Original Research

# Impact of the implementation of an evidence-based guideline on diagnostic testing, management, and clinical outcomes for infants with bronchiolitis

Ricardo Henao-Villada, Monica P. Sossa-Briceño and Carlos E. Rodríguez-Martínez

## Abstract

**Background:** Although bronchiolitis poses a significant health problem in low- and middle-income countries (LMICs), to the best of our knowledge, to date it has not been determined whether evidence-based bronchiolitis clinical practice guidelines (CPGs) complemented by standardized educational strategies reduce the use of unnecessary diagnostic tests and medications and improve clinically important outcomes in LMICs.

**Methods:** In an uncontrolled before and after study, we assessed the impact of the implementation of an evidence-based bronchiolitis CPG on physician behavior and the care of infants with bronchiolitis by comparing pre-guideline (March to August 2014) and post-guideline (March to August 2015) use of diagnostic tests and medications through an electronic medical record review in a children's hospital in Bogota, Colombia. We also sought to assess the impact of the implementation of the CPG on clinically important outcomes such as lengths of stay, hospital admissions, intensive care admissions, and hospital readmissions.

**Results:** Data from 662 cases of bronchiolitis (pre-guideline period) were compared with the data from 703 cases (post-guideline period). On comparing the pre- and post-guideline periods, it was seen that there was a significant increase in the proportion of patients with an appropriate diagnosis and treatment of bronchiolitis (36.4% *versus* 44.5%, $p = 0.003$), and there were statistically significant decreases in the use of a hemogram (33.2% *versus* 26.6%, p=0.010), procalcitonin (3.9% *versus* 1.6%, *p*=0.018), nebulized beta-2 agonists (45.6% *versus* 3.4%, $p < 0.001$), nebulized anticholinergics (3.3% versus 1.4%, p= 0.029), and nebulized epinephrine (16.2% *versus* 7.8%, $p < 0.001$). Likewise, a significant increase in the use of nebulized hypertonic saline was seen (79.6% *versus* 91.7%, $p < 0.001$). However, implementation of the CPG for bronchiolitis was not associated with significant changes in clinically important outcomes.

**Conclusions:** The development and implementation of a good quality bronchiolitis CPG is associated with a significant increase in the proportion of cases with an appropriate diagnosis and treatment of the disease in the context of a university-based hospital located in the capital of an LMIC. However, we could not demonstrate an improvement in clinically important outcomes such as any of the bronchiolitis severity parameters.

***Keywords:*** bronchiolitis, clinical practice guidelines, clinical practice variation, diagnostic tests, health resources, implementation, quality of care

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## Introduction

Acute bronchiolitis represents the most important cause of lower respiratory tract infection during the first year of life and is the leading reason for hospitalization for infants beyond the neonatal period [Leader and Kohlhase, 2003]. The disease is usually associated with substantial direct and indirect costs, not only for healthcare systems,

but also for families and society as a whole [Paramore *et al.* 2004]. Bronchiolitis poses a significant health problem in high-income countries, but it is an even greater problem in low- and middle-income countries (LMICs), due to higher mortality rates [Berman, 1991].

Although several clinical practice guidelines (CPGs) of acceptable quality have been developed [Rodríguez-Martínez *et al.* 2016], there is still significant unexplained variability in the clinical practice [Christakis *et al.* 2005; Florin *et al.* 2014]. This variability has been associated with inappropriate use and overuse of medications with insufficient evidence of effectiveness [Ochoa Sangrador *et al.* 2014] and the use of unnecessary diagnostic tests [Rodríguez Martínez and Sossa Briceño, 2011], generating unnecessary and costly resource use with no improvement in important clinical outcomes [Christakis *et al.* 2005]. In an attempt to reduce the variability in clinical practice for bronchiolitis, several different CPGs have been developed [Rodríguez Martínez *et al.* 2016], but many physicians fail to prescribe in accordance with these CPGs [Florin *et al.* 2014]. This lack of impact of CPGs on physician behavior has been deemed to be associated with the persistence of variability in the use of medications, diagnostic tests, and resources despite lack of strong evidence supporting recommendations for their routine use [Florin *et al.* 2014].

