SYSTEMATIC REVIEW

Effects of evidence-based clinical practice guidelines in cardiovascular health care quality improvements: A systematic review [version 1; peer review: 1 approved]

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Abstract

Background: The development of clinical practice guidelines (CPGs) has increasing global growth; however, the certainty of impact on patients and health systems, as well as the magnitude of the impact, is not apparent. The objective of this systematic review was to assess the effectiveness of the application of CPGs for the improvement of the quality of health care in three domains: structure, process and results in the patient for the management of cardiovascular disease.

Methods: We followed the methods described by the Cochrane Handbook and present a descriptive analysis because of the high heterogeneity found across the included studies. We searched the Cochrane Central Register of Controlled Trials, MEDLINE and EMBASE databases, as well as the grey literature, between 1990 and June 2016. No language restrictions were applied. Only randomised clinical trials (RCTs) were selected. Three authors independently carried out the data extraction, using a modified version of the Cochrane Effective Practice and Organization of Care form.

Results: Of the total of 84 interventions included in the nine RCTs evaluated, three (4%) were related to health care structure, 54 (64%) to the health care delivery process and 27 (32%) to patient outcomes. Regarding the impact of using the CPGs, in 55 interventions (65%), there were no significant differences between control and experimental groups. In four interventions (5%), the result favoured the control group, and the result favoured the intervention group on 25 of the interventions (30%).

Conclusions: This systematic review showed that CPGs could be useful to improve the process and structure of health care and, to a lesser extent, to improve the results in patients. However, evidence was weak. There are probably still undiscovered variables that interfere with the use of the CPGs and, therefore, with their impact. Therefore, more studies of good quality are needed.

Registration: PROSPERO CRD42013003589.

Keywords
Clinical Practice Guidelines, CPG, effect, health care quality
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Competing interests: No competing interests were disclosed.

Grant information: IHCAI Foundation, the sponsor of the Cochrane Center for Central America and the Spanish-speaking Caribbean, provided the necessary to carry out this review such as access to databases, full-text articles and other resources.

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Introduction

This review refers to the changes in the quality of healthcare services that are direct consequences of the systematic use of clinical practice guidelines (CPGs). Donabedian (1988) states that before evaluating health care, we must first decide how to define “quality” and whether it depends only on the actions of physicians or if it also depends on contributions from the patients and the healthcare system.

Defining quality is challenging since it is not easy to characterise coherently and objectively. Health must be analysed from a holistic point of view, and guideline developers must determine the ideal amount of influence health should receive from individual preferences and social components. We must also understand the relationship between structural characteristics and healthcare processes, as well as their results in health services (Donabedian, 1988).

Since the 1990s, increasing numbers of CPGs are being developed. However, it is unknown whether these high-quality recommendations have a beneficial impact on patient health. Despite the high number of recently published CPGs, there are few studies on their effectiveness in improving clinical outcomes, the process and structure quality throughout the healthcare system.

After an exhaustive search, only two systematic reviews (SR) we found on this topic, but this SR did not cover the three domains of evaluation of quality and international perspective together.

This review sought to assess whether the quality of health care improves in patients with the cardiovascular disease when using CPGs vs standard professional medical practice. The primary aim was to assess the impact of the CPGs for the management of cardiovascular diseases on healthcare quality, in terms of patient outcomes, management process, and healthcare structure.

Methods

We designed a methodology aimed to find and analyse studies measuring the impact of CPGs on the improvement of quality in health care services in the three areas proposed by Donabedian (Donabedian, 1988): structure, process, and patient outcomes. From the very beginning of the process when the authors wrote this review protocol, it was clear that these items would not be easy to measure and, as the search and data extraction moved forward, it became harder to synthesise the information delivered by the different studies included. The main obstacle was the inconsistency observed in the different outcome measures used by the studies, which included continuous as well as dichotomous values for different clinical conditions and interventions. The intervention definition read as any planned action taken to modify the clinical practice and use of the clinical guidelines for influencing in the clinical practice. The authors followed the methodological recommendations described in the Cochrane Handbook (Higgins & Green, 2012). This review is registered with PROSPERO (ID: CRD420130035889).

