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Journal:	<i>BMJ Paediatrics Open</i>
Manuscript ID	bmjpo-2021-001111
Article Type:	Original research
Date Submitted by the Author:	29-Mar-2021
Complete List of Authors:	Klem, Nicolai; University of Oslo, Department of General Practice Skjerven, Håvard Ove; Oslo University Hospital Nilsen, Beate; Oslo Accident and Emergency Outpatient Clinic Brekke, Mette; University of Oslo, Department of General Practice Vallahsnes, Odd Martin; University of Oslo, Department of General Practice
Keywords:	Health services research, Virology, Therapeutics

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Treatment for acute bronchiolitis before and after implementation of new national guidelines: an observational study from primary and secondary care in Oslo, Norway

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Word count: 2328

What is known about the subject

- Treatment guidelines for acute bronchiolitis no longer recommend the use of nebulized adrenaline
- Guidelines, often made in the specialist health services for specific conditions, are often perceived not to fit the primary care population

What this study adds

- The successful implementation of a new treatment guideline for acute bronchiolitis, reduced the use of nebulized adrenaline both in primary and secondary care
- An inverse rise in the use of nebulized saline was seen in both settings, though not specifically recommended
- Use of antibiotics remained low

ABSTRACT

Background: Acute bronchiolitis treatment guidelines changed in Norway in 2013, no longer recommending the use of nebulized adrenaline. We aimed to assess whether these changes were successfully implemented in both primary and secondary care. Secondary aims were to compare the difference in management of acute bronchiolitis patients in primary and secondary care between 2009 and 2017.

Methods: We retrospectively registered data on demographics, clinical features and management from electronic medical records of all infants (<12 months of age) diagnosed with acute bronchiolitis at a primary care centre (Oslo Accident and Emergency Outpatient Clinic) and a secondary care centre (Oslo University Hospital) in Norway in 2009, 2014, and 2017. All patient records were individually reviewed to ensure data accuracy.

Results: We included 680 (36.3%) patients from primary care and 1195 (63.7%) from secondary care. There was a reduction in the use of nebulized adrenaline from 2009 to 2017 from 66.9% to 16.1% of cases ($p<0.001$) in primary care and from 59.1 % to 4.9 % ($p<0.001$) in secondary care. In parallel, there was an increase in the use of nebulized saline treatment, from 0.8% to 53.8% ($p<0.001$) in primary care and from 39.3% to 65.3% ($p<0.001$) in secondary care. The decrease in the use of nebulized racemic adrenaline occurred earlier in secondary care than in primary care; 13.4 % vs 56.1%, respectively, in 2014.

Conclusions: Implementation of the new guidelines on the treatment of acute bronchiolitis were successfully implemented in both primary and secondary care.

Key words: Compliance, treatment guidelines, bronchiolitis, nebulizer treatment, racemic adrenaline, saline, RS-virus, antibiotic treatment, primary vs secondary care

INTRODUCTION

Bronchiolitis is an acute viral lower respiratory tract infection affecting infants below one year of age.(1) Multiple treatment options have been recommended and used throughout different regions and time periods, including nebulized beta-2-agonists, nebulized racemic adrenaline, systemic corticosteroids, antibiotics, and nebulized hypertonic saline.(1-4) Mecklin et al. showed that all of these options were used in infants below 12 months of age with bronchiolitis between 2000 and 2015 in Tampere, Finland, with an increasing use of nebulized hypertonic saline.(5) In 2013, nebulized racemic adrenaline was removed from the Norwegian national acute bronchiolitis treatment guidelines(6) as a consequence of the Bronchiolitis All-Study SE Norway that found no difference in patient outcomes in children given nebulized racemic adrenaline vs. children given nebulized saline.(2) In general, recently published guidelines from different regions recommend supportive care only and a minimal handling strategy in the treatment for acute bronchiolitis patients.(7-10)

Adherence to clinical guidelines in general practice has room for improvements.(11) One plausible explanation is that guidelines are often made by secondary care specialists for specific conditions that do not necessarily fit the primary care population.(12) The Norwegian guidelines for acute bronchiolitis are made by paediatricians for secondary care, but parts of the guidelines have been used also in Norwegian primary care.(6) To the best of our knowledge, no studies have compared how the same changes in a clinical guideline have been implemented in both primary and secondary care.

Aims

The primary aim of the study was to determine whether the new national treatment guidelines for acute bronchiolitis in Norway, published in 2013, were implemented in primary and

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3 secondary care. Secondary aims were to compare the difference in management of acute
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5 bronchiolitis patients in primary and secondary care between 2009 and 2017.
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11 **METHODS**

12 **Study design**

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15 A retrospective observational study of children < 12 months of age presenting with acute
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17 bronchiolitis at the Oslo Accident and Emergency Outpatient Clinic (OAEOC) or at the Oslo
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19 University Hospital, Division of Paediatric and Adolescent Medicine (OUH), in Oslo,
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21 Norway, in 2009, 2014, and 2017.
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28 **Settings**

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30 The Norwegian healthcare system is two-tiered, with primary care holding a gate-keeping
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32 function for secondary care. Unless triaged directly for hospital treatment by the ambulance
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34 service, patients at all ages are assessed in primary care, usually by local family physicians
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36 during office hours, or at primary care emergency outpatient clinics at weekends and nights. If
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38 the primary care doctor decides that the patient needs secondary care, the patient is transferred
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40 to hospital.
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47 In Oslo, the main primary care emergency clinic is the OAEOC, open 24 hours a day, 365
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49 days a year. Diagnostic and treatment resources include chest X-rays, point-of-care blood
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51 tests, and nebulizer treatment. Oslo is the capital city of Norway and had 666 759 inhabitants
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53 as per 1.1.2017.(13) The paediatric population (children < 18 years of age) in the OAEOC
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55 catchment area was 137 233 as per 1.1.2017, while the OUH catchment area, covering 12 of
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57 15 city districts, encompassed 110 958.(13)
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Participants

We included all patients below the age of 12 months diagnosed with bronchiolitis at the OAEOC or the OUH from the 1st of January to the 31st of December of the three years 2009, 2014, and 2017.