Previous evidence has suggested that development of CPGs alone may not change physician behavior; it may also be necessary to execute an implementation strategy showing how the recommendations can be put into practice [Florin *et al.* 2014]. The development and implementation of evidence-based clinical pathways has been shown to positively impact clinically important outcomes such as use of unnecessary diagnostic tests, use of medications with insufficient evidence of effectiveness, and length of stay [Perlstein *et al.* 1999; Wilson *et al.* 2002]. However, to the best of our knowledge, no previous study has investigated if the development and implementation of evidence-based bronchiolitis CPGs improve clinically important outcomes in LMICs. Additionally, while some studies have found good self-reported compliance with local bronchiolitis CPGs, this method of reporting compliance is potentially inaccurate and could provide information of what physicians think they do rather than what they actually do [Barben *et al.* 2008; Touzet *et al.* 2007].

The objective of the present single-center study was to assess the impact of the implementation of an evidence-based bronchiolitis CPG on physician behavior and the care of infants with bronchiolitis by comparing pre-guideline and post-guideline use of diagnostic tests and medications through an electronic medical record review in one of the most representative children's hospitals in Bogota, Colombia. We also sought to assess the impact of the implementation of the CPG on clinically important outcomes such as length of stay, hospital admissions, intensive care admissions, and hospital readmissions.

## Methods

### Study site

The Fundación Hospital La Misericordia is a tertiary care university-based children's hospital located in the metropolitan area of Bogota, the capital city of Colombia, a tropical LMIC located in South America. The hospital has 287 beds and serves the city of Bogota (7,363,782 inhabitants) as well as other cities of the country. For the latter, it mainly functions as a referral center that admits about 12,000 children (of which about 2000 are due to bronchiolitis) and registers more than 60,000 emergency room visits per year (of which about 3000 are due to bronchiolitis). The majority of admissions to the hospital come from the emergency department and from inpatient transfers from outlying primary and secondary clinics and hospitals. All emergency and inpatient services are provided with the assistance of pediatricians, residents, interns, and medical students.

### Guideline development

The evidence-based bronchiolitis CPG used in the present study was developed by a team comprised of resident pediatricians, pediatric pulmonologists, and clinical epidemiologists, supported by the Institute for Clinical Investigations, Universidad Nacional de Colombia. Because international CPGs from authoritative sources may not be directly applicable to a local setting and rigorous guideline development often carries significant personnel, resource, and time implications, the team decided to adapt high quality existing CPGs.

For this purpose, the first step was to conduct a systematic search for CPGs on the diagnosis or treatment of acute viral bronchiolitis in infants

published from 2010 to 2013, with no language restriction. We did not search for CPGs published before 2010 because evidence-based CPGs need to be updated regularly and the resultant CPG developed was concerned with the most up-to-date evidence. The systematic search for CPGs was carried out by searching in the TRIP (Turning Research into Practice) database web sites of major international agencies that elaborate or compile CPGs, clearinghouse websites, Google, Google Scholar, and the US National Library of Medicine database (through PubMed). A trial search coordinator with the Iberoamerican Cochrane Collaboration provided search support for the review team authors.

The process of identification and selection of appropriate and relevant documents yielded three CPGs for further quality evaluation. The AGREE II instrument was used to evaluate the quality of the selected CPGs because this tool is currently the most widely accepted and validated instrument for appraising the quality of CPGs [Brouwers *et al.* 2010]. In total, two independent reviewers with experience in developing and appraising CPGs evaluated the three selected CPGs using the AGREE II instrument, which was pilot-tested to ensure proper use. After comparing the scores of the three selected CPGs, the CPG of the Spanish National Healthcare System [Working Group of the Clinical Practice Guideline on Acute Bronchiolitis and Sant Joan de Déu Foundation, 2010] was rated as 'recommended', and was the selected CPG for the adaptation process.

However, due to the fact that classic adaptation of CPGs could also involve a long and costly process, the team developed and used a short-term strategy for the adaptation process [Galindo *et al.* 2014]. The adaptation of the selected CPG started in September 2013, and was carried out over a period of 6 months. The complete adaptation process comprised the following steps: (1) creating a coordinating committee; (2) prioritizing the conditions for the CPG; (3) building the Guidelines Adaptation Group; (3) defining the guideline's scope and objectives; (4) searching for the CPG; (5) selecting related titles (two reviewers); (6) assessing the quality using the AGREE II instrument (two reviewers); (7) selecting the guidelines to be adapted; (8) defining the relevance of the adapted CPG questions (five maximum); (9) assessing the need for a new question to be answered; (10) searching for tables of evidence; (11) validating the qualification of the

evidence; (12) adjusting the recommendations to the local context; and (13) drawing up the final document [Galindo *et al.* 2014].

