Supplementary Tables:
Palivizumab Data

	Study Details		Methodology			Population			Outcomes Relating to RSV	Conclusions	Quality Scores		
	Citation	**Country**	**Study Design**	**Health status**	**Duration**	**Inclusion criteria**	**Exclusion criteria**	**N**	**Outcome**	**Conclusion**	**Evidence Level**	**Item Bank**	**JADAD**
1	Abadesso et al. J Hosp Infect. 2004;58:38-41.	Portugal	Retrospective single center study	High risk	1998-1999	High-risk infants in a NICU during an outbreak of RSV	NR	NR	2 outbreaks were described. In the 1st, standard infection control measures were successful. In the 2nd, infection control measures were unsuccessful (mortality rate: 12.5%). Palivizumab was then given to all infants in the unit at a cost of €401/patient: no additional RSV cases were identified.	Palivizumab may have supported the infection control measures in minimizing the RSV outbreak, indicating its potential for controlling nosocomial RSV infection.	3	NA	NA
2	Abusamra et al. Arch Dis Child. 2012;97: A25*	UK	Retrospective single center study	High risk	2006-2010	Infants <6 months with CHD; children <2 years with CLD on home oxygen; children <2 years with congenital immunodeficiency	NR	61	41/61 patients completed immuno-prophylaxis. None of those who completed prophylaxis was diagnosed RSV+. AEs were mild. Vial sharing was used to reduce costs.	RSV prophylaxis is safe and efficacious in high risk infants.	3	8	NA
3	Ambrose et al. Hum Vaccin Immunother.2014;10:2785-8.	USA	Retrospective multicenter study	Preterm or BPD	NA	Information on palivizumab efficacy by high-risk group using data derived from 3 significant clinical trials	NA	250,500 eligible for prophylaxis	The population-weighted efficacy estimate for palivizumab was 68%. Prevalence of BPD/CHD contributed to a higher efficacy result.	Palivizumab is efficacious in reducing RSVH at a rate higher than that observed in initial clinical trials.	3	NA	NA
4	Anderson et al. Pediatr Infect Dis J. 2017;36:699-704.	USA	Post hoc analysis of a prospective multicenter study	High risk	2002-2006	Children born <36 wGA aged ≤12 months; children <24 months of age with HS-CHD, and/ or CLD of prematurity who required medical intervention	NR	849	443/849 infants received palivizumab. RSV was identified in 47% of the cohort. When adjusted for confounds, palivizumab effectiveness was calculated as 58%, and at 62% in preventing ICU admissions.	Palivizumab prevents RSVH and ICU admissions in high-risk infants.	2	10	NA
5	Atkins et al. Pediatr Infect Dis J. 2000;19:138-43.	USA	Prospective/ retrospective single center study	Preterm	Pre-prophylaxis: 1994-1996 Prophylaxis: 1996-1998	Preterm infants born at ≤32 weeks at risk for RSVH and born 6 months before or during the winter season	Neonatal inpatients; patients that left the clinic's outpatient system during the 1st winter of life	Pre-prophylaxis: 159 Post-prophylaxis: 195	In the pre-prophylaxis era, 35/159 (22%) of high-risk infants had RSVH. In the post-prophylaxis era, 17/195 (8.7%) of high-risk infants had RSVH, a significant decrease.	RSV prophylaxis significantly reduces RSVH in high-risk infants as well as reducing healthcare costs.	3	10	NA
6	Baysal et al. Eur Heart J. 2013;34:691-692.*	Turkey	Prospective single center study	CHD	NR	Children <2 years old with LRTI	NR	419	241/419 patients with LRTI had hemodynamically unstable CHD. 29 CHD patients were given palivizumab. Prophylaxis reduced inpatient treatment from 59% to 14%. Mortality was 2% (1 infant).	Palivizumab prophylaxis is effective in infants with CHD. Diagnostic measures should be optimized to isolate RSV-LRTI to enable relevant treatment.	2	3	NA

7	Bellavance et al. Paediatr Child Health. 2006;11:19-23.	Canada	Retrospective multicenter study	CHD	2002-2003 and 2003-2004	Infants with CHD prescribed palivizumab	Infants prescribed palivizumab without CHD	2002-2003: 45 2003-2004: 146	The number of children receiving >5 doses significantly increased from 10/45 (22%) in 2002-2003 to 57/128 (45%) in 2003-2004. 117/146 children (80%) receiving palivizumab in 2003-2004 met CPS guidelines versus 38/45 children (84%) in 2002-2003 (i.e., pre-guideline publication) (non-significant). Patients not meeting CPS criteria were >24 months at time of 1st dose, had hemodynamically insignificant CHD or lesions adequately corrected by surgery.	The number of children with CHD receiving palivizumab prophylaxis increased significantly following publication of CPS guidelines. The majority of children were eligible for palivizumab according to current CPS criteria. More patients received >5 doses in 2003-2004 than in 2002-2003.	3	7	NA
8	Bjornson et al. Eur Respir J. 2015;46:PA3625.*	Canada	Retrospective multicenter study	CF	2000-2009	Data on RSVH and respiratory infections in infants with CF <2 years of age	NR	130	6/130 infants (43 palivizumab; 87 non-palivizumab) had 8 RSVH. For RSVH, there were no differences between non/prophylaxed groups in ICU LOS (mean 5.0±5.7, n=2), O_2 use (mean 6.5±0.7, n=2) or total LOS (mean 34.5±36.1, n=6). There were no SAEs related to palivizumab.	Palivizumab prophylaxis did not predict RSVH. There were no differences in RSVH and respiratory infections or morbidities between groups. However, despite the sample size, power may have been insufficient to detect differences.	3	10	NA
9	Blanken et al; Dutch RSV Neonatal Network. N Engl J Med. 2013;368:1791-9.	Netherlands	Prospective multicenter study	Preterm	2008-2010	Infants born at 33-35 wGA aged ≤6 months at the start of the RSV season and with no previous wheezing issues	CHD; BPD; DS; other serious congenital disorders; MV at birth; treated with surfactant; physician-diagnosed wheeze prior to RSV season start	429	Palivizumab treatment resulted in a significantly reduced incidence of RSVH (0.9% versus 5.1%) and a relative reduction of 61% in the total number of wheezing days during the 1st year of life. During this time, the proportion of infants with recurrent wheeze was 10 percentage points lower in patients treated with palivizumab.	In otherwise healthy preterm infants, palivizumab treatment resulted in a significant reduction in wheezing days during the 1st year of life, even after the end of treatment. These findings implicate RSV infection as an important mechanism of recurrent wheeze during the 1st year of life in such infants, via pulmonary epithelial damage and immunological changes in the lungs creating long-term hyper-responsiveness.	1	13	4
10	Bonnet et al. Acta Pediatrica. 2011;100:59.*	Europe	Retrospective multicenter study	HS-CHD	2000-2008	Infants <24 months with HS-CHD at time of initial palivizumab dose during the RSV season (1 Sep–30 Apr). Controls were infants with HS-CHD <32 months at the end of the RSV season for which they would have had RSV prophylaxis	Corrected CHD; uncomplicated small atrial or ventricular septal defects or patent ductus arteriosus; receipt of palivizumab before approval for use; involvement in study in a prior RSV season	1009 per study arm	Compared with controls, fewer prophylaxed infants experienced RSV (1.9% versus 1.7%, respectively). Overall numbers of deaths (all cause) were similar for prophylaxed infants (9/1009) and control infants (10/1009).	No additional safety concerns associated with the administration of palivizumab were reported.	3	11	NA
11	Butt et al. Cardiol Young. 2014;24:337-43.	Canada	Retrospective single center study	CHD	2003-2009	Hospital medical records of all children with CHD and RSVH	RSV as secondary diagnosis	30	10/30 of hospitalized infants qualified for prophylaxis (HS-CHD), of which 4/10 received palivizumab. 185 infants with HS-CHD received prophylaxis over the 7-year period. The rate of RSV infection in all infants with HS-CHD was 2.2% (4/185).	The data demonstrate good palivizumab efficacy in prevention of RSVH in infants with HS-CHD	3	10	NA
12	Butt et al. Eur J Pediatr. 2011;170:907-13.	Canada	Retrospective single center study	None	2003-2009	PICU admissions for RSV infection	NR	181	RSV accounted for 5.7% of PICU admissions. 84% were <2 years of age. 70.2% had no comorbidities. 3.3% had received palivizumab prophylaxis and >88% were not eligible for prophylaxis under current guidelines.	The number of high-risk infants being admitted to the PICU with RSV has reached a plateau. Any further reductions in admissions will only occur with universal vaccination.	3	10	NA

13	Carbonell-Estrany et al. Pediatrics. 2010;125:e35-51.	Multi-national	Prospective multicenter study	Preterm or CLD	NR	Preterm infants aged ≤6 months at enrolment or children aged ≤24 months with CLD	NR	6635	Motavizumab recipients had a 26% relative reduction in RSVH versus palivizumab recipients. Motavizumab was superior to palivizumab for reduction of RSV-specific outpatient ARIs.	Children receiving prophylaxis with motavizumab or palivizumab had low rates of RSVH; motavizumab recipients experienced 50% fewer medically attended infections than palivizumab recipients.	1	12	5
14	Carrera et al. Minerva Pediatr. 2013;65:505-12.	Italy	Prospective single center study	NR	NR	Infants hospitalized with a case history indicative of RSV	NR	8	Symptomatic infants given palivizumab at the onset of infection demonstrated significant clinical improvement.	The results are promising but require verification via RCT.	4	NA	NA
15	Carroll et al. J Allergy Clin Immunol. 2017;139:66-71.	USA	Retrospective multicenter study	Asthma	1996-2003	Children aged 4.5-6 years enrolled in KPNC or TennCare during the 1st year of life and who had received immuno-prophylaxis according to AAP recommendations	NR	6571 (4 mutually exclusive eligibility groups: CLD; preterm <29 wGA; preterm <32 wGA; other eligibility)	Asthma at 4.5-6 years affected 45%, 23%, 19%, and 17% of children in the CLD, <29 wGA, 29-32 wGA, and other eligibility groups. Overall, the majority of infants received at least 1 dose of RSV immunoprophylaxis. Compared with the non-prophylaxed group, infants with ≥70% adherence were more likely to have CLD (45% versus 22%), lower median birth weight (1179 versus 1510 grams), be SGA (8% versus 4%), and have longer median birth hospital LOS (50 versus 31 days). Adherence to RSV prophylaxis was not associated with decreased asthma. However, children with ≥70% adherence had decreased odds of asthma versus ≤20% adherence (OR: 0.62; CI, 0.50-0.78).	Non-significant associations on prevention of asthma in specific preterm groups. Highlights the need for larger studies and prospective cohorts and provide estimates of potential preventive effect sizes in high-risk children.	3	11	NA
16	Carroll et al. Pediatr Infect Dis J. 2012;31:e229-31.	USA	Survey	CLD, preterm or CHD	2001-2009	Infants enrolled between 2001-2007 RSV seasons, aged <1 at enrolment	Unknown response to palivizumab question	1557	Adherence to palivizumab recommendations for infants with CLD and/or prematurity increased from 33% in 2001-2002 to over >80% in 2005-2007.	In this real-world assessment of adherence to palivizumab, there was increasing adherence to AAP recommendations during the 6-year period, but 17% of treated infants still did not meet AAP eligibility criteria.	4	NA	NA
17	Chadha et al. South Med J. 2012;105:399-404.	USA	Retrospective multicenter study	None	2004-2009	Infants scheduled to receive palivizumab for each RSV season	NR	1956	Infants <29 wGA received 34-48% of their total eligible palivizumab doses, whereas infants 29-31 wGA received 36-46% of doses. The rate of RSV emergency department visits and inpatient admissions did not differ significantly across years.	Healthcare professionals must work harder to identify and follow-up with patients who qualify for palivizumab dosing, including infants who meet criteria for a 2nd season as suboptimal in preterm infants insured by the South Carolina Medicaid program.	3	5	NA
18	Chan et al; CARESS investigators. Pediatr Infect Dis J. 2015;34:e290-7.	Canada	Registry	None	2005-2014	Infants recruited into CARESS	NR	19,253	An infant was considered adherent if they received all of their expected injections or ≥5 injections within appropriate inter-dose intervals. Adherence was more likely in infants with higher maternal education and those with siblings. Adherence was less likely in infants of aboriginal descent, with mothers who smoke, and older infants. Adherence was significantly associated with lower incidence of RSV infection (OR: 0.74; CI: 0.60-0.93) but not with RSVH. However, in those hospitalized for RSV, adherence was significantly associated with incidence of intubation, LOS, ICU stay and respiratory support.	Adherence may have implications in children with less severe RSV infections and those who are already hospitalized for a RSV infection.	4	NA	NA

