Efektywniejsza profilaktyka zakażenia wirusem RS (Better RSV prophylaxis)

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What is Respiratory Syncytial Virus (RSV)?

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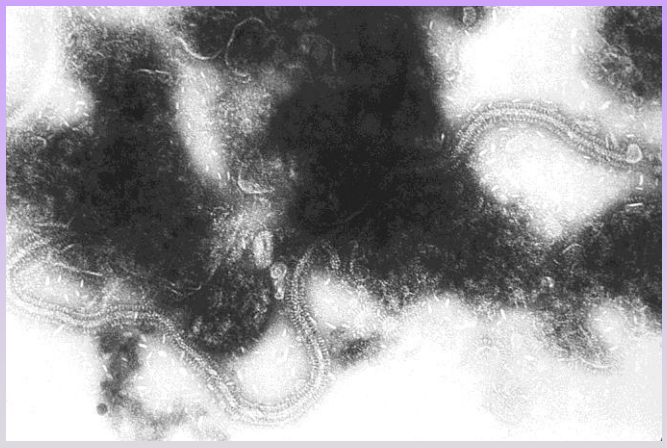
Respiratory Syncytial Virus



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Respiratory Syncytial Virus

- 60% of infants are infected during their first RSV season and nearly all children become infected with the virus by 2–3 years of age.
- Before prophylaxis for RSV, many at-risk infants developed bronchiolitis necessitating hospitalization.
- Natural infection with RSV does not produce lasting immunity.
- Infants can become infected more than once during RSV season.

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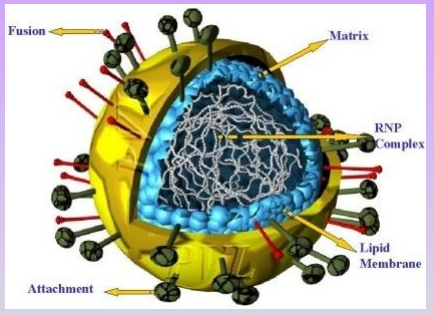
Respiratory Syncytial Virus

- RSV is a single-stranded RNA virus of related to the Paramyxoviridae
- This is the same family as viruses such as those causing measles and mumps for which there is effective vaccination.



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Respiratory Syncytial Virus

- RSV is now as of 2016 a member of the family Pneumovirinae (formerly a subfamily of Paramyxoviridae).
- The name derives from that fact that RSV forms into syncytia, a multinucleated mass of cytoplasm that is not separated into individual cells.
- F proteins on the surface of the virus cause the cell membranes on nearby cells to merge, forming these syncytia

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RSV Targets

- RSV has 10 genes encoding 11 proteins
- NS1 and NS2 inhibit type I interferon activity.
- N encodes nucleocapsid protein that associates with the genomic RNA forming the nucleocapsid.
- M encodes the Matrix protein required for viral assembly.
- SH, G and F form the viral coat, the
  - F (fusion) and G (glycoproteins) are essential for virus to penetrate the cell.
  - These are important in determining whether there is an appropriate antibody response.
- M2 is the second matrix protein also required for transcription
  - M2-1 (elongation factor) and
  - M2-2 (transcription regulation),
- L encodes the RNA polymerase.
- Phosphoprotein P is a cofactor for L.

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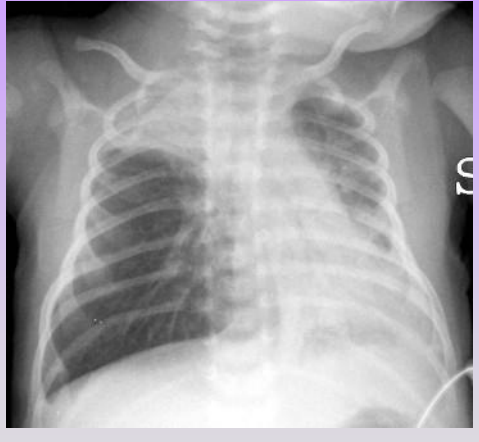
Bronchiolitis



Journal of Medical Case Reports 2008, 2:212

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Immunoprophylaxis

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Prevention

- Good handwashing and keeping at risk infants away from infected individuals is ideal.
- Early attempts at vaccine production were not successful
- A vaccine trial in 1960s using an inactivated virus (FI-RSV), actually increased disease severity in children who received vaccine.

