

## Bronchiolitis clinical practice guidelines implementation: surveillance study of hospitalized children in Jordan

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### ABSTRACT

**Introduction:** Bronchiolitis is a leading cause of hospital admissions and death in young children. Clinical practice guidelines (CPG) to diagnose and manage bronchiolitis have helped healthcare providers to avoid unnecessary investigations and interventions and to provide evidence-based treatment. Aim of this study is to determine the effect of implementing CPG for the diagnosis and management of bronchiolitis in a tertiary hospital in Jordan.

**Methods:** The study compared children (age <24 months) diagnosed with bronchiolitis and who required admission to King Abdullah University Hospital in Irbid during the winter of 2017 (after CPG implementation) and age-matched children admitted in the winter of 2016. The proportion of patients receiving diagnostic tests and treatments in the two groups were compared.

**Results:** Eighty-eight and 91 patients were diagnosed with bronchiolitis before and after CPG implementation, respectively. Respiratory syncytial virus rapid antigen detection testing decreased after CPG implementation [n=64 (72.7%) vs n=46 (50.5%), p=0.002]. However, there was no significant change in terms of other diagnostic tests. The use of nebulized salbutamol [n=44 (50%) vs n=29 (31.9%), p=0.01], hypertonic saline [n=39 (44.3%) vs n=8 (8.8%), p<0.001], and inappropriate antibiotics [n=31 (35.2%) vs n=15 (16.5%), p=0.004] decreased after CPG implementation. There was no difference in mean LOS (standard deviation; SD) between the pre- and post-CPG groups [3.5 (2) vs 4 (3.4) days, p=0.19]. The mean cost of stay (SD) was 449.4 (329.1) US dollars for pre-CPG compared to 507.3 (286.1) US dollars for the post-CPG group (p=0.24).

**Conclusion:** We observed that the implementation of CPG for bronchiolitis diagnosis and management helped change physicians' behavior toward evidence-based practices. However, adherence to guidelines must be emphasized to improve practices in developing countries, focusing on the rational use of diagnostic testing, and avoiding use of unnecessary medications when managing children with a diagnosis of bronchiolitis.

**Key words:** Bronchiolitis; clinical practice guidelines; developing countries; implementation; Jordan.

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## Introduction

Bronchiolitis is a leading cause of hospital admissions and death in young children worldwide, resulting in a substantial burden on healthcare services [1]. Bronchiolitis-associated morbidity and mortality are predominantly reported in developing countries [2]. In Jordan, bronchiolitis caused by respiratory syncytial virus (RSV) and other viruses are a major cause of respiratory tract infections in hospitalized children [3,4].

The diagnosis of bronchiolitis is clinical, as it is based on history and physical examination; routine diagnostic or radiographic testing is not required [5,6]. Regarding the management of bronchiolitis, there is no role for bronchodilators (salbutamol) [7], epinephrine, or corticosteroids [8]. Antibiotics are not indicated unless concomitant bacterial infection is present [6].

Clinical practice guidelines (CPG) to diagnose and manage bronchiolitis have been issued in many countries [5,9,10]. Although a lack of compliance with CPG and variations in practice in managing inpatient bronchiolitis have been reported [11-13], implementing CPG has helped healthcare providers to reduce variations in practice, providing evidence-based treatment, the avoidance of unnecessary investigations and interventions, and the appropriate utilization of healthcare resources [14-18].

There are no Jordanian national guidelines for diagnosing and managing bronchiolitis. Jordanian physicians rely on published international guidelines for managing pediatric bronchiolitis. Consequently, there are variations in healthcare planning and the degree of use of diagnostic and therapeutic measures in bronchiolitis management. To our knowledge, no study has addressed the effect of implementing international guidelines for inpatient management of bronchiolitis in developing countries including Jordan. Thus, we conducted this study to determine the effect of implementing international guidelines on the diagnosis and management of bronchiolitis in an academic-based hospital in Jordan which could help in guiding physicians toward evidence based medical practice and optimizing the utility of health resources.

