

BMJ Open Factors associated with higher quality of clinical practice guidelines and their recommendations for the pharmacological treatment of depression: a systematic review

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To cite: Gabriel FC, de Melo DO, Stein AT, *et al.* Factors associated with higher quality of clinical practice guidelines and their recommendations for the pharmacological treatment of depression: a systematic review. *BMJ Open* 2023;**13**:e067390. doi:10.1136/bmjopen-2022-067390

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2022-067390>).

Received 11 August 2022
Accepted 11 March 2023



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ABSTRACT

Objective The objective of this study was to assess the quality of clinical practice guidelines (CPGs) for the pharmacological treatment of depression along with their recommendations and factors associated with higher quality.

Design We conducted a systematic review that included CPGs for the pharmacological treatment of depression in adults.

Data sources We searched for publications from 1 January 2011 to 31 December 2021, in MEDLINE, Cochrane Library, Embase, PsycINFO, BVS and 12 other databases and guideline repositories.

Eligibility criteria for selecting studies We included CPGs containing recommendations for the pharmacological treatment of depression in adults at outpatient care setting, regardless of whether it met the U.S. National Academy of Medicine criteria, or not. If a CPG included recommendations for both children and adults, they were considered. No language restriction was applied.

Data extraction and synthesis Data extraction was also conducted independently and in duplicate, a process that was validated in a previous project. The quality of the CPGs and their recommendations were assessed by three independent reviewers using Appraisal of Guidelines for Research and Evaluation (AGREE II) and Appraisal of Guidelines for Research and Evaluation-Recommendations Excellence (AGREE-REX). A CPG was considered to be of high quality if AGREE II Domain 3 was $\geq 60\%$; while their recommendations were considered high if AGREE-REX Domain 1 was $\geq 60\%$.

Results Seventeen out of 63 (27%) CPGs were classified as high quality, while 7 (11.1%) had high-quality recommendations. The factors associated with higher-scoring CPGs and recommendations in the multiple linear regression analyses were 'Handling of conflicts of interest', 'Multiprofessional team' and 'Type of institution'. 'Inclusion of patient representative in the team' was also associated with higher-quality recommendations.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ To increase the reliability of the quality assessment of the guidelines and recommendations, three reviewers independently conducted the assessment using both AGREE II and AGREE-REX evaluation tools. Before the assessment, the appraisers underwent rigorous training to ensure consistency in their evaluations.
- ⇒ The study was based on a comprehensive literature search on the pharmacological treatment of depression conducted in 17 databases using a sensitive strategy.
- ⇒ The inclusion of studies published in different languages made it difficult to include all documents present on the websites of specific institutions.

Conclusions The involvement of professionals from diverse backgrounds, the handling of conflicts of interest, and the inclusion of patients' perspectives should be prioritised by developers aiming for high-quality CPGs for the treatment of depression.

INTRODUCTION

Depression is a serious mental health problem that causes severe professional, economic, social and personal incapacitation.^{1 2} The Global Burden of Disease Study 2017 estimated that more than 264 million people worldwide were affected by depression.³ Moreover, according to the WHO, approximately 800 000 cases of suicide per year are attributable to this disease.⁴ The prevalence of depression has increased considerably in the last few years,^{5 6} overloading healthcare systems.⁷ The COVID-19 pandemic increased

the prevalence of mental illness even further, generating an extra need of resources to overcome the burden of mental health disorders.⁸ While a growing number of depression cases are being recognised and treated, rates of poor outcomes at 1 year in community populations remain high.⁹ The optimisation of health resources for the treatment of depression by implementing evidence-based health interventions is challenging,¹⁰ but necessary. In this scenario, adherence to high-quality clinical practice guidelines (CPGs) is vital.

CPGs are documents that contain recommendations for the optimisation of patient care, developed through the systematic review of evidence and analysis of the risks, benefits and costs of interventions for each clinical health condition.¹¹ However, the potential benefits of a CPG depend on its quality. Only high-quality CPGs have the potential of facilitating expected positive outcomes in care of patients with depression, facilitating the clinical decision-making process, enhancing the education process of patients and professionals on the best practices, reducing unnecessary clinical variability, and improving the cost-effectiveness of healthcare.¹²

