Open access Original research

BMJ Open International variation in evidencebased emergency department management of bronchiolitis: a retrospective cohort study

Marie-Pier Lirette, ^{1,2} Nathan Kuppermann, ^{3,4} Yaron Finkelstein, ^{1,5} Roger Zemek , ^{6,7} Amy C Plint, ^{6,7} Todd Adam Florin , ^{8,9} Franz E Babl , ^{10,11} Stuart Dalziel, ^{12,13} Stephen Freedman , ^{14,15} Damian Roland, ^{16,17} Mark David Lyttle , ^{18,19} David Schnadower, ²⁰ Dale Steele , ^{21,22} Ricardo M Fernandes, ^{23,24} Derek Stephens, ⁵ Anupam Kharbanda, ²⁵ David W Johnson, ^{15,26} Charles Macias, ^{27,28} Javier Benito, ²⁹ Suzanne Schuh , ^{5,30} for the Pediatric Emergency Research Networks (PERN)

To cite: Lirette M-P. Kuppermann N, Finkelstein Y, et al. International variation in evidence-based emergency department management of bronchiolitis: a retrospective cohort study. BMJ Open 2022;12:e059784. doi:10.1136/ bmjopen-2021-059784

Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi. org/10.1136/bmjopen-2021-059784).

Received 02 December 2021 Accepted 02 February 2022

Check for updates

@ Author(s) (or their employer(s)) 2022. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by

For numbered affiliations see end of article.

Correspondence to

Dr Suzanne Schuh: suzanne.schuh@sickkids.ca

ABSTRACT

Objectives We aimed to evaluate the international variation in the use of evidence-based management (EBM) in bronchiolitis. We hypothesised that management consistent with full-EBM practices is associated with the research network of care, adjusted for patient-level characteristics. Secondary objectives were to determine the association between full-EBM and (1) hospitalisation and (2) emergency department (ED) revisits resulting in hospitalisation within 21 days.

Design A secondary analysis of a retrospective cohort

Setting 38 paediatric EDs belonging to the Paediatric Emergency Research Network in Canada, USA, Australia/ New Zealand UK/Ireland and Spain/Portugal.

Patients Otherwise healthy infants 2-11 months old diagnosed with bronchiolitis between 1 January 2013 and 31 December, 2013.

Outcome measures Primary outcome was management consistent with full-EBM, that is, no bronchodilators/ corticosteroids/antibiotics, no chest radiography or laboratory testing. Secondary outcomes included hospitalisations during the index and subsequent ED visits. Results 1137/2356 (48.3%) infants received full-EBM (ranging from 13.2% in Spain/Portugal to 72.3% in UK/ Ireland). Compared with the UK/Ireland, the adjusted ORs (aOR) of full-EBM receipt were lower in Spain/Portugal (aOR 0.08, 95% CI 0.02 to 0.29), Canada (aOR 0.13 (95% CI 0.06 to 0.31) and USA (aOR 0.16 (95% CI 0.07 to 0.35). EBM was less likely in infants with dehydration (aOR 0.49 (95% CI 0.33 to 0.71)), chest retractions (aOR 0.69 (95% CI 0.52 to 0.91)) and nasal flaring (aOR 0.69 (95% CI 0.52 to 0.92)). EBM was associated with reduced odds of hospitalisation at the index visit (aOR 0.77 (95% CI 0.60 to 0.98)) but not at revisits (aOR 1.17 (95% CI 0.74 to 1.85)). Conclusions Infants with bronchiolitis frequently do not receive full-EBM ED management, particularly those outside of the UK/Ireland. Furthermore, there is marked variation in full-EBM between paediatric emergency networks, and full-EBM delivery is associated with lower

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ While studies have examined international variation of specific aspects of bronchiolitis care, there is lack of data on the international use of practices consistent with full-evidence-based management for bronchiolitis and related association with patient outcomes.
- ⇒ Use of a large international database with patientlevel data optimises generalisability of the results, enables adjustment of the associations for disease severity and provides data for emergency department-based international deimplementation strategies of low-value bronchiolitis interventions.
- ⇒ A large sample size provides high statistical precision.
- ⇒ Use of the international standards for retrospective chart reviews and the methodology to select records and to blind abstractors from the study hypotheses minimises the selection and ascertainment biases.
- ⇒ While this database was collected in 2013, the definition of the optimal bronchiolitis management used in this study remains the treatment target to this day: experts currently continue to convey the need for intensive de-implementation of low-value bronchiolitis care to enhance the adoption of bestpractice management of bronchiolitis.

likelihood of hospitalisation. Given the global bronchiolitis burden, international ED-focused deimplementation of non-indicated interventions to enhance EBM is needed.

INTRODUCTION

Reducing unnecessary medical interventions is a global priority, enhanced by the current pandemic crisis.² The Choosing Wisely initiative has prioritised healthcare and reduced the use of ineffective interventions.



Bronchiolitis, the leading cause of emergency department (ED) visits and hospitalisations in infants,³ has an asthma-like phenotype and many world regions and hospitals have previously adopted asthma-related interventions in bronchiolitis. Because subsequent evidence demonstrated that routine pharmacotherapy,⁴ chest radiography⁵ and laboratory testing⁶ have no proven benefit in bronchiolitis management, the standard of bronchiolitis care consists of oxygen therapy, airway support and hydration.⁷⁸ Because of the practice vs evidence disparity, we are now faced with the challenging task to 'deimplement' various unwarranted bronchiolitis interventions.⁹

To this effect, the uptake of the best bronchiolitis management evidence into clinical practice in the ED is suboptimal. Bronchiolitis management guidelines universally emphasise supportive management quidelines universally emphasise supportive management quality improvement (QI) experts endorse this goal. Furthermore, a Paediatric Health Information Systems database bronchiolitis study from the USA demonstrated a decrease in ED bronchodilator use but no associated reduction in hospitalisation, supporting the American Academy of Pediatrics recommendation to limit routine administration of bronchodilator in bronchiolitis. Nonetheless, many institutions continue to use nonevidence-based approaches, which lead to undue patient morbidity and places a significant burden on healthcare systems worldwide.

