Respiratory Syncytial Virus Prophylaxis in Neurologic and Muscular Disorders in the Canadian Respiratory Syncytial Virus Evaluation Study of Palivizumab

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Background: This study aimed to examine the risk of respiratory-related hospitalization in children with neurologic and muscular disorders (NMDs) who received respiratory syncytial virus (RSV) prophylaxis in the Canadian RSV Evaluation Study of Palivizumab.

Methods: The Canadian RSV Evaluation Study of Palivizumab is a prospective registry of children who received ≥1 palivizumab injection among 32 Canadian sites. Demographic data were collected at enrollment, and respiratory events were documented monthly. Cox proportional hazard analyses were conducted to compare respiratory illness-related hospitalization (RIH) and RSV-related hospitalization (RSVH) among children with NMD and those prophylaxed for standard indications (SI) and complex medical disorders.

Results: Group differences were found in enrollment age and weight, birth weight, household-crowding, neonatal stay and supplemental oxygen requirement (all P < 0.05). RIH and RSVH incidences were 19.2%, 3.3% (NMD, n = 605); 6.0%, 1.5% (SI, n = 20,335), 9.4%, 1.6% (complex medical disorders, n = 4063), respectively. Children with NMD had a higher risk of RIH (hazard ratio [HR]: 1.90; 95% confidence interval [CI]: 1.41–2.56; P < 0.0005) than those with SI. RSV risk was greater in children with NMD compared with both the SI (HR: 2.26; 95% CI: 1.38–3.72, P < 0.0001) and complex medical disorders groups (HR: 2.74; 95% CI: 1.55–4.84, P = 0.001). Children with more severe infantile onset NMD had a higher risk of RSVH than those with general hypotonic disorders (HR: 1.69; 95% CI: 1.06–2.68; P = 0.027) but not RS VH.

Conclusions: Children with NMD who received palivizumab had a higher risk of both RIH and RSVH. Our results imply that all children with NMD, regardless of disease severity, are at risk for respiratory-related illness and RSV infection.

Key Words: palivizumab, neuromuscular, comparison, outcomes, hospitalization

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Respiratory syncytial virus (RSV) is one of the leading causes of viral-related lower respiratory tract infection in infants and young children. Seasonal outbreaks usually peak during the winter months in temperate climates and during the hot rainy season in tropical areas. The majority of children worldwide are infected by RSV at least once within the first 2 years of life. Clinical manifestations of RSV infection are generally mild, and mortality rates are low in healthy term infants. Premature infants and children predisposed with high-risk medical conditions including chronic lung disease and significant congenital heart disease are at an increased risk of RSV-related hospitalization (RSVH), intensive care unit admission and death.

Growing evidence suggests that children with neurologic and muscular disorders (NMDs) may also be at high risk for RSV infection and related severe respiratory complications. Children with NMD commonly exhibit ineffective clearance of airway secretions from the upper respiratory tract because of reduced muscle tone and functional residual capacity. Children with NMD, similarly, have poor control over their swallowing and coughing mechanisms.

As a result, children with NMD are prone to recurrent aspiration of RSV-infected upper airway secretions, which may lead to subsequent inflammation of the lower respiratory tract, pneumonia or respiratory failure and necessitate prolonged hospitalization.

Palivizumab (Synagis) (AbbVie Inc., Chicago, IL, USA) is a humanized monoclonal antibody approved for prophylaxis in children with established risk factors for severe RSV infection. Current pediatric guidelines with regard to RSV prophylaxis in children with NMD are incomplete because of the small number of subjects enrolled in published studies, the low strength of evidence in clearly defining the incidence, morbidity and mortality associated with RSV in NMD, effects of risk factors and the absence of robust data from prospective controlled studies in this population. Hence, the actual risk of severe RSV infection and the efficacy of palivizumab prophylaxis in children with NMD remains poorly understood.

As part of the Canadian RSV Evaluation Study of Palivizumab (CARESS), the present study aimed to examine the risk of respiratory illness-related hospitalization (RIH) and RSVH in children with NMD who received RSV prophylaxis.

