Canadian and United Kingdom/Ireland Practice Patterns in Lumbar Puncture Performance in Febrile Neonates with Bronchiolitis

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Abstract

Background: Serious bacterial infections in young infants with bronchiolitis are rare. Febrile infants <1 month old with bronchiolitis often receive a lumbar puncture (LP), despite limited data for this practice and lack of clinical practice guidelines for this population.

The primary objective was to investigate practice patterns in performance of LPs in the Emergency Department (ED) management of febrile infants aged ≤ 30 days with bronchiolitis.

Methods: A cross-sectional survey of two national pediatric emergency research networks in Canada (PERC) and the United Kingdom/Ireland (PERUKI) was conducted January to November 2017 using a modified Dillman technique. The survey was preceded by a clinical vignette describing a well-appearing, 21-day-old infant with low-grade fever, respiratory findings typical of bronchiolitis, and no perinatal SBI risk features.

Results: The response rate from PERC was 169/250 (68%) and 172/201(86%) from PERUKI. Nine physicians in training were excluded, leaving 332 eligible participants. Although most physicians believe that neonates with bronchiolitis rarely have meningitis [PERC 141/161 (87.6%); PERUKI 154/171(90%)] and feel comfortable diagnosing bronchiolitis in this group [PERC 136/161(84.5%); PERUKI 143/171(83.6%)], there was significant variation in the proportion who would be likely/very likely to perform an LP [PERC 100/161(62.1%); PERUKI 15/171 (8.8%)] ($p<0.0001$). Practice in Canada, < 10 years in practice, and lack of comfort with diagnosing bronchiolitis represent multivariable predictors of LP; OR 23.7 (95% CI 11.7 to 47.9), 2.3 (95% CI 1.2 to 4.2)

and 2.5 (95% CI 1.1 to 5.0), respectively. Rapid knowledge of RSV positivity would decrease LP probability from 35.4% to 20.2%.

Conclusion: Estimated probability of performing LPs and other interventions in otherwise healthy febrile neonates with bronchiolitis is highly variable between emergency physicians in Canada and the UK/Ireland. Network, < 10 years in ED practice, and comfort level with diagnosing bronchiolitis in newborns constitute independent predictors of the likelihood of LP performance.

What is known: Infants <1 month of age with bronchiolitis and fever often receive full sepsis work-up with lumbar puncture, despite lack of evidence for this practice, and lack of clinical practice guidelines for this population.

As a recent international study found large variation among emergency departments, clinicians looking after febrile newborns with bronchiolitis in different geographic global regions may also adopt different diagnostic approaches.

What this study adds: In this survey of pediatric emergency physicians in the national emergency networks in Canada and in the United Kingdom /Ireland, we found substantial practice variation in diagnostic strategies in newborns with bronchiolitis, with those in the Canadian network more likely to perform a lumbar puncture. Less practice experience and less comfort with diagnosing bronchiolitis was also associated with greater tendency to perform a lumbar puncture. Future multi-national outcomes research is needed to establish the best practice guidelines and decrease the costs of care in this population.

INTRODUCTION

Bronchiolitis represents the most common cause for infant hospitalization and a common reason for Emergency Department (ED) visits.([1](#), [2](#)) Fever constitutes a common clinical sign of bronchiolitis, yet in very young infants the fever poses a dilemma for clinicians: is the fever a consequence of the bronchiolitis, or a superimposed serious bacterial infection (SBI)?([1-3](#)) These infants are not vaccinated and are susceptible to perinatally acquired pathogens.([3](#))

Clinical practice guidelines recommend routine comprehensive screening for SBI in febrile infants under 1 month of age without a clear source of infection.([4](#), [5](#)) Since the incidence of concurrent SBI in febrile infants with bronchiolitis is less than 2%, leading bronchiolitis clinical practice guidelines (CPG) do not endorse routine laboratory investigations.([1-3](#)) However, there is currently no guidance on the management of febrile infants with bronchiolitis in the first month of life. Many such children routinely undergo a full sepsis work up, including a lumbar puncture (LP), despite published evidence that meningitis occurs in less than 1% of these infants.([3](#), [6](#), [7](#)) However, given the rarity of bacterial meningitis in young infants with fever and bronchiolitis, a major limitation of the available evidence is lack of optimal power for accurate risk assessment of this outcome. Therefore the aforementioned practice needs to be evaluated in the context of potential utility and possible adverse effects of this procedure in bronchiolitis.([8](#), [9](#))

A recent international study found large variation in practice patterns of bronchiolitis management between EDs.([10](#)) It is therefore possible that clinicians looking after febrile newborns with bronchiolitis in different geographic global regions may adopt different

diagnostic approaches. This information constitutes an important initial step for creating further evidence about best practice management and optimizing resource utilization in this sub-population.