While studies have examined international variation of specific aspects of bronchiolitis care, ^{6 10 19} there is lack of data regarding the international use of best practices for bronchiolitis. Given the substantial healthcare consumption and financial burden of bronchiolitis, such knowledge can be used to optimise resource use and healthcare outcomes through focused deimplementation strategies of low-value interventions.⁹

We conducted a planned secondary analysis of a multicentre, multinational, retrospective cohort study of infants with bronchiolitis who presented to the EDs associated with five Paediatric Emergency Research Networks (PERN) in Canada, the USA, Spain/Portugal, the UK/ Ireland and Australia/New Zealand who are members of the PERN.²⁰ The primary objective was to evaluate the variation across research networks in evidence-based bronchiolitis management (EBM) in the EDs. We hypothesised there would be an association between management consistent with full-EBM and the research network where the infants were treated. Secondary objectives were to examine the association between full-EBM provision and (A) hospitalisation at the index ED visit and (B) return ED visit for bronchiolitis within 21 days resulting in hospitalisation.

METHODS

Study design and population

We conducted a multicentre retrospective cohort study of previously healthy infants 2–11 months old with bronchiolitis in 38 PERN EDs. The PERN is an international umbrella network with these individual networks: the Pediatric Emergency Research Canada (PERC), the Pediatric Emergency Medicine Collaborative Research Committee (PEM-CRC) and the Pediatric Emergency Care Applied Research Network (PECARN) in the USA, the Paediatric Research in Emergency Departments International Collaborative (PREDICT) in Australia and New Zealand, the Paediatric Emergency Research UK and Ireland (PERUKI) and the Research in European Pediatric Emergency Medicine (REPEM) network in Spain and Portugal. ¹⁰

Infants with bronchiolitis, defined a priori as the first presentation of respiratory distress with a viral respiratory tract infection, who presented to the PERN EDs between 1 January2013 and 31 December 2013 were included in the study. 8 Infants previously enrolled or diagnosed with bronchiolitis more than 1 month prior to the index ED visit were excluded, as were infants with known congenital heart disease, coexistent chronic lung disease, liver or kidney disease, immunodeficiency, neuromuscular, neurological or bone disease, and those with metabolic or genetic conditions. To maximise generalisability of the study results, we have included infants with a history of prematurity who had healthy lungs. Because febrile infants less than 2 months old with viral infections have non-negligible risks for serious bacterial infections, we limited this study to infants 2 months of age or older.²¹ Bronchiolitis diagnosis in infants aged 12 months and older may overlap with asthma, and we have therefore excluded this age group.²²

Study protocol

Patient study data were collected according to international standards for retrospective chart reviews. ²³ All study variables were defined a priori and itemised in a manual of operations with a source hierarchy for all data points. To standardise data extraction across networks, site investigators were educated in site-specific and study-specific terms for the collection of individual variables. Site investigators also trained local study staff in study procedures and were responsible that data were recorded according to the manual of operations.

Potentially eligible patients were identified by searching the medical record for ED discharge diagnoses of bronchiolitis or respiratory syncytial virus infection (International Classification of Disease 10 or 9 codes J 21.0, 21.8, 21.9 or 466.1). Because of the large number of bronchiolitis cases seen at each participating institution, we aimed to select a random sample of bronchiolitis cases at each site ED. Potentially eligible infants were therefore randomly identified, by a random number generating programme, for medical record review. Because the charts to be reviewed for eligibility and subsequent review were identified at random, there was a low probability of a selection bias. The chart reviewers were aware that the study concerned bronchiolitis management but were unaware of specific hypotheses and details about what the optimal bronchiolitis management consisted of. Therefore, it is unlikely



that the cases who received full-EBM were selected preferentially, and a significant ascertainment bias was not probable.

Abstracted data included patient demographics, presenting symptoms, physical examination findings, laboratory and radiographic investigations, medications administered in the ED and prescribed at ED discharge, disposition and return ED visits for bronchiolitis within 21 days, with and without hospitalisation.

Outcome measures

The primary outcome measure was receipt of management consistent with full-EBM in the ED, as per the recommendations by national bronchiolitis guidelines.^{7 8 11-16} With the exception of some guidelines allowing a monitored trial of bronchodilators/epinephrine in select infants, 11 12 14 16 the message to minimise pharmacotherapy and testing has been common to all national bronchiolitis guidelines published since 2006.^{7 8 11-16} Therefore, full-EBM was a priori defined as receipt of none of the following in the ED and, when relevant, no prescription for such at ED discharge: inhaled bronchodilators, hypertonic saline or epinephrine, systemic or inhaled corticosteroids, antibiotics in the absence of a documented bacterial infection (eg, suspected sepsis, otitis media, urinary tract infection, pneumonia), chest radiography unless the infant was admitted to the intensive care unit (ICU), nasopharyngeal viral testing unless the infant was hospitalised (cohorting reasons), blood tests, urinalyses in afebrile infants (temperatures <38.0°C in ED triage) and urine cultures in those with fever (temperature \geq 38.0°C in triage) who were \geq 3 months old. Secondary outcomes included (A) hospitalisation from the ED at the index ED visit and (B) return ED visits for bronchiolitis within 21 days of the initial discharge home resulting in hospitalisation.

Analyses

We sought to have $\geq 80\%$ power at a 5% significance level to assess the association between EBM and the network. Based on previous international studies, we estimated that 30% of patients would receive full-EBM. ^{6 10 19} Assuming a requirement of 20 patients with the outcome of interest for each of the 12 independent predictor variables examined, we aimed to include at least 240 patients with full-EBM. ²⁴

Participant characteristics were analysed with descriptive statistics, using proportions and 95% CI for categorical data, means with SD for normally distributed continuous data and medians with IQR for continuous data with non-normal distributions. The two US networks were treated as a single network, to ensure no participants were counted twice.

Bivariable logistic regression was used to examine the association between each candidate predictor variable and full-EBM. These variables were selected because of their plausible association with EBM and adopted from previous studies of bronchiolitis practice patterns. ⁶ 10 19

They included the research network, poor feeding, documented dehydration, nasal flaring/grunting, chest retractions, oxygen saturation in triage in room air, respiratory rate and apnoea. We performed multivariable logistic regression analysis to determine independent associations between full-EBM as a binary dependent variable and the candidate predictor variables. Because management by full-EBM was likely correlated with individual EDs, we incorporated the ED as a random effect. We also used multiple logistic regression analyses to examine the association between full-EBM and (A) hospitalisation for bronchiolitis at the index ED visit, (B) ED revisits for bronchiolitis within 21 days resulting in hospitalisation, adjusted for network and disease severity.

