TRENDS IN RISK OF RESPIRATORY SYNCYTIAL VIRUS HOSPITALIZATIONS IN PRETERM INFANTS OVER A 10-YEAR PERIOD

Amanda M. Kong, DrPH,[1] Isabelle H. Winer, MPH,[1] David Diakun, BS,[1] Adam Bloomfield, MD,[2] Tara Gonzales, MD[2]
[1]*IBM Watson Health, Cambridge, MA, USA* [2]*Sobi, Waltham, MA, USA*

Contact Information:
Amanda M. Kong, DrPH
Lead Researcher
IBM Watson Health
akong@us.ibm.com

Background

- Prior to 2014, the American Academy of Pediatrics (AAP) recommended respiratory syncytial virus (RSV) immunoprophylaxis (RSV-IP) to reduce the risk of severe RSV hospitalization (RSVH) for certain infants < 35 weeks gestational age (wGA).
- After 2014, the AAP no longer recommended use among infants born > 29 wGA without other medical conditions.[1]
- RSV-IP utilization subsequently decreased among these infants, as well as infants born < 29 wGA for whom RSV-IP is still currently recommended.[2]

Objective

- To describe and compare RSVH rates among preterm (PT) infants < 35 wGA and term infants ≥ 37wGA from 2009-2019.

Methods

Study Design and Data Source

- This retrospective cohort study used administrative claims data from the IBM MarketScan Commercial Database and the IBM MarketScan Multi-State Medicaid Database.

Study Design and Data Source

- We identified infants born between 7/1/2008 and 6/30/2019, who could be linked to a birth hospitalization record, were discharged alive from birth hospitalization, had a valid code for wGA at birth, and were < 6 months old at any point during an RSV season (November to March).
- Infants with a diagnosis-related group (DRG) indicating they were born full-term and had no major health problems were classified as term.
- PT infants born at < 35 wGA were classified by wGA using diagnosis codes.
- Infants were excluded if they met any of the following criteria:
  - Evidence of complex, rare medical conditions (cystic fibrosis, immunodeficiency, congenital anomalies of the respiratory system, neuromuscular, immunological or genetic conditions, or organ transplants)
  - Evidence of chronic lung disease of prematurity
  - Evidence of congenital heart disease
  - A DRG code of full-term with major health problems or preterm with unknown wGA, or diagnosis codes indicating birth at 35-36 wGA (late PT)
  - ≥ 6 months old for the entire first RSV season after birth

Outcomes

- We calculated the number of contributed infant-seasons as the days of follow-up at < 6 months old during the RSV season divided by the number of days in an RSV season (151 days).
- The RSVH rates during each RSV season for infants < 6 months are presented as the number of hospitalizations per 100 infant-seasons.
  - We identified RSVHs by ICD-9-CM (079.6, 466.11, or 480.1) and ICD-10-CM (B974, J121, J205, or J210) diagnosis codes on inpatient claims.
- To account for seasonal variation in virus circulation which may impact absolute RSVH rates, we calculated unadjusted rate ratios for PT infants relative to term infants.
- We fit difference-in-difference models using Poisson family generalized linear models (GLMs) with a log link to determine if there was a change in relative rates for PT infants compared to terms infants after the guidance change by comparing the 5 seasons before the guidance change combined to the 5 seasons after the guidance change combined.
- Next, we evaluated trends over 10 years using Poisson family GLMs including a linear b-spline term for year to determine if trends in relative risk for PT infants vs. term infants changed after the guidance change.
- P values < 0.05 were considered statistically significant.