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Am J Epidemiol. 1969 Apr;89(4):422-34.

Development of Immunoprophylaxis

- 1996: FDA approved the intravenous polyclonal antibody RSV immune globulin (RSV-IVIG, Respigam)
  - Prepared from donors selected for high serum titers of RSV neutralizing antibody (not available)
- 1998: FDA approved palivizumab (Synagis)
  - First monoclonal antibody developed into vaccine, for use as immunoprophylaxis for children ≤2 yrs at risk for severe RSV infection

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Comparison of RSV-IVIG with Palivizumab

Characteristics	RSV-IVIG (Respigam)	Palivizumab (Synagis)
Type of immunoglobulin	Polyclonal	Monoclonal
Method of administration	IV	IM
Contraindicated in infants with hemodynamically significant CHD	Yes	No
Protects against other viral infections	Yes	No
Decreased AOM	Yes	No
Risk of fluid overload in BPD	Yes	No
Blood product	Yes	No
Interferes with routine childhood immunization	Yes	No
Dosage	750mg/k/dose	15mg/k/g/dose
Dosing interval	Monthly	Monthly
# of doses / season	5	5

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Prevention

- Palivizumab is a monoclonal antibody directed against RSV surface fusion protein (F protein).
- It replaced earlier methods of prophylaxis by administration of RSV-IG
- It is given by monthly injections, typically begun just prior to the RSV season and should be continued for five months.

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Prevention

- PREVENT Trial demonstrated an overall reduction in RSV hospitalization of 43%
- The IM-pact RSV trail demonstrated a 39% reduction in hospitalization of infants with CLD and a 78% reduction in those without CLD.
- In infants 32 -35 weeks, an 80% reduction overall in RSV related hospitalization; in those without chronic lung disease, an 82% reduction.
- IM-pact RSV demonstrated a “Need to Treat” of 16 to prevent one hospitalization.

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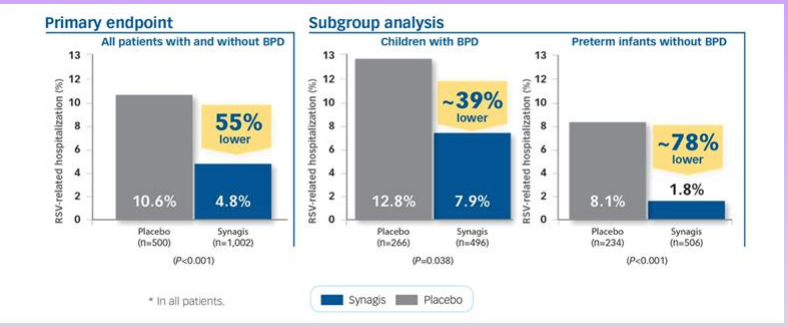
The IMpact-RSV Study Group. Palivizumab, a humanized respiratory syncytial virus monoclonal antibody, reduces hospitalization from respiratory syncytial virus infection in high-risk infants. Pediatrics. 1998;102:531-537.

The PREVENT Study Group. Reduction of respiratory syncytial virus hospitalization among premature infants and infants with bronchopulmonary dysplasia using respiratory syncytial virus immune globulin prophylaxis. Pediatrics 1997;99:93-99.



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The IMpact-RSV Study Group. Palivizumab, a humanized respiratory syncytial virus monoclonal antibody, reduces hospitalization from respiratory syncytial virus infection in high-risk infants. Pediatrics. 1998;102:531-537.

Revision History of AAP Guidance

- In 2009 and 2012, the AAP began developed increasingly restrictive guidance for the use of palivizumab
- August 2014, the AAP released its updated policy for palivizumab prophylaxis – this statement expires in five years.
- However, there has been no change in the FDA indication for palivizumab.

