

Supplementary Information: Data Extraction Table

	Study Details	Methodology				Population						Outcomes		Quality Scores		
	Citation	Country	Study Design	Intervention	Duration	Inclusion criteria	Exclusion criteria	Disease status	N	Gender	Mean age at admission	Outcomes relating to RSV	Conclusions	Evidence Level	Item Bank	JADAD
1	Alvaro et al. 2000.	Italy	Retrospective multicenter study	None	May-June 1999	None - survey of Italian pediatricians	None	RSV infection necessitating hospitalization	344 pediatricians interviewed	NR	NR	Participating pediatricians considered prematurity (30.6%), BPD (30.4%), immunodeficiency (21.6%), or CHD (14.9%) to be conditions resulting in high-risk of severe RSV infection.	80% of pediatricians interviewed were dissatisfied with the current treatment availability for severe RSV infection.	4	5	NA
2	Anak et al. 2010.	Turkey	Retrospective multicenter study	Oncology	2006 and 2009	Pediatric oncology patients receiving therapy with or without HSCT	None	Confirmed RSV infection	2006: 30 patients 2009: 15 patients	NR	NR	2006: RSV was detected in 6/30 symptomatic patients. 4/6 were neutropenic; 2/6 were not neutropenic but immunocompromised due to oncology treatment. 2009: RSV was detected in 9/15 patients, of which 2 were asymptomatic. No deaths were reported.	It is recommended that strict RSV infection control measures are used in patients with cancer, including delaying chemotherapy and using prophylaxis or treatment measures such as ribavirin and IVIG.	4	9	NA
3	Arnold et al. 1999.	Canada	Retrospective analysis of a prospective multicenter study	None	1993-1995	NR	NR	Confirmed RSV infection	159	NR	NR	159 infants from a cohort of 1516 had underlying respiratory issues. Of these, 91 patients had BPD prior to RSV infection. Patients using home oxygen were significantly more likely to be admitted to ICU during RSVH.	RSV morbidity is similar in BPD and other respiratory conditions.	3	10	NA
4	Asner et al. 2013.	Canada	Prospective single center study	Immuno-deficiency	2006-2011	Immunodeficient children <18 years presenting with RTI during/on admission. Patients <5 years old were prospectively enrolled. Data on children >5 years were retrospectively collected	Immunocompromised children with other comorbidities qualifying for RSV prophylaxis based on current Canadian guidelines	RSV URTI or RSV LRTI	117 RSV+ immunocompromised patients	Male: 47%	Median age at RSV diagnosis: 2.7 years	Median duration of RSVH was 9 days. 28 were admitted to ICU (10 HSCT/SOT; 4 leukemia/solid tumor; 14 congenital immunodeficiencies). 5 patients died (3 immunodeficiency; 1 chronic granulomatous disease; 1 SOT).	There are serious potential consequences of RSV infection in younger children with underlying congenital immunodeficiencies; these patients may benefit from preventative strategies.	2	10	NA
5	Avetisyan et al. 2009.	Sweden	Retrospective multicenter study	Allo-HSCT	2000-2007	Allo-HSCT patients (children and adults) diagnosed with RSV	None	Confirmed RSV infection	275 allo-HSCT patients	Male: Female: 25:7	Median age at RSV diagnosis: 40.4 years	32/275 identified patients (26 adults; 6 children) were diagnosed with confirmed RSV infection. 28 of these were given ribavirin therapy for a median of 22.5 days. 3 patients died from RSV. RSV patients had increased later respiratory dysfunction compared to controls.	RSV in allo-HSCT patients has low attributable mortality but continued respiratory dysfunction.	3	11	NA

6	Bate et al. 2009.	UK	Retrospective multicenter study	Oncology	2003-2005	Children < 15 years with ICD-10 codes relating to hematological malignancy or solid tumors and infectious disease as cause of death	NR	Confirmed RSV infection	734 total deaths	NR	NR	82/734 deaths were infection-related, contributing to 25% of hematological malignancy deaths and 5% of solid tumor deaths. No significant yearly differences were identified. 3/10 viral deaths were due to RSV.	Infection is an important contributor to deaths in children with malignancies.	2	11	NA
7	Blanchard et al. 2006.	USA	Case Report	Immuno-suppression following liver transplant	NR	Two patients, 8 months and 20 months of age, admitted with severe RSV infection 2 and 10 months post-transplant, respectively	NR	Confirmed RSV infection	NR	NR	NR	Patient 1 had increased respiratory rate with flaring and retractions, and coarse breath sounds with wheezing. Chest X-ray showed increased peribronchial markings (no focal consolidation). She was intubated for 13 days, and tested RSV+/shed virus for 25 days. Patient 2 post-operatively developed sepsis. After completion of antibiotics she developed tachypnea and bilateral expiratory wheezing. Chest X-ray showed peribronchial thickening (no focal lesions). She continued to test RSV+ for 5 days following her first positive panel.	Transplant recipients often have atypical presentations. Severity can vary. Viral shedding tends to be prolonged in transplant recipients.	4	NA	NA