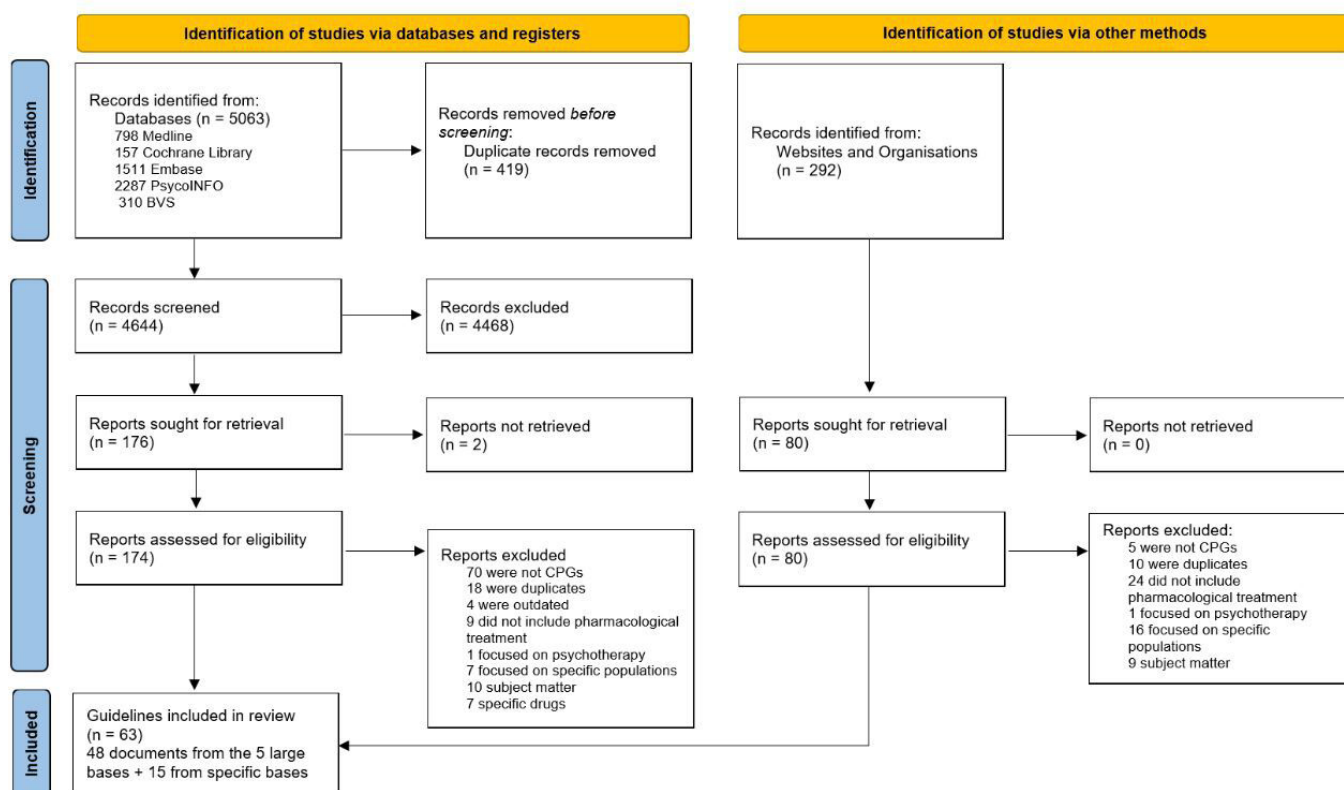
Nevertheless, there are some challenges associated with high-quality CPGs. The development of rigorous CPGs is a time-consuming and expensive task. High-quality CPGs need to be supported by systematic reviews which

require significant time, effort and technical capacity to complete.¹¹ Guidelines need to be developed by a multi-professional, independent team of experts that do not have competing interests. They also need to be continuously updated in response to new and relevant evidence, their development should be transparent and reproducible, and they need to consider patients' values and preferences.^{11 13} Furthermore, the final documents of the guidelines need to be clear, well-organised and user-friendly.^{12 14}

With the aim of providing support to guideline developers and users, some instruments have been developed to evaluate CPG quality. The most used tool for this purpose is the Appraisal of Guidelines for Research and Evaluation (AGREE II).^{13 15 16} AGREE II has been validated and translated into several languages and provides online training and a clearly written user manual. This popular instrument enables a broad CPG quality assessment,¹⁷ however it does not consider the quality of its recommendations.

To address this knowledge gap, the AGREE team developed an evidence-based AGREE II add-on, called the Appraisal of Guidelines for Research and Evaluation-Recommendations Excellence (AGREE-REX), which enables the critical assessment of the recommendations of CPGs by their developers and users.¹⁸⁻²⁰ It is important

Figure legend



Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *Br Med J*. 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: <http://www.prisma-statement.org/>.

Figure 1 Flowchart of clinical practice guidelines (CPG) selection.

Table 1 Characteristics of the included clinical practice guidelines (CPGs)

Characteristic, no. (%)	n=63
Handling of conflicts of interest	11 (17.5)
Multiprofessional team	23 (36.5)
Inclusion of patient representative in the team	6 (9.5)
Governmental funding	24 (38.1)
Type of institution or organisation	
Independent researcher/University	19 (30.2)
Professional society	25 (39.7)
Governmental	19 (30.2)
Year of publication	
2011 to 2015	27 (42.9)
2016 to 2021	36 (57.1)

to note that AGREE-REX assesses the clinical credibility of the recommendations, meaning that it checks whether the recommendations have covered the key elements that make them more applicable to a particular context.¹⁷ AGREE-REX considers that for a recommendation to be both high-quality and reliable, it must consider the values of the CPG developers and policy makers, in addition to patient preferences, and additional factors such as the clinical applicability and purpose of the CPG.¹⁸ AGREE-REX complements the AGREE II evaluation by providing an evaluation of key elements that underpin the development of the recommendations. Therefore, for a complete evaluation of CPG quality, it is important to appraise both the general quality of the CPGs and its recommendations' quality.