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	2014 AAP	2012 AAP	FDA Approved Label (NPA)
≤ 28 6/7 weeks	No Change	No Change	Recommended
29-31 weeks	Not recommended	≤ 6 months at start of RSV season	≤ 6 months at start of RSV season
32-34 weeks	Not recommended	Not recommended unless other qualifiers exist	≤ 6 months at start of RSV season
35 weeks	Not recommended	Not recommended unless other qualifiers exist	≤ 6 months at start of RSV season
Bronchopulmonary Dysplasia/Chronic Lung Disease of Prematurity (BPD/CLDP)	CLDP < 32 wks wGA and O_2 for > 28 days if < 12 months. If 12-24 months, meds or O_2 within 6 months	≤ 24 months at start of RSV season if requires oxygen or meds in prior 6 months	≤ 24 months at start of RSV season
Hemodynamically Significant-Congenital Heart Disease (HS-CHD)	12-24 months at start of RSV season; no longer recommended	≤ 24 months at start of RSV season	≤ 24 months at start of RSV season

Hospitalization

- Of the preterm infants 32-35 weeks gestation who were <6 months on November 1, 4.9% were hospitalized with RSV-related illnesses each season.
- Pre-school aged siblings and daycare attendance increased the risk of RSV disease.
- Among the subset of 32-34 week gestation infants eligible under a risk-related criteria, the RSV-related hospitalization rate was 9.1%.

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Forbes M, Kumar V, Yogev R, Wu X, Robbie G, Ambrose CS. Serum palivizumab level is associated with decreased severity of respiratory syncytial virus disease in high-risk infants. Hum Vaccin Immunother 2014;10. Ambrose CS, Anderson EJ, Simoes EA, et al. Respiratory syncytial virus disease in preterm infants in the U.S. born at 32-35 weeks gestation not receiving immunoprophylaxis. The Pediatric infectious disease journal 2014;33:576-82.

RSV related Hospitalization Decreases

- A study by Blanken, et al., supports the original evidence presented in the IMpact RSV trial.
- Palivizumab decreased RSV-related hospitalization in 33-35 week gestation infants by 82%, whereas the original IMpact study described a 78% decrease.

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The IMpact-RSV Study Group. Palivizumab, a humanized respiratory syncytial virus monoclonal antibody, reduces hospitalization from respiratory syncytial virus infection in high-risk infants. . Pediatrics 1998;102:531-7.
Blanken MO, Rovers MM, Molenaar JM, et al. Respiratory syncytial virus and recurrent wheeze in healthy preterm infants. N Engl J Med 2013;368:1791-9.

Cochrane Review

- A Cochrane review using data from a number of randomized controlled trials found high quality evidence to support the association of palivizumab and reduction in RSV-related hospitalization (RR 0.49, 95% CI 0.37-0.64) as well as high quality evidence to support an association of palivizumab and reduction in RSV ICU admissions (RR 0.5, 95% CI 0.3-0.81).

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Andabaka T, Nickerson JW, Rojas-Reyes MX, Rueda JD, Bacic Vrca V, Barsic B. Monoclonal antibody for reducing the risk of respiratory syncytial virus infection in children. Cochrane database of systematic reviews (Online) 2013;4:CD006602.

High Risk Patients

- Winterstein, et al., evaluated 247,566 patients in Florida and Texas to determine the age at which at-risk infants born from 32-34 weeks gestation experienced a risk of developing RSV equivalent to that of term babies.
- At one month of age, these babies had a risk of being hospitalized equivalent to that of term babies.
- Based on this assessment, they described a risk equivalence at 1 month of age.

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Winterstein AG, Knox CA, Kubilis P, Hampp C. Appropriateness of age thresholds for respiratory syncytial virus immunoprophylaxis in moderate-preterm infants: a cohort study. JAMA Pediatr 2013;167:1118-24.

High Risk Patients

- RSV-related hospitalization rate of these preterm infants was 3.1% in Florida and 4.5% in Texas.
- Incomplete coding and testing for RSV was a consistent issue.
- Increasingly preterm infants were at higher risk for hospitalization and the issues pertaining to disparity could not be separately identified in the populations studied.

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Winterstein AG, Knox CA, Kubilis P, Hampp C. Appropriateness of age thresholds for respiratory syncytial virus immunoprophylaxis in moderate-preterm infants: a cohort study. JAMA Pediatr 2013;167:1118-24.

High Risk Patients

- In another at-risk population in Florida, Winterstein, et al., demonstrated palivizumab prophylaxis was associated with a reduction in severe RSV infection.
- Analysis of the Kids' Inpatient Database of hospitalizations between 2000-2009 (n=325,494) showed that bronchiolitis hospitalizations increased by 29% in the sub-group where there was an FDA indication for palivizumab prophylaxis.