8	Bloemers et al. 2007.	Netherlands	Prospective/retrospective multicenter study	DS	1976-2005 2003-2005	Children with DS hospitalized for RSV infection	Palivizumab prophylaxis; death <2 years of age unrelated to RSV	Confirmed RSV infection	395	M: 58.5%	NR	141/395 (35.7%) of RSVH children with DS had HS-CHD. A further 27.3% had non-significant CHD. RSVH rate was higher in DS/HS-CHD children than preterm DS (11.9% vs 9.4%).	HS-CHD and prematurity are independent risk factors for RSVH in children with DS (which is itself an independent risk factor).	2	11	NA
9	Byington et al. 2015.	USA	Retrospective multicenter study	None	2000-2011	Children <2 years with RSV in the Healthcare Cost and Utilization Project Kids' Inpatient Database (KID) or Pediatric Health Information System (PHIS)	NR	ICD codes for RSV	Total: 872,658	NR	NR	Most RSV-associated mortality occurred between November-March, with 70-77% of deaths in the KID data sets and 61-71% in the PHIS data sets. The majority of deaths in both datasets occurred in infants aged ≤12 months (85% [KID] and 77% [PHIS]).	RSVH and mortality have decreased in the 21st century. Infants, especially those with chronic comorbidities, represent the majority of RSV deaths.	2	11	NA
10	Calvo et al. 2015. <sup>a</sup>	Spain	Prospective, multicenter study	None	2011-2012	Children <5 years old admitted to hospital with confirmed RSV infection	Incomplete data	Confirmed RSV infection	225 comorbid children 460 non-comorbid matches	Male 58%	Mean 35 months	77% of hospitalized children had an underlying disease, predominantly respiratory (66%), cardiovascular (20%) or neurologic (11%).	Children >2 years with underlying disease are 8.7 times more likely to have RSVH versus other children <2 years.	1	12	NA
11	Campbell et al. 2015.	USA	Prospective single center study	Allo-HSCT	2005-2010	Part of a surveillance study of allo-HSCT patients (children and adults) tested for virus before undergoing transplant	NR	Confirmed RSV infection	458 patients tested	Male without pre-HSCT virus: 62.3% Male with pre-HSCT virus: 62.9%	Median age without pre-HSCT virus: 51 years Median age with pre-HSCT virus: 44 years	Respiratory viruses were seen in 116/458 pre-HSCT patients. Infected patients were significantly younger (46% <18 years versus 23% >18 years old) and more likely to have serious comorbidities. Mortality risk was higher in infected patients.	Symptomatic patients should be tested for viruses and transplant delayed, where practical.	1	12	NA

12	Chemaly et al. 2014.	USA	Retrospective multicenter study	Oncology	1998-2009	Children <18 years with cancer diagnosed with RSV infection	NR	Confirmed RSV infection	59 cases identified	Male: 49%	Median age: 5 years	73% of 59 cases were community-acquired. 76% of patients received chemotherapy <1 month before RSV diagnosis, and 39% received corticosteroids. 81% presented with URTI, of which 37% progressed to LRTI, which was associated with increased use of ICU resources. 3 patients with nosocomial RSV and coinfections died.	Severity of immunodeficiency is an important factor in the risk of severe infection and mortality in this population.	3	10	NA
13	Chu et al. 2014.	USA	Retrospective single center study	Oncology	2007-2008; 2012	Nosocomial outbreaks of RSV in a cancer center	NR	Confirmed RSV infection	2007-8: 51 2012: 24	NR	NR	In the 2007-8 outbreak, 1 patient (2%) died of RSV pneumonia. 67% of sequenced samples were identical. In the 2012 outbreak, no deaths were reported, and 90% of samples were identical.	The results indicate that an outpatient clinic can act as a source of nosocomial infection and control interventions should possibly be implemented.	3	10	NA
14	Chu et al. 2016.	USA	Retrospective single center study	Oncology	2008-2013	Children with hematologic malignancy or hematopoietic/SOT with outpatient RSV infection	NR	Confirmed RSV infection	54	Male hematologic malignancy: 49% Male SOT: 50% Male HSCT: 71%	Median hematologic malignancy: 7.8 years Median solid organ transplant: 4.8 years Median HSCT: 6.0 years	54 outpatients were RSV+, but 37 infections (69%) were potentially acquired via clinic. Those with fever were significantly more likely to be hospitalized. Patients with a hematologic malignancy were significantly less likely to be hospitalized. No RSV deaths were reported.	The study concluded that a significant burden of RSV takes place in immunocompromised children in the outpatient setting.	3	10	NA
15	Deschamp et al. 2015.	USA	Prospective multicenter study	CF	NR	Regularly evaluated infants with confirmed CF	NR	Confirmed RSV infection	13 infants	Male viral infection: 40%	Median age at infection: 17.8 weeks	10/13 infants tested positive for a respiratory virus over a period of 11 months. Rhinovirus was the most commonly identified virus: RSV was identified in only 1 patient.	Respiratory viruses are common in infants with CF, and can be prevalent in asymptomatic patients.	2	10*	NA
16	Doering et al. 2006.	Austria/ Germany	Retrospective analysis	None	1998-1999 2001-2002	Preterm infants (29-35 wGA) admitted to NICU	Prophylaxis; nosocomial infection; positive RSV test >3 days post-admission	Confirmed RSV infection	1158	NR	NR	110/1158 infants were admitted for ARI. 57/1158 were admitted for RSV (31/57 laboratory-confirmed). 48 children of the cohort had RSVH before their first birthday. No significant differences were seen between infants aged 29-32 or 33-35 wGA.	The incidence rate reported here is similar to that reported in other studies in Canada and Austria.	2	9	NA
