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# **Quality assessment of asthma clinical practice guidelines: a systematic appraisal**

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## ABSTRACT

**Background:** The quality and potential impact of available clinical guidelines for asthma management has not been systematically evaluated. We therefore evaluated the quality of clinical practice guidelines (CPGs) for asthma.

**Methods:** We performed a systematic search of scientific literature published between 2000 and 2010 to identify and select CPGs related to asthma management. We searched guideline databases, guideline developers' websites and MEDLINE. Four independent reviewers assessed the eligible guidelines using the AGREE II instrument. We calculated the overall agreement among reviewers with the Intraclass Correlation Coefficient (ICC).

**Results:** Eighteen CPGs published between the years 2000-2010 were selected from a total of 1,005 references. The overall agreement among reviewers was moderate (ICC: 0.78; 95%CI 0.62-0.90). The mean scores for each AGREE domain were: *Scope and Purpose* 44.1% (range: 10.0-79.0%); *stakeholder involvement* 33.8% (range: 4.0-66.0%); *rigor of development* 32.4% (range: 8.0-64.0%); *clarity and presentation* 52.1% (range: 17.0-85.0%); *applicability* 21.1% (range: 3-55%); and *editorial independence* 25% (range: 0-58%). None of the appraised guidelines had a score higher than 60% (recommended). Half of the appraised guidelines were recommended with modifications (9/18) or not recommended (9/18) for using in clinical practice. We observed improvement over time in guidelines' overall quality ( $p=0.01$ ; guidelines from 2001-2006 vs. 2007-2009).

**Conclusions:** The quality of guidelines for asthma care is low although it has improved over time. Greater efforts are needed to provide high quality guidelines that can be used as a reliable tool for clinical decision-making in this field.

## ABREVIATION LIST

AGREE: Appraisal for Research Guidelines Evaluation

BMJ: British Medical Journal

CAEP/CTS: Canadian Association of Emergency Physicians and the Canadian Thoracic Society.

CI: Confidence interval

CPG's: Clinical Practice Guidelines

GEMA: Spanish Guideline for Asthma Management

GINA: Global Initiative for Asthma

ICC: Intraclass Correlation Coefficient

ICSI: Institute for Clinical Systems Improvement

IPCRG: Institute for primary care respiratory group

IUATLD: International Union Against Tuberculosis and Lung Disease

JAMA: Journal of American Medical Association

MESH: Medical Subject Heading

NAEPP: National Asthma Education and Prevention Program

NGC: National Guidelines Clearinghouse

NHMRC: National Health and Medical Research Council

NICE: National Institute for Health and Clinical Excellence

SIGN: Scottish Intercollegial Guidelines Network

WHO: World Health Organization

## INTRODUCTION

Asthma is a major worldwide cause of morbidity and mortality with considerable differences among countries<sup>1</sup>. In response to this epidemiological scenario, several different entities have organized expert panels to develop clinical guidelines for the appropriate diagnosis and management of the disease. Despite numerous initiatives to optimize care of patients with asthma, the outcomes and level of disease control remain unsatisfactory.

Clinical Practice Guidelines (CPGs) are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances. CPGs aim to formulate explicit, specific recommendations that if adopted in clinical practice<sup>2</sup>, will produce better results for patients, decrease risks and promote cost-effective practices<sup>3-5</sup>. However, their potential to improve patient care and resource use depends not only on their quality but also on their dissemination and implementation strategies<sup>3,4,6</sup>.

There is often a mismatch between recommendations and handling of patients with asthma. An example of this is the under treatment and overuse of respiratory medication in these patients<sup>7</sup>. A recent retrospective analysis of initial therapy in patients with mild persistent asthma showed that only 24.9% were started, according to guidelines recommendations, on inhaled corticosteroids<sup>8</sup>. In this sense, one of the objectives of the guidelines is to reduce the gap between physician behavior and scientific evidence<sup>9</sup>.

Little is still known about the process and factors responsible for the lack of adherence of physicians to guidelines. In order to develop strategies to enhance these issues, the underlying barriers must be identified. Grimshaw and Russell indicated that explicit guidelines improve clinical practice, when they are introduced in the context of rigorous evaluations<sup>10</sup>.

Therefore, quality improvement and optimum dissemination and implementation of asthma guidelines, appear to be important objectives.

To our knowledge, the quality of asthma guidelines has not yet been systematically evaluated<sup>11-13</sup>. We therefore conducted this study to assess the quality of available asthma guidelines.

## **METHODS**

### **Identification of Guidelines**

An exhaustive search (from January 2000 to November 2010) was performed (Supplemental Table-1). We initially searched guideline databases and clearinghouses using the term 'asthma'. The process was completed by searching MEDLINE (through PubMed) using a combination of text free terms and their corresponding MeSH terms and limiting the results with a filter to retrieve guidelines as follow: (Practice Guideline OR Guidelines OR Practice Guideline OR Guideline OR Consensus Development Conference OR Practice Guidelines as TopicMeSH) AND ("Asthma"Mesh OR asthma\*ti). The search was limited to documents published in four languages: English, Spanish, French and Portuguese. Two reviewers (AA and ES) independently evaluated all search results to determine the inclusion or exclusion of references. Disagreements were resolved by discussion.

### **Selection of Guidelines**

CPGs aimed to provide diagnostic and therapeutic recommendations on care for children AND/OR adolescents AND adults were included. The documents were considered as a guideline if they met the following criteria: to provide practical clinical recommendations for children, adolescents or adults, collect all related documents and supporting materials. Documents without recommendations, secondary publications and guidelines about asthma subtypes or phenotypes were excluded (i.e. Allergic Rhinitis and Asthma or Difficult to Treat Asthma).