19	Chang et al. Pediatr Cardiol. 2010;31:90-5.	USA	Retrospective multicenter study	CHD	2000-2006	Children <2 years of age with RSV-related principal diagnosis in the Californian OSHPD database	NR	Total RSVH: 53,207	Of 53,207 total hospitalizations, 3.0% had CHD and 0.5% had HS-CHD. 5 deaths were reported in the HS-CHD population; 4/5 occurred prior to the 2003 AAP guidelines. RSVH was reduced by 19% for HS-CHD patients (approx. 7 RSVH/ year) after 2003.	Since 2003, the impact of palivizumab recommendations for this population has been limited. Cost-benefit analyses for prophylaxis need further study.	3	11	NA
20	Chávez-Bueno et al. Pediatr Infect Dis J. 2007;26:1089-93.	USA	Retrospective single center study	High risk	2001-2005	Children with RSVH who received ≥1 dose of IV palivizumab, either alone or in combination with ribavirin	NR	31	31 patients received palivizumab and 25 patients (80%) also received ribavirin. 18/31 patients had signs of LRTI, 17 were hypoxemic, 10 required ICU admission, and 5 were intubated. 2 deaths were reported. No treatment-related AEs were observed.	Treatment of RSV in high risk children with IV palivizumab alone or in combination with ribavirin was well tolerated and associated with decreased mortality compared with previous reports.	3	9	NA
21	Chemaly et al. J Pediatr Hematol Oncol. 2014;36:e376-81.	USA	Retrospective single center study	Cancer	1998-2009	Children ≤18 years with cancer who had been diagnosed with RSV infection	NR	59	No significant differences were observed in rates of progression to LRTI and RSV-associated mortality for patients receiving antiviral therapy at the URTI stage versus those who did not. However, patients with LRTI had significantly better outcomes when treated with aerosolized ribavirin plus immune-modulators (mainly palivizumab) versus aerosolized ribavirin alone.	Ribavirin did not show any benefit in reducing LRTI or mortality; however, addition of palivizumab to the treatment regimen may be potentially beneficial, especially for children with LRTI.	3	10	NA
22	Chen et al; CARESS investigators. PLoS One. 2015;10:e0134711.	Canada	Prospective multicenter study	High risk	2008-2013	Infants who received >1 dose of palivizumab during the 2008-2013 RSV seasons	NR	13,025	52 of the cohort experienced an AE other than a respiratory infection. Of these, 6 (0.05%) patients had a total of 14 hypersensitivity reactions that were deemed potentially related to palivizumab.	A small proportion of infants (0.05%) in the CARESS registry experienced AEs that had a potential relationship with palivizumab; these appeared to be unpredictable in terms of onset. Overall, palivizumab appears to be a safe and well-tolerated antibody for RSV prophylaxis in high-risk children.	3	11	NA
23	Chu et al. Circulation. 2014;130:A16190.*	USA	Retrospective multicenter study	CHD	1997-2009	RSVH in children <24 months with HS-CHD in the Kids' Inpatient Database before and after implementation of 2003 AAP guidelines	NR	2205	2205 RSVH in children <24 months with HS-CHD were reported. Median LOS was 23 days versus 4 days in all children with RSVH (n=463,918) and mortality was 5% versus 0.1% in all children with RSVH. The number of RSVH were highest in 1997 and decreased significantly following FDA approval of palivizumab and again following introduction of AAP policy.	RSVH in infants with HS-CHD has declined significantly alongside the approval of palivizumab, although this population continues to experience high morbidity and mortality following RSVH.	3	10	NA
24	Clark et al. Biol Blood Marrow Transplant. 2016; 22:S19-481.*	USA	Retrospective single center study	HSCT	2009-2014	Patients who underwent HSCT on the pediatric transplant service	NR	275	128/275 patients were prophylaxed. 46/275 patients had a RSV+ swab: 40/46 of which were in the prophylaxis cohort and 12 were considered prophylaxis failures. Only 3 RSVHs occurred, all in the failure group.	Palivizumab did not appear to decrease RSV infection rates in HSCT patients. Palivizumab was safe and well-tolerated.	3	11	NA
25	Cohen et al; Palivizumab Outcomes Registry Group. Pediatr Cardiol. 2008;29:382-7.	USA	Prospective multicenter study	CHD	2000-2004	Registry of infants with CHD prophylaxed with palivizumab	NR	1500	The cumulative RSVH rate was 1.9% among patients with CHD who received prophylaxis. Among subjects with cyanotic and acyanotic CHD, hospitalization rates were 2.6% and 1.6%, respectively.	The registry data shows low RSVH rates in infants with CHD prophylaxed with palivizumab in line with AAP guidelines.	3	10	NA

26	Cox et al. J Hosp Infect. 2001;48:186-92.	UK	Case report	Preterm	1999	Preterm infants in a special care baby unit during a hospital outbreak of RSV	NR	15	Standard infection prevention controls failed to contain the spread of RSV. 7 infants were infected and 8 further high-risk preterm infants were given palivizumab. None of the prophylaxed infants became RSV+.	Further study into the role of palivizumab in the control of hospital RSV outbreaks is required.	4	NA	NA
27	Danziger-Isakov et al. Pediatr Transplant. 2012; 16:638-44.	USA	Survey	Lung transplant	NR	Physicians from 28 lung transplant centers participating in the IPLTC (voluntary collaboration of physicians practicing at centers who perform lung transplants in children <18)	NR	28 programs	18/28 programs responded with a median of 53 transplants (8-355). RSV testing occurred in asymptomatic (6/17) and symptomatic (17/17) patients via PCR or DFA. Many centers offer prophylaxis (9/17) and treatments (14/17), but strategies are not uniform. Transplant candidates received prophylaxis (IM and/or IV) at 10 sites, with 9 following national (5) or local (4) guidelines. Medications include inhaled (6), oral (4), or IV (4) ribavirin, plus IGIV (9), steroids (8), and IV (2) or IM (3) palivizumab.	This study shows noticeable variation in prophylaxis and treatment practices among centers participating in the IPLTC and identifies a need for a consensus of practice.	4	NA	NA
28	De Fontbrune et al. Clin Infect Dis. 2007;45:1019-24.	France	Retrospective single center study	HSCT	1999-2006	Patients who underwent HSCT on the pediatric transplant service diagnosed with RSV	NR	40	19/40 patients were prophylaxed -palivizumab was initiated a median of 2 days after RSV diagnosis. No AEs were reported. Prophylaxis did not limit progression from URTI to LRTI, and had no effect on survival rate.	Palivizumab had no effect on outcome in this population.	3	10	NA
29	Diehl et al. J Manag Care Pharm. 2010;16:23-31.	USA	Retrospective multicenter study	None	2006-2007	Infants ≤24 months who received at least 1 dose of palivizumab during the 2006-2007 RSV season	NR	245	14/73 (19.2%) compliant infants had at least 1 respiratory-related hospital admission compared with 37/172 (21.5%) non-compliant infants. There was a significant difference in the proportion of infants with at least 1 respiratory-related ER visit: 15.1% (n=11) of compliant infants versus 28.5% (n=49) noncompliant infants. There were no RSV-related ER visits in either group and no significant differences between groups in the proportion with at least 1 RSV-related office visit (9.6% compliant infants versus 5.8% noncompliant infants). RSVH occurred in 0 (0.0%) compliant and 2 (1.2%) noncompliant infants.	Approximately 30% of infants who received palivizumab during the 2006-2007 RSV season were compliant with dosing recommendations. Compliance was associated with a lower proportion of infants with at least 1 respiratory-related ER visit but not with any other study outcome. Median palivizumab per patient costs were higher for the compliant group, but there was no significant between-group difference in total median per patient cost (palivizumab drug plus respiratory-related medical cost).	3	10	NA
30	Dizdar et al. J Hosp Infect. 2010;75:292-4.	Turkey	Case report	High risk	2009	High-risk infants in a NICU during an outbreak of RSV	NR	NR	11 preterm infants tested RSV+; additional testing identified 2 asymptomatic cases. Cross-infection precautions were taken and all remaining preterm infants were prophylaxed with palivizumab. 2 further RSV+ cases were identified 2 days after prophylaxis.	This (at the time of writing) is the largest NICU RSV outbreak to be identified promptly using rapid testing and minimized using infection control measures and prophylaxis.	4	NA	NA
31	Drummond et al. Pediatric Pulmonology. 2016;51:688-95.	France	Retrospective multicenter study	Childhood interstitial lung disease	2007-2013	Children <24 months with interstitial lung disease treated with corticosteroids	NR	24	RSVH rates (305/1000 patient-seasons) and median LOS (7 days) were higher in children with interstitial lung disease. RSVH rates were not significantly different between children with and without palivizumab prophylaxis.	Children with interstitial lung disease on corticosteroid treatment are at high risk of RSVH. Further research is needed to define the efficacy of palivizumab in this population.	3	10	NA

32	Duppenthaler et al. Swiss Med Wkly. 2001;131:146-51.	Switzerland	Retrospective single center study	NR	1998-2000	Children <16 years hospitalized for RSV infection; resident in Canton of Bern	RSV not detected for 72 hours after hospitalization; RSV in absence of respiratory illness	242	Of 242 RSVH, 216 (89.3%) and 26 (10.7%) occurred in children without and with risk factors, respectively. Patients without and with risk factors had similar clinical courses with respect to ICU admission rate. Former preterm infants were significantly older at admission.	The impact of palivizumab on the prevention of RSVH in Bern, Switzerland, is expected to be small, and the approved indications may not target infants at greatest risk for severe disease.	3	11	NA
33	Escobar et al. J Pediatric Infect Dis Soc. 2013;2:205-14.	USA	Retrospective multicenter study	NR	1998-2006	Children adhering to the AAP guidelines from KPNC and TennCare databases	NR	15,707 (4 mutually exclusive eligibility groups: CLD; preterm <29 wGA; preterm <32 wGA; other eligibility)	Immunoprophylaxis increased over the study period, from 15% for all eligible groups in 1998 to 54% in 2007. Adherence was highest among babies with CLD (KPNC 67% and TennCare 55%). Non-adherence (0% adherence) was greatest among infants of African-American mothers (AOR: 1.32; CI: 0.98–1.78); those with mothers with less than a high school education (AOR: 1.58; CI: 1.09–2.30) in KPNC; and in infants of Hispanic mothers in TennCare (AOR: 1.65; CI: 1.24–2.20). In KPNC, 0.11% of ineligible term infants and 5% of ineligible premature infants received immuno-prophylaxis; the corresponding proportions in TennCare were 1% and 11%.	Overall adherence with AAP guidelines has increased over time. Considerable overuse and underuse of immunoprophylaxis are evident with identifiable risk groups to target for improvement.	3	10	NA
34	Faldella et al. J Chemother. 2010;22:30-5.	Italy	Prospective single center study	Preterm	2000-2004	30-month follow up of infants born at ≤32 wGA and <2 years of age at time of potential respiratory hospitalization	NR	225	32/225 infants were hospitalized for RTI during the follow-up period. A similar rate of RTI hospitalization was seen in both prophylaxed and non-prophylaxed groups. However, limited to infants hospitalized during their 1st RSV season and with a chronological age <6 months at admission, incidence rates for hospitalization were significantly six-fold lower in palivizumab recipients.	Palivizumab prophylaxis is a useful tool for preventing RTI hospitalization in young preterm infants during the RSV season.	2	10	NA
35	Fanos et al. J Chemother. 2009;21:302-10.	Italy	Prospective multicenter study	Prematurity	2004-2006	Infants born at ≤35 wGA between May 1 2004 and Feb 28 2005; palivizumab prophylaxis in 1st RSV season; not hospitalized in 1st RSV season; involved in follow-up respiratory programs	Treatment for BPD/CLD within 6 months; MV within 3 months prior to enrolment; CHD; immune-deficiency; serious congenital or chromosomal abnormalities; life expectancy of ≤6 months; participating in another clinical study	260	32.3% of infants experienced at least 1 respiratory episode, 3.8% required short hospitalization because of LRTI, 8.5% had physician-documented recurrent wheezing, and 48.8% required airway medications/ antibiotics during follow-up. 10 (3.8%) infants were hospitalized due to respiratory-related problems but only 1 patient was tested for RSV (negative result).	The patient outcomes identified in the study were low in the 2nd RSV season among preterm infants who had received prior palivizumab prophylaxis. Palivizumab contributes to low rates of hospitalization in subsequent RSV seasons in infants born ≤35 weeks.	2	10	NA
36	Farber et al. Pediatrics. 2016;138:e20160627.	USA	Retrospective multicenter study	Preterm	2012-2014	≤6 months at the start of RSV season (on or after Apr 1) and born before Dec 31 of their 1st year's RSV season	<29 or >36 wGA; chronic respiratory disease; HS-CHD; pulmonary hypertension; HSCT or other transplantation; severe genetic syndrome; heart failure; CLD of prematurity; <3 months of health plan eligibility during the RSV season in 1st year of life	2031(29-32 wGA) 12,066 (33-36 wGA)	In 29-32 wGA infants, palivizumab was associated with significantly reduced RSVH rates (3.1% versus 5.0%) but increased non-RSV bronchiolitis diagnoses (3.3% versus 1.9%). There were no significant differences by palivizumab status for 33-36 wGA infants.	In infants born at 29-32 wGA without comorbidities, palivizumab was associated with reduced RSVH but increased 'bronchiolitis without RSV' diagnoses.	3	11	NA

37	Feltes et al. Pediatr Res. 2011;70:186-91.	Multi-national	Prospective multicenter study	HS-CHD	2005-2008	Children aged ≤24 months with HS-CHD	Patients with uncomplicated or non-significant CHD	1236	Approximately 93% of motavizumab and 50% of palivizumab patients reported an AE. Skin events occurred in 19.3% of motavizumab recipients and 16.2% of palivizumab recipients. RSVH rates were similar between groups.	The drugs had a similar safety profile in infants with CHD, with the exception of a small increase in skin events following motavizumab. The evidence is consistent with a larger study of motavizumab versus palivizumab in preterm infants.	1	13	3
38	Feltes et al; Cardiac Synagis Study Group. J Pediatr. 2003;143:532-540.	USA	Prospective multicenter study	HS-CHD	1998-2002	Children aged ≤24 months with HS-CHD or unoperated/partially corrected CHD	Unstable respiratory or cardiac status; cardiac surgery expected within 2 weeks; ventilator support; expected survival <6 months; HIV; RSV infection; use of investigational agents or RSV therapy in previous 3 months	1287	Palivizumab recipients had a significant 45% relative reduction in RSVH, a significant 56% reduction in RSVH LOS per 100 children, and a significant 73% reduction in total RSVH days with increased supplemental oxygen per 100 children.	Palivizumab was safe, well-tolerated, and effective for prophylaxis of serious RSV disease in young children with HS-CHD.	1	13	4
39	Figueras-Aloy et al; IRIS Study Group. Pediatr Infect Dis J. 2008;27:788-93.	Spain	Prospective two-cohort study	NR	2005-2007	Preterm infants born between $32^{1-}35^{0}$ wGA; discharged during the infectious RSV season or aged ≤6 months at the season start (Oct 1^{st})	Previous study inclusion; nosocomial RSV; known renal or hepatic impairment; immunodeficiency; chronic seizure disorder; CHD with cyanosis or heart failure; chromosomal anomalies; congenital metabolic diseases; major congenital anomalies	5441	The incidence of RSVH was significantly lower in children receiving palivizumab (1.3% versus 4.1%) and came out as an independent factor in a multiple regression analysis (OR: 0.25; CI: 0.13– 0.49).	Palivizumab significantly reduced rates of RSVH.	2	11	NA
40	Friedman et al. Clin Pediatr (Phila). 2016;55:724-37.	USA	Survey of pediatric specialists	NA	NR	Neonatologists, pediatricians, pediatric pulmonologists and pediatric cardiologists	NR	555 respondents (from both surveys)	Most neonatologists and pediatricians (>82.7%) reported a high clinical need for RSV immunoprophylaxis in preterm infants <32 wGA. Pediatric pulmonologists and pediatric cardiologists suggested that health conditions indicative of CLD of prematurity and HS-CHD confer eligibility for RSV immunoprophylaxis. Agreement with the changes in the 2014 AAP guidance for RSV immunoprophylaxis was mixed.	Survey findings may provide a basis to improve education about risk for severe RSV disease and evaluate changes in physician use of RSV immunoprophylaxis based on the 2014 guidance.	4	NA	NA
41	Frogel et al. J Perinatol. 2008;28:511-7.	USA	Prospective multicenter study	Healthy	2000-2004	Cohort of children receiving ≥1 dose of palivizumab during the RSV season	NR	19,548 enrolments	38.6% of <32 wGA infants (3023/7826); 8.3% of 32-35 wGA infants (777/9317); and 22.9% of >35 wGA infants (549/2400) had CLD as a risk factor for RSVH. In prophylaxed infants, the overall RSV rate was 1.3%.	Prophylaxis results in low RSV rates in high risk infants.	3	8	NA
42	Giebels et al. Pediatr Pulmonol. 2008;43:169-74.	Canada	Retrospective single center study	CF	1997-2005	Review of prophylaxed children <18 months in their 1^{st} RSV season following diagnosis with CF	NR	Prophylaxed : 35 Non-prophylaxed: 40	3/40 non-prophylaxed infants were hospitalized for confirmed RSV. None of the palivizumab recipients were hospitalized for confirmed RSV.	Palivizumab prophylaxis may be beneficial for infants with CF.	3	10	NA
43	Granbom et al. Acta Paediatr. 2014;103:840-5.	Sweden	Retrospective multicenter study	CHD	2010-2012	Patients <2 years with and without CHD hospitalized with respiratory tract and RSV infections	NR	219	The calculated RR of children with CHD being hospitalized with RSV infection was 2.06 (CI 1.6–2.6) compared with children without CHD. Approximately half of patients (49%) born before the RSV season and 25% born during the RSV season did not start treatment as recommended by guidelines.	Having CHD increased the rate and estimated RR of RSVH. The guidelines were not followed for a large proportion of children born during a RSV season and need updating.	3	10	NA

