Pharmacotherapy in Bronchiolitis at Emergency Department Discharge: A Pediatric Emergency Research Networks (PERN) Retrospective Cohort Study

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Abstract

Background: Clinical guidelines advise against pharmacotherapy in bronchiolitis. However, little is known about global variability in prescribing practices for bronchiolitis at Emergency Department (ED) discharge.

Primary objective: To evaluate global variation in the proportion of infants discharged from the ED prescribed pharmacotherapy, i.e. inhaled albuterol or oral/inhaled corticosteroids. We hypothesized there would be significant global variation in prescribing practice, after adjustment for patient-level characteristics. We also examined the association between pharmacotherapy at discharge and ED re-visits and hospitalizations for bronchiolitis.

Methods: We conducted a planned secondary analysis of a multinational, retrospective cohort study of the Pediatric Emergency Research Network. Previously healthy infants <12 months old discharged with bronchiolitis in 2013 from 38 EDs in Canada, US, Australia & New Zealand, UK & Ireland, and Spain & Portugal were included. Primary outcome: pharmacotherapy prescription at ED discharge. Secondary outcomes: ED re-visits and hospitalizations within 21 days.

Findings: 317/1,566 (20 %) infants were prescribed pharmacotherapy. While corticosteroid prescriptions were infrequent (0% Spain & Portugal, 6 % U.S.), those for albuterol ranged from 5 % in the UK & Ireland to 32 % in the U.S. ($p<0.0001$).

Compared to UK & Ireland, odds ratios (ORs) for prescription of pharmacotherapy were: 9.22 (95%CI 1.70-50.0) Spain & Portugal, 8.20 (2.79-24.10) U.S., 5.17 (1.61-16.70) Canada, and 1.21 (0.36-4.10)

Australia & New Zealand. After adjustment for clustering by site, treatment at discharge was associated with older age (OR 1.23, 1.16-1.30), oxygen saturation (OR 0.92, 0.85-0.99), chest retractions (OR 1.88, 1.26-2.79), network ($p<0.001$) and site ($p<0.001$).

303/1566 (19 %) infants returned to the EDs and 129/303 (43 %) were hospitalized. Discharge pharmacotherapy was not associated with re-visits ($p=0.55$) or hospitalizations ($p=0.50$).

Interpretation: Substantial use of ineffective medications in infants with bronchiolitis at ED discharge is common, with marked practice differences between countries and EDs. The results of this study emphasize the need for enhanced knowledge translation and de-prescribing efforts to optimize and unify the management of bronchiolitis.

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Background

Bronchiolitis is the leading cause of infant hospitalizations in the United States and other western countries.[1,2] The use of pharmacotherapy has not been shown to improve bronchiolitis outcomes, prompting professional societies around the world to advise against its routine use.[3-13] However, the impact of international bronchiolitis practice guidelines on unwarranted use of resources continues to be suboptimal.[14-18] Substantial variation in the use of pharmacotherapies in bronchiolitis is associated with major costs and persists in North America and elsewhere.[8,9,11,14,19-28]

Although previous studies of use of pharmacotherapies in bronchiolitis have focused on their administration in the emergency department (ED) and inpatient settings,[14,15,19-22,26,29,30] studies which have documented pharmacotherapies prescribed at discharge from medical encounters have focused on community hospitals,[31] hospitalized children,[32,33] and non-hospital based ambulatory practices.[34] Recently it has been reported that children with bronchiolitis often receive non-evidence based

interventions while in the ED,[25] but little is known about ED discharge prescribing practices in bronchiolitis.

