PEER REVIEW HISTORY

BMJ Paediatrics Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	RETROSPECTIVE AUDIT OF GUIDELINES FOR INVESTIGATION AND TREATMENT OF BRONCHIOLITIS: A FRENCH PERSPECTIVE
AUTHORS	Benhamida, Myriam; BIHOUEE, Tiphaine; Verstraete, Marie; Gras Le Guen, Christèle; Launay, Elise

VERSION 1 - REVIEW

REVIEWER	Mittal, Vineeta UT Southwestern Medical Center & Children's Health System Dallas, Texas USA Competing interests: None
REVIEW RETURNED	25-Jul-2017

GENERAL COMMENTS	This is a well written manuscript and addresses variation in practice in management of bronchiolitis in France and authors have successfully implemented the guidelines to show that variation can be significantly reduced. Few comments for consideration: 1. Methods: -why did the authors choose 1 year age cut off when typical bronchiolitis age is 2 years. -Mention that you looked at healthy children and sub classifies premature babies. What about children with complex comorbidities? were they included? -The process of guideline development is well described. How did the authors manage "change"? -describe how education and buy-in was obtained from those involved. Physician behavior change is hard. You clearly got it! How? Results -well described. Discussions -Please have subheading so it is easier to read. Example: reduced overuse of tests, Reduced overuse to treatment, Cost savings. Would suggest to add a small paragraph on how over utilization is a burden on healthcare and not a good practice. -Would recommend briefly describing implementation strategies including challenges and wins. -Why did the use of amoxicillin go up?

REVIEWER	Traves, Donna Derbyshire Childrens Hospital England Competing interests: none to declare
REVIEW RETURNED	01-Aug-2017

GENERAL COMMENTS	The study is well designed to look at the issue raised in the introduction, that too many interventions are carried out on patients with bronchiolitis in France. The comparison of management before and after new HUGO guidelines quite clearly demonstrates that it is possible to reduce the interventions undertaken, which is encouraging. I do wonder however, whether the study is more of an audit of compliance with guidelines or a quality improvement project rather than a scientific study?. there are a few additional comments that I feel would enhance the paper,. Line 31 - it states "either" one year before or after. This might be better phrased "looking at" one year before and after. line 33 - I am unclear as to why both treatment associated with a diagnostic test is needed. why can it not only look at treatments and interventions not routinely recommended individually? line 63 . the grammar of "But, while" does not make sense in the sentence. this should be re-phrased. Line 72 - the grammar of "And, in " is not good grammar and should be changed! line 108 - in the interventions, you mention criteria being established to differentiate asthma from bronchiolitis. It would be good to see these and have them in an appendix/ reference so that the actual differences can be assessed. line 111 - the HUGO bronchiolitis guidelines are referenced throughout the paper and in the interventions, it would be good to see at least a summary of these so that the reader can understand what the paper is based on. line 125 - I very much like the inclusion and exclusion criteria. the study population looking at those infants less than 1 year, with a viral prodrome leading to wheeze will ensure that older children with different set of respiratory illness and pathology will not be included. The results are very applicable to a general paediatric population. Results - line 167 - there seems to be a very high admission rate for children with bronchiolitis seen in the emergency department. I am interested to know whether the children seen in emergency department are self referrals, GP referrals or those directed there by a medical professional. It would be interesting to compare this data to other data regarding rates of admissions for bronchiolitis in other units/ countries. I note that there is no difference in the length of stay in the patient groups 1 and 2, despite the reduced interventions. The paper states that other research shows length of stay up to 3 days compared to 2 days in this study, more can be made of this showing that interventions really do not affect length of stay and are deemed unnecessary. Funding:

	line 266 - "This work was supported by any grant" please can this be clarified as to whether there was funding or which grant was used - or is this a typing error?!

REVIEWER	Johnson, Lara W. Texas Tech University Health Sciences Center 3601 4th St MS9406 Lubbock, TX 79430 Competing interests: None
REVIEW RETURNED	05-Aug-2017