44	Grimaldi et al. Pediatr Infect Dis J. 2004;23:1081-5.	France	Prospective multicenter study	BPD	1999-2002	All children ≤32 wGA with BPD hospitalized for RSV infection	No predefined criteria for hospitalization and transfer to pediatric intensive care, was left to the choice of each physician responsible for care	N per season: 123; 144; 154	The incidence of BPD in surviving preterm infants was 25%, 13.5 and 17.9% (by season). The RSVH rate in this population decreased significantly (46.2% vs 11.8 and 3.8%), predominantly due to prophylaxis in later seasons.	The study supports the efficacy of prevention of RSV bronchiolitis by palivizumab in severely premature infants with BPD.	2	9	1
45	Grimaldi et al; Burgundy Perinatal Network. Pediatr Pulmonol. 2007;42:189-92.	France	Prospective multicenter study	Preterm	1999-2004	Infants born ≤30 weeks without BPD	NR	NR	In this preterm cohort, the RSVH rate was reduced significantly in the 2 seasons with palivizumab prophylaxis versus the 3 previous RSV seasons, with an NNT of 6.	The study yielded favorable results, compared to other post-marketing studies. However, healthcare organizational differences could account for the lack of favorable results.	2	9	1
46	Groothuis JR. Eur J Clin Microbiol Infect Dis. 2003;22:414-7.	Multi-national	Prospective multicenter study	Preterm	2000-2001	Infants born at ≤35 wGA and a chronologic age of <6 months without CLD	NR	285	6 AEs were considered possibly related to palivizumab: rhinitis, cough, fever, pharyngitis, bronchiolitis, and diarrhea. No deaths were reported. 6/20 hospitalizations from the total cohort were RSV+.	Palivizumab is a safe, well tolerated prophylactic therapy in 29-32 wGA infants without CLD.	3	10	1
47	Groothuis JR. Pediatr Infect Dis J. 2001;20:628-30.	USA	Prospective multicenter study	Preterm or BPD	1998-1999	Infants born at ≤35 wGA and chronologic age of <6 months; children aged ≤24 months with BPD	NR	565	Only 39 patients reported AEs thought to be related to palivizumab, none of which were severe. The estimated RSVH rate was 2.1%, based on those infants who were tested for RSV.	This study reaffirmed the safety and tolerability of palivizumab; <2% discontinued the study due to AEs. Palivizumab is the on license, safe and effective drug available to prevent RSV in high risk infants (as written at the time of original publication).	3	10	1
48	Groves et al. Pediatr Pulmonol. 2016;51:379-85.	Northern Ireland	Retrospective single center study	CF	1997-2007	Children diagnosed via neonatal screening	Children born outside of Northern Ireland	92 (Non-recipient cohort: 47 Recipient cohort: 45)	RSVH rate was 13%. The RR of RSV infection in palivizumab non-recipients versus recipients was 4.78. Those who received palivizumab were significantly less likely to be admitted to hospital for RSV-related LRTI than non-palivizumab recipients (2/45 [3 days] versus 10/47 [10 days]).	Palivizumab was effective in reducing RSVH in CF patients.	4	10	NA
49	Grupo de Hospitales Benazuza. An Esp Pediatr. 2002;56:293-7.	Spain	Prospective multicenter study	High risk	2000-2001	Infants meeting prophylaxis recommendations	NR	283	10.6% of palivizumab-prophylaxed newborns were later hospitalized with bronchiolitis. Of these, 3.9% were attributed to RSV. Prophylaxed infants born <31 wGA had a higher rate of hospitalization compared to 31-32 wGA infants.	The differences in responses based on wGA status may account for variations in reported palivizumab efficacy in other studies.	2	11	1
50	Hampp et al. J Pediatr. 2010;156:953-9.	USA	Retrospective multicenter study	CLD, preterm, CHD, CF, immuno-deficiency	1998-2005	Children continuously eligible between September and February	NR	302,101 children-seasons	Of 302,101 children-seasons, 6089 were associated with 24,469 doses of palivizumab. In the 2004/2005 season, 73.6% of children with CLD, 67.6% children <32 wGA, 37% with CHD, 26.4% with CF, and 19.4% with severe immunodeficiency received immune-prophylaxis. Multiple indications increased likelihood for prophylaxis from 34.9% to 80.4%. Full season coverage was consistent across indications, at ~70%. From the 1998/1999 season through the 2004/2005 season, 8038 doses were administered during 2051 children-seasons without any indication; mostly (69.6%) where premature children had exceeded the recommended age range for prophylaxis.	High utilization rates were found in children with multiple indications, and compliance with a monthly schedule was consistently high. One third of doses were administered outside of guidelines, suggesting suboptimal utilization of resources in the absence of prior authorization.	3	10	NA

51	Hashmi et al. Ir Med J. 2000;93:284.	Ireland	Retrospective single center study	High risk	1999-2000	High-risk preterm infants selected for palivizumab prophylaxis	NR	7	None of the infants who received palivizumab reported a RSV infection.	Palivizumab was found to be effective in this population but its cost is prohibitive. Large studies are warranted for economic and practical use.	3	6	NA
52	Henckel et al. Pediatr Infect Dis J. 2004;23:27-31.	Sweden	Retrospective multicenter study	High risk	1999-2002	Infants hospitalized for RSV <1 year of age (<24 months in infants with CLD)	NR	818	A total of 818/62,225 infants were hospitalized with confirmed RSVH over the 3 seasons monitored, corresponding to a rate of 1.4%, 1% and 1.5% per year. 235/62,225 infants were prophylaxed, and 13/235 (13/818) had RSVH.	The data illustrate that the benefits of palivizumab are small in a large population, but the costs are substantial. Even in high-risk groups, most infants will not require hospitalization.	3	10	NA
53	Houweling et al. Pharmacoepidemiology and Drug Safety. 2013;22;339.	The Netherlands	Retrospective multicenter study	Preterm, CHD or BPD	1999-2007	All infants born between 1 Apr 1999 and 31 Mar 2007 from The Netherlands Perinatal Registry	NR	3321	Only 15% were recipients of palivizumab, with the majority born <32 wGA and mean age at 1st use was 3.1 months. The strongest predictor of receiving palivizumab was being born <32 wGA (OR: 49.1; CI: 31.5-76.4). However, among the infants born <32 wGA, 50% still did not receive palivizumab. Sub-analyses among this group showed that the likelihood of receiving palivizumab was higher for infants born in later years, having RDS or being hospitalized in the RSV season.	In the Netherlands, Palivizumab is mostly prescribed to infants born <32 wGA, according to Dutch guidelines. Use has increased over the years. However, not all children addressed in the label indication are receiving Palivizumab.	3	6	NA
54	Iğde et al. Allergy: Eur J Allergy Clin Immunol. 2016;71:534.*	Turkey	Prospective single center study	Asthma	2008-2011	Children 2-5 years old	NR	339	Preterm infants prophylaxed with palivizumab showed significantly different wheezing rates to term infants at the ages of 2-5 years. Non-prophylaxed preterm infants were reported to have higher rates than prophylaxed preterms but similar rates of wheezing to term infants at 2-5 years.	The study supports the benefit of administration of palivizumab to preterm infants to reduce the risk of asthma development.	3	6	1
55	Kingston et al. Ir Med J. 2010;103:141-4.	Ireland	Survey	CLD	NR	Survey administered to 1 consultant neonatologist or pediatrician in a maternity center	NR	20 centers	10 centers had in-house protocols, 3 centers used the AAP guidelines, 2 centers preferred the UK Joint Committee on Vaccination and Immunization guidelines and 3 centers did not have a set protocol. 4 participants felt its use impacted on hospital admissions and 61% believed its use was cost-effective.	The budgetary implication for immunoprophylaxis with palivizumab in Ireland is estimated at €1.5-2 million annually. Given current pharmaco-economic constraints there is a need to implement a national protocol on RSV immunoprophylaxis.	4	NA	NA
56	Klimek et al. Przegl Lek. 2009;66:34-8.#	Poland	Prospective single center study	Preterm	2004-2008	Very preterm infants	Infants with indications for prophylaxis other than prematurity	55	3.6% of prophylaxed children were hospitalized for RSV. Prophylaxis was most effective in low weight preterm infants and those not receiving respiratory medication on discharge from neonatal care.	RSV is beneficial for low birth weight infants with or without BPD.	3	7	1
57	Kool-Houweling et al. Acta Paediatr. 2015;104:927-32.	The Netherlands	Retrospective multicenter study	None	1999-2007	All infants born between 1 Apr 1999 and 31 Mar 2007	Infants hospitalized during the whole RSV season	3231	Only 15% of the 3231 infants who met the licensed indications received palivizumab: the strongest predictor was birth <32 wGA (OR: 49.1 [CI 31.5–76.4]). However, 50% of infants born <32 wGA did not receive palivizumab: sub-analyses showed that the probability increased for infants born in later years, those who had RDS and those hospitalized during the RSV season.	Only 15% of eligible infants received palivizumab and they were mostly born <32 wGA, in line with Dutch guidelines. There was an increase in proportion of palivizumab users over the study period due to changing guidelines; however, the national guidelines are not fully adhered to and other factors may influence the decision not to prescribe palivizumab.	3	9	NA

58	Krilov et al. BMC Pediatrics. 2014;14:261.	USA	Retrospective multicenter study	Preterm, CLD or HS-CHD	2003-2009	Birth hospital discharge before Oct 1; continuous insurance eligibility from birth through Apr 30; ≥1 palivizumab use from Aug 1 to end of season; high-risk status (≤34 wGA or CLD of prematurity or HS-CHD)	Children born during the RSV season	8443	Partially prophylaxed infants were significantly more likely to have RSVH than fully prophylaxed infants (11.7% versus 7.9%). RSVH rates ranged from 8.5% to 24.8% in preterm, CHD, and CLDP infants with partial prophylaxis. After adjusting for potential confounders, partially prophylaxed infants had 21% greater odds of hospitalization versus fully prophylaxed infants (OR 1.21, CI 1.09-1.34).	RSVH rates were significantly higher in high-risk Medicaid infants with partial palivizumab prophylaxis compared with fully prophylaxed infants. These findings suggest that reduced and/or delayed dosing is less effective.	3	10	NA
59	Kurz et al. J Hosp Infect. 2008;70:246-52.	Austria	Case report	High risk	NR	High risk infants in a NICU during an outbreak of RSV	NR	11	1 infant presented with confirmed RSV. Following diagnosis, infection control measures were implemented and all other NICU patients were prophylaxed with palivizumab. No further cases were reported.	Palivizumab, when used with routine infection control measures, appears to prevent the spread of RSV infection in the NICU.	4	NA	NA
60	La Gamma et al. Am J Perinatol. 2015;32:1017-23.	USA	Retrospective multicenter study	Preterm (≤36 wGA)	2006-2011	Infants ≤36 wGA who were discharged home after birth during the November-March RSV seasons	NR	NR	Among infants ≤36 wGA discharged home during the RSV season, 21.4-27.0% had a record of palivizumab receipt before discharge. Among infants ≤30 wGA, palivizumab receipt was 82.3-88.8%. Receipt varied considerably at the hospital level, from 0-100%.	The identified gaps in recommended care can help inform future implementation of palivizumab and other interventions to help improve the health of high-risk preterm infants in the United States.	3	6	NA
61	Lacaze-Masmonteil et al. Arch Dis Child. 2004;89:562-7.	France	Prospective multicenter study	Preterm	2000	Cohort of infants born at <33 wGA with no BPD at 39 wGA and no prophylaxis	NR	2813	7.2% of infants without BPD and without prophylaxis were readmitted at least once for RSV during the epidemic season. Children born at <31 wGA, having IUGR, or living in a single-parent family had significantly higher risk of readmission for LRTI or RSV LRTI. 6.1% of 376 children submitted for prophylaxis were readmitted at least once for RSV. RSVH rate was 20.1% in the non-prophylaxed group and 8.4% in the prophylaxed group. 2 RSV deaths were reported in non-prophylaxed infants.	1 in 4 non-prophylaxed preterm infants without BPD were readmitted ≥1 time for any reason. ~20% of these readmissions were related to RSV infection.	2	11	1
62	Lacaze-Masmonteil et al. Drug Saf. 2003;26:283-91.	Multi-national	Prospective multicenter study	High risk	1999-2000	Aged ≤2 years; born at ≤35 wGA and had BPD requiring medical management within 6 months prior to the RSV season or judged to be at risk for serious RSV infection	Hospitalized; required MV; active illness/ infection at enrolment; known renal or hepatic dysfunction; chronic seizure disorder; CHD; immunodeficiency; palivizumab allergy; treatment with RSV IGIV < 3 months prior to enrolment; previous treatment with other mAB	71 1st palivizumab season 63 2nd palivizumab season	No 1st or 2nd season subjects experienced a significant anti-palivizumab antibody response. 12.7% 1st season and 12.7% 2nd season subjects experienced ≥1 SAEs; most were respiratory and all were considered not or probably not related to palivizumab. No deaths occurred.	Monthly palivizumab injections were not associated with adverse immune responses or AEs in young children receiving palivizumab for 1 or 2 seasons. Children receiving palivizumab for a 2nd season did not experience more SAEs than those receiving it for the 1st time.	3	9	1
63	Lacaze-Masmonteil et al; French Pediatricians' Group of Synagis® Patients' Name-Based Programs. Pediatr Pulmonol. 2002;34:181-8.	France	Prospective multicenter study	NR	1999-2000	Children <6 months at inclusion and born at <33 wGA with a history of BPD; children <2 years and born at <36 wGA having had treatment for BPD over the previous 6 months	NR	516	RSVH occurred in 39/516 prophylaxed children (7.6% of the total cohort). Among those 39 children, 10 (1.9% of the total) required admission into ICU; 4 required MV. No RSV deaths were reported.	The RSVH rate in this high-risk cohort was comparable to the rate previously observed in the BPD subgroup of prophylaxed children in the IMpact-RSV trial.	3	11	NA