At the OAEOC, eligible patients were identified from the patient registration lists in the electronic medical records. If the triage nurse had described airway illness as the presenting complain in a child below the age of 12 months, the case notes were reviewed by study personnel and the patient included if given a bronchiolitis diagnosis (R78 in the International Classification of Primary Care, 2nd edition (ICPC-2))(14) or treated for bronchiolitis with relevant bronchiolitis symptoms noted. At the OUH, all contacts involving patients below the age of 12 months with a diagnosis of bronchiolitis (J21 in the International Classification of Diseases and Related Health Problems (ICD-10))(15) were identified through an electronic search in the medical records. Electronic patient records for each acute admission were reviewed. In both settings, patients were included case by case, while planned follow-up contacts were excluded. Hence, one patient could be included several times as different cases.

We reviewed 5233 patient records at the OAEOC and 1520 at the OUH, yielding 680 included cases from the OAEOC and 1195 from the OUH.

Variables

We registered demographic data (gender, age), vital signs (heart rate, oxygen saturation, respiratory rate, temperature), and clinical signs of respiratory distress (retractions, cyanosis). Furthermore, we registered treatment given, including nebulized medication (racemic

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3 adrenaline, saline, salbutamol), oxygen, high-flow nasal oxygen, ventilatory support
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5 (continuous positive airway pressure (CPAP), bilevel positive airway pressure (BPAP),
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7 respirator), nasogastric tube feeding, antipyretics, steroids, and antibiotics. Supplementary
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9 investigations were also registered, including C-reactive protein (CRP), nasopharyngeal
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11 swabs for virus and atypical bacterial agents, and chest X-rays. At the OAEOC, a CRP point-
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13 of-care test was used, not measuring values < 5 mg/L, while the OUH used a laboratory CRP
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15 test. Finally, we registered length of stay, whether the patient was transferred to hospital from
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17 the OAEOC, whether nebulizer home treatment was initiated, and whether the patient re-
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19 presented to the clinic within 48 hours.
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26 **Statistical methods**

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28 All data were analysed in IBM SPSS version 26 (IBM Corp., Chicago, IL). Pearson's chi-
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30 square test was used to compare frequencies. For continuous data, one-way analysis of
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32 variance (ANOVA) was used. Kruskal-Wallis test was used for the CRP data, which did not
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34 follow the normal distribution. The significance level was set to 5 percent. Imputation for
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36 missing data was not performed.
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42 **Ethics**

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44 The study was a quality improvement study, as per the Norwegian Law on Health Personnel
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46 §26, retrospectively collecting anonymous data already registered in patient records.
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48 Accordingly, the need for approval from an ethics committee was waived, as was the need to
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50 obtain consent to participate. The study was approved by the Oslo University Hospital
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52 Information Security and Privacy Office, and by the director of the Department of Emergency
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54 General Practice at the City of Oslo Health Agency.
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RESULTS

We included 680 cases from primary care and 1195 cases from secondary care. Mean age was higher in primary care than in secondary care, 6.1 months versus 4.8 months ($p < 0.001$). The gender distribution was similar, with 60.9 % boys in both settings. Clinical characteristics are shown in table 1.

There was a reduction in the use of nebulized racemic adrenaline treatment from 2009 to 2017; from 66.9 % (162/242) of cases to 16.1 % (32/199) ($p < 0.001$) in primary care and from 59.1 % (257/435) to 4.9 % (19/386) ($p < 0.001$) in secondary care (table 2).

Simultaneously, there was an increase in the use of nebulized saline treatment; from 0.8 % (2/242) to 53.8 % (107/199) ($p < 0.001$) in primary care and from 39.3 % (171/435) to 65.3 % (252/386) ($p < 0.001$) in secondary care. The decrease in the use of nebulized racemic adrenaline occurred earlier in secondary care (13.4 % (50/374) in 2014) than in primary care (56.1 % (134/239) in 2014).

In secondary care, there was also a reduction from 2009 to 2017 in the use of nebulized salbutamol from 14.5 % (63/435) of cases to 6.5 % (25/386) ($p = 0.001$), an increase in the use of oxygen supplement from 9.9 % (43/435) to 19.4 % (75/386) ($p < 0.001$), and of antipyretics from 6.2 % (27/435) to 13.0 % (50/386) ($p = 0.004$) (table 2). In-hospital antibiotic use was low throughout the study period; 1.9 % in 2009, 2.7 % in 2014 and 4.3 % in 2017 ($p = 0.136$). Antibiotic home-treatment initiated from the hospital was reduced from 4.6 % (20/435) to 2.8 % (11/386) ($p = 0.047$).

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3 Furthermore, there was a decrease in the use of chest X-ray as a diagnostic tool, from 4.1 %
4 (10/242) to none ($p < 0.001$) in primary care and from 31.0 % (135/435) to 19.2 % (74/386)
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6 (p < 0.001) in secondary care (table 2). At the hospital, microbiological tests were performed
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8 in 72.6 % (867/1195) of the children. RS-virus was the main agent throughout, found in 69.3
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10 % (601/867) of the samples (table 3).
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19 **DISCUSSION**

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21 In accordance with the guidelines published in 2013, the use of nebulized racemic adrenaline
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23 was substantially reduced from 2009 to 2017 in both primary and secondary care. The change
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25 occurred earlier (2014) in secondary than in primary care. In the same period, the use of
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27 nebulized saline increased and antibiotics decreased in both settings. In hospital, the use of
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29 oxygen and antipyretics increased.
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35 The new treatment guidelines were implemented already in 2014 in secondary care and well
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37 implemented in primary care in 2017. One can argue that this was fairly successful, as
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39 implementation of guidelines are known to take time.(16, 17) Our results show slower
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41 adaption to the guidelines in primary care than in secondary care. There is research suggesting
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43 low adherence to guidelines in primary care,(11) which would support our findings. Primary
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45 care physicians experience several barriers for adherence to guidelines, where lack of
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47 awareness and lack of familiarity are the two most commonly reported.(18, 19) As physicians
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49 in primary care manage patients of all ages with a wide spectrum of illnesses, the
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51 implementation of guidelines for specific illnesses might not get general attention.(12) The
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53 Bronchiolitis All-Study SE was conducted at the OUH previously to the guideline
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60 implementation, directly involving most doctors and nurses attending the acute ward.(2, 20)