17	Doucette et al. 2016.	USA	Retrospective multicenter study	High-risk infants	1997-2012	High-risk infants <1 year old identified using the Kids' Inpatient Database	NR	Confirmed RSV infection	461,625 RSVH	NR	NR	RSVH rates were significantly higher in 'high-risk' infants with CLD, CHD, DS (without CHD) or congenital airway anomalies. Over the study period, RSVH decreased in infants with CLD and high-risk CHD, likely due to increased prophylaxis. RSV mortality decreased over time, but use of mechanical ventilation and costs of RSVH increased.	RSVH rates have decreased over recent years in 'high-risk' infants, potentially due to increased prophylaxis.	2	10	NA

18	El Saleeby et al. 2008.	USA	Retrospective multicenter study	Oncology	1997-2005	Patients <21 years old with neoplasia, HSCT, immunodeficiency or hematologic disorders and a positive RSV test	NR	Confirmed RSV infection	58 cases	Male: 62.1%	Median 4.29 years	54/58 cases were diagnosed between October - March. The most common symptoms were cough, rhinitis, and fever. 36% of patients had RSVH for a median of 7 days. 5 patients died from RSV-LRTI, but each was severely immunocompromised. Age <2 years and lymphopenia at RSV diagnosis were predictors of LRTI progression.	The results require confirmation but indicate that young patients with cancer, or patients with cancer with significant lymphopenia, are at highest risk of RSV and RSV-mortality.	3	10	NA
19	El-Bietar et al. 2015.	USA	Prospective single center study	HSCT	2008-2013	Patients (pediatric and adult) undergoing HSCT	NR	Confirmed RSV infection	349 patients evaluated	NR	NR	15/349 transplant patients developed a URTI a median of 151 days post-HSCT. 3/349 patients reported an LRTI a median of 33 days post-HSCT. 15/18 patients were on immune-suppressants at this time. No RSV deaths were recorded.	None reported.	3	9*	NA
20	Ernst et al. 2012.	Germany	Case Report	HSCT	-	14 year old girl with acute lymphoblastic leukemia given HSCT	NR	Confirmed RSV infection	NR	NR	NR	After allogeneic HSCT, the patient suffered 5 viral reactivations/ infections, including acyclovir-resistant HSV-1 esophagitis, HHV-6 encephalitis, rotavirus gastroenteritis, RSV pneumonia, and ADV esophagitis. No blood screens revealed any signs of infection.	Viral re-infections are a common complication of allogeneic HSCT, and repeated screens for early diagnosis are recommended.	4	NA	NA
21	Feldman et al. 2015.	USA	Retrospective single center study	Liver transplant	2004-2013	Children <18 years that underwent a liver transplant	NR	Confirmed RSV infection	2554 transplant patients	NR	NR	511/2554 patients reported a viral respiratory infection, predominantly RSV (7.2%), influenza (6.6%) or rotavirus (5.8%). In the first 12 months following transplant, 4.0% of patients experienced RSVH. The RSV mortality rate was 4.9%.	Vaccine-preventable illnesses occur up to 66 times more often in transplant patients compared to the general pediatric population, predominantly in the first 2 years after transplant.	3	9*	NA
22	Fjaerli et al. 2004.	Norway	Retrospective multicenter study	None	1993-2000	Children <2 years old admitted to hospital with bronchiolitis	NR	Confirmed RSV infection	764	M: 63%	Median 6 months	93% of infants had 1 hospitalization; 7% had ≥2 hospitalizations. Mean annual hospitalization rates were 21.7/1.000 children <1 year and 14.1/1.000 children <2 years. 77 infants were in ≥1 high-risk groups.	Hospitalization incidences and RSV outcomes were in agreement with other studies. Hospital LOS and morbidity was high in preterm children, children with CHD and in children with trisomy 21.	3	11	NA
23	Garcia et al. 2007.	USA	Prospective single center study	CF	1998-1999	Children (7-18 years) with confirmed CF	Living ≥90 miles from the center; blood transfusion received within <3 months	Confirmed RSV infection	44 patients	Male CF patients: 61.4%	NR	56 LRTIs and 18 hospitalizations were recorded during the RSV season. 16/44 children had an RSV infection (9 aged 7-12 years; 7 aged 12-18 years), predominantly between October - January. There was no increase in hospitalization rate due to infection.	The clinical impact of respiratory viruses in populations with lung disorders, such as CF, should be further studied to identify the associated morbidity.	2	10	NA

24	Gooch et al. 2011.	USA	Retrospective multicenter study	DS	2001-2007	Data on children <2 years old with DS without CHD taken from I3 Medical Claims Database matched with control term infants	NR	Confirmed RSV infection	196 Infants with DS	Male: 47.5%	NR	196 DS infants were matched to 784 controls. 3.6% of DS infants had RSVH: 3.6% of DS study infants versus 0.8% control infants.	Infants <2 years with DS without CHD are at increased risk of RSVH.	2	8*	NA