64	Li et al; CARESS Investigators. Pediatr Infect Dis J. 2017;36:445-450.	Canada	Prospective multicenter study	HS-CHD	2005-2015	Children <2 years of age with HS-CHD	NR	1909	1380/1909 infants received prophylaxis in the 1st year; 529/1380 infants received prophylaxis in both years. RSVH rates in the 1st and 2nd year were 10.6% and 1.7%. Cox regression showed that RSVH risk was similar across both years.	The findings suggest that infants with HS-CHD in their 2nd year are equally at risk for RSVH as infants in the 1st year, and therefore, are suitable for prophylaxis.	3	10	1
65	Linder et al. Clin Epidemiol. 2015;7:45–51.	Sweden	Survey	NA	2005-2010	Children born <26 wGA; children with BPD; children with HSHD	NR	2317	Of 582,822 children, 2317 (0.4%) were identified as high-risk for RSV infection according to Swedish recommendations. In total, 943 children had a palivizumab prescription recorded. In a random sample of 176 children at high-risk for RSV infection and with no records of palivizumab prescription fills, 47% had been treated with palivizumab according to medical records. The records underestimated palivizumab treatment by 49% in preterm children, 42% in children with BPD, and 23% in those with HS-CHD.	Improvement of the information concerning drugs administered in-hospital for the Swedish national registers is required to enable accurate information on the efficacy and safety of the drug.	4	NA	NA
66	Linnane et al. Multidiscip Respir Med. 2015;10:32.	Ireland	Retrospective single center study	CF	2004-2009	Children with CF <24 months who received palivizumab during their 1st year of life (once a month for up to 7 months)	NR	19 (30 in control group)	Prophylactic palivizumab did not prevent hospitalization for 10/19 patients, 3 of whom were affected by RSV. This was significantly greater than in the control group, where no hospitalizations were recorded.	The study does not provide unequivocal support for prophylactic use of palivizumab in CF patients <2 years old. Although, should reported incidence of RSVH increase, there is scientific plausibility for a suitably-powered palivizumab RCT.	3	7	NA
67	Mansbach et al. Pediatr Emerg Care. 2007;23:362-7.	USA	Prospective multicenter study	Bronchiolitis	NR	Emergency department patients >2 years with an attending physician diagnosis of bronchiolitis	NR	624	According to AAP recommendations, 35 children (6%) should have received palivizumab, but only 17 did. Prophylaxis with palivizumab did not differ by region. ED clinical presentations were similar when comparing children that did/not receive prophylaxis. Those receiving palivizumab were significantly more likely to come to the ED using systemic corticosteroids (22% vs 7%) and to be treated with corticosteroids (31% vs 15%). Both groups were at similar risk of hospitalization (52% vs 39%).	Only half of children presenting to the ED with bronchiolitis who met the AAP criteria for palivizumab prophylaxis received the treatment. ED visits present an opportunity to educate families about RSV prophylaxis.	3	4	1
68	Manzoni et al. Pediatr Infect Dis J. 2016;36:2-8.	Canada / Italy	Prospective multicenter study	Preterm or underlying disorders	2012-2014	Preterm infants; infants with underlying disorders; received palivizumab	NR	14,468	RSVH was significantly more frequent in Group 2 (with underlying disorders) compared to Group 1 (preterm infants). Infants with neuromuscular disorders (7.88%), airway anomalies (5.95%), BPD (4.75%) and HS-CHD (4.10%) had the highest RSVH incidences.	RSVH rates are higher in infants given palivizumab for reasons other than prematurity. It is uncertain whether these findings relate to inadequate current palivizumab dosing protocols or to a specific increased RSVH risk inherent in infants with severe underlying comorbidities.	3	11	1
69	Medrano López et al; CIVIC Study Group. Pediatr Infect Dis J. 2010;29:1077-82.	Spain	Prospective multicenter study	None	2004-2008	Children < 24 months of age with HS-CHD diagnosed with acute respiratory infection	Non-HS-CHD; HIV; involvement in other clinical trials; children that developed ARIs while hospitalized for another reason	2613	96/2613 patients required RSVH with a 3.6% specific admission rate. The cumulative RSVH rate was reported to be 1.9% among children with CHD who received prophylaxis.	Hospital admission rate and infection severity are important issues in HS-CHD. RSV was the most common virus found in children that required hospital admission for ARI. Strict adherence to prophylaxis guidelines should be kept to decrease respiratory admissions.	2	10	1

70	Michaels et al. Pediatr Transplant. 2009;13:451-6.	USA	Retrospective multicenter study	SOT	NR	Survey of SOT programs about their RSV prevention and treatment strategies	NA	NA	49% of responding SOT programs use RSV prophylaxis to candidates and/or recipients; 97% of centers used palivizumab. Strategies varied depending on the age of the patient and the organ type being transplanted.	More RSVH data is needed to affect strategies for RSV prophylaxis in this population.	4	NA	NA
71	Milczewska et al. Pediatria Polska. 2008;83:264-9.#	Poland	NR	Preterm	2005-2007	Preterm infants with or without BPD prophylaxed with palivizumab	NR	27	Of the study group, 7 infants had no RTIs; 16 infants experienced 1-3 infections; 4 infants had pneumonia requiring hospitalization.	The study confirms previous reports that palivizumab significantly reduces hospitalization frequency.	3	4	1
72	Mitchell et al. Eur Resp J. 2013;42:P3612.*	Canada	Prospective multicenter study	CF	2005-2012	Infants who received >1 dose of palivizumab during the 2005-2012 RSV seasons	NR	Total cohort: 13,310	In terms of RSVH, CF infants were not significantly different from infants with other underlying medical disorders (0.55% vs 2.21%) or those meeting indications for prophylaxis (1.47%). Cox analysis showed no effect of CF on RSVH risk compared to infants with other underlying disorders.	Despite overall differences in respiratory illness, RSVH rates appear similar in CF to infants with other underlying disorders or those that meet the indications for prophylaxis.	3	9	1
73	Mitchell et al. Eur Resp J. 2013;42:P4319.*	Canada	Prospective multicenter study	Neuromuscular disease	2005-2012	Infants who received >1 dose of palivizumab during the 2005-2012 RSV seasons	NR	Total cohort: 13,311	RSVH prevalence was higher in infants with neuromuscular impairments versus infants with other underlying medical disorders (5.23% vs 1.56%) or those meeting indications for prophylaxis (1.21%). Cox proportional hazard analysis showed increased risk of RSVH in infants with neuromuscular impairments compared to infants meeting indications for prophylaxis.	Infants with neuromuscular impairments are at higher risk of respiratory infection and RSVH compared to infants with other medical disorders or those meeting indications for prophylaxis. These data support palivizumab prophylaxis in this population.	3	9	1
74	Mitchell et al. Pediatr Pulmonol. 2006;41:1167-74.	Canada	Retrospective multicenter study	High risk	1995-2002	Infants <36 wGA	NR	1733	In Calgary, RSVH was significantly reduced from 7.3% pre-palivizumab versus 3.0% post-palivizumab. In Edmonton, where palivizumab was not offered, no change in RSVH was seen (5.0% versus 7.1%).	A palivizumab RSV prevention program for high risk infants reduced RSVHs, providing "real life" evidence of the benefits of the prophylaxis strategy.	3	10	NA
75	Mitchell et al. Eur Resp J. 2014;44:P1259.*	Canada	Prospective multicenter study	CAA	2005-2012	Infants who received >1 dose of palivizumab during the 2005-2012 RSV seasons	NR	Total cohort: 13,311	Infants with CAA had a respiratory infection rate of 12.9% compared to infants prophylaxed for other underlying disorders (9.9%) and those meeting palivizumab indications (5.9%). Of 40/309 CAA infants hospitalized for respiratory infection, 4 tested RSV+. Cox analysis showed no increase in 1st RSVH compared to the other groups.	This is the largest report of CAA infants receiving palivizumab. Despite differences in risk factors, infants with CAA appear to have similar RSVH hazards to infants with other medical disorders and those meeting indications for palivizumab.	3	9	1
76	Mitchell et al. Am J Respir Crit Care Med. 2017;195:A1196.*	Canada	Prospective multicenter study	CAA	2005-2015	Infants who received >1 dose of palivizumab across 32 hospital sites	NR	CAA: 850 Medical disorder: 2982 Standard indication: 17,604	Infants with CAA had a respiratory illness-related hospitalization rate of 11.6% versus infants with underlying medical disorders (10.1%) and standard indication infants (6.3%) and had a significantly increased hazard versus the other groups. RSVH hazard was 1.6% versus 1.58% and 1.35%, respectively.	CAA infants experienced increased respiratory illness-related hospitalization risk relative to infants with underlying medical disorders or standard indication infants. Hazard for RSVH appeared similar across indications, possibly due to the smaller CAA sample size.	3	9	1
77	Mitchell et al; CARESS investigators. Pediatr Infect Dis J. 2011;30:651-5.	Canada	Prospective multicenter study	High risk	2005-2009	Infants who received >1 dose of palivizumab during the 2005-2009 RSV seasons	NR	5286	3741 patients (70.8%) were prophylaxed for being preterm, 449 (8.5%) for BPD/CLD, 508 (9.6%) for CHD, and 588 (11.1%) for other reasons. The RSVH rate was calculated as 1.38%. No deaths considered related to palivizumab were reported.	The RSVH rate was within the range found in previous reports (1.3%-5.3%), but did not match the declining rates of the US Palivizumab Outcomes Registry, potentially due to increased testing for RSV when hospitalized and increasing rates of prophylaxis in high-risk infants.	2	10	1

78	Mochizuki et al. Am J Respir Crit Care Med. 2017;196:29-38.	Japan	Retrospective multicenter study	Preterm	2007-2008	Preterm infants (33-35 wGA) followed for 1st 6 years of life	NR	444 (349 received palivizumab during the 1st year of life)	At 6 years, atopic asthma was not different in the groups: 15.3 versus 18.2% in the treated and untreated groups, respectively. Physician-diagnosed recurrent wheeze was observed in 15.3% versus 31.6% (p=0.003).	Palivizumab prophylaxis administered to preterm infants did not suppress onset of atopic asthma but resulted in a significantly lower incidence of recurrent wheezing during the 1st 6 years.	2	8	0
79	Navér et al. Acta Paediatr. 2004;93:1470-3.	Sweden	Prospective multicenter study	Preterm	2000-2002	Preterm infants born <36 wGA and <2 years old with RSVH	NR	5800	390/5800 infants were given palivizumab: 76% were in accordance with Swedish recommendations. 218 (3.8%) children <36 wGA, 97 children (5.4%) <33 wGA, 33 (6.7%) children <29 wGA, and 8 (5.7%) <26 wGA and <2 years old had RSVH. The NNT to avoid 1 RSVH in children <36 wGA was 48.	Palivizumab should be used restrictively, recommended only for infants with CLD <1 year of age and under active treatment.	3	10	1
80	Notario et al. Pediatric Health Med Ther. 2014;5:43-8.	Multi-national	Retrospective multicenter study	Preterm	1996-1997	Infants ≤35 wGA and ≤6 months of age; ≤24 months old with diagnosis of BPD requiring ongoing treatment	Hospitalization at study entry lasting >30 days; MV; life expectancy <6 months; RSV infection; hepatic or renal dysfunction; seizure disorder; immunodeficiency; IgG product allergy; RSV IGIV within <3 months; previous palivizumab, other mAB, RSV vaccines, or other investigational agents; HS-CHD	724	Palivizumab consistently reduced RSVH (64.5%–100%) versus placebo in preterm infants without BPD in all gestational age groups. Notable relative reductions in RSVH risk were seen in the moderate/late preterm groups (82% for both the 32–34 & 32–35 wGA).	Palivizumab effectively reduced RSVH rates in preterm infants, particularly the moderate/late preterm groups.	2	10	NA
81	Null D Jr et al. Pediatr Infect Dis J. 2005;24:1021-3.	USA	Prospective multicenter study	High risk	1996-1998	Children who had received palivizumab within the IMpact RSV trial	NR	55	2 children (4%) had RSVH infection during the study. Both hospitalizations were brief (1 and 3 days) and neither required MV or ICU admission. Injections of palivizumab were well tolerated; AEs judged to be related to palivizumab were reported in 4 children (7%).	Palivizumab given in the year after initial palivizumab prophylaxis was 'safe and well-tolerated'.	3	7	1
82	O'Connell et al. J Hosp Infect. 2011;77:338-42.	Ireland	Case report	High risk	2010	High risk infants in a NICU during an outbreak of RSV	NR	NR	4 infants were RSV+. PCR was used to confirm infection and palivizumab was given to all infants in the NICU. No further symptomatic cases were identified within the unit.	Infection control is a challenge in high occupancy units.	4	NA	NA
83	Oh et al; Composs Investigators. Pediatr Infect Dis J. 2002;21:512-8.	Canada	Prospective multicenter study	Preterm and/or BPD	1999-2000	Infants ≤32 wGA and ≤6 months of age; ≤24 months old with diagnosis of BPD requiring ongoing treatment	Language barrier; receipt of palivizumab as part of other clinical trial during study period	444	The estimated incidence of RSVH was 2.4%, with a higher rate in children with BPD (6.0%) versus preterm only (1.6%). 2% of subjects discontinued palivizumab for AEs.	Palivizumab prophylaxis during the RSV season was well-tolerated and associated with a low rate of RSVH.	2	10	1