Missing data were managed using listwise deletion, as the amount of missing data was minimal (<5%). Overall significance was set at an alpha level 0.05 (two sided). Statistical analysis was performed using version SAS V.9.4 system for Windows and PROC GLIMMIX (SAS Institute).

Patient and public involvement

Because this was a retrospective study with no patient identifiers, this aspect does not apply.

RESULTS

Study population

A total of 5205 potentially eligible infants were identified, of whom 2183 (41.9%) met exclusion criteria, leaving 3022 eligible participants. Of these, 2356 (80%) infants had full data on all variables and constituted the study population. These included 476 (20%) infants treated at eight Canadian paediatric EDs (PERC), 717 (30.4%) at ten EDs in the USA (PEM-CRC and PECARN), 496 (21.0%) at eight EDs in Australia/New Zealand (PREDICT), 591 (25.1%) at nine EDs in UK/Ireland (PERUKI) and 76 (3.2%) infants at three EDs in Spain/Portugal (REPEM). Of the 2356 study infants, 1550 (65.8%) were discharged home from the ED, 769 (32.6%) were admitted to an inpatient unit and 37 (1.6%) to ICU. Demographic and clinical characteristics of the infants are summarised in table 1.

Evidence-based management

A total of 1137/2356 (48.3%) infants received management consistent with full-EBM. The proportions of infants receiving EBM were 152/476 (31.9%) in Canada, 242/717 (33.8%) in the USA, 306/496 (61.7%) in Australia/New Zealand, 427/591 (72.3%) in the UK/Ireland and 10/76 (13.2%) in Spain/Portugal. The proportional use of full-EBM at individual EDs ranged from 3.2% to 87.0% (median 28.8%; IQR 8.0%–81.0%).

Receipt of full-EBM was less likely in severe bronchiolitis and more likely in infants managed in the UK/Ireland and Australia/New Zealand (table 2). In the multivariable analysis, delivery of full-EBM was more common in well-hydrated infants without nasal flaring/grunting or



Table 1 Demographic and clinical characteristics of the study population

	Networks						
Variables	Canada N=476	USA N=717	Australia New Zealand	UK Ireland N=591	Spain Portugal		
					-		
Age (months)*	5.3±2.7	5.2±2.5	5.8±2.7	5.1±2.6	4.4±2.7		
Temperature °C	37.5±0.8	37.6±0.0	37.0±0.8	37.0±0.8	37.9±1.1		
History of poor feeding	304 (63.9)	343 (47.8)	274 (55.1)	341 (57.6)	33 (43.4)		
Chest retractions	305 (64.1)	536 (74.7)	434 (87.3)	375 (63.3)	61 (80.3)		
Respiratory rate (bpm)†	48.0±13.0	50.1±13.0	49.6±12.2	46.7±11.1	52.9±10.1		
Oxygen saturation (%)*	96.8±3.6	96.6±3.3	97.0±2.8	97.3±2.6	96.9±2.4		
Reported/observed apnoea	24 (5.0)	39 (5.4)	31 (6.2)	29 (4.9)	1 (1.3)		
Dehydration	50 (10.5)	61 (8.5)	76 (15.3)	30 (5.1)	0 (0.0)		
Nasal flaring/grunting	82 (17.2)	152 (21.2)	87 (17.5)	37 (6.3)	8 (10.5)		
Suspected bacterial infection	38 (8.0)	116 (16.2)	29 (5.8)	29 (4.9)	12 (15.8)		

Data are (n, %).

*Mean±SD.

†breaths per minute (bpm)

chest retractions and was inversely associated with oxygen saturation (table 2).

After adjusting for patient-level variables, the use of full-EBM varied widely and was significantly higher in the UK/Ireland than in Canada, the USA or Spain/Portugal (table 2, figure 1). Compared with the UK/Ireland, the odds of EBM were 92% lower in Spain/Portugal, 87%

lower in Canada, 84% lower in the USA and 25% lower in Australia/New Zealand (table 2).

EBM and hospitalisation at Index ED visit

The hospitalisation rates were 216/496 (43.5%) in Australia/New Zealand, 33/76 (43.4%) in Spain/Portugal, 273/717 (38.1%) in the USA, 174/591 (29.4%)

Table 2	Association	between	evidence-	based	management	and	patient	characteristics
---------	-------------	---------	-----------	-------	------------	-----	---------	-----------------

Variables	Evidence-based management (EBM) N=1137	No evidence-based management N=1219	Bivariate OR 95% CI	Multivariable OR 95% CI	Multivariable p value
Reported poor feeding N (%)	612 (53.8)	683 (55.9)	0.78 (0.65 to 0.95)	0.99 (0.80 to 1.22)	0.89
Respiratory rate in ED (bpm)*	47.8 (11.6)	49.7 (13)	1.05 (1.02 to 1.10)	0.99 (0.95 to 1.04)	0.82
Oxygen saturation in ED (%)*†	97.3 (2.5)	96.5 (3.5)	0.89 (0.86 to 0.92)	0.91 (0.88 to 0.95)	0.0001
Dehydration in ED*	70 (6.2)	147 (12.0)	0.39 (0.28 to 0.56)	0.49 (0.33 to 0.71)	0.0002
Nasal flaring/grunting	116 (10.2)	250 (20.5)	0.54 (0.41 to 0.71)	0.69 (0.52 to 0.92)	0.012
Apnoea	50 (4.4)	74 (6.1)	0.68 (0.45 to 1.03)	0.78 (0.49 to 1.23)	0.28
Chest retractions	782 (75.6)	929 (82.3)	0.56 (0.43 to 0.72)	0.69 (0.52 to 0.91)	0.008
Country					<0.0001
Canada			0.18 (0.14 to 0.24)	0.13 (0.06 to 0.31)	<0.0001
USA			0.20 (0.16 to 0.25)	0.16 (0.07 to 0.35)	<0.0001
Australia and New Zealand			0.62 (0.48 to 0.80)	0.75 (0.32 to 1.77)	0.52
UK and Ireland			Reference	Reference	Reference
Spain and Portugal			0.06 (0.03 to 0.12)	0.08 (0.02 to 0.29)	0.0001

Data are n (%).

