M, Kennedy EB, Byrne N, et al. The management of depression in patients with cancer: a clinical practice guide. J OncolPract 2016;12(8):747-56. doi:10.1200/JOP.2016.011072.	Subject matter
Ostacher MJ, Tandon R, Suppes T. Florida best practice psychotherapeutic medication guidelines for adults with bipolar disorder: a novel, practical, patient-centered guide for clinicians. J Clin Psychiatry 2016;77(7):920-6. doi:10.4088/JCP.15cs09841. Available in: http://www.embase.com/search/results?subaction=viewrecord &from=export&id=L611538719.	Subject matter
Pfennig A, Bschor T, Falkai P, et al. The diagnosis and treatment of bipolar disorder: recommendations from the current S3 guideline. Dtsch Arztebl Int 110(6):92-100. doi:10.3238/arztebl.2013.0092.	Subject matter
Rosenblat JD, McIntyre RS. Treatment recommendations for DSM-5-defined mixed features. CNS Spectr 2017;22(2):147-54. doi:10.1017/S1092852916000432.	Subject matter
Alexopoulos GS. Pharmacotherapy for late-life depression. J Clin Psychiatry 2011;72(1):e04. doi:10.4088/JCP.7085tx2cj.	Not a CPG
Andreescu C, Reynolds CF III. Late-life depression: evidencebased treatment and promising new directions for research and clinical practice. Psychiatr Clin North Am 2011;34(2):335-55. doi:10.1016/j.psc.2011.02.005.	Not a CPG
Arnow BA, Steidtmann D, Blasey C, et al. The relationship between the therapeutic alliance and treatment outcome in	Not a CPG

two distinct psychotherapies for chronic depression. J Consult Clin Psychol 2013; 81(4):627-38. doi:10.1037/a0031530.	
Ayub-Dargél A, Masson M, Henry C. The RANZCP guidelines: managing mood disorders in the real world. Aust N Z J Psychiatry 2016;50(12): 1198-9. doi:10.1177/0004867416676373.	Not a CPG
Bland P. Raising standards of care for patients with depression. Practitioner 2011;255(1740):21-5.	Not a CPG
Boffin N, Bossuyt N, Declercq T, et al. Incidence, patient characteristics and treatment initiated for GP-diagnosed depression in general practice: results of a 1-year nationwide surveillance study. Fam Prac 2012;29(6):678-87. doi:10.1093/fampra/cms024.	Not a CPG
Bohra HM, Novak M. Depression in patients with chronic kidney disease. CANNT J 2015;25(3):34-8.	Not a CPG
Busch FN, Sandberg LS. Combined treatment of depression. Psychiatr Clin North Am 2012;35(1):165-79. doi:10.1016/j.psc.2011.10.002.	Not a CPG
Cohen A. The QOF, NICE, and depression. Br J Gen Pract 2011;61(590):549. doi:10.3399/bjgp11X593785.	Not a CPG
Baumann S, Benson-Martin J, Cossie Q, et al. SASOP treatment guidelines for psychiatric disorders: eminence or evidence based? S Afr JPsychiatr 2019;20(2):a529. doi10.4102/sajpsychiatry.v20i2.529.	Not a CPG
Cosgrove L, Shaughnessy AF, Wheeler EE, et al. The American Psychiatric Association's guideline for major depressive disorder: a commentary. Psychother Psychosom 2012;81(3):186-8. doi:10.1159/000335523.	Not a CPG
Cuijpers P. Effective therapies or effective mechanisms in treatment guidelines for depression? Depress Anxiety 2013;30(11):1055-7. doi:10.1002/da.22205.	Not a CPG
Cuijpers P. Combined pharmacotherapy and psychotherapy in the treatment of mild to moderate major depression? JAMA Psychiatry 2014;71(7):747-8. doi:10.1001/jamapsychiatry.2014.277.	Not a CPG
De Coteau PA, Byrne CD, Russell, V. The HSE/ICGP guidelines on the management of depression and anxiety disorders in primary care. Ir Med J 2012;105(7):251.	Not a CPG
Desseilles M, Witte J, Chang TE, et al. Assessing the adequacy of past antidepressant trials: a clinician's guide to	Not a CPG

the antidepressant treatment response questionnaire. J Clin Psychiatry 2011;72(8):1152-4. doi:10.4088/JCP.11ac07225.	
Canadian Agency for Drugs and Technologies in Health. Diagnosing, Screening, and Monitoring Depression in the Elderly: A Review of Guidelines. Ottawa, ON: CADTH; 2015.	Not a CPG
Canadian Agency for Drugs and Technologies in Health. Antidepressants in Elderly Patients with Major and Minor Depression: A Review of Clinical Effectiveness and Guidelines. Ottawa, ON: CADTH; 2015.	Not a CPG
Gensichen J, Harter M, Klesse C, et al. Germany's national clinical practice guideline (S3) for unipolar depression—What is important for family practice? ZFA 2011;87(5):223-30. doi:10.3238/zfa.2011.0223.	Not a CPG
Geoffroy PA, Bellivier F. The RANZCP mood disorders guidelines: an easy step-by-step toolbox for daily practice. Aust N Z J Psychiatry 2016;50(10):1014-5. doi:10.1177/0004867416667829.	Not a CPG
Gitlin M. The Royal Australian and New Zealand College of Psychiatrists clinical guidelines for mood disorders: kudos and quarrels. Aust NZPsychiatry 2016;50(10):937-8. doi:10.1177/0004867416668038	Not a CPG
Grobler, G. An overview of depression treatment guidelines. Abstracts 2nd African College of Neuropsychopharmacology Congress 30-31 July 2016 Stellenbosch, Western Cape, South Africa. ActaNeuropsychiatr 2016;28(s3):1-15. doi:10.1017/neu.2016.37.	Not a CPG
Heilmann KE, Wagner M, Riedel-Heller S, et al. Treating late life depression with antidepressants: a summary of recommendations in international guidelines. Fortschr Neurol Psychiatr 2015;83(7):381-91. doi:10.1055/s-0035-1553315.	Not a CPG
Horgan D, Dodd S. Combination antidepressants—use by GPs and psychiatrists. Aust Fam Physician 2011;40(6):397-400.	Not a CPG
Kasper S. Editorial. World J Biol Psychiatry 2013;14(5):333. doi:10.3109/15622975.2013.819703.	Not a CPG
Kendall T, Pilling S, Glover N, et al. Guidelines in mental health - national and international perspectives. Int Rev Psychiatry 2011;23(4):314-7. doi:10.3109/09540261.2011.607431.	Not a CPG