84	Ohler et al. Am J Health Syst Pharm. 2013;70:1342-6.	NR	Retrospective single center study	NR	2005-2009	Group 1: hospitalized Oct 2005-Apr 2007 with inpatient doses of palivizumab throughout the RSV season followed by outpatient doses; Group 2: hospitalized Oct 2007-Apr2009 received 1 dose of palivizumab before discharge followed by outpatient doses	NR	207 (Group 1: 112; Group 2: 95)	7 patients were hospitalized for RSV infection (5 in Group 1 versus 2 in Group 2, p=0.4564). No RSV-related deaths occurred. Significantly more inpatient doses were administered to Group 1 versus Group 2 (1.7 versus 1). Limiting inpatient palivizumab to 1 dose before discharge resulted in institutional cost savings of more than $60,000 annually.	RSVH rates did not significantly differ between NICU patients who received inpatient prophylactic palivizumab monthly and those who received only 1 dose before discharge.	3	7	NA
85	Oncel et al. Turk J Pediatr. 2012;54:344-51.	Turkey	Retrospective multicenter study	Preterm	2010-2011	Infants born at ≤32 wGA separated into 2 groups depending on palivizumab status (prophylaxed versus non-prophylaxed).	NR	Prophylaxed: 201 Non-prophylaxed: 71	No palivizumab-related AEs were reported. 6.5% of prophylaxed and 7% of non-prophylaxed infants were hospitalized for LRTI. In ≤28 wGA infants, prophylaxis resulted in a 38.75% decrease in LRTI hospitalization versus no prophylaxis.	The study indicated that palivizumab reduced LRTI hospitalization rates in infants born at ≤28 wGA, but showed no cost benefit at any gestational age.	3	10	NA
86	Ovsyannikov et al. 2012.*	Russia	Prospective multicenter study	High risk	2012	Children eligible for palivizumab prophylaxis	NR	156	Immunization with palivizumab led to a reduction in LRTI frequency (0.064 to 0.014) and hospitalization (0.048 to 0.01). Some minor AEs but no SAEs were reported.	RSV prophylaxis with palivizumab in high-risk infants is safe and effective.	3	9	NA
87	Ozyurt et al. Pediatr Pulmonol. 2015;50:1025-32.	Turkey	Retrospective single center study	CHD	Control: 2009-2010 Prophylaxis: 2010-2012	Control group: infants with CHD aged 0-2 years; Prophylaxis group: Infants <1 year old with CHD	NR	Control: 96 Prophylaxis: 91	Rate of LRTI, LRTI hospitalization, and ICU admission were significantly higher in the control group versus the prophylaxed group. Palivizumab was shown to reduce LRTI hospital admissions by 65% (multiple admissions by 82%), hospitalizations by 74% (multiple by 40%), diagnosis of severe LRTI by 71%, ICU admissions by 65%, and mortality by 49%.	Palivizumab prophylaxis is associated with significant reductions in LRTI diagnoses and hospitalizations.	3	10	NA
88	Paes et al. Pediatr Infect Dis J. 2014;33:e29-33.	Canada	Prospective multicenter study	DS	2006-2012	Any child receiving ≥1 dose of palivizumab in the CARESS registry	Language barrier; receipt of palivizumab as part of other clinical trial during study period	DS: 600 Standard Indication: 11,081 Other Illness: 1629	RSVH incidence rates were similar for DS (1.53%), standard indications (1.45%) and other illnesses (2.27%). There were no differences in RSVH based on group or prophylaxis compliance. No prophylaxis-related deaths were reported.	RSVH rates were low in infants with DS following prophylaxis with palivizumab. Risks were similar to those found in other prophylaxed groups.	3	11	NA
89	Paes et al. Eur J Clin Microbiol Infect Dis. 2012;31:2703-11.	Canada	Prospective multicenter study	Preterm	2006-2011	Any child with no underlying disorder receiving ≥1 dose of palivizumab	Language barrier; receipt of palivizumab as part of other clinical trial during study period	6654	Infants ≤32 wGA (Group 1) were compared to 33–35 wGA infants (Group 2) following prophylaxis. RSV rates were similar for Group 1 (1.5%) and Group 2 (1.4%).	RSVH is similar in infants ≤32 wGA and 33–35 wGA. Prophylaxis of 33–35 wGA infants is beneficial and cost-effective, and should be performed to target the highest risk infants.	3	10	NA
90	Paes et al. Eur J Pediatr. 2012;171:833-41.	Canada	Prospective multicenter study	High risk	2006-2010	Any child receiving ≥1 dose of palivizumab	Language barrier; receipt of palivizumab as part of other clinical trial during study period	Group 1: 4880 Group 2: 952	A greater proportion of Group 2 infants (those with medical disorders) were hospitalized for respiratory infection and RSV than Group 1 (preterm). Being in Group 2 was associated with an increased risk of respiratory infection but not RSVH. Risk of RSVH was similar in both groups.	In infants receiving palivizumab, those with underlying medical disorders are at higher risk for respiratory events than preterm infants. Risk of RSVH, however, is similar.	3	11	NA

91	Parmigiani et al. Acta Biomed Ateneo Parmense. 2001;72:109-13.	Italy	Prospective single center study	High risk	1999-2001	Infants born ≤28 wGA with BPD at 28 days of age and need for pharmacological respiratory therapy on NICU discharge; control group: infants born at ≤28 wGA with BPD at 28 days of age without therapy	NR	Palivizumab: 11 Control: 8	Palivizumab prophylaxis was associated with mild and transient AEs. No infant in either group was diagnosed with RSV infection.	The data indicates that palivizumab is safe for use in very preterm infants with BPD. Further research is necessary to determine palivizumab efficacy of in this population.	3	8	1
92	Parnes et al; Palivizumab Outcomes Registry Study Group. Pediatr Pulmonol. 2003;35:484-9.	USA	Prospective multicenter study	High risk	2000-2001	Infants receiving palivizumab prophylaxis	NR	Season 1: 2116 Season 2: 305	Total RSVH rate was 2.9%. The rate varied with risk group: 5.8% in infants with CLD, and 2.1% in preterm infants without CLD. Nearly 50% of hospitalizations occurred within the 1st and 2nd injection intervals, suggesting the importance of early RSV protection.	These data support palivizumab prophylaxis for severe RSV infection in high-risk infants.	3	10	1
93	Pedraz et al; IRIS Study Group. Pediatr Infect Dis J. 2003;22:823-7.	Spain	Prospective/ retrospective multicenter study	Preterm	1998-2002	Cohort of non-prophylaxed and a cohort of prophylaxed infants, all ≤32 wGA and ≤6 months	Nosocomial RSV infection	Non-prophylaxed: 1583 Prophylaxed: 1919	The RSVH rate in the prophylaxed cohort was 3.95% versus 13.25% in non-prophylaxed infants. 1 RSV-related death was reported in the non-prophylaxed group. Significant risk factors for RSVH in both cohorts included low wGA; age <3 months at RSV season onset; school-aged siblings; and lower parental education.	These data show that palivizumab is effective at reducing RSVH in high-risk preterm infants.	2	10	1
94	Perrin et al. Pediatrics. 2012;129:55-61.	USA	Prospective multicenter study	None	2009-2011	Infants with known risk factors for RSV, e.g. preterm	NR	247	In the 2009–2010 season, 161 children were enrolled to receive palivizumab, 86 of whom (53%) met AAP guidelines. In contrast, in 2010–2011, a total of 85 children were enrolled to receive palivizumab, and 73 (86%) met the guidelines. However, of the children selected within the AAP guidelines, only 29% received the appropriate number of doses, whereas 62% and 9% received fewer or excessive doses, respectively; these findings were similar for the 2 seasons.	In a primary practice, use of palivizumab outside of the AAP guidelines was frequent and manifested as inadequate indications or inadequate number of doses.	3	9	1
95	Pinquier et al. Arch Pediatr. 2009;16:1443-52.	France	Prospective multicenter study	Preterm	2005-2006	Infants who had received palivizumab prophylaxis	Lack of parental consent	1371	Admission for RSVH after palivizumab prophylaxis was 2.47% (37/1371). Prophylaxis was well tolerated.	Marketing Authorization was well observed among participating centers, and palivizumab was shown to be safe.	3	10	1
96	Resch et al. Int J Infect Dis. 2017;57:50-3.	Austria	Retrospective single center study	Preterm	2004-2012	Preterm infants up to 28 weeks 6 days GA followed over 2 consecutive RSV seasons	Lost to follow-up	287	17/287 tested RSV+ during the study period and 14/287 experienced RSVH. 214/287 infants received palivizumab prophylaxis. 11/214 infants with palivizumab recommendation had RSV infection during the 1st RSV season.	Respiratory morbidity was high and did not seem to be altered by palivizumab prophylaxis. A substantial burden of RSV disease in this population in the era of palivizumab was seen, mainly focused on the 1st RSV season.	3	9	NA
97	Resch et al. Eur J Clin Microbiol Infect Dis. 2006;25:120-2.	Austria	Prospective/ retrospective multicenter study	None	2001-2003	Cohort of preterm infants (29-32 wGA) born between 1 Jun 2001 - 31 Dec 2002	NR	801	104/801 patients were hospitalized due to respiratory infection. 34.6% hospitalizations were RSV-related (36 infants). The overall RSVH rate was 4.5%, rising to 5.7% in infants ≤5 months. 3/90 (3.3%) infants with adequate prophylaxis had RSVH versus 12/148 (8.1%) with inadequate prophylaxis.	The high number of inadequate or incomplete courses of palivizumab prophylaxis administered in our observational study indicates further efforts are required in order to improve compliance.	2	10	1

98	Rutkowska et al. Pediatria Polska. 2011;86:317-25.#	Poland	Retrospective multicenter study	BPD	NR	Preterm infants with BPD	NR	557	436 respiratory episodes were recorded. 22.9% of patients experienced an RTI after 1 dose of palivizumab, declining to 7.5% after the 5th dose. 91 RTI hospitalizations were recorded. 3.6% of infants reported AEs following prophylaxis. No mortality due to RSV was recorded.	Palivizumab prophylaxis was provided in line with guidelines; it was effective at reducing RTIs and should be a mandatory program.	3	9	NA
99	Santos et al. Pediatrics. 2012;130:e1695-9.	USA	Case report	Acute lymphocytic leukemia	NR	2 patients with acute lymphocytic leukemia and persistent RSV infection during chemotherapy	NR	2	In both patients, RSV infection cleared within 72 hours of receiving palivizumab.	IV palivizumab may be suitable for treating persistent RSV in immunocompromised infants.	4	NA	NA
100	Simões et al. J Allergy Clin Immunol. 2010;126:256-62.	Multi-national	Prospective multicenter study	Preterm	2001-2005	Preterm infants (<36 wGA) without CLD and no history of RSV vaccination	MV at enrollment; life expectancy of <6 months; known immunodeficiency	Family atopy: 220 No family atopy: 201	The relative protective effect of palivizumab on physician-diagnosed recurrent wheezing through the ages of 2-5 years was 68% in those with no family history of asthma and 80% in those with no family history of atopy or food allergies. Palivizumab did not have a significant effect in subgroups with a family history of food allergies or atopy.	RSV prophylaxis decreases the risk of recurrent wheezing in non-atopic children, suggesting that RSV predisposes to recurrent wheezing in an atopy-independent mechanism.	2	12	1
101	Simões et al. J Pediatr. 2007;151:34-42.	Multi-national	Prospective multicenter study	Preterm	2001-2005	Preterm infants (≤35 wGA) who had received palivizumab and were not hospitalized for RSV; preterm infants who never received palivizumab	MV at enrollment; CHD; renal, hepatic or seizure disorder; life expectancy of <6 months; known immunodeficiency; receipt of other RSV therapies	Palivizumab: 191 Non-palivizumab: 230 Non-palivizumab, non-RSV hospitalized: 154	Significantly fewer incidences of recurrent wheezing (49% relative reduction) and physician-diagnosed recurrent wheezing (51% relative reduction) were reported in palivizumab-treated subjects versus 230 untreated subjects and the non-RSVH subgroup over the 24-month follow-up.	The data indicate that palivizumab prophylaxis of RSV may reduce subsequent recurrent wheezing in preterm infants.	2	12	1
102	Simon et al. Klin Pediatr. 2011;223:292-8.	Germany	Retrospective multicenter study	None	2002-2007	Children <2 years who received palivizumab between 1 Sep and 31 May during the corresponding season	1st immunization performed outside 1 September and 31 May; age >24 months at 1st administration	10,616	Of infants receiving palivizumab, median wGA at birth was 29, and 31% had CHD. The risk of SAEs possibly/probably related to palivizumab was 0.2/1000 administrations. The worst-case RSVH rate was 2.5% in prophylaxed children.	Palivizumab prophylaxis is effective against RSVH. The achievement of optimal adherence is ongoing.	3	9	NA
103	Sorrentino et al. Pediatr Infect Dis J. 2000;19:1068-171.	USA	Retrospective multicenter study	Preterm	1998-1999	Infants born at ≤35 weeks, <2 years old at time of 1st injection and received at least 1 dose of palivizumab	NR	1839	Infants given prophylaxis reported an RSVH rate of 2.3% (42/1839). Within this, prophylaxed infants with CLD had a 4% RSVH rate (16/399) and prophylaxed preterms without CLD had a 2.1% rate (26/1227).	Only 2.3% of children receiving palivizumab prophylaxis were hospitalized with RSV, which compares favorably with the rates observed in the pivotal IMpact-RSV trial (4.8%).	3	10	NA
104	Speer et al. Pediatr Infect Dis J. 2008;27:559-61.	USA	Prospective multicenter study	CF	2000-2004	Infants who received ≥1 dose of palivizumab; diagnosis of CF	NR	91	No infants with CF who received prophylaxis were hospitalized as a result of RSV LRTI.	Evaluations of palivizumab use in infants with CF could be warranted.	3	7	1