*Mean (±SD).

†For every 1% decrease in saturation below 100%, multivariable odds of EBM decreased by 9%.

bpm, breaths per minute; ED, emergency department.

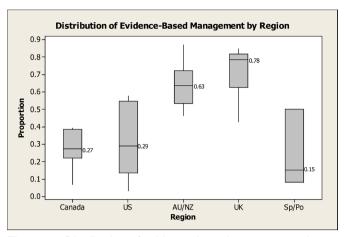


Figure 1 Distribution of evidence-based management by country. Proportions in boxes indicate medians and IQRs. AU/NZ, Australia/New Zealand; Sp/Po, Spain/Portugal.

in the UK/Ireland and 110/476 (23.1%) in Canada. After adjustment for patient-level characteristics and the network, infants with full-EBM had 23% lower odds of hospitalisation than those without full-EBM (table 3). There was no significant association between hospitalisation for bronchiolitis and the network (table 3).

EBM and **ED** revisits with hospitalisation

Of the 1550 discharged infants, 153 (9.9%) returned to the ED within 21 days and were hospitalised at the return visit. The proportions of children with revisits requiring hospitalisation were 66/417 (15.8%) in the UK/Ireland, 5/38 (13.2%) in Spain/Portugal, 27/280 (9.6%) in Australia/New Zealand, 37/444 (8.3%) in the USA and 18/366 (4.9%) in Canada. After adjustment for patient-level variables and the network, there was no significant

association between full-EBM and hospitalisation at the return visit (OR 1.17 (95% CI 0.74 to 1.85), p=0.50).

DISCUSSION

In this large international study, we demonstrated that infants with milder bronchiolitis and those managed in the UK/Ireland were more likely to receive full-EBM compared with infants with more severe disease and those treated in EDs in North America or Spain/Portugal. After adjustment for patient-level variables, infants with bronchiolitis given full-EBM were less likely to be hospitalised. However, EBM was not associated with an increased risk of subsequent hospitalisations.

A substantial proportion of infants with bronchiolitis did not receive full-EBM. Understanding the clinicians' decision-making process represents a critical component in improving overall evidence-based care. A qualitative study highlighted severity of illness as an important element influencing practice variation and illustrated that many clinicians were more comfortable 'doing less' when caring for well-appearing infants. The findings of our study underscore this concept.

Infants in the UK/Ireland had the highest rates of full-EBM. While this phenomenon is likely multifactorial, medical, cultural and societal differences between countries appear to have an important effect. ²⁶ ²⁷ Management approaches in North America favour overtreatment, ¹⁰ ²⁷ reflecting a perceived need to 'do something'. For example, in a cross-sectional study comparing practice patterns in the management of febrile neonates with bronchiolitis in Canada to those in UK/Ireland. British and Irish clinicians claimed to be more

Variable N (%)	Hospitalisation N=806	No hospitalisation N=1550	Bivariate OR (95% CI)	Multivariable OR (95% CI)	P value
Evidence-based management	337 (41.8)	799 (51.6)	0.57 (0.46 to 0.71)	0.77 (0.60 to 0.98)	0.03
Oxygen saturation*† (%)	96.6±4.0	97.6±2.1	1.35 (1.30 to 1.41)	1.31 (1.25 to 1.37)	< 0.0001
Nasal flaring/grunting	211 (26.2)	155 (10.0)	3.69 (2.82 to 4.84)	2.60 (1.92 to 3.51)	<0.0001
Apnoea	79 (9.8)	44 (2.8)	3.99 (2.60 to 6.12)	4.34 (2.61 to 7.21)	< 0.0001
Chest retractions	716 (92.3)	993 (71.7)	4.94 (3.59 to 6.81)	3.32 (2.36 to 4.67)	<0.0001
Poor feeding	541 (67.1)	753 (48.6)	2.47 (2.01 to 3.03)	1.87 (1.46 to 2.38)	<0.0001
Country					0.85
Canada			reference	reference	
USA			1.78 (0.52 to 6.11)	1.67 (0.46 to 5.98)	0.36
Australia/New Zealand			1.92 (0.52 to 7.12)	1.96 (0.50 to 7.63)	0.33
UK/Ireland			1.00 (0.28 to 3.55)	1.49 (0.40 to 5.57)	0.99
Spain/Portugal			1.92 (0.30 to 12.15)	2.49 (0.37 to 16.91)	0.49



comfortable in omitting a lumbar puncture while their Canadian colleagues were more risk averse.²⁷

The observed practice variation may also be explained in part by differences in judicial and financial systems. Clinicians in the USA often face higher liability risks, which may lead to the practice of 'defensive medicine'.²⁸ In contrast, the National Health Service in the UK compels clinicians to consider resource utilisation and interventions may therefore differ.²⁹ Different sources of practice guidelines may also play a role in guideline adherence. For example, the UK guidelines are published by the National Institute for Health and Care Excellence which, as an agency of the National Health Service, may carry more influence than national specialty societies elsewhere. However, pay-for-performance systems rewarding institutions meeting specific quality metrics are being introduced in North America, which will likely lead to enhanced evidence-based care.

