Supplementary Information: Data Extraction Table

	Study Details	Methodology				Population								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	Altman et al. 2000.	USA	Prospective single centre study	None	1994-1996	Patients with cardiac disease with RSVH	Patients with non-significant cardiac diagnoses	Virologically confirmed RSV infection	1091 RSVH	NR	16 months. 61% > 12 months	63/1091 (6%) of children with RSVH had hsCHD. 5/63 (7.9%) infants had >1 RSVH in the same RSV season. 1 death was reported.	RSV remains an issue for children with hsCHD into the second year of life, impacting perioperative surgery management in CHD children.	1	10	NA
2	Baysal et al. 2013.	Turkey	Prospective single centre study	None	NR	Children <2 years old diagnosed with LRTI	NR	NR	419	NR	NR	241/419 (57.5%) hospitalized patients had hsCHD. CHD carried a hospitalization rate of 14%. Average LOS was 9.9 days and 30% of RSV-CHD patients were admitted to PICU. 1 death was recorded.	RSV is a substantial cause of morbidity in children with CHD in developing countries.	1	3*	NA
3	Bonillo Perales et al. 2000.	Spain	Prospective single centre study	None	1997-2000	All neonatal infants	None	Bronchiolitis admission	12,895	NR	3.1 months	455/12,895 neonates (3.52%) were hospitalized for bronchiolitis. The incidence rate in infants with CHD was 9.8% vs 3.18% in term infants.	Neonatal mechanical ventilation, BPD and CHD are more closely linked to RSV bronchiolitis admission than wGA.	1	10	NA
4	Boyce et al. 2000.	USA	Retrospective multicentre study	None	1989-1993	Children <3 years old enrolled at birth in Tennessee Medicaid	NR	Confirmed RSV or bronchiolitis infection	248,652 child-years	M: 51%	<3 years	A rate of 81.6 RSVH per 100 child years in infants <12 months old was reported. Infants with BPD, CHD, other conditions or preterm birth had a higher risk of RSV.	Children <24 months with BPD have high rates of RSVH. After the first year, children with CHD or prematurity have similar rates to low risk infants <12 months old.	3	11	NA
5	Butt et al. 2014.	Canada	Retrospective single centre study	Prophylaxis	2003-2009	Children with CHD and RSVH	RSV not primary admission diagnosis	Confirmed RSV infection	30	M: 53.3%	15.1 months	12/30 (40%) of cardiac patients with RSVH had hsCHD, and 27/30 (90%) had acyanotic disease. 4 had received prophylaxis. 53.3% were admitted to PICU for a median of 11 days. 1 death was reported.	185 infants ≤2 years with hsCHD received prophylaxis. Breakthrough RSV infections occurred in 2.2%, demonstrating good efficacy of palivizumab in this population.	3	11	NA
6	Byington et al. 2015	USA	Retrospective multicentre study	None	2000-2011 (sporadically)	Children <2 years with an ICD-9-CM code	NR	ICD codes for RSV	Total: 872,658	NR	NR	70-77% of RSV-associated mortality in the KID datasets and 61-71% in the PHIS datasets occurred between November-March. The majority of deaths occurred in infants aged ≤12 months (85% in the KID dataset and 77% in the PHIS dataset).	RSVH and mortality have decreased in the 21st century. Infants, especially those with complex chronic conditions, represent the majority of RSV-associated deaths in the United States.	2	11	NA

7	Chang et al. 2010.	USA	Retrospective multicentre study	Prophylaxis	2000-2002 2004-2006	Discharge data on RSVH in children <2 years before and after palivizumab prophylaxis introduced.	Patients with missing data	ICD codes for RSV	Total 53,207 RSVH	NR	NR	3.0% of RSVH were in children with CHD, and 0.5% in those with hsCHD. 5 deaths were reported in CHD RSV children. Approximately 7 fewer RSVHs/year were reported in CHD infants after prophylaxis introduced.	Prophylaxis had a limited effect on the number of RSVHs in infants with hsCHD, suggesting that further investigation is warranted.	2	11	NA