Table 2 Clinical practice guidelines (CPGs) descriptive statistics for AGREE II and AGREE-REX Scores, n=63

Instrument domain	Mean±SD	Median (IQR)
AGREE II		
Scope and purpose	62.4±19.4	63 (46–78)
Stakeholder involvement	40.9±23.4	39 (22–59)
Rigour of development	39.4±26.4	35 (14–63)
Clarity of presentation	68.4±18.5	70 (57–83)
Applicability	29.3±21.3	23 (13–39)
Editorial independence	50.0±24.5	53 (33–72)
AGREE-REX		
Clinical applicability	36.3±19.2	35 (19–50)
Values and preferences	17.7±14.0	14 (7–25)
Implementability	35.1±15.7	33 (25–44)
The CPGs included were published between 1 January 2011 and 31 January 2021.		
AGREE II, Appraisal of Guidelines for Research and Evaluation; AGREE-REX, Appraisal of Guidelines for Research and Evaluation-Recommendations Excellence; SD, standard deviation.		

Some studies have already assessed the quality of CPGs for the pharmacological treatment of depression using AGREE II. However, the main focus of these studies was not on the quality of the documents or the factors related to high-quality. Furthermore, patient characteristics were either more restricted or included other chronic conditions, which did not specifically address depression.²¹ To our knowledge, no study has assessed the quality of recommendations for the pharmacological treatment of depression using AGREE-REX.

By identifying the factors associated with high-quality CPG recommendations for the pharmacological treatment of depression, we can evaluate the areas for improvement that can help developers enhance their processes and create superior quality CPGs and recommendations. Therefore, our study aimed to assess the quality of CPGs for the treatment of depression and their recommendations and identify the factors associated with higher quality.

METHODS

The methods for this systematic review have already been previously reported in our published protocol²² and are only briefly described here. Our methodology involved: (1) The identification of CPGs, (2) Extraction of CPGs' characteristics, (3) Appraisal of CPGs' quality using AGREE II, (4) Appraisal of the quality of CPG recommendations with AGREE-REX, and (5) Analysis of factors associated with the quality of CPGs and their recommendations.

The identification and appraisal of CPGs was initially conducted to elaborate a comparison of high-quality recommendations for the pharmacological treatment of depression. As a post hoc analysis, we then explored the factors associated with high-quality guidelines and recommendations.

We searched for publications from 1 January 2011 to 31 December 2021, in MEDLINE, Cochrane Library, Embase, PsycINFO, BVS (Virtual Health Library Regional Portal) and 12 other databases and guideline repositories (online supplemental material). The obtained citations were screened to select potentially eligible articles, which were obtained as full texts and reviewed to assess inclusion. Both previous steps were performed independently and in duplicate. Data extraction was also conducted independently and in duplicate, a process that was validated in a previous project.^{21–23}

The quality of the CPGs was appraised by a team of multidisciplinary researchers trained according to a previously published protocol.²² A final consolidated score ranging from 0% to 100% was obtained per AGREE II and AGREE-REX domains. More information on the methodology is provided in the published protocol.²² Data were summarised by standard statistical methods and analysed using simple and multiple linear regression. Data were processed and analysed with IBM SPSS v.25.0. The detailed methodology is outlined in in online

**Table 3** Contribution of CPG characteristics to AGREE II Domain 3 and AGREE-REX Domain 1 Scores (n=63)

Characteristics	Univariate analysis			Multivariable analysis		
	B	95% CI	P value	B	95% CI	P value
AGREE II Domain 3						
Handling of conflicts of interest	43.2	29.2 to 57.2	<0.001	20.4	7.9 to 32.9	0.002
Multiprofessional team	41.1	31.7 to 50.4	<0.001	22.2	10.2 to 34.2	<0.001
Inclusion of patient representative in the team	36.8	15.7 to 57.8	0.001	3.7	-11.5 to 18.9	0.627
Governmental funding	20.2	7.3 to 33.1	0.003	0.3	-12.5 to 13.1	0.964
Type of institution						
Independent researcher/university	Ref.	-	-	Ref.	-	-
Professional society	31.1	18.5 to 43.7	<0.001	17.8	7.6 to 27.9	0.001
Governmental	42.2	28.7 to 55.6	<0.001	19.8	4.5 to 35.1	0.012
Publication year >2015	-3.3	-16.9 to 10.4	0.631	0.5	-7.6 to 8.7	0.898
AGREE-REX Domain 1						
Handling of conflicts of interest	30.0	19.7 to 40.3	<0.001	12.8	3.4 to 22.2	0.008
Multiprofessional team	27.0	19.6 to 34.5	<0.001	11.2	2.2 to 20.3	0.016
Inclusion of patient representative in the team	31.3	16.7 to 45.9	<0.001	11.1	-0.3 to 22.6	0.056
Governmental funding	11.9	2.4 to 21.5	0.016	1.0	-8.7 to 10.6	0.841
Type of institution						
Independent researcher/university	Ref.	-	-	Ref.	-	-
Professional society	25.4	16.4 to 34.4	<0.001	17.0	9.4 to 24.6	<0.001
Governmental	29.1	19.5 to 38.7	<0.001	15.2	3.7 to 26.7	0.010
Publication year >2015	-1.6	-11.5 to 8.2	0.740	1.0	-5.2 to 7.1	0.748