Study searches

We did a systematic search using the following electronic databases for primary studies (randomised controlled trials (RCTs)): Cochrane Central Register of Controlled Trials (CENTRAL). The Cochrane Library, including the Cochrane EPOC (Cochrane Effective Practice and Organization of Care) specialised database; MEDLINE; EMBASE; CINAHL; PsycINFO; LILACS; Health Technology Assessment Databases and Web of Science, Science Citation Index, and Social Sciences Citation Index.

The review authors combined search strategy for indexed terms and developed free text terms. We included searches of grey literature in different sources, such as reports of the world and regional conferences, academic theses and scientific reports not published in indexed journals. We searched for studies published between January 1990 and June 2016, without any language restriction. An advanced search strategy is available as Extended data, Appendix 1 (Ramirez et al., 2019).

Study selection

We analysed the studies found through the search strategy, and two authors independently selected the articles according to the following inclusion criteria: RCT measuring the change in health care when using CPGs on cardiovascular disease. The study should measure the change in any of the three health care domains (structure, process, and patient outcomes).

Data extraction

Three authors independently performed data extraction using a modified shorter version of the Cochrane Collaboration EPOC Data Collection Checklist translated into Spanish. Apart from preparing the Spanish version, we eliminated several items not applicable to this review, given that we only included RCTs. We used a standardised digital form for data extraction and analysis. We used Review Manager software (RevMan 5.3) for the data analysis.

We assessed the risk of bias (quality) according to the Cochrane Handbook (Higgins & Green, 2012). We found very high variability, so the study results were introduced as a narrative in the Results.

Because of the variability between the measurements of the effect of the impact of CPGs on the change of quality in the studies included in this review, it was not possible or appropriate to perform a meta-analysis; therefore, it was not possible to measure the statistical heterogeneity.

Results

Study identification and selection

After removing duplicates, the search yielded 4279 potential studies. We evaluated the titles and abstracts of the studies and excluded 4051. Of these, we selected 96 studies after assessing the full texts.
Study characteristics
For the analysis, we organised the studies according to the topic or pathology being the core subject of the CPG, and for this report, we only selected RCTs on cardiovascular diseases, because this theme accounts for the higher number of original articles. In total, we selected nine RCTs (Figure 1). Characteristics of the included studies are available as Extended data, Appendix 2 (Ramirez et al., 2019).

We included nine RCTs analysing cardiovascular diseases (Beaulieu et al., 2004; Berner et al., 2003; Ellis et al., 2000; Guadagnoli et al., 2004; Hand et al., 2014; Jäntti et al., 2007; Kiessling & Henriksson, 2002; Tierney et al., 2003; Tsuyuki et al., 2015). All trials were carried out between 2000 and 2015, five in the United States of America, two in Canada, one in Finland and one in Sweden. Eight articles addressed outpatient care and three inpatient care. The CPGs included in the selected trial looked at the following clinical problems: management of stable angina pectoris (over 65 years), unstable angina, dyslipidemia, acute infarction, heart failure and blood pressure. Besides, the trials included perioperative cardiac evaluations of patients with non-cardiac surgery, cardiopulmonary resuscitation and secondary prevention in patients having coronary artery disease.

A number of the 4,279 studies found in the initial search were not randomised clinical trials, as the authors described in their titles or abstracts. When assessing the full-text articles, we found that many were cluster trials and observational studies with a “before and after” design.

Quality of evidence assessment
As for the quality of the evidence, we observed the presence of a high or unclear risk of bias for allocation concealment (selection bias), blinding of participants and personnel (performance bias), and blinding of outcome assessment (detection bias), which can be explained by the nature of the interventions studied. We found several types of systematic errors: random sequence generation (selection bias), incomplete outcome data (attrition bias) and selective reporting (reporting bias). We found that the interventions measured yielded outcomes assessed with moderate to low evidence certainty according to the GRADE classification.

Risk of bias assessment
Analysing the risk of bias in the nine included RCTs studies found the random sequence generation (selection bias) assessment had a low risk of bias (between 50–75%) for allocation concealment (selection bias) 33% low, 33% unknown and 33% high risk of bias. The blinding of participants and personnel (performance bias) obtained almost 50% high risk of bias. The blinding of outcome assessments (detection bias) obtained a 50% low and 50% uncertain risk of bias. Incomplete outcome data (attrition bias) obtained between a 50 and 75% low risk of bias. For the selective reporting (reporting bias), there was a 100% low risk of bias. Finally, other types of bias had a low risk of between 50 and 75% (Figure 2).