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Winterstein AG, Hampp C, Saidi A. Effectiveness of palivizumab prophylaxis in infants and children in Florida. Pharmacoepidemiol Drug Saf 2012;21:53-60.
Hasegawa K, Tsugawa Y, Brown DF, Mansbach JM, Camargo CA, Jr. Trends in bronchiolitis hospitalizations in the United States, 2000-2009. Pediatrics 2013;132:28-36.
McLaurin K, Ambrose CS. Clarifying costs and benefits of respiratory syncytial virus immunoprophylaxis. Pediatrics 2014;133:e1101.

RSV Hospitalizations

- In a study conducted by Hall, et al., RSV-related hospitalizations among preterm and term infants were evaluated in 3 US counties.
- RSV acute respiratory illness was tallied and relative risk was identified by age from birth certificate data.
- Although this study has been used as justification for reduced immunoprophylaxis, the study included an insufficient number of premature infants.

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RSV Hospitalizations

- Premature infants represented only 10% of the 2,140 subjects studied.
- Although RSV rates in this study were not found to be significantly different between preterm and term infants, 70% of the palivizumab eligible patients in the study populations had received palivizumab.
- African American infants greater than or equal to 6 months of age were hospitalized more often.

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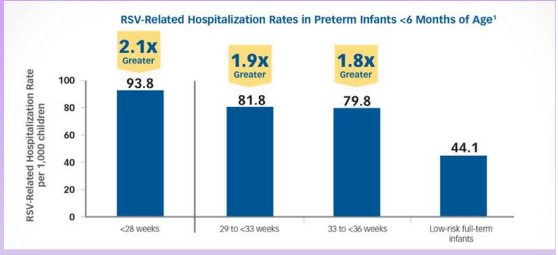
Hall CB, Weinberg GA, Blumkin AK, et al. Respiratory syncytial virus-associated hospitalizations among children less than 24 months of age. Pediatrics 2013;132:e341-8.

RSV Hospitalizations

- Boyce, et al., identified a two-fold higher hospitalization rate for preterm infants.
- This higher rate of hospitalization might drop if adequate prophylaxis could be assured.



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Boyce TG, Mellen BG, Mitchel EF, Jr., Wright PF, Griffin MR. Rates of hospitalization for respiratory syncytial virus infection among children in medicaid. The Journal of pediatrics 2000;137:865-70.
Carroll KN, Griffin MR, Edwards KM, et al. Adherence to guidelines for respiratory syncytial virus immunoprophylaxis among infants with prematurity or chronic lung disease in three United States counties. The Pediatric infectious disease journal 2012;31:e229-31.

SENTINEL I

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Evan J. Anderson, Leonard R. Krilov, John P. DeVincenzo, Paul A. Checchia, Natasha Halasa5, Eric A. F. Simões, Joseph B. Domachowske, Michael L. Forbes, Pia S. Pannaraj9, Scott J. McBride, Kimmie K. McLaurin, Veena R. Kumar, Christopher S. Ambrose. SENTINEL1: An Observational Study of Respiratory Syncytial Virus Hospitalizations among U.S. Infants Born at 29 to 35 Weeks' Gestational Age Not Receiving Immunoprophylaxis. Amer J Perinatol 2017; 34(01): 51-61. DOI: 10.1055/s-0036-1584147

SENTINEL 1

- Objective: characterize RSV-confirmed hospitalizations (RSVHs) among US preterm infants born at 29–35 wGA not receiving RSV IP during the 2014–2015 and 2015–2016 RSV seasons (ClinicalTrials.gov Identifier: NCT02273882).
- Patients were stratified according to illness severity.

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SENTINEL 1

- Infant inclusion criteria:
  - Born at 29–35 weeks GA (29 weeks, 0 days through 35 weeks, 6 days)
  - Laboratory-confirmed, community-acquired or nosocomial RSV disease
  - <12 months of age at time of the index RSVH admission
  - Hospitalized ≥24 hours specifically for the diagnosed RSV disease (the index RSVH)

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- Earlier gestational age and younger chronologic age were associated with a higher risk of ICU admission and need for MV (**Figures 2a and 2b**).