The primary objective of this multi-national survey of two pediatric emergency research networks in Canada and the United Kingdom/Ireland which are part of a large international collaborative pediatric emergency research network was to compare the proportions of emergency physicians who would be very likely/likely to perform an LP in a febrile, well-appearing full-term 21-day-old infant with a typical presentation of mild bronchiolitis and without perinatal sepsis-associated risk factors. We hypothesized there would be a significant difference in this outcome between the networks.

METHODS

Study Design and Population

In accordance with the modified Dillman's Total Design Method for contact and follow up,[\(11\)](#) we used purposive cluster sampling and sent this international electronic survey to all staff emergency physicians who were also members of the Pediatric Emergency Research Canada (PERC) and the Pediatric Emergency Research in the United Kingdom and Ireland (PERUKI) collaborative research networks, using comprehensive membership and email lists of both organizations. We excluded physicians in training, those no longer practicing emergency medicine, and physicians who did not treat children. The survey period took place from January to March 2017 in Canada, and from September to November 2017 in the United Kingdom and Ireland. Physicians received a letter informing them that their participation was voluntary and responses confidential. Non-responders were sent three subsequent reminders. We tracked the characteristics of

the respondents and non-respondents to assess participation bias. Prior to the administration of the survey, the research ethics boards of the lead hospital and of both network associations approved the survey, under the relevant research governance principles of each country.

Survey Content and Development

The survey was preceded by a clinical vignette describing a hypothetical case of an alert and well hydrated 21-day-old full-term infant with low-grade rectal fever, nasal congestion, mild to moderate respiratory distress typical of bronchiolitis, and no high-risk perinatal features for SBI.([5](#), [12](#)) (Figure 1) Due to the absence of a validated questionnaire instrument for management of neonatal bronchiolitis, we have employed the survey technique described by Streiner and Norman.([13](#)) We utilized the evidence from the literature regarding the suggested management of febrile newborns,([5](#), [12](#)) clinical criteria for the diagnosis and recommended use of laboratory testing in bronchiolitis,([1](#), [2](#)) and published level of risk for meningitis in young febrile infants with bronchiolitis.([3](#), [6](#), [7](#)) Listed authors with content and survey methodology expertise generated, pre-tested the survey questions for ambiguity, redundancy and proper question sequence, revised the questions and also reduced the number of questions. We have also calculated the Cronbach's alpha to test for internal consistency of survey questions related to the use of lumbar punctures in bronchiolitis.

The following domains constituted the survey infrastructure:1) participants' demographics (6 questions), 2) participants' knowledge about a)recommended management of febrile newborns in general, b)typical clinical presentation of bronchiolitis, c)published risk of bacterial meningitis in febrile neonates with

bronchiolitis, and d) the physicians' level of comfort with diagnosing bronchiolitis in a febrile neonate (5 questions), 3) estimated probability of performing the LP, other laboratory tests, chest radiography, use of intravenous antibiotics and hospitalization of the index case as well as the reasons behind this practice (6 questions), 4) estimated level of probability of utilizing the aforementioned testing and management strategies in the event of rapid availability of a positive RSV test (5 questions) and 5) estimated maximum level of tolerable evidence-based risk of bacterial meningitis required to forego routine LP performance in well-appearing febrile full-term newborns with mild bronchiolitis (1 question). The primary outcome was the LP performance as this test represents the most controversial investigation in this population.

The response options included a five-point Likert scale ranging from either “strongly agree to “strongly disagree” or from “very likely” to “very unlikely”, as appropriate for a given question. The reported agreement results included those where participants designated either strong or moderate level of agreement with or level of likelihood of a given event.