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3 This would suggest a higher awareness and familiarity to the new guidelines at the hospital,
4 leading to faster adaptation. We consider full time employees and internal education programs
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8 at both clinics crucial for successful implementation.
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12 Apart from the primary care delay in implementing the new guidelines, we found similar
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14 changes in the initial treatment of patients with acute bronchiolitis in primary and secondary
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16 care. The increase in nebulized saline use is not evidence based and not recommended by
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18 national guidelines. Overtreatment is an acknowledged challenge in medicine,(21) and there
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20 is a possibility that the increasing use of nebulized saline is a consequence of the urge of
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22 health care personnel to do something, by providing any specific therapy, rather than what
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24 actually benefits the patients.
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31 The reduction in the use of nebulized beta-2-agonists is supported by new guidelines and
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33 research,(2, 9, 22-25) and is a focus across the world.(24, 25) Antibiotic treatment is not
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35 recommended for acute bronchiolitis,(9, 26, 27) and overuse is a known problem.(28-30) Our
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37 results showed a very low use of antibiotics, consistently below 5 %, compared to other
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39 countries, where rates in the range of 3.5–11.1 % are reported.(28)
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46 We found a steady rise in the use of highflow oxygen in the hospital setting. Recent research
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48 has not clearly shown that this is beneficial for acute bronchiolitis treatment.(31, 32) Hospital
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50 length of stay did not change during the study time period. However, there was an increase in
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52 the proportion of patients discharged within 24 hours, from 49.9 % to 61.4 %, signifying that
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54 a majority of hospital bronchiolitis patients only need a short period of supportive care.
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3 No more than 40 % of the bronchiolitis patients at the OAEOC were sent on to secondary
4 care. This contribution to reducing hospital emergency department crowding is an advantage
5 of a gate keeping primary care emergency health service. The availability of nebulizer
6 treatment and short-term observation gives the OAEOC the capacity to treat and observe
7 children with a wide variety of airway symptoms, and hence better to identify the patients in
8 need of hospital treatment.
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12 The main agent causing bronchiolitis is known to be RS-virus,(33, 34) as was the case in our
13 study, with Rhinovirus the second most common agent. Two or more agents were found in
14 more than one out of four children, less frequently than the 61% co-infections found by
15 Skjerven et al. in their review from 2016.(35) A relationship between viral findings and the
16 severity of respiratory disease in infants with acute bronchiolitis has not been established,
17 though it has been suggested that high genomic load can lead to longer hospital stay and more
18 use of oxygen and ventilatory support.(35, 36)
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38 **Strengths and limitations**

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40 Our study included a large patient population from both primary and secondary care.
41 Encompassing the two largest emergency departments for children in Oslo, our study
42 population is representative of the city population. Though patients were not included if
43 managed at other smaller primary care clinics, or referred by them or the ambulance service
44 directly to the neighbouring paediatric hospital covering the remaining 3 of 15 city districts,
45 this number is probably small and the population is most likely similar to ours. We therefore
46 consider our results to be representative for the population of children with acute bronchiolitis
47 needing primary and/or hospital care in Norway.
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3 The medical journal of every study subject was thoroughly examined by the first author,
4 ensuring as complete and accurate data as possible.
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10 Eligible patients were found retrospectively, and we sought to limit selection bias by having
11 clear and strict inclusion criteria. Still, some interpretation was necessary in the primary care
12 setting in cases where bronchiolitis had not been set as the main diagnosis and the patient was
13 included based on the case notes. Only the first author reviewed the patient records. This
14 secured a more consistent inclusion of patients, but at the same time carried the risk of
15 increased selection bias.
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26 Since the inclusion of some patients was based on strict criteria from case notes, we may have
27 missed some patients in the primary care group receiving ICPC-2 symptoms diagnoses rather
28 than the specific diagnosis of acute bronchiolitis. This may also partly explain why the
29 number of included patients was lower at the OAEOC than the OUH. Furthermore, the
30 ambulance service brings severely sick patients directly to hospital, hence bypassing the
31 OAEOC.
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42 **Conclusion**

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44 There was a large and highly significant reduction in the use of nebulized racemic adrenaline
45 treatment after the introduction of new national guidelines in 2013, both in primary and
46 secondary health care. Simultaneously, there was an increase in the use of nebulized saline.
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48 Implementation of the new guidelines occurred earlier in the hospital setting than in primary
49 care.
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Acknowledgements

We thank the Department of Microbiology at the Oslo University Hospital for making the microbiological data available to us.

Funding statement

Dr Klem received a six months scholarship from the Norwegian Committee on Research in General Practice (Allmenntmedisinsk Forskningsutvalg (AFU)), a committee of the Norwegian College of General Practitioners.

Data sharing statement

Data are currently not available for sharing. Several manuscripts based on the data set are in preparation. Requests concerning the data may be sent to the corresponding author.

Authors' contributions

NK conceived and designed the study, collected and analysed the data, and drafted and revised the manuscript. HOS, MB, and BN contributed to designing the study and revised the manuscript. OMV contributed to designing the study, revised the manuscript, and supervised the project.

Competing interests:

The authors have no conflicts of interest to disclose.

Patient and public involvement

Patients were not involved in designing the study, but will be involved in disseminating the results to the wider patient community.

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Table 1. Demographics and clinical features of children treated for acute bronchiolitis in primary care and at hospital in Oslo, Norway, before and after introduction of new treatment guidelines in 2013

	Primary care ^b			Hospital ^b		
	2009 <i>n</i> = 242	2014 <i>n</i> = 239	2017 <i>n</i> = 199	2009 <i>n</i> = 435	2014 <i>n</i> = 374	2017 <i>n</i> = 386
Gender						
Girls (<i>n</i> (%))	99 (41.0)	91 (38.1)	76 (38.2)	180 (41.4)	142 (38.0)	145 (37.6)
Boys (<i>n</i> (%))	143 (59.0)	148 (61.9)	123 (61.8)	255 (58.6)	232 (62.0)	241 (62.4)
Age (months, mean ± SD)	6.4 ± 3.3	6.2 ± 3.4	5.7 ± 3.3	4.9 ± 3.1	5.0 ± 3.4	4.6 ± 3.2
Heart rate (per minute, mean ± SD)	152.6 ± 22.3	151.5 ± 37.4	155.0 ± 21.0	147.7 ± 19.4	148.1 ± 21.6	151.4 ± 19.1**
Respiratory rate (per minute, mean ± SD)	50.0 ± 12.0	49.2 ± 11.7	51.9 ± 11.3	50.7 ± 11.4	50.0 ± 11.1	48.4 ± 10.4*
Oxygen saturation (% , mean ± SD)	96.5 ± 3.0	96.0 ± 5.0	96.4 ± 2.8	97.1 ± 3	96.8 ± 3.9	97.1 ± 2.7
Retractions (<i>n</i> (%))	126 (52.1)	163 (68.2)	136 (68.3)*	253 (58.2)	197 (52.7)	237 (61.4)*
Cyanosis (<i>n</i> (%))	2 (0.8)	2 (0.8)	3 (1.5)	4 (0.9)	4 (1.1)	4 (1.0)
Temperature (°C, mean ± SD)	37.5 ± 0.9	37.4 ± 0.9	37.4 ± 0.9	37.7 ± 0.8	37.6 ± 0.8	37.5 ± 0.8*
CRP (mg/L, median (IQR)) ^a	10 (5–14)	6 (5–18.5)	5 (5–11.5)**	7.0 (1.5–17.6)	7.8 (1.7–20.6)	7.0 (1.4–18)