## Evaluation of Guidelines

The *Appraisal of Guidelines for Research and Evaluation* (AGREE II) instrument was used<sup>14,15</sup>. The AGREE II instrument provides criteria for assessing the quality of the methods used for guideline development and the quality of their reports, providing an assessment of predictive validity of the guideline<sup>16,17</sup>.

The AGREE II consists of 23 key items organized into 6 domains, followed by 2 global rating items (“Overall Assessment”). Each domain captures a unique dimension of guideline quality (Supplemental Table-2). The score for each domain is calculated as a percentage of the maximum possible score for that domain and its standardized range (0% to 100%)<sup>14</sup>.

Each guideline included was evaluated by four independent reviewers (AA, ES, GR, and VP) with experience in developing and appraising guidelines. The final overall recommendation about each one of the included guidelines was based on an overall judgment taking into account the scores of all items<sup>14</sup>. We also evaluated whether guidelines included a search strategy in at least one database and classified the quality of evidence and graded the strength of recommendations. Those who met both requirements were considered evidence based.

## Statistical Analysis

A descriptive statistical analysis through the calculation of the total standardized score value by each reviewer, and the value per domain was performed. Agreement between the four reviewers was determined by the intra-class correlation coefficient (CCI). Descriptive values were provided. A score of 60% average was chosen (standardization of total points as a percentage over maximum points) to establish the proportion of guidelines which scored points above this level in each domain. The intra-class correlation coefficient (ICC) with a 95% confidence interval (CI) as an overall indicator of agreement among the reviewers for each of the 23 items of the AGREE II instrument was calculated. According to the scale proposed by Landis and Koch, the degree of agreement between 0.01 and 0.20 is slight, from 0.21 to 0.40 is fair, from 0.41 to 0.60 is moderate, from 0.61 to 0.80 is substantial and from 0.81 to 1.00 is

very good<sup>18</sup>. Due to a temporal non-homogeneous distribution of 18 included CPGs, we compared CPGs before and after a date (Not updated versions versus previous versions). To test the hypothesis of whether guideline quality improved over time, each guideline was evaluated, starting from 2001, exploring change over time and using a student t-test. All tests were two-sided and the significance level used was 5% (alpha=0.05). Software used for the analysis was SPSS (v-15.0).

## RESULTS

### Literature Search

A total of 1005 references were retrieved. Among them 908 articles were excluded due to inappropriate references (not-Asthma CPGs) and 97 selected. Later on 79 references were excluded for including only children or adults (n=18), assess asthma phenotypes (n=27) or duplicated data (n=34). Two guidelines that included adolescents and adults but exclude children were assessed<sup>19,20</sup>. Finally, 18 documents underwent for full evaluation with AGREE II<sup>14</sup> (Figure-1).

Among the 18 selected CPGs (Table-1), 3 were international (more than two countries)<sup>21-23</sup>, 3 from United States<sup>24,25</sup>, 2 from United Kingdom<sup>26,27</sup>, and Spain<sup>28,29</sup>, and one from each of the following countries: Australia-New Zealand<sup>30</sup>, Brazil<sup>31</sup>, Canada<sup>32</sup>, Finland<sup>33</sup>, France<sup>20</sup>, India<sup>34</sup>, Singapore<sup>35</sup>, South Africa<sup>19</sup>. CPGs were published between 2000-2010. The overall reviewer's agreement for the evaluation with the AGREE II instrument was substantial (ICC: 0.78; 95%CI 0.62-0.90).

### Scope and Purpose

Table-2 shows the AGREE II domain-standardized scores for asthma CPGs and overall recommendation. The mean score for the scope and purpose domain was 44.1% (range, 10-79%), indicating that, on average, 44% of the criteria for scope and purpose were met. Most guidelines (16/18) scored below 60% for this domain<sup>28,37</sup>. Only two guidelines clearly defined

their scope and global objectives, and specifically defined their related clinical field and target populations<sup>28,37</sup>.

### **Stakeholder Involvement**

Overall, the mean score for this domain was 33.8% (range, 4-66%). There was only one guideline scoring above 60% (Table-2)<sup>29</sup>. The patients or their representatives were involved in the development of two guidelines<sup>20, 29</sup>.

### **Rigor of Development**

The mean score for this domain was 32.0% (range, 8-64%). Only one guideline clearly described the criteria for selecting evidences and recommendations (score above 60%) (Table-2)<sup>26</sup>.

### **Clarity of Presentation**

The mean score for this domain was 52.1% (range, 17-85%). In this domain, 6/18 guidelines scored above 60% and three of them received the highest value found in all domains: 85%, 83% and 81%, respectively (Table-2)<sup>24,26,29</sup>.

### **Applicability**

The lowest score was observed in this domain (Table-2), with a mean value of 21.1% (range, 3-55%). In general, there was little information regarding potential organizational barriers, cost implications and tools for application.

### **Editorial Independence**

The mean score in this domain was 57% (range, 27.7-100%). Only 4/18 (22.2%) of the guidelines included information about the potential conflicts of interest of guideline institutions

or members (Table-2)<sup>24,26,28,29</sup>. One out of the three international guidelines was supported by pharmaceutical industry.