MATERIALS AND METHODS

CARESS is a prospective, longitudinal, observational, open-cohort study of children who received at least 1 injection of palivizumab for RSV prophylaxis. There are 32 participating sites located across Canada. Children were ineligible for enrollment if they were simultaneously receiving palivizumab in another clinical trial or if their caregivers were incapable of communicating in either English or French. Research ethics board approval was obtained for the study at each participating site, and investigational procedures conformed to the Declaration of Helsinki guiding principles. Written informed consent was obtained from the parents or legal guardian of each study participant before the collection of any patient-related information.
Children were enrolled at the beginning of the RSV season (November to March) after the first dose of palivizumab. Demographics, medical history, neonatal course and palivizumab administration were recorded during the child’s first hospital visit by the treating physician or the attending research nurse. Data on palivizumab utilization and adherence, adverse events and any other complications related to respiratory infection were subsequently obtained during monthly follow-up telephone interviews.

If a child required hospitalization for respiratory illness, additional information regarding the hospital course such as length of hospital stay, requirement of mechanical ventilation and RSV test results were obtained following parental or legal guardian consent. RIH was defined as both RSV-positive and negative respiratory-related hospitalizations. A RHI with a positive laboratory test for RSV was categorized as a RSVH. RSV-positivity was confirmed on nasopharyngeal swabs, aspirates or washes by enzyme, immunofluorescent assay or polymerase chain reaction. All information collected were anonymously coded and electronically logged into the registry.

Definitions of Study Groups

There are currently more than 150 NMDs delineated by Muscular Dystrophy Canada and the World Federation of Neurology, and the definition of NMD encompasses a wide variety of disorders that involve skeletal muscle innervation. In the present study, eligible subjects were classified as having NMD based on their diagnosis at study enrollment, irrespective of their primary indication for RSV prophylaxis. The diagnoses included infants who had general hypotonia and those who had hypotonia associated with specific neuro-muscular disorders of infantile onset, irrespective of the underlying level of neurologic lesion (eg, central nervous system, motor neuron, neuromuscular junction, nerve and muscle). Examples of general hypotonic conditions included hypoxic-ischemic encephalopathy, syndromes (eg, Prader-Willi), chromosomal disorders and migration and demyelinating conditions (group 1). Specific neuro-muscular disorders of infantile onset comprised medical conditions such as spinal muscular atrophy, muscle disorders (eg, myotonic dystrophy, centronuclear and nemaline myopathy), mitochondrial and glycogen storage myopathies or arthrogryposis (group 2). Since children with infantile-onset myopathies may be more susceptible to respiratory complications because of the severity of muscular compromise compared with those with general hypotonia, we postulated that group 2 may be at a greater risk for RIH and RSVH than group 1. While children with Down syndrome are also known to have hypotonia during their initial development, this group was excluded from the present study because the risk of RSVH in children with Down syndrome who received palivizumab has been previously assessed by the CARESS investigators.

Children who received prophylaxis for approved, standard indications (SI) and other off-label, complex medical disorders (CMDs) were also included in the present study as comparator groups. The SI group consisted of infants who were born prematurely as well as those who had chronic lung disease or significant congenital heart disease and are currently approved for RSV prophylaxis by the majority of international pediatric advisory bodies. Children with CMD represented those who were individually approved provincially for off-label palivizumab based on the severity of their underlying illness. Examples of medical conditions included in the CMD group are cystic fibrosis, congenital airway anomalies, immunodeficiency and pulmonary disorders.

Definition of Palivizumab Adherence

The CARESS study defines palivizumab-adherent children as those who received ≥5 injections or at least the expected number of palivizumab injections within the recommended time intervals between injections. The recommended time intervals refer to 16–35 days between the first and second injections and 25–35 days between subsequent injections. Overall, this definition of adherence takes into account both the duration of the RSV season and the pharmacokinetic properties of palivizumab.

Statistical Analyses

Data were analyzed using IBM SPSS Statistics v25.0 (IBM Corp., Armonk, NY). Median values and their corresponding interquartile range were reported for continuous variables with nonparametric distribution. Differences in baseline demographics, neonatal characteristics, treatment adherence and hospitalization events were assessed using χ² test for categorical variables and t test or Kruskal-Wallis H test for continuous variables. A P value of less than 0.05 was considered statistically significant.

RIH and RSVH incidences were calculated for descriptive purposes. The formulae used to determine the incidences have been previously described. In brief, the incidence of RIH was obtained by dividing the number of children who were hospitalized for respiratory illness by the total number of children in the corresponding cohort. This RIH value was then multiplied by the number of children within each cohort with positive RSV lab results and further divided by the total number of children who were tested for RSV infection to obtain the RSVH incidence.

