RSV-related hospitalization and outpatient palivizumab use in very preterm (born at < 29 wGA) infants: 2003-2020

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CONCLUSIONS

- This study extends the existing literature by demonstrating higher rates of RSVH and poorer RSVH outcomes in very preterm infants relative to term infants in both Commercially insured and Medicaid insured populations.
- Despite evidence that palivizumab reduces RSVH severity, rates of outpatient palivizumab utilization were suboptimal among very preterm infants throughout the study period.
- Targeted interventions to increase awareness among providers and caregivers as well as remove barriers to access, particularly among Medicaid patients, may improve RSV immunoprophylaxis coverage in medically fragile, preterm infants.

INTRODUCTION

- Respiratory syncytial virus (RSV) is the leading cause of bronchiolitis and pneumonia in children under one year.[1] Infants born preterm have the highest rates of RSV related hospitalizations.[2-5]
  - Infants of gestational age less than 29 weeks experience the highest rate of adverse outcomes associated with RSV infection.
- Palivizumab has been used to prevent severe RSV disease in children with specific health conditions and those born at <36 weeks gestational age (wGA) since its FDA approval in 1998.
  - In infants <29 wGA, palivizumab prophylaxis has been consistently recommended since 1998 despite changes in the recommendations for other preterm infants.
- Previous research has described trends in palivizumab use and RSV-related hospitalizations (RSVH) among term and preterm infants, but limited data are available for very preterm infants.[2-4]

OBJECTIVES

- To characterize palivizumab prophylaxis and RSV-related hospitalization among very preterm (<29 wGA) infants.

METHODS

Study Design and Data Source

- This retrospective observational cohort used de-identified claims from infant patients in the Merative MarketScan Commercial and Multi-State Medicaid administrative claims databases.
- The MarketScan Commercial Database contains the inpatient, outpatient, and outpatient prescription drug experience of employees and their dependents, covered under a variety of fee-for-service and managed care health plans, including over 190 million lives over the 2003-2020 time frame across all geographic regions of the United States. Over the same time frame, the MarketScan Multi-State Medicaid Database contains the pooled healthcare experience of Medicaid over 30 million enrollees from 9 to 13 (varying by year) geographically distributed states.

Patient Selection

- Infants born between 7/1/2003 and 6/30/2020 at less than 29 wGA ("very preterm") or greater than 37 wGA ("term") and discharged alive were identified.
- Inpatient claims were required to have a diagnosis code for RSV in any position.
- Infants with evidence of health conditions such as congenital heart disease and cystic fibrosis were excluded.

Analysis

- During RSV seasons (November to March) from 2003 to 2020, claims incurred by infants while they were <12 months old were evaluated for outpatient administration of palivizumab and RSVH.
- The number of contributed infant-seasons were calculated as the days of follow-up at < 12 months old during the RSV season divided by the number of days in an RSV season (151 days). Infants were required to be less than 12 months old at some point during an RSV season (November to March).

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Analysis, continued

- Bivariate analyses were conducted to test for differences in outcomes in very preterm infants by palivizumab use (with versus without palivizumab) and to compare outcomes in very preterm and term infants.
- The relative risk of RSVH and 95% confidence intervals were calculated overall and for three wGA strata (<25 wGA, 25-26 wGA, 27-28 wGA) to compare the risk of RSVH in very preterm and term infants.

RESULTS

Study Population and Palivizumab Administration

- The study included 40,123 very preterm infants (27,029 in Medicaid) and 4,421,942 term infants (2,496,284 in Medicaid (See table 1).
- The overall rate of outpatient palivizumab administration in very preterm infants was similar in Commercially insured (57.1%) and Medicaid insured infants (56.2%%).
- Less than 0.1% of term infants received outpatient palivizumab administration.