## Methods

### Study design and setting

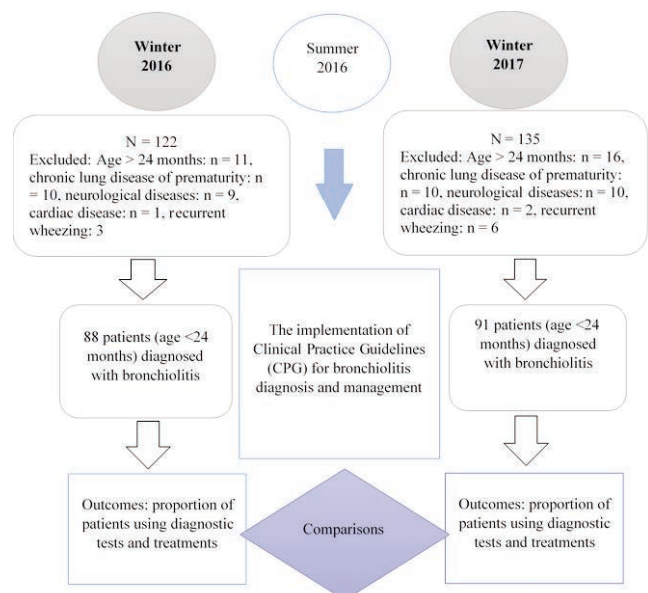
Clinical surveillance of children admitted with acute respiratory infection (ARI) to King Abdullah University Hospital (KAUH) was conducted during the 3-month winter period (January to March) of 2016 [4] and 2017 (*data unpublished*). CPG for bronchiolitis diagnosis and management were implemented in the pediatric department of KAUH during the summer of 2016. We studied the effect of implementing CPG on diagnostic testing and management of children <24 months who had a diagnosis of bronchiolitis and required admission during the winter of 2017 compared to their counterparts admitted before the implementation of CPG in 2016 by comparing the proportions of patients receiving diagnostic tests and treatments. Winter is the peak of ARI/bronchiolitis in Jordan [3]. Diagnostic testing used in the methodology of the surveillance studies in 2016 and 2017 was not included in this study or used for comparison. Ethical approval for the ARI surveillance was given by the Institutional Review Board of Jordan University of Science and Technology.

KAUH is an academic-based hospital affiliated with Jordan University of Science and Technology and is a tertiary medical center in the city of Irbid, Northern Jordan. It has a pediatric ward and patients are cared for by pediatric specialists and subspecialists. Patients are admitted through the emergency department, outpatient clinics, or referred from other hospitals.

## Study population

We selected children who had a clinical diagnosis of bronchiolitis among patients with ARI. Demographic and detailed clinical data of patients were collected on admission by trained pediatric residents. Data included: age, gender, gestational age, smoking exposure, day care attendance, breast feeding history and presenting symptoms (fever, cough, rhinorrhea, wheezing, apnea, difficulty breathing and cyanosis). Physical examination findings at the time of presentation were recorded, including SpO<sub>2</sub> readings, respiratory rate, axillary temperature, retractions, flaring, grunting and auscultatory findings: wheezing and crackles. Tachypnea was defined as a respiratory rate  $\geq 60$ /min for infants younger than 2 months,  $\geq 50$ /min for infants 2 to 12 months old, and  $\geq 40$ /min for children 12 to 60 months old. Severe disease was defined as any sign of respiratory distress (tachypnea, grunting, flaring, retractions, cyanosis), apnea, altered mental status, or SpO<sub>2</sub> <90%. Diagnostic and management plans were obtained from the electronic health record (EHR) system for each patient. Children who required intensive care unit admission or ventilator management, had chronic lung disease of prematurity, cardiac disease, chronic pulmonary disease, immunodeficiency, neurological disease, genetic abnormality or developed two or more previous episodes of wheezing attacks were excluded from the study (Figure 1).

Chest X-rays (CXRs) of all studied patients admitted during the study period in 2016 and 2017 were interpreted by a pediatric radiologist who was blinded to the diagnosis. Presence of a secondary bacterial diagnosis was documented when having bacterial urinary tract infection, bacteremia, or bacterial meningitis. Antibiotic use during hospitalization based on evidence of bacterial infection, including positive urine culture, positive blood culture, positive cerebrospinal fluid culture, acute otitis media, or possible pneumonia diagnosis clinically and by CXR (presence of consolidation interpreted by one radiologist), was considered as appropriate use.