8	Cilla et al. 2006.	Spain	Retrospective single centre study	None	1996-2000	Children <2 years old admitted for acute, community-acquired RSV infection	NR	Confirmed RSV infection	357	M: 53.5%	NR	Associations were found between RSV and maternal age, CHD, suburban residence, and birth between July-December. 8/357 (2.2%) had congenital cardiac malformations.	Infants with has CHD have increased risk of RSVH	3	10	NA
9	Duppenthaler et al. 2004.	Switzerland	Prospective multicentre study	None	1997-2003	Children with CHD <2 years old admitted for RSV infection	NR	Confirmed RSV infection	Total 729	NR	NR	10/729 (1.4%) of patients had CHD. Hospitalization rates in CHD patients <12 months were 2.0/100 child years, and 0.5/100 child years in children 12-24 months old (corresponding to 1.2 and 0.2 in children without CHD). 1 death was reported.	RSVH rates in children <24 months with CHD were lower than previous reports from the USA: the risk was only two times greater in children with CHD compared to non-CHD.	1	10	NA
10	Eriksson et al. 2002.	Sweden	Prospective single centre study	None	1987-1998	All children hospitalized for RSV infection	NR	Virologically confirmed RSV infection	1354	M: 54%	Median 2.7 months	Hospitalization rates across the RSV seasons varied from 28-64% for infants with CHD compared to 0.8-1.4% in infants without risk factors. Complications resulting in PICU admission were more common in infants with risk factors.	The study found lower population rates of RSVH and complications than previouslyreported.	3	10	NA
11	Fjaerli et al. 2004.	Norway	Retrospective multicentre 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 21.7/1000 children <1 year and 14.1/1000 children <2 years. 77 children belonged to ≥1 high-risk groups, e.g. preterm birth, DS and CHD.	RSVH rates and outcomes were in agreement with other studies. Hospital LOS and morbidity was high in preterm children, children with CHD and children with DS.	3	11	NA
12	Friedman et al. 2016.	USA	Retrospective multicentre study	None	1997-2012	Children 12-23 months admitted for RSV	NR	ICD codes for RSV	1,085,181 CHD ICD-9 codes and 4468 RSVH	NR	NR	Children with CHD had a mean RSVH LOS of 4.4 days versus 2.3 days without CHD. Mechanical ventilation and inpatient mortality were higher for children with CHD (11.4% and 1.6%, respectively) than children without CHD, (2.3% and 0.1%, respectively).	In the second year of life, several specific CHD diagnoses were associated with substantial risk for RSVH, mechanicalventilation, and mortality.	2	10	NA
13	Granbom et al. 2014.	Sweden	Prospective multicentre study	Prophylaxis	2010-2012	Children with CHD <2 years hospitalized for RSV	NR	ICD codes for RSV	219	NR	NR	The calculated RR of children with CHD experiencing RSVH was 2.06 (95% CI 1.6–2.6; p < 0.0001) compared with children without CHD.	Having CHD increased the rate and estimated RR of RSVH in these children.	2	10	NA

14	Grimaldi et al 2002.	France	Retrospective multicentre study	None	1999-2000	Infants with RSVH	NR	Confirmed RSV infection	484	M: 59.6%	5 months	13/484 (2.7%) of infants with RSVH had CHD. Multivariate analysis showed 3 significant independentfactors associated with risk of ICU admission for RSV: preterm birth <32 weeks (OR = 0.86 [0.75-0.98]), neonatal respiratory distress (OR = 4.23 [1.31 to 13.03]) and CHD (OR = 5.26 [1.02 to 21.01]).	At risk populations for severe RSV bronchiolitis with PICU admission should include all very preterm infants with respiratory distress syndrome.	1	10	NA
15	Hervás et al. 2012.	Spain	Retrospective single centre study	None	1995-2006	Children <2 years hospitalized for acute bronchiolitis	NR	ICD-9 codes for acute bronchiolitis ; RSV bronchiolitis ; RSV pneumonia; RSV not otherwise specified.	2384	M: 58%	3.9 months	77% of admissions were in infants aged <6 months. 62.7% of bronchiolitis admissions were for RSV. The majority of RSVH occurred between November and March. RSV was associated with increased LOS, increased risk of ICU admission, and oxygen use.	Preterm infants of <32 wGA, CHD, and atelectasis/ condensation were main risk factors for ICU admission in both RSV and non-RSV bronchiolitis. RSV bronchiolitis seems to be a more severe disease than that caused by other viruses.	3	11	NA