## Overall Evaluation

After weighting the scores of all guidelines, reviewers classified them as follows: none of the guidelines as “recommended”, nine (50%) as “recommended with modifications”<sup>20,21,24,26,28-30,32,35,37</sup> and nine (50%) as “not recommended”<sup>19,22,23,25,27,31-34</sup>. Finally, our study showed an improvement of the overall score over time in the development of CPG (guidelines from 2001-2006 vs. 2007-2009;  $p < 0.01$  (Table 3).

## DISCUSSION

Clinical practice guidelines have been developed to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances. Although the principles for developing CPGs are well established, the increase in production of CPGs has been associated by an increasing concern about the variations in guideline recommendations and quality<sup>40</sup>. Over the past decade, a significant number of guidelines have been published on asthma; however, no previous study of asthma CPGs quality assessment has been published.

There are two important findings in the present review. The average score across domains of asthma guidelines is low; however, their quality has improved over time. *Clarity of Presentation*, and *Editorial Independence* domains showed the highest average scores and *Applicability* the lowest. The scores for *Stakeholder Involvement* and *Rigor of Development* domains remained below 50%.

The *Applicability domain* addresses the potential organizational, behavior and cost implications of guidelines implementation. In the present study this domain score was disappointingly low. A previous review reported similar results for this domain in other

conditions, arguing that it could happen because the guideline panels considered the development and implementation of the guidelines as separate activities<sup>40</sup>. Accordingly, panels do not pay proper attention to the potential barriers of guidelines implementation.

The *Stakeholder Involvement* domain addresses the degree to which the guideline represents the views of its intended users. The implementation of CPGs requires both the contribution and experience of the multidisciplinary medical team and the patients' point of view. The effect of sharing patient-clinician responsibilities regarding treatment decisions, treatment adherence, and asthma-related clinical outcomes has been recently evaluated. Compared with standard care, involving patients in decisions regarding their management have shown promising results<sup>41</sup>. With a few notable exceptions, in diabetes<sup>42</sup> and cardiovascular risk assessment<sup>43</sup>, current versions of evidence-based guidelines do not address patient preferences or include tools for shared decision making<sup>44</sup>. Asthma CPGs are not the exception with a score below 50%.

*Rigor of Development* domain is closely linked to the confidence that can be placed in a guideline. This domain evaluates the process used to locate and synthesize the evidence and to formulate and update the recommendations. The low score in this domain (32%) could be due to the lack of methodological expertise of guideline teams or the lack of resources of these institutions<sup>40</sup>. CPGs with the highest score in this domain were those that used a formal system to rate the quality of the evidence and graded the strength of recommendations<sup>26, 24</sup>. The most up to date system, GRADE, was used in only one of the included guidelines<sup>26</sup>.

The *Scope and Purpose domain* addresses the overall aim of the guideline, the clinical question and the target population. Regarding this domain, only two CPGs obtained scores higher than 60%<sup>28,37</sup>. This was related with lack of details in description of overall objective(s), health question and target population definition. This finding is a matter of concern given that this issue should be easily tackled and well developed in the initial stages of any guideline, as it will have an enormous influence in the rest of the work. A problem of developing guidelines

for asthma management lies partly on the ambiguity and inaccuracy in the asthma definition in general. This ambiguity may be related to the lack of consensus among specialists. On one side there are authors that consider asthma a pathophysiological phenomenon and not a disease, whereas others consider it a syndrome. Hence, there is no an established gold standard for diagnosing asthma. These important issues were addressed only by one of the included guidelines<sup>26</sup>.

*Editorial Independence* and *Clarity of Presentation* domains address potential conflicts of interest, language and format, respectively. They were the domains with the highest scores. Six<sup>24,26-28,30,35</sup> of 18 evaluated CPGs (33%) were developed by Public Agencies/Government, 9/18 (50%)<sup>19,21,22,25, 29,33,36-38</sup> by Private Entities or Medical Societies and 3/18 by both<sup>20,31,34</sup>. Five guidelines (28%) reported funding from the pharmaceutical Industry<sup>19,21,24,29,30</sup>. Sniderman et al. suggest that individuals who receive benefits from companies whose products are discussed should not be part of the decision making<sup>45</sup>. The results of the present study suggest that funding source of asthma guidelines does not influence quality. There is a variety of funding sources among the recommended guidelines: three received support from Pharmaceutical Industry<sup>21,24,29</sup>, three from public funding<sup>26,28,35</sup> and three were developed by Medical Societies<sup>20,30,37</sup>. Interestingly, the non-recommended guidelines were not supported by Pharmaceutical Industry.

In the present analysis we found that asthma CPGs published between 2007 and 2009 were of higher quality and more likely to be recommended than those published from 2001-2006. We chose these time periods post-hoc taking into account the temporal distribution of the included guidelines and without looking at the AGREE-II results. The low scores in several of the domains are concerning with the poor performance in “Rigor of Development”, which was the most problematic. This finding reflects a lack of methodological expertise which is often related with a lack of adequate resources. The use of the GRADE in only one guideline could be related with the latter finding, since this requires advanced knowledge to be implemented.

Most of our findings are consistent with those reported by a previous systematic review<sup>40</sup>, with the quality improving over time, but scores remain moderate to low. There were some differences in our work in relation with this earlier systematic review. For example, as opposed to this systematic review, the domain Editorial Independence scored was the highest in our evaluation and showed an improvement over time.