Kongsuk T. Clinical practice guideline major depressive disorder for general practitioners. Value Health 2013;16(7): A695. doi:10.1016/j.jval.2013.08.2091.	Not a CPG
Kurian BT, Grannemann B, Trivedi MH. Feasible evidencebased strategies to manage depression in primary care. Curr Psychiatr Rep 2012;14(4):370-5. doi:10.1007/s11920-0120290-y.	Not a CPG
Laux G. Update treatment of depression—S3 Guideline, internet- based psychotherapy, antidepressants and driving ability. Nervenheilkunde 2016;35(10):691-6. doi:10.1055/s-0037- 1616433.	Not a CPG
Leadholm AKK, Rothschild AJ, Nolen WAet al. The treatment of psychotic depression: is there consensus among guidelines and psychiatrists? J Affect Disord 145(2): 214-20. doi:10.1016/j.jad.2012.07.036.	Not a CPG
Malhi G, Oakley-Browne M, Hay P. Clinical practice guidelines project (CPG project) overview. Aust NZ JPsychiatr 2015;49(Supp 1):30. doi:10.1177/0004867415578344.	Not a CPG
Manning JS, Jackson WC. Providing guideline-concordant assessment and monitoring for major depression in primary care. J Clin Psychiatry 2015;76(1):e3. doi:10.4088/JCP.13013tx7c.	Not a CPG
Mathys M, Mitchell BG. Targeting treatment-resistant depression. JPharm Pract 2011;24(6):520-33. doi:10.1177/0897190011426972.	Not a CPG
Morris DW, Trivedi MH. Measurement-based care for unipolar depression. Curr Psychiatry Rep 2011;13(6);446-58. doi:10.1007/s11920-011-0237-8.	Not a CPG
Nelson JC. Foreword. CNSDrugs 2013;27:3-4. doi:10.1007/s40263-012-0027-9.	Not a CPG
Nutt DJ. Highlights of the international consensus statement on major depressive disorder. J Clin Psychiatry 2011;72(6):e21. doi:10.4088/JCP.9058tx2c.	Not a CPG
Ogasawara K, Ozaki N. Review of the new treatment guideline for major depressive disorder by the Japanese Society of Mood Disorders. Brain Nerve 2012;64(10):1159-65. In Japanese.	Not a CPG
Oldham J. Fine-tuning our treatment strategies. J Psychiatr Pract 2011;17(3):157.	Not a CPG

doi:10.1097/01.pra.0000398408.13750.8d.	
Pai N. Are the Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders meeting the needs of clinicians? Aust N Z J Psychiatry 2016;50(10):1015-6. doi:10.1177/0004867416667828.	Not a CPG
Patkar AA, Pae C-U. Atypical antipsychotic augmentation strategies in the context of guideline-based care for the treatment of major depressive disorder. CNS Drugs 2013;27(Suppl 1):S29-S37. doi:10.1007/s40263-012-0031-0.	Not a CPG
Rawlins M. Ten years of NICE mental health guidelines. Int Rev Psychiatry 2011;23(4):311-3. doi:10.3109/09540261.2011.606804.	Not a CPG
Reisdorf S. Revision of the national health care guidelines on unipolar depression. MedMonatss Pharm 2016;39(4):171-2.	Not a CPG
Roberge P, Fournier L, Brouillet H, et al. A provincial adaptation of clinical practice guidelines for depression in primary care: a case illustration of the ADAPTE method. J Eval Clin Pract 2015;21(6):1190-8. doi:10.1111/jep.12404.	Not a CPG
Schuklenk U, Vathorst SVD. Treatment-resistant major depressive disorder and assisted dying. J Med Ethics 2015;41(8), 577-83. doi:10.1136/medethics-2014-102458.	Not a CPG
Schulte-Korne G, Krick K. In reply. Dtsch Arztebl Int 2014;111(18):330. doi:10.3238/arztebl.2014.0330c.	Not a CPG
Tomba E, Fava GA. Treatment selection in depression: the role of clinical judgment. Psychiatr Clin North Am 2012;35(1):87-98. doi:10.1016/j.psc.2011.11.003.	Not a CPG
Treuer T, Liu C-Y, Salazar G, et al. Use of antidepressants in the treatment of depression in Asia: guidelines, clinical evidence, and experience revisited. Asia Pac Psychiatry 2013;5(4):219-30. doi:10.1111/appy.12090.	Not a CPG
Tundo A, Calabrese JR, Proietti L, et al. Short-term antidepressant treatment of bipolar depression: are ISBD recommendations useful in clinical practice? J Affect Disord 2015;171:155-60. doi:10.1016/j.jad.2014.09.019.	Not a CPG
Van Avendonk M, van Weel-Baumgarten E, van der Weele G, et al. Summary of the Dutch College of General Practitioners' practice guideline "Depression". Ned Tijdschr Geneeskd 2012;156(38):A5101.	Not a CPG
Vinberg M, Levinsen MF, Kessing LV. Treatment-resistant	Not a CPG

depression is treatable. Ugeskr Laeger 2011;173(9):651-4.	
Wang HR, Bahk WM, Park YM, et al. Korean medication algorithm for depressive disorder: comparisons with other treatment guidelines. Psychiatry Investig 2014;11(1):1-11. doi:10.4306/pi.2014.11.1.1.	Not a CPG
Won E, Park SC, Han KM, et al. Evidence-based, pharmacological treatment guideline for depression in Korea, revised edition. J Korean Med Sci 2014;29(4):468-84. doi:10.3346/jkms.2014.29.4.468.	Not a CPG
Xiang YT, Hu C, Wang G, et al. Prescribing patterns of antidepressants, antipsychotics and mood stabilizers in bipolar patients misdiagnosed with major depressive disorder in China. Hum Psychopharmacol 2012;27(6):626-31. doi:10.1002/hup.2262.	Not a CPG
Yang J, Han C, Yoon HK, et al. Experiences and barriers to implementation of clinical practice guideline for depression in Korea. BMC Psychiatry 2013;13:150. doi:10.1186/1471244X-13 - 150.	Not a CPG
Zimmerman M. Symptom severity and guideline-based treatment recommendations for depressed patients: implications of DSM-5's potential recommendation of the PHQ-9 as the measure of choice for depression severity. Psychother Psychosom 2012;81(6):329-32. doi:10.1159/000342262.	Not a CPG
Zimmerman M, Martinez JH, Friedman M, et al. How can we use depression severity to guide treatment selection when measures of depression categorize patients differently? J Clin Psychiatry 2012;73(10):1287-91. doi:10.4088/JCP.12m07775.	Not a CPG
Malhi GS, Outhred T, Hamilton A, et al. Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders: major depression summary. Med J Aust 2018;208(4):175-80. doi:10.5694/mja17.00659.	Not a CPG
Evidence-Based Clinical Practice Guidelines for Depression in Adults on Traditional Korean Medicine; 2016.	Not found
S3-Leitlinie/Nationale Versorgungs Leitlinie Unipolare Depression; 2015. In German.	Language
Depression. Adapted Evidence-based Guideline. Ucrania; 2014 - ^enpecia. AganTOBaHaKaÍHÍnHaHacTaHOBa. In Ukrainian.	Language