**Figure 1. Flowchart of the study design.**

## Guidelines development and implementation

Summary key points for diagnosing and managing bronchiolitis were developed from the American Academy of Pediatrics CPG for diagnosing and managing bronchiolitis (Table 1) [5]. They were drafted and revised by a pediatric pulmonologist and two pediatric infectious disease specialists. The CPG were made accessible online in the EHR system of the hospital with the assistance of the health information technology department. An order set was developed from the CPG and implemented in the EHR. A PowerPoint (Microsoft Corp., Redmond, WA) presentation with the content of the CPG was explained to practicing doctors including residents in an educational session in the pediatric department. Afterward, a demonstration of how to access the CPG and the order-set in the EHR was conducted for a mini-group of pediatric residents. Pediatric residents rotate in pediatric wards, emergency department and outpatient clinics, and all had received education. All pediatric patients at KAUH in pediatric wards, emergency department and outpatient clinics are managed by pediatric residents and specialists who were all included in CPG training. Investigators ensured all residents had received educational training via marking checklist for attendance. Some of the investigators were also clinical attending physicians supervising the residents caring for bronchiolitis patients during the 2016-2017 time period of the study. The CPG was implemented for patients admitted with bronchiolitis prior to the winter of 2017. A repeated educational session of bronchiolitis CPG content and order-set was delivered to the residents in 2017. Application of CPG in 2017 was randomly checked during clinical rounds, and periodically by interviewing the residents.

## Outcome measures

The demographic and clinical characteristics of patients admitted with a bronchiolitis diagnosis were compared between 2017 (after CPG) and 2016 (before CPG). The outcome measure was the proportion of patients using diagnostic tests and treatments. Diagnostic tests included complete blood count (CBC), blood culture, urine analysis and culture, CXR, rapid RSV antigen testing, influenza reverse transcriptase-polymerase chain reaction testing. Treatments included nasal bulb suctioning, bronchodilators (scheduled nebulized salbutamol), single trial of salbutamol, nebulized hypertonic saline, inhaled and systemic steroids, antibiotics (inappropriate use), and chest physiotherapy. Difference in use of antibiotics between two groups was adjusted for the variables: prematurity, white blood cell count (WBC), CXR findings of consolidation and atelectasis, and secondary bacterial diagnosis. Secondary outcomes were the mean length of hospital stay (LOS) and admission cost.

## Statistical analysis

Statistical analysis was conducted using SPSS version 20 (IBM, Armonk, NY, USA). Data are described using means (standard deviation (SD)) for continuous variables and numbers and percentages for categorical variables. The differences in the means of continuous variables between pre-CPG and post-CPG implementation were analyzed using the independent *t*-test and the differences between proportions were analyzed using the Chi-square test. The difference in the use of antibiotics between the two time periods was analyzed using binary logistic regression to adjust for important variables. A *p* of <0.05 was considered statistically significant.

## Results

### Demographic and clinical characteristics

A total of 88 and 91 patients were diagnosed with bronchiolitis before and after CPG implementation, respectively. No significant differences were found in demographic data between both groups as shown in Table 2. Regarding the clinical presentation (Table 2), the post-CPG group had significantly greater occurrences of difficulty breathing, apnea, hypoxia (SpO<sub>2</sub> <94%), and requirement for oxygen supplementation. Retraction and flaring occurred more significantly in the pre-CPG group. Severe disease was more frequent in the post-CPG group (*p*=0.009) (Table 2).

### LOS and cost

There was no difference in mean LOS (SD) between the pre- and post-CPG groups [3.5 (2) vs 4 (3.4) days, *p*=0.19]. The mean cost of stay (SD) was 318.7 (233.4) Jordanian dinars (JD) (449.4 (329.1) US dollars) for pre-CPG compared to 359.8 (202.9) JD (507.3 (286.1) US dollars) for the post-CPG group (*p*=0.24) (Table 2).

### Diagnostic testing

The use of RSV rapid antigen detection declined significantly after CPG implementation (*p*=0.002) (Table 3). The frequencies of CBC, blood culture, urinalysis, urine culture, CXR, and influenza testing did not change after CPG (Table 3).