### Guideline content

The resultant CPG after the adaptation process recommends against routine use of diagnostic tests such as a hemogram, C-reactive protein, and procalcitonin and suggested that C-reactive protein and procalcitonin should be ordered only for infants with suspected serious bacterial infections. Likewise, the CPG recommends against routine use of chest radiography, suggesting that it should be ordered only for infants with diagnostic uncertainty, severe disease, or an atypical disease course.

With respect to the pharmacological treatment, the CPG also recommends against routine use of inhaled bronchodilators (beta 2 agonists, anticholinergics), nebulized epinephrine, and anti-inflammatories (inhaled or systemic corticosteroids), but allows for the option of a monitored trial of inhaled bronchodilators or nebulized epinephrine, continuing their administration only if there is a documented positive clinical response to the trial using an objective means of evaluation. Finally, the CPG also recommends that nebulized hypertonic saline could be administered to infants hospitalized for bronchiolitis in order to shorten hospital stay, but recommends against its use in the emergency department.

### Guideline implementation

Standardized educational strategies were implemented in the study hospital in two phases between February and March 2015. The first phase was carried out in February 2015 and comprised individual educational interventions targeting general practitioners and pediatricians working in the emergency department and in the general ward. The second phase was carried out in March 2015 and involved group educational interventions targeting pediatric residents, general practitioners, and pediatricians. A Power Point presentation showing levels of evidence and grades for the main recommendations of the newly-developed CPG was used in the second phase. Both phases were complemented by an interactive session of questions and answers. Additionally, in both phases each participant was given written material containing the levels of evidence and grades for the main recommendations

of the newly developed CPG and a validated scale for assessing the severity of bronchiolitis. The above mentioned implementation strategy was complemented by the availability of an easily accessible written version of the CPG in the electronic medical record platform.

### Study design and study population

We conducted an uncontrolled before and after study through a review of the hospital's electronic medical record of patients 24 months of age and younger who were admitted to the emergency department or who were hospitalized with a discharge diagnosis of acute bronchiolitis (ICD-10 codes J21, J21.0, J21.1, J21.8, J21.9) during the pre-guideline (March to August 2014) and post-guideline (March to August 2015) periods. We chose these two time periods because they roughly coincided with the main bronchiolitis season in the city [Rodríguez *et al*. 2014].[17] Eligible patients were identified by daily review of the electronic medical record of the emergency department and the general ward and were confirmed by consultation with the physician caring for the patient. Due to the fact that patients with subsequent bronchiolitis readmissions are usually managed differently from those who present with their first episode, we analyzed only the data regarding the first admission. However, hospital readmission was analyzed as an outcome measure. Patients with incomplete data were excluded from the analysis.

After reviewing the electronic medical record, we collected the following demographic, clinical, and disease-related information: date of emergency department attendance or admission, age, gender, presence of underlying disease conditions (prematurity, pre-existing respiratory conditions, bronchopulmonary dysplasia, congenital heart disease, and pulmonary hypertension), use of diagnostic tests (hemogram, C-reactive protein, procalcitonin, and chest radiography), use of medications (beta 2 agonists, anticholinergics, epinephrine, inhaled and systemic corticosteroids, or antibiotics), type of virus identified, if a bronchiolitis severity classification was used, and if so, which scale for assessing the severity was used and what the severity level the disease was. In the same manner, we collected information related to outcomes of care or bronchiolitis severity parameters such as length of stay, hospital admissions, intensive care admissions, assisted ventilation requirement, ambulatory oxygen requirement, and hospital readmissions.