Analyses

To detect a difference (agreed upon by the investigators as clinically important) of 15% in the proportion of ED physicians in PERC versus the PERUKI intending to “likely” or “very likely” perform an LP in the index case, and assuming a 80% LP rate in PERC and 65% in the PERUKI with 80% power, a minimum of 138 participants per network were needed (276 participants total).[\(14\)](#)

Differences in physician characteristics between PERC and PERUKI participants were analyzed using the chi-square statistic. We also used the chi-square test to examine other

relevant differences in proportions. The association between the LP performers versus non-performers (defined as “likely or very likely” to perform this test) and other candidate predictors of this outcome were analyzed using the binomial logistic regression analysis. The candidate predictor variables were the network, physician years in practice, formal pediatric emergency medicine (PEM) training (yes vs no), full-time vs part-time (<50% full-time equivalent) ED practice, “comfortable” or “very comfortable” with diagnosing bronchiolitis in a newborn (versus a lower comfort level), and knowledge about evidence-based probability of meningitis in young febrile infants with bronchiolitis (“agree” or “strongly agree” with the statement that very young febrile infants with bronchiolitis rarely have bacterial meningitis or sepsis versus a lower level of agreement or lack of related knowledge). Predictor variables associated with the outcome in the bivariate analysis with a p-value <0.2 were included in the multivariable logistic regression analysis. We used Wald and likelihood ratios to remove the non-contributory variables from the model and the Hosmer-Lemeshow test was employed to test the goodness-of-fit of the model.

RESULTS

Respondents and Non-Respondents

The survey was distributed to a total of 451 members across the networks (PERC: 250, PERUKI: 201). The response rate in PERC was 169/250 (68%) and in PERUKI 172/201(86%), yielding a total response rate of 341/451 (76%). Nine physicians in training were removed for a total of 332 eligible participants. Significantly more physicians in PERC have been PEM-trained and practicing in pediatric EDs for 10 years or more compared to PERUKI (Table 1). The proportions of PERC participants vs non-

respondents were comparable with respect to ED practice for more than 10 years (55% vs 58%), PEM training (65% vs 51%) and full-time ED work (89% vs 82%). The same was true for the PERUKI network- ED practice >10 years: 33% vs 25%, PEM training 53% vs 38%.

Cronbach's alpha for the survey was 0.88, indicating an excellent internal consistency.[\(15\)](#)

Table 1

Characteristics of PERC versus PERUKI Network Participants.

Characteristic, N (%)	PERC N= 161	PERUKI N=171	P value
Years in practice: ≥ 10	89 (55.3)	43 (25.1)	<0.0001
PEM trained	105 (65.2)	90 (52.6)	0.03
University-affiliated PED	159 (98.8)	115 (67.3)	<0.0001
Comfortable diagnosing newborn bronchiolitis	136 (84.5)	143 (83.6)	0.60
Estimated probability of bacterial meningitis in index case unlikely/highly unlikely	141 (87.6)	154 (90.0)	0.48
Availability of rapid RSV testing $\geq 75\%$ of the time	31 (19.3)	35 (20.5)	0.78
Full-time ED practice*	143 (88.8)	113 (66.1)	<0.0001

PEM: Pediatric Emergency Medicine

PED: Pediatric Emergency Department

RSV: Respiratory Syncytial Virus

PERC: Pediatric Emergency Research Canada

PERUKI: Pediatric Emergency Research United Kingdom and Ireland

* More than 50% of total clinical practice time

Knowledge about Management of Febrile Newborns and Risk of Meningitis in Bronchiolitis

Virtually all participants were in agreement about the typical clinical presentation of bronchiolitis [PERC: 161/161 (100%); PERUKI: 169/171 (98.8%)]. The majority agreed that febrile infants under three months of age with bronchiolitis rarely have bacterial meningitis [PERC: 141/161 (87.6%); PERUKI: 154/171 (90%)] and feel comfortable/very comfortable making a diagnosis of bronchiolitis in newborns [PERC: 136/161(84.5%); PERUKI: 143/171(83.6%)]. However, significantly more participants in Canada interpret the current scientific evidence as suggesting that well-appearing febrile neonates with bronchiolitis should undergo a full sepsis work-up compared to their U.K./Ireland counterparts [PERC: 152/161(94.4%); PERUKI: 120/171(70.2%)], $p<0.0001$).