105	Stewart et al. BMC Infect Dis. 2013;13:334.	USA	Retrospective multicenter study	NR	2003-2009	Subjects born and discharged from hospital before RSV season and received ≥1 palivizumab dose during their 1st RSV season identified from a large US commercial health insurance database	Infants born during the RSV season (Oct 1 -April 30)	5003	Subjects were deemed compliant if they received ≥5 palivizumab doses without gaps (>35 days) and their 1st dose was received by November. 30.62% of subjects were deemed non-compliant and had significantly higher unadjusted rates of RSVH compared to compliant subjects during both observation periods (post-index: 6.1 vs 2.8 per 100 infant seasons; RSV season: 5.9% vs 2.3%). In multivariate analyses, non-compliance was significantly associated with higher risk of RSVH (HR: 2.01). Of 225 RSVH observed during the RSV season, 61 (27%) occurred before the 1st dose of palivizumab.	Subjects who did not receive monthly dosing of palivizumab throughout the RSV season had significantly higher rates of RSVH. RSVHs prior to the 1st dose of palivizumab suggest some dosing was started too late.	3	10	NA
106	Tavsu et al. Am J Perinatol. 2014;31:667-72.	Turkey	Prospective single center study	Preterm	2009-2011	Infants born <32 wGA and hospitalized in the NICU	CHD; CLD; other serious comorbidity	Palivizumab: 39 Control: 41	RSVH rates were found to be significantly lower in the palivizumab group both at the year of prophylaxis and in the following year (OR 1.32 [1.11–1.57]). No significant differences between groups were reported for child development indices.	Palivizumab reduced RSVH and RSV LRTI in the prophylaxed year and the year after without impacting infant development.	2	12	3
107	Tchana et al. Giornale Italiano di Cardiologia. 2011;12:42S-43S.*	Italy	Retrospective single center study	CHD	2004-2011	Infants with CHD eligible for prophylaxis	NR	28	22/28 eligible infants received RSV prophylaxis. Of the 6 that did not receive prophylaxis, 5 later became RSV+. Of the 22 prophylaxed infants, only 1 infant (who did not complete the course) later became RSV+.	Proper use of RSV prophylaxis is effective and recommended for infants with HS-CHD.	3	5	NA
108	The IMpact-RSV Study Group. Pediatrics. 1998; 102:531-7.	Multi-national	Prospective multicenter study	BPD or preterm	1996-1997	≤35 wGA infants ≤6 months or younger or ≤24 months or younger with clinical diagnosis of BPD requiring ongoing medical treatment	HS-CHD; hospitalization expected to last >30 days at study entry; MV; life expectancy <6 months; active/recent RSV infection; known hepatic/renal dysfunction; seizure disorder; immune-deficiency; allergy to IgG products; RSVIG within <3 months; previous receipt of palivizumab, RSV vaccines, other mAB or investigational agents	1502	Monthly prophylaxis was associated with a 55% reduction in RSVH in both preterm children and those with BPD. Children receiving prophylaxis had significantly fewer days of RSVH.	Monthly IM administration of palivizumab is safe and effective for prevention of serious RSV in preterm children and those with BPD.	1	12	3
109	Thomas et al. J Pediatr Hematol Oncol. 2007;29: 227-32.	USA	Decision analysis	BMT	NR	Decision tree of RSV-related mortality in children receiving palivizumab after BMT	NA	NA	Palivizumab prophylaxis was associated with a 10% survival increase in BMT patients (absolute increase 83% to 92%) with an NNT of 12.	The model indicates a positive effect of palivizumab on survival in pediatric BMT patients. The model requires support from a suitable RCT.	4	NA	NA

110	Turner et al. Cardiol Young. 2009;19:346-51.	UK (Scotland)	Prospective single center study	Congenital cardiac malformation	1999-2007	NR	NR	NR	The annual number of children receiving palivizumab rose more than 5-fold, from 17 in the 1999-2000 season to 115 in 2004-2005, then declined to 63 in 2006-2007, following publication of recommendations of the Joint Committee on Vaccination and Immunization of the UK Department of Health. Prior to the recommendations, 35/44 (80%) patients with congenital cardiac malfunction who received palivizumab in the 2005-2006 season deviated from the current recommendations, compared to 5/51 (10%) who received palivizumab for non-cardiac indications. No patients who received palivizumab required PICU admission with proven RSV infection over the 8-year period.	The number of children receiving palivizumab initially increased significantly, although it has now fallen following implementation of national recommendations. Much prescribing, particularly for children with congenital cardiac malfunction, did not fulfil current recommendations. The absence of admissions to pediatric intensive care reflects the success of targeted immunization in our population.	2	2	1
111	Turti et al. BMC Res Notes. 2012;5:484.	Russia	Prospective multicenter study	BPD	2009-2010	Children born at ≤35 wGA and aged ≤6 months at enrollment; aged ≤24 months with a clinical diagnosis of BPD within 6 months before enrollment; aged ≤24 months with un-operated/ partially corrected HS-CHD	Hospitalization or MV at enrolment; life expectancy <6 months; active respiratory illness or other infection; known renal/ hepatic impairment; history of seizures (exc. neonatal seizures); unstable neurologic disorder; prior receipt of RSV prophylaxis	100	94/100 subjects completed their dosing schedule. There were no RSVHs or deaths. 6/7 subjects hospitalized for respiratory/ cardiac conditions had an RSV test: all were negative. Only 3 mild AEs were thought to be possibly related to palivizumab.	Palivizumab prophylaxis was efficacious against RSV and well-tolerated in high-risk children in the Russian Federation.	3	10	1
112	Vagnarelli et al. Acta Biomed Ateneo Parmense. 2000;71:573-5.	Italy	Prospective single center study	Preterm	1999-2000	NICU newborns meeting AAP prophylaxis guidelines	NR	8	None of the infants who received palivizumab reported RSVH. 2/8 reported mild, transient AEs.	Palivizumab was safe and effective in this population.	3	7	1
113	van Beek et al. Clin Dev Immunol. 2013;2013: 801581.	Multi-national	Prospective multicenter study	DS	NR	DS caregivers (e.g. pediatricians)	NR	68	39 caregivers surveyed had knowledge of the increased risk of severe RSV infection in children with DS, while 6 were unaware of the increased risk. The use of palivizumab in children with DS varied from never (5.6%) to all children (3.8%). 30 graded that it was important to have a statement on the use of RSV prophylaxis in DS in existing guidelines.	Most pediatricians are aware that children with DS have increased risk of severe RSV. Respondents felt that a statement on RSV prophylaxis in DS guidelines was important, but this was rarely present at this time.	4	10	NA
114	Vendetti et al. Hosp Pediatr. 2016;6:354-8.	NR	Retrospective multicenter study	None	2009-2013	Infants who received non-discharge palivizumab; high risk patients- defined as those with CLD, CHD or prematurity	NR	1263	1263 patients (80% classified as high-risk) received at least 1 dose of non-discharge palivizumab. Among high-risk patients, predictors of receipt of non-discharge palivizumab included longer LOS, institution, and comorbid conditions. Most low-risk patients (88%) who received non-discharge palivizumab had no comorbid conditions. Non-discharge palivizumab use varied widely among institutions. Overall, 25 eligible patients developed RSV, 17 of whom received non-discharge palivizumab.	Despite current recommendations, palivizumab for prevention of RSV was common, even among patients at low risk of severe RSV.	3	5	NA

115	Winterstein et al. Pediatr Pulmonol. 2013;48:874-84.	USA	Retrospective multicenter study	CF	1999-2006	Infants with CF aged 0-2 years identified using the National CF Registry	Palivizumab prophylaxis during month before cohort entry	Patient seasons with palivizumab use: 575 Patient seasons without palivizumab: 2300	The matched cohort of 1974 infants (2875 infant seasons) experienced 32 RSVH (3.9/ 1000 season months). Compared to periods of no use, the adjusted HR for palivizumab use was 0.57 (CI: 0.20–1.60) for RSVH.	The results suggested a small positive effect of palivizumab on RSV in this population, but overall RSV incidence was low in the cohort.	3	11	NA
116	Winterstein et al. Pharmacoepidemiol Drug Saf. 2012;21:53-60.	USA	Retrospective multicenter study	None	1998-2004	Cohort of children ≥3 months old eligible for Florida Medicaid	NR	645,313	6463 RSVH were recorded, with an incidence rate of 22.3/1000 patient-years of RSV season. HRs for RSVH were 0.89 (CI: 0.71–1.12), 0.56 (CI: 0.46–0.69), and 0.71 (CI: 0.51–0.97) for first, subsequent, and former use of palivizumab, respectively.	Palivizumab was associated with reduction in RSVH with protection appearing to extend past the current monthly dosing schedule.	3	11	NA
117	Wu et al. Pediatrics. 2004;114:e554-6.	USA	Prospective single center study	Preterm (≤30 wGA)	2001-2002	Infants aged 30 wGA at birth remaining in the NICU at 1 month of age	Infants with acute illness; multiple congenital anomalies; CHD; known hepatic or renal dysfunction	24	Midpoint palivizumab concentrations after the 1st dose were 45.6±13.0 μg/mL; 71% (17/24) of infants maintained optimal palivizumab concentrations (≥40 μg/mL). 16 infants were given 2 doses and 6 were given 3 doses while in the NICU. Midpoint concentrations after 2nd dose were significantly higher than those after 1st dose. Likewise, trough concentrations before 3rd dose were 51.9±7.8 μg/mL and higher than those before 2nd dose; all 6 infants showed concentrations >40 μg/ml.	Very premature infants had sustained optimal protective serum concentrations only after the 2nd dose of palivizumab; 77% of infants tested had trough concentrations <40 μg/mL before the 2nd dose. Additional studies are needed to establish the optimal timing of the initial dose and optimal dosing interval of palivizumab in this most vulnerable population.	2	8	1
118	Yi et al. Pediatrics. 2014;133:1031-7.	Canada / Netherlands	Retrospective multicenter study	DS	Prophylaxed: 2005-2012 Non-prophylaxed: 2003-2005	Palivizumab-treated children with DS	NR	Prophylaxed DS: 532 Non-prophylaxed DS: 233	8 treated and 23 untreated children experienced RSVH. IRR was 3.63-fold higher for untreated children. No significant differences between groups for age at RSVH or RSVH LOS were identified.	These results indicate that palivizumab prophylaxis is associated with a significant reduction in RSVH rate in children with DS during the 1st 2 years of life.	3	10	NA
119	Yoshihara et al. Pediatrics. 2013;132:811-8.	Japan	Prospective multicenter study	Preterm	2007-2008	Preterm infants 33-35 wGA born between Jul 1 and Dec 31 2007	SGA (<22.5 SD of reference birth weight); CLD; history of respiratory diseases requiring MV; received < 3 doses of palivizumab during 1st 6 months of life	Prophylaxed: 349 Non-prophylaxed: 95	Recurrent wheezing was seen in 18/95 (18.9%) in the untreated group, and 22/345 (6.4%) in the palivizumab group: a ~threefold lower rate (RR: 0.34 [CI 0.19–0.60], p<0.001). children who received palivizumab had significantly fewer subsequent outpatients visits for respiratory disease (12.1 vs 14.1 visits/person for control infants; RR: 0.88 [CI 0.83–0.94], p<0.001). There was no difference in number of hospitalizations due to respiratory disease.	Palivizumab prophylaxis administered to 33-35 wGA infants is associated with significantly lower incidence of recurrent wheezing during the 1st 3 years of life.	2	10	1
120	Zembles et al. Am J Health Syst Pharm. 2016; 73:405-8.	USA	Quality-improvement project	None	2014-2015	NA	NA	NA	During the 2014-15 RSV season (after implementation of the revised AAP guidelines), the number of palivizumab doses administered at the hospital declined by 56% from the previous RSV season. 97% of doses were administered for appropriate indications.	Standardized, comprehensive guidelines with defined criteria for palivizumab prophylaxis can be more cost-effective without impacting on morbidity or mortality.	4	NA	NA

AAP: American Academy of Pediatrics; AE: adverse event; AOR: Adjusted odds ratio; ARI: acute respiratory infection; BMT: bone marrow transplantation; BPD: bronchopulmonary dysplasia; CAA: congenital airway abnormalities; CARESS: Canadian Registry of Palivizumab; CF: cystic fibrosis; CHD: congenital heart disease; CI: confidence interval; CLD: chronic lung disease; CPS: Canadian Paediatric Society; DS: Down syndrome; DFA: direct fluorescent antibody staining; ER: emergency room; FDA: Food and Drug Administration; HIV: human immunodeficiency virus; HR: hazard ratio; HS-CHD: hemodynamically significant congenital heart disease; HSCT: Hematopoietic stem cell transplantation; ICU: intensive care unit; IGIV: Intravenous Immunoglobulin; IM: intramuscular; IPLTC: International Pediatric Lung Transplant Collaborative; IRR: incidence rate ratio; IUGR: intrauterine growth restriction; IV: intravenous; KPNC: Kaiser Permanente Northern California; LOS: length of stay; LRTI: lower respiratory tract infection; mAB: monoclonal antibody; MV: mechanical ventilation; NA: not applicable; NICU: neonatal intensive care unit; NNT: number needed to treat; NR: not reported; OR: odds ratio; OSHPD: Office of Statewide Health Planning and Development; PCR: polymerase chain reaction; PICU: pediatric intensive care unit; RCT: randomized controlled trial; RDS: respiratory distress syndrome; RR: relative risk; RSV: respiratory syncytial virus; RSV+: respiratory syncytial virus positive; RSVH: respiratory syncytial virus hospitalization; RTI: respiratory tract infection; SAE: serious adverse event; SGA: small for gestational age; SOT: solid organ transplant; URTI: upper respiratory tract infection; wGA: week's gestational age

* conference abstract # foreign language

Ribavirin Data

	Study Details		Methodology			Population			Outcomes Relating to RSV	Conclusions	Quality Scores		
	Citation	**Country**	**Study Design**	**Health status**	**Duration**	**Inclusion criteria**	**Exclusion criteria**	**N**	**Outcome**	**Conclusion**	**Evidence Level**	**Item Bank**	**JADAD**
1	Anak et al. Pediatr Pulmonol. 2010;45:307-11.	Turkey	Case report	Oncology	2006-2009	Pediatric patients hospitalized for hemato-oncological diseases	NA	6	5/6 patients with RSV antigen were treated with 0.2–0.4 g/kg IGIV and specific antiviral therapy, oral ribavirin (20–25 mg/kg/day in 3 doses). 5 patients recovered fully, although 2 were retreated due to recurrent RSV antigen and respiratory symptoms within 2 weeks.	Oral ribavirin with IGIV may be an option in the treatment of RSV, particularly when other forms of antivirals are not available.	4	NA	NA
2	Chávez-Bueno et al. Pediatr Infect Dis J. 2007;26:1089-93.	USA	Retrospective single center study	High-risk	2001-2005	Children with RSVH who received ≥1 dose of IV palivizumab, either alone or in combination with ribavirin	NR	31	31 patients received palivizumab and 25 patients (80%) also received ribavirin. 18/31 patients had signs of LRTI, 17 were hypoxemic, 10 required ICU admission, and 5 were intubated. 2 deaths were reported. No treatment-related AEs were observed.	Treatment of RSV in high risk children with IV palivizumab alone or in combination with ribavirin was well tolerated and associated with decreased mortality compared with previous reports.	3	9	NA
3	Chemaly et al. J Pediatr Hematol Oncol. 2014;36:e376-81.	USA	Retrospective single center study	Oncology	1998-2009	Children ≤18 years with cancer who had been diagnosed with RSV infection	NR	59	No significant differences were observed in the rates of progression to LRTI and RSV-associated mortality for patients receiving antiviral therapy at URTI stage versus those who did not. However, patients with LRTI had significantly better outcomes when treated with aerosolized ribavirin plus immunomodulators (mainly palivizumab) when compared with aerosolized ribavirin alone.	Ribavirin did not show any benefit in reducing LRTI or mortality; however, addition of palivizumab to the treatment regimen may be potentially beneficial, especially for children with LRTI.	3	10	NA
4	Colinas Herrero et al. An Esp Pediatr. 1997;46:143-7.#	Spain	Retrospective single center study	Bronchiolitis	1987-1994	Children hospitalized with bronchiolitis	NR	153	The impact of bronchiolitis was higher in urban areas, and during the winter. RSV was identified in 90.8% of patients. Younger patients were significantly more likely to have a more severe disease course than older children, and often had a history of prematurity or neonatal respiratory issues. Treatment with ribavirin significantly improved respiratory distress in infected infants.	Ribavirin is a useful treatment for moderate/severe RSV infection.	3	9	NA
5	Danziger-Isakov et al. Pediatr Transplant. 2012;16:638-44.	USA	Survey	Lung Transplant	NR	Physicians from 28 lung transplant centers participating in the IPLTC (voluntary collaboration of physicians practicing at centers who perform lung transplants in children <18)	NR	28 programs	18/28 programs responded with a median of 53 transplants (8-355). RSV testing occurred in asymptomatic (6/17) and symptomatic (17/17) patients via PCR or DFA. Many centers offer prophylaxis (9/17) and treatments (14/17), but strategies are not uniform. Transplant candidates received prophylaxis (IM and/or IV) at 10 sites, with 9 following national (5) or local (4) guidelines. Medications include inhaled (6), oral (4), or IV (4) ribavirin, plus IVIG (9), steroids (8), and IV (2) or IM (3) palivizumab.	This study shows noticeable variation in prophylaxis and treatment practices among centers participating in the IPLTC and identifies a need for a consensus of practice.	4	NA	NA