Cox proportional hazard regressions using a backward conditional method were performed to evaluate the relative risk of RIH and RSVH between groups. The number of days from study enrollment to the subject’s first RIH or RSVH was used to evaluate risk for the respective outcome. Demographic, neonatal and adherence variables that were significantly different between groups and not multicollinear were included as covariates. The relative risk of RIH and RSVH was first compared between all children with NMD (groups 1 and 2), SI and CMD. Hazard ratio (HR), 95% confidence interval (CI) and P value are reported for each regression analysis. Pairwise group assessments were also performed to specifically compare the NMD group with the SI group and the CMD group with the CMD group. A subgroup analysis was also conducted to examine whether the severity of underlying NMD influences the risk of RIH and RSVH by comparing children with general hypotonia (group 1) versus children with more severe neurologic disorders with primary muscular involvement (group 2). Cox proportional hazard regressions were also used in post hoc analyses to compare risk of RIH and RSVH between infants who received prophylaxis for NMD with and without risk factors for RSV (prematurity, chronic lung disease, significant congenital heart disease and pulmonary hypertension).

RESULTS

Over the past 12 consecutive RSV seasons (2005–2017), a total of 25,003 children who received palivizumab were enrolled in CARESS: NMD [n = 605 (2.4%)], SI [n = 20,335 (81.3%)] and CMD [n = 4063 (16.3%)]. Those with NMD received on average, 5 ± 1 palivizumab injections per RSV season and 395 (65.3%) NMD patients received ≥5 or at least the expected number of palivizumab injections within the recommended time intervals between injections (see Table, Supplemental Digital Content 1, http://links.lww.com/INF/D435). SI patients received on average, 4 ± 1 doses of palivizumab and 64.2% were fully adherent. The CMD group received an average of 5 ± 1 palivizumab doses and 68.6% were fully adherent based on both adherence definitions. As depicted in Supplemental Digital Content 1 (table, http://links.lww.com/INF/D435), adherence to palivizumab was significantly different between the 3 groups.
During the neonatal period, infants with NMD had longer enrollment weight only differed between the NMD group and the SI group. The median birth weight of NMD subjects was higher than SI subjects and 380 CMD subjects had a total of 1405 and 493 RIH events, respectively. Of the hospitalized children, 19 children from group 1 and 4 children from group 2 were RSV-positive. The resulting RSVH incidences were 3.3% (NMD), 1.5% (SI) and 1.6% (CMD). The burden of illness associated with RSVH is described in Table 2. A higher proportion of RSV-positive children with NMD were hospitalized with pneumonia compared with the other groups while a higher proportion of RSV-positive children with SI were hospitalized with apnea. In addition, RSV-positive children with NMD had also significantly longer durations of intensive care unit stay compared with the CMD and SI groups.

Cox proportional hazard analysis was adjusted for variables that were significantly different between groups [see Table 1 and Supplemental Digital Content 1 (table, http://links.lww.com/INF/D435)]. Figure 1A compares the RHI and RSVH hazard curves between the NMD, SI and CMD groups. NMD subjects had a higher risk of RIH compared with the SI group (HR: 1.90; 95% CI: 1.41–2.56; P < 0.0005) but were similar to the CMD group (HR: 1.33; 95% CI: 0.96–1.86; P = 0.090). Children with NMD were also at a higher risk of RSVH compared with both the SI group (HR: 2.26; 95% CI: 1.38–3.72; P = 0.001) and the CMD group (HR: 2.74; 95% CI: 1.55–4.84; P = 0.001).

**Post Hoc Analyses**

A subgroup analysis of the NMD group was conducted to determine the relative risk of RIH and RSVH between children with general hypotonia in group 1 [n = 498 (82.3%)] and those with more severe neurologic disorders with muscle involvement in group 2 [n = 107 (17.7%)]. Average number of palivizumab injections and adherence rates were similar between the 2 groups. Patients in group 2 were significantly older at study enrollment, had longer gestation and weighed more both at birth and study enrollment compared with patients from group 1. Patients in group 2 were also less likely to live in crowded home conditions and be a twin or triplet. In addition, patients in group 2 experienced shorter durations of hospital stay [group 1 median (IQR): 39 (19–85) vs. group 2: 32 (7–66); χ² = 4.81; P = 0.028], were less likely to require respiratory support (61.0% in group 1 vs. 50.5% in group 2; χ² = 4.08; P = 0.043) and oxygen therapy (62.9% in group 1 vs. 50.5% in group 2; χ² = 5.66; P = 0.017) and were less prone to sepsis during the neonatal period (23.7% in group 1 vs. 12.1% in group 2; χ² = 6.92; P = 0.009). RIH was documented in 87 group 1 subjects and 29 group 2 subjects. Of the hospitalized children with NMD, 15 children from group 1 and 4 children from group 2 were RSV-positive, resulting in RSVH incidences of 3.2% (group 1) and 0.9% (group 2) respectively.