There are some limitations in the present review that should be discussed. The observational study design does not allow us to establish causal relationships between the guidelines quality and other outcomes. Additionally, our review included CPGs in four languages, and excluded consensus of asthma subtypes or guidelines directed only to the pediatric population. In the case of the language criteria it is likely that those omitted, from less developed countries, were of lower quality than the ones included. To this extent our evaluation would be overestimating the quality of asthma guidelines. In the case of pediatric guidelines, to the extent that those guidelines are of better quality than our sample we will be underestimating the quality of asthma guidelines. We think this is unlikely. Our review has some strengths. We performed an exhaustive search and four reviewers performed evaluation with good concordance. Finally, our team included clinical experts and methodologists with wide experience in CPGs.

In conclusion, currently available asthma CPGs present important limitations. However, these guidelines have improved over time and most could continue improving, particularly in the areas of development, patient participation (integrating their “views and preferences”) and implementation. Greater efforts are needed to provide high quality guidelines that can be used as a reliable tool for clinical decision-making.

**Author's contributions:**

AA and PA designed the study. AA, ES, VP and GR acquired the data. IG led the statistical analysis. AA and PA analyzed, interpreted the data and drafted the manuscript. All authors made substantial contributions for important intellectual and approved the final manuscript. AA coordinated the study.

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### **Legend of the Figures**

Figure 1. Study flow diagram for asthma guidelines assessment.

### **Definitions of abbreviations:**

CPG= Clinical Practice Guidelines; AGREE II= Appraisal of Guidelines Research and Evaluation

**Table 1.** Included clinical practice guidelines on asthma management

| <b>Title</b>                                                                                                                                                                 | <b>Country</b>       | <b>Organization (Type)</b>                                                                                                 | <b>Year of Publication</b> | <b>Population</b>      |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|----------------------------------------------------------------------------------------------------------------------------|----------------------------|------------------------|
| Global Initiative for Asthma: Global strategy for asthma management and prevention <sup>21</sup>                                                                             | International        | Global initiative for asthma (GINA) <sup>+</sup>                                                                           | 2009                       | Children and adults    |
| Guidelines for the diagnosis and management of asthma <sup>24</sup>                                                                                                          | United States        | National Asthma Education and Prevention Program (NAEPP) <sup>+</sup>                                                      | 2007                       | Children and adults    |
| Spanish Guideline for asthma management <sup>29</sup>                                                                                                                        | Spain                | Sociedad Española de Neumología y Cirugía Torácica (SEPAR) y otras 8 sociedades científicas médicas españolas <sup>±</sup> | 2009                       | Children and adults    |
| British Guideline on the management of asthma <sup>26</sup>                                                                                                                  | Scotland, UK         | Scottish Intercollegial Guidelines Network (SIGN) <sup>+</sup>                                                             | 2008                       | Children and adults    |
| Canadian asthma consensus guidelines <sup>36</sup>                                                                                                                           | Canada               | Canadian Asthma Consensus Report <sup>±</sup>                                                                              | 2003                       | Children and adults    |
| Guía de práctica clínica sobre asma <sup>28</sup>                                                                                                                            | Spain                | Servicio Vasco de Salud <sup>+</sup>                                                                                       | 2007                       | Children and adults    |
| Asthma management handbook <sup>30</sup>                                                                                                                                     | Australia-New Zeland | National Asthma Council Australia <sup>+</sup>                                                                             | 2006                       | Children and adults    |
| IV Brazilian Guideline for asthma management <sup>31</sup>                                                                                                                   | Brazil               | Brazilian Health <sup>‡</sup>                                                                                              | 2006                       | Children and adults    |
| Diagnosis and management of asthma <sup>37</sup>                                                                                                                             | United States        | Institute for Clinical Systems Improvement <sup>+</sup> (ICSI)                                                             | 2008                       | Children and adults    |
| General principles for the diagnosis and management of asthma <sup>25</sup>                                                                                                  | United States        | Michigan Quality Improvement Consortium <sup>±</sup>                                                                       | 2008                       | Children and adults    |
| Management of asthma <sup>35</sup>                                                                                                                                           | Singapur             | Singapur Ministry of Health <sup>+</sup>                                                                                   | 2008                       | Children and adults    |
| Management of asthma <sup>22</sup>                                                                                                                                           | International        | International primary care respiratory group guidelines <sup>±</sup>                                                       | 2007                       | Children and adults    |
| Long-Term Management of asthma <sup>33</sup>                                                                                                                                 | Finland              | Finnish Medical Society <sup>±</sup>                                                                                       | 2006                       | Children and adults    |
| Management of asthma: a guide to the essentials of good clinical practice <sup>38</sup>                                                                                      | International        | International Union Against Tuberculosis and Lung Diseases <sup>±</sup> (IUATLD)                                           | 2006                       | Children and adults    |
| Guidelines for the chronic asthma in adolescents and adults <sup>19</sup>                                                                                                    | South African        | South African Thoracic Society <sup>±</sup>                                                                                | 2007                       | Adolescents and adults |
| Evidence-based guideline on primary care management of asthma <sup>27</sup>                                                                                                  | UK                   | North of England Asthma Guideline Development Group <sup>+</sup>                                                           | 2001                       | Children and adults    |
| Recommandations pour le suivi médical des patients asthmatiques adultes et adolescents (Recommendations for the management of asthmatic adolescents and adult) <sup>20</sup> | France               | French language Society of Pneumology <sup>‡</sup>                                                                         | 2005                       | Adolescents and adults |
| Guidelines for Management of Asthma at Primary and Secondary Levels of Health Care In India <sup>34</sup>                                                                    | India                | WHO-Government of India Collaborative Programme (2004-2005) <sup>‡</sup>                                                   | 2005                       | Children and adults    |