### Outcomes

As the primary outcome of interest, we defined *a priori* a composite outcome score, which we termed 'appropriate diagnosis and treatment of bronchiolitis'. This composite outcome score aggregated the use of diagnostic tests (hemogram, C-reactive protein, procalcitonin, and chest radiography), the use of medications (nebulized beta 2 agonists, inhaled beta 2 agonists, nebulized anticholinergics, inhaled anticholinergics, nebulized epinephrine, inhaled corticosteroids, systemic corticosteroids, antibiotics, and nebulized hypertonic saline), and the use of a scale for assessing the severity of bronchiolitis. Each of these 14 items had a binary score: 0 indicating that the diagnostic test or the medication was not used and 1 indicating that they were used (except for the use of a scale for assessing the severity of bronchiolitis, which also had a binary score, but with 0 indicating that a scale was used and 1 indicating that it was not used). The total score was calculated by adding up the scores for the 14 items, resulting in a total score ranging from 0–14 (best to worst). A composite outcome score >3 was designated as 'inappropriate diagnosis and treatment of bronchiolitis', whereas scores ≤3 were deemed as 'appropriate diagnosis and treatment of bronchiolitis', provided they did not include the use of anticholinergics (nebulized or inhaled) or corticosteroids (inhaled or systemic). Additionally, the use of nebulized hypertonic saline was deemed as appropriate for inpatients but not for outpatients.

Secondary outcomes included bronchiolitis severity parameters such as length of stay, hospital admissions, intensive care admissions, assisted ventilation requirement, ambulatory oxygen requirement, and hospital readmissions. The study protocol was approved by the local ethics board.

### Statistical analysis

Continuous variables are presented as mean standard deviation (SD) or median interquartile range (IQR), whichever is appropriate. Categorical variables are presented as numbers (percentage). The differences in the proportion of use of diagnostic tests and medications and categorical bronchiolitis severity variables between pre-guideline and post-guideline assessment periods were evaluated using the McNemar test. The difference in length of stay between pre-guideline and post-guideline periods was assessed using the

paired Student's *t*-test or the Wilcoxon signed-rank test, whichever was appropriate. We used general linear models (GLMs) to examine the association between the implementation of the guideline and the 'appropriate diagnosis and treatment of bronchiolitis', adjusting for baseline values and potential confounders. Likewise, we used GLMs to examine the association between the implementation of the guideline and bronchiolitis severity parameters, adjusting for baseline values and potential confounders. Results of the multivariate analyses are presented as an odds ratio (OR) with their respective 95% confidence interval (CI). All statistical tests were two-tailed, and the significance level used was $p < 0.05$. The data were analyzed with the statistical package Stata, version 12.0 (Stata Corporation, College Station, TX, USA).

## Results

### Characteristics of the study population

After reviewing the electronic medical record, a total of 1365 cases of bronchiolitis were identified using ICD-10 codes. Data from 662 cases of bronchiolitis (188 who attended the emergency department and 474 inpatients) from the 6-month period before implementation of the CPG (March to August 2014) were compared with the data from 703 cases (170 who attended the emergency department and 533 inpatients) from the 6-month period after implementation of the CPG (March to August 2015). Of the 1365 included patients, 756 (55.4%) were males, and the median (IQR) age was 5.0 (2.0–9.0) months. The age group distribution was: 850 (62.3%) less than 6 months, 374 (27.4%) between 7 and 12 months, and 126 (9.2%) between 13 and 24 months. As expected, in both years the majority of cases of bronchiolitis (873, 63.9%) occurred during the 3-month period from March to May, the main rainy season in the city. Regarding the presence of underlying disease conditions, it was found that 104 (7.6%) patients had a history of prematurity, 28 (2.1%) patients had a history of previous respiratory disease, 11 (0.8%) patients had a history of congenital heart disease, and 11 (0.8%) patients had an underlying neurologic disease. Of the total of 1354 cases of bronchiolitis, 499 (36.6%) had respiratory syncytial virus infections, 22 (1.6%) had adenovirus infections, 5 (0.4%) had influenza infections, and in the remaining 839 (61.4%) cases no virus was

identified or no test was ordered for identifying the causative virus. There were significant differences in the months of disease occurrence and the type of viral respiratory infection between pre-guideline and post-guideline periods (Table 1). The remaining demographic and clinical characteristics measured did not differ between study periods (Table 1).

### Use of diagnostic tests

Use of diagnostic tests in the 6-month period before implementation of the CPG was as follows: hemogram in 220 patients (33.2%), C-reactive protein in 119 (18.0%), procalcitonin in 26 (3.9%), and chest radiography in 315 (47.6%).

Use of diagnostic tests in the 6-month period after implementation of the CPG was as follows: hemogram in 187 patients (26.6%), C-reactive protein in 149 (21.2%), procalcitonin in 11 (1.6%), and chest radiography in 307 (43.7%).