The studies with the lowest and highest risk of bias (Kiessling & Henriksson, 2002 and Jäntti et al., 2007, respectively) were chosen to be evaluated with the GRADE methodology and to build a summary of findings table. The aim of doing this GRADE table was obtaining the rank of possible grades of the evidence certainty found in the 84 interventions from the nine studies included. The results of these studies produced moderate-to-low evidence certainty, according to the GRADE classification (see Table 1 and Table 2).
Figure 2. Overall bias risk chart of all included studies.

Table 1. Evaluation of the Certainty of the Evidence for the Jäntti 2007 study on cardiopulmonary resuscitation, according to the GRADE classification.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Average duration (seconds ± SE)</th>
<th>Relative effect (p)</th>
<th>Nr of participants (studies)</th>
<th>Certainty of the evidence (GRADE)</th>
<th>Relevance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Average with ERC 2000</td>
<td>Average with ERC 2005</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total time without flow (s)</td>
<td>393 ± 19</td>
<td>190 ± 23</td>
<td>p &lt; 0.001</td>
<td>34 Control Group: 17 Intervention Group: 17 (1 RCT (Randomized Controlled Trial))</td>
<td>MODERATE 1,2</td>
</tr>
<tr>
<td>Delay to start CPR (s)</td>
<td>8 ± 6</td>
<td>8 ± 4</td>
<td>p = 0.949</td>
<td>34 Control Group: 17 Intervention Group: 17 (1 RCT (Randomized Controlled Trial))</td>
<td>LOW 1,3</td>
</tr>
</tbody>
</table>

ERC: European Resuscitation Council
SE: Standard deviation
p: significance

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of the effect

Explanations

1. For the generation of the random sequence (selection bias) the risk is High: sealed, numbered and opaque envelopes were used for the randomisation of the cases to be treated. It is not clear why people with less work experience or no academic degree were assigned to the ERC 2000. For the allocation concealment (selection bias) the risk is High: It is likely that by nature of the study the allocation concealment of the selection could not be made. For blinding of participants and staff (performance bias) the risk is High: It is likely that the nature of the study could not prevent participants from knowing which group they belonged to (which CPG they were using). For blinding of the outcome evaluation (detection bias) the risk is Low: A computer automatically collected data. In other risks of bias, the risk of bias is High: The description of the study design was not clear; therefore, we assumed that the study has a high risk of bias.

2. P < 0.001

3. P 0.949
Is the active implementation more effective compared to passive implementation as it was used in the control group to improve secondary prevention of coronary artery disease?

Patient or population: person with coronary artery disease.

Intervention: Active implementation (general practitioners participated in learning dialogues using the CPG on secondary prevention of coronary artery disease, method of recurrent cases in their primary care centers)

Control: Passive implementation (the CPG was mailed to general practitioners and presented at a conference)


<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Average Change of active versus passive implementation of the CPG (%) (95% CI)</th>
<th>Relative effect (p)</th>
<th>Nb of participants (studies)</th>
<th>Certainty of the evidence (GRADE)</th>
<th>Relevance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Group</td>
<td>0.7% (CI -4.1 a 5.9)</td>
<td>-</td>
<td>176 Control Group: 88 Intervention Group: 88 (1 RCT (Randomized Controlled Trial))</td>
<td>MODERATE1,2</td>
<td>IMPORTANT</td>
</tr>
<tr>
<td></td>
<td>Difference in percentage of LDL change at 2 years [Mean (mmol / L)]</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Intervention Group</td>
<td>-9.3 % (CI -15.8 a -2.9)</td>
<td>p &lt; 0.05</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Difference in percent change in total cholesterol at 2 years [Mean (mmol / L)]</td>
<td>1.8% (CI -2.2 a 5.9)</td>
<td>-6.0 % (CI -10.4 a -1.5)</td>
<td>p &gt; 0.05</td>
<td>176 Control Group: 88 Intervention Group: 88 (1 RCT (Randomized Controlled Trial))</td>
</tr>
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<td></td>
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</tbody>
</table>