Figure 2a. Proportion of Infants with RSV-confirmed ICU Admissions by Chronologic Age Group

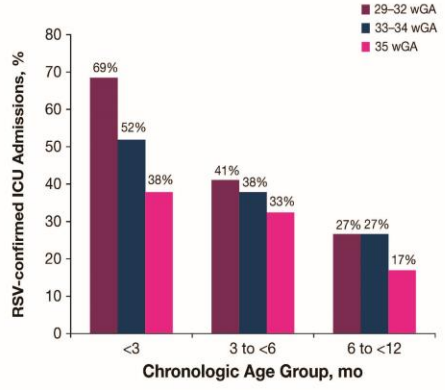
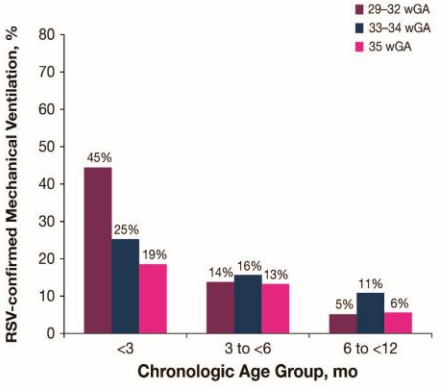


Figure 2b. Proportion of Infants with Need for RSV-confirmed Mechanical Ventilation by Chronologic Age Group



ICU=intensive care unit; RSV=respiratory syncytial virus; wGA=weeks' gestational age.

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SENTINEL 1

- In 29–35 wGA preterm infants <6 months not receiving RSV IP, RSV illness can result in ICU admissions and mechanical ventilation (MV).
- Consistent with previous RSV studies
- Earlier gestational age and younger chronologic age were associated with a higher risk for both compared with later gestational age and older chronologic age.
- The incidence of RSV was higher at younger chronologic age and at earlier gestational age.

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Truven Database

- Following a change in palivizumab dosing patterns for the 2014-2015 season, with a decline in RSV prophylaxis, the TRUVEN study demonstrated hospitalization increases among infants born at 29-34 wGA and aged <3 months.
- Compared with the 2013–2014 season, RSV hospitalization increased by 2.7-fold (p=0.02) in the at-risk group. RSV hospitalizations for infants 29-34 wGA were up to seven times higher than normal term infants

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Kong AM, Krilov LR, Fergie J, Goldstein M, Diakun D, Wade SW, 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. 2017.

The Second Season

- Investigation of serious RSV disease in preterm infants from the 2 seasons after AAP 2014 policy
- RSV immunoprophylaxis was significantly lower in preterm infants born in 2014–2016 vs. 2012–2014, reflecting the AAP 2014 policy.
- 2.5–5 times higher risk for preterm infants <6 months old to be hospitalized than full-term infants in 2014–2015; this increased to approximately a 3.5–5.5 times higher risk in 2015–2016

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Goldstein M; Krilov LR; Fergie J; McLaurin KK; Wade S; Diakun D; Bloomfield A; Kong AM. Respiratory syncytial virus hospitalization rates and costs among full-term and preterm infants before and after implementation of the 2014 American Academy of Pediatrics guidance on immunoprophylaxis. Academy of Managed Care Pharmacy (AMCP) Nexus, October 16–19, 2017; Dallas, Texas

The Second Season

- U.S. commercial and Medicaid insurance claims from >1.5 million infants aged <1 year. The study not only found an increased RSV hospitalization risk among preterm infants but also higher costs associated with the hospitalizations.
- The Average cost for an RSV hospitalization during the 2014–2016 RSV seasons for commercially insured infants <3 months was $17,416 for full-term infants vs. $39,174 for infants 29–34 wGA. Medicaid infants <3 months had an average cost of $9,824 for full-term infants vs. $22,316 for infants 29–34 wGA.