6	Edell et al. Pediatr Pulmonol. 1998;25:154-8.	USA	Retrospective single center study	Healthy	1994-1995	Otherwise healthy infants <6 months of age with severe RSVH	NR	41	Ribavirin treatment significantly reduced the prevalence of reactive airway disease versus controls, in terms of the proportion of patients developing airway reactivity (59% versus 89%) and the number of episodes of reactive airway disease (31 versus 70).	The data indicates that ribavirin reduces the prevalence of airway reactivity.	3	7	NA
7	Edell et al. Chest. 2002;122:935-9.	USA	Prospective single center study	Healthy	1997-1999	Otherwise healthy infants with severe RSV	Upper or lower respiratory tract symptoms >5 days; preterm birth; history of RSV bronchiolitis; cardiopulmonary disease; neurologic impairment; immunocompromised; parent with asthma or atopic disease	49	In the year following RSV infection, the ribavirin group had significantly fewer episodes (2.7 versus 6.4) and reduced severity of reactive airway disease and respiratory hospitalization LOS (25 days/100 patients versus 90 days/100 patients) compared to a conservative treatment group.	Early ribavirin treatment of RSV in previously healthy infants reduces incidence and severity of reactive airway disease as well as respiratory illness-related hospitalization.	1	8	2
8	Everard et al. Respir Med. 2001;95:275-80.	UK	Prospective single center study	Healthy (no high risk factors)	NR	Infants hospitalized with moderately severe bronchiolitis	Infants with risk factors for severe disease	40	No significant differences in clinical improvement over 24 hours, time to discharge, bronchial responsiveness at 6 months of age, frequency of significant respiratory symptoms over the 1st year of life or frequency of bronchodilators and inhaled steroids during the year of follow-up were observed between the ribavirin and placebo groups.	The study found no clinical benefit from the use of ribavirin in acute illness or the subsequent year in infants hospitalized with bronchiolitis.	1	11	3
9	Guerguerian et al. Am J Respir Crit Care Med. 1999;160:829-34.	Canada	Prospective single center study	Healthy	1994-1997	Infants <1 year of age with MV for respiratory distress secondary to RSV in the ICU	Cyanotic CHD; CHD associated with pulmonary hypertension; chronic respiratory disease associated with BPD; CF; chronic aspiration; pulmonary hypoplasia; neuromuscular disease; central hypoventilation syndrome; altered airway protection; immune deficiency; chronic liver disease; renal failure; previous ribavirin; MV for >24 h prior to aerosol treatment; nosocomial RSV	41	Ribavirin aerosols were well tolerated. No related deaths were reported. Ribavirin therapy resulted in no significant differences in length of ventilation, aerosol therapy, ICU LOS, total O_2 therapy, and hospitalization.	Aerosolized ribavirin was not effective at reducing length of ventilation and course of illness in otherwise healthy infants ventilated for respiratory distress secondary to RSV bronchiolitis.	1	13	3
10	Kimpen et al. Pediatr Infect Dis J. 1997;16:479-81.	NR	Questionnaire	None	NR	ESPID members	NR	88 centers	Ribavirin was used occasionally for high risk patients in 34 centers, although 16 hospitals followed the guidelines of the Red Book Committee of the AAP. There were no centers using ribavirin for all patients. Bronchodilator treatment was used universally in various combinations for all patients in 54 centers and for all high risk patients in 15. Corticosteroids were used by >80% of ESPID colleagues in various combinations of administration routes.	The lack of effective treatment for RSV bronchiolitis and the controversy in the literature concerning antiviral, bronchodilator and anti-inflammatory therapy leads to inconsistent treatment strategies.	4	NA	NA

11	Krilov et al. Pediatr Infect Dis J. 1997;16:273-6.	USA	Retrospective multicenter study	None	(1986-1987) 1993-1994	Follow up of infants with RSVH between 1986-87	NR	100	Children treated with ribavirin reported significantly fewer incidences of bronchitis in the intervening years (13/33 ribavirin versus 44/67 non-ribavirin). When matched by age at initial infection, ribavirin patients had longer ICU LOS during RSVH.	A good long term prognosis was reported in infants treated with ribavirin. No long term AEs on pulmonary function were detected, despite slightly more severe illness at RSV presentation.	3	10	NA
12	Law et al. Pediatrics. 1997;99:E7.	Canada	Prospective multicenter study	High-risk groups (CHD/CLD; preterm; RSVH ≤6 weeks; early hypooxia)	1993-1994	Children with acute RSV infection divided into subsets of: CHD, CLD, 6 weeks of age, ≤36 wGA, early hypoxia.	Compromised immunity; nosocomial infection	1205	In each subset, non-ventilated ribavirin patients had significantly longer RSVH LOS (2-3 days longer) than patients without ribavirin. Duration of hypoxia was significantly increased. ICU LOS increased for all ribavirin subgroups except CHD. Ribavirin therapy was not significantly associated with any outcome measures for ventilated patients.	The data raise doubts about the clinical effectiveness of ribavirin in high risk infants and children. However, ribavirin was used for sicker children, which may have influenced outcome via selection bias.	3	11	NA
13	Long et al. Pediatr Infect Dis J. 1997;16:1023-8.	USA	Prospective single center study	None	NR	Children enrolled in in randomized trials of ribavirin	NR	54	Recurrent LRTI was reported at least once for 79% of the ribavirin and 73% of placebo group. In the first 5 years after RSV, 54% of the ribavirin group and 50% of the placebo group reported wheezing.	Children in the ribavirin treatment group did not have exacerbated respiratory symptoms versus the control group, and their pulmonary function measurements were equal to the placebo-treated group, suggesting no long term AE or benefit of ribavirin therapy.	3	7	NA
14	Meert et al. Crit Care Med. 1994;22:566-72.	USA	Prospective single center study	MV	1991-1993	Children requiring MV for RSVH	Intubated for RSV-related apnea; received aerosolized ribavirin for >1 day before requiring MV	41	Ribavirin patients were not significantly different from placebo patients for number of ventilator days, oxygen days, ICU or hospital LOS.	Ribavirin aerosol therapy is safe for MV children with severe RSV, although ribavirin does not appear to significantly impact clinical outcomes.	1	11	3
15	Moler et al. J Pediatr. 1996;128:422-8.	USA and Canada	Prospective multicenter study	MV	NR	Infants with RSV-associated respiratory failure undergoing MV	MV not managed by a pediatric intensive care service; cardiopulmonary arrest before hospital arrival; nosocomial RSV; first received ribavirin ≥72 hours after initiation of MV	223	91/223 infants received ribavirin during MV. Multivariate analysis showed that use of ribavirin during MV was associated with significantly prolonged duration MV. Mortality rates did not significantly differ.	Ribavirin administration during MV in previously well infants with RSVH was not associated with reductions in mortality rates or duration of ventilation.	3	11	NA
16	Molinos-Quintana et al. Bone Marrow Transplant. 2013;48:265-8.	Spain	Prospective single center study	HSCT	2010-2012	Children undergoing HSCT	NR	6	6 patients had 9 episodes of RSV, of which 4 were LRTI. Patients showed favorable clinical responses to IV ribavirin, with 100% survival and no progression to LRTI in the remaining 5 URTI. No AEs due to ribavirin were reported.	IV Ribavirin was effective and well tolerated by HSCT patients, without associated side effects.	3	9	1
17	Ohmit et al. J Clin Epidemiol. 1996;49:963-7.	USA	Retrospective single center study	None	1986-1992	Children with confirmed RSV, hospitalized over 7 epidemic periods	NR	768	Multivariate analysis demonstrated that ribavirin treatment was significantly associated with increased hospital LOS.	The study was unable to confirm if the effect of ribavirin on RSVH LOS was due to a treatment AE or a perceived need to complete the course of therapy.	3	9	NA
18	Rodriguez et al. Arch Pediatr Adolesc Med. 1999;153:469-74.	USA	Prospective multicenter study	Healthy	1983-1992	Infants ≥1 month old with RSV LRTI and expected hospital LOS of ≥3 days	Chronic pulmonary disease; preterm	Ribavirin: 24 Placebo: 11	For follow-up years 1 to 3, more reactive airway disease, wheezing, and pneumonia were reported in the placebo than the ribavirin group (non-significant). An asthma challenge test showed greater reactivity in the placebo group (non-significant).	Ribavirin exposure showed no long-term effects on reactive airway disease, wheezing and pneumonia. Weighted severity scores suggest a long-term beneficial effect of ribavirin therapy.	3	11	3
19	Sanchez et al. Clinical Intensive Care. 2001;12:169-72.	USA	Retrospective multicenter study	Preterm	1990-1997	Infants born at <36 wGA receiving MV for confirmed RSV infection	CHD	Ribavirin: 21 Control: 20	No significant differences were identified in the pediatric risk of mortality score, duration of MV, ICU or RSVH LOS.	Aerosolized ribavirin has no significant impact on decreasing hospital morbidity and/or mortality in preterm infants.	2	8	NA

AAP: American Academy of Pediatrics; AE: adverse event; BPD: bronchopulmonary dysplasia; CF: cystic fibrosis; CHD: congenital heart disease; CLD: chronic lung disease; DFA: direct fluorescent antibody staining; ESPID: European Society for Paediatric Infectious Diseases; HSCT: Hematopoietic stem cell transplantation; ICU: intensive care unit; IGIV: Intravenous Immunoglobulin; IM: intramuscular; IPLTC: International Pediatric Lung Transplant Collaborative; IV: intravenous; LOS: length of stay; LRTI: lower respiratory tract infection; MV: mechanical ventilation; NA: not applicable; NR: not recorded; PCR: polymerase chain reaction; RSV: respiratory syncytial virus; RSVH: respiratory syncytial virus hospitalization; URTI: upper respiratory tract infection; wGA: week's gestational age # Foreign language

RSV-IGIV Data

	Study Details		Methodology			Population			Outcomes Relating to RSV	Conclusions	Quality Scores		
	Citation	**Country**	**Study Design**	**Health status**	**Duration**	**Inclusion criteria**	**Exclusion criteria**	**N**	**Outcome**	**Conclusion**	**Evidence Level**	**Item Bank**	**JADAD**
1	Anak et al. Pediatr Pulmonol. 2010;45:307-11.	Turkey	Case report	Oncology	2006-2009	Pediatric patients hospitalized for hemato-oncological diseases	NA	6	5/6 patients with RSV antigen were treated with 0.2–0.4 g/kg IGIV and oral ribavirin (20–25 mg/kg/day in 3 doses). 5 patients recovered fully, although 2 were retreated due to recurrent RSV antigen and respiratory symptoms within 2 weeks.	Oral ribavirin with IGIV may be an option in the treatment of RSV, particularly when other forms of antivirals are not available.	4	NA	NA
2	Danziger-Isakov et al. PediatrTransplant. 2012; 16:638-44.	USA	Survey	Lung Transplant	NR	Physicians from 28 lung transplant centers participating in the IPLTC (voluntary collaboration of physicians practicing at centers who perform lung transplants in children <18)	NR	28 programs were surveyed	18/28 programs responded with a median of 53 transplants (8-355). RSV testing occurred in asymptomatic (6/17) and symptomatic (17/17) patients via PCR or DFA. Many centers offer prophylaxis (9/17) and treatments (14/17), but strategies are not uniform. Transplant candidates received prophylaxis (IM and/or IV) at 10 sites, with 9 following national (5) or local (4) guidelines. Medications include inhaled (6), oral (4), or IV (4) ribavirin, plus IGIV (9), steroids (8), and IV (2) or IM (3) palivizumab.	This study shows noticeable variation in prophylaxis and treatment practices among centers participating in the IPLTC and identifies a need for a consensus of practice.	4	NA	NA
3	DeVincenzo et al. Bone Marrow Transplant. 2000;25:161-5.	USA	Prospective multicenter study	BMT	1991-1996	RSV+ children with a suspected immunodeficiency disease (e.g. HIV/AIDS) or another life-threatening illness	Patients with a previous reaction to an immune globulin product	11	6 patients showed resolution of RSV symptoms after 1 dose of RSV-IGIV. Serum RSV neutralizing titers were measured in 5 patients and showed a 3- to 30-fold increase 24 h after RSV-IGIV infusion. 4 patients reported mild adverse events, of which 1 (tachycardia) was considered related to RSV-IGIV. 1/11 (9.1%) patients died from RSV (91% survival).	RSV-IGIV may increase survival in immunocompromised children undergoing BMT above that seen in these patients treated with ribavirin alone.	2	9	1
4	Groothuis et al. N Engl J Med. 1993;329:1524-30.	USA	Prospective multicenter study	CHD, BPD or preterm	NR	<4 years old at study start (children <12 months preferred) with CHD/cardiomyopathy, BPD, or preterm birth (≤35 wGA) and a chronologic age of <6 months	Immunodeficiency; poorly controlled heart or renal failure; ventilator dependence; expected survival of <6 months	249	Frequency of all LRTI was reduced by 48%, and frequency of moderate and severe LRTI was reduced by 62%. Children in the high-dose group were hospitalized 63% less than controls, with a shorter LOS. The greatest improvement was among preterm infants and infants with BPD. A multivariate model showed that high-dose RSV-IGIV significantly reduced RSV incidence by 75%. Incidence following low-dose IGIV was not significantly different.	Administration of high doses of RSV-IGIV is a safe and effective means of preventing LRTI in infants and young children at high risk for this disease.	1	12	3
5	Groothuis et al. Pediatrics. 1995;95:463-7.	USA	Prospective multicenter study	BPD	NR	Infants born at ≤35 wGA and a chronologic age of <6 months	Immunodeficiency; poorly controlled heart or renal failure; ventilator dependence; expected survival of <6 months	162	In the high-dose (750 mg) RSV-IGIV group, 14.5% of the analyzed nasopharyngeal specimens grew into a virus, versus 19.1% in the control group. High-dose RSV-IGIV recipients had a lower incidence of RSV and RSVH.	Prophylaxis with RSV-IGIV is safe and (at the time of original publication) currently the only effective means to prevent severe RSV in high-risk preterm infants.	1	11	3