25	Hiatt et al. 1999.	USA	Prospective single center study	Cystic fibrosis	1988-1991	Infants <2 years with CF; age-matched controls	NR	Confirmed RSV infection	30 infants with CF 28 controls	CF Male: Female: 15:13 Control Male: Female: 20:10	NR	Overall rates of respiratory illnesses were similar for all children, but infants with CF were x4 more likely to develop acute LRTI. 68% of controls had RSV during the season versus 23% of CF infants; a significant difference. However, 3 infants with CF had RSVH versus 0 controls.	Infants with CF have a high risk for LRTI and subsequent hospitalization.	2	11	NA
26	Hutspardol et al. 2015.	Canada	Retrospective multicenter study	HSCT	2000-2012	Children <18 years who had received HSCT	NR	Confirmed RSV infection	844 HSCT patients	NR	Median patient age: 7.5 years	96/844 patients were diagnosed with respiratory viral infection; 54 were within the first 100 days after HSCT. Of the 54, 15 were RSV + (8 LRTI; 7 URTI) with a median time of diagnosis of 14 days after HSCT. 35/54 occurred between October-March. 1 RSV-related death was reported (6.7% mortality).	The authors proposed that it may be preferable to avoid patient admissions during the respiratory infection season when practical, particularly in Canada, where seasons vary considerably.	3	11	NA
27	Kim et al. 2014.	USA	Retrospective multicenter study	HSCT	1988-2011	Patients that had undergone HSCT at either of 2 centers	NR	Confirmed RSV infection	181 HSCT patients with RTI	Male: 60%	Median patient age: 40.0 years	138/181 patients had RSV URTI at median 49 days post-transplant; 43 progressed to LRTI. 6/181 were <2 years old; 20 were 2-14 years old. Smoking, lymphocyte count at onset, and total body conditioning irradiation were risk factors linked with progression to LRTI.	Lower respiratory disease is a cause of mortality in HSCT patients and risk factors such as smoking and lymphocyte count may increase risk of RSV progression.	3	11	NA
28	Kristensen et al. 1998.	Denmark	Retrospective, multicenter study	None	1995-1996	Infants <6 months hospitalized for RSV infection	NR	Confirmed RSV infection	459	M: 56.4%	NR	The incidence rate of RSV was 34/1000/seasons, equivalent to 32/1000/season in term infants and 66/1000/season in preterm infants. 15.9% of hospitalized infants were comorbid and were more likely to suffer more severe infection courses.	RSV infection was reported as milder in East Denmark than elsewhere, but RSV continues to be a considerable burden to the Danish healthcare system.	2	10	NA
29	Kristensen et al. 2012.	Denmark	Retrospective, multicenter study	None	1997-2003	Birth cohort of Danish children <2 years	None	ICD codes for RSV	452, 205	NR	NR	12,498/452,205 (2.8%) had RSVH. 2720 infants had CHD, of which 292 (10.7%) had RSVH. Duration of hospitalization was increased in children with CHD.	Chronic disease is an important risk factor for RSVH.	2	10	NA

30	Lerret et al. 2013.	USA	Case Report	Liver transplant	-	Patient 1 was hospitalized at 16 months for respiratory distress while awaiting transplant; Patient 2 was 36 wGA preterm who received a liver transplant at 2.5 years of age.	None	Confirmed RSV infection	NR	NR	NR	Patient 1 was hospitalized at 16 months for respiratory distress. Still hospitalized at 19 months, he was recorded as RSV+. He was given palivizumab and oxygen support, but died 18 days after infection diagnosis. Patient 2 had a history of reactive airway disease and CHD. He was admitted 3 months post-transplant for fever and respiratory issues, and later diagnosed RSV+ and post-transplant lymphoproliferative disorder. Immunosuppressive treatment was reduced and RSV treatment, mechanical ventilation and high-frequency oscillatory support given, but he died 68 days after infection diagnosis.	There is significant morbidity associated with liver transplant patients. The authors proposed widening prophylaxis guidelines to include patients with chronic liver disease/liver transplant recipients aged ≤ 24 months and liver transplant recipients <36 months of age with underlying pulmonary conditions.	4	NA	NA
31	Liu et al. 2009.	USA	Retrospective, multicenter study	Lung transplant	1988-2005	Data on pediatric lung transplant recipients identified by chart review and provided by 14 different centers	NR	Confirmed RSV infection	576 transplant patients	NR	NR	79/576 patients (13.8%) developed a viral respiratory infection within 12 months post-transplant (mean 3.4 months); 25% of these had >1 infection (mean 1.3). RSV was responsible for 20.8% of infections. RSV and influenza were the most common causes identified during the winter months. Subjects with a viral infection were significantly younger (9.7 years versus 13.1 years), were more likely to have received living donor or bilateral cadaveric transplants, and be younger at transplant (greatest risk: 0-5.4 years).	Post-lung transplantation has the highest mortality rate of pediatric SOT procedures, and respiratory viral infection is a risk factor for death within the first 12 months after transplantation.	2	10	NA