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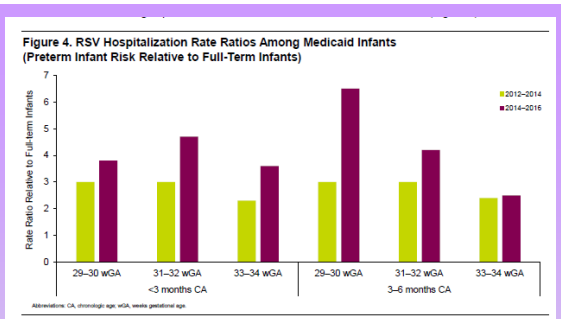
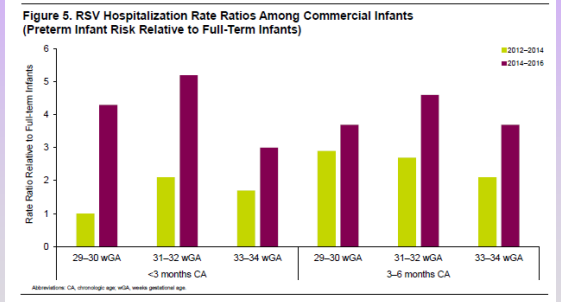
Goldstein M; Krilov LR; Fergie J; McLaurin KK; Wade S; Diakun D; Bloomfield A; Kong AM. Respiratory syncytial virus hospitalization rates and costs among full-term and preterm infants before and after implementation of the 2014 American Academy of Pediatrics guidance on immunoprophylaxis. Academy of Managed Care Pharmacy (AMCP) Nexus, October 16–19, 2017; Dallas, Texas





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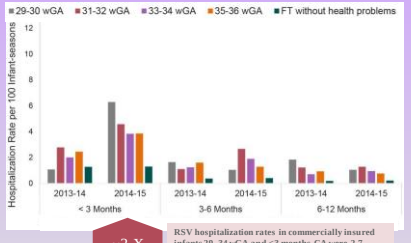
Goldstein M; Krilov LR; Fergie J; McLaurin KK; Wade S; Diakun D; Bloomfield A; Kong AM. Respiratory syncytial virus hospitalization rates and costs among full-term and preterm infants before and after implementation of the 2014 American Academy of Pediatrics guidance on immunoprophylaxis. Academy of Managed Care Pharmacy (AMCP) Nexus, October 16–19, 2017; Dallas, Texas

RSV Hospitalization Rates Among Infants for 2013–2014 and 2014–2015 (Absolute Risk)

Retrospective study

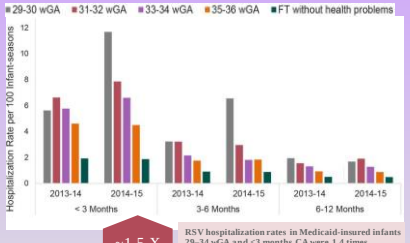
Commercial



~3 X GREATER

RSV hospitalization rates in commercially insured infants 29–34 wGA and <3 months CA were 2.7 times greater in the 2014–2015 season compared with the 2013–2014 season (95% CI, 1.2–6.0, P=0.02)

Medicaid



~1.5 X GREATER

RSV hospitalization rates in Medicaid-insured infants 29–34 wGA and <3 months CA were 1.4 times greater in the 2014–2015 season compared with the 2013–2014 season (95% CI, 1.0–1.9, P=0.03)

CA=chronological age; CI=confidence interval; FT=full term.
Kong AM, et al. Am J Perinatol. Online at: DOI: 10.1055/s-0037-1606352. Accessed November 7, 2017.

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RSV Hospitalization Rate Ratios Among Infants 2012–2016 (Preterm Infant Risk Relative to Full-term Infants)

- **There was a statistically significant increase in risk of RSVH for preterm infants 29–34 wGA compared with full-term infants**
- **The difference-in-difference was 2.0 (95% CI, 1.4–2.8, P<0.0001) for commercial patients, and 1.5 (95% CI, 1.2–1.7, P<0.0001) for Medicaid patients**

Goldstein M, et al. Poster presented at: Academy of Managed Care Pharmacy (AMCP) Nexus, Dallas, TX, October 16-19, 2017.

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Morbidity and Mortality

- Children at high risk for RSV include those with other co-morbidities besides prematurity, including chronic lung disease and congenital heart disease.
- Welliver, et al., described a series of patients with severe underlying comorbidities, as well as those with nosocomial RSV who appear to be at increased risk for death after RSV hospitalization.

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Welliver RC, Sr., Checchia PA, Bauman JH, Fernandes AW, Mahadevia PJ, Hall CB. Fatality rates in published reports of RSV hospitalizations among high-risk and otherwise healthy children. Current medical research and opinion 2010;26:2175-81.