AGREE II, Appraisal of Guidelines for Research & Evaluation; Domain 3, Rigour of Development; AGREE-REX, AGREE Recommendations Excellence; Domain 1, Clinical Applicability; B, linear regression coefficient representing the variable absolute impact (ie, increase or decrease) on the score; CI, confidence interval; P value, statistical significance.

supplemental material 1, while the reasons for excluding CPGs are shown in online supplemental material 2.

Patient and public involvement

No patient was involved.

RESULTS

CPG identification

We retrieved 5063 documents from the search and removed 419 duplicates; thus, we screened 4644 references. We discarded non-relevant references and retrieved 174 full texts to check their eligibility (two full texts could not be retrieved). A total of 126 documents were excluded and 48 documents were included after the full-text review. Moreover, we identified 15 documents from the guidelines' repositories. Ultimately, 63 CPGs were included in this study (see [figure 1](#)).

Characteristics of CPGs

[Table 1](#) provides a summary of the characteristics of the included CPGs. Most were published after 2015 (36, 57.1%), 11 (17.5%) reported how conflicts of interest were handled and only 6 (9.5%) included patient representatives in the development team.

Appraisal of the quality of the guidelines and their recommendations

[Table 2](#) presents descriptive statistics for the AGREE II and AGREE-REX Scores. Among the 63 CPGs, domains with low mean scores on the AGREE II ($\leq 50\%$) were 'Stakeholder Involvement', 'Rigour of Development' and 'Applicability', while for the AGREE-REX, the mean scores in all domains were below 50%. The results of the appraisal of the CPGs' domains using the AGREE II and AGREE-REX are shown in [table 1](#) in the online supplemental material 3. [Table 3](#) presents the contribution of CPG characteristics to AGREE II Domain 3 and AGREE-REX Domain 1 scores.

Seventeen (27.0%) CPGs were classified as high quality according to AGREE II (Domain 3, Rigour of Development $\geq 60\%$).²⁴⁻⁴⁰ Moreover, seven (11.1%) CPGs were also considered to have high-quality recommendations (AGREE-REX Domain 1, Clinical Applicability $\geq 60\%$).²⁴⁻³¹ All CPGs classified as being of high quality by AGREE-REX were also considered high quality according to AGREE II (online supplemental material).

Factors associated with higher quality

In the univariate analyses, all factors except publication year >2015 were found to have statistically significant

associations with AGREE II Domain 3 and AGREE-REX Domain 1. For AGREE II Domain 3, the multiple linear regression analysis showed that 'Handling of conflicts of interest', 'Multiprofessional team' and 'Type of institution' were statistically significant factors associated with increased scores. Regarding 'Type of institution', both 'Professional society' and 'Governmental institutions' presented higher scores when compared with 'Independent researcher/University'. The remaining factors (ie, 'Inclusion of patient representative in the team', 'Governmental funding' and 'Publication yr.>2015') did not reach statistical significance.

When considering AGREE-REX Domain 1, the same three factors were deemed to have a significant association with higher scores in the multiple linear regression model: 'Handling of conflicts of interest', 'Multiprofessional team' and 'Type of institution'. Similarly, for AGREE-REX Domain 1, institutions represented by 'Independent researcher/University' were those found to have lower scores when compared with 'Professional society' and 'Governmental institutions'. However, it is important to note that 'Inclusion of patient representative in the team' reached borderline statistical significance ($p=0.056$) and was associated with higher AGREE-REX Domain 1 scores.

DISCUSSION

In this systematic review, we identified 63 CPGs for the treatment of depression in adults. We found that few guidelines were classified as high quality according to AGREE II (17/63, 27.0%) and even fewer were considered to have high-quality recommendations according to AGREE-REX (7/63, 11.1%). The factors associated with higher-scoring CPGs (AGREE II Domain 3) and recommendations (AGREE-REX Domain 1) in our multiple linear regression analyses were 'Handling of conflicts of interest', 'Multiprofessional team' and 'Type of institution', with 'Professional society' and 'Governmental institutions' presenting higher scores when compared with 'Independent researcher/University'. Additionally, 'Inclusion of patient representative in the team' was found to have borderline statistical significance ($p=0.056$) with higher AGREE-REX Domain 1 Scores, which are related to improved clinical applicability.

In the multivariable analysis, 'Inclusion of patient representative in the team' was no longer significant in the model analysing AGREE II Domain 3 (Rigour of Development). This finding could be explained by the small number of CPGs with this particular characteristic declared, which may produce less reliable estimates and wide CIs in a more saturated model. In addition, 'Governmental funding' lost its statistical significance, probably because it may be a surrogate marker of the involvement of 'Governmental institutions'.

