Lower respiratory tract infection caused by respiratory syncytial virus. The short-term and the long-term efficacy of corticosteroids
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Chapter 1
Hospitalisations for bronchiolitis in the Netherlands from 1991 through 1999

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Abstract

Background
Respiratory Syncytial virus (RSV) is the causative agent in the majority of the bronchiolitis hospital admissions in infants and young children. To analyse trends in pediatric bronchiolitis hospitalisations in The Netherlands an observational study was performed.

Methods
From January 1991 through December 1999 the number of bronchiolitis hospitalisations for children up to 4 years of age were compared with the number of asthma and pneumonia hospitalisations, as well as with trends in the number of national RSV detections. In addition, the number of patients with known risk factors for severe RSV disease (bronchopulmonary dysplasia, congenital heart disease and prematurity) and the number of patients admitted to two pediatric intensive care units (PICU) with RSV lower respiratory tract infection were analysed.

Results
The number of bronchiolitis hospitalisations increased 2.8 times from 1022 in season-year 1991–1992 to 2918 in season-year 1998–1999 (p value for trend 0.003), whereas neither the number of asthma nor of pneumonia hospitalisations changed significantly. The number of RSV detections showed the same increasing pattern as the bronchiolitis admissions. However, this trend did not reach statistical significance. We observed no changes in the number of patients belonging to riskgroups, neither in the number of PICU RSV admissions during the study period.

Conclusions
We found an increase in number of pediatric bronchiolitis hospitalisations in The Netherlands from 1991 through 1999, which may have an important socio-economic impact.

Introduction
Respiratory syncytial virus (RSV) is the most important respiratory pathogen in infancy, causing lower respiratory tract infection in about 30% of the cases, with bronchiolitis being the most common manifestation. In general, about 1% to 2% of the children with RSV disease needs to be hospitalised for monitoring and supportive therapy. It has been demonstrated that from 1980 through 1989 bronchiolitis hospitalisations have increased in The Netherlands. To assess trends in hospitalisation for bronchiolitis from 1991 through 1999 in The Netherlands we performed this descriptive analysis.
Methods

Study design
Hospital discharge data from January 1991 through December 1999 for children up to 4 years of age were obtained from the National Medical Registration (LMR Prismant, Utrecht, The Netherlands), that obtains discharge data of more than 95% of the hospitals in The Netherlands. We planned to compare trends in bronchiolitis hospitalisations with trends in hospital admissions of other common acute respiratory diseases in infancy and childhood in the same age group. Therefore, data with the following International Classification of Diseases, ninth revision, clinical modification (ICD-9-CM, www.cdc.gov/nchs) codes were selected: bronchiolitis (code 466.1), asthma (code 493) and bacterial pneumonia (code 481, 486, 4822, 4823, 4824, 4828, 4829). In order to analyse whether trends in bronchiolitis hospitalisations could be related to trends in number of RSV detections, virological data were obtained from the Dutch Working Group on Clinical Virology in co-operation with the National Institute of Public Health and the Environment (RIVM). The RIVM registers weekly the positive RSV results of 17 virological laboratories, that represent approximately 50% of all laboratories performing RSV tests in The Netherlands (RIVM, unpublished data). In addition, to compare bronchiolitis hospitalisations with the number of patients at risk for a severe course of RSV disease we also analysed annual hospitalisation data of patients with bronchopulmonary dysplasia (BPD, code 7707) and congenital heart disease (CHD, code 745 and 746) as well as the number of premature births in The Netherlands (data obtained from the National Neonatology Registration, Prismant, Utrecht, The Netherlands). Finally, to analyse whether there have been a change in disease severity, we counted all children admitted to the paediatric intensive care unit (PICU) of both the Emma Children’s Hospital (Amsterdam), as well as the Wilhelmina Children’s Hospital (Utrecht) with the discharge diagnosis RSV lower respiratory tract infection (RSV-LRTI) from 1991 through 1999. Both are tertiary care university hospitals with a 10 to 14 bed multidisciplinary PICU, each with on the average 550 admissions annually, and represent 25% to 30% of the total PICU beds in The Netherlands.