Comparisons were done across all three years at each setting: **p* < 0.05, ***p* < 0.01, ****p* < 0.001.

^aCRP test used in primary care setting did not specify values < 5 mg/L. Values <5 mg/L are set as 5

^bExcept for two statistically significant changes in vital signs among the hospital patients; a rise in heart rate from 2009 to 2017; 147.7 ± 19.4 to 151.4 ± 19.1 (*p* < 0.01), and a fall in respiratory rate in the same time period; 50.7 ± 11.4 to 48.4 ± 10.4 (*p* < 0.05), there were no significant differences in vital signs or symptoms between the patient populations in the two settings, nor across the years at each setting.

CRP: C-reactive protein; IQR: interquartile range; SD: standard deviation.

Table 2. Management of children with acute bronchiolitis in primary care and at hospital in Oslo, Norway before and after introduction of new treatment guidelines in 2013

	Primary care			Hospital		
	2009 <i>n</i> = 242	2014 <i>n</i> = 239	2017 <i>n</i> = 199	2009 <i>n</i> = 435	2014 <i>n</i> = 374	2017 <i>n</i> = 386
Nebulized racemic adrenaline (<i>n</i> (%))	162 (66.9)	134 (56.1)	32 (16.1)***	257 (59.1)	50 (13.4)	19 (4.9)***
Nebulized saline (<i>n</i> (%))	2 (0.8)	52 (21.8)	107 (53.8)***	171 (39.3)	278 (74.3)	252 (65.3)***
Nebulized salbutamol (<i>n</i> (%))	5 (2.1)	9 (3.8)	4 (2.0)	63 (14.5)	36 (9.6)	25 (6.5)**
Oxygen supplement (<i>n</i> (%))	5 (2.1)	4 (1.7)	4 (2.0)	43 (9.9)	86 (23.0)	75 (19.4)***
Betamethasone (<i>n</i> (%))	16 (6.6)	13 (5.4)	9 (4.5)	29 (6.7)	16 (4.3)	14 (3.6)
Antipyretics (<i>n</i> (%))	7 (2.9)	20 (8.4)	5 (2.5)**	27 (6.2)	34 (9.1)	50 (13.0)***
Chest X-ray (<i>n</i> (%))	10 (4.1)	0 (0.0)	0 (0.0)***	135 (31.0)	67 (17.9)	74 (19.2)***
Referral to hospital (<i>n</i> (%))	93 (38.4)	107 (44.8)	79 (39.7)	Not applicable		
Hospitalization days (<i>mean</i> ± <i>SD</i>)				2.7 ± 3.8	2.7 ± 3.0	2.2 ± 2.4
Hospitalized less than 24 hours (<i>n</i> (%))				217 (49.9)	197 (52.7)	237 (61.4)**
Highflow nasal oxygen (<i>n</i> (%))				0 (0.0)	20 (5.3)	38 (9.8)***
CPAP/BPAP (<i>n</i> (%))				19 (4.4)	27 (7.2)	23 (6.0)
Respirator/mechanical ventilation (<i>n</i> (%))	Not applicable			6 (1.4)	7 (1.9)	7 (1.8)
Nasogastric tube (<i>n</i> (%))				40 (9.2)	43 (11.5)	56 (14.5)
Microbiological nasopharyngeal testing				303 (69.7)	278 (74.3)	286 (74.1)
Antibiotics in hospital (<i>n</i> (%))				8 (1.9)	10 (2.7)	16 (4.3)
Antibiotics home treatment (<i>n</i> (%))	4 (1.7)	1 (0.4)	1 (0.5)	20 (4.6)	6 (1.6)	11 (2.8)*
Nebulization home-treatment (<i>n</i> (%))	Not applicable			227 (52.2)	231 (61.8)	238 (61.7)**
Recontact within 48 hours (<i>n</i> (%))	39 (16.1)	35 (14.6)	32 (16.1)	37 (8.5)	39 (10.4)	50 (13.0)

Comparisons were done across all three years at each setting: **p* < 0.05, ***p* < 0.01, ****p* < 0.001.

BPAP: Bilevel positive airway pressure; CPAP: continuous positive airway pressure; SD: standard deviation.

Table 3 – Microbiological results from nasopharynx swabs in children with acute bronchiolitis treated at hospital in Oslo, Norway, before and after introduction of new treatment guidelines in 2013

	2009	2014	2017
	<i>n</i> = 303	<i>n</i> = 278	<i>n</i> = 286
RS-virus (<i>n</i> (%))	181 (59.7)	206 (74.1)	214 (74.8)
Rhinovirus (<i>n</i> (%))	^a	126 (45.3)	117 (40.9)
Other viruses (<i>n</i> (%))	63 (20.8)	78 (28.1)	73 (25.5)
Bacteria (<i>n</i> (%))	5 (1.7)	0 (0.0)	4 (1.4)
Two or more agents (<i>n</i> (%))	11 (3.6) ^a	79 (28.4)	56 (19.6)
Negative results (<i>n</i> (%))	87 (28.7) ^a	16 (5.8)	12 (4.2)

^aRhinovirus was not tested for in 2009.

RS-virus: Respiratory syncytial virus.