We identified several domains with suboptimal performance as evaluated with the AGREE II and AGREE-REX tools. With the AGREE II tool, the worst-scored domains

were 'Applicability', 'Rigour of development' and 'Stakeholder involvement'. These findings show that CPGs may not always be based on the best evidence. Many currently available CPGs do not improve the quality of care for patients and may lead to the waste of scarce resources.^{41–43}

In other words, low scores in AGREE II Domain 3 (Rigour of Development) may indicate that most pharmacological treatments for depression did not report or perform the methodological processes expected for high-quality guidelines. Therefore, these CPGs had low or no use of appropriate development methods, selection and synthesis of evidence, and recommendations.

With the AGREE-REX tool, all three domains—'Clinical applicability', 'Values and preferences' and 'Implementability'—received low scores. The domain with the worst quality was 'Values', signalling that CPGs did not address the preferences of professionals, policy makers, developers or patient representatives in their recommendations. The values of policy makers are frequently missing, although some CPGs mention the term 'equity'—one of the values and preferences—as an important concept and as a factor considered in its development. Low scores in Domain 2 (Values) have also been found when applying AGREE-REX in CPGs for different health conditions.²⁰ Considering that therapeutic failure and adverse events in depression treatment are not uncommon, considering the values of patients, professionals, developers and policy/decision makers might be central to ensuring the effectiveness of a CPG.

In AGREE-REX Domain 1 (Clinical Applicability), we identified that the CPGs failed to clearly report the analysis of the quality of the studies, develop a list of relevant treatment outcomes (eg, quality of life, symptomatic remission, response) and appoint a patient representative as a team member. Finally, regarding AGREE-REX Domain 3 (Implementability), CPGs did not mention the anticipated impact when implementing recommendations and in the formal analysis of costs beyond the definitions of audit criteria to verify such implementation. Finally, low scores in AGREE II Domain 5 (Applicability) and AGREE-REX Domain 3 (Implementability) reveal a lack of consideration to implement strategies for clinical practice, which may lead to an ineffective interpretation of the best available evidence in practice.

We found that the handling of conflicts of interest was relevant in determining a high-quality status for a CPG and its recommendations. Such results call attention to previous reports supporting that simply declaring conflicts of interest is not enough.⁴⁴ Declaring potential conflicts of interests is not sufficient to avoid bias in the CPG development. Handling these conflicts by removing participants with conflicts from specific discussions, from voting or from the guideline group is essential to maintain rigour and transparency in the development process. The mean score of the 'Editorial independence' domain in AGREE II, the domain that includes how to handle conflicts of interest, was 50.0, contrasting with the mean scores of the highest-scored domains: 'Clarity of presentation' with

68.4 and 'Scope and purpose' with 62.4. This indicates a need for increasing attention to improve 'Handling of conflicts of interest' when developing a CPG.

We also found that a 'Multiprofessional team' was associated with higher quality in CPGs and their recommendations. These results may support the implementation of multiprofessional teams working together and sharing different practices and knowledge may offer improved results for patients, organisations and health systems.^{45 46}

According to our analyses, 'Inclusion of patient representative in the team' may also be important for the quality of recommendations. Considering patients unique views, preferences and values regarding treatment benefits and harms enriches CPGs, helps minimise disease stigmatisation and improves adherence to treatment.⁴⁷⁻⁵⁰

A study by Zafra-Tanaka *et al*⁵¹ analysed the quality and characteristics of 11 CPGs for depression published from January 2014 to May 2018 using the AGREE II instrument. Their findings revealed that <50% of these CPGs (5/11) have shared their search strategies or listed the studies used to develop the recommendations (4/11).⁵¹ These information gaps make it more difficult to understand the possible biases such as potential conflicts of interest in the formulation of the recommendations provided in CPGs, thereby undermining health professionals' trust in these guidelines. Only 18% of the CPGs (2/11) have included patient representatives in their development team. Another relevant finding of this study was that only 27% (3/11) of the CPGs had a score of $\geq 70\%$ in AGREE II Domain 3 (methodological rigour).

In addition, in a systematic review conducted by our group, the Chronic Diseases and Informed Decisions Research Group (CHRONIDE),²¹ the methodological rigour was evaluated using AGREE II for 421 CPGs for treating chronic non-communicable diseases (including depression) in primary healthcare, <25% of those CPGs (99/421) were considered as having high quality. Of all the CPGs evaluated in the study, 31 CPGs were for treating depression. Of these, only 45% (14/31) were considered high quality ($\geq 60\%$ in AGREE II Domain 3). Remarkably, no associations between geographical region and quality of CPGs were found, unlike the findings of other studies.^{52 53} Inclusion of >20 authors, being developed by government institutions and disclosure of financing support were associated with a higher quality based on logistic regression analysis. The authors raised a point that the government institutions have more financial and human resources for developing CPGs, which is generally a lengthy and costly process. Moreover, the study also revealed that Domain 4 (Applicability) received lower scores in the AGREE II assessment, either for the CPGs to treat depression or for the CPGs as a whole.