On comparing the pre- and post-guideline periods, it was seen that there were statistically significant decreases in the use of hemogram ($p = 0.010$) and procalcitonin ($p = 0.018$).

### Use of medications

Rates of use of medications for each study period are presented in Table 2.

On comparing pre- and post-guideline periods, it was seen that there were statistically significant decreases in the use of nebulized beta 2 agonists ($p < 0.001$), nebulized anticholinergics ($p = 0.029$), and nebulized epinephrine ($p < 0.001$). Additionally, there was a statistically significant increase in the use of nebulized hypertonic saline in the post-guideline period ($p < 0.001$). Rates of use of inhaled beta 2 agonists, inhaled anticholinergics, corticosteroids, and antibiotics did not differ between study periods.

### Use of a bronchiolitis severity classification

There was no significant difference in the rate of use of a bronchiolitis severity classification between pre-guideline and post-guideline periods (2.7% *versus* 2.4%, $p = 0.73$). Among those patients that had severity classification, there were no statistical significant differences regarding the

**Table 1.** Demographic and clinical characteristics of the patients included in the study, according to the study period.

| Variable | Pre-guideline period (n = 662) | Post-guideline period (n = 703) | p-value |
|---|---|---|---|
| Age (months), median (IQR) | 5.0 (2.0-9.0) | 5.0 (2.0-9.0) | 0.637 |
| Sex (male/female) | 376/286 | 380/323 | 0.308 |
| Months of disease occurrence | | | |
|     March to May | 459 (69.3%) | 414 (58.9%) | <**0.001** |
|     June to August | 202 (30.5%) | 289 (41.1%) | <**0.001** |
| Presence of underlying disease conditions | | | |
|     Prematurity | 54 (8.2%) | 50 (7.1%) | 0.467 |
|     Previous respiratory disease | 10 (1.5%) | 18 (2.6%) | 0.171 |
|     Congenital heart disease | 8 (1.2%) | 3 (0.4%) | 0.106 |
|     Underlying neurologic disease | 8 (1.2%) | 3 (0.4%) | 0.106 |
| Type of viral respiratory infection | | | |
|     Respiratory syncytial virus | 220 (33.2%) | 279 (39.7%) | **0.013** |
|     Other viruses | 18 (2.7%) | 9 (1.2%) | 0.056 |
|     No virus isolation | 318 (48.0%) | 298 (42.4) | **0.036** |
|     No test was ordered | 106 (16.0%) | 117 (16.6%) | 0.753 |

**Table 2.** Use of medications, according the study period.

| Medication | Pre-guideline period (n = 662) | Post-guideline period (n = 703) | p-value |
|---|---|---|---|
| Bronchodilators | | | |
|     Nebulized beta 2 agonists | 302 (45.6%) | 24 (3.4%) | <**0.001** |
|     Inhaled beta 2 agonists | 465 (70.2%) | 483 (68.7%) | 0.421 |
|     Nebulized anticholinergics | 22 (3.3%) | 10 (1.4%) | **0.029** |
|     Inhaled anticholinergics | 10 (1.5%) | 11 (1.6%) | 1.00 |
| Nebulized epinephrine | 107 (16.2%) | 55 (7.8%) | <**0.001** |
| Anti-inflammatories | | | |
|     Inhaled corticosteroids | 16 (2.4%) | 17 (2.4%) | 1.00 |
|     Systemic corticosteroids | 43 (6.5%) | 37 (5.3%) | 0.389 |
| Nebulized hypertonic saline | 527 (79.6%) | 645 (91.7) | <**0.001** |
| Antibiotics | 71 (10.7%) | 64 (9.1%) | 0.444 |

bronchiolitis severity when comparing pre-guideline and post-guideline periods ($p = 0.081$).

### Bronchiolitis severity parameters
On comparing the pre- and post-guideline periods, it was found that there were no statistically significant differences in outcomes of care or bronchiolitis severity parameters such as length of stay [4.0 (0.0–7.0) *versus* 5.0 (2.0–8,0), $p = 0.37$], hospital admissions (71.6% *versus* 75.8%, $p = 0.07$), intensive care admissions (1.2% *versus* 0.7%, $p = 0.39$), assisted ventilation requirement (0.5% *versus* 0.1%, $p = 0.63$), ambulatory oxygen requirement (35% *versus* 37.8%, $p = 0.20$), and hospital readmissions (1.5% *versus* 0.6%, $p = 0.18$).