BMJ Paediatrics Open

Treatment for acute bronchiolitis before and after implementation of new national guidelines: a retrospective observational study from primary and secondary care in Oslo, Norway

Journal:	<i>BMJ Paediatrics Open</i>
Manuscript ID	bmjpo-2021-001111.R1
Article Type:	Original research
Date Submitted by the Author:	30-Apr-2021
Complete List of Authors:	Klem, Nicolai; University of Oslo, Department of General Practice Skjerven, Håvard Ove; Oslo University Hospital Nilsen, Beate; Oslo Accident and Emergency Outpatient Clinic Brekke, Mette; University of Oslo, Department of General Practice Vallersnes, Odd Martin; University of Oslo, Department of General Practice
Keywords:	Health services research, Virology, Therapeutics

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3 **Treatment for acute bronchiolitis before and after**
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6 **implementation of new national guidelines: a retrospective**
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5 **Word count:** 2395
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10 **What is known about the subject**
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- 13 • Treatment guidelines for acute bronchiolitis no longer recommend the use of
14 nebulized adrenaline
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 - 16 • Guidelines, often made by hospital specialists for hospital care, are often perceived not
17 to fit the primary care population
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26 **What this study adds**
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- 29 • The successful implementation of a new treatment guideline for acute bronchiolitis,
30 reduced the use of nebulized adrenaline both in primary and secondary care
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 - 32 • An inverse rise in the use of nebulized saline was seen in both settings, though not
33 specifically recommended
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 - 36 • Use of antibiotics remained low
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ABSTRACT

Background: Acute bronchiolitis treatment guidelines changed in Norway in 2013, no longer recommending the use of nebulized adrenaline. We aimed to assess whether these changes were successfully implemented in both primary and secondary care. Secondary aims were to compare the difference in management of acute bronchiolitis patients in primary and secondary care between 2009 and 2017.

Methods: We retrospectively registered data on demographics, clinical features and management from electronic medical records of all infants (<12 months of age) diagnosed with acute bronchiolitis at a primary care centre (Oslo Accident and Emergency Outpatient Clinic) and a secondary care centre (Oslo University Hospital) in Norway in 2009, 2014, and 2017. All patient records were individually reviewed to ensure data accuracy.

Results: We included 680 (36.3%) patients from primary care and 1195 (63.7%) from secondary care. There was a reduction in the use of nebulized adrenaline from 2009 to 2017 from 66.9% to 16.1% of cases ($p<0.001$) in primary care and from 59.1 % to 4.9 % ($p<0.001$) in secondary care. In parallel, there was an increase in the use of nebulized saline treatment, from 0.8% to 53.8% ($p<0.001$) in primary care and from 39.3% to 65.3% ($p<0.001$) in secondary care. The decrease in the use of nebulized racemic adrenaline occurred earlier in secondary care than in primary care; 13.4 % vs 56.1%, respectively, in 2014.

Conclusions: Implementation of the new guidelines on the treatment of acute bronchiolitis were successfully implemented in both primary and secondary care.

Key words: Compliance, treatment guidelines, bronchiolitis, nebulizer treatment, racemic adrenaline, saline, RS-virus, antibiotic treatment, primary vs secondary care

INTRODUCTION

Bronchiolitis is an acute viral lower respiratory tract infection affecting infants below one year of age.(1) Multiple treatment options have been recommended and used throughout different regions and time periods, including nebulized beta-2-agonists, nebulized racemic adrenaline, systemic corticosteroids, antibiotics, and nebulized hypertonic saline.(1-4) Mecklin et al. showed that all of these options were used in infants below 12 months of age with bronchiolitis between 2000 and 2015 in Tampere, Finland, with an increasing use of nebulized hypertonic saline.(5) In 2013, nebulized racemic adrenaline was removed from the Norwegian national acute bronchiolitis treatment guidelines(6) as a consequence of the Bronchiolitis All-Study SE Norway that found no difference in patient outcomes in children given nebulized racemic adrenaline vs. children given nebulized saline.(2) In general, recently published guidelines from different regions recommend supportive care only and a minimal handling strategy in the treatment for acute bronchiolitis patients.(7-10)

Adherence to clinical guidelines in general practice has room for improvements.(11) One plausible explanation is that guidelines are often made by secondary care specialists for specific conditions that do not necessarily fit the primary care population.(12) The Norwegian guidelines for acute bronchiolitis are made by paediatricians for secondary care, but parts of the guidelines have been used also in Norwegian primary care.(6) To the best of our knowledge, no studies have compared how the same changes in a clinical guideline have been implemented in both primary and secondary care.

Aims

The primary aim of the study was to determine whether the new national treatment guidelines for acute bronchiolitis in Norway, published in 2013, were implemented in primary and secondary care. Secondary aims were to compare the difference in management of acute bronchiolitis patients in primary and secondary care between 2009 and 2017.

METHODS

Study design

A retrospective observational study of children < 12 months of age presenting with acute bronchiolitis at the Oslo Accident and Emergency Outpatient Clinic (OAEOC) or at the Oslo University Hospital, Division of Paediatric and Adolescent Medicine (OUH), in Oslo, Norway, in 2009, 2014, and 2017.

Settings

The Norwegian healthcare system is two-tiered, with primary care holding a gate-keeping function for secondary care. Unless triaged directly for hospital treatment by the ambulance service, patients at all ages are assessed in primary care, usually by local family physicians during office hours, or at primary care emergency outpatient clinics at weekends and nights. If the primary care doctor decides that the patient needs secondary care, the patient is transferred to hospital.

In Oslo, the main primary care emergency clinic is the OAEOC, open 24 hours a day, 365 days a year. Diagnostic and treatment resources include chest X-rays, point-of-care blood tests, and nebulizer treatment. Oslo is the capital city of Norway and had 666 759 inhabitants

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3 as per 1.1.2017.(13) The paediatric population (children < 18 years of age) in the OAEOC
4 catchment area was 137 233 as per 1.1.2017, while the OUH catchment area, covering 12 of
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8 15 city districts, encompassed 110 958.(13)
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10 11 12 **Participants**

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14 We included all patients below the age of 12 months diagnosed with bronchiolitis at the
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2014, and 2017.