### Table 1. Neonatal Hospitalization Events by Indication

<table>
<thead>
<tr>
<th>Hospitalization event</th>
<th>NMD, n = 605</th>
<th>SI, n = 20,335</th>
<th>CMD, n = 4063</th>
<th>χ²</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of neonatal stay, d, median (IQR)</td>
<td>38 (18–82)</td>
<td>35 (19–63)</td>
<td>15 (3–48)</td>
<td>904.86</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Respiratory support (%)</td>
<td>358 (59.2)</td>
<td>13,046 (64.2)</td>
<td>1576 (38.8)</td>
<td>904.17</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Oxygen therapy (%)</td>
<td>8 (2–35)</td>
<td>9 (3–34)</td>
<td>24 (8.2)</td>
<td>34.27</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Days on oxygen therapy, median (IQR)*</td>
<td>60 (70.7)</td>
<td>10,211 (50.2)</td>
<td>1657 (40.8)</td>
<td>154.71</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Documented necrotizing enterocolitis (%)</td>
<td>22 (6–73)</td>
<td>10 (2–42)</td>
<td>10 (2–32)</td>
<td>54.29</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Surgery for patent ductus arteriosus (%)</td>
<td>35 (5.8)</td>
<td>1010 (5.0)</td>
<td>112 (2.8)</td>
<td>39.38</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Documented sepsis*</td>
<td>131 (21.7)</td>
<td>2742 (13.8)</td>
<td>431 (10.6)</td>
<td>63.16</td>
<td>&lt;0.0005</td>
</tr>
</tbody>
</table>

*Denotes variables that had a significant contribution to the Cox regression models.

### Table 2. Hospitalization Events by Indication During RSVH

<table>
<thead>
<tr>
<th>Hospitalization event</th>
<th>NMD, n = 19</th>
<th>SI, n = 259</th>
<th>CMD, n = 61</th>
<th>χ²</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of stay, d, median (IQR)</td>
<td>7 (3–12)</td>
<td>5 (3–9)</td>
<td>5 (3–9)</td>
<td>0.61</td>
<td>0.736</td>
</tr>
<tr>
<td>Apnea (%)</td>
<td>7 (30.5)</td>
<td>44 (17.1)</td>
<td>3 (4.9)</td>
<td>6.17</td>
<td>0.046</td>
</tr>
<tr>
<td>Bronchiolitis (%)</td>
<td>12 (62.2)</td>
<td>208 (80.9)</td>
<td>40 (65.6)</td>
<td>8.84</td>
<td>0.012</td>
</tr>
<tr>
<td>Decreased oxygen saturation (%)</td>
<td>11 (57.9)</td>
<td>114 (46.3)</td>
<td>28 (47.5)</td>
<td>0.95</td>
<td>0.623</td>
</tr>
<tr>
<td>Inability to maintain oral intake (%)</td>
<td>10 (52.6)</td>
<td>110 (42.8)</td>
<td>24 (39.3)</td>
<td>1.05</td>
<td>0.592</td>
</tr>
<tr>
<td>Pneumonia (%)</td>
<td>8 (42.1)</td>
<td>50 (19.5)</td>
<td>18 (29.5)</td>
<td>7.26</td>
<td>0.027</td>
</tr>
<tr>
<td>Respiratory arrest (%)</td>
<td>1 (5.3)</td>
<td>6 (2.3)</td>
<td>2 (3.3)</td>
<td>0.69</td>
<td>0.708</td>
</tr>
<tr>
<td>Respiratory distress (%)</td>
<td>18 (78.9)</td>
<td>179 (70.2)</td>
<td>50 (82.0)</td>
<td>3.89</td>
<td>0.148</td>
</tr>
<tr>
<td>Respiratory support (%)</td>
<td>7 (36.8)</td>
<td>87 (33.6)</td>
<td>22 (36.1)</td>
<td>0.20</td>
<td>0.907</td>
</tr>
<tr>
<td>Length of respiratory support, d, median (IQR)*</td>
<td>14 (3–36)</td>
<td>4 (2–8)</td>
<td>4 (2–7)</td>
<td>5.36</td>
<td>0.068</td>
</tr>
<tr>
<td>ICU admission (%)</td>
<td>7 (36.8)</td>
<td>74 (28.6)</td>
<td>11 (18.0)</td>
<td>3.73</td>
<td>0.155</td>
</tr>
<tr>
<td>Length of ICU stay, d, median (IQR)*</td>
<td>14 (6–24)</td>
<td>5 (3–9)</td>
<td>3 (3–6)</td>
<td>6.45</td>
<td>0.040</td>
</tr>
<tr>
<td>Intubation (%)</td>
<td>4 (21.1)</td>
<td>33 (12.7)</td>
<td>5 (8.2)</td>
<td>2.33</td>
<td>0.312</td>
</tr>
<tr>
<td>Length of intubation, d, median (IQR)*</td>
<td>19 (8–34)</td>
<td>6 (4–10)</td>
<td>4 (3–8)</td>
<td>2.29</td>
<td>0.317</td>
</tr>
</tbody>
</table>