[Depressive Disorder. Depressie (M44)]; 2012. In Dutch.	Language
Herrmann M, Gensichen J. Guidelines in general practice: the example depression. Psychiatrie 2015;66:119-24.	Language
Kuroki T, Tanaka T. [Threshold of application of antidepressant drugs for treatment of depressive disorder]. Seishin Shinkeigaku Zasshi 2015;117(4):269-76. In Japanese.	Language
Semba J. [Proper use of novel antidepressants in psychiatric clinical practice]. Seishin Shinkeigaku Zasshi. 2014;116(2):138-143. In Japanese.	Language
Yamada K. [Evidence of treatment for depressive episodes of bipolar disorder]. Seishin Shinkeigaku Zasshi 2011;113(9):873-9. In Japanese.	Language
Siu AL, US Preventive Services Task Force (USPSTF). Screening for depression in adults: US Preventive Services Task Force recommendation statement. JAMA 2016;315(4):380-7. doi:10.1001/jama.2015.18392.	Language
Thase ME. Recommendations for screening for depression in adults. JAMA 2016;315(4):349-50. doi:10.1001/jama.2015.18406.	Language
Patejuk-Mazurek I. Selected antidepressants and anxiolytics: practical guidelines and case studies. Psychiatria 2017;14(3):135-42.	Language
Clinical Practice Guidelines: Depression in Adolescents and Young Adults. Melbourne, Australia: NHMCRC; 2015.	Focused on special groups
Rayner L, Price A, Hotopf M, et al. The development of evidence-based European guidelines on the management of depression in palliative cancer care. Eur J Cancer 2011;47(5):702-12. doi:10.1016/j.ejca.2010.11.027.	Focused on special groups
World Health Organization. Pharmacological Interventions (Antidepressants) for 433 People with Dementia Who Have Associated Depression. Geneva, Switzerland: WHO; 2015. Available from: https://www.who.int/mental_health/mhgap/evidence/dementia /q4/en/. Accessed August 1, 2017.	Focused on special groups
Colquhoun DM, Bunker SJ, Clarke DM, et al. Screening, referral and treatment for depression in patients with coronary heart disease. Med J Aust 2013;198(9):483-4. doi:10.5694/mja13.10153.	Focused on special groups
Galician Health Technology Assessment Agency. Clinical	Outdated

Practice Guideline on the Management of Major Depression in Adults. Santiago de Compostela, Spain: Galician Health Technology Assessment Agency; 2008.	
National Collaborating Centre for Mental Health (UK). Depression. The Treatment and Management of Depression in Adults. Leicester, UK: British Psychological Society; 2010.	Outdated
Lam RW, Parikh SV, Michalak EE, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) consensus recommendations for functional outcomes in major depressive disorder. Ann Clin Psychiatr 2015;27(2):142-9.	Outdated
Agency for Healthcare Research and Quality. Detecting Depression in Older Adults with Dementia. Ann Arbor, MI: University of Michigan Health System; [s.d].	Outdated
Adult Depression in Primary Care. Bloomington, MN: ICSI; 2013.	Outdated
Galletly C, Castle D, Dark F, et al. Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for the management of schizophrenia and related disorders. Aust N Z J Psychiatry 2016;50(5):410-72. doi:10.1177/0004867416641195.	Outdated
Karyotaki E, Smit Y, Cuijpers P, et al. The Long-term Efficacy of Psychotherapy, Alone or in Combination with Antidepressants, in the Treatment of Adult Major Depression. Good Clinical Practice (GCP). Brussels, Belgium: Belgian psychotherapy Health Care Knowledge Centre (KCE); 2014. Available from: pression_Report_0.pdf. Accessed June 30, 2017.	Focused on psychotherapy
Goracci A, Forgione RN, De Giorgi R, Coluccia A, Cuomo S, Fagiolini A. Practical guidance for prescribing trazodone extended-release in major depression. Expert Opin Pharmacother. 2016;17(3):433-41. doi: 10.1517/14656566.2016.1133587	Subject matter

Appendix 1. Systematic search strategies

Medline (PubMed website)

(((“Guideline”[Publication Type] OR Guideline as Topic”[Mesh] OR ‘Practice Guideline”[Publication Type] OR ‘Health Planes Guidelines’[Mesh]) OR ‘Clinical Protocols’[Mesh])) OR (‘Consensus Development Conference, NIH” [Publication Type] OR (‘Consensus Development Conference, NIH” [Publication Type] OR (‘Consensus”[Mesh]))) OR Standard of Care[Mesh] “ Guideline” Publication Type] OR ‘Guideline as Topic’[Mesh] OR ‘Practice Guideline”[Publication Type] OR ‘Health Planes Guidelines’[Mesh]) OR ‘Clinical Protocols’[Mesh])) OR (‘Consensus Development Conference, NIH” [Publication Type] OR (‘Consensus Development Conference, NIH” [Publication Type] OR (‘Consensus”[Mesh]))) OR Standard of Care[Mesh]))) AND ((Depressive Disorder [Mesh] AND Depressive Disorder, Major [Mesh] OR Depressive Disorders OR disorder, Depressive OR Disorders, Depressive OR Neurosis, Depressives OR Depressive Neuroses OR Depressive Neurosis OR Neuroses, Depressive OR Depressions, Endogenous OR Endogenous Depression OR Endogenous Depressions OR Depressive Syndrome OR Depressive Syndromes OR Syndrome, Depressive OR Syndromes, Depressive OR depression, Neurotic OR Depressions, Neurotic OR Neurotic depression OR Neurotic Depressions OR Melhancholia OR Melancholias OR Unipolar Depression OR Depression, Unipolar OR Depressions, Unipolar OR Unipolar Depressions)))

Cochrane

# 1	MeSH descriptor: [Guideline] explode all trees
# 2	MeSH descriptor: [Consensus] explode all trees
# 3	MeSH descriptor: [Clinical Protocols] explode all trees
# 4	#1 OR #2 OR #3
# 5	MeSH descriptor: [Depression] explode all trees
# 6	#4 AND #5

Embase

((practice guideline/mj OR ‘consensus development’/exp/mj OR ‘clinical protocol’/mj AND (‘depression’/exp) AND (2011:py OR 2012:py OR 2013:py OR 2014:py OR 2015:py OR 2016:py AND [embase]/lim)

Appendix 2. Reasons for excluding clinical practice guideline (CPG)

Reference of the excluded CPG	Reasons for exclusion
Institute for Clinical Systems Improvement. Adult Depression in Primary Care. Bloomington, MN: ICSI; 2016.	Duplicate
Austin M-P, Highet N, The Expert Working Group. Mental Health Care in the Perinatal Period: Australian Clinical Practice Guideline. Melbourne, Australia: Centre of Perinatal Excellence; 2017.	Duplicate
Grinspun, D, Bajnok I, Rey M. Delirium, Dementia, and Depression in Older Adults: Assessment and Care. Toronto, Canada: Registered Nurses' Association of Ontario; 2016.	Duplicate
National Guideline Clearinghouse. Delirium, Dementia, and Depression in Older Adults: Assessment and Care. Rockville, MD: Agency for Healthcare Research and Quality (AHRQ); 2016. Available from: https://www.guideline.gov. Accessed January 19, 2017.	Duplicate
National Institute for Health and Care Excellence. Depression in Adults: Recognition and Management. 2009. Available from: https://www.nice.org.uk/gui dance/cg90/evidence. Accessed June 30, 2017.	Duplicate
Boltz M (Ed.). Evidence-based Geriatric Nursing Protocols for Best Practice. New York, NY: Springer; 2012.	Duplicate
Depression. University of Michigan Health System. NGC:008672.	Duplicate
Álvarez Ariza M, Atienza Merino G, Ávila González MJ, et al. GPC sobre el Manejo de la Depresión en el Adulto. Madrid, Spain: Ministerio de Sanidad, Servicios Sociales e Igualdad; 2014.	Duplicate
National Guideline Clearinghouse. Depression (Singapore). Rockville, MD: Agency for Healthcare Research and Quality (AHRQ); 2012. Available from https://www.guideline.gov/summaries/summary/39324. Accessed October 19, 2016.	Duplicate
Austin M-P, Highet N, The Expert Working Group. Mental Health Care in the Perinatal Period: Australian Clinical Practice Guideline. Melbourne, Australia: Centre of Perinatal Excellence; 2017.	Duplicate