### Appropriate diagnosis and treatment of bronchiolitis
There was a statistically significant increase in the proportion of patients with an appropriate diagnosis and treatment of bronchiolitis between pre-guideline and post-guideline periods (36.4% *versus* 44.5%, $p = 0.003$).

**Table 3.** Predictors of appropriate diagnosis and treatment of bronchiolitis through multivariate analysis.

| Variable | OR (CI 95%) | *p*-value |
|---|---|---|
| Age | 0.93 (0.91–0.96) | <**0.001** |
| Absence of any underlying disease condition | 2.02 (1.14–3.59) | **0.016** |
| RSV as the causative virus identified | 1.33 (1.06–1.68) | **0.014** |
| Bronchiolitis occurring from March to May | 1.24 (0.98–1.56) | 0.067 |
| Implementation of the CPG | 1.31 (1.05–1.64) | **0.017** |

CI, confidence interval; CPG, Clinical Practice Guideline; OR, odds ratio; RSV, respiratory syncytial virus.

### Predictors of appropriate diagnosis and treatment of bronchiolitis through multivariate analysis

Multivariate analyses were conducted to determine independent factors associated with an appropriate diagnosis and treatment of bronchiolitis. The predictor variables included in the multivariate models were age, presence of underlying disease conditions, the type of virus identified, the months of disease occurrence, and the implementation of the CPG. After controlling for these potential confounders, it was found that the implementation of the CPG (OR 1.31; CI 95% 1.05–1.64; *p* = 0.017), age (OR 0.93; CI 95% 0.91–0.96; *p* < 0.001), respiratory syncytial virus (RSV) as the causative virus identified (OR 1.33; CI 95% 1.06–1.68; *p*= 0.014), and the absence of any underlying disease condition (OR 2.02; CI 95% 1.14–3.59; *p* = 0.016) were independent predictors of an appropriate diagnosis and treatment of bronchiolitis in our sample of patients (Table 3).

### Predictors of bronchiolitis severity parameters through multivariate analyses

Multivariate analyses were conducted in order to determine independent factors associated with bronchiolitis severity parameters. Implementation of the CPG was not statistically associated with length of stay, hospital admissions, intensive care admissions, assisted ventilation requirement, ambulatory oxygen requirement, or hospital readmissions (data not shown).

### Discussion

The present study suggests that the development and implementation of a good quality CPG for bronchiolitis is associated with a significant increase in the proportion of cases with an appropriate diagnosis and treatment of the disease.

This appropriate diagnosis and treatment of bronchiolitis was mainly due to a decrease in use of diagnostic tests such as a hemogram and procalcitonin and changes in the use of medications such as nebulized beta 2 agonists, nebulized anticholinergics, nebulized epinephrine, and nebulized hypertonic saline. However, implementation of the CPG for bronchiolitis was not associated with significant changes in outcomes of care or bronchiolitis severity parameters such as length of stay, hospital admissions, intensive care admissions, assisted ventilation requirement, ambulatory oxygen requirement, or hospital readmissions.

The findings of the present study point to the usefulness of the implementation of a good quality bronchiolitis CPG in impacting physician's behavior with respect to the use of unnecessary diagnostic tests and the use of medications with insufficient evidence of effectiveness. This optimization of the use of diagnostic tests and treatments could help to reduce the variability in the clinical practice and the direct costs of bronchiolitis, leading to a more efficient diagnostic and therapeutic approach to the disease. Additionally, the findings of the present study provide further evidence of the effectiveness of a strategy for implementing a bronchiolitis CPG, which is one of the main flaws of the majority of the available bronchiolitis CPGs [Rodríguez-Martínez *et al.* 2016]. Although we could not demonstrate a significant change in clinically important outcomes such as length of stay, hospital admissions, intensive care admissions, assisted ventilation requirement, ambulatory oxygen requirement, or hospital readmissions, the significant increase in the proportion of cases with an appropriate diagnosis and treatment of the disease is probably associated with lower use of resources and with a lower proportion of the adverse effects of unnecessary medications or

treatments. However, our study was not designed to measure the above factors.