*Calculations of median and IQR are based on only those who received respiratory support, intensive care or intubation. All patients who experienced a RSVH were included in the Kruskal-Wallis H test to obtain the χ² statistics and corresponding P values.

ICU indicates intensive care unit; IQR, interquartile range.
There were no between-group differences in the burden of illness associated with RSVH. As shown in Figure 1B, children in group 2 had a higher risk of RIH than group 1 (HR: 1.69; 95% CI: 1.06–2.68; \( P = 0.027 \)) while controlling for demographic and neonatal course differences between the 2 groups. The risk of RSVH did not differ between the 2 groups (HR: 0.96; 95% CI: 0.28–3.38; \( P = 0.955 \)).

In a post hoc analysis comparing children primarily prophylaxed for NMD (n = 253) and children with NMD and risk factors for RSV (n = 352), no differences in risks of RIH (HR: 1.15; 95% CI: 0.77–1.70; \( P = 0.492 \)) or RSVH (HR: 0.65; 95% CI: 0.23–1.84; \( P = 0.414 \)) were found between groups when controlling for relevant demographic and neonatal variables.

**DISCUSSION**

The CARESS study was established in 2004 and has since become the largest prospective pediatric registry for children who received RSV prophylaxis. More than 25,000 infants and young children living in Canada have been enrolled over the past 12 RSV seasons (2005–2017), providing real-world evidence on palivizumab utilization and adherence, as well as on the risk of hospitalization in children with different medical disorders. In the current study, children with NMD were shown to have a significantly higher risk of RIH compared with children with SI. In addition, the risk of RSVH was greater in children with NMD relative to both the SI group and the CMD group. Moreover, children with more severe NMD had a greater risk of RIH compared with children with general hypotonia within the NMD subgroup.

The higher risk of RIH and RSVH in children with NMD in our study may be attributed to their underlying muscle weakness, which, as previously mentioned, renders them more vulnerable to severe respiratory complications. Such observations have also been documented in an English population-based birth cohort study using the national Hospital Episodes Statistics database, the relative risk of RSVH in infants <1 year old with cerebral palsy was 2.4 (95% CI: 1.5–4.0) and 1.7 (95% CI: 1.3–2.4) in those with other nervous system congenital abnormalities, when compared with healthy term infants. In addition, in a large international collaborative prospective cohort study of 13,368 palivizumab-prophylaxed children, those with NMD were determined to be at a 3.7 times (95% CI: 2.1–6.6; \( P < 0.001 \)) higher risk of RSVH than preterm neonates. Moreover, the Pediatric Investigators Collaborative Network on Infections in Canada compared RSVH outcomes in children with chronic lung disease (n = 91, 57.2%) and those with NMD (n = 6, 3.8%) and found similar risk in both groups.
Children with neurogenic disorders compared with those with chronic lung disease were hospitalized with RSV at an older mean age (3.12 vs. 1.18 years) and a higher proportion were admitted to intensive care (50% vs. 35%) and required mechanical ventilation (33% vs. 23%). In a prospective cohort study of children with combined group I and II NMD versus those without NMD, Wilke-Kemmann et al confirmed that the median age at RSVH was higher (14 vs. 5 months) and was significantly associated with a greater risk of intensive care admission, need for mechanical ventilation and attributable mortality (all P < 0.02). The findings further support the importance of prophylaxis in children with NMD.