McDermott B, Baigent M, Chanen A, et al. Clinical Practice Guidelines: Depression in Adolescents and Young Adults. Melbourne, Australia: Agency for Healthcare Research and Quality; 2010.	Duplicate
Michigan Quality Improvement Consortium Guideline. Primary Care Diagnosis and Management of Adults with Depression. Detroit, MI: MQIC; 2018. Available from: http://mqic.org/guidelines.htm. Accessed October 19, 2016.	Duplicate
National Institute for Health and Clinical Excellence. Depression in Children and Young People: Identification and Management in Primary, Community and Secondary Care. Leicester, UK: British Psychological Society; 2005.	Duplicate
Michigan Quality Improvement Consortium Guideline. Primary Care Diagnosis and Management of Adults with Depression. Detroit, MI: MQIC; 2018. Available from: http://mqic.org/guidelines.htm. Accessed October 19, 2016.	Duplicate
Connolly KR, Thase ME. If at first you don't succeed: a review of the evidence for antidepressant augmentation, combination and switching strategies. Drugs 2011;71(1):43-64. doi:10.2165/11587620-000000000-00000.	Duplicate
National Institute for Health and Care Excellence. Common Mental Health Disorders. Identification and Pathways to Care. London, UK: NICE; 2011.	Without pharmacological treatment
Grinspun, D, Bajnok I, Rey M. Delirium, Dementia, and Depression in Older Adults: Assessment and Care. Toronto, Canada: Registered Nurses' Association of Ontario; 2016.	Duplicate
Joffres M, Jaramillo A, Dickinson J, et al. Recommendations on screening for depression in adults. CMAJ 2013;185(9):775-82. doi:10.1503/cmaj.130403.	Without pharmacological treatment
Boltz M (Ed.). Evidence-based Geriatric Nursing Protocols for Best Practice. New York, NY: Springer; 2012.	Duplicate
Patten SB. Updated CANMAT guidelines for treatment of major depressive disorder. Can J Psychiatry 2016; 61(9):504-5. doi:10.1177/0706743716660034.	Without pharmacological treatment
Rush AJ, Aaronson ST, Demyttenaere K. Difficult-to-treat depression: a clinical and research roadmap for when remission is elusive. Aust N Z J Psychiatry 2019;53(2):109-18. doi:10.1177/0004867418808585.	Without pharmacological treatment
Frye MA. Clinical practice: bipolar disorder--a focus on depression. N Engl J Med 2011;364(1):51-9.	Focused on special groups

Malhi GS, Bassett D, Boyce P, et al. Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders. Aust N Z J Psychiatry 2015;49(12):1087-206. doi:10.1177/0004867415617657.	Duplicate
Andersen BL, DeRubeis RJ, Berman BS, et al. Screening, assessment, and care of anxiety and depressive symptoms in adults with cancer: an American Society of Clinical Oncology guideline adaptation. J Clin Oncol 2014;32(15):1605-19. doi:10.1200/JCO.2013.52.4611.	Subject matter
American Medical Directors Association. Guideline Summary: Depression in the Long Term Care Setting. Columbia, MD: AMDA; 2011.	Subject matter
Joffres M, Jaramillo A, Dickinson J, et al. Recommendations on screening for depression in adults. CMAJ 2013;185(9):775-82. doi:10.1503/cmaj.130403.	Subject matter
Li M, Kennedy EB, Byrne N, et al. The management of depression in patients with cancer: a clinical practice guide. J OncolPract 2016;12(8):747-56. doi:10.1200/JOP.2016.011072.	Subject matter
Ostacher MJ, Tandon R, Suppes T. Florida best practice psychotherapeutic medication guidelines for adults with bipolar disorder: a novel, practical, patient-centered guide for clinicians. J Clin Psychiatry 2016;77(7):920-6. doi:10.4088/JCP.15cs09841. Available in: http://www.embase.com/search/results?subaction=viewrecord &from=export&id=L611538719.	Subject matter
Pfennig A, Bschor T, Falkai P, et al. The diagnosis and treatment of bipolar disorder: recommendations from the current S3 guideline. Dtsch Arztebl Int 110(6):92-100. doi:10.3238/arztebl.2013.0092.	Subject matter
Rosenblat JD, McIntyre RS. Treatment recommendations for DSM-5-defined mixed features. CNS Spectr 2017;22(2):147-54. doi:10.1017/S1092852916000432.	Subject matter
Alexopoulos GS. Pharmacotherapy for late-life depression. J Clin Psychiatry 2011;72(1):e04. doi:10.4088/JCP.7085tx2cj.	Not a CPG
Andreescu C, Reynolds CF III. Late-life depression: evidencebased treatment and promising new directions for research and clinical practice. Psychiatr Clin North Am 2011;34(2):335-55. doi:10.1016/j.psc.2011.02.005.	Not a CPG
Arnow BA, Steidtmann D, Blasey C, et al. The relationship between the therapeutic alliance and treatment outcome in	Not a CPG

two distinct psychotherapies for chronic depression. J Consult Clin Psychol 2013; 81(4):627-38. doi:10.1037/a0031530.	
Ayub-Dargél A, Masson M, Henry C. The RANZCP guidelines: managing mood disorders in the real world. Aust N Z J Psychiatry 2016;50(12): 1198-9. doi:10.1177/0004867416676373.	Not a CPG
Bland P. Raising standards of care for patients with depression. Practitioner 2011;255(1740):21-5.	Not a CPG
Boffin N, Bossuyt N, Declercq T, et al. Incidence, patient characteristics and treatment initiated for GP-diagnosed depression in general practice: results of a 1-year nationwide surveillance study. Fam Prac 2012;29(6):678-87. doi:10.1093/fampra/cms024.	Not a CPG
Bohra HM, Novak M. Depression in patients with chronic kidney disease. CANNT J 2015;25(3):34-8.	Not a CPG
Busch FN, Sandberg LS. Combined treatment of depression. Psychiatr Clin North Am 2012;35(1):165-79. doi:10.1016/j.psc.2011.10.002.	Not a CPG
Cohen A. The QOF, NICE, and depression. Br J Gen Pract 2011;61(590):549. doi:10.3399/bjgp11X593785.	Not a CPG
Baumann S, Benson-Martin J, Cossie Q, et al. SASOP treatment guidelines for psychiatric disorders: eminence or evidence based? S Afr JPsychiatr 2019;20(2):a529. doi10.4102/sajpsychiatry.v20i2.529.	Not a CPG
Cosgrove L, Shaughnessy AF, Wheeler EE, et al. The American Psychiatric Association's guideline for major depressive disorder: a commentary. Psychother Psychosom 2012;81(3):186-8. doi:10.1159/000335523.	Not a CPG
Cuijpers P. Effective therapies or effective mechanisms in treatment guidelines for depression? Depress Anxiety 2013;30(11):1055-7. doi:10.1002/da.22205.	Not a CPG
Cuijpers P. Combined pharmacotherapy and psychotherapy in the treatment of mild to moderate major depression? JAMA Psychiatry 2014;71(7):747-8. doi:10.1001/jamapsychiatry.2014.277.	Not a CPG
De Coteau PA, Byrne CD, Russell, V. The HSE/ICGP guidelines on the management of depression and anxiety disorders in primary care. Ir Med J 2012;105(7):251.	Not a CPG
Desseilles M, Witte J, Chang TE, et al. Assessing the adequacy of past antidepressant trials: a clinician's guide to	Not a CPG