### Treatment measures

There was a significant increase in the use of nasal bulb suctioning after CPG implementation (*p*<0.001) (Table 4). Use of nebulized salbutamol and hypertonic saline decreased in the post-CPG group compared to the pre-CPG group (*p*=0.014 and *p*<0.001, respectively) (Table 4). The rate of inhaled or systemic steroid use was low in both groups. Antibiotic use was not affected by CPG implementation. However, inappropriate antibiotic use (no evi-

**Table 1. Summary of clinical practice guidelines for diagnosing and managing bronchiolitis.**

- Diagnosis of bronchiolitis and assessment of disease severity should be based on history and physical examination
- Laboratory studies and chest radiography should not be routinely ordered for diagnosis of bronchiolitis
- Salbutamol should not be used
- Epinephrine should not be used
- Nebulized hypertonic saline 3% should not be routinely used, and may be considered for children with a diagnosis of bronchiolitis and have length of stay >72 hours
- Inhaled and systemic steroids should not be used
- Antibiotics should not be administered to patients with bronchiolitis unless there is concomitant bacterial infection
- Chest physiotherapy should not be used
- Consider nasal suctioning in infants with respiratory distress due to nasal blockage with secretions
- Nasogastric or intravenous fluids should be administered for patients who cannot tolerate oral hydration



dence of bacterial infection or pneumonia) reduced significantly after CPG ( $p=0.004$ ) (Table 4).

After adjustment for factors, including prematurity,  $WBC > 15,000$ , presence of CXR findings (atelectasis and consolidation), and having a secondary bacterial diagnosis, a significant decline in the use of antibiotics was noted in the post-CPG group compared to the pre-CPG group (odds ratio: 0.2, 95% confidence interval: 0.1-0.6,  $p=0.003$ ).  $WBC > 15,000$  and secondary bacterial diagnosis were significantly associated with antibiotic use among the tested variables in the regression model ( $p < 0.001$  and  $p = 0.003$ , respectively) (Table 5).

## Discussion

Our study showed that implementing international CPG and making them accessible in the EHR system was helpful in minimizing the unnecessary use of medications for managing inpatient bronchiolitis in a tertiary medical center in Jordan. However, no change was noted in the ordering diagnostic tests (CBC, blood culture, urine culture, CXR) except for RSV testing which declined after CPG implementation. Our results were similar to those of a multicenter cohort study in the US in which CPG did not significantly reduce the ordering of tests unless they were used for longer periods [17].

RSV antigen detection testing was successfully reduced after CPG. However, half of the patients were tested for RSV after the intervention, a value considered higher than previously reported [19]. Routine viral testing to detect the etiology of bronchiolitis is not recommended based on evidence but it can assist in the cohorting of patients and avoiding unnecessary antibiotic use [20]. Influenza testing frequency was not changed, possibly explained by the fact that the period of our study coincided with the influenza epidemic season in Jordan [21], where antiviral therapy is available and can be helpful [22].

Our study showed that doctors leaned towards ordering diagnostic tests and the evaluation of serious bacterial infection which has been associated with increased LOS and antibiotic overuse and a low-positive yield in patients with bronchiolitis [23]. In our study, WBC count was significantly associated with antibiotic use in the logistic regression analysis. Almost all patients in both pre- and post-CPG groups had CBC testing which highlights the lack of specific indication and a routine practice that was not changed after CPG.

Physicians were not adherent to the recommendation of not ordering CXR routinely, as CXR was ordered in all cases of admitted bronchiolitis before and after CPG. Patients after CPG tended to have more severe disease presentations which may partly explain this finding. Our result is similar to that of a study low- and middle-income countries (LMIC) that demonstrated no change in CXR use after CPG implementation [15]. Previous research in developed countries [14,16,24] showed a significant decrease in CXR use after CPG. Factors leading to overuse of CXR by physicians in managing bronchiolitis in developing or LMIC countries need to be studied. Perhaps physicians might not feel confident relying on clinical assessment for diagnosing bronchiolitis, or they are concerned about missing cases of bacterial pneumonia cases; for example, children in Jordan are not vaccinated against streptococcus pneumonia. When residents were asked about reasons of ordering tests in patients with bronchiolitis, responses included: fear of missing another diagnosis as urinary tract infection in a febrile child below the age of 2 years or pneumonia in a child with respiratory symptoms, ordering all the labs earlier is better than waiting for the results if another diagnosis is suspected later in the course of the illness and sometimes lack of awareness of the

sequences of ordering unnecessary tests.