32	Lo et al. 2013.	USA	Retrospective, multicenter study	Oncology, solid organ transplant or HSCT	1993-2006 (Transplant) 2000-2005 (Oncology)	Pediatric HSCT and SOT recipients	NR	Confirmed RSV infection	2375 patients	Male infection: 51%	Median 4.3 years at infection	166/2375 patients had a respiratory infection (39% HSCT; 38% SOT; 23% malignancies). 96% of infections involved hospitalization. RSV was the most common infection (42% of cases). Almost half of nosocomial infections were RSV. 49% of respiratory infections were in patients of recent antibody therapy.	Respiratory viral infections are a common cause of morbidity and mortality in immunocompromised children, particularly those undergoing HSCT or SOT.	3	10	NA
33	Luján-Zilbermann et al. 2001.	USA	Retrospective, single center study	HSCT	1994-1997	Pediatric HSCT patients with positive respiratory virus cultures	NR	Confirmed RSV infection	281 cases	Male: 69%	NR	32/181 of HSCT cases had a respiratory infection in the first 12 months following transplant. RSV was responsible for 14% of infections, behind hPIV, adenovirus and influenza A. RSV infections trended in early winter.	Respiratory viruses are common infections in pediatric patients in the year following HSCT.	3	10	NA

34	McCarthy et al. 1999.	UK	Retrospective, single center study	HSCT	1993-1998	Recipients of bone marrow allografts	NR	Confirmed RSV infection	336 patients	NR	Median patient age: 10.6 years	26/336 (6.3%) patients were diagnosed as RSV+. 5/26 (19.2%) patients died of RSV infection. Acute myeloid leukemia and unrelated donor transplants were associated with a worsened outcome.	Further research is required to identify risk factors for RSV infection in immunocompromised patients.	3	10	NA
35	Medrano López et al. 2009.	Spain	Prospective, multicenter study	DS and/or CHD	2006-2007	Patients <24 months old with DS and/or CHD	NR	Confirmed RSV infection	1085 patients followed	Total Male DS: 59.6% Total Male non-DS: 56.3%	Median age at study DS: 8.5 Median age at study: non-DS: 15.7 months	147/1085 patients followed were hospitalized with a respiratory infection. The RSV admission rate was 4.4%, and was higher in children with DS (7.8%) versus non-DS (3.2%). However, RSV immunoprophylaxis rates were lower in DS (39.9%) versus non-DS (83.4%).	RSVH is higher in DS patients without HS-CHD and without immunoprophylaxis.	1	11	NA
36	Mendoza Sanchez et al. 2006.	Spain	Retrospective, single center study	Oncology or HIV	1989-2003	Children ≤14 years old diagnosed with cancer or HIV	Patients with other acquired immunodeficiencies	Confirmed RSV infection	129 HIV 218 Oncology	Male respiratory infection: 41%	Male respiratory infection median: 52 months Female respiratory infection: 56 months	26/129 (20%) of patients with HIV and 27/218 (12%) oncology patients had an identified respiratory viral infection. RSV was the most frequently identified virus (43% of cases). Nosocomial infection was suggested in 40% of cases. 63% of HIV patients and 70% of oncology patients with a respiratory infection were hospitalized. 52% of infected oncology patients incurred delayed chemotherapy due to respiratory infection. 2 oncology patients (7%) died as a result of RSV infection.	Preventative measures against respiratory infection are necessary in children with HIV or undergoing anti-cancer treatment due to the high potential for nosocomial infection and the substantial subsequent morbidity.	3	11	NA
37	Miller et al. 1996.	USA	Case Report	Renal transplant	1985-1993	Five renal transplant patients <4 years old diagnosed with post-transplant RSV infection	NR	Confirmed RSV infection	NR	NR	NR	RSV infection was reported 1-7 months post-transplant. The course of infection was similar to that in otherwise healthy children. 3 patients developed acute rejection during or after infection (successfully treated with corticosteroids).	There may be an association between RSV and transplant rejection, but more data are required. If diagnosed early, RSV infection does not appear to result in increased mortality in these patients.	4	NA	NA
38	Moreno-Perez et al. 2014. <sup>a</sup>	Spain	Prospective, multicenter study	None	2011-2012	Children <5 years old admitted to hospital with confirmed RSV infection	Incomplete data	Confirmed RSV infection	225 children with comorbidities 460 matched children without comorbidities	Comorbid Male: Female: 1:1.47 Non-comorbid Male: Female: 1:1.64	Comorbid group median: 12.49 months Non-comorbid group median: 2.96 months	Children with comorbidities (respiratory [64%]; cardiovascular [25%]; neurological [12%] (other [all <10%]) were significantly older on admission than controls. Infants with respiratory comorbidities had more oxygen therapy; cardiac/ metabolic patients had more mechanical ventilation. Higher pneumonia diagnoses were seen in comorbid children (18.2%) versus controls (9.3%).	Severity of RSV infection is higher in children with underlying comorbidities than in otherwise healthy children.	2	12	NA