Morbidity and Mortality

- RSV is a leading cause of worldwide morbidity, and mortality in children less than five years of age and causes approximately 3.4 million hospitalizations and greater than 66,000 deaths per year in this group.
- Although 99% of these deaths occur in developing countries, of all infectious diseases affecting children worldwide, only malaria is more deadly.

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Nair H, Nokes DJ, Gessner BD, Dherani M, Madhi SA, Singleton RJ, et al. Global burden of acute lower respiratory infections due to respiratory syncytial virus in young children: a systematic review and meta-analysis. Lancet. 2010;375(9725):1545-55. 2. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V,et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden o f Disease Study 2010. Lancet. 2012;380(9859):2095-128.

The Financial Issue

- An analysis by McLauren, et al., demonstrated modeled costs of 55 to 85% less than list pricing using a blended drug discount of 33% coupled with seasonal and patient weight considerations.
- For this model, contemporary hospitalization claim data were used to quantify payer-related costs and cost neutrality was demonstrated in patient groups up to 34 weeks gestation.

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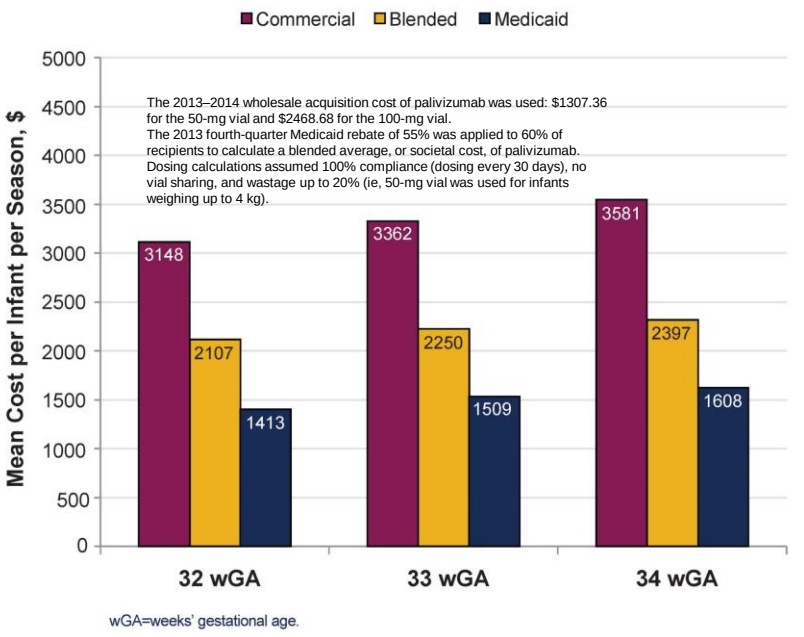
Smart KA, Paes BA, Lanctot KL. Changing costs and the impact on RSV prophylaxis. Journal of medical economics 2010;13:705-8.
Shi N, Palmer L, Chu B-C, et al. Association of RSV lower respiratory tract infection and subsequent healthcare use and costs: a Medicaid claims analysis in early-preterm, late-preterm, and full-term infants. Journal of medical economics 2011;14:335-40.
Meissner HC, Kimberlin DW. RSV immunoprophylaxis: does the benefit justify the cost? Pediatrics 2013;132:915-8.
McLaurin K, Ambrose CS. Clarifying costs and benefits of respiratory syncytial virus immunoprophylaxis. Pediatrics 2014;133:e1101

Average 2013–2014 Cost of Palivizumab for Infants 32–34 wGA



wGA=weeks' gestational age.

The Financial Issue

- Medicaid-related cost discounts were most significant, and prophylaxis of patients in this cohort produced a cost savings.
- However, physician fee, follow-up costs, parent time off work, and patient factors including "cost" of discomfort from RSV disease were not considered in either commercial or government insurance programs.

Smart KA, Paes BA, Lanctot KL. Changing costs and the impact on RSV prophylaxis. Journal of medical economics 2010;13:705-8.
Shi N, Palmer L, Chu B-C, et al. Association of RSV lower respiratory tract infection and subsequent healthcare use and costs: a Medicaid claims analysis in early-preterm, late-preterm, and full-term infants. Journal of medical economics 2011;14:335-40.
Meissner HC, Kimberlin DW. RSV immunoprophylaxis: does the benefit justify the cost? Pediatrics 2013;132:915-8.
McLaurin K, Ambrose CS. Clarifying costs and benefits of respiratory syncytial virus immunoprophylaxis. Pediatrics 2014;133:e1101

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The Financial Issue

- Extension of this model to include these considerations and dosing according to the full FDA indication may provide additional cost reduction and further tip the balance towards justification for prophylaxis.