Management of the Index Case

The infant described in the vignette would be likely/very likely subjected to an LP by 100/161(62.11%) emergency physicians in Canada, in contrast to 15/171 (8.77%) physicians in the U.K./Ireland (difference 0.53, 95% CI 0.45 to 0.62, $p < 0.0001$, OR 17.0, 95% CI 9.19 to 31.63). Among the 61 physicians in Canada and the 156 physicians in the U.K./Ireland who chose to forgo lumbar puncture, the stated reasons for not performing the test included a low perceived risk of bacterial meningitis (PERC: 48%, PERUKI: 63%), concern about augmenting respiratory distress/parental discomfort (PERC: 29%, PERUKI: 35%) and a higher perceived risk of the procedure compared to the risk of meningitis (PERC: 9%, PERUKI: 13%). Table 2 illustrates the contrast in the differences in the overall management of the index infant between networks, highlighting that

investigations and interventions are more frequently performed by the PERC participants. Treatment in Canada, ED practice for less than 10 years and lack of physician comfort with the diagnosis of newborn bronchiolitis represent significant multivariable predictors of LP performance (Table 3). Rapid knowledge of RSV positivity would significantly decrease the estimated probability of LP performance and of projected antibiotic treatments - Table 4.

Table 2

Probability of Management in Febrile Newborns with Bronchiolitis in Study

Networks.

Variable, N (%)	PERC N=161	PERUKI N=171	Bivariate Odds Ratio	95% CI	P value
Lumbar puncture	100 (62.1)	15 (8.7)	17.0	9.2 to 31.6	<0.0001
Blood culture	139 (86.3)	47 (27.4)	16.7	9.5 to 29.2	<0.0001
Complete blood count	138 (85.7)	49 (28.7)	14.9	8.6 to 25.9	<0.0001
Urine culture	137 (85.1)	44 (25.7)	16.4	9.5 to 28.6	<0.0001
Chest radiograph	76 (47.2)	22 (12.9)	6.1	3.5 to 10.4	<0.0001
Nasal PCR for RSV	112 (69.6)	86 (50.3)	2.3	1.4 to 3.5	0.0003
Antibiotics	94 (58.4)	24 (14.0)	8.6	5.0 to 14.6	<0.0001
Hospitalization	134 (83.2)	106 (62.0)	3.0	1.8 to 5.1	<0.0001
No investigations	13 (8.1)	67 (39.2)	0.14	0.05 to 0.22	<0.0001

PCR: Polymerase Chain Reaction

RSV: Respiratory Syncytial Virus

PERC: Pediatric Emergency Research Canada

PERUKI: Pediatric Emergency Research United Kingdom and Ireland

Table 3**Multivariable Predictors of Lumbar Puncture in Febrile Neonatal Bronchiolitis**

Characteristics	Odds Ratio (95% CI)	P-value
Network (PERC vs PERUKI)	23.7 (11.7 to 47.9)	<0.0001
Years in practice < 10	2.3 (1.2 to 4.2)	0.009
PEM-trained (yes vs no)	0.8 (0.4 to 1.5)	0.5
Lack of comfort with bronchiolitis diagnosis*	2.5 (1.1 to 5.0)	0.02

PERC: Pediatric Emergency Research Canada

PERUKI: Pediatric Emergency Research United Kingdom and Ireland

PEM: Pediatric Emergency Medicine

*very uncomfortable, uncomfortable, neither comfortable nor uncomfortable

Table 4**Probability of Interventions with and without Positive RSV Test in Study Networks.**

Variable, N (%)	PERC N=161	PERUKI N=171	Total relative change (%)	Relative change Canada (%)	Relative change U.K. (%)
LP overall	100 (62.1%)	15 (8.8%)	↓41.7	↓39.0	↓60.2
LP with positive RSV	61 (37.9%)	6 (3.5%)			
Antibiotics overall	94 (58.3%)	24 (14.0 %)	↓34.7	↓33.0	↓41.7
Antibiotics with positive RSV	63 (39.1%)	14 (8.2%)			
Hospitalization overall	134 (83.2%)	106 (62.0%)	↓12.5	↓9.0	↓17.0
Hospitalization with positive RSV	122 (75.8%)	88 (51.5%)			

LP: Lumbar Puncture

RSV: Respiratory Syncytial Virus

PERC: Pediatric Emergency Research Canada

PERUKI: Pediatric Emergency Research United Kingdom and Ireland

How Risk Averse are the Emergency Physicians?