Table 1. Number of Infants and Infant-Seasons Contributed and Payer

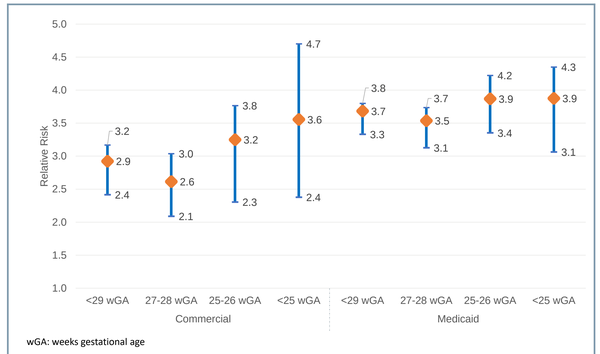
	Commercial		Medicaid	
Gestational Age Cohort	Infants	Infant-Seasons	Infants	Infant-Seasons
All infants				
Full term (37+ weeks)	1,925,658	1,745,600.9	2,496,284	2,358,873.1
Very Preterm Infants (<29 weeks)	13,094	9630.5	27,029	20,346.1
27-28 weeks	7,368	5564.8	14,678	11,445.3
25-26 weeks	3,919	2779.3	8,424	6,135.3
<25 weeks	1,807	1286.4	3,927	2,765.5

Birth Characteristics of Very Preterm and Term Infants

- In the Commercially insured population, very preterm infants had markedly longer birth hospitalizations on average than term infants (76.1 days vs. 3.0 days), much greater rates of NICU admission (97.1% vs. 1.3%), and greater rates of mechanical ventilation (38.6% vs. 0.2%) (p<.001 for all).
- Similarly, the Medicaid-insured population had significantly longer birth hospitalizations (75.1 days vs. 3.1 days), higher rates of NICU admission (97.9% vs. 1.3%), and mechanical ventilation (38.5% vs. 0.2%) were observed in very preterm infants.
- Among very preterm infants, birth hospitalizations were longer and proportional with NICU stays, mechanical ventilation, and BPD were higher in preterm infants with palivizumab use than in preterm infants without palivizumab use.
- The Commercially insured population who received palivizumab had significantly longer birth hospitalizations (80.7 vs. 69.2 days, p<.001), higher rates of NICU stays (99.5% vs. 93.5%, p<.001), and higher use of mechanical ventilation (39.8% vs. 36.8%, p<.001). A similar pattern was found among infants in the Medicaid population. The infants who received palivizumab had longer birth hospitalizations (80.5 days vs. 67.3%, p<.001), higher rates of NICU stays (99.6% vs. 95.5%, p<.001) and higher rates of mechanical ventilation (40.0% vs. 36.3%, p<.001).

Risk of RSV Hospitalization (Term vs. Very Preterm)

- Rate of RSVH in very preterm infants ranged from 1.0 per 100 infant seasons (in the 2004-2005 RSV season) to 4.4 (in the 2019-2020 season) in Commercially insured infants, and 3.5 (2013-2014 RSV season) to 8.4 (2003-2004 RSV season) in Medicaid insured infants.
- The relative risk of RSVH was inversely related to wGA at birth in both the Commercially insured and Medicaid insured populations, with the highest relative risk observed in infants <25 wGA at birth. (Figure 1)

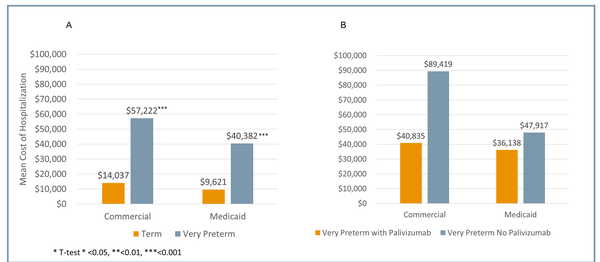


wGA: weeks gestational age

Figure 1: Relative Risk of RSV Hospitalization In Very Preterm vs. Term Infants

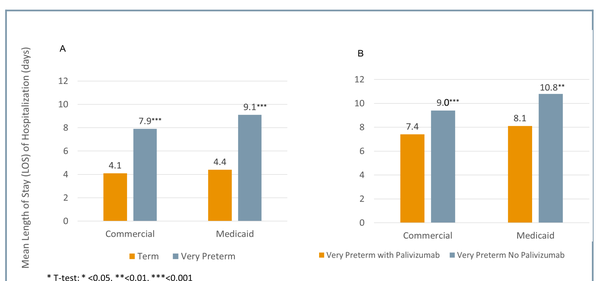
RSV Hospitalization: Costs and Utilization (Term vs. Very Preterm)