We also found that infants with full-EBM were less likely to be hospitalised, independent of bronchiolitis severity. Chest radiography represents one of the most frequently employed non-evidence-based interventions in bronchiolitis, ⁶ and is associated with frequent false-positive diagnoses of pneumonia and unwarranted antibiotic use. ⁵ ⁶ Clinicians may be more inclined to hospitalise infants with radiographic findings for observation or for intravenous antibiotics, which may in part explain the association between full-EBM and lower hospitalisation rates found in our study. ³⁰

Several strategies help enhance provision of EBM in bronchiolitis. Characteristics of guideline recommendations are known to be associated with guideline uptake³¹ and improve EBM of bronchiolitis. 32 For example, the Australian guidelines explicitly include infants with atopy in their recommendation against inhaled β_0 agonists. 15 However, guideline publication alone does not necessarily result in practice change, 32 highlighting a need for robust multifaceted QI initiatives in the ED,³ which are highly effective in improving adherence to national recommendations.³³ ³⁴ A large QI study in the USA demonstrated improved ED performance in the management of bronchiolitis, with rates of non-effective interventions approaching those reported in the UK.³⁴ A redesign of a bronchiolitis clinical pathway and order set which specifically recommends against therapies and tests rather than just removing them has been recently shown to lead to a substantial decrease in bronchodilator use in bronchiolitis in the USA, without negative impact on other outcome measures.³⁵

Because of associated system and behavioural challenges, widely adopted use of low-value care is difficult to deimplement. The international variation found in this study may reflect that some practices, such as bronchodilator use, were never adopted in some countries, while other regions are making slow progress to remove them. To this effect, experts suggest employment of multifaceted approaches involving both system-based and family-centred interventions. Two recent USA Paediatric

Health Information Systems database studies demonstrate a decreasing trend in the use of bronchodilators and other interventions in bronchiolitis since the publication of the 2014American Academy of Pediatrics guideline, without associated change in outcomes. 18 38 The authors attribute this emerging success to increasing guideline uptake based on reinforcement of the AAP guidelines in clinical pathways, higher awareness of healthcare overuse and adoption of Choosing Wisely measures. 38 39 International deimplementation strategies are also essential for wide-ranging adoption of bronchiolitis best practices. 40 A recent cluster randomised trial from Australia and New Zealand represents the first international effort showing that targeted interventions addressing factors influencing bronchiolitis management can successfully deimplement unnecessary care.41

This study has several limitations. The specifics of our definition of bronchiolitis vary between countries and some cases may have been assigned alternate diagnoses. Because this database was collected before the most recent guideline updates, ^{7 8 14 15} the current variation in EBM may be smaller. However, the practice reported in this study occurred 7 years after publication of major bronchiolitis guidelines from the USA, the UK, Australia and Spain, 11 13 16 with attendant evidence of substantial practice variation after the 2006 guideline publication. 42 Evidence confirms that the interval of evidence-to-practice translation is decades-long.⁴⁰ While there has been a decrease in the use of several non-recommended bronchiolitis interventions since the most recent guideline update in the USA, 18 38 experts convey continued need for improved deimplementation of low-value bronchiolitis care³⁸ to enhance EBM-based practice. The definition of the optimal EBM-based bronchiolitis management used in this study has not significantly changed between the initial and the most recent publication of the USA bronchiolitis guideline, 8 16 and remains the treatment target to this day.³⁸ The retrospective design may have led to some variables being inaccurately captured and some infants discharged home may have been subsequently admitted to other institutions. Our results may not be fully representative of the management of all infants with bronchiolitis within a given region as our study included a limited number of paediatric EDs from each country. This may be particularly true of Spain and Portugal where few EDs participated. In addition, the results of this study are not generalisable to infants younger than 2 months of age whose management is more controversial and who tend to have more severe illness.³² Because of the public health measures related to the current COVID-19 epidemic, there has been a recent temporary shift in respiratory syncytial virus (RSV) epidemiology. 43 Because COVID-19related bronchiolitis may represent a disease with different outcomes, 44 the results of this study may not be fully applicable to that population. However, the best principles of bronchiolitis management remain unchanged.

In this large international study, we found that a significant proportion of infants with bronchiolitis do not



receive full EBM in the ED, particularly those treated outside of the UK/Ireland, with marked practice variation between networks. Provision of full EBM was associated with lower likelihood of hospitalisation. Given the magnitude of the bronchiolitis burden worldwide, these results emphasise the need for enhanced ED-focused international deimplementation efforts to optimise the adoption of best-practice management of bronchiolitis.

Author affiliations

¹Division of Pediatric Emergency Medicine, The Hospital for Sick Children, Toronto, Ontario, Canada

²Department of Pediatrics, University of Toronto, Toronto, Ontario, Canada ³The Departments of Emergency Medicine and Pediatrics, University of California Davis School of Medicine, Sacramento, California, USA

⁴University of California Davis Health System, Sacramento, California, USA
 ⁵Hospital for Sick Children Research Institute, University of Toronto, Toronto, Ontario, Canada

⁶Division of Pediatric Emergency Medicine, Children's Hospital of Eastern Ontario, Ottawa, Ontario, Canada

⁷Division of Pediatric Emergency Medicine, University of Ottawa, Ottawa, Ontario, Canada

⁸Department of Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA

⁹Department of Pediatrics, Ann and Robert H Lurie Children's Hospital of Chicago, Chicago, Illinois, USA

¹⁰Emergency Department, Murdoch Childrens Research Institute, Melbourne, Victoria. Australia

¹¹The University of Melbourne/The Royal Children's Hospital CICH, Parkville, Victoria, Australia

¹²Emergency Department, Starship Children's Health, Auckland, Auckland, New Zealand

¹³Departments of Surgery and Paediatrics: Child and Youth Health, The University of Auckland, Auckland, New Zealand

¹⁴Department of Pediatrics, Sections of Pediatric Emergency Medicine and Gastroenterology, Alberta Children's Hospital Research Institute, Calgary, Alberta, Canada

¹⁵University of Calgary Cumming School of Medicine, Calgary, Alberta, Canada
¹⁶Paediatric Emergency Medicine Leicester Academic (PEMLA) Group, Leicester Royal Infirmary, Leicester, UK

¹⁷SAPPHIRE Group, Health Sciences, University of Leicester, Leicester, UK

¹⁸Emergency Department, Bristol Royal Hospital for Children, Bristol, UK
¹⁹Faculty of Health and Applied Life Sciences, University of the West of England, Bristol, UK

²⁰Division of Emergency Medicine, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA

²¹Pediatric Emergency Medicine, Hasbro Children's Hospital, Providence, Rhode Island, USA

²²Departments of Emergency Medicine, Pediatrics and Health Services, Policy & Practice, Brown University, Providence, Rhode Island, USA

²³Department of Pediatrics, Hospital de Santa Maria, Lisboa, Portugal

²⁴Laboratory of Clinical Pharmacology and Therapeutics, Faculty of Medicine, Universidade de Lisboa Instituto de Medicina Molecular, Lisboa, Portugal