GENERAL COMMENTS	The authors report the results of a quality improvement initiative in a single center to provide care for patients with bronchiolitis consistent with international guidelines. The authors were able to achieve significant reductions in the utilization of diagnostic testing and treatments. The authors focus on only three weeks of each bronchiolitis season (pre and post). Suggestions to improve the manuscript: 1) There are several instances of somewhat awkward sentence construction and word choice, which may occasionally be confusing to the reader. A thorough editing with minor stylistic rewrites would be appropriate. There are also typos in the tables. 2) The authors refer to this as a QI intervention, but have chosen to use a more epidemiological approach in reporting the data. Seldom do QI interventions work this completely. It would be interesting to understand the implementation science aspect of this work with greater detail regarding the implementation of the guidelines, problems, lessons learned, impact over time and sustainability of change. 3) Although the authors do present a sample size calculation supporting the number of subjects included, looking at only three weeks per season may introduce bias. Performance during those very busy times may be consistently better or worse than it might be at another time. This should be discussed in the limitations section. 4) In general, a more expanded limitations section would be welcome. 5) Although there is an indication that data were being collected retrospectively, were the members of the care team aware of the study as it was occurring after the care process changes? 7) If the focus of this study is reporting the QI work, then more information is needed to adequately describe the QI process. This study is relevant and important in describing improvement of bronchiolitis inpatient care in France. However, significant revisions are required to more adequately explain the methodology in the context of QI.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Comments to the Author
This is a well written manuscript and addresses variation in practice in management of bronchiolitis in France and authors have successfully implemented the guidelines to show that variation can be significantly reduced. Few comments for consideration:

1. Methods:
1.1- why did the authors choose 1 year age cut off when typical bronchiolitis age is 2 years.

Answer: Thank you for your comment. To explain, the target population for the HUGO bronchiolitis guidelines was children from birth to one year of age. That is why this age was the cut off for inclusion in our study. There were also several other reasons why we chose this cut-off age:

a) In France, epidemiologic data suggest that the peak frequency of bronchiolitis in infants is between 2 and 8 months.

[Consensus conference on the management of infant bronchiolitis. Paris, France, 21 September 2000. Proceedings]. *Arch Pédiatrie Organe Off Sociéte Fr Pédiatrie* 2001;**8 Suppl 1**:1s–196s

b) It ensured that older children with different sets of respiratory illness or pathology would not be included.

c) In the NEMJ in 2016 Meissner wrote, “various definitions of bronchiolitis have been proposed, but the term is generally applied to a first episode of wheezing in infants younger than 12 months of age.”

Meissner HC. Viral Bronchiolitis in Children. *N Engl J Med* 2016;**374**:62–72. doi:10.1

d) There are also several others major studies that have chosen this cut-off age:
- Cunningham S, Rodriguez A, Adams T, *et al.* Oxygen saturation targets in infants with bronchiolitis (BIDS): a double-blind, randomised, equivalence trial. *Lancet Lond Engl* 2015;**386**:1041–8.
- Silver AH, Esteban-Cruciani N, Azzarone G, *et al.* 3% Hypertonic Saline - Versus Normal Saline in Inpatient Bronchiolitis: A Randomized Controlled Trial. *Pediatrics* 2015;**136**:1036–43.
- Akenroye AT, Baskin MN, Samnaliev M, *et al.* Impact of a Bronchiolitis Guideline on ED Resource Use and Cost: A Segmented Time-Series Analysis. *Pediatrics* 2014;**133**:e227–34.

We added a sentence to explain this choice and added the corresponding references in the Methods section

See lines 121-122: ” The cut-off age of one year was decided upon according to the current literature.”

1.2 Mention that you looked at healthy children and sub classifies premature babies. What about children with complex comorbidities? were they included?

Answer: Thank you for your comment. We opted for a pragmatic study, so we did not exclude patients with comorbidities. The comorbidities are detailed in the online resource 2.

We have also added this information in greater detail in the Results section. Please see line 172: “Twenty-four children had comorbidities (see online resource 2).”

Online resource 2

	2011 n=13	2013 n = 11
congenital heart disease	4	2
other malformation	2	2
chronic neurological disease	0	2
neonatal respiratory distress	5	3
mild bronchopulmonary dysplasia	0	1
sickle cell disease	0	1
child abuse	2	0

1.3 The process of guideline development is well described. How did the authors manage "change"?

Answer: Thank you for your compliment and comment. The new guidelines were presented and explicated daily to nurses and medical staff over two weeks in order to ensure that they were understood by all the healthcare professionals in charge of children with bronchiolitis. The new protocol was also posted in medical and nurses offices.

See lines 111-116: “The guidelines were implemented by the NUH in September 2012 by holding team meetings involving pediatric nurses, physicians, and trainees. These inter-professional meetings occur annually at the start of bronchiolitis season. Daily brief meeting (just following the usual morning meeting) with physicians and nurses were also organized during the 14 first days of the epidemic seasons to discuss difficulties and a summary of the guidelines was posted in the emergency and the general pediatric wards. The guidelines were integrated into the NUH guidelines book, and they are readily accessible online via the hospital’s intranet website.”

1.4 Describe how education and buy-in was obtained from those involved. Physician behavior change is hard. You clearly got it! How?