Results

Table 1. Number of infants and infant-seasons contributed at < 6 months old

	N of Infants Contributing Follow-Up at <6 Months Old	N of Infant-Seasons Contributed at <6 Months Old	N of RSVH During Contributed Infant-Season
Commercial			
Preterm Infants <29 wGA	5,833	2,307.8	74
Preterm Infants 29-34 wGA	52,535	25,217.7	722
Preterm Infants 29-30 wGA	5,924	2,644.0	79
Preterm Infants 31-32 wGA	12,305	5,816.1	203
Preterm Infants 33-34 wGA	34,306	16,757.6	440
Term Infants	1,111,670	568,473.8	6,486
Medicaid			
Preterm Infants <29 wGA	12,116	4,817.4	320
Preterm Infants 29-34 wGA	85,099	42,553.0	2,181
Preterm Infants 29-30 wGA	10,680	4,934.3	323
Preterm Infants 31-32 wGA	21,298	10,428.6	609
Preterm Infants 33-34 wGA	53,121	27,190.2	1,249
Term Infants	1,492,943	796,745.7	13,962

RSVH, respiratory syncytial virus hospitalization; wGA, weeks gestational age

- 58,368 commercially-insured and 97,215 Medicaid-insured infants born at <35 wGA contributed 27,526 and 47,370 RSV seasons, respectively, at <6 months old (Table 1).
- These PT infants were compared to 1,111,670 commercially-insured and 1,492,943 Medicaid-insured term infants who contributed 568,474 and 796,746 RSV seasons, respectively, at <6 months old (Table 1).
- There were 796 RSVH among commercially-insured PT infants, 6,486 RSVH among commercially-insured term infants, 2,501 RSVH among Medicaid-insured PT infants, and 13,962 RSVH among Medicaid-insured term infants during the 10 seasons in the database.
- Across the 10 seasons, RSVH rates ranged from 1.5 to 5.4 RSVH per 100 infant-seasons from <29 wGA infants, 1.6 to 4.3 RSVH per 100 infant-seasons for 29-34 wGA infants, and 0.9 to 1.4 RSVH per 100 infant-seasons for term infants among the commercially-insured population (Figure 1A).
- Across the 10 seasons, RSVH rates ranged from 4.0 to 9.3 RSVH per 100 infant-seasons from <29 wGA infants, 3.6 to 6.6 RSVH per 100 infant-seasons for 29-34 wGA infants, and 1.4 to 2.4 RSVH per 100 infant-seasons for term infants among the Medicaid-insured population (Figure 1B).
- In every wGA cohort and at every timepoint, the RSVH rate was higher among PT infants than among term infants leading to unadjusted rate ratios greater than 1 (Figure 2A and 2B).
- Unadjusted rate ratios comparing PT to term infants increased after the 2014 recommendation change for both commercially-insured and Medicaid-insured infants (Figure 2A and 2B).
- Based on the difference-in-difference models, the relative rate of RSVH for PT infants vs. term infants was significantly higher in the 5 seasons after the guidance change than in the 5 seasons before the guidance change (Table 2).
  - The relative rate for RSVH for infants born at 29-34 wGA vs. term infants nearly doubled (1.95, 95% CI 1.67-2.27) after the guidance change for commercially-insured infants and increased by 70% (1.70, 95% CI 1.55-1.86) for Medicaid-insured infants.
  - Significant increases in relative rates were also found for infants <29 wGA compared to term after the guidance change.

Figure 1. RSV Hospitalization Rates for A) Commercially-insured and B) Medicaid-insured Infants <6 Months Old

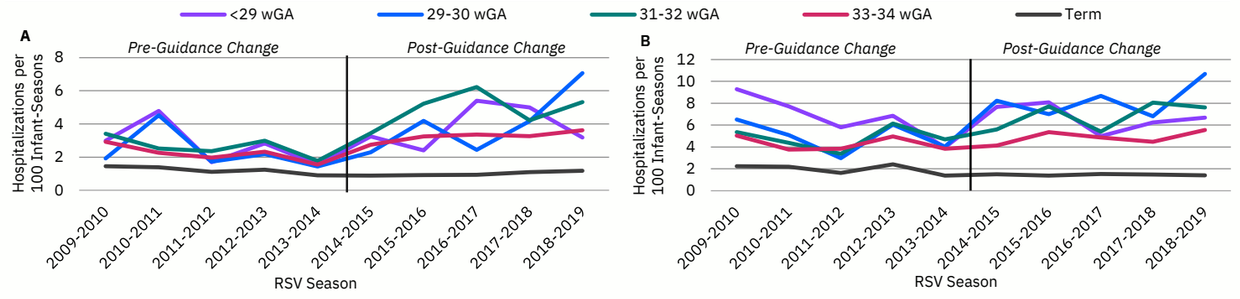

Figure 2. Rate Ratios for RSV Hospitalization Rates for A) Commercially-insured and B) Medicaid-insured Infants <6 Months Old