²⁵Department of Pediatric Emergency Medicine, Children's Minnesota, Minneapolis, Minnesota, USA

²⁶Departments of Pediatrics, Emergency Medicine, and Physiology and Pharmacology, Alberta Children's Hospital Research Institute, Calgary, Alberta, Canada

²⁷Division of Pediatric Emergency Medicine, UH Rainbow Babies and Children's Hospital, Cleveland, Ohio, USA

²⁸Case Western Reserve University, Cleveland, Ohio, USA

²⁹Pediatric Emergency Department, Cruces University Hospital, Barakaldo, Spain ³⁰Division of Pediatric Emergency Medicine, The Hospital for Sick Children,

Department of Pediatrics, University of Toronto, Toronto, Ontario, Canada

Twitter Todd Adam Florin @toddflorin1, Damian Roland @damian_roland and Mark David Lyttle @mdlyttle

Acknowledgements We thank Judy Sweeney (RN, BScN) and Maggie Rumantir (MD) for their generous contribution to coordinating this study, Lejla Halilovic (BSc) and Kinza Naeem (BSc) for their administrative assistance with the study and the following PERN colleagues without whom this study couldn't have happened.

Collaborators PECARN: Aderonke O. Adekunle-Ojo, MD (Texas Children's Hospital, Houston, TX): Lalit Baiai, MD, MPH (Department of Pediatrics, Children's Hospital Colorado, Aurora, CO); Daniel Cohen, MD (Nationwide Children's Hospital, Columbus, OH); Marisa Louie, MD (University of Michigan, Ann Arbor, MI); Elizabeth Powell, MD. MPH (Ann and Robert H. Lurie Children's Hospital of Chicago, Chicago, IL): Richard Ruddy, MD (Cincinnati Children's Hospital Medical Centre, Cincinnati, OH); Ashvin Shenoy, MD (School of Medicine, University of California Davis School of Medicine, Sacramento, CA), PERC: Samina Ali, MDCM, FRCP(C) (Stollery Children's Hospital, Edmonton, AB, Canada); Eleanor Fitzpatrick, RN (Izaak Walton Killam Hospital, Halifax, NS, Canada); Serge Gouin, MD, FRCP(C) (Centre Hospitalier Universitaire Saint-Justine Hospital, University of Montreal, Montreal, QC, Canada); Terry P. Klassen, MD, FRCP(C), MSc (Manitoba Institute of Child Health, University of Manitoba, Winnipeg, MB, Canada); Garth Meckler, MD, MSHS, FAAP, FRCP(C) (British Columbia Children's Hospital, Vancouver, BC, Canada); Amita Misir, MD (London Health Sciences Centre Children's Hospital, London, ON, Canada); Judy Sweeney, RN, BScN (The Hospital for Sick Children, Toronto, ON, Canada). PERUKI: Fawaz Arshad, BMBS (Leicester Royal Infirmary Children's Emergency Department, Leicester, UK); Carol Blackburn, MBChB (Our Lady's Children's Hospital, Dublin, Ireland): Eleftheria Boudalaki, Ptychion latrikes (City Hospitals Sunderland National Health Service Foundation Trust, Sunderland, UK); Sian Copley, MBBS (City Hospitals Sunderland National Health Service Foundation Trust, Sunderland, UK); Kathryn Ferris, MB BCh BAO (Royal Belfast Hospital for Sick Children, Belfast, UK); Stuart Hartshorn, MBChir (Birmingham Children's Hospital, Birmingham, UK); Christopher Hine MBChB (Birmingham Children's Hospital, Birmingham, UK); Julie- Ann Maney, MB BCh BAO (Royal Belfast Hospital for Sick Children, Belfast, UK); Fintan McErlean (Royal Belfast Hospital for Sick Children, Belfast, UK); Niall Mullen, MB BCh (City Hospitals Sunderland National Health Service Foundation Trust, Sunderland, UK); Katherine Potier de la Morandiere, MBChB (Royal Manchester Children's Hospital, Manchester, UK); Stephen Mullen, MB BCh BAO (Royal Belfast Hospital for Sick Children, Belfast, UK); Juliette Oakley, MB BCh (The Noah's Ark Children's Hospital for Wales, Cardiff, UK); Nicola Oliver, MBBS (Bristol Royal Hospital for Children, Bristol, UK); Colin Powell, MD (The Noah's Ark Children's Hospital for Wales, Cardiff, UK); Vandana Rajagopal, MBBS (The Noah's Ark Children's Hospital for Wales, Cardiff, UK); Shammi Ramlakhan, MBBS (Sheffield Children's Hospital, Sheffield, UK); John Rayner, MBChB (Sheffield Children's Hospital, Sheffield, UK); Sarah Raywood, MB BCh (Royal Manchester Children's Hospital, Manchester, UK); Damian Roland, MBBS, (Leicester Royal Infirmary Children's Emergency Department, Leicester, UK); Siobhan Skirka, MBChB (Our Lady's Children's Hospital, Crumlin, Dublin, UK); Joanne Stone, MBChB (Sheffield Children's Hospital, Sheffield, UK). PREDICT: Meredith Borland, MBBS, FRACGP, FACEM (Princess Margaret Hospital for Children, Perth, WA, Australia); Simon Craig, MBBS (Monash Medical Centre, Melbourne, VIC, Australia); Amit Kochar, MD (Women's and Children's Hospital, Adelaide, SA, Australia); David Krieser, MBBS (Sunshine Hospital, St Albans, VIC, Australia); Cara Lacey, MBBS (Sunshine Hospital, St Albans, VIC, Australia); Jocelyn Neutze, MBChB (Middlemore Hospital, Auckland, New Zealand); Karthikeyan Velusamy, MD (Townsville Hospital, Douglas, QLD, Australia). REPEM: Javier Benito, MD, PHD (Pediatric Emergency Department, Cruces University Hospital, Barakaldo, Bizkaia, Spain); Ana Sofia Fernandes, MD (Santa Maria Hospital, Lisbon, Portugal); Joana Gil, MD (Santa Maria Hospital, Lisbon, Portugal); Natalia Paniagua, MD (Cruces University Hospital, Barakaldo, Bizkaia, Spain); Gemma Claret Teruel, MD (Hospital Sant Joan de D.u, Barcelona, Spain); Yehezkel Waisman, MD (Schneider Children's Medical Center of Israel, Petah Tigva, Israel). Research Network and Development of Pediatric Emergency Medicine in Latin America: Pedro Bonifacio Rino, MD (Hospital de Pediatria Prof. Dr Juan P. Garrahan, Buenos Aires, Argentina). PERN Executive Committee: Stuart R. Dalziel (Chair), Nathan Kuppermann (Vice Chair), James Chamberlain (PECARN), Santiago Mintegi (REPEM), Rakesh Mistry PEM-CRC), Lise Nigrovic (PEM-CRC), Amy C. Plint (PERC), Damien Roland (PERUKI), Patrick Van de Voorde (REPEM). PERN Networks: Participating networks include the following: PECARN, PEM-CRC of the American Academy of Pediatrics, PERC, PERUKI, PREDICT, REPEM, and the Red de Investigacion y Desarrollo de la Emergencia Pediatrica Latinoamericana, which means Research Network and Development of Pediatric Emergency Medicine in Latin America (Argentine-Uruguayan network).