Answer: Thank you for your comment. In comparison to the results of other quality improvement studies, such as those reported in Ralston’s systematic review, we encountered better reduction rates for unnecessary diagnostic tests and treatments. This level of success is probably linked to the design of our intervention, as it was a voluntary local collaborative work. A large team of NUH medical staff (e.g. pediatricians, pediatric pulmonologists, and emergency physicians) were involved in generating the HUGO guidelines and in their presentation in inter-professional team meetings. Having a large team engagement led by a site champion is one of the major determinants of success for a bronchiolitis quality improvement program, as found by Ralston et al. in their multicentric study. Moreover the collaborative nature of the work helps to overcome clinical practice inertia and to promote evidence based medicine.

See lines 261-269 in Discussion section

“DETERMINANTS OF SUCCESS OF QUALITY IMPROVEMENT PROGRAMM

In comparison to the results of other quality improvement studies, such as those reported in Ralston's systematic review [18], we encountered better reduction rates for unnecessary diagnostic tests and treatments. This level of success is probably linked to the design of our intervention, as it was a voluntary local collaborative work. A large team of NUH medical staff (e.g. pediatricians, pediatric pulmonologists, and emergency physicians) were involved in generating the HUGO guidelines and in their presentation in inter-professional team meetings. Having a large team engagement led by a site champion is one of the major determinants of success for a bronchiolitis quality improvement program, as found by Ralston et al. in their multicentric study [25]. Moreover the collaborative nature of the work helps to overcome clinical practice inertia and to promote evidence based medicine [29]."

2. Results
-well described.

3. Discussions
3.1 Please have subheading so it is easier to read. Example: reduced overuse of tests, Reduced overuse to treatment, Cost savings. Would suggest to add a small paragraph on how over utilization is a burden on healthcare and not a good practice.

Answer: Thank you for this suggestion. We have added the subheadings and also changed the order of some paragraphs to enhance relevance. The burden of over utilization on LOS are described. And the consequences of overuse of CXR and chest physiotherapy are detailed too.

See Discussion section for subheadings

See line 241-242: "In addition, reducing unnecessary care provided benefits in term of LOS and was costs saving."

3.2 Would recommend briefly describing implementation strategies including challenges and wins.

Answer : Thank you for this suggestion. We added a paragraph addressing this comment. See lines 261-269.

3.3 Why did the use of amoxicillin go up?

Answer: Thank you for your comment. Based on the nature of French bacterial ecology, especially for *Haemophilus influenzae*, the HUGO guidelines recommend choosing amoxicillin in case of a concomitant bacterial infection. It is worth noting that while the amoxicillin rate increased to 86.36%, the proportion of clavulanic acid-amoxicillin antibiotic prescriptions dropped to 4.54%

Reviewer: 2

Comments to the Author
The study is well designed to look at the issue raised in the introduction, that too many interventions are carried out on patients with bronchiolitis in France. The comparison of management before and after new HUGO guidelines quite clearly demonstrates that it is possible to reduce the interventions undertaken, which is encouraging.

I do wonder however, whether the study is more of an audit of compliance with guidelines or a quality improvement project rather than a scientific study?

there are a few additional comments that I feel would enhance the paper,.

1- Line 31 - it states "either" one year before or after. This might be better phrased "looking at" one year before and after.

Answer: Thank you for your comment. We apologize for this phrasing error, and we have made the correction and we have submitted the revised manuscript for English editing (the first version had also been edited for English by professional).
See lines 31-33 : “This retrospective before/after design study was conducted in the general pediatric unit of a tertiary level of care French hospital, looking at one year before (i.e. the winter of 2011-2012) and one year after (i.e. the winter of 2013-2014) implementation of the guidelines”

2- line 33 - I am unclear as to why both treatment associated with a diagnostic test is needed. why can it not only look at treatments and interventions not routinely recommended individually?

Answer: Thank you for your comment. We made the choice to use a composite outcome build with the two main resources that tend to be misused in bronchiolitis in order to capture the overall impact of the HUGO guidelines. Indeed, the proportion of patient having both treatment associated with a unnecessary diagnostic test was 45% before guidelines implementation. But the use of each treatment and diagnostic test not routinely recommended by the guidelines were evaluated too. We discussed this point in the Discussion section.

See lines 277-282: “We made the choice of a composite outcome associating treatment and diagnostic test, this outcome could appear heterogeneous. Nevertheless treatment and diagnostic testing were the two main resources that tend to be misused in bronchiolitis. Having a composite outcome allowed us to capture the overall impact of the HUGO guidelines. Moreover the use of each treatment and diagnostic test not routinely recommended by the guidelines were evaluated separately too and we showed a clinically and statistically significant reduction of most of the inadequate tests or treatments”

3- line 63 . the grammar of "But, while" does not make sense in the sentence. this should be re-phrased.