the antidepressant treatment response questionnaire. J Clin Psychiatry 2011;72(8):1152-4. doi:10.4088/JCP.11ac07225.	
Canadian Agency for Drugs and Technologies in Health. Diagnosing, Screening, and Monitoring Depression in the Elderly: A Review of Guidelines. Ottawa, ON: CADTH; 2015.	Not a CPG
Canadian Agency for Drugs and Technologies in Health. Antidepressants in Elderly Patients with Major and Minor Depression: A Review of Clinical Effectiveness and Guidelines. Ottawa, ON: CADTH; 2015.	Not a CPG
Gensichen J, Harter M, Klesse C, et al. Germany's national clinical practice guideline (S3) for unipolar depression—What is important for family practice? ZFA 2011;87(5):223-30. doi:10.3238/zfa.2011.0223.	Not a CPG
Geoffroy PA, Bellivier F. The RANZCP mood disorders guidelines: an easy step-by-step toolbox for daily practice. Aust N Z J Psychiatry 2016;50(10):1014-5. doi:10.1177/0004867416667829.	Not a CPG
Gitlin M. The Royal Australian and New Zealand College of Psychiatrists clinical guidelines for mood disorders: kudos and quarrels. Aust NZPsychiatry 2016;50(10):937-8. doi:10.1177/0004867416668038	Not a CPG
Grobler, G. An overview of depression treatment guidelines. Abstracts 2nd African College of Neuropsychopharmacology Congress 30-31 July 2016 Stellenbosch, Western Cape, South Africa. ActaNeuropsychiatr 2016;28(s3):1-15. doi:10.1017/neu.2016.37.	Not a CPG
Heilmann KE, Wagner M, Riedel-Heller S, et al. Treating late life depression with antidepressants: a summary of recommendations in international guidelines. Fortschr Neurol Psychiatr 2015;83(7):381-91. doi:10.1055/s-0035-1553315.	Not a CPG
Horgan D, Dodd S. Combination antidepressants—use by GPs and psychiatrists. Aust Fam Physician 2011;40(6):397-400.	Not a CPG
Kasper S. Editorial. World J Biol Psychiatry 2013;14(5):333. doi:10.3109/15622975.2013.819703.	Not a CPG
Kendall T, Pilling S, Glover N, et al. Guidelines in mental health - national and international perspectives. Int Rev Psychiatry 2011;23(4):314-7. doi:10.3109/09540261.2011.607431.	Not a CPG

Kongsuk T. Clinical practice guideline major depressive disorder for general practitioners. Value Health 2013;16(7): A695. doi:10.1016/j.jval.2013.08.2091.	Not a CPG
Kurian BT, Grannemann B, Trivedi MH. Feasible evidencebased strategies to manage depression in primary care. Curr Psychiatr Rep 2012;14(4):370-5. doi:10.1007/s11920-0120290-y.	Not a CPG
Laux G. Update treatment of depression—S3 Guideline, internet- based psychotherapy, antidepressants and driving ability. Nervenheilkunde 2016;35(10):691-6. doi:10.1055/s-0037- 1616433.	Not a CPG
Leadholm AKK, Rothschild AJ, Nolen WAet al. The treatment of psychotic depression: is there consensus among guidelines and psychiatrists? J Affect Disord 145(2): 214-20. doi:10.1016/j.jad.2012.07.036.	Not a CPG
Malhi G, Oakley-Browne M, Hay P. Clinical practice guidelines project (CPG project) overview. Aust NZ JPsychiatr 2015;49(Supp 1):30. doi:10.1177/0004867415578344.	Not a CPG
Manning JS, Jackson WC. Providing guideline-concordant assessment and monitoring for major depression in primary care. J Clin Psychiatry 2015;76(1):e3. doi:10.4088/JCP.13013tx7c.	Not a CPG
Mathys M, Mitchell BG. Targeting treatment-resistant depression. JPharm Pract 2011;24(6):520-33. doi:10.1177/0897190011426972.	Not a CPG
Morris DW, Trivedi MH. Measurement-based care for unipolar depression. Curr Psychiatry Rep 2011;13(6);446-58. doi:10.1007/s11920-011-0237-8.	Not a CPG
Nelson JC. Foreword. CNSDrugs 2013;27:3-4. doi:10.1007/s40263-012-0027-9.	Not a CPG
Nutt DJ. Highlights of the international consensus statement on major depressive disorder. J Clin Psychiatry 2011;72(6):e21. doi:10.4088/JCP.9058tx2c.	Not a CPG
Ogasawara K, Ozaki N. Review of the new treatment guideline for major depressive disorder by the Japanese Society of Mood Disorders. Brain Nerve 2012;64(10):1159-65. In Japanese.	Not a CPG
Oldham J. Fine-tuning our treatment strategies. J Psychiatr Pract 2011;17(3):157.	Not a CPG

doi:10.1097/01.pra.0000398408.13750.8d.	
Pai N. Are the Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders meeting the needs of clinicians? Aust N Z J Psychiatry 2016;50(10):1015-6. doi:10.1177/0004867416667828.	Not a CPG
Patkar AA, Pae C-U. Atypical antipsychotic augmentation strategies in the context of guideline-based care for the treatment of major depressive disorder. CNS Drugs 2013;27(Suppl 1):S29-S37. doi:10.1007/s40263-012-0031-0.	Not a CPG
Rawlins M. Ten years of NICE mental health guidelines. Int Rev Psychiatry 2011;23(4):311-3. doi:10.3109/09540261.2011.606804.	Not a CPG
Reisdorf S. Revision of the national health care guidelines on unipolar depression. MedMonatss Pharm 2016;39(4):171-2.	Not a CPG
Roberge P, Fournier L, Brouillet H, et al. A provincial adaptation of clinical practice guidelines for depression in primary care: a case illustration of the ADAPTE method. J Eval Clin Pract 2015;21(6):1190-8. doi:10.1111/jep.12404.	Not a CPG
Schuklenk U, Vathorst SVD. Treatment-resistant major depressive disorder and assisted dying. J Med Ethics 2015;41(8), 577-83. doi:10.1136/medethics-2014-102458.	Not a CPG
Schulte-Korne G, Krick K. In reply. Dtsch Arztebl Int 2014;111(18):330. doi:10.3238/arztebl.2014.0330c.	Not a CPG
Tomba E, Fava GA. Treatment selection in depression: the role of clinical judgment. Psychiatr Clin North Am 2012;35(1):87-98. doi:10.1016/j.psc.2011.11.003.	Not a CPG
Treuer T, Liu C-Y, Salazar G, et al. Use of antidepressants in the treatment of depression in Asia: guidelines, clinical evidence, and experience revisited. Asia Pac Psychiatry 2013;5(4):219-30. doi:10.1111/appy.12090.	Not a CPG
Tundo A, Calabrese JR, Proietti L, et al. Short-term antidepressant treatment of bipolar depression: are ISBD recommendations useful in clinical practice? J Affect Disord 2015;171:155-60. doi:10.1016/j.jad.2014.09.019.	Not a CPG
Van Avendonk M, van Weel-Baumgarten E, van der Weele G, et al. Summary of the Dutch College of General Practitioners' practice guideline "Depression". Ned Tijdschr Geneeskd 2012;156(38):A5101.	Not a CPG
Vinberg M, Levinsen MF, Kessing LV. Treatment-resistant	Not a CPG