The findings reported by Zafra-Tanaka *et al*⁵¹ and Molino *et al*²¹ (the CHRONIDE Group) demonstrate that professionals and policy makers should know that only few CPGs for adults with depression demonstrate high developmental rigour. In addition, the relevance of including the patient's viewpoints, highlighted by Zafra-Tanaka *et*

al,⁵¹ converges to low quality of applicability detected by Molino *et al*.²¹ Thus, the findings indicate that healthcare policy makers should invest in improving the developmental rigour of CPGs to attain the confidence of professionals using them and, on the implementation, and monitoring of recommendations to ensure their applicability. Following these principles, the role of CPGs as a tool to promote evidence-based health is safeguarded.

This article has several strengths. First, we conducted a comprehensive search across 17 CPG databases and repositories. To ensure a comprehensive quality assessment of the guidelines and recommendations, three independent raters were trained rigorously and used both AGREE II and AGREE-REX evaluation tools. This contributed to increase the reliability of quality assessment. Moreover, the use of AGREE-REX is still incipient and at the time of writing fewer than 10 studies have used this tool for the appraisal of the quality of CPGs recommendations.

Nevertheless, this study also has some limitations. To better evaluate the guidelines and their recommendations, whenever possible, we reviewed their supplemental materials and the methodological guidance of their institutions. However, the search for these documents was conducted in the organisations' websites, and we may have missed additional relevant documents that may impact the final evaluations. Moreover, the inclusion of studies published in different languages made it difficult to include all documents present on the websites of specific institutions.

Another aspect is that although most included CPGs were published after the release of The Diagnostic and Statistical Manual of Mental Disorders V (DSM-V) in 2013, some of them may have relied on DSM-IV definitions. However, since the evaluation of CPG quality does not specifically involve diagnostic criteria, it is unlikely that this could influence the results observed in this study.

Finally, as there were very few CPGs classified as high quality, we obtained wide CIs for the associations, which creates uncertainty regarding the estimates. Therefore, caution is recommended when interpreting our results. However, this possible limitation does not lessen the relevance of our work since, at least to our knowledge, this is the first study to assess the quality of recommendations of CPGs for the treatment of depression and to explore the factors associated with higher-quality CPGs and their recommendations.

CONCLUSION

We identified 63 CPGs for the pharmacological treatment of depression in adults, with 27.0% classified as high quality and 11.1% as having high-quality recommendations. The factors 'Handling of conflicts of interest', 'Multiprofessional team' and 'Type of institution' were significantly associated with higher quality in AGREE II Domain 3 and AGREE-REX Domain 1, followed by 'Inclusion of patient representative in the team', which may have an important role in AGREE-REX Domain 1.

CPG developers should be aware of the above characteristics to obtain more reliable and implementable recommendations. They should focus on improving quality as a whole and, more emphatically, on developing better recommendations rather than creating new ones with similar limitations.

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Acknowledgements The authors thank Ana Paula Callejo and Beatriz Minguzzi for their invaluable assistance in helping them better understand the method of appraisal for CPGs.

Contributors FCG, DdM, ATS, IDF, DTC and ER conceived the main idea behind this manuscript. FCG, IDF, ATS and ER wrote the manuscript. GCHF-M, IbDS, CdSR, MCR, RF and TR critically revised the manuscript and made important intellectual contributions to its development. All authors read and approved the final version of the manuscript. FCG is responsible for the overall content as guarantor.

Funding This work was supported by the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPQ) (no. 141811/2020–0) and the Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP), Programa de Pesquisa para o SUS-Gestão Compartilhada em Saúde (PPSUS) (no. 2019/03883-7).

Competing interests IDF is the current leader of the AGREE collaboration.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