Contributors M-PL conceived the study, co-wrote the study protocol and wrote the manuscript. NK designed the study, provided major input into the concept of the study and drafting and revision of the manuscript. YF designed the study, provided major input into the concept of the study and drafting and revision of the manuscript. RZ designed the study, provided major input into the concept and



analysis of the study and drafting and revision of the manuscript. ACP designed the study, provided major input into the concept and analysis of the study and drafting and revision of the manuscript. TAF designed the study, drafted the manuscript and revised it for intellectual content. FEB designed the study, drafted the manuscript and revised it for intellectual content. SD designed the study, drafted the manuscript and revised it for intellectual content. SF designed the study, drafted the manuscript and revised it for intellectual content. DR designed the study, drafted the manuscript and revised it for intellectual content. MDL designed the study, drafted the manuscript and revised it for intellectual content. DayS (Schnadower) designed the study, drafted the manuscript and revised it for intellectual content. DalS designed the study, drafted the manuscript and revised it for intellectual content. RMF designed the study, drafted the manuscript and revised it for intellectual content. DeS conducted the analysis and revised the manuscript for intellectual content. AK designed the study, drafted the manuscript and revised it for intellectual content, DWJ designed the study, drafted the manuscript and revised it for intellectual content. CM designed the study, provided extensive database support, drafted the manuscript and revised it for intellectual content. JB designed the study, drafted the manuscript and revised it for intellectual content. SS conceived the study, co-wrote the study protocol, wrote the manuscript and revised it critically for intellectual content. SS is the guarantor of the study.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval The parent PERN study related to this database was approved by the Research Ethics Boards of all participating institutions, as was the current secondary analysis (REB approval number 1000039075). Because this was a retrospective study, the Research Ethics Board waved the parental consent.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. Data are available on reasonable request. Deidentified patient data are available from Derek Stephens at derste1@outlook.com to researchers with funded study protocol whose proposed use of the data has been approved for a specific purpose, with a signed data access agreement.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

ORCID iDs

Roger Zemek http://orcid.org/0000-0001-7807-2459
Todd Adam Florin http://orcid.org/0000-0002-4387-2605
Franz E Babl http://orcid.org/0000-0002-1107-2187
Stephen Freedman http://orcid.org/0000-0003-2319-6192
Mark David Lyttle http://orcid.org/0000-0002-8634-7210
Dale Steele http://orcid.org/0000-0002-5689-0255
Suzanne Schuh http://orcid.org/0000-0001-7567-6919

REFERENCES

- Ross J, Santhirapala R, MacEwen C, et al. Helping patients choose wisely. BMJ 2018:k2585.
- 2 Cutler D. How will COVID-19 affect the health care economy? JAMA Health Forum 2020;1:e200419.
- 3 Troeger C, Blacker B, Khalil IA, et al. Estimates of the global, regional, and national morbidity, mortality, and aetiologies of lower respiratory infections in 195 countries, 1990–2016: a systematic analysis for the global burden of disease study 2016. Lancet Infect Dis 2018;18:1191–210.
- 4 Fernandes RM, Bialy LM, Vandermeer B, et al. Glucocorticoids for acute viral bronchiolitis in infants and young children. Cochrane Database Syst Rev 2013;41.
- 5 Schuh S, Lalani A, Allen U, et al. Evaluation of the utility of radiography in acute bronchiolitis. J Pediatr 2007;150:429–33.
- 6 Zipursky A, Kuppermann N, Finkelstein Y, et al. International practice patterns of antibiotic therapy and laboratory testing in bronchiolitis. Pediatrics 2020;146:e20193684.