At the OAEOC, eligible patients were identified from the patient registration lists in the
electronic medical records. If the triage nurse had described airway illness, or symptoms
associated with airway illness, as the presenting complaint in a child below the age of 12
months, the case notes were reviewed by study personnel and the patient included if given a
bronchiolitis diagnosis (R78 in the International Classification of Primary Care, 2nd edition
(ICPC-2))(14) or treated for bronchiolitis with relevant bronchiolitis symptoms noted. At the
OUH, all contacts involving patients below the age of 12 months with a diagnosis of
bronchiolitis (J21 in the International Classification of Diseases and Related Health Problems
(ICD-10))(15) were identified through an electronic search in the medical records. Electronic
patient records for each acute admission were reviewed. In both settings, patients were
included case by case, while planned follow-up contacts were excluded. Hence, one patient
could be included several times as different cases.

We reviewed 5233 patient records at the OAEOC and 1520 at the OUH, yielding 680
included cases from the OAEOC and 1195 from the OUH.

Variables

We registered demographic data (gender, age), vital signs (heart rate, oxygen saturation, respiratory rate, temperature), and clinical signs of respiratory distress (retractions, cyanosis). Furthermore, we registered treatment given, including nebulized medication (racemic adrenaline, saline, salbutamol), oxygen, high-flow nasal oxygen, ventilatory support (continuous positive airway pressure (CPAP), bilevel positive airway pressure (BPAP), respirator), nasogastric tube feeding, antipyretics, steroids, and antibiotics. Supplementary investigations were also registered, including C-reactive protein (CRP), nasopharyngeal swabs for virus and atypical bacterial agents, and chest X-rays. At the OAEOC, a CRP point-of-care test was used, not measuring values < 5 mg/L, while the OUH used a laboratory CRP test. Finally, we registered length of stay, whether the patient was transferred to hospital from the OAEOC, whether nebulizer home treatment was initiated, and whether the patient re-presented to the clinic within 48 hours.

Statistical methods

All data were analysed in IBM SPSS version 26 (IBM Corp., Chicago, IL). Pearson's chi-square test was used to compare frequencies. For continuous data, one-way analysis of variance (ANOVA) was used. Kruskal-Wallis test was used for the CRP data, which did not follow the normal distribution. The significance level was set to 5 percent. Imputation for missing data was not performed.

Ethics

The study was a quality improvement study, as per the Norwegian Law on Health Personnel §26, retrospectively collecting anonymous data already registered in patient records.

Accordingly, the need for approval from an ethics committee was waived, as was the need to

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3 obtain consent to participate. The study was approved by the Oslo University Hospital
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5 Information Security and Privacy Office, and by the director of the Department of Emergency
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7 General Practice at the City of Oslo Health Agency.
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11 12 13 14 **RESULTS**

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16 We included 680 cases from primary care and 1195 cases from secondary care. Mean age was
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18 higher in primary care than in secondary care, 6.1 months versus 4.8 months ($p < 0.001$). The
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20 gender distribution was similar, with 60.9 % boys in both settings. Clinical characteristics are
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22 shown in table 1.
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28 There was a reduction in the use of nebulized racemic adrenaline treatment from 2009 to
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30 2017; from 66.9 % (162/242) of cases to 16.1 % (32/199) ($p < 0.001$) in primary care and
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32 from 59.1 % (257/435) to 4.9 % (19/386) ($p < 0.001$) in secondary care (table 2).
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36 Simultaneously, there was an increase in the use of nebulized saline treatment; from 0.8 %
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38 (2/242) to 53.8 % (107/199) ($p < 0.001$) in primary care and from 39.3 % (171/435) to 65.3 %
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40 (252/386) ($p < 0.001$) in secondary care. The decrease in the use of nebulized racemic
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42 adrenaline occurred earlier in secondary care (13.4 % (50/374) in 2014) than in primary care
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44 (56.1 % (134/239) in 2014).
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49 In secondary care, there was also a reduction from 2009 to 2017 in the use of nebulized
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51 salbutamol from 14.5 % (63/435) of cases to 6.5 % (25/386) ($p = 0.001$), an increase in the
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53 use of oxygen supplement from 9.9 % (43/435) to 19.4 % (75/386) ($p < 0.001$), and of
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55 antipyretics from 6.2 % (27/435) to 13.0 % (50/386) ($p = 0.004$) (table 2). In-hospital
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57 antibiotic use was low throughout the study period; 1.9 % in 2009, 2.7 % in 2014 and 4.3 %
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3 in 2017 ($p = 0.136$). Antibiotic home-treatment initiated from the hospital was reduced from
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5 4.6 % (20/435) to 2.8 % (11/386) ($p = 0.047$).
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10 Furthermore, there was a decrease in the use of chest X-ray as a diagnostic tool, from 4.1 %
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12 (10/242) to none ($p < 0.001$) in primary care and from 31.0 % (135/435) to 19.2 % (74/386)
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14 ($p < 0.001$) in secondary care (table 2). At the hospital, microbiological tests were performed
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16 in 72.6 % (867/1195) of the children. RS-virus was the main agent throughout, found in 69.3
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18 % (601/867) of the samples (table 3).
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26 **DISCUSSION**