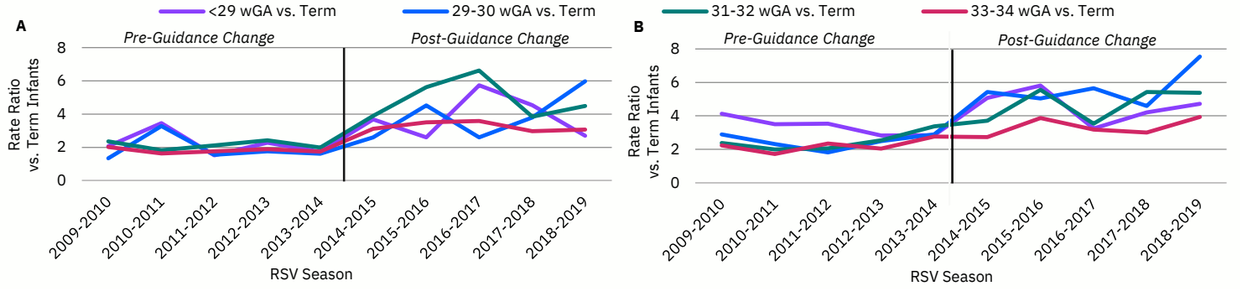

Table 2. Results from Difference-in-Difference (DiD) Models Comparing Relative Rates of RSVH for Preterm vs. Term Infants

	Commercially-Insured		Medicai-Insured	
Gestational age	DiD for RSVH Rates 2014-2019 vs. 2009-2014 (95% CI)	*P* value	DiD for RSVH Rates 2014-2019 vs. 2009-2014 (95% CI)	*P* value
<29 wGA	1.73 (1.10, 2.74)	0.019	1.37 (1.10, 1.71)	0.006
29-34 wGA	1.95 (1.67, 2.27)	<0.001	1.70 (1.55, 1.86)	<0.001
29-30 wGA	2.02 (1.30, 3.15)	0.002	2.23 (1.78, 2.80)	<0.001
31-32 wGA	2.27 (1.71, 3.01)	<0.001	1.89 (1.60, 2.23)	<0.001
33-34 wGA	1.81 (1.49, 2.20)	<0.001	1.52 (1.35, 1.70)	<0.001

- The longitudinal 10-year models indicated that after the increase in relative rates in the 2014-2015 season immediately after the guidance change, the increased relative rate for preterm vs. term infants persisted for each of the 5 seasons after the guidance changed.
- The increase was stable, meaning that the difference between preterm and term infants did not increase or decrease in the seasons after the guidance change.

References

[1] American Academy of Pediatrics Committee on Infectious Diseases. Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection. Pediatrics. 2014;134(2):415-420.
[2] Kong AM et al. The 2014–2015 national impact of the 2014 American Academy of Pediatrics guidance for respiratory syncytial virus immunoprophylaxis on preterm infants born in the United States. Am J Perinatol. 2018;35:192-200.

Limitations

- This study is subject to limitations common to all retrospective administrative claims, including that all records are subject to coding limitations and data entry errors.
- RSV test results are not captured in claims data; however, the AAP does not recommend routine RSV testing during RSV season as it rarely alters clinical management.
- The sample sizes were smaller for infants born at younger gestational ages, which leads to less stable trends over the 10-year period.
- The study was restricted to infants with commercial or Medicare insurance, and the findings may not extend to infants with other insurance or no insurance.

Conclusions

- After the change in AAP recommendations for RSV-IP, we found increases in RSVH rates for infants born at 29-34 wGA compared to term infants ≥ 37wGA, which persisted during the 5 seasons after the guidance change.
- We observed the same trend, though with a smaller effect size, among infants born at < 29 wGA for whom RSV-IP remains recommended.[1]

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