depression is treatable. Ugeskr Laeger 2011;173(9):651-4.	
Wang HR, Bahk WM, Park YM, et al. Korean medication algorithm for depressive disorder: comparisons with other treatment guidelines. Psychiatry Investig 2014;11(1):1-11. doi:10.4306/pi.2014.11.1.1.	Not a CPG
Won E, Park SC, Han KM, et al. Evidence-based, pharmacological treatment guideline for depression in Korea, revised edition. J Korean Med Sci 2014;29(4):468-84. doi:10.3346/jkms.2014.29.4.468.	Not a CPG
Xiang YT, Hu C, Wang G, et al. Prescribing patterns of antidepressants, antipsychotics and mood stabilizers in bipolar patients misdiagnosed with major depressive disorder in China. Hum Psychopharmacol 2012;27(6):626-31. doi:10.1002/hup.2262.	Not a CPG
Yang J, Han C, Yoon HK, et al. Experiences and barriers to implementation of clinical practice guideline for depression in Korea. BMC Psychiatry 2013;13:150. doi:10.1186/1471244X-13 - 150.	Not a CPG
Zimmerman M. Symptom severity and guideline-based treatment recommendations for depressed patients: implications of DSM-5's potential recommendation of the PHQ-9 as the measure of choice for depression severity. Psychother Psychosom 2012;81(6):329-32. doi:10.1159/000342262.	Not a CPG
Zimmerman M, Martinez JH, Friedman M, et al. How can we use depression severity to guide treatment selection when measures of depression categorize patients differently? J Clin Psychiatry 2012;73(10):1287-91. doi:10.4088/JCP.12m07775.	Not a CPG
Malhi GS, Outhred T, Hamilton A, et al. Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders: major depression summary. Med J Aust 2018;208(4):175-80. doi:10.5694/mja17.00659.	Not a CPG
Evidence-Based Clinical Practice Guidelines for Depression in Adults on Traditional Korean Medicine; 2016.	Not found
S3-Leitlinie/Nationale Versorgungs Leitlinie Unipolare Depression; 2015. In German.	Language
Depression. Adapted Evidence-based Guideline. Ucrania; 2014 - ^enpecia. AganTOBaHaKaÍHÍnHaHacTaHOBa. In Ukrainian.	Language

[Depressive Disorder. Depressie (M44)]; 2012. In Dutch.	Language
Herrmann M, Gensichen J. Guidelines in general practice: the example depression. Psychiatrie 2015;66:119-24.	Language
Kuroki T, Tanaka T. [Threshold of application of antidepressant drugs for treatment of depressive disorder]. Seishin Shinkeigaku Zasshi 2015;117(4):269-76. In Japanese.	Language
Semba J. [Proper use of novel antidepressants in psychiatric clinical practice]. Seishin Shinkeigaku Zasshi. 2014;116(2):138-143. In Japanese.	Language
Yamada K. [Evidence of treatment for depressive episodes of bipolar disorder]. Seishin Shinkeigaku Zasshi 2011;113(9):873-9. In Japanese.	Language
Siu AL, US Preventive Services Task Force (USPSTF). Screening for depression in adults: US Preventive Services Task Force recommendation statement. JAMA 2016;315(4):380-7. doi:10.1001/jama.2015.18392.	Language
Thase ME. Recommendations for screening for depression in adults. JAMA 2016;315(4):349-50. doi:10.1001/jama.2015.18406.	Language
Patejuk-Mazurek I. Selected antidepressants and anxiolytics: practical guidelines and case studies. Psychiatria 2017;14(3):135-42.	Language
Clinical Practice Guidelines: Depression in Adolescents and Young Adults. Melbourne, Australia: NHMCRC; 2015.	Focused on special groups
Rayner L, Price A, Hotopf M, et al. The development of evidence-based European guidelines on the management of depression in palliative cancer care. Eur J Cancer 2011;47(5):702-12. doi:10.1016/j.ejca.2010.11.027.	Focused on special groups
World Health Organization. Pharmacological Interventions (Antidepressants) for 433 People with Dementia Who Have Associated Depression. Geneva, Switzerland: WHO; 2015. Available from: https://www.who.int/mental_health/mhgap/evidence/dementia /q4/en/. Accessed August 1, 2017.	Focused on special groups
Colquhoun DM, Bunker SJ, Clarke DM, et al. Screening, referral and treatment for depression in patients with coronary heart disease. Med J Aust 2013;198(9):483-4. doi:10.5694/mja13.10153.	Focused on special groups
Galician Health Technology Assessment Agency. Clinical	Outdated

Practice Guideline on the Management of Major Depression in Adults. Santiago de Compostela, Spain: Galician Health Technology Assessment Agency; 2008.	
National Collaborating Centre for Mental Health (UK). Depression. The Treatment and Management of Depression in Adults. Leicester, UK: British Psychological Society; 2010.	Outdated
Lam RW, Parikh SV, Michalak EE, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) consensus recommendations for functional outcomes in major depressive disorder. Ann Clin Psychiatr 2015;27(2):142-9.	Outdated
Agency for Healthcare Research and Quality. Detecting Depression in Older Adults with Dementia. Ann Arbor, MI: University of Michigan Health System; [s.d].	Outdated
Adult Depression in Primary Care. Bloomington, MN: ICSI; 2013.	Outdated
Galletly C, Castle D, Dark F, et al. Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for the management of schizophrenia and related disorders. Aust N Z J Psychiatry 2016;50(5):410-72. doi:10.1177/0004867416641195.	Outdated
Karyotaki E, Smit Y, Cuijpers P, et al. The Long-term Efficacy of Psychotherapy, Alone or in Combination with Antidepressants, in the Treatment of Adult Major Depression. Good Clinical Practice (GCP). Brussels, Belgium: Belgian psychotherapy Health Care Knowledge Centre (KCE); 2014. Available from: pression_Report_0.pdf. Accessed June 30, 2017.	Focused on psychotherapy
Goracci A, Forgione RN, De Giorgi R, Coluccia A, Cuomo S, Fagiolini A. Practical guidance for prescribing trazodone extended-release in major depression. Expert Opin Pharmacother. 2016;17(3):433-41. doi: 10.1517/14656566.2016.1133587	Subject matter

Appendix 1. Systematic search strategies

Medline (PubMed website)