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28 In accordance with the guidelines published in 2013, the use of nebulized racemic adrenaline
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30 was substantially reduced from 2009 to 2017 in both primary and secondary care. The change
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32 occurred earlier (2014) in secondary than in primary care. In the same period, the use of
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34 nebulized saline increased and antibiotics decreased in both settings. In hospital, the use of
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36 oxygen and antipyretics increased.
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42 The new treatment guidelines were implemented already in 2014 in secondary care and well
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44 implemented in primary care in 2017. One can argue that this was fairly successful, as
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46 implementation of guidelines are known to take time.(16, 17) Our results show slower
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48 adaption to the guidelines in primary care than in secondary care. There is research suggesting
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50 lower adherence to guidelines in primary care,(11) which would support our findings. Primary
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52 care physicians experience several barriers for adherence to guidelines, where lack of
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54 awareness and lack of familiarity are the two most commonly reported.(18, 19) As physicians
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56 in primary care manage patients of all ages with a wide spectrum of illnesses, the
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3 implementation of guidelines for specific illnesses might not get general attention.(12) The
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5 Bronchiolitis All-Study SE was conducted at the OUH previously to the guideline
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7 implementation, directly involving most doctors and nurses attending the acute ward.(2, 20)
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10 This would suggest a higher awareness and familiarity to the new guidelines at the hospital,
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12 leading to faster adaptation. We consider full time employees and internal education programs
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14 at both clinics crucial for successful implementation.
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20 Apart from the primary care delay in implementing the new guidelines, we found similar
21
22 changes in the initial treatment of patients with acute bronchiolitis in primary and secondary
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24 care. The increase in nebulized saline use is not evidence based and not recommended by
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26 national guidelines. Overtreatment is an acknowledged challenge in medicine,(21) and there
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28 is a possibility that the increasing use of nebulized saline is a consequence of the urge of
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30 health care personnel to do something, by providing any specific therapy rather than what is
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32 evidence based management.
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39 The reduction in the use of nebulized beta-2-agonists is supported by new guidelines and
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41 research,(2, 9, 22-25) and is a focus across the world.(24, 25) Antibiotic treatment is not
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43 recommended for acute bronchiolitis,(9, 26, 27) and overuse is a known problem.(28-30) Our
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45 results showed a very low use of antibiotics, consistently below 5 %, compared to other
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47 countries, where rates in the range of 3.5–11.1 % are reported.(28)
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52 We found a steady rise in the use of highflow oxygen in the hospital setting. Recent research
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54 has not clearly shown that this is beneficial for acute bronchiolitis treatment.(31, 32) Hospital
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56 length of stay did not change during the study time period. However, there was an increase in
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3 the proportion of patients discharged within 24 hours, from 49.9 % to 61.4 %, signifying that
4 a majority of hospital bronchiolitis patients only need a short period of supportive care.
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10 No more than 40 % of the bronchiolitis patients at the OAEOC were sent on to secondary
11 care. This contribution to reducing hospital emergency department crowding is an advantage
12 of a gate keeping primary care emergency health service. The availability of nebulizer
13 treatment and short-term observation gives the OAEOC the capacity to treat and observe
14 children with a wide variety of airway symptoms, and hence better to identify the patients in
15 need of hospital treatment.
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26 The main agent causing bronchiolitis is known to be RS-virus,(33, 34) as was the case in our
27 study, with Rhinovirus the second most common agent. Two or more agents were found in
28 more than one out of four children, less frequently than the 61% co-infections found by
29 Skjerven et al. in their review from 2016.(35) A relationship between viral findings and the
30 severity of respiratory disease in infants with acute bronchiolitis has not been established,
31 though it has been suggested that high genomic load can lead to longer hospital stay and more
32 use of oxygen and ventilatory support.(35, 36)
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45 **Strengths and limitations**

46 Our study included a large patient population from both primary and secondary care.
47 Encompassing the two largest emergency departments for children in Oslo, our study
48 population is representative of the city population. Though patients were not included if
49 managed at other smaller primary care clinics, or referred by them or the ambulance service
50 directly to the neighbouring paediatric hospital covering the remaining 3 of 15 city districts,
51 this number is probably small and the population is most likely similar to ours. We therefore
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3 consider our results to be representative for the population of children with acute bronchiolitis
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5 needing primary and/or hospital care in Norway.
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10 The medical journal of every study subject was thoroughly examined by the first author,
11 ensuring as complete and accurate data as possible. Clinical signs, diagnostic investigations,
12 or treatments not mentioned in the patient records were considered not present or not
13 performed. This may have resulted in some underreporting, though not enough to have an
14 impact on our conclusions.
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23 Eligible patients were found retrospectively, and we sought to limit selection bias by having
24 clear and strict inclusion criteria. Still, some interpretation was necessary in the primary care
25 setting in cases where bronchiolitis had not been set as the main diagnosis and the patient was
26 included based on the case notes. Only the first author reviewed the patient records. This
27 secured a more consistent inclusion of patients, but at the same time carried the risk of
28 increased selection bias.
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40 Since the inclusion of some patients was based on strict criteria from case notes, we may have
41 missed some patients in the primary care group receiving ICPC-2 symptoms diagnoses rather
42 than the specific diagnosis of acute bronchiolitis. However, the patient records of all
43 individuals with related symptom diagnoses was manually screened to identify signs and
44 symptoms in order to identify acute bronchiolitis. This may also partly explain why the
45 number of included patients was lower at the OAEOC than the OUH. Furthermore, the
46 ambulance service brings severely sick patients directly to hospital, hence bypassing the
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Conclusion

There was a large and highly significant reduction in the use of nebulized racemic adrenaline treatment after the introduction of new national guidelines in 2013, both in primary and secondary health care. Simultaneously, there was an increase in the use of nebulized saline. Implementation of the new guidelines occurred earlier in the hospital setting than in primary care.

Acknowledgements

We thank the Department of Microbiology at the Oslo University Hospital for making the microbiological data available to us.

Funding statement

Dr Klem received a six months scholarship from the Norwegian Committee on Research in General Practice (Allmenntmedisinsk Forskningsutvalg (AFU)), a committee of the Norwegian College of General Practitioners.

Data sharing statement

Data are currently not available for sharing. Several manuscripts based on the data set are in preparation. Requests concerning the data may be sent to the corresponding author.

Authors' contributions

NK conceived and designed the study, collected and analysed the data, and drafted and revised the manuscript. HOS, MB, and BN contributed to designing the study and revised the

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3 manuscript. OMV contributed to designing the study, revised the manuscript, and supervised
4 the project.
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10 **Competing interests:**

11
12 The authors have no conflicts of interest to disclose.
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15 **Patient and public involvement**

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17 Patients were not involved in designing the study, but will be involved in disseminating the
18 results to the wider patient community.
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Confidential: For Review Only

Table 1. Demographics and clinical features of children treated for acute bronchiolitis in primary care and at hospital in Oslo, Norway, before and after introduction of new treatment guidelines in 2013