6	Redding et al. Arch Pediatr Adolesc Med. 1999;153: 503-7.	USA	Prospective single center study	BPD or preterm	1996-1997	Infants born < 35 wGA and <6 months of age OR preterm children aged <2 years with chronic respiratory disease	NR	76	3/76 (4%) of children receiving RSV-IGIV were hospitalized for RSV bronchitis or pneumonia versus 2/65 (3%) of control infants (both with CHD). The hospitalization rate was 5% in infants with BPD and 0% in preterm infants without lung disease.	The risk of RSVH in healthy preterm infants <6 months is low. Current indications for RSVIG may need inclusion of specific clinical characteristics rather than basing treatment on gestational age.	2	11	1
7	Rodriguez et al. Pediatrics. 1997;100:937-42.	USA	Prospective multicenter study	None	NR	Previously healthy infants <2 years; hospitalized for RSV+ bronchiolitis and/or pneumonia; showing acute lower respiratory symptoms for <4 days with a respiratory score of ≥2.5	Patients with cardio-pulmonary disease; immunodeficiency disease; serum IgA deficiency; renal failure; <32 wGA; previous reaction to blood products	98	Mean RSVH LOS was 4.58 days for the RSV-IGIV group versus 5.52 days for the placebo group. Children with more severe illness had 1.6 fewer hospital days and 2.7 days shorter ICU stays after RSV-IGIV versus placebo, but infants with modest respiratory illness did not receive any benefit from RSV-IGIV therapy.	No evidence was reported that treatment with RSV-IGIV resulted in reduced RSVH or ICU LOS, although some beneficial trends were seen for infants with more severe disease.	1	11	3
8	Rodriguez et al. Pediatrics. 1997;99:454-61.	USA	Prospective multicenter study	High risk	NR	Infants <2 years with BPD, CLD, CHD, or prematurity (<32 wGA); hospitalized with a history of LRTI of <4 days	Poorly controlled congestive heart failure; renal failure; pre-RSV ventilator dependency; life expectancy <6 months; pre-treatment with ribavirin; previous reaction to blood products; immune-deficiency	102	RSV-IGIV had no significant effect on hospital LOS, ICU LOS, or duration of mechanical ventilation versus placebo, or in respiratory score over time.	RSV-IGIV treatment is safe for children with BPD, CHD, or preterm birth RSVH, but is not efficacious in reducing illness severity.	1	11	3
9	Simoes et al. J Pediatr. 1998;133:492-9.	USA	Prospective multicenter study	CHD	1992-1995	Children <48 months with CHD or cardiomyopathy	Immunodeficiency disease; recent RSV; previous reaction to blood products; poor venous access; renal failure; ventilator dependency; life expectancy of <6 months	416	32/214 in the control group were hospitalized with RSV versus 21/202 of the RSV-IGIV group. 26 deaths (13 in each group) occurred during the trial (no trial significance reported).	RSV-IGIV had no significant impact on preventing RSVH in children with CHD.	1	13	3
10	The PREVENT Study Group. Pediatrics. 1997;99:93-9.	USA	Prospective multicenter study	BPD or preterm	1994-1995	Children ≤24 months with BPD and supplemental oxygen in the past 6 months; preterm infants ≤6 months	Hospitalization during randomization; MV; life expectancy <6 months; active/recent RSV infection; known IgA deficiency or immunodeficiency; previous reaction to blood products; current or previous (<2 months) IGIV; renal impairment	510	RSV-IGIV prophylaxis was associated with a 41% reduction in the incidence of RSVH, 53% reduction in RSV LOS and 60% reduction in days needing oxygen support. ICU LOS and mechanical ventilation for RSV were not significantly different between the treatment groups.	Monthly administration of RSV-IGIV was safe, well tolerated, and was effective in reducing the incidence and LOS of RSVH.	1	12	3
11	Wenzel et al. Am J Med. 2002;112:627-33.	USA	Prospective single center study	High risk	NR	Children with CLD or BPD	Prophylaxis with low-dose RSV-IGIV (150 mg/kg); history of cardiac disease	RSVIG: 13 Control: 26	The FEV_1/FVC ratio was significantly higher in the RSV-IGIV group than controls. There was a greater proportion of children with normal lung function in the RSV-IGIV group, and airway conductance was more likely to be normal in this group. Atopy was significantly less common in the RSV-IGIV group, with a lower number of asthma attacks, colds, and missed school days.	The results suggest that RSV prophylaxis with RSV-IGIV in infancy may have long-term effects on respiratory and immunologic criteria for asthma. However, larger-scale studies are needed.	2	10	1

AIDS: acquired immunodeficiency syndrome; BMT: bone marrow transplantation; BPD: bronchopulmonary dysplasia; CHD: congenital heart disease; CLD: chronic lung disease; DFA: direct fluorescent antibody staining; FVC: forced vital capacity; FEV: forced expiratory volume; HIV: human immunodeficiency virus; ICU: intensive care unit; IgA: Immunoglobulin A; IGIV: intravenous immunoglobulin; IM: intramuscular; IPLTC: International Pediatric Lung Transplant Collaborative; IV: intravenous; LOS: length of stay; LRTI: lower respiratory tract infection; MV: mechanical ventilation; NA: not applicable; NR: not reported; PCR: polymerase chain reaction; RSV: respiratory syncytial virus; RSV+: respiratory syncytial virus positive; RSVH: respiratory syncytial virus hospitalization; wGA: week's gestational age

Other Data

	Study Details		Methodology				Population			Outcomes Relating to RSV	Conclusions	Quality Scores		
	Citation	**Country**	**Study Design**	Intervention	Health status	Duration	**Inclusion criteria**	**Exclusion criteria**	**N**	**Outcome**	**Conclusion**	**Evidence Level**	**Item Bank**	**JADAD**
1	Carbonell-Estrany et al. Pediatrics 2010;125:e35-51.	Multi-national	Prospective multicenter study	Palivizumab/ motavizumab	Preterm or CLD	NR	Preterm infants aged ≤6 months at enrolment or children aged ≤24 months with CLD	NR	6635	Motavizumab recipients had a 26% relative reduction in RSVH compared with palivizumab recipients. Motavizumab was superior to palivizumab for reduction of RSV-specific outpatient ARIs.	Children receiving prophylaxis with motavizumab or palivizumab had low rates of RSVH; motavizumab recipients experienced 50% fewer medically attended infections than palivizumab recipients.	1	12	5
2	Escobar et al. J Pediatric Infect Dis Soc. 2013;2:205-14.	USA	Retrospective multicenter study	Palivizumab/ RespiGam	NR	1998-2006	Children adhering to the AAP guidelines from KPNC and TennCare databases	NR	15,707 (4 mutually exclusive eligibility groups: CLD; preterm <29 wGA; preterm <32 wGA; and other eligibility)	Immunoprophylaxis increased over the study period, from 15% for all eligible groups in 1998 to 54% in 2007. Adherence was highest among babies with CLD (KPNC 67% and TennCare 55%). Non-adherence (0% adherence) was greatest among infants of African-American mothers (AOR: 1.32; CI: 0.98–1.78); those with mothers with less than a high school education (AOR: 1.58; CI: 1.09–2.30) in KPNC; and in infants of Hispanic mothers in TennCare (AOR: 1.65; CI: 1.24–2.20). In KPNC, 0.11% of ineligible term infants and 5% of ineligible premature infants received immuno-prophylaxis; the corresponding proportions in TennCare were 1% and 11%.	Overall adherence with AAP guidelines has increased over time. Considerable overuse and underuse of immunoprophylaxis are evident with identifiable risk groups to target for improvement.	3	10	NA
3	Feltes et al. Pediatr Res. 2011;70:186-91	Multi-national	Prospective multicenter study	Palivizumab/ motavizumab	HS-CHD	2005-2008	Children aged ≤24 months with HS-CHD	Patients with uncomplicated or non-significant CHD	1236	Approximately 93% of motavizumab and 50% of palivizumab patients reported an AE. Skin events occurred in 19.3% of motavizumab recipients and 16.2% of palivizumab recipients. RSVH rates were similar between groups.	The drugs had a similar safety profile in infants with CHD, with the exception of a small increase in skin events following motavizumab. The evidence is consistent with a larger study of motavizumab versus palivizumab in preterm infants.	1	13	3
4	Glenn et al. Vaccine. 2013;31:524-32.	USA	Prospective multicenter study	RSV F vaccine	Healthy	NR	Healthy adults 18-49 years of age	NR	150	The vaccine was well-tolerated, with no evidence of toxicity or SAEs. Both RSV A and B neutralization was significantly increased in vaccinated versus placebo individuals at Day 60.	This Phase I study showed that the RSV F nanoparticle vaccine was well tolerated. Neutralization, anti-RSV F IgG titers and palivizumab-competing antibodies were induced at levels that have been associated with decreased risk of RSVH.	1	13	3
5	Glenn et al. J Infect Dis. 2016;213:411-22.	USA	Prospective multicenter study	RSV F vaccine	Healthy	NR	Healthy non-pregnant women 18-35 years of age	NR	330	The vaccine was well tolerated, with primary AEs of injection site reactions. Anti-F IgG antibodies rose 6.5-15.6-fold, with significantly higher levels in 2-dose, adjuvant regimens. Palivizumab-competitive antibody levels increased up to 325 μg/mL at day 56.	This Phase II study showed that the vaccine appeared safe, immunogenic, and reduced RSV infections.	1	13	3
6	Griffin et al. Antimicrob Agents Chemother. 2017;61:e01714-16.	USA	Prospective single center study	MEDI8897	Healthy	2014-2015	Healthy normotensive men or women; aged 18-49 years; body weight of 45-110 kg	Acute illness or fever ≥99.5°F; previous receipt of mAB; receipt of drug therapy in <7 days or any vaccine in <14 days; receipt of investigational therapy	136	The mean half-life of MEDI8897 was 85- 117 days, and the bioavailability after 300 mg administration was 77%. Time to maximum concentration following IM dosing was 5 to 9 days. The safety profile of MEDI8897 was similar to placebo.	This Phase I study supports the commencement of clinical studies of MEDI8897 in infants to provide protection throughout the RSV season. MEDI8897 has increased potency and a longer half-life compared to palivizumab.	1	12	2

								within 120 days prior to or 360 days after dosing; receipt of immunoglobulin or blood products in prior 6 months; clinically significant abnormal laboratory values						
7	O'Brien et al. Lancet Infect Dis. 2015;15:1398-408.	USA	Prospective multicenter study	Motavizumab	Preterm	2004-2010	Infants aged ≤6 months born at 36 wGA on a Native American reservation	CLD of prematurity; hospital admission at randomization; present or past wheezing; RSV infection; medical disorders; receipt of palivizumab; receipt of any antibody within 3 months of randomization	2127	After ITT analysis, motavizumab resulted in an 87% relative reduction (RR: 0.13; 95% CI: 0.08-0.21) RSVH (21/1417 [2%] of participants who received motavizumab; 80/710 [11%] of 710 participants who received placebo, p<0.0001). SAEs were less common in motavizumab (212 [15%]) than placebo (148 [21%]). Hypersensitivity events were more common in motavizumab (208 [14.7%]) than placebo (87 [12.3%], p=0.14). There was no effect on rates of medically attended wheezing in children aged 1-3 years (190 [14.9%] motavizumab versus 90 [14.0%] placebo).	Motavizumab significantly reduced the RSV-associated inpatient and outpatient burden and set a benchmark for the efficacy of RSV prevention strategies.	1	11	5
8	Ramilo et al. Pediatr Infect Dis J. 2014;33:703-9.	USA	Prospective multicenter study	Motavizumab	Healthy	2006-2008	Previously healthy infants; ≥36 wGA; ≤12 months of age at randomization; hospitalized for LRTI with a documented positive RSV test	Antiviral treatment for current RSV infection before randomization; use of steroids within 30 days of randomization; medically significant underlying illness; intubation for ventilator support at randomization; previous supplemental O_2 use or MV; receipt of palivizumab or other immunoglobulin during the 2 months before randomization	118	In each study group, median RSV load decreased at a similar rate from baseline to study day 7. Median duration of hospitalization was 3.05, 2.99 and 2.88 days for motavizumab 30 mg/kg, motavizumab 100 mg/kg and placebo groups, respectively. 6 (8%) motavizumab and 0 placebo recipients were admitted to ICU and 4 required MV. The incidence of wheezing episodes during the 12-month follow up was comparable for all 3 groups.	Motavizumab had no appreciable effect on RSV viral load or illness severity in infants with RSVH.	1	10	5
9	Schepens et al. J Infect Dis. 2011;204:1692-701.	Belgium	*In vitro* study	F-VHHb nanobodies	NA	NA	Vero cells; BALB/c mice	NA	NR	F-VHHb nanobodies blocked RSV infection by inhibiting fusion without impairing RSV attachment to target cells. In mice, intranasal bivalent RSV F–specific nanobodies were protective against RSV infection.	The authors stated that therapeutic treatment with these nanobodies after RSV infection could reduce viral replication and reduce pulmonary inflammation. Nanobodies are promising options for RSV treatment.	4	NA	NA

AAP: American Academy of Pediatrics; AE: adverse event; AOR: adjusted odds ratio; ARI: acute respiratory infection; CHD: congenital heart disease; CLD: chronic lung disease; HS-CHD: hemodynamically significant congenital heart disease; ICU: intensive care unit; IgG: Immunoglobulin G; IM: intramuscular; ITT: intent to treat; LRTI: lower respiratory tract infection; KPNC: Kaiser Permanente Northern California; mAB: monoclonal antibody; MV: mechanical ventilation; NA: not applicable; NR: not reported; RR: relative risk; RSV: respiratory syncytial virus; RSVH: respiratory syncytial virus hospitalization; SAE: serious adverse event; wGA: week's gestational age