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REFERENCES

- Chisholm D, Sweeny K, Sheehan P, *et al.* Scaling-up treatment of depression and anxiety: a global return on investment analysis. *Lancet Psychiatry* 2016;3:415–24.
- Thompson C. *Affective disorders: the instruments of psychiatric research*. London: John Wiley & Sons, 2010.
- GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the global burden of disease study 2017. *Lancet* 2018;392:1789–858.
- World Health Organization. *Depression and other common mental disorders: global health estimates [internet]*. Geneva: WHO, 2017. Available: <http://apps.who.int/iris/bitstream/10665/254610/1/WHO-MSD-MER-2017.2-eng.pdf>
- Moreno-Agostino D, Wu Y-T, Daskalopoulou C, *et al.* Global trends in the prevalence and incidence of depression: a systematic review and meta-analysis. *J Affect Disord* 2021;281:235–43.
- Murray CJL, Barber RM, Foreman KJ, *et al.* Global, regional, and national disability-adjusted life years (dalis) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990–2013: quantifying the epidemiological transition. *Lancet* 2015;386:2145–91.
- Cipriani A, Furukawa TA, Salanti G, *et al.* Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis. *Lancet* 2018;391:1357–66.
- COVID-19 Mental Disorders Collaborators. Global prevalence and burden of depressive and anxiety disorders in 204 countries and territories in 2020 due to the COVID-19 pandemic. *Lancet* 2021;398:1700–12.
- Spijker J, Bijl RV, de Graaf R, *et al.* Determinants of poor 1-year outcome of DSM-III-R major depression in the general population: results of the Netherlands mental health survey and incidence study (nemesi). *Acta Psychiatr Scand* 2001;103:122–30.
- Collins PY, Patel V, Joestl SS, *et al.* Grand challenges in global mental health. *Nature* 2011;475:27–30.
- Institute of Medicine. *Clinical practice cpgs we can trust (US)*. Washington, DC: National Academies Press, 2011.
- Brignardello-Petersen R, Carrasco-Labra A, Guyatt GH. How to interpret and use a clinical practice guideline or recommendation: users' guides to the medical literature. *JAMA* 2021;326:1516–23.
- AGREE Next Steps Consortium. The AGREE-II instrument [electronic version]. [place unknown]: AGREE. 2017. Available: <http://www.agreetrust.org> [Accessed 7 May 2018].
- Swinglehurst D. Evidence-Based guidelines: the theory and the practice. *Evidence-Based Healthcare and Public Health* 2005;9:308–14.
- Hoffmann-Eßer W, Siering U, Neugebauer EAM, *et al.* Guideline appraisal with agree II: systematic review of the current evidence on how users handle the 2 overall assessments. *PLoS One* 2017;12:e0174831.
- Hoffmann-Eßer W, Siering U, Neugebauer EAM, *et al.* Guideline appraisal with agree II: online survey of the potential influence of agree II items on overall assessment of guideline quality and recommendation for use. *BMC Health Serv Res* 2018;18:143.
- Brouwers MC, Kho ME, Browman GP, *et al.* Agree II: advancing Guideline development, reporting and evaluation in health care. *CMAJ* 2010;182:E839–42.
- AGREE-REX Research Team. The appraisal of CPGs research & evaluation-recommendation excellence (AGREE-REX) [internet] AGREE. 2017. Available: <https://www.agreetrust.org/wp-content/uploads/2019/04/AGREE-REX-2019.pdf> [Accessed 17 May 2019].