Statistical analysis
Statistical analysis was performed with the SPSS package for Windows, version 9.0 (SPSS Inc., Chicago, Ill.). Trends in hospitalisation were tested with linear regression analysis. A p value of <0.05 was considered statistically significant.
Results
To analyse trends in hospitalisations per 'RSV-season-year' monthly admission data of bronchiolitis, asthma and pneumonia were clustered from July until June the year thereafter. During 8 season-years the number of bronchiolitis hospitalisations among children up to 4 years of age significantly increased from 1022 in season-year 1991–1992 to 2918 in season-year 1998–1999 (Table 1.1 and Figure 1.1). There has been no significant change in annual number of live births during the same period (Yearbook Statistics Netherlands 1991-2000, data not shown). Neither the number of asthma nor of pneumonia hospitalisations changed significantly during the same period (Table 1.1 and Figure 1.1).
Although the number of RSV detections clustered per season-year showed the same increasing pattern as the bronchiolitis hospitalisations (Figure 1.1) this trend was statistically not significant (Table 1.1).
There was no significant change in the number of patients hospitalised with bronchopulmonary dysplasia (range from 97 to 171), with congenital heart disease (range from 1689 to 2106) nor in the number of premature births (range from 1402 to 1993) during the study period.
Finally, the bronchiolitis hospitalisations were compared with the number of RSV-LRTI admissions on the two PICU’s. Although the number of PICU patients with RSV-LRTI per RSV-season-year increased significantly during the study period (p value for trend 0.04), there was no significant trend in the proportion of PICU patients compared to the bronchiolitis hospitalisations per season-year.

Discussion
We found that the number of bronchiolitis hospitalisations in The Netherlands has increased from 1991 through 1999. An increase of bronchiolitis hospitalisations has also been reported in other countries since the 1980s.\(^3\)
The explanation of the increase in bronchiolitis hospitalisations is probably multifactorial. Changes in admission criteria for bronchiolitis may have played a role, but are difficult to quantify. Shay et al suggested that increased use of pulse oximetry in emergency departments could have contributed to the observed increase of bronchiolitis admissions in the USA.\(^3\) Although no data are available on the use of pulse oximetry in children with bronchiolitis seen on the emergency departments in The Netherlands it is known that nowadays over 80% of the hospitalised children with RSV bronchiolitis are monitored with pulse oximetry.\(^4\)
RSV bronchiolitis has many features in common with asthma and a diagnostic shift from asthma to bronchiolitis may have occurred during the period under study. This may have been guided by the introduction of the rapid direct immunofluorescence RSV tests that were introduced in the mid-1980s in The Netherlands. Although the prevalence of asthma in developed countries has increased during the study period, the severity of asthma and the hospitalisations probably did not change.\(^5\) Therefore,
if a diagnostic shift from asthma to bronchiolitis largely has contributed to the increase of the bronchiolitis admissions a concomitant decrease in asthma hospitalisations should be expected, which is not the case. However, this should be interpreted with caution since also other factors such as standardised and improved treatment for asthma may have influenced the number of asthma hospitalisations. RSV is the most common cause of bronchiolitis in infancy and childhood, and an increase of RSV infections among infants may have caused the increase in bronchiolitis hospitalisations. Although the number of national RSV detections showed the same pattern as the bronchiolitis hospitalisations this trend was not significant, making this explanation less likely.

Neither the number of patients with BPD or CHD nor the number of premature births did show a significant change during the study period, indicating that a change in number of patients at risk for severe disease has not contributed to the increase in bronchiolitis hospitalisations.

Finally, the number of patients admitted with RSV-LRTI to the two participating PICU’s did not show a proportional increase compared to the total number of bronchiolitis hospitalisations, which gives an indication that disease severity did not change dramatically during the study period.

In conclusion, we found an increase in the number of bronchiolitis hospitalisations in The Netherlands from 1991 through 1999. This increase may have an important impact on health care costs, and underscores the need for further development of an effective vaccine against RSV. In addition, national guidelines for hospitalisation indications for bronchiolitis may be important to limit the number of bronchiolitis hospitalisations.
Table 1.1

<table>
<thead>
<tr>
<th>Condition</th>
<th>R square</th>
<th>Regression coefficient (95% Confidence Interval)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchiolitis</td>
<td>0.78</td>
<td>234 (111 to 357)</td>
<td>0.003</td>
</tr>
<tr>
<td>Asthma</td>
<td>0.35</td>
<td>53 (-19 to 126)</td>
<td>0.13</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>0.21</td>
<td>-22 (-66 to 21)</td>
<td>0.26</td>
</tr>
<tr>
<td>RSV detections</td>
<td>0.14</td>
<td>65 (-97 to 227)</td>
<td>0.36</td>
</tr>
</tbody>
</table>

* RSV-season-year: July - June

Figure 1.1
Total number of bronchiolitis, asthma and pneumonia hospitalisations among children up to 4 years of age and total number of RSV detections from 17 virological laboratories in the Netherlands during 8 RSV-season-years from 1991/1992 through 1998/1999. (RSV-season-year: July - June)
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References