The findings of the present study are in line with previous research intended to assess the impact of implementing bronchiolitis CPGs on resource use. Kotagal and colleagues reported a significant decrease in the proportion of patients who received albuterol after the implementation of an evidence-based CPG [Kotagal *et al.* 2002]. Mittal and colleagues demonstrated a significant reduction in the use of tests and treatments (hemogram, chest radiography, bronchodilators, corticosteroids, and antibiotics) after the implementation of a CPG that included the presence of an easily accessible online CPG document [Mittal *et al.* 2014]. Likewise, after the implementation of an evidence-based CPG, Perlstein and colleagues reported a 30% decrease in the use of at least one beta-agonist therapy, as well as a significant decrease in nasopharyngeal washings for RSV, chest radiographs, respiratory therapies, and mean costs for respiratory care services [Perlstein *et al.* 1999]. However, in contrast to our findings, previous reports in the literature have shown significant improvements in outcomes of care or bronchiolitis severity parameters such as length of stay (LOS) and hospital admissions after the implementation of the CPG. Kotagal and colleagues reported a significant decrease in length of stay after the implementation of an evidence-based CPG [Kotagal *et al.* 2002]. Likewise, Perlstein and colleagues reported a 30% decrease in the rate of hospital admissions and a decrease of 17% in the mean LOS after the implementation of an evidence-based CPG [Perlstein *et al.* 2000]. These discordant results can be explained, at least in part, by a residual confounding bias (where the OR of the intervention is specifically biased downward) due to the fact that a known potential confounder, severity of bronchiolitis, could not be included in the multivariate models because a disease severity classification was used only in 2.4% of cases. This is a viable hypothesis, because local epidemiological surveillance reports in the city (Secretary of Health of Bogota) showed an increase in the severity of acute lower respiratory infections in the first semester of 2015 compared with the same period in 2014 [Secretary of Health of Bogota, 2015]. An alternative explanation is that, as opposed to the use of diagnostic tests, if there has been a failure to demonstrate that the use of medications such as bronchodilators and nebulized epinephrine (which accounts for the highest proportion of

changes between pre-guideline and post-guideline periods) has a significant impact on clinically important outcomes, this does not necessarily mean that the choice not to use them does have a significant impact on these outcomes. It is simply that the disease follows its natural course, and there are no significant differences between administering and not administering these medications. Another finding that deserves attention is that in the post-guideline period, the use of nebulized bronchodilators decreased whereas the use of inhaled bronchodilators remained unchanged. The reason for this is not clear but it could be attributed to the fact that the CPG implemented in the study promotes the use of the inhaled instead of the nebulized form in order to perform the monitored trial with bronchodilators.

We are aware that our research may have two limitations. The first is that we used an uncontrolled before and after study to determine the impact of the implementation of an evidence-based bronchiolitis CPG on physician behavior and the care of infants with bronchiolitis. Although it is not possible to definitely attribute any observed changes to the intervention with the foregoing design of the study, it is very probable that the observed changes in physician behavior and the care of infants with bronchiolitis were attributable to the intervention, because no other factors or interventions occurred during the study periods to which those significant changes could be ascribed. The second is that we used a nonvalidated definition for an appropriate diagnosis and treatment of bronchiolitis. Although other studies have used different definitions of an appropriate diagnosis and treatment of the disease [Ochoa Sangrador *et al.* 2013; Acuña-Cordero *et al.* 2014], these definitions have not been validated and have not included variables that we considered important, such as the use of a scale for assessing the severity of the disease. Finally, our results need to be interpreted with caution, because residual confounding cannot be excluded. The main strength of the study is that it offers crucial evidence for the impact of a relatively simple intervention in a LMIC, aimed at improving the diagnosis and the management of a disease that is an important cause of morbidity and mortality in these countries.

In conclusion, the findings of the present study show that the development and implementation of a good quality bronchiolitis CPG is associated with a significant increase in the proportion of

cases with an appropriate diagnosis and treatment of the disease in the context of a university-based hospital located in the capital of an LMIC. However, although the improvement in the proportion of cases with an appropriate diagnosis and treatment of the disease was due to changes in the proportion of the use of diagnostic tests and medications as recommended in a good quality CPG, we could not demonstrate an improvement in clinically important outcomes. Further studies, with a sample of patients/physicians more representative of the whole country, and taking into account the severity of bronchiolitis as a potential confounder, will need to be undertaken in the future. Additionally, future research on a validated definition of an appropriate diagnosis and treatment of bronchiolitis should be undertaken.

### Conflict of interest statement
The authors declare that there is no conflict of interest in preparing this article.

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