- 19 Brouwers MC, Spithoff K, Kerkvliet K, *et al.* Development and validation of a tool to assess the quality of clinical practice guideline recommendations. *JAMA Netw Open* 2020;3:e205535.
- 20 Florez ID, Brouwers MC, Kerkvliet K, *et al.* Assessment of the quality of recommendations from 161 clinical practice guidelines using the appraisal of guidelines for research and evaluation-recommendations excellence (AGREE-REX) instrument shows there is room for improvement. *Implement Sci* 2020;15:79.
- 21 Molino C de GRC, Leite-Santos NC, Gabriel FC, *et al.* Factors associated with high-quality guidelines for the pharmacologic management of chronic diseases in primary care: a systematic review. *JAMA Intern Med* 2019;179:553–60.
- 22 Gabriel FC, Stein AT, de Melo DO, *et al.* Recommendations for the pharmacological treatment of treatment-resistant depression: a systematic review protocol. *PLoS One* 2022;17:e0267323.
- 23 Chronide.org [internet]. [place unknown]: chronide. 2019. Available: <https://www.chronide.org/>
- 24 Ministerio de Salud (COL). 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: guía de práctica clínica (bogotá: minsalud). 2013. Available: <http://www.ietsi.org.co/reportes-ietsi/Documentacion%20Reportes/Gu%C3%ADa.Completa.Depresion.2013.pdf> [Accessed 30 Jun 2017].
- 25 Ministerio de Salud. *Depresión em personas de 15 años y más: CL*. Santiago: Minsal, 2013.
- 26 National Institute for Health and Care Excellence. *Depression in adults: recognition and management*. London: NICE, 2009. Available: <https://www.nice.org.uk/guidance/cg90/evidenc>
- 27 Härter M, Schorr S, Schneider F, eds. *S3-leitlinie: nationale versorgungseitlinie unipolare depression langfassung*. 2nd ed. Berlin: Springer, 2015.
- 28 Instituto de Evaluación de Tecnologías en Salud e Investigación (PE). *Guía de práctica clínica para el tamizaje y el manejo del episodio depresivo leve en el primer nivel de atención*. Lima: EsSalud, 2019. Available: http://www.essalud.gob.pe/ietsi/pdfs/tecnologias_sanitarias/GPC_Depresion_V_Extensa.pdf
- 29 American Psychological Association. *Clinical practice guideline for the treatment of depression across three age cohorts*. Washington, DC: American Psychological Association, 2019. Available: <https://www.apa.org/depression-guideline/guideline.pdf>
- 30 Management of Major Depressive Disorder Working Group. *VA/dod clinical practice guideline for the management of major depressive disorder*. 3rd ed. Washington, DC: United States Department of Veterans Affairs, US Department of Defence, 2016.
- 31 Trangle M, Gursky J, Haight R, *et al.* *Depression in primary care*. Bloomington, MN: ICSI, 2016. Available: https://www.icsi.org/CPGs_more/catalog_CPGs_and_more/catalog_CPGs/catalog_behavioral_health_CPGs/depression
- 32 Kaiser Permanente care management institute. *Diagnosis and treatment of depression in adults: 2012 clinical practice guideline*. Oakland, CA: KPCMI, 2012.
- 33 García-Herrera P, Noguera MEV, Muñoz CM, *et al.* *Guía de práctica clínica para el tratamiento de la depresión en atención primaria*. Málaga: Hospital Regional Universitario “Carlos Haya”, 2011.
- 34 Working group of the clinical practice guideline on the management of depression in adults. *Clinical practice guideline on the management of depression in adults*. Madrid: Ministerio de Sanidade, Servicios Sociales e Igualdad, 2014.
- 35 Registered nurses' association of Ontario. *Delirium, dementia, and depression in older adults: assessment and care*. 2nd ed. Toronto, ON: RNAO, 2016.
- 36 Qaseem A, Barry MJ, Kansagara D, *et al.* Nonpharmacologic versus pharmacologic treatment of adult patients with major depressive disorder: a clinical practice guideline from the American College of physicians. *Ann Intern Med* 2016;164:350–9.
- 37 Instituto Mexicano del Seguro Social. *Guía de práctica clínica gpc: diagnóstico y tratamiento de la depresión en el adulto mayor en el primer nivel de atención*. Ciudad de México: IMSS, 2011.
- 38 Secretaría de Salud, S. (MX). *Diagnóstico y tratamiento del trastorno depresivo en el adulto*. Ciudad de México: Secretaría de Salud, 2015.
- 39 Secretaría de Salud, S. (MX). *Diagnóstico y tratamiento del trastorno depresivo en el adulto: intervenciones de enfermería para la detección, atención y control de la depresión en el adulto mayor en los tres niveles de atención*. Ciudad de México: Secretaría de Salud, 2016.
- 40 Chua HC, Chan LL, Chee KS, *et al.* *Depression*. Singapore: Ministry of Health, 2012. Available: <http://www.smj.org.sg/sites/default/files/5302/5302cpg1.pdf>
- 41 Alonso-Coello P, Irfan A, Solà I, *et al.* The quality of clinical practice guidelines over the last two decades: a systematic review of guideline appraisal studies. *Qual Saf Health Care* 2010;19:e58.
- 42 Bancos I, Cheng T, Prokop LJ, *et al.* Endocrine clinical practice guidelines in North America. A systematic assessment of quality. *J Clin Epidemiol* 2012;65:520–5.
- 43 Don-Wauchope AC, Sievenpiper JL, Hill SA, *et al.* Applicability of the agree II instrument in evaluating the development process and quality of current national Academy of clinical biochemistry guidelines. *Clin Chem* 2012;58:1426–37.
- 44 MacQueen G, Santaguida P, Keshavarz H, *et al.* Systematic review of clinical practice guidelines for failed antidepressant treatment response in major depressive disorder, dysthymia, and subthreshold depression in adults. *Can J Psychiatry* 2017;62:11–23.
- 45 Hopkins D. *Framework for action on interprofessional education and collaborative practice*. Geneva: WHO, 2010.
- 46 Oosterhuis WP, Bruns DE, Watine J, *et al.* Evidence-Based guidelines in laboratory medicine: principles and methods. *Clin Chem* 2004;50:806–18.
- 47 Armstrong MJ, Mullins CD, Gronseth GS, *et al.* Impact of patient involvement on clinical practice guideline development: a parallel group study. *Implement Sci* 2018;13:55.
- 48 Tong A, Tunnicliffe DJ, Lopez-Vargas P, *et al.* Identifying and integrating consumer perspectives in clinical practice guidelines on autosomal-dominant polycystic kidney disease. *Nephrology (Carlton)* 2016;21:122–32.
- 49 Cronin RM, Mayo-Gamble TL, Stimpson S-J, *et al.* Adapting medical guidelines to be patient-centered using a patient-driven process for individuals with sickle cell disease and their caregivers. *BMC Hematol* 2018;18:12.
- 50 Rocha FL, Hara C, Paprocki J. Doença mental e estigma. *Rev Med Minas Gerais* 2015;25:590–6.
- 51 Zafra-Tanaka JH, Goicochea-Lugo S, Villarreal-Zegarra D, *et al.* Characteristics and quality of clinical practice guidelines for depression in adults: a scoping review. *BMC Psychiatry* 2019;19:76.
- 52 Owolabi M, Olowoyo P, Miranda JJ, *et al.* Gaps in hypertension guidelines in low- and middle-income versus high-income countries: a systematic review. *Hypertension* 2016;68:1328–37.
- 53 Bayona H, Owolabi M, Feng W, *et al.* A systematic comparison of key features of ischemic stroke prevention guidelines in low- and middle-income vs. high-income countries. *J Neurol Sci* 2017;375:360–6.