39	Murray et al. 2014.	UK	Retrospective, multicenter study	None	2007-2008	Birth cohort of infants followed up to 1 year of age	Hospitals with insufficient records	Confirmed RSV infection	296,618	NR	Median 120 days	7189 infants were hospitalized with a primary diagnosis of bronchiolitis, equal to 24.2/1000 infants. 28% were coded as RSV. Admission rates were higher among preterm infants (47.3/1000 infants vs 22.4/1000 for term infants). DS and cerebral palsy were risk factors for admission.	Most (85%) infants who are admitted to hospital with bronchiolitis in England are born at term, with no known predisposing risk factors for severe RSV infection, although risk of admission is higher in known risk groups.	2	11	NA
40	Pisesky et al. 2016.	Canada	Retrospective, single center study	None	2010-2011	Children <3 years old potentially hospitalized for RSV	Children admitted to NICU immediately after birth	Confirmed RSV infection	2287	NR	NR	The proportion DS children with RSVH (0.7%) was significantly higher than the number of children with DS in the total population cohort (0.1%). Of the total RSV cohort, 16.3% had ≥1 major risk factor.	RSV incidence has not changed over time, indicating that prevention of infection has not progressed.	2	9	NA
41	Pockett et al. 2013.	UK	Retrospective, multicenter study	CF; insulin-dependent type I diabetes; cancer; epilepsy	2001-2008	Children <5 years old admitted with a primary diagnosis of RSV or rotavirus gastroenteritis	Multiple diagnoses or readmission	Confirmed RSV infection	101,784 healthy controls 17,420 eczema controls 486 cases	NR	RSV mean: 1.0 years	333/486 (68.5%) of cases had RSVH versus 94,252/101,784 (92.6%) of healthy controls, compared to otherwise healthy controls, cases were hospitalized for longer (8.9 days versus 2.0 days) and had a greater cost of treatment (£533 versus £84).	The majority of rotavirus and RSV infections occur in otherwise healthy children, but exhibit a more serious disease course in children with comorbidities such as CF, diabetes, cancer or epilepsy.	2	11	NA
42	Purcell et al. 2004	USA	Retrospective single center study	None	1991-2002	All patients discharged with a diagnosis of RSV LRTI during 9/11 RSV seasons between July 1, 1991 and June 30, 2002	NR	Confirmed RSV infection	3308 admissions	NR	NR	A significantly higher percentage of patients age <6 weeks, with/out CHD, prematurity, or neurologic disease had longer LOS, were admitted to PICU and used mechanical ventilation versus children with no risk factors, with numbers increasing as number of risk factors increased from 0 to ≥3.	Children with ≥3 risk factors for RSV are at increased risk of more severe RSV disease course.	3	9	NA
43	Robinson et al. 2015.	Canada	Prospective, multicenter study	HSCT or SOT	2010-2013	Children <18 years old who had received HSCT or SOT in the last 2 years and a confirmed RSV infection within the study period	NR	Confirmed RSV infection	24 cases	Male: 77%	Median HSCT: 6.4 years Median SOT: 5.9 years	5/24 (21%) had RSV diagnosed in the first month post-transplant. One death was reported in a lung-transplant recipient. The estimated incidence of RSVH in the first 2 years following transplant was 5/488 (1.0%) for HSCT recipients and 13/274 (4.7%) for SOT.	Prevention of nosocomial transmission should be prioritized in these patients, and additional research is required to determine risk factors for poor outcomes following RSV infection.	4	11	NA
44	Sánchez-Luna et al. 2016.	Spain	Prospective, multicenter study	DS	2012-2014	Infants <1 year old with or without DS	HS-CHD; BPD; <35 wGA; nosocomial RSV infection; parental language barrier; lack of consent; major neonatal surgery	Confirmed RSV infection	93 infants with DS 68 non-DS controls	Male (total): 63.3%	Mean age (total):7.8 months	RSVH was significantly higher in DS patients (44.1%) compared to non-DS patients (7.7%). 23.2% of DS cases had received prophylaxis with palivizumab, versus 0% in the non-DS group.	Patients with DS should be considered within recommendations for RSV immunoprophylaxis.	2	11	NA



45	Simon et al. 2008 <sup>a</sup>	Germany	Prospective, multicenter study	None	1999-2005	All patients with RSV infection	None	Confirmed RSV infection	1568	Male community acquired (total): 58.3% Male nosocomial (total): 56.7%	Community RSV: 160 days Nosocomial: 113 days	Of the 1568 documented RSV infections, 6% were nosocomial and 94% were community acquired. 55% of nosocomial infections occurred in preterms. The nosocomial group showed a significantly higher proportion of risk factors such as prematurity, CLD, mechanical ventilation, CHD and neuromuscular impairment.	Nosocomial RSV infections display higher additional risk factors and are associated with a more complicated course of disease.	2	11	NA
46	Simon et al. 2008 <sup>b</sup>	Germany	Retrospective analysis	Oncology	NR	RSV-infected pediatric patients with cancer	NR	Confirmed RSV infection	39	Male: 43.6%	Median: 33 months	44% of patients received supplemental oxygen, 5 were admitted to ICU and 1 received mechanical ventilation. RSVH resulted in a median of 7 inpatient days..	RSV infection in children with cancer undergoing treatment with non-myeloablative conventional chemotherapy may result in significant complications and additional days of inpatient treatment.	3	NA	NA