Legend: <sup>±</sup> Private Medical Entities or Medical Societies; <sup>+</sup> Public Agencies/Government; <sup>‡</sup> Both (Private Medical Entities or Medical Societies and Public agencies/Government)

**Table 2.** AGREE II domain-standardized scores for CPGs on asthma and overall guideline assessment

| Guideline                                                                               | Scope and Purpose <sup>1</sup><br>(%) | Stakeholder Involvement <sup>2</sup><br>(%) | Rigor of Development <sup>3</sup><br>(%) | Clarity of Presentation <sup>4</sup><br>(%) | Applicability <sup>5</sup><br>(%) | Editorial Independence <sup>6</sup><br>(%) | Overall Guideline Assessment   |
|-----------------------------------------------------------------------------------------|---------------------------------------|---------------------------------------------|------------------------------------------|---------------------------------------------|-----------------------------------|--------------------------------------------|--------------------------------|
| Global Initiative for Asthma. 2009 <sup>21</sup>                                        | 51                                    | 44                                          | 46                                       | 78                                          | 55                                | 29                                         | Recommended with modifications |
| Guidelines for the diagnosis and management of asthma (NAEPP) <sup>24</sup>             | 57                                    | 52                                          | 58                                       | 83                                          | 35                                | 58                                         | Recommended with modifications |
| Spanish Guideline for asthma management (GEMA) <sup>29</sup>                            | 57                                    | 66                                          | 55                                       | 81                                          | 20                                | 38                                         | Recommended with modifications |
| British Guideline on the management of asthma <sup>26</sup>                             | 49                                    | 46                                          | 64                                       | 85                                          | 53                                | 50                                         | Recommended with modifications |
| Canadian Asthma Consensus Guidelines <sup>32</sup>                                      | 31                                    | 19                                          | 20                                       | 44                                          | 9                                 | 13                                         | Not Recommended                |
| Guía de practica clínica sobre asma (Vasca) <sup>39</sup>                               | 79                                    | 53                                          | 51                                       | 78                                          | 30                                | 58                                         | Recommended with modifications |
| Asthma Management Handbook <sup>30</sup>                                                | 44                                    | 36                                          | 23                                       | 68                                          | 19                                | 17                                         | Recommended with modifications |
| IV Brazilian Guideline for asthma management <sup>31</sup>                              | 11                                    | 4                                           | 8                                        | 17                                          | 10                                | 0                                          | Not recommended                |
| Diagnosis and management of asthma <sup>35</sup>                                        | 61                                    | 48                                          | 42                                       | 44                                          | 27                                | 50                                         | Recommended with modifications |
| General principles for the diagnosis and management of asthma <sup>23</sup>             | 57                                    | 25                                          | 20                                       | 46                                          | 3                                 | 17                                         | Not recommended                |
| Management of asthma (Singapore) <sup>33</sup>                                          | 58                                    | 28                                          | 28                                       | 49                                          | 22                                | 25                                         | Recommended with modifications |
| Management of asthma. IPCRG <sup>20</sup>                                               | 29                                    | 18                                          | 15                                       | 32                                          | 11                                | 27                                         | Not recommended                |
| Long-Term Management of asthma <sup>21</sup>                                            | 42                                    | 29                                          | 30                                       | 44                                          | 7                                 | 15                                         | Not recommended                |
| Management of asthma: a guide to the essentials of good clinical practice <sup>21</sup> | 60                                    | 18                                          | 10                                       | 26                                          | 34                                | 21                                         | Not recommended                |
| Guidelines for the chronic asthma in adolescents and adults <sup>17</sup>               | 17                                    | 17                                          | 15                                       | 47                                          | 8                                 | 8                                          | Not recommended                |
| Evidence-based guideline on primary care management of asthma <sup>25</sup>             | 10                                    | 25                                          | 35                                       | 49                                          | 7                                 | 10                                         | Not recommended                |
| French Language Society of Pneumology <sup>18</sup>                                     | 57                                    | 55                                          | 51                                       | 40                                          | 16                                | 8                                          | Recommended with modifications |
| India Guidelines <sup>32</sup>                                                          | 25                                    | 26                                          | 13                                       | 26                                          | 11                                | 8                                          | Not recommended                |

<sup>1</sup>Degree to which the overall objectives of the guideline and the clinical questions covered.

<sup>2</sup>Degree to which the guideline represents the views of its intended consumers.

<sup>3</sup>To what extent systematic methods for formulating the recommendations were taken into account.

<sup>4</sup>Clarity of the guidelines and whether the recommendations are specific and unambiguous.

<sup>5</sup>Evaluation of guideline implementation issues.

<sup>6</sup>Evaluation of the presence of conflict of interest.