To address this knowledge gap, we conducted a planned secondary analysis of a multicenter, multi-national, retrospective cohort study of previously healthy infants with bronchiolitis who presented to any of the EDs associated with six pediatric emergency research networks (national research-focused groups of pediatric EDs) in Canada, the United States, Spain & Portugal, United Kingdom & Ireland or Australia & New Zealand who are members of the Pediatric Emergency Research Network (PERN). The primary objective was to evaluate the variation across research networks in the proportion of infants who were discharged from the ED and were prescribed either inhaled bronchodilators or systemic/inhaled corticosteroids for home use. Although discouraged by clinical practice guidelines,[3-12] we believe these medications are commonly prescribed despite little evidence of benefit.[14,26,28,29,35-39] A recent National Institutes of Health- funded investigation of de-implementation studies points out paucity of such efforts[40] and the Choosing Wisely initiative has been focusing on systematically improving value of healthcare by reducing use of ineffective therapies[41]. The information in this study provides background data for future de-implementation efforts to unify the standards and decrease costs of care for this common disease. We hypothesized that that there would be significant association between prescription for pharmacotherapy at ED discharge and the network where the infant presented, after adjustment for patient-level characteristics. Secondary objectives were to examine the association between the prescriptions for these medications at ED discharge and subsequent return visits to the ED and hospitalizations for bronchiolitis.

Methods

Study Design and Population

We conducted a retrospective cohort study at 38 pediatric EDs in 8 countries, all of which are member sites of the PERN.[42] The PERN is an international collaborative research network comprised of six

national or regional networks, including: 1) Pediatric Emergency Research Canada (PERC); 2) Pediatric Emergency Medicine Collaborative Research Committee (PEM-CRC) and Pediatric Emergency Care Applied Research Network (PECARN) in the United States; 3) Paediatric Research in Emergency Departments International Collaborative (PREDICT) in Australia & New Zealand; 4) Paediatric Emergency Research United Kingdom & Ireland (PERUKI); and 5) Research in European Paediatric Emergency Medicine (REPEM) in Spain & Portugal. The annual patient volume in the participating EDs ranged from 20,000 to 120,000. The initial study approved by the Research Ethics Boards of all participating institutions addressed practice variation in the proportions of infants hospitalized from the ED who also receive evidence-based supportive therapies during hospital stay.

The study population in this secondary analysis consisted of infants younger than 12 months, diagnosed with bronchiolitis in the ED between January 1, 2013 and December 31, 2013, and discharged home. This time period contained the most recent data available at the time of the ethics review. We defined bronchiolitis as the first presentation of acute respiratory distress with upper respiratory tract symptoms.[9,10] This definition included only children with no previous visits to a health care provider for bronchiolitis symptoms 1 month or more prior to the index ED visit. We excluded infants who received a previous diagnosis of bronchiolitis ≥1 month prior to the index episode, those with co-existent lung disease, congenital heart disease, immunodeficiency, neuromuscular/neurologic/bone disease, metabolic/genetic, kidney or liver disease, infants hospitalized at the index ED visit and those previously enrolled in the study.

Patient Identification and Study Execution

We collected patient study data according to standard methods for retrospective chart reviews,[43] with all study variables defined *a priori* in keeping with international definitions. We itemized these variables in a manual of operations with data source hierarchy, which was used by all site investigators and site abstractors. In order to standardize research process, site investigators were educated in data extraction

procedures on site-and study- specific terms (such as dehydration) and they reviewed the case report forms to ensure information clarity. This was important because of the heterogeneity of health care systems involved.

At each hospital, we identified the medical records of consecutive infants who presented to the ED within the study period and had an International Classification of Disease 9 or 10 discharge diagnosis of bronchiolitis/RSV bronchiolitis (codes J 21·0, 21·8, 21·9/466·1). Using a random number generator, each site identified a random sample of records for review. Trained abstractors assessed eligibility and recorded data into a secure web-based database until at least 50 records were included in the initial study from each site.

Abstracted data included patient demographics, presenting symptoms and physical examination findings in the ED, vital signs and oxygen saturation measured on room air in ED triage, and medications which were given prior to ED arrival, administered in the ED and prescribed at ED discharge. Subsequent ED attendances and hospitalizations for bronchiolitis within 21 days of the index ED visit were documented.