Answer: Thank you for this suggestion. We have made this correction.

See line 61: “In 2014 and 2015…”

4- Line 72 - the grammar of "And, in " is not good grammar and should be changed!

Answer: Thank you for your comment. We made the correction.
See line 71: “By comparison, Ralston et al. have proposed…”

5- line 108 - in the interventions, you mention criteria being established to differentiate asthma from bronchiolitis. It would be good to see these and have them in an appendix/ reference so that the actual differences can be assessed.

Answer: Thank you for your comment. The criteria are mentioned in the online resource 1. We added a referral to this online resource in the Methods section.

See line 106-107: “Criteria to distinguish childhood asthma from acute viral bronchiolitis were established (see online resource 1).”

And see line 109-110 : “All these recommendations were summarized in the HUGO bronchiolitis guidelines (see online resource 1)[12]”

6- line 111 - the HUGO bronchiolitis guidelines are referenced throughout the paper and in the interventions, it would be good to see at least a summary of these so that the reader can understand what the paper is based on.
Answer: Thank you for your comment. We have addressed this issue above.

7- line 125 - I very much like the inclusion and exclusion criteria. the study population looking at those infants less than 1 year, with a viral prodrome leading to wheeze will ensure that older children with different set of respiratory illness and pathology will not be included. The results are very applicable to a general paediatric population.

Results -
8- line 167 - there seems to be a very high admission rate for children with bronchiolitis seen in the emergency department. I am interested to know whether the children seen in emergency department are self referrals, GP referrals or those directed there by a medical professional. It would be interesting to compare this data to other data regarding rates of admissions for bronchiolitis in other units/ countries.

Answer: Thank you for your comment. We did not collect this information for the present study, but previous French data suggest that one third of the children presenting at pediatric emergency room are referred by GP or a medical professional and two thirds are self referrals.

Reference : Les urgences hospitalières, qu'en sait-on ? Albert VUAGNAT. 2013
http://drees.solidarites-sante.gouv.fr/IMG/pdf/panorama2013_dossier01.pdf

9- I note that there is no difference in the length of stay in the patient groups 1 and 2, despite the reduced interventions. The paper states that other research shows length of stay up to 3 days compared to 2 days in this study, more can be made of this showing that interventions really do not affect length of stay and are deemed unnecessary.

Answer: Thank you for this suggestion. We completed Table 2 with the data concerning LOS, ICU admission all-cause 7-day readmission and added a sentence the Discussion section to address your comment. See Table 2.

See Line 2241-242: "Our results also suggest that reducing unnecessary care provided benefits in term of LOS and was cost-saving."

Funding:
line 266 - "This work was supported by any grant" please can this be clarified as to whether there was funding or which grant was used - or is this a typing error?!

Answer: Thank you for this comment**.** This was, in fact, a typing error which we have corrected.

See line 302: "No funding supported this work."

"

Reviewer: 3

Comments to the Author
The authors report the results of a quality improvement initiative in a single center to provide care for patients with bronchiolitis consiswe aptent with international guidelines. The authors were able to achieve significant reductions in the utilization of diagnostic testing and treatments. The authors focus on only three weeks of each bronchiolitis season (pre and post).

Suggestions to improve the manuscript:

1) There are several instances of somewhat awkward sentence construction and word choice, which may occasionally be confusing to the reader. A thorough editing with minor stylistic rewrites would be appropriate. There are also typos in the tables.
Answer: Thank you for this comment. We had the revised manuscript edited by professional and corrected the typos in the Tables.

2) The authors refer to this as a QI intervention, but have chosen to use a more epidemiological approach in reporting the data. Seldom do QI interventions work this completely. It would be interesting to understand the implementation science aspect of this work with greater detail regarding the implementation of the guidelines, problems, lessons learned, impact over time and sustainability of change.

Answer: Thank you for this comment. The success is probably linked to the design of our intervention, as it was a voluntary local collaborative work. A large team of NUH medical staff (e.g. pediatricians, pediatric pulmonologists, and emergency physicians) were involved in generating the HUGO guidelines and in their presentation in interprofessional team meetings. Moreover the collaborative nature of the work helps to overcome clinical practice inertia and to promote evidence based medicine. Finally having a large team engagement led by a site champion is one of the major determinants of success for a bronchiolitis quality improvement program, as found by Ralston et al. in their multicentric study, and it was the case in Nantes University Hospital. The next step of this work will be to evaluate the implementation of HUGO guidelines in the others HUGO centers, were medical staff were less involved in generating the guidelines and to assess the determinants of success for the guideline implementation. We detailed the way of implementation in the Methods section and we added a paragraph in the Discussion section.