**Table 3.** Quality assessment of asthma guidelines across time(2001-2006 vs. 2007-2009).

| <b>Domain</b>           | <b>Guidelines from 2001-2006<br/>(mean ± SD)</b> | <b>Guidelines from 2007-2009<br/>(mean ± SD)</b> | <b>p-value</b> |
|-------------------------|--------------------------------------------------|--------------------------------------------------|----------------|
| Scope and Purpose       | 0.30 ± 0.17                                      | 0.53 ± 0.15                                      | 0.01           |
| Stakeholder             | 0.26 ± 0.16                                      | 0.39 ± 0.16                                      | 0.13           |
| Rigor of development    | 0.24 ± 0.15                                      | 0.38 ± 0.18                                      | 0.09           |
| Clarity of presentation | 0.39 ± 0.17                                      | 0.60 ± 0.21                                      | 0.35           |
| Applicability           | 0.12 ± 0.04                                      | 0.27 ± 0.17                                      | 0.02           |
| Editorial independence  | 0.12 ± 0.08                                      | 0.35 ± 0.18                                      | 0.04           |
| <b>Overall</b>          | <b>0.24 ± 0.11</b>                               | <b>0.41 ± 0.15</b>                               | <b>0.01</b>    |

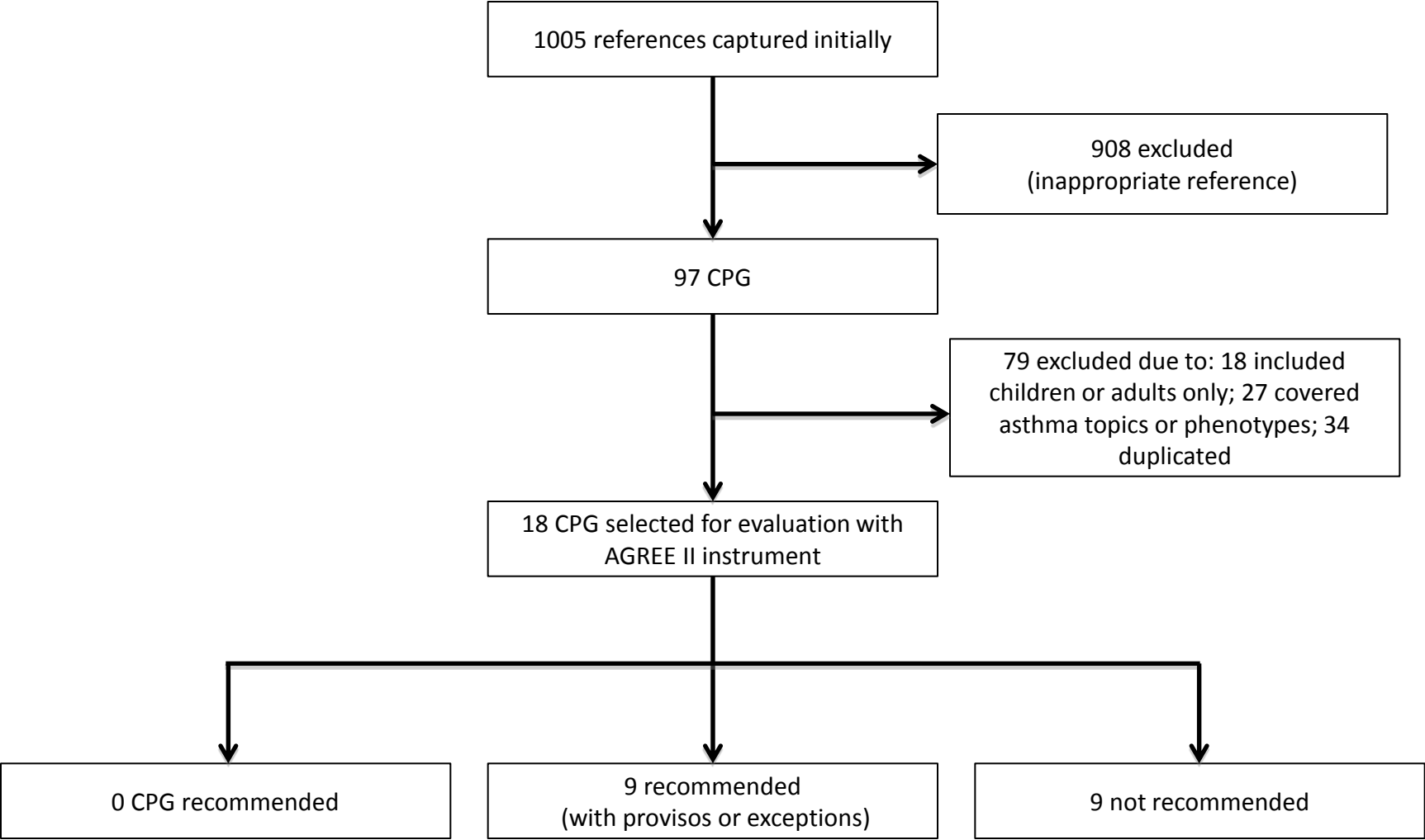


Fig 1. Identification and evaluation of clinical practice guidelines for the diagnosis and treatment of asthma. CPG= Clinical Practice Guidelines; AGREE II= Appraisal of Guidelines Research and Evaluation.