Outcome Measures

The primary outcome measure was defined *a priori* as a prescription at ED discharge of at least one of the following medications: albuterol (salbutamol) administered via metered dose inhaler or nebulizer, or corticosteroids given by mouth or by inhalation. We have not collected information on oral albuterol (salbutamol) and decongestants as these medications are rarely prescribed in tertiary care pediatric hospitals. Secondary outcomes included a) ED re-visit for bronchiolitis within 21 days of the index ED discharge, and b) ED re-visits for bronchiolitis which resulted in bronchiolitis-related hospitalization within 21 days of the index ED discharge. This time frame was chosen for defining subsequent ED re-visits or hospitalization because bronchiolitis symptoms may persist for 21 days.[28,44,45]

Analyses

The sample size required for this study was estimated to provide 80% power at a 5% significance level to assess the primary association between the use of pharmacotherapy (bronchodilators and /or corticosteroids) at ED discharge and the pediatric research network in which the patient was seen, adjusting for patient-level characteristics listed below which may impact this association. Based on a previous study,[25] we assumed that 20% of discharged infants would be prescribed pharmacotherapy. Planning the examination of 11 independent variables and requiring 10 patients with the outcome of interest per predictor variable evaluated and allowing for moderate average correlation between independent variables, we needed to analyze at least 220 infants with and 880 infants without prescribed pharmacotherapies.[46]

We used proportions to describe categorical data and means with standard deviations or medians with interquartile ranges for continuous data. Relevant 95% confidence intervals were calculated around proportions. PEM-CRC and PECARN networks were treated as a single network in the analysis, as there is significant overlap between sites and both are based in the United States. Of note, the PECARN and PEM-CRC networks represent separate networks of mutually exclusive different sites within the United States. Therefore, no patient or site was counted twice in the analysis.

Bivariable logistic regression was used to examine the association between each explanatory variable and discharge pharmacotherapy. Thereafter, multivariable logistic regression analysis was performed to determine the association between discharge pharmacotherapy as a binary dependent variable and potential predictors. Because the ED physicians may be more inclined to prescribe pharmacotherapy in older infants with more severe disease, we evaluated the following independent variables: age, poor feeding by history, dehydration observed by the ED treating physician, nasal flaring/grunting, chest retractions, oxygen saturation, respiratory rate, and the research network in which the patient was

evaluated. Predictors with univariate p-values <0.2 were included in the multivariate analysis. To examine clustering of discharge pharmacotherapy by site, we incorporated the treating site (ED) as a random effect. To ensure the data was missing at random, we have carried out a multiple imputation procedure and repeated the analyses with the imputed and the full-data sets. Because the pattern for missing data was identified as arbitrary, we used the fully conditional specification method for imputing missing data for continuous and categorical data.[47]

We also used logistic regression analyses to examine the association between pharmacotherapy at discharge from the ED and subsequent ED re-visits and hospitalizations for bronchiolitis. These associations were adjusted for the variables previously found to impact these bronchiolitis outcomes i.e. network, age, gender,[48] nasal flaring, chest retractions and oxygen saturation. The analyses were done using SAS version 9·4 and PROC GLIMMIX (SAS Institute Inc.).

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Findings

Study Population

A total of 5,305 potentially eligible infants were identified at the 38 sites. Of these, 1,580 met exclusion criteria, leaving 3,725 eligible participants. Of these, 1,466 infants were admitted to hospital and 2,259 (60·6%) were discharged home. The hospitalization rate from the ED was 39% and varied between 30% (Spain& Portugal) and 46% (Australia& New Zealand).

A total of 1,566 discharged infants had full data on all study variables: 320 were discharged home from eight Canadian pediatric EDs [PERC], 452 from 10 EDs in the United States [PEM-CRC and

PECARN], 294 children from eight EDs in Australia & New Zealand [PREDICT], 432 from nine EDs in UK & Ireland [PERUKI] and 68 infants were discharged from three EDs in Spain & Portugal [REPEM].

The demographic and clinical characteristics of the discharged infants are described in Table 1.