Implementing CPG was helpful in minimizing the inappropriate use of antibiotics. Overuse of antibiotics is a major health issue, and needs to be targeted to lessen cost, side effects, and antimicrobial resistance [25]. We determined that cases requiring antibiotics were based on evidence, including the presence of secondary bacterial diagnosis (positive bacterial cultures: urinary tract infection,

**Table 2. Comparison of demographic and clinical characteristics of patients pre- and post- clinical practice guidelines.**

Variable	Pre-CPG	Post-CPG	p
Age (months), mean (SD)	7.3 (5.6)	6.6 (5.1)	0.35
Sex			0.67
Female	31 (35.2)	29 (32.2)	
Male	57 (64.8)	61 (67.8)	
Gestational age			0.91
Premature	13 (14.8)	14 (15.4)	
Full term	75 (85.2)	77 (84.6)	
Smoking exposure	52 (59.1)	56 (61.5)	0.74
Day care attendance	13 (14.8)	14 (15.4)	0.91
Breast feeding	70 (79.5)	62 (68.1)	0.08
Axillary temperature $>38^{\circ}\text{C}$	44 (60.3)	42 (46.2)	0.07
Rhinorrhea	59 (67)	66 (72.5)	0.42
Cough	80 (90.9)	87 (95.6)	0.21
Wheezing	54 (61.4)	58 (63.7)	0.74
Apnea	3 (3.4)	25 (27.5)	$<0.001^*$
Difficulty breathing	67 (76.1)	80 (87.9)	0.04*
Cyanosis	11 (12.5)	20 (22)	0.09
Tachypnea	60 (68.2)	50 (54.9)	0.07
SpO <sub>2</sub>			0.007*
$>94$	60 (68.2)	41 (45.1)	
90-94	12 (13.6)	19 (20.9)	
$<90$	16 (18.2)	31 (34.1)	
Retractions	45 (51.1)	31 (34.1)	0.02*
Flaring	35 (39.8)	14 (15.4)	$<0.001^*$
Grunting	15 (17)	9 (9.9)	0.16
Wheezing	47 (53.4)	44 (48.4)	0.50
Crackles	36 (40.9)	5 (5.5)	$<0.001^*$
Severe disease	65(73.9)	81(89)	0.009*
Chest radiograph findings			
Interstitial markings	36 (40.9)	34 (38.2)	0.71
Hyperinflation	25 (28.4)	18 (20.2)	0.20
Atelectasis	12 (13.6)	22 (24.7)	0.06
Peribronchial thickening	45 (51.1)	47 (52.8)	0.82
Consolidation	13 (14.8)	12 (13.3)	0.78
Normal radiographic findings	30 (34.1)	22 (24.7)	0.17
White blood count			0.29
$<15000$	58 (67.4)	68 (74.7)	
$>15000$	28 (32.6)	23 (25.3)	
Respiratory syncytial virus positive	19 (21.6)	21(23.1)	0.81
Secondary diagnosis	25 (28.4)	37 (40.7)	0.09
Length of stay, days			0.78
$<3$	54 (61.4)	54 (59.3)	
$>3$	34 (38.6)	37 (40.7)	
Length of stay (mean), days	3.47 (2)	4.04 (3.5)	0.19
Total cost mean (SD), US\$	449.4 (329.1)	507.3 (286.1)	0.24

Data presented as number and (%); SD, standard deviation; \*statistically significant at  $p < 0.05$ .

meningitis, and bacteremia) or pneumonia in both groups. Other studies showed that CPG did not reduce the use of antibiotics in bronchiolitis [15,17,24] possibly because of the presence of concomitant bacterial infection requiring antibiotics that was not identified.

In our study, CPG helped to decrease the use of nebulized salbutamol as in previous studies [14,24]. A trial of bronchodilator is not recommended considering evidence in managing bronchiolitis [5]. However, the use of a single salbutamol trial did not change after CPG. This could be because it was administered in the emergency department prior to admission or was given to address parents' dissatisfaction when their children were not getting any treatment. Reports indicate that a rationale for medication prescription by practitioners in bronchiolitis could be the expectation of parents [26].

The role of nebulized hypertonic saline in bronchiolitis is controversial [27]. The American Academy of Pediatrics recommends the use of nebulized hypertonic saline (3%) in the inpatient setting for non-severe bronchiolitis as it may decrease LOS in cases where LOS exceeds 3 days [5,28,29]. Before CPG, there was an overuse of hypertonic saline in the study population, and this declined significantly after CPG.