A total of 18/161 (11.1%) physicians in Canada require a zero percent risk of meningitis to forego an LP, in contrast to 5/171 (2.9%) of PERUKI participants (difference 8.3%, 95% CI 0.02 to 0.14, $p = 0.003$). Among the participants in the U.K. and Ireland, the claimed tolerance for the risk level of $>1\%$ for meningitis in this population is 42/171 (24.6%) without performing an LP. In contrast, 6/161 (3.7%) participants in Canada would accept a meningitis risk of $>1\%$ to forego an LP (difference 20.9%, 95% CI 0.14 to 0.28, $p < 0.001$).

DISCUSSION

This study demonstrates that the estimated probability of performing an LP and other investigations in otherwise healthy febrile neonates with bronchiolitis is highly variable among emergency physicians in Canada and in the U.K./Ireland. The network, length of ED practice, and the physician level of comfort with diagnosing bronchiolitis in febrile neonates constitute multivariable predictors of the likelihood of LP performance. To our knowledge, this is the first examination of management strategies in this population.

While the North American guidelines for diagnosis and management of bronchiolitis are outlined in both the American Academy of Pediatrics and the Canadian Pediatric Society position statements,^(1, 2) the PERUKI network utilizes the National Institute for Health

and Care Excellence (NICE) guidelines.(16) These guidelines are similar in their recommendations for minimizing diagnostic work-up for infants with typical bronchiolitis.(1, 2, 16) However, while the NICE guideline notes that infants less than 3 months of age are at risk for deterioration,(16) all three guidelines target infants 1 to 24 months of age, making the management considerations in infants less than one month of age challenging.(1, 2, 16)

As a result, there are no published guidelines on the diagnosis, diagnostic work up, and management of febrile infants less than one month of age with bronchiolitis. Physicians practicing in both North America and in the U.K./Ireland have similar recommended standards of care for febrile newborns with no apparent fever source, which involve full sepsis work up including blood culture, urine culture, and LP.(4, 17) Therefore, many physicians likely default to these guidelines when looking after febrile newborns in the context of a suspected viral source such as bronchiolitis. While this hypothesis is reflected in our practice findings in Canada, our colleagues in the U.K./Ireland adopt a less aggressive approach.

We can hypothesize that this difference may in part relate to higher risk aversion among our Canadian colleagues, as suggested by a higher proportion of the physicians in Canada professing to require zero meningitis risk to forego a LP in febrile newborns with bronchiolitis compared to those in the U.K./Ireland. Risk minimizers have low tolerance for adverse outcomes and adopt conservative approaches to lower the risk of potential liability.(18) In contrast, test minimizers rely on thorough clinical evaluation to avoid potentially unnecessary interventions when the risk of serious outcomes is low. This description may characterize some of our U.K./Ireland participating colleagues. A

systematic review of 34 studies of malpractice claims from both North America and the U.K., found that meningitis was the most commonly missed pediatric diagnosis.[\(19\)](#) Concern about potential litigation in Canada may motivate the physicians to proceed with an LP, despite their acknowledged low risk of meningitis in the index case. The context of healthcare delivery may also impact the differences in intervention rates. As the National Health System in the U.K. compels clinicians to consider the costs of resource utilization, investigations may well differ as a result of these undocumented pressures. This is supported by an evidence of much lower rates of computerized tomography utilization in head injured patients in the U.K. compared to Canada.[\(20\)](#) A previous study showed a higher rate of brief infant hospitalizations in the UK compared to fewer but longer admissions in Ontario, Canada.[\(21\)](#) The stated reasons for this disparity included differences in support in early infancy, the strictly enforced 4 hour ED disposition policy in the U.K., and a greater presence of pediatric emergency clinicians in the EDs in Canada. [\(21\)](#) Therefore, underlying differences in the clinical risk assessment and in the health care system pressures may both contribute to the interventional difference between the U.K. and Canada found in our study.