Prescriptions for Bronchodilators and Corticosteroids at ED discharge

A total of 317/1566 (20 %) discharged infants were prescribed either inhaled salbutamol/albuterol or oral/inhaled corticosteroids at ED discharge. Of these, 300 (19 %) participants were instructed to take inhaled salbutamol/albuterol, 44 (3 %) were sent home on oral corticosteroids and 6 (0.4%) received prescriptions for inhaled corticosteroids (some patients received prescriptions for a combination of these medications). Of the 351 discharged infants who received a therapeutic trial of inhaled salbutamol/albuterol in the ED, 300 (86 %) also received prescriptions for this medication at ED discharge.

While the use of corticosteroids was uniformly low across networks, participants in Canada, the United States, and Spain & Portugal were more likely to be prescribed salbutamol/albuterol on discharge compared to their counterparts in Australia & New Zealand and United Kingdom & Ireland (Table 2). Children prescribed at least one of these treatments were older and more likely to present to the ED with nasal flaring/grunting and chest retractions than those without these prescriptions (Table 3).

Using the United Kingdom & Ireland as a reference (lowest rate of discharge pharmacotherapy use), the respective multivariable ORs for the prescription for either salbutamol (albuterol) or corticosteroids were 9·22 for Spain & Portugal (95% CI 1·70-49·96), 8·20 for the United States (95% CI 2.·79-24·11), 5·17 for Canada (95% CI 1·61-16·67), and 1·21 for Australia & New Zealand (95% CI 0·36 – 4·10). Figure 1 illustrates the variation in the prescriptions for bronchodilators and/or corticosteroids at ED discharge between and within networks.

Both the site and the network represented significant sources of variation in the use of albuterol/corticosteroids, independent of the patient-level characteristics ($p<0{\cdot}001$ for both). The proportional use of at least one of the discharge pharmacotherapies per site ranged from 0 to 64 % (Figure 1). After adjustment for clustering by site and other covariates, the prescription for pharmacotherapy at ED discharge was associated with increasing age (multivariable OR 1·23 (95% CI 1·16 – 1·30, $p<0{\cdot}0001$) [i.e. for each month increase in age, the odds of the outcome increased by 23%], decreasing oxygen saturation (OR 0·92; 95% CI 0·85 – 0·99, $p=0{\cdot}03$) [for each percentage point decrease in saturation below 100%, the odds of the outcome increased by 8%], chest retractions (OR1·88 (95% CI 1·26-2·79, $p=0{\cdot}002$) and network ($p<0{\cdot}001$). The multiple imputation procedure did not change these results.

Pharmacotherapy prescriptions and patient outcomes after ED discharge

Of the 1,566 discharged infants, 303 (19 %) returned to the ED with ongoing bronchiolitis symptoms within 21 days of the index ED visit. Of these, 129 (43%) were admitted to hospital for bronchiolitis within this time interval. The re-visit rate to the ED ranged from 16 % (Canada) to 25 % (Spain & Portugal), $p=0{\cdot}14$. Specifically, 54/317 (17 %) infants prescribed pharmacotherapy returned for continued symptoms versus 249/1,249 (20 %) of their non-treated counterparts ($p=0{\cdot}24$). After adjusting for clustering by site, network, age and gender,[48] the re-visits were not associated with prescription for pharmacotherapy at ED discharge (OR 1·13, 95% CI 0·77-1·65, $p=0{\cdot}55$)

The rates of the re-visit related hospitalizations for bronchiolitis ranged from 5 % in Canada to 15 % in Spain & Portugal: 25/317 (8 %) infants prescribed pharmacotherapy were hospitalized upon return to the ED versus 104/1249 (8 %) infants without prescriptions ($p=0{\cdot}99$). After adjusting for clustering by site, age, gender [48], nasal flaring, chest retractions, oxygen saturation and network, hospitalizations were not associated with prescription for pharmacotherapy at ED discharge (OR 1·20, 95% CI 0·71-2·01, $p=0{\cdot}50$).