CI: Confidence interval
p: significance

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

For the generation of the random sequence (selection bias) the risk of bias is Uncertain: Not described. For allocation concealment (selection bias) the risk is low: general practitioners and patients did not know in which research group they were assigned. For blinding of participants and staff (performance bias) the risk is low: General practitioners were not aware of being involved in the study and a blinded nurse on which group each patient belonged to, was the one who handled the paperwork, protocols of the investigation and had no contact with general practitioners. For blinding of the outcome assessment (detection bias), the risk is Low: The research codes and databases were not disclosed until the authors completed the statistical analysis. For incomplete results data (attrition bias), the risk is Low: The study used the intention-to-treat analysis and indicated that the follow-up for two years was 86%. For the particular report (notification bias) the risk is Low: The research codes and databases were not disclosed until the authors completed the statistical analysis. For Other biases the risk is Low: None known

Assessment of study outcomes

The authors grouped the outcomes in simple relative and absolute numbers. There was not a global estimate of the measurements of the effects included in the studies because of the considerable variability of measuring units, as well as the clinical heterogeneity found among the studies included. The measurement of the outcomes reported in the studies was dichotomous, continuous or nominal; the majority were dichotomous and were used to measure the mastery of the process, e.g. the number of patients receiving an adequate treatment following a recommendation versus those who did not.

Of the total of 84 interventions included in the nine RCTs evaluated, three (4%) corresponded to the health care structure
domain, 54 interventions (64%) to the domain health care delivery and 27 interventions (32%) to the domain of patient results. Regarding the impact of CPG use, we found that in 55 interventions (65%) there was no significant difference between the control and experimental groups.

In four interventions (5%) the outcome favoured the control group (comparison of the measure of compliance of the recommendations (the average adjusted by the patient characteristics, the setting, and the number of measures applied per patient)). The measure of effects (odds ratio (OR)) regarding the conditions acute myocardial infarction and heart failure, separated by care provided by a cardiologist or primary care physicians, were as follows: acute myocardial infarction, cared by a cardiologist OR 0.81 (95% CI: 0.79 to 0.83), and cared by a primary care physician OR 0.73 (95% CI: 0.71 to 0.76); heart failure, cared by a cardiologist OR 0.88 (95% CI: 0.86 to 0.90), and care by a primary care physician OR 0.79 (95% CI: 0.76 to 0.81).

The result favoured the intervention group for 25 interventions (30%). Some of the recommendations were: use of antplatelet medication during the 24-hour hospital stay, a study of the left ventricle ejection fraction, total cholesterol and LDL measurements, cardiopulmonary resuscitation, and degree of compliance with CPGs recommendations.

**Discussion**

Methodological efforts have been made to develop trustworthy CPGs. However, it still seems that some of these CPGs are far from the reality of the clinical practice (Institute of Medicine (US) Committee on Standards for Developing Trustworthy Clinical Practice Guidelines, 2011).

It is essential to emphasise the main findings from the outcome analysis. It is surprising that most of the studies did differentiate between the control and experimental groups regarding the improvements with the use of CPGs. The effects of recommendations of the interventions included in the nine RCTs on the areas of health care structure (4%) and patient outcomes were the least studied (32%). This fact could lead us to assume that researchers have given more importance to the evaluation of using (or not using) the recommendations in the area of the process, instead of their direct impact on the patient health.

The changes observed in the patient progression were generally modest. In the six studies evaluating patient outcomes (27 interventions), four of them reported a positive result for seven measurements (26%) of the interventions. For example, the study by Ellis et al. (2000) measured the difference in the average change of total cholesterol (mg/dl) and reported a decrease of 7.4 mg/dl in favour of the intervention. It is essential to mention that these measures were mostly surrogate variables. Only one study reported variables for clinical results (Tierney et al., 2003), with 13 interventions, but found no meaningful differences in the results between the groups.

Most of the studies (eight) reported results in the process area and showed favourable results for the intervention in six studies with 16 measurements. This fact reflects the reluctance of health care providers to use CPGs and means that only 30% of these interventions followed the recommendations given by the CPGs.