- In the Commercially insured population, the cost of RSVH was more than four times higher for infants born at less than 29 wGA compared to term (Figure 2A).
- Length of stay doubled (Figure 3A), rate of ICU admissions tripled, and use of mechanical ventilation was more common in very preterm infants compared to term (Figure 4A).
- Results were similar in the Medicaid population.



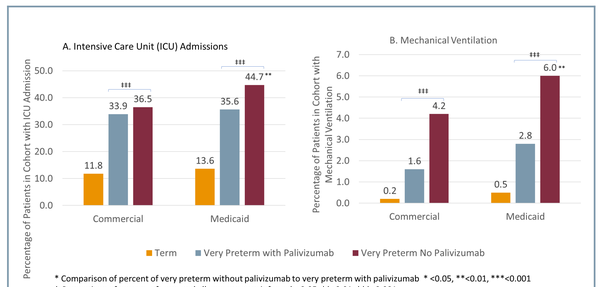
* T-test * <0.05, **<0.01, ***<0.001

Figure 2: Cost of RSV-Related Hospitalization in Term and Very Preterm Infants by Payer and Palivizumab Use



* T-test: * <0.05, **<0.01, ***<0.001

Figure 3. Length of RSV Hospitalization in Very Preterm Infants by Payer and Palivizumab Use



* Comparison of percent of very preterm without palivizumab to very preterm with palivizumab * <0.05, **<0.01, ***<0.001
‡ Comparison of percent of term and all very preterm infants ‡ <0.05, ‡‡<0.01, ‡‡‡<0.001

Figure 4. Healthcare Utilization in Term and Very Preterm Infants by Payer and Palivizumab Use

RSV Hospitalization in Very Preterm, With and Without Palivizumab

- In the Commercially-insured population, the cost of RSVH was less than one half as much among infants who received palivizumab compared to those who did not. Within the Medicaid-insured population, costs were about 25% lower for infants receiving palivizumab (Figure 2B).
- Length of stay for RSVH was significantly shorter in very preterm infants with palivizumab use (Figure 3B).
- Rates of ICU admission and rates of mechanical ventilation were lower among Medicaid-insured infants with palivizumab. These same trends were not statistically significant among commercially-insured infants with or without palivizumab (Figure 4). However, the length of ICU admission in this population was significantly shorter in infants with palivizumab use (9.5 days [SD 7.2] vs. 13.7 days [SD19.2]).

Limitations

- This study is subject to limitations common to all retrospective administrative claims studies such as coding errors and omission of unbilled/over-the-counter services.
- Data on inpatient administration of palivizumab is not available in this database and only outpatient administrations are measured.
- The study was restricted to infants with commercial or Medicaid insurance, and the findings may not extend to infants with other insurance or no insurance.

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DISCLOSURES

- Abiola Oladapo, Tara Gonzales, and Matthew Wojdyla are employed by Sobi, Inc. ("Sobi"). Elizabeth Packnett, Isabelle Winer, Heather Larkin, and David Diakun are employed by Merative (IBM Watson Health at the time of the study) which received funding from Sobi to conduct this study. Mitchell Goldstein and Vincent C. Smith are paid consultants of Sobi. This research was presented in part at the 2022 38th Annual Advances in Care Conference – Advances in Therapeutics and Technology: Critical Care of Neonates, Children, and Adults in Snowbird, Utah.