47	Small et al. 2002	USA	Retrospective single center study	Allo/Auto-HSCT	1994-1999	Allo-HSCT patients	NR	Confirmed RSV infection	548 (154 children <19 years])	RSV: 64.6% Non-RSV: 60.8%	RSV: 20.3 years Non-RSV: 32.0 years	Children were more likely to develop RSV than adults (17.5% vs 5.3%) (RR 3.29, 95% CI, 1.92–5.64). The incidence of RSV following allo-or auto-HSCT was 5.7% and 1.5%, respectively. 72% of patients received aerosolized ribavirin and/or RSV-IGIV, including 23/25 patients diagnosed with RSV pneumonia. 3 patients died of RSV following an unrelated HSCT.	It is common for immunosuppressed individuals to progress from URTI to pneumonia: if left untreated this can become fatal.	3	10	NA
48	Somayaji et al. 2017	Canada/USA	Retrospective multi-center study	CF	2003-2009	All persons in the CF Foundation Patient Registry during the study period.	NR	NR	12,702 children (<18 years)	Male CF (<18 years): 51.1%	NR	The primary outcome was CF pulmonary exacerbation requiring IV antibiotics/ hospitalization. An annual increase in pulmonary exacerbations occurred during the winter months, and was temporally associated with increased influenza/ RSV activity. RSV activity was associated with increased exacerbation risk in children (RR 1.05, 95% CI 1.02-1.07, p < 0.001).	Prophylaxis and/or vaccination strategies against viral pathogens should be explored in this vulnerable population.	2	10	NA
49	Stagliano et al. 2015	USA	Retrospective multi-center study	DS	2005-2011	Children <3 years	Patients who received prophylaxis	Confirmed RSV infection	633 200	Total Male DS: 49.5% Total Male non-DS: 51%	DS: 9.8 months Non-DS: 3.5 months	DS had a greater adjusted hazard ratio for RSVH than most risk factors for patients with DS aged 0-23 months (3.21) or 24-36 months (5.07). The median LOS of children with and without DS was 4 days versus 2 days (P < .001). Patients with DS had a greater risk of requiring respiratory support (relative risk 5.5; 95% CI, 2.5-12.3).	DS is independently associated with an increased risk for RSVH. Children with DS are older at time of RSVH and have more severe RSV illness than non-DS children. This increased risk for hospitalization continues beyond 24 months.	2	9	NA

50	Sung et al. 2008	USA	Retrospective review of three trials	<i>de novo</i> AML	2003-2005; 1996-2002; 1989-1995	Only patients with <i>de novo</i> AML	NR	Confirmed RSV infection	2078	NR	NR	Prevalence of RSV infection ranged from 0-1% in induction and 0.3-2.2% in consolidation. 4 died from RSV (RSV-specific mortality: 0.2%). The risk of RSV-related mortality among RSV infection episodes was high (4/40, 10%).	The risk of RSV infection in pediatric AML patients is low and RSV infection contributes to mortality in 0.2% of all children. However, children with AML who experience RSV infections are at high risk of RSV-related mortality.	3	NA	NA
51	Thorburn. 2009.	UK	Prospective/retrospective cohort study	Mortality	1999-2007	Children hospitalized to PICU with RSV bronchiolitis	NR	Confirmed RSV infection	2009	NR	NR	98.5% of 406 RSV+ patients admitted to PICU required mechanical ventilation; 35 children died. The overall PICU RSV mortality was 8.6% (standardized mortality ratio: 0.76). The RSVH mortality rate was 1.7%. 18 deaths were directly RSV-related (PICU 4.4%; hospital 0.9%). 17 died from non-pneumonitis causes after becoming RSV-. All RSV deaths had pre-existing medical conditions. Risk factors for death were pre-existing disease (RR 2.36), cardiac anomaly (RR 2.98) and nosocomial RSV infection (RR 2.89).	Pre-existing disease/co-morbidity is associated with a significantly higher risk of death from severe RSV infection. Nosocomial RSV infection is an additional major risk factor for death in children with severe RSV infection.	2	8	NA
52	Tran et al. 2013	USA	Retrospective single center study	Abdominal organ transplant	2008-2011	Patients between 6 months - 18 years and tracheally extubated >24 hours after transplant surgery	Patients with no evidence of increased work of breathing or hypoxemia requiring oxygen therapy	Confirmed RSV infection	25	NR	24 months	RSV was identified in 5 subjects with an associated mortality of 40% despite reduced immunosuppression and administration of palivizumab. 9 patients required oxygen supplementation at discharge.	Significant mortality was observed in this cohort with previous LTRI, younger age and greater immunosuppression are risk factors for serious RSV disease.	3	10	NA
53	Vettenranta et al. 1996	Finland	Case studies	Oncology	1993-1994	Patients in a pediatric oncology ward with a severe RSV infection	NR	Confirmed RSV infection	6	Male: 40%	24 months	All patients were receiving intense chemotherapy at the time of RSV infection. The clinical course of RSV infection involved upper respiratory tract symptoms followed by pneumonia with 1 case being fatal and the others recovering within 3-4 weeks of diagnosis. 4/6 received inhaled and 3/6 received IV ribavirin.	RSV remains a potential cause for morbidity and even mortality among children immunocompromised through chemotherapy. This highlights a need for rapid diagnostics and prevention of the spread of disease in a pediatric hematology/oncology unit.	4	NA	NA