Discussion

This large international study of infants diagnosed with bronchiolitis conducted in pediatric EDs of a global consortium of pediatric emergency research networks, demonstrates substantial inter-network and inter-site variation in the use of prescriptions for bronchodilators and corticosteroids at ED discharge. This practice does not appear to be associated with subsequent bronchiolitis-related ED re-visits and hospitalizations. Most infants treated with inhaled salbutamol/albuterol in the ED received prescriptions to continue this medication after discharge home.

Several factors may have contributed to these results. Previous evidence shows a lack of benefit associated with the use of both salbutamol/albuterol and corticosteroids in bronchiolitis.[9,10,35-38,49-51] However, successful dissemination and implementation efforts require multidisciplinary and multi-faceted strategies which may take many years to successful fruition.[52,53] Interestingly, the direction of research evidence is an important factor in the implementation of results: trial results with lack of treatment benefit tend to carry less impact on clinical ED practice than positive results.[54] This phenomenon may in part account for the challenge to curtail the use of medications in bronchiolitis, which are clearly beneficial in diseases with a similar phenotype such as asthma.

It is important to highlight the high "non-intervention" rates in the UK & Ireland and in Australia & New Zealand compared to North America. While the reasons for these disparities remain uncertain, they are likely multifactorial. Notably, the bronchiolitis clinical practice guidelines in the UK& and Australia have traditionally encouraged physicians not to use bronchodilators[5,8] However, this recommendation only became firm in the US guidelines in 2014.[9] Furthermore, the Australasian guideline goes one step further and explicitly discourages bronchodilator use in young infants with bronchiolitis who also have a personal or family history of atopy[13] The clinical diagnosis of bronchiolitis in Australia & New Zealand permits multiple presentations within the first two years of life, and trials of salbutamol there are usually confined to older patients presenting with subsequent episodes of bronchiolitis-like phenotype.

In addition, the practice of paediatric emergency medicine in the UK also appears to be generally less intervention-intensive compared to Canada.[55]

Because selective use of β_2 agonists in bronchiolitis does not improve clinical outcomes[3-12,49-51] most albuterol-treated infants could reasonably have been expected to have been discharged home without these medications. However, this was not the case. It is unlikely that any of the study infants diagnosed with bronchiolitis had their first episode of asthma, as this diagnosis is rare in infants <12 months of age and we mitigated this possibility by strictly adhering to the conservative and specific American Academy of Pediatrics (AAP) definition of bronchiolitis.[9,10,25] A plausible explanation for the continued use of albuterol after discharge may be perceived benefit of the trial of β_2 agonists in the ED due to the bias of the treating physician. The physicians knew which children had been treated and may have anticipated some related therapeutic value in the ED or after discharge home.[33,56] Furthermore, the study cohort was treated just before the publication of the most recent AAP, NICE and Australasian bronchiolitis guidelines which do not advocate for a trial of inhaled bronchodilators.[3,5,9] Therefore, current use of bronchodilators may be lower than that detected in our study.

There are few published studies specifically addressing the use of pharmacotherapy prescriptions at ED discharge in bronchiolitis. Most studies which report data on the use of medications after medical encounters for bronchiolitis focus on other objectives, targeted different populations and have utilized other study designs.[20,32-34] For example, one study focused on ethnic differences in bronchiolitis management and reported much higher ongoing corticosteroid use with Hispanic children.[32] However, hospitalized infants up to 2 years of age were included, some of whom may have had a history of recurrent wheezing.[32] Both of these characteristics augment the probability of alternate diagnoses such as asthma.[57] In a further study of bronchiolitis management in Canadian community hospitals the authors report a much higher use of pharmacotherapy compared to the current study: 36% of discharged infants left the ED with inhaled bronchodilators, 10% with oral corticosteroids and 15% were prescribed

inhaled corticosteroids.[20] In contrast to the mainly tertiary care pediatric EDs participating in the current study, physicians in community hospitals may have less access to treatment guidelines[58] and may be less familiar with recent literature regarding bronchiolitis management.[20,59] A small U.S. study found that virtually all infants with bronchiolitis without a clinical response to albuterol in the ED had orders to continue albuterol during hospitalization and the majority of those without inpatient response to albuterol were discharged with albuterol for home use.[33] Our study confirms frequent continued use of ineffective medications in bronchiolitis at a global level.