**Supplemental Table 1.** Sites searched for identification of clinical practice guidelines

| <b>Guidelines developers</b>                                                              | <b>Web sites</b>                                                                                                              | <b>Number of References (Searching)</b> |
|-------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|
| NICE                                                                                      | <a href="http://www.nice.org.uk/">http://www.nice.org.uk/</a>                                                                 | 108                                     |
| SIGN (Scottish Intercollegiate Guidelines Network)                                        | <a href="http://www.sign.ac.uk/">http://www.sign.ac.uk/</a>                                                                   | 138                                     |
| New Zealand Guidelines Group                                                              | <a href="http://www.nzgg.org.nz/guidelines">http://www.nzgg.org.nz/guidelines</a>                                             | 5                                       |
| NHMRC (National Health and Medical Research Council)                                      | <a href="http://www.nhmrc.gov.au/">http://www.nhmrc.gov.au/</a>                                                               | 82                                      |
| ICSI                                                                                      | <a href="http://www.icsi.org">http://www.icsi.org</a>                                                                         | 5                                       |
| American Thoracic Society                                                                 | <a href="http://www.thoracic.org">http://www.thoracic.org</a>                                                                 | 5                                       |
| European Respiratory Society                                                              | <a href="http://www.ers-education.org/pages/default.aspx?id=2005">http://www.ers-education.org/pages/default.aspx?id=2005</a> | 1                                       |
| British Thoracic Society                                                                  | <a href="http://www.brit-thoracic.org.uk/library-guidelines.aspx">http://www.brit-thoracic.org.uk/library-guidelines.aspx</a> | 1                                       |
| Biblioteca de Guías de Práctica Clínica del Sistema Nacional de Salud. Gobierno de España | <a href="http://portal.guiasalud.es/web/guest/home">http://portal.guiasalud.es/web/guest/home</a>                             | 23                                      |
| <b>Compiler Entities, Registries or Clearinghouses:</b>                                   |                                                                                                                               |                                         |
| NGC (National Guidelines Clearinghouse)                                                   | <a href="http://www.guidelines.gov/">http://www.guidelines.gov/</a>                                                           | 37                                      |
| <b>Generic databases or search engines:</b>                                               |                                                                                                                               |                                         |
| MEDLINE (PubMed)                                                                          | <a href="http://www.ncbi.nlm.nih.gov/pubmed/">http://www.ncbi.nlm.nih.gov/pubmed/</a>                                         | 171                                     |
| TRIP database                                                                             | Guidelines in <a href="http://www.tripdatabase.com">http://www.tripdatabase.com</a>                                           | 412                                     |
|                                                                                           | US                                                                                                                            | 56                                      |
|                                                                                           | UK                                                                                                                            | 218                                     |
|                                                                                           | OTHERS                                                                                                                        | 25                                      |
|                                                                                           | CANADA                                                                                                                        | 48                                      |
|                                                                                           | AUSTRALIA AND NZ                                                                                                              | 65                                      |
| Excelencia Clínica                                                                        | <a href="http://www.excelenciaclinica.net">www.excelenciaclinica.net</a>                                                      | 17                                      |
|                                                                                           | <b>TOTAL</b>                                                                                                                  | <b>1005</b>                             |

**Supplemental Table 2.** List of items of the AGREE II instrument

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                            |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------|
| To continuation the areas that instrument AGREE II values and the criteria are exposed that one of them includes each. Each criterion is equivalent to a question that is done to him to the CPG and, on the base of the answer obtained after examining the content of the guide, will receive a score. The score obtained by each domain (sum of the obtained one by each criterion) is considered of independent form for the global valuation of the guide. |                                                                                                            |
| — <b>Domain 1</b> (items 1-3): Scope and purpose                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                            |
| Is concerned with the overall aim of the guideline, the specific clinical questions and the target patient population.                                                                                                                                                                                                                                                                                                                                          |                                                                                                            |
| Item 1:                                                                                                                                                                                                                                                                                                                                                                                                                                                         | The overall objective(s) of the guideline is (are) specifically described                                  |
| Item 2:                                                                                                                                                                                                                                                                                                                                                                                                                                                         | The health question(s) covered by the guideline is (are) specifically described.                           |
| Item 3:                                                                                                                                                                                                                                                                                                                                                                                                                                                         | The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described. |
| — <b>Domain 2</b> (items 4-6): Stakeholder involvement                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                            |
| Focuses on the extent to which the guideline represents the views of its intended users.                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                            |
| Item4:                                                                                                                                                                                                                                                                                                                                                                                                                                                          | The guideline development group includes individuals from all relevant professional groups.                |
| Item 5:                                                                                                                                                                                                                                                                                                                                                                                                                                                         | The views and preferences of the target population (patients, public, etc.) have been sought.              |
| Item 6:                                                                                                                                                                                                                                                                                                                                                                                                                                                         | The target users of the guideline are clearly defined.                                                     |
| — <b>Domain 3</b> (items 7-14): Rigor of development                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                            |
| Relates to the process used to gather and synthesis the evidence, the methods to formulate the recommendations and to update them.                                                                                                                                                                                                                                                                                                                              |                                                                                                            |
| Item 7:                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Systematic methods were used to search for evidence.                                                       |
| Item 8:                                                                                                                                                                                                                                                                                                                                                                                                                                                         | The criteria for selecting the evidence are clearly described.                                             |
| Item 9:                                                                                                                                                                                                                                                                                                                                                                                                                                                         | The strengths and limitations of the body of evidence are clearly described.                               |
| Item 10:                                                                                                                                                                                                                                                                                                                                                                                                                                                        | The methods for formulating the recommendations are clearly described.                                     |
| Item 11:                                                                                                                                                                                                                                                                                                                                                                                                                                                        | The health benefits, side effects, and risks have been considered in formulating the recommendations.      |
| Item 12:                                                                                                                                                                                                                                                                                                                                                                                                                                                        | There is an explicit link between the recommendations and the supporting evidence.                         |
| Item 13:                                                                                                                                                                                                                                                                                                                                                                                                                                                        | The guideline has been externally reviewed by experts prior to its publication.                            |
| Item 14:                                                                                                                                                                                                                                                                                                                                                                                                                                                        | A procedure for updating the guideline is provided.                                                        |
| — <b>Domain 4</b> (items 15-17): Clarity and presentation                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                            |
| Deals with the language and format of the guideline.                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                            |
| Item 15:                                                                                                                                                                                                                                                                                                                                                                                                                                                        | The recommendations are specific and unambiguous.                                                          |
| Item16:                                                                                                                                                                                                                                                                                                                                                                                                                                                         | The different options for management of the condition or health issue are clearly presented.               |
| Item 17:                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Key recommendations are easily identifiable.                                                               |
| — <b>Domain 5</b> (items 18-21): Applicability                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                            |
| Pertains to the likely organizational, behavioral and cost implications of applying the guideline.                                                                                                                                                                                                                                                                                                                                                              |                                                                                                            |
| Item18:                                                                                                                                                                                                                                                                                                                                                                                                                                                         | The guideline describes facilitators and barriers to its application.                                      |
| Item 19:                                                                                                                                                                                                                                                                                                                                                                                                                                                        | The guideline provides advice and/or tools on how the recommendations can be put into practice.            |
| Item 20:                                                                                                                                                                                                                                                                                                                                                                                                                                                        | The potential resource implications of applying the recommendations have been considered.                  |
| Item 21:                                                                                                                                                                                                                                                                                                                                                                                                                                                        | The guideline presents monitoring and/or auditing criteria.                                                |
| — <b>Domain 6</b> (items 22-23): Editorial independence                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                            |
| Is concerned with the independence of the recommendations and acknowledgement of possible conflict of interest from the guideline development group.                                                                                                                                                                                                                                                                                                            |                                                                                                            |
| Item 22:                                                                                                                                                                                                                                                                                                                                                                                                                                                        | The views of the funding body have not influenced the content of the guideline.                            |
| Item 23:                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Competing interests of guideline development group members have been recorded and addressed.               |