54	von Renesse et al. 2009	Germany	Prospective, multicenter study	None	1999-2005	RSV patients	None	Confirmed RSV infection	1541	NR	Ventilated mechanically median: 4.2 months Control group median: 4.8 months	In 1541 patients there were 1568 RSV infections. 60% of the group ventilated mechanically had at least 1 additional risk factor for severe course of infection (prematurity 50%, CLD 20%, CHD 35% and immunodeficiency 20%).	Children treated by long term mechanical ventilation may acquire RSV infection by transmission by droplets or caregivers and face an increased risk of severe course of RSV infections.	2	10	NA

55	Wang et al. 1995.	Canada	Prospective, multicenter study	None	1993	Children <2 years with RSVH; any RSVH children with underlying cardiac disease, pulmonary disease, or immunosuppression	Patients >2 years with only asthma	Confirmed RSV infection	689	NR	9.1 months (median 4.9 months)	The mean RSVH LOS was 7 days; 110 patients were admitted to ICU, 63 used mechanical ventilation, and 6 died. In addition to known risk factors for increased morbidity, aboriginal race (via maternal race), a history of apnea or respiratory arrest during acute illness before hospitalization, and pulmonary consolidation were identified as relevant risk factors.	Patients with underlying diseases and, possibly, those of aboriginal race should be targeted for RSV vaccine trials.	2	11	NA
56	Wilkesmann et al. 2007.	Germany	Prospective, multicenter study	NMI	1999-2005	All pediatric inpatients with RSV	NR	Confirmed RSV infection	NMI: 73 Control: 1495	NMI: 58.9% Control: 58.1%	NMI: 430 days Control: 145 days	1568 RSV infections in 1541 patients were seen. 73 (4.7%) had a clinically relevant NMI (e.g. cerebral palsy); 41 (56%) NMI patients had ≥1 additional risk factor (prematurity, CHD, CLD, immuno-deficiency). Median age at diagnosis was higher in NMI patients (14 versus 5 months); they had a greater risk of seizures (15.1% versus 1.6%), and a higher proportion had to be mechanically ventilated (9.6% versus 1.9%). Mortality was significantly higher in the NMI group (5.5% versus 0.2%).	Children with clinically relevant NMI face an increased risk for severe RSV and therefore should be a cofactor in the decision algorithm of passive immunization.	2	11	NA
57	Zachariah et al. 2011.	USA	Retrospective, multicenter study	Spina bifida without anencephaly, cleft palate, lung agenesis or dysgenesis, biliary atresia	1997-2004	Data on RSVH for patients <21 years old	NR	Confirmed RSV infection	3417 births with congenital malformations	NR	NR	77 RSVH took place in 3417 identified patients (65 with no RSV risk factors). When compared against a cohort without malformations, children with spina bifida without anencephaly, cleft palate, lung agenesis, hypoplasia or dysplasia, or biliary atresia were statistically more likely to have RSVH within the first 2 years of life.	Children with particular congenital malformations have a higher risk for RSVH and a more severe disease course in the first 2 years of life.	2	9	NA
58	Zachariah et al. 2012.	USA	Retrospective, multicentre study	DS	1995-2006	Children and adolescents <21 years old	RSV infection after the first week of hospitalisation	Confirmed RSV infection	16, 355	DS <1 yr: 68.2% No-DS <1 yr: 56.0% DS (1-2 yrs): 63.5% No DS (1-2 yrs): 54.8%	DS <1 yr: 2 months No-DS <1 yr: 4 months DS (1-2 yrs): 17 months No DS (1-2 yrs): 16 months	Children with DS had a significantly higher risk than did those without DS for RSVH (OR, 5.99; 95% CI, 6.68-5.38), even in the absence of other underlying conditions (OR 3.5; 95% CI, 3.10-4.12). Children with DS with RSVH presented significantly more frequently with fever, chest radiography consolidation, and need for bronchodilator therapy.	Children with DS have a higher risk of RSVH even in the absence of coexisting risk factors. They present more often with fever and more often have radiographic consolidation.	2	10	NA

\* Conference abstract; <sup>9</sup> Moreno-Perez et al and Calvo et al report the same study under separate publications; <sup>b</sup> Simon et al (b) is a subset analysis of Simon et al (a).

ADV: adenovirus; AML: acute myeloid leukemia; ARI: acute respiratory infection; BPD: bronchopulmonary dysplasia; CF: cystic fibrosis; CHD: congenital heart disease; CI: confidence interval; CLD: chronic lung disease; DS: Down syndrome; HHV-6: human herpes virus 6; HIV: human immunodeficiency virus; hPIV: human parainfluenza virus; HS-CHD: hemodynamically significant CHD; HSCT: hematopoietic stem cell transplantation; HSV-1: herpes simplex virus type 1; ICD: international statistical classification of diseases and related health problems; ICU: intensive care unit; IV: intravenous; IVIG: intravenous immunoglobulin; LOS: length of stay; LRTI: lower respiratory tract infection; NA: not available; NMI: neuromuscular impairment; NR: not reported; PICU: pediatric intensive care unit; RR: relative risk; RSV: respiratory syncytial virus; RSVH: RSV hospitalization; RTI: respiratory tract infection; SOT: solid organ transplant; SSV-1: spindle-shaped virus 1; URTI: upper respiratory tract infection; wGA: weeks' gestational age