Approximately 1 of 3 infants were nonadherent to palivizumab prophylaxis, which may be because of several factors including Aboriginal status, ethnicity, smoking in the household, having siblings and level of maternal education. Previously, nonadherence has been associated with higher odds of testing positive for a RSV infection and greater burden of illness; however, adherence was not a significant predictor of RIH or RSVH in the present study.

In a subgroup analysis, we have shown that relative to children with general hypotonia (group 1), those with more severe neuromuscular disorders (group 2) are 1.69 times more likely to be hospitalized for respiratory illness but are similar in terms of their susceptibility to RSV infection. The higher incidence of RIH in group 2 compared with group 1 aligns with our predictions as we expected children with more severe NMD to have weaker respiratory muscles, which would result in greater difficulties clearing aspirated upper airway secretions from the lower respiratory tract. It is possible that the higher probability of aspiration may have increased the likelihood of airway obstruction and potentiated respiratory emergencies that necessitated hospitalization in group 2 children.

Kristensen et al similarly investigated the risk of RSVH in children with chronic medical conditions registered in the Danish National Patient Registry. Of the 10,616 subjects assessed, children with group 1 disorders including cerebral palsy (n = 905), encephalocoele (n = 542) and spina bifida (n = 172) had an increased risk of RSVH compared with hospitalized but otherwise healthy children. However, children with group 2 disorders including spinal muscular atrophy (n = 39) and other neuromuscular conditions of congenital onset (n = 344) were not at significant risk for RSVH. Collectively, the results imply that children with general acquired hypotonia were more susceptible to RSVH than those who had neuromuscular disorders of infantile onset, which differs from our findings of no differences in RSVH risk between the groups. This discrepancy may be attributable to the differences in demographic characteristics and environmental factors between the CARESS and Danish population such as tobacco exposure and single parenthood, which have previously been independently associated with RSV risk. On the other hand, the conflicting results may simply be because of the fact that all CARESS patients were prophylaxed with palivizumab whereas only 118 children (0.03%) with a broad spectrum of congenital chronic conditions in the Danish cohort received >1 dose of palivizumab. Nevertheless, these RIH and RSVH results need further clarification in prospective studies of children with NMD who have and have not received prophylaxis.

No differences in the risk of RIH and RSVH were found between children with NMD only and children with NMD and risk factors for RSV. These findings suggest that the risk for respiratory illness and lower respiratory infection hospitalization associated with NMD during early childhood is independent of comorbid risk factors.

There are some limitations in this study that merit consideration. First, a comparative control arm of children who did not receive prophylaxis was not available. However, with little known about the hospitalization risk of children with NMD who receive palivizumab, comparisons with children who receive palivizumab for approved SIs may be just as important. Second, the low number of children with NMD hospitalized for RSVH (n = 19) may have hindered our ability to detect clinically relevant morbidities among hospitalized children and compare these with those who have not received prophylaxis in the scientific literature. However, this is a common challenge for all studies that evaluate outcomes in children with NMD because of the relatively low incidence. Last, not every child was tested for RSV following respiratory hospitalization. Therefore, our results may have underestimated the true incidence of RSVH in children who received prophylaxis.

In conclusion, respiratory outcomes and hospitalization risks were evaluated in 605 children with NMD who received palivizumab during the respective RSV season. Findings revealed a higher risk of both RIH and RSVH among children with NMD compared with those with SI and CMD even though the true incidence of RSVH in this study may have been underestimated. Children with more severe NMD of infantile onset were also shown to have a higher risk of RIH compared with those with general hypotonia; however, the RSVH risk did not differ between the 2 NMD groups. Altogether, our findings imply that all children with NMD, regardless of the severity of their underlying hypotonia, are at risk for respiratory-related illness and RSV infection despite prophylaxis. Future cost-effectiveness analyses, alongside studies that compare palivizumab-treated children with NMD versus palivizumab-un-treated control subjects are warranted to precisely assess the benefit of palivizumab prophylaxis in children with NMD.


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