A prospective bronchiolitis study at 30 EDs within the United States found no association between unscheduled visits following discharge from the ED and pharmacotherapy used within one week of the re-visit.[48] While that study did not specifically focus on medications prescribed at ED discharge, our study confirms this lack of association on an international scale and also highlights that the receipt of prescriptions for bronchodilators and corticosteroids does not affect subsequent hospitalizations for bronchiolitis.

While the current study found a relatively low overall rate of pharmacotherapy prescription use at ED discharge, there remains room for improvement, especially in North America and Spain & Portugal. While the bronchiolitis guidelines aim to minimize overtreatment,[3-12] future elaboration of guidelines on discharge management may be beneficial. Implementation of the evidence-based quality improvement strategies, clinical practice pathways and quality collaboratives[22,60,61,62] targeted for ED practice may also help us improve bronchiolitis care. A recent multi-center U.S. quality improvement study reported lower rates of bronchodilator use than the U.S. rates detected in our study, with some study sites reaching achievable benchmark of bronchodilator administration approaching the rate attained in the U.K. These quality improvement efforts indicate ongoing fruitful U.S. efforts to decrease the use of non-effective medications.[63]

Furthermore, experts have recently identified the need for research of multicomponent de-implementation strategies for limiting the use of ineffective health care practices. These include electronic clinical decision support systems, pay-for-performance feedback, and close collaboration among all relevant stakeholders, including Choosing Wisely and Canadian De-prescribing Network.[40,42,64-66] Achievable benchmarks of care parameters have also been recommended to minimize unnecessary bronchiolitis care.[67] It is possible that the less-interventional approach to bronchiolitis management adopted by colleagues in the United Kingdom & Ireland and Australia & New Zealand may indeed reflect this benchmark standard to minimize the continued use of ineffective medications in bronchiolitis elsewhere.

Because this was an analysis of an existing database, certain study limitations exist. An important limitation is the reliance on a documented diagnosis of bronchiolitis. While we have used the definition of bronchiolitis suggested by the AAP, the details of this definition vary internationally to some extent. Therefore, some bronchiolitis cases may have received other diagnoses and may have been missed in the study. Furthermore, some historical, clinical and management variables may also not have been accurately captured. The retrospective design precluded us from ascertaining if some return visits have occurred outside of the participating hospitals. Missing data introduced another limitation. However, the multiple imputation correction did not change the study results.This suggests that the pattern of missing data did not result in a major systematic bias.[68]

Missing data on atopy precluded us from adjustment of the analyses for this variable. While previous bronchiolitis studies show lack of association between the effect of bronchodilators and corticosteroids and atopy,[35,44] information about atopy may have influenced prescribing practices at ED discharge. We have used a 21-day interval to define return visits for the index bronchiolitis episode. While this time frame should have been long enough for follow-up of the initial illness,[44,45] some returning patients may have had a new infection with a different virus strain rather than persistent infection from the same virus

strain.[69] Finally, this study was performed in a modest number of pediatric EDs within each country and the results may not be representative of all infants with bronchiolitis within a given region.

In conclusion, in this multicenter, multi-national study, we found that substantial use of ineffective medications in infants with bronchiolitis at ED discharge is common, with marked practice differences between countries and EDs. Prescribing pharmacotherapy was not associated with the likelihood of bronchiolitis-related ED re-visits and subsequent hospitalizations. Given the global magnitude of this practice, the high prevalence of bronchiolitis and global fiscal health care realities, these results emphasize the need for enhanced knowledge translation and de-implementation efforts to optimize and unify the management of bronchiolitis.