Literature shows that the risk of SBI in young febrile infants with bronchiolitis is very low, and the main bacterial co-infection is a UTI.[\(3\)](#) Ralston et al. conducted a systematic review summarizing the risk of occult SBI in infants less than 60-90 days old with bronchiolitis. In the 11 included studies, 5/1749 infants had bacteremia (0.3%), none had meningitis and UTIs were diagnosed in 3.3% of infants.[\(3\)](#) While the systematic review did not find differences in rates of SBI in newborns versus older infants, an important limitation was a relative paucity of studies targeting young infants and a small number of

newborns with bronchiolitis.(3, 7) As a result, lack of adequate power prevents us from making firm conclusions about accurate risk estimates for the risk of meningitis in this population. Therefore, future multi-site research on this topic would be beneficial.

Interestingly, knowledge of rapid RSV positivity was found to considerably reduce the projected rate of diagnostic tests and antibiotic use in both networks. Although the majority of infants hospitalized with bronchiolitis have positive RSV tests,(2) there is currently no data supporting the impact of RSV testing on clinical outcomes in typical bronchiolitis.(6, 22) While a recent meta-analysis of 789 neonates with bronchiolitis demonstrated no cases of bacterial meningitis, the authors showed a comparable incidence of SBI (usually UTI) in RSV positive babies (11.5%) and those negative for RSV (15.3%).(7, 23) Therefore, based on current evidence, routine RSV testing is not indicated to guide further management in bronchiolitis. This notion of resource stewardship is also in keeping with recent Choosing Wisely® initiatives about the need for medical testing and treatments, that could not only cause potential harm to patients but could also add avoidable costs to the healthcare system.(24) Hopefully, future research will enlighten us on potential benefit of RSV testing in very young febrile infants with bronchiolitis.

Other discrepancies in the management of bronchiolitis have been recently reported. A study of 3,725 infants with bronchiolitis showed large differences in the use of evidence-based supportive therapies and investigations between EDs and networks in North America, United Kingdom/Ireland, Spain/Portugal and Australia/New Zealand.(10) The current study demonstrates a similar variation in the management of newborn

bronchiolitis and suggests the need for enhancing current evidence and identification of international best practices for this population.

A strength of this international survey is the high participation rate (76%), with the response rate much higher compared to the 52% in most surveys.[\(25\)](#) Nevertheless, we cannot rule out participation bias. However, our responders and non-responders had similar characteristics, and the resulting bias was therefore likely relatively minor.

Importantly, survey results may not accurately reflect actual practice. Therefore, future directions should include large multi-centre examination of practice patterns of diagnostic testing and outcomes in young infants with bronchiolitis. While these results obtained from a diverse international population are likely generalizable to other academic EDs, their generalizability to community EDs may be limited.

In conclusion, we found a large practice variation between the national emergency networks in Canada and in the U.K./Ireland in the diagnostic work up of febrile infants under 30 days of age with bronchiolitis. Future multi-national research needs to provide accurate clinical outcome estimates in this subpopulation in order to establish the best practice and management guidelines, optimize resource utilization, and decrease the costs of care.

AUTHOR CONTRIBUTIONS

L. S. conceived the study, wrote the study protocol, supervised data extraction and wrote the manuscript.

S. S. conceived the study, wrote the study protocol, supervised data extraction, co-wrote the manuscript.

M. L. aided in study design, supervised data extraction, drafted the manuscript and revised it for intellectual content.

D.R. aided in study design, revised the manuscript for intellectual content.

D. S. conducted the statistical analysis, drafted and revised the manuscript for intellectual content.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

CONFLICT OF INTEREST

The authors have no conflicts of interest relevant to this article to disclose.

FINANCIAL DISCLOSURE

The authors have no financial relationships relevant to this article to disclose.

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FIGURE LEGEND

Figure 1: Vignette with a hypothetical index case