However, most of the studies included in this review used multiple strategies to implement the CPGs (electronic notifications in a digital file, cell phone applications, letters, phone calls, printed material), and the authors do not tailor to every recommendation (the implementation strategy is usually the same for every recommendation within a CPG). A more specific approach, based on the results of the analysis of the obstacles hindering the adoption of every recommendation separately, might improve the use and effect of the recommendations in practice.

**Conclusions**

There is an imbalance between the number of CPGs developed and the number of high-quality studies evaluating their effectiveness. The study demonstrates weak evidence about the benefit of CPGs for improving the quality of the healthcare process and structure and, to a lesser extent, for improving patient outcomes. There are still undiscovered variables that may interfere with the use of the CPGs and, therefore, with their impact. Therefore, more studies of good quality are still needed.

The variation in the effects of the recommendations of the CPGs suggests that it would be useful to focus on the analysis of the adherence limitations, as well as on designing implementation strategies adapt every recommendation, instead of considering the CPGs as a whole. Further research is still needed to determine which factors related to the CPGs and their specific recommendations are essential to predict the use of CPGs, and thus achieve better patient outcomes.

**Implications for practice**

The initial objective of this review was to strengthen the development programs for CPG by evaluating their effects on the quality of health care and to give reliable evidence to sustain the decision-making process related to the construction of CPGs in medium- and low-income countries. Even the research evidence is not strong enough to support the CPGs as a tool to improve the practice for a better quality of care, the results of this review must need to be interpreted with caution. Definitely. It seems the standard application used so far must be reviewed and must incorporate new psychosocial strategies oriented toward driving change in clinical practice and the doctor-patient relationship. We need reaching the right hands at the right time. It is necessary to emphasise that the standard implementation used so far must be reviewed, and must incorporate new psychosocial strategies oriented toward driving change in clinical practice and the doctor-patient relationships.

For an adequate implementation of a CPG, it is necessary to take into account the possible costs and benefits that will be necessary to know the expected results precisely. The health systems that build CPGs must maximise their efforts to get health care personnel to follow the recommendations of the CPGs and make an effort to evaluate their impact.
Implications for research
Since research in this field is so new, and the results of this study were not conclusive, more research is needed to evaluate the change that CPGs could make to the quality of health care, emphasising the less studied areas, such as the structure of health care services and patient outcomes.

Data availability
Underlying data
All data underlying the results are available as part of the article and no additional source data are required.

Extended data

This project contains the following extended data:
- Appendix 1 Advanced Search Strategy
- Appendix 2 Characteristics of included studies English version

References

Reporting guidelines

Grant information
IHCAI Foundation, the sponsor of the Cochrane Center for Central America and the Spanish-speaking Caribbean, provided the necessary to carry out this review such as access to databases, full-text articles and other resources.

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Acknowledgments
Thanks to the professors of the School of Epidemiology of the University of Frontera Temuco, Chile, and the advisor of the Master’s thesis, Mario Delgado MD, PhD, for his contribution and suggestions of the proposed protocol of the review.

Author information
Anggie Ramírez-Morera and Juan Carlos Vazquez are PhD candidates at Autonomous University of Barcelona.
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Version 1

Reviewer Report 24 July 2019

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Yasser Sami Abdel Dayem Amer
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Thank you for the invitation to review this well-conducted systematic review.

The study under review is very interesting for the evidence-based clinical practice guidelines (CPGs)- and for the healthcare quality and safety- research communities.

Moreover, I would like to congratulate the authors for this work with some minor comments with the aim of improving the content and message of this distinguished study.

Abstract:

1. I recommend replacing the phrase ‘results in patients’ with ‘patient outcomes’ as it is more commonly used in the field of quality and safety in healthcare. Additionally, the authors have used it for the rest of the MS.

Introduction:

2. I would recommend adding recent definitions of both CPGs and healthcare quality (HCQ) as nowadays clinicians are getting increasingly interested in the fields of evidence-based medicine (EBM) and HCQ either from a research perspective or through engagement in their respective healthcare organizational accreditation. The HCQ definition and description of EB-CPGs are already in the PROSPERO protocol, please include them here as well.