Research in context

Evidence before this study

Bronchiolitis is a common illness in infancy and the leading cause of infant hospitalization in the Western world. Previous work suggests that pharmacotherapy does not change the clinical course of bronchiolitis, and its use has been discouraged by professional societies worldwide. However, many clinicians continue to administer medications to infants with bronchiolitis, with marked international practice variation and substantial healthcare costs. Although infants with bronchiolitis seeking Emergency Department (ED) care often receive non-recommended pharmacotherapy while in the ED, there is a substantial knowledge gap regarding the practice patterns of prescriptions for non-recommended medications at ED discharge. On June 28th 2018 we carried out a PubMed search using the following search terms: “bronchiolitis/viral bronchiolitis” plus “bronchodilators” or “corticosteroids” plus “patient discharge” or “hospital /emergency discharge”, “patient re-admission/re-hospitalization,” “infant” in the Ovid Medline and EMBASE databases. We found 4 articles which reported documented the use of these medications for bronchiolitis at discharge from medical encounters. However, these

articles focused on hospitalized infants, community EDs, and outpatient clinic practices, and none examined the use of discharge pharmacotherapy in more than one country. Eleven other articles described the use of pharmacotherapy in the ED or inpatient setting. We found no studies of bronchiolitis that reported the use of bronchodilators or corticosteroids at discharge from pediatric EDs at an international level.

Added value of this study

This multi-national study provides a comprehensive assessment of the variation and disparity in the pharmacological management of acute bronchiolitis in infants discharged from ED care across five national research networks in eight countries on three continents. To our knowledge, this is the first study comparing ED discharge treatment practices of infant bronchiolitis globally, employing all available data from established collaborative ED networks. Our findings will inform future global practice to de-prescribe non-effective medications in bronchiolitis and de-implement the use of non-recommended interventions, in an effort to unify and improve the standards and decrease the cost of care of infants with bronchiolitis. Lower use of pharmacotherapy at ED discharge in bronchiolitis would also decrease the potential for treatment-related adverse events and minimize parental expectations of benefit from non-indicated medications.

Implications of all the available evidence

Substantial use of ineffective medications in infants with bronchiolitis at ED discharge is common, with marked practice differences between countries and EDs. The continued use of ineffective treatments emphasizes the need for enhanced knowledge translation and de-implementation efforts to optimize and unify the management of bronchiolitis. Further research into supportive bronchiolitis management strategies, such as clarifying the benefit of non-pharmacologic therapies, may also be beneficial.

Author Contributions

Dr. Jamal conceived the study, co-wrote the study protocol and wrote the manuscript.
Dr. Finkelstein helped design the study, provided major input into the concept and analysis of the study and drafting and revision of the manuscript.
Dr Kuppermann designed the study, provided major input into the concept and analysis of the study and drafting and revision of the manuscript.
Dr Freedman designed the study, provided major input into the concept and analysis of the study and drafting and revision of the manuscript.
Dr Florin designed the study, provided major input into the concept and analysis of the study and drafting and revision of the manuscript.
Dr. Babl designed the study, drafted the manuscript and revised it for intellectual content.
Dr. Dalziel designed the study, drafted the manuscript and revised it for intellectual content.
Dr. Zemek designed the study, provided major input into the concept and analysis of the study and drafting and revision of the manuscript.
Dr. Plint designed the study, drafted the manuscript and revised it for intellectual content.
Dr. Steele designed the study, drafted the manuscript and revised it for intellectual content.
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Dr. Johnson designed the study, drafted the manuscript and revised it for intellectual content.
Mr. Stephens conducted the analysis and revised the manuscript for intellectual content.
Dr. Kharbanda designed the study, drafted the manuscript and revised it for intellectual content.
Dr Rolland designed the study, drafted the manuscript and revised it for intellectual content.
Dr. Lyttle designed the study, drafted the manuscript and revised it for intellectual content.
Dr. Macias designed the study, provided extensive database support, drafted the manuscript and revised it for intellectual content.
Dr. Fernandes designed the study, drafted the manuscript and revised it for intellectual content.
Dr. Benito designed the study, drafted the manuscript and revised it for intellectual content.
Dr. Schuh conceived the study, co-wrote the study protocol, wrote the manuscript and revised it critically for intellectual content

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