(((“Guideline”[Publication Type] OR Guideline as Topic”[Mesh] OR ‘Practice Guideline”[Publication Type] OR ‘Health Planes Guidelines’[Mesh]) OR ‘Clinical Protocols’[Mesh])) OR (‘Consensus Development Conference, NIH” [Publication Type] OR (‘Consensus Development Conference, NIH” [Publication Type] OR (‘Consensus”[Mesh]))) OR Standard of Care[Mesh] “ Guideline” Publication Type] OR ‘Guideline as Topic’[Mesh] OR ‘Practice Guideline”[Publication Type] OR ‘Health Planes Guidelines’[Mesh]) OR ‘Clinical Protocols’[Mesh])) OR (‘Consensus Development Conference, NIH” [Publication Type] OR (‘Consensus Development Conference, NIH” [Publication Type] OR (‘Consensus”[Mesh]))) OR Standard of Care[Mesh]))) AND ((Depressive Disorder [Mesh] AND Depressive Disorder, Major [Mesh] OR Depressive Disorders OR disorder, Depressive OR Disorders, Depressive OR Neurosis, Depressives OR Depressive Neuroses OR Depressive Neurosis OR Neuroses, Depressive OR Depressions, Endogenous OR Endogenous Depression OR Endogenous Depressions OR Depressive Syndrome OR Depressive Syndromes OR Syndrome, Depressive OR Syndromes, Depressive OR depression, Neurotic OR Depressions, Neurotic OR Neurotic depression OR Neurotic Depressions OR Melhancholia OR Melancholias OR Unipolar Depression OR Depression, Unipolar OR Depressions, Unipolar OR Unipolar Depressions)))

Cochrane

# 1	MeSH descriptor: [Guideline] explode all trees
# 2	MeSH descriptor: [Consensus] explode all trees
# 3	MeSH descriptor: [Clinical Protocols] explode all trees
# 4	#1 OR #2 OR #3
# 5	MeSH descriptor: [Depression] explode all trees
# 6	#4 AND #5

Embase

((practice guideline/mj OR ‘consensus development’/exp/mj OR ‘clinical protocol’/mj AND (‘depression’/exp) AND (2011:py OR 2012:py OR 2013:py OR 2014:py OR 2015:py OR 2016:py AND [embase]/lim)

Appendix 2. Reasons for excluding clinical practice guideline (CPG)

Reference of the excluded CPG	Reasons for exclusion
Institute for Clinical Systems Improvement. Adult Depression in Primary Care. Bloomington, MN: ICSI; 2016.	Duplicate
Austin M-P, Highet N, The Expert Working Group. Mental Health Care in the Perinatal Period: Australian Clinical Practice Guideline. Melbourne, Australia: Centre of Perinatal Excellence; 2017.	Duplicate
Grinspun, D, Bajnok I, Rey M. Delirium, Dementia, and Depression in Older Adults: Assessment and Care. Toronto, Canada: Registered Nurses' Association of Ontario; 2016.	Duplicate
National Guideline Clearinghouse. Delirium, Dementia, and Depression in Older Adults: Assessment and Care. Rockville, MD: Agency for Healthcare Research and Quality (AHRQ); 2016. Available from: https://www.guideline.gov. Accessed January 19, 2017.	Duplicate
National Institute for Health and Care Excellence. Depression in Adults: Recognition and Management. 2009. Available from: https://www.nice.org.uk/gui dance/cg90/evidence. Accessed June 30, 2017.	Duplicate
Boltz M (Ed.). Evidence-based Geriatric Nursing Protocols for Best Practice. New York, NY: Springer; 2012.	Duplicate
Depression. University of Michigan Health System. NGC:008672.	Duplicate
Álvarez Ariza M, Atienza Merino G, Ávila González MJ, et al. GPC sobre el Manejo de la Depresión en el Adulto. Madrid, Spain: Ministerio de Sanidad, Servicios Sociales e Igualdad; 2014.	Duplicate
National Guideline Clearinghouse. Depression (Singapore). Rockville, MD: Agency for Healthcare Research and Quality (AHRQ); 2012. Available from https://www.guideline.gov/summaries/summary/39324. Accessed October 19, 2016.	Duplicate
Austin M-P, Highet N, The Expert Working Group. Mental Health Care in the Perinatal Period: Australian Clinical Practice Guideline. Melbourne, Australia: Centre of Perinatal Excellence; 2017.	Duplicate

McDermott B, Baigent M, Chanen A, et al. Clinical Practice Guidelines: Depression in Adolescents and Young Adults. Melbourne, Australia: Agency for Healthcare Research and Quality; 2010.	Duplicate
Michigan Quality Improvement Consortium Guideline. Primary Care Diagnosis and Management of Adults with Depression. Detroit, MI: MQIC; 2018. Available from: http://mqic.org/guidelines.htm. Accessed October 19, 2016.	Duplicate
National Institute for Health and Clinical Excellence. Depression in Children and Young People: Identification and Management in Primary, Community and Secondary Care. Leicester, UK: British Psychological Society; 2005.	Duplicate
Michigan Quality Improvement Consortium Guideline. Primary Care Diagnosis and Management of Adults with Depression. Detroit, MI: MQIC; 2018. Available from: http://mqic.org/guidelines.htm. Accessed October 19, 2016.	Duplicate
Connolly KR, Thase ME. If at first you don't succeed: a review of the evidence for antidepressant augmentation, combination and switching strategies. Drugs 2011;71(1):43-64. doi:10.2165/11587620-000000000-00000.	Duplicate
National Institute for Health and Care Excellence. Common Mental Health Disorders. Identification and Pathways to Care. London, UK: NICE; 2011.	Without pharmacological treatment
Grinspun, D, Bajnok I, Rey M. Delirium, Dementia, and Depression in Older Adults: Assessment and Care. Toronto, Canada: Registered Nurses' Association of Ontario; 2016.	Duplicate
Joffres M, Jaramillo A, Dickinson J, et al. Recommendations on screening for depression in adults. CMAJ 2013;185(9):775-82. doi:10.1503/cmaj.130403.	Without pharmacological treatment
Boltz M (Ed.). Evidence-based Geriatric Nursing Protocols for Best Practice. New York, NY: Springer; 2012.	Duplicate
Patten SB. Updated CANMAT guidelines for treatment of major depressive disorder. Can J Psychiatry 2016; 61(9):504-5. doi:10.1177/0706743716660034.	Without pharmacological treatment
Rush AJ, Aaronson ST, Demyttenaere K. Difficult-to-treat depression: a clinical and research roadmap for when remission is elusive. Aust N Z J Psychiatry 2019;53(2):109-18. doi:10.1177/0004867418808585.	Without pharmacological treatment
Frye MA. Clinical practice: bipolar disorder--a focus on depression. N Engl J Med 2011;364(1):51-9.	Focused on special groups