Additional relevant studies to cite here:
(i) about the relation between EBM and HCQ:
(ii) an earlier similar key review:
Grimshaw J, Russell I: Effect of clinical guidelines on medical practice: a systematic review of

page 3, left column, para 4:
3. '..After an exhaustive.....only two systematic reviews (SRs)......, but *these SRs* did not....' Please add citations for these two references (SRs).

4. '..and international perspective together.' What do you mean by an 'international perspective'; of what; (i.e. of CPGs, of healthcare quality, or of cardiovascular healthcare?), please clarify or re-write.

page 3, right column, para 4:
5. Regarding the data extraction modified and translated from the EPOC checklist, was it validated and if not, why the authors felt they did not need to? Additionally, please provide the readers who would be interested in the replication of this research with this tool as an online supplementary here.

It was indeed mentioned with a link in the PROSPERO protocol (https://fs20.formsite.com/mtristan/form41/index.html, attached on Appendix 3) but the link did not work, giving an error!
Moreover, I checked the (Extended data) links in the OSF Home but could not retrieve it.

6. Please delete the duplicated sentence; 'We used a standardized digital ..........and analysis'.

page 3, right column, para 7:
7. The #87 studies that were planned to be included in another analysis were not mentioned here since the final included were 9 rather than 96 studies. Please elaborate on this in this location.

8. Figure 1. PRISMA flow chart:
#87 of studies to include in other *analyses*.

Tables 1 and 2.: the GRADE quality assessments and the explanations for the certainty of evidence were very well conducted and written.

9. Table 1: please, if feasible, replace the question in the GRADE SoF table; ‘.....the results for cardiopulmonary resuscitation?’ with ‘.....the outcomes for cardiopulmonary resuscitation?’

page 7, left column para 1:
10. Once more, please replace ‘patient results’ with ‘patient outcomes’.

Discussion:
11. '..However, it still seems that some of these CPGs are...'

page 7, right column, para 2:
12. As part of discussing ‘multiple strategies to implement the CPGs’, I would recommend adding insights and citing these relevant keynote articles that discuss multi-faceted CPGLI strategies and their importance:

(i) Grol R, Wensing M. Improving patient care: the implementation of change in health care (in Dutch: Implementatie: effective verbetering van de patiëntenzorg). Amsterdam: Reed Business
Education; 2013.


page 7, right column, para 4:

13. ‘...... as well as on designing implementation strategies adapt every recommendation...’

Do you mean "designing implementation strategies AND adapt every recommendation..." if so add a comma ',' or "designing implementation strategies (by) adapting every recommendation". Additionally, I suggest to add:

"...initiate a pilot implementation of specific recommendation(s) instead of considering implementation of the CPGs as a whole".

page 7, right column, para 5:

14. Implications for practice The initial objective of this review was to strengthen the development programs for CPGs (plural)

15. The results of this review must need to be interpreted with caution.

It reads better either (the results of this review must be interpreted with caution.) or (the results of this review need to be interpreted with caution.).

16. ‘It is necessary to emphasise that the standard CPG implementation used so...’

page 7, right column, para 6:

17. ‘For an adequate implementation of a CPG, it is necessary to take into account the possible costs, risks, and benefits

Finally, I would like to congratulate the authors once more on this work and invite all interested researchers to conduct similar research using this robust methodology to study the impact of EB-CPG implementation on all different healthcare specialties in addition to their effects on the interdisciplinary workflows and transitions of care between different specialties and services in healthcare.

References

4. Gagliardi AR, Brouwers MC, Bhattacharyya OK, Guideline Implementation Research and Application Network: A framework of the desirable features of guideline implementation tools (GItools): Delphi survey

**Are the rationale for, and objectives of, the Systematic Review clearly stated?**
Yes

**Are sufficient details of the methods and analysis provided to allow replication by others?**
Yes

**Is the statistical analysis and its interpretation appropriate?**
Yes

**Are the conclusions drawn adequately supported by the results presented in the review?**
Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Pediatrics, child healthcare, evidence-based healthcare, knowledge translation, quality and safety in healthcare, healthcare informatics, and implementation and improvement sciences and research in general

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

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