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Smart KA, Paes BA, Lanctot KL. Changing costs and the impact on RSV prophylaxis. Journal of medical economics 2010;13:705-8.
Shi N, Palmer L, Chu B-C, et al. Association of RSV lower respiratory tract infection and subsequent healthcare use and costs: a Medicaid claims analysis in early-preterm, late-preterm, and full-term infants. Journal of medical economics 2011;14:335-40.
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The Financial Issue

- Threshold analysis in the 33–35 wGA subgroup demonstrates an adjusted RSV-hospitalization baseline risk of 17.94% or higher would result in an ICER (incremental cost-effectiveness ratio) below the £30,000 per quality-adjusted life-year threshold for cost effective therapy.
- Palivizumab is cost-effective versus no prophylaxis in the United Kingdom in many subgroups; palivizumab would be a cost-effective use of National Health Service resources.

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Bentley A, Filipovic I, Gooch K, and Büsch K. A cost-effectiveness analysis of respiratory syncytial virus (RSV) prophylaxis in infants in the United Kingdom. Health Economics Review http://www.healtheconomicsreview.com/content/3/1/18

The Issue of Disparity

- The economic impact to families outside of the healthcare system is not considered.
- The inability to provide for the care of an affected infant without a parent or guardian at home to attend to the frequent needs of these infants may perpetuate the cycle of poverty.

- While there is a high level of evidence that RSV prophylaxis is effective, considerable debate remains regarding best strategies for prevention of RSV in neonatal and pediatric patients.

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NPA 2018 RSV Prevention Guideline

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NPA and RSV

- NPA became aware of grassroots efforts at the level of many state and local organizations, protesting the decision to reduce the eligibility for RSV prophylaxis, and beginning in 2009, we commissioned our own guidelines.
- The most recent guidelines are available at www.nationalperinatal.org.
- The National Perinatal Association 2018 RSV Prophylaxis Guidelines were published in the October 2017 “Neonatology Today”.

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2018 NPA Recommendations

Indication	Chronological Age	Dosing
Areas Where Strong Data Exist		
Chronic lung disease requiring medical management	Less than 24 months at start of RSV season	Monthly during RSV season
Born at <28 0/7 weeks' gestational age (wGA)	Less than 12 months at start of RSV season	Monthly during RSV season
Born at 28 0/7-32 0/7 wGA	Less than 6 months at start of RSV season	Monthly during RSV season
Born at 32 1/7-35 6/7 wGA	Less than 6 months at start of RSV season with significant provider- identified risk factors.	Monthly during RSV season
Hemodynamically Significant Congenital Heart Disease	Less than 24 months at start of RSV season unless cardiology waiver obtained	Monthly during RSV season
Areas Where Individualized Guidance is Indicated		
Neuromuscular Disease affecting respiratory function	Less than 24 months at start of RSV season	Monthly during RSV season
Congenital abnormalities of the airways (e.g., Congenital Diaphragmatic Hernia)	Less than 24 months at start of RSV season	Monthly during RSV season
Immune Disorders (e.g., HIV, SCID, DiGeorge, IgA deficiency, Hypergammaglobulinemia)	Less than 24 months at start of RSV season unless infectious disease or immunology waiver obtained	Monthly during RSV season
Cystic Fibrosis, Primary Ciliary Dyskinesia, or other rare lung disease resulting in chronic respiratory insufficiency	Less than 24 months at start of RSV season; consultation with pediatric pulmonology suggested	Monthly during RSV season

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Respiratory Syncytial Virus Prophylaxis

- The cost of prophylaxis should be weighed against the risk of severe RSV disease requiring hospitalization and associated costs to the family as well as perceived long term consequences.
- A pediatrician or primary care provider is in the best position to assess and interpret relative risk factors.
- The most consistently identified factors associated with increased risk of RSV are child care attendance, school-aged siblings, young chronological age and maternal smoking.

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