Despite the increase in the proportion of patients that received appropriate diagnosis and treatment, there was no change in LOS after CPG as reported previously [15]. However, other confounding variables could have attributed to LOS such as disease severity. A higher number of patients in the post-CPG group were hypoxic and had a severe disease presentation which could have necessitated a relatively longer LOS to facilitate oxygen supplementation and appropriate care. Although the post-CPG group had a non-significantly higher rate of a secondary diagnosis than the pre-CPG group, this could have influ-

enced LOS in order for the patient to receive required treatment.

The total cost of stay was not changed after CPG. Other non-healthcare-related factors could have influenced the total cost such as the parents' preference for particular hospital accommodation services which have more than one option with variable expenses.

### Strengths and limitations

Our study included patients with bronchiolitis who were enrolled based on clinical diagnosis not on discharge diagnosis codes as in other studies [16,17]. This reduced the possibility of missing or misdiagnosing cases of bronchiolitis and allowed the recognition of severe disease. Moreover, we determined the presence of comorbidities and excluded them from the study, as they could have increased the risk of severe disease and influenced management plan, LOS, and cost. Further, we identified the presence of concomitant bacterial illness and justified antibiotic use which helped in recognizing antibiotic overuse in our study.

Our study was limited by its small sample size and perhaps, extending the duration of patient enrollment would have validated our findings.

**Table 3. Comparison of diagnostic tests used pre- and post-clinical practice guidelines implementation.**

Diagnostic testing	Pre-CPG	Post-CPG	p
Complete blood count	86 (97.7)	91 (100)	0.15
Blood culture	54 (61.4)	50 (54.9)	0.38
Urine analysis and culture	36 (40.9)	36 (39.6)	0.85
Chest radiography	88 (100)	91 (100)	No statistics computed#
Respiratory syncytial virus	64 (72.7)	46 (50.5)	0.002*
Influenza testing	40 (45.5)	37 (40.7)	0.51

Data presented as number and (%); CPG, clinical practice guidelines; #number is equal in both groups; \*statistically significant at p<0.05.

**Table 4. Treatments of patients pre- and post-clinical practice guidelines implementation.**

Diagnostic testing	Pre-CPG	Post-CPG	p
Therapeutic intervention	Pre-CPG	Post-CPG	p
Nasal suctioning	9 (10.2)	83 (91.2)	<0.001*
Scheduled salbutamol	44 (50)	29 (31.9)	0.01*
Salbutamol trial	24 (27.3)	21 (23.1)	0.52
Nebulized hypertonic saline	39 (44.3)	8 (8.8)	<0.001*
Inhaled corticosteroid	3(3.4)	3(3.3)	0.97
Systemic steroids	8 (9.1)	5 (5.5)	0.35
Antibiotics	52 (59.1)	44 (48.4)	0.15
Inappropriate antibiotic use (no indication)	31 (35.2)	15 (16.5)	0.004*
Chest physiotherapy	7 (8.0)	8 (8.8)	0.840

Data presented as number and (%); \*statistically significant at p<0.05.

**Table 5. Comparison of antibiotic use pre- and post-clinical practice guidelines.**

	OR	95% confidence interval	p
Antibiotic use (post-CPG vs pre-CPG)	0.23	0.09, 0.62	0.003*
<b>Variables affecting antibiotic use</b>			
Gestational age (premature vs. full term)	1.10	0.26, 4.62	0.901
White blood cell count ≥15,000 v vs <15,000)	4.23	1.62, 11.05	0.003*
Gender (female vs male)	1.39	0.54, 3.58	0.497
Chest radiograph finding (consolidation vs no consolidation)	3.67	0.49, 27.55	0.207
Chest radiograph finding (atelectasis vs no atelectasis)	1.68	0.58, 4.88	0.337
Secondary bacterial diagnosis	248.21	28.85, 2135.65	0.000*

Logistic regression analysis for variables could have affected antibiotic use in both groups of patients pre- and post-CPG; CPG, clinical practice guidelines; #number is equal in both groups; \*statistically significant at p<0.05.

oping countries that have healthcare systems with limited resources. These findings orient physicians and stakeholders in the health care sector in Jordan to the necessity of establishing and implementing CPG for managing inpatients with bronchiolitis. Barriers to implement CPG and adherence to minimizing unnecessary diagnostic testing and treatment need to be assessed for improving clinical practice and optimizing resource utilization.

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