	Primary care ^b			Hospital ^b		
	2009 <i>n</i> = 242	2014 <i>n</i> = 239	2017 <i>n</i> = 199	2009 <i>n</i> = 435	2014 <i>n</i> = 374	2017 <i>n</i> = 386
Gender						
Girls (<i>n</i> (%))	99 (41.0)	91 (38.1)	76 (38.2)	180 (41.4)	142 (38.0)	145 (37.6)
Boys (<i>n</i> (%))	143 (59.0)	148 (61.9)	123 (61.8)	255 (58.6)	232 (62.0)	241 (62.4)
Age (months, mean ± SD)	6.4 ± 3.3	6.2 ± 3.4	5.7 ± 3.3	4.9 ± 3.1	5.0 ± 3.4	4.6 ± 3.2
Heart rate (per minute, mean ± SD)	152.6 ± 22.3	151.5 ± 37.4	155.0 ± 21.0	147.7 ± 19.4	148.1 ± 21.6	151.4 ± 19.1**
Respiratory rate (per minute, mean ± SD)	50.0 ± 12.0	49.2 ± 11.7	51.9 ± 11.3	50.7 ± 11.4	50.0 ± 11.1	48.4 ± 10.4*
Oxygen saturation (% , mean ± SD)	96.5 ± 3.0	96.0 ± 5.0	96.4 ± 2.8	97.1 ± 3	96.8 ± 3.9	97.1 ± 2.7
Retractions (<i>n</i> (%))	126 (52.1)	163 (68.2)	136 (68.3)*	253 (58.2)	197 (52.7)	237 (61.4)*
Cyanosis (<i>n</i> (%))	2 (0.8)	2 (0.8)	3 (1.5)	4 (0.9)	4 (1.1)	4 (1.0)
Temperature (°C, mean ± SD)	37.5 ± 0.9	37.4 ± 0.9	37.4 ± 0.9	37.7 ± 0.8	37.6 ± 0.8	37.5 ± 0.8*
CRP (mg/L, median (IQR)) ^a	10 (5–14)	6 (5–18.5)	5 (5–11.5)**	7.0 (1.5–17.6)	7.8 (1.7–20.6)	7.0 (1.4–18)

Comparisons were done across all three years at each setting: **p* < 0.05, ***p* < 0.01, ****p* < 0.001.

^aCRP test used in primary care setting did not specify values < 5 mg/L. Values <5 mg/L are set as 5

^bExcept for two statistically significant changes in vital signs among the hospital patients; a rise in heart rate from 2009 to 2017; 147.7 ± 19.4 to 151.4 ± 19.1 (*p* < 0.01), and a fall in respiratory rate in the same time period; 50.7 ± 11.4 to 48.4 ± 10.4 (*p* < 0.05), there were no significant differences in vital signs or symptoms between the patient populations in the two settings, nor across the years at each setting.

CRP: C-reactive protein; IQR: interquartile range; SD: standard deviation.

Table 2. Management of children with acute bronchiolitis in primary care and at hospital in Oslo, Norway before and after introduction of new treatment guidelines in 2013

	Primary care			Hospital		
	2009 <i>n</i> = 242	2014 <i>n</i> = 239	2017 <i>n</i> = 199	2009 <i>n</i> = 435	2014 <i>n</i> = 374	2017 <i>n</i> = 386
Nebulized racemic adrenaline (<i>n</i> (%))	162 (66.9)	134 (56.1)	32 (16.1)***	257 (59.1)	50 (13.4)	19 (4.9)***
Nebulized saline (<i>n</i> (%))	2 (0.8)	52 (21.8)	107 (53.8)***	171 (39.3)	278 (74.3)	252 (65.3)***
Nebulized salbutamol (<i>n</i> (%))	5 (2.1)	9 (3.8)	4 (2.0)	63 (14.5)	36 (9.6)	25 (6.5)**
Oxygen supplement (<i>n</i> (%))	5 (2.1)	4 (1.7)	4 (2.0)	43 (9.9)	86 (23.0)	75 (19.4)***
Betamethasone (<i>n</i> (%))	16 (6.6)	13 (5.4)	9 (4.5)	29 (6.7)	16 (4.3)	14 (3.6)
Antipyretics (<i>n</i> (%))	7 (2.9)	20 (8.4)	5 (2.5)**	27 (6.2)	34 (9.1)	50 (13.0)***
Chest X-ray (<i>n</i> (%))	10 (4.1)	0 (0.0)	0 (0.0)***	135 (31.0)	67 (17.9)	74 (19.2)***
Referral to hospital (<i>n</i> (%))	93 (38.4)	107 (44.8)	79 (39.7)	Not applicable		
Hospitalization days (<i>mean</i> ± <i>SD</i>)				2.7 ± 3.8	2.7 ± 3.0	2.2 ± 2.4
Hospitalized less than 24 hours (<i>n</i> (%))				217 (49.9)	197 (52.7)	237 (61.4)**
Highflow nasal oxygen (<i>n</i> (%))				0 (0.0)	20 (5.3)	38 (9.8)***
CPAP/BPAP (<i>n</i> (%))				19 (4.4)	27 (7.2)	23 (6.0)
Respirator/mechanical ventilation (<i>n</i> (%))	Not applicable			6 (1.4)	7 (1.9)	7 (1.8)
Nasogastric tube (<i>n</i> (%))				40 (9.2)	43 (11.5)	56 (14.5)
Microbiological nasopharyngeal testing				303 (69.7)	278 (74.3)	286 (74.1)
Antibiotics in hospital (<i>n</i> (%))				8 (1.9)	10 (2.7)	16 (4.3)
Antibiotics home treatment (<i>n</i> (%))	4 (1.7)	1 (0.4)	1 (0.5)	20 (4.6)	6 (1.6)	11 (2.8)*
Nebulization home-treatment (<i>n</i> (%))	Not applicable			227 (52.2)	231 (61.8)	238 (61.7)**
Recontact within 48 hours (<i>n</i> (%))	39 (16.1)	35 (14.6)	32 (16.1)	37 (8.5)	39 (10.4)	50 (13.0)

Comparisons were done across all three years at each setting: **p* < 0.05, ***p* < 0.01, ****p* < 0.001.

BPAP: Bilevel positive airway pressure; CPAP: continuous positive airway pressure; SD: standard deviation.

Table 3 – Microbiological results from nasopharynx swabs in children with acute bronchiolitis treated at hospital in Oslo, Norway, before and after introduction of new treatment guidelines in 2013

	2009	2014	2017
	<i>n</i> = 303	<i>n</i> = 278	<i>n</i> = 286
RS-virus (<i>n</i> (%))	181 (59.7)	206 (74.1)	214 (74.8)
Rhinovirus (<i>n</i> (%))	^a	126 (45.3)	117 (40.9)
Other viruses (<i>n</i> (%))	63 (20.8)	78 (28.1)	73 (25.5)
Bacteria (<i>n</i> (%))	5 (1.7)	0 (0.0)	4 (1.4)
Two or more agents (<i>n</i> (%))	11 (3.6) ^a	79 (28.4)	56 (19.6)
Negative results (<i>n</i> (%))	87 (28.7) ^a	16 (5.8)	12 (4.2)

^aRhinovirus was not tested for in 2009.

RS-virus: Respiratory syncytial virus.