Malhi GS, Bassett D, Boyce P, et al. Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders. Aust N Z J Psychiatry 2015;49(12):1087-206. doi:10.1177/0004867415617657.	Duplicate
Andersen BL, DeRubeis RJ, Berman BS, et al. Screening, assessment, and care of anxiety and depressive symptoms in adults with cancer: an American Society of Clinical Oncology guideline adaptation. J Clin Oncol 2014;32(15):1605-19. doi:10.1200/JCO.2013.52.4611.	Subject matter
American Medical Directors Association. Guideline Summary: Depression in the Long Term Care Setting. Columbia, MD: AMDA; 2011.	Subject matter
Joffres M, Jaramillo A, Dickinson J, et al. Recommendations on screening for depression in adults. CMAJ 2013;185(9):775-82. doi:10.1503/cmaj.130403.	Subject matter
Li M, Kennedy EB, Byrne N, et al. The management of depression in patients with cancer: a clinical practice guide. J OncolPract 2016;12(8):747-56. doi:10.1200/JOP.2016.011072.	Subject matter
Ostacher MJ, Tandon R, Suppes T. Florida best practice psychotherapeutic medication guidelines for adults with bipolar disorder: a novel, practical, patient-centered guide for clinicians. J Clin Psychiatry 2016;77(7):920-6. doi:10.4088/JCP.15cs09841. Available in: http://www.embase.com/search/results?subaction=viewrecord &from=export&id=L611538719.	Subject matter
Pfennig A, Bschor T, Falkai P, et al. The diagnosis and treatment of bipolar disorder: recommendations from the current S3 guideline. Dtsch Arztebl Int 110(6):92-100. doi:10.3238/arztebl.2013.0092.	Subject matter
Rosenblat JD, McIntyre RS. Treatment recommendations for DSM-5-defined mixed features. CNS Spectr 2017;22(2):147-54. doi:10.1017/S1092852916000432.	Subject matter
Alexopoulos GS. Pharmacotherapy for late-life depression. J Clin Psychiatry 2011;72(1):e04. doi:10.4088/JCP.7085tx2cj.	Not a CPG
Andreescu C, Reynolds CF III. Late-life depression: evidencebased treatment and promising new directions for research and clinical practice. Psychiatr Clin North Am 2011;34(2):335-55. doi:10.1016/j.psc.2011.02.005.	Not a CPG
Arnow BA, Steidtmann D, Blasey C, et al. The relationship between the therapeutic alliance and treatment outcome in	Not a CPG

two distinct psychotherapies for chronic depression. J Consult Clin Psychol 2013; 81(4):627-38. doi:10.1037/a0031530.	
Ayub-Dargél A, Masson M, Henry C. The RANZCP guidelines: managing mood disorders in the real world. Aust N Z J Psychiatry 2016;50(12): 1198-9. doi:10.1177/0004867416676373.	Not a CPG
Bland P. Raising standards of care for patients with depression. Practitioner 2011;255(1740):21-5.	Not a CPG
Boffin N, Bossuyt N, Declercq T, et al. Incidence, patient characteristics and treatment initiated for GP-diagnosed depression in general practice: results of a 1-year nationwide surveillance study. Fam Prac 2012;29(6):678-87. doi:10.1093/fampra/cms024.	Not a CPG
Bohra HM, Novak M. Depression in patients with chronic kidney disease. CANNT J 2015;25(3):34-8.	Not a CPG
Busch FN, Sandberg LS. Combined treatment of depression. Psychiatr Clin North Am 2012;35(1):165-79. doi:10.1016/j.psc.2011.10.002.	Not a CPG
Cohen A. The QOF, NICE, and depression. Br J Gen Pract 2011;61(590):549. doi:10.3399/bjgp11X593785.	Not a CPG
Baumann S, Benson-Martin J, Cossie Q, et al. SASOP treatment guidelines for psychiatric disorders: eminence or evidence based? S Afr JPsychiatr 2019;20(2):a529. doi10.4102/sajpsychiatry.v20i2.529.	Not a CPG
Cosgrove L, Shaughnessy AF, Wheeler EE, et al. The American Psychiatric Association's guideline for major depressive disorder: a commentary. Psychother Psychosom 2012;81(3):186-8. doi:10.1159/000335523.	Not a CPG
Cuijpers P. Effective therapies or effective mechanisms in treatment guidelines for depression? Depress Anxiety 2013;30(11):1055-7. doi:10.1002/da.22205.	Not a CPG
Cuijpers P. Combined pharmacotherapy and psychotherapy in the treatment of mild to moderate major depression? JAMA Psychiatry 2014;71(7):747-8. doi:10.1001/jamapsychiatry.2014.277.	Not a CPG
De Coteau PA, Byrne CD, Russell, V. The HSE/ICGP guidelines on the management of depression and anxiety disorders in primary care. Ir Med J 2012;105(7):251.	Not a CPG
Desseilles M, Witte J, Chang TE, et al. Assessing the adequacy of past antidepressant trials: a clinician's guide to	Not a CPG

the antidepressant treatment response questionnaire. J Clin Psychiatry 2011;72(8):1152-4. doi:10.4088/JCP.11ac07225.	
Canadian Agency for Drugs and Technologies in Health. Diagnosing, Screening, and Monitoring Depression in the Elderly: A Review of Guidelines. Ottawa, ON: CADTH; 2015.	Not a CPG
Canadian Agency for Drugs and Technologies in Health. Antidepressants in Elderly Patients with Major and Minor Depression: A Review of Clinical Effectiveness and Guidelines. Ottawa, ON: CADTH; 2015.	Not a CPG
Gensichen J, Harter M, Klesse C, et al. Germany's national clinical practice guideline (S3) for unipolar depression—What is important for family practice? ZFA 2011;87(5):223-30. doi:10.3238/zfa.2011.0223.	Not a CPG
Geoffroy PA, Bellivier F. The RANZCP mood disorders guidelines: an easy step-by-step toolbox for daily practice. Aust N Z J Psychiatry 2016;50(10):1014-5. doi:10.1177/0004867416667829.	Not a CPG
Gitlin M. The Royal Australian and New Zealand College of Psychiatrists clinical guidelines for mood disorders: kudos and quarrels. Aust NZPsychiatry 2016;50(10):937-8. doi:10.1177/0004867416668038	Not a CPG
Grobler, G. An overview of depression treatment guidelines. Abstracts 2nd African College of Neuropsychopharmacology Congress 30-31 July 2016 Stellenbosch, Western Cape, South Africa. ActaNeuropsychiatr 2016;28(s3):1-15. doi:10.1017/neu.2016.37.	Not a CPG
Heilmann KE, Wagner M, Riedel-Heller S, et al. Treating late life depression with antidepressants: a summary of recommendations in international guidelines. Fortschr Neurol Psychiatr 2015;83(7):381-91. doi:10.1055/s-0035-1553315.	Not a CPG
Horgan D, Dodd S. Combination antidepressants—use by GPs and psychiatrists. Aust Fam Physician 2011;40(6):397-400.	Not a CPG
Kasper S. Editorial. World J Biol Psychiatry 2013;14(5):333. doi:10.3109/15622975.2013.819703.	Not a CPG
Kendall T, Pilling S, Glover N, et al. Guidelines in mental health - national and international perspectives. Int Rev Psychiatry 2011;23(4):314-7. doi:10.3109/09540261.2011.607431.	Not a CPG

Kongsuk T. Clinical practice guideline major depressive disorder for general practitioners. Value Health 2013;16(7): A695. doi:10.1016/j.jval.2013.08.2091.	Not a CPG
Kurian BT, Grannemann B, Trivedi MH. Feasible evidencebased strategies to manage depression in primary care. Curr Psychiatr Rep 2012;14(4):370-5. doi:10.1007/s11920-0120290-y.	Not a CPG
Laux G. Update treatment of depression—S3 Guideline, internet- based psychotherapy, antidepressants and driving ability. Nervenheilkunde 2016;35(10):691-6. doi:10.1055/s-0037- 1616433.	Not a CPG
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