See lines 111-116: “The guidelines were implemented by the NUH in September 2012, by holding team meetings involving pediatric nurses, physicians, and trainees. These interprofessional meetings take place every year at the start of bronchiolitis season. Daily brief meetings (just following the usual morning meeting) with physicians and nurses were also organized during the 14 first days of the epidemic seasons to discuss difficulties and a summary of the guidelines was posted in the emergency and the general pediatric wards. The guidelines were integrated into the NUH guidelines book, and they are readily accessible online via the hospital’s intranet website.”

See lines 260-269:

“DETERMINANTS OF SUCCESS OF QUALITY IMPROVEMENT PROGRAM:

In comparison to the results of other quality improvement studies, such as those reported in Ralston’s systematic review [18], we encountered better reduction rates for unnecessary diagnostic tests and treatments. This level of success is probably linked to the design of our intervention, as it was a voluntary local collaborative work. A large team of NUH medical staff (e.g. pediatricians, pediatric pulmonologists, and emergency physicians) were involved in generating the HUGO guidelines and in their presentation in inter-professional team meetings. Having a large team engagement led by a site champion is one of the major determinants of success for a bronchiolitis quality improvement program, as found by Ralston et al. in their multicentric study [25]. Moreover, the collaborative nature of the work helps to overcome clinical practice inertia and to promote evidence based medicine [29].”

3) Although the authors do present a sample size calculation supporting the number of subjects included, looking at only three weeks per season may introduce bias. Performance during those very busy times may be consistently better or worse than it might be at another time. This should be discussed in the limitations section.

Answer: Thank you for your comment. Indeed, it may introduce a bias. However, the bias was the same for the two periods of evaluation, as we analysed the three major bronchiolitis epidemic weeks. In a later study, we will try to included the whole season.

See lines 273-276: “It may have introduced bias: performance during those times may be consistently better or worse than it might be at another time. But the bias was the same for the two inclusion periods. We hypothesized that the workload is similar year-over-year during those busy weeks.”

4) In general, a more expanded limitations section would be welcome.
Answer: Thank you for your comment. We added some points of limitations according to the comments of the reviewers.

See lines 272-282: “The main limitation of this study was its retrospective, monocentric before vs. after design. In order to limit bias, we choose to evaluate the same unit during the three major bronchiolitis epidemic weeks. It may have introduced bias: performance during those times may be consistently better or worse than it might be at another time. But the bias was the same for the two inclusion periods. We hypothesized that the workload is similar year-over-year during those busy weeks. There was no major change in the way the unit was run, senior medical staff, or nurse teams between the two periods. We made the choice of a composite outcome associating treatment and diagnostic test, this outcome could appear heterogeneous. Nevertheless treatment and diagnostic testing were the two main resources that tend to be misused in bronchiolitis. Having a composite outcome allowed us to capture the overall impact of the HUGO guidelines. Moreover the use of each treatment and diagnostic test not routinely recommended by the guidelines were evaluated separately too and we showed a clinically and statistically significant reduction of most of the inadequate tests or treatments.”

5) Although there is an indication that data were being collected retrospectively, were the members of the care team aware of the study as it was occurring after the care process changes?

Answer: Thank you for your comment. We began designing the study in April 2014, at which time the members of the care team were not aware that a study would take place for the two periods analyzed. We added this detail.

See line 132: “Data were collected by the retrospective review of medical files in October 2014”

7) If the focus of this study is reporting the QI work, then more information is needed to adequately describe the QI process.

Answer: Thank you for this comment. The process of HUGO guideline implementation is described in material and methods. We added some details in the Methods sections (lines 111-116), and we added general information on the QI process in the Discussion section (see line 273-282). We also added a summary of the HUGO bronchiolitis guidelines in the online resource 1 and we also checked that all relevant information on quality improvement was reported in our manuscript according to SQUIRE guideline. We also added a sentence in the abstract to mention quality improvement.

See answer to point 2) above for citation

See online resource 1

See lines 103-104: “This study was reported according to the SQUIRE (Standards for Quality Improvement Reporting Excellence) reporting guidelines.”

See online resource 5 with completed SQUIRE checklist.

See abstract lines 28-29 : “We hypothesize that the implementation of these guidelines contributed to the quality improvement of the management of bronchiolitis in our hospital.”

This study is relevant and important in describing improvement of bronchiolitis inpatient care in France. However, significant revisions are required to more adequately explain the methodology in the context of QI.