- 7 guideline N. Bronchiolitis in children: diagnosis and management. NICE, 2015.
- 8 Ralston SL, Lieberthal AS, Meissner HC, et al. Clinical practice guideline: the diagnosis, management, and prevention of bronchiolitis. *Pediatrics* 2014:134:e1474–502.
- 9 Cheston CC, Vinci RJ. Overuse of continuous pulse oximetry for bronchiolitis: the need for Deimplementation science. *JAMA* 2020:323:1449.
- 10 Schuh S, Babl FE, Dalziel SR, et al. Practice variation in acute bronchiolitis: a pediatric emergency research networks study. Pediatrics 2017;140:e20170842.
- 11 Working Group of the Clinical Practice Guideline on Acute Bronchiolitis; Sant Joan de Déu Foundation Fundació Sant Joan de Déu, coordinator; Clinical Practice Guideline on Acute Bronchiolitis; Quality Plan for the Spanish National Healthcare System of the Spanish Ministry for Health and Social Policy; Catalan Agency for Health Technology Assessment. Clinical practice guidelines in the Spanish national healthcare system: CAHTA No. 2007/05, 2010.
- 12 Baraldi E, Lanari M, Manzoni P, et al. Inter-society consensus document on treatment and prevention of bronchiolitis in newborns and infants. Ital J Pediatr 2014;40:65.
- 13 Baumer JH. Sign guideline on bronchiolitis in infants. Arch Dis Child 2006;92:ep149–51.
- 14 Friedman JN, Rieder MJ, Walton JM, et al. Bronchiolitis: recommendations for diagnosis, monitoring and management of children one to 24 months of age. Paediatr Child Health 2014;19:485–91.
- 15 O'Brien S, Borland ML, Cotterell E, et al. Australasian bronchiolitis guideline. J Paediatr Child Health 2019;55:42–53.
- American Academy of Pediatrics Subcommittee on Diagnosis and Management of Bronchiolitis. Diagnosis and management of bronchiolitis. *Pediatrics* 2006;118:1774–93.
- 17 Breakell R, Thorndyke B, Clennett J, et al. Reducing unnecessary chest x-rays, antibiotics and bronchodilators through implementation of the NICE bronchiolitis guideline. Eur J Pediatr 2018;177:47–51.
- 18 Shanahan KH, Monuteaux MC, Nagler J, et al. Early use of bronchodilators and outcomes in bronchiolitis. *Pediatrics* 2021;148:e2020040394.
- 19 Jamal A, Finkelstein Y, Kuppermann N, et al. Pharmacotherapy in bronchiolitis at discharge from emergency departments within the pediatric emergency research networks: a retrospective analysis. Lancet Child Adolesc Health 2019;3:539–47.
- 20 Klassen TP, Acworth J, Bialy L, et al. Pediatric emergency research networks: a global initiative in pediatric emergency medicine. Pediatr Emerg Care 2010;26:541–3.
- 21 McDaniel CE, Ralston S, Lucas B, et al. Association of diagnostic criteria with urinary tract infection prevalence in bronchiolitis: a systematic review and meta-analysis. JAMA Pediatr 2019;173:269.
- 22 Korppi M. Virus-induced wheezing in infants aged 12-24 months and bronchiolitis in infants under 6 months are different clinical entities. Acta Paediatr 2015;104:e539.
- 23 Kaji AH, Schriger D, Green S. Looking through the retrospectoscope: reducing bias in emergency medicine chart review studies. *Ann Emerg Med* 2014;64:292–8.
- 24 Peduzzi P, Concato J, Kemper E, et al. A simulation study of the number of events per variable in logistic regression analysis. J Clin Epidemiol 1996;49:1373–9.
- 25 Jakobsen JC, Gluud C, Wetterslev J, et al. When and how should multiple imputation be used for handling missing data in randomised clinical trials – a practical guide with flowcharts. BMC Med Res Methodol 2017;17:162.
- 26 Haskell L, Tavender EJ, Wilson C, et al. Understanding factors that contribute to variations in bronchiolitis management in acute care settings: a qualitative study in Australia and New Zealand using the theoretical domains framework. BMC Pediatr 2020;20:189.
- 27 Simone L, Lyttle MD, Roland D. Canadian and United Kingdom -Practice Patterns in the use of Lumbar Punctures in Neonates with Bronchiolitis. *Emerg Med J* 2019;36:148–53.
- 28 Kessler DP, Summerton N, Graham JR. Effects of the medical liability system in Australia, the UK, and the USA. *The Lancet* 2006;368:240–6.
- 29 Harron K, Gilbert R, Cromwell D, et al. International comparison of emergency Hospital use for infants: data linkage cohort study in Canada and England. BMJ Qual Saf 2018;27:31–9.
- 30 Bryan MA, Desai AD, Wilson L, et al. Association of bronchiolitis clinical pathway adherence with length of stay and costs. *Pediatrics* 2017;139:e20163432.
- 31 Grol R, Grimshaw J. From best evidence to best practice: effective implementation of change in patients' care. *The Lancet* 2003;362:1225–30.



- 32 Kirolos A, Manti S, Blacow R, *et al.* A systematic review of clinical practice guidelines for the diagnosis and management of bronchiolitis. *J Infect Dis* 2020;222:S672–9.
- 33 Ralston SL, Garber MD, Rice-Conboy E, et al. A multicenter collaborative to reduce unnecessary care in inpatient bronchiolitis. Pediatrics 2016:137.
- 34 Mussman GM, Lossius M, Wasif F, et al. Multisite emergency department inpatient collaborative to reduce unnecessary bronchiolitis care. *Pediatrics* 2018;141:e20170830.
- 35 Dunn M, Muthu N, Burlingame CC, et al. Reducing albuterol use in children with bronchiolitis. *Pediatrics* 2020;145:e20190306.
- 36 Prasad V, Ioannidis JP. Evidence-Based de-implementation for contradicted, unproven, and aspiring healthcare practices. *Implement Sci* 2014;9:1.
- 37 Hiscock H, Neely RJ, Warren H, et al. Reducing unnecessary imaging and pathology tests: a systematic review. *Pediatrics* 2018;141:e20172862.
- 38 House SA, Marin JR, Hall M, et al. Trends over time in use of Nonrecommended tests and treatments since publication of the

- American Academy of pediatrics bronchiolitis guideline. *JAMA Netw Open* 2021;4:e2037356.
- 39 American Academy of Pediatrics. Choosing W. Ten things physicians and patients should question, 2021.
- 40 Wilson CL, Johnson D, Oakley E, et al. Knowledge translation studies in paediatric emergency medicine: a systematic review of the literature. J Paediatr Child Health 2016;52:112–25.
- 41 Haskell L, Tavender EJ, Wilson CL. Effectiveness of targeted interventions on treatment of infants with bronchiolitis: a randomized clinical trial. *JAMA Pediatr* 2021.
- 42 Florin TA, Byczkowski T, Ruddy RM, et al. Variation in the management of infants hospitalized for bronchiolitis persists after the 2006 American Academy of pediatrics bronchiolitis guidelines. J Pediatr 2014;165:e781:786–92.
- 43 Van Brusselen D, De Troeyer K, ter Haar E, et al. Bronchiolitis in COVID-19 times: a nearly absent disease? *Eur J Pediatr* 2021;180:1969–73.
- 44 Grimaud E, Challiol M, Guilbaud C, et al. Delayed acute bronchiolitis in infants hospitalized for COVID-19. *Pediatr Pulmonol* 2020;55:2211–2.