**Supplemental Table 3.** Shortcomings and actions to improve guideline quality

(Appraisal of Guidelines, Research and Evaluation domains)

| <b>Appraisal of Guidelines, Research and Evaluation domain</b> | <b>Deficiencies</b>                                                                                                                                                                                                                                    | <b>Actions</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|----------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b><i>Scope and purpose</i></b>                                | <ol style="list-style-type: none"> <li>1 Lack of information on purpose and target population.</li> <li>2 Lack of information about the scope or too broad scopes.</li> </ol>                                                                          | <ol style="list-style-type: none"> <li>1 Provide specific information and clear summaries, which is less time-consuming than improving the process or methodology.</li> <li>2 Consider limiting number the scope and/or the number of questions in each guideline. Focus on questions that are important to patients and clinicians. Panels for guideline development should priorities their efforts and identify which questions should be answered first.</li> </ol>      |
| <b><i>Stakeholder involvement</i></b>                          | <ol style="list-style-type: none"> <li>1 Lack of multidisciplinary teams.</li> <li>2 Low participation of patients or no consideration of patients' views.</li> </ol>                                                                                  | <ol style="list-style-type: none"> <li>1 Involve several related disciplines</li> <li>2 Contact patient organization for feed-back at early stages and along the whole process, of guideline developing. Include patients in guideline panels. Consider searching for qualitative and other types of research about patient's values and preferences.</li> </ol>                                                                                                             |
| <b><i>Rigor of development</i></b>                             | <ol style="list-style-type: none"> <li>1 Lack of methodological expertise.</li> <li>2 Lack of information about methods.</li> </ol>                                                                                                                    | <ol style="list-style-type: none"> <li>1 Involve librarians and methodologists in the guideline development process.</li> <li>2 Include more information about the methods in the guidelines. Use addenda for including search strategies, databases consulted, literature selection process, system used to evaluate the quality of the evidence and grading of recommendations, and evidence tables. In electronic documents, hyperlinks can be helpful.</li> </ol>        |
| <b><i>Clarity and presentation</i></b>                         | <ol style="list-style-type: none"> <li>1 Vague recommendations or statements that do not imply a specific action.</li> <li>2 Thick, textbook-like documents with recommendations hidden in the text. Lack of summaries for use in practice.</li> </ol> | <ol style="list-style-type: none"> <li>1 Refrain from including material in guidelines that is not directly relevant to the needs of the guideline users.</li> <li>2 Avoid classic textbook-like guidelines. Minimize background sections. Provide specific information and clear summaries.</li> </ol>                                                                                                                                                                      |
| <b><i>Applicability</i></b>                                    | <ol style="list-style-type: none"> <li>1 Lack of information about the dissemination and implementation strategies.</li> <li>2 Absence of criteria for monitoring and/or audit.</li> </ol>                                                             | <ol style="list-style-type: none"> <li>1 Need to integrate these issues in the development phase. Relevant professionals with the relevant expertise should be incorporated in the development group in early stages.</li> <li>2 Guideline groups should explicitly acknowledge the need to consider barriers, costs, indicators or criteria for monitoring locally when implementing or adapting a guideline.</li> </ol>                                                    |
| <b><i>Editorial independence</i></b>                           | Lack of or insufficient information on the presence of conflicts of interest in guideline developers (economic and/or intellectual)                                                                                                                    | <ol style="list-style-type: none"> <li>1 Public and explicit declaration of all type of conflicts of interest of guideline panels is a must.</li> <li>2 Institutions should be transparent about their conflicts of interest policies and funding sources. Guideline members should reveal any financial ties with industry and any potential intellectual conflicts. The latter includes authorship of studies or grant funding in a related area of healthcare.</li> </ol> |