16	Khongphatthanayothin et al. 1999.	USA	Retrospective multicentre study	Surgical outcomes	1990-1995	All children with discharge diagnoses of CHD and RSV receiving cardiac surgery <6 months after infection	NR	Virologically confirmed RSV infection	25	Male Group 1: 53.8% Male Group 2: 66.7%	Group 1: median 86 days Group 2: median 116 days	Group 1 patients had cardiac surgery while symptomatic for RSV. Two patients died and 17 cases of postoperative complications were reported: pulmonary hypertension, adult respiratory distress syndrome, tracheal stenosis, ventricular dysfunction, secondary infection, pericardial effusion and deep vein thrombosis. Group 2 patients had surgery *after* RSV infection. None died, and only 2 cases of minor complications were reported.	Cardiac surgery performed while symptomatic for RSV is associated with high risk of post-operative complications. Risk increases with earlier surgery.	4	9	NA
17	Kristensen et al. 2012.	Denmark	Retrospective multicentre 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%) were RSVH. 2720 infants had CHD, of which 292 (10.7%) were RSVH. Hospital LOS was increased in children with CHD.	Chronic disease is an important risk factor of RSVH	2	10	NA
18	Kristensen et al. 2009.	Denmark	Retrospective multicentre study	None	1996-2003	Children <14 years with ICD coded cardiac malformations or other heart disease	None	Confirmed RSV infection	3239 children with heart disease	Female: 52.7%	362 days	331/3239 (10.2%) of children with heart disease had a positive RSV test. Multivariate analyses showed that DS, cardiomyopathy and hsCHD were predictors of RSVH	Incidence rate of RSVH in children <24 months with heart disease was 56.5/1000 child-years	2	12	NA
19	Lanari et al. 2004.	Italy	Prospective multicentre study	None	1999-2000	Cohort of children <2 years hospitalized for LRTI	None	NR	1214	NR	NR	42/1214 (3.5%) infants hospitalized for RSV had non-surgically corrected CHD, and were associated with increased hospital LOS and oxygen therapy. Nosocomially acquired RSV infection was higher in CHD than in non-CHD infants (9.8% vs 2.9).	Infants with CHD have a high risk of nosocomially acquired RSV infection.	3	NA	NA

20	Li et al. 2016.	Canada	Prospective multicentre study	Prophylaxis	2005-2015	Infants <24 months with hsCHD who had received prophylaxis were recruited	None	Confirmed RSV infection	1st year of life: 1380; 2nd year of life: 529	1st year of life: 53.3% male; 2nd year of life: 52.6% male	1st year of life: 4.2 months; 2nd year of life: 17.8 months	Infants prophylaxed in their second year had a more complicated neonatal course, with significantly longer LOS (51.2 versus 24.9 days) compared with those in the first year. The respiratory hospitalization and RSVH rates in the first and second years were 11.2%; 10.6% and 2.3%; 1.7% respectively.	Infants in the first and second year of life had a similar RSVH hazard. This suggests that infants in the second year with hsCHD, who remain unstable, are equally at risk for RSVH and merit prophylaxis.	1	11	NA
21	Meberg et al. 2006.	Norway	Prospective single centre study	Costs of hospitalization	1987-2004	Cohort of live born infants	None	Confirmed RSV infection	43,470 total	NR	NR	527/43,470 (1.2%) of infants born at the hospital had CHD. All were < 2 years old. 500 were exposed to RSV. RSVH was significantly higher in CHD vs non-CHD children (4.8% vs 2%), and increased to 9.2% in severe CHD.	For better cost-effectiveness, RSV prophylaxis should only be considered in infants with severe CHD.	1	10	NA
22	Meberg et al. 2000.	Norway	Prospective single centre study	None	1982-1996	Cohort of live born infants	None	None	35,218	NR	NR	360/35218 (1%) of infants had CHD. At follow-up, 154/360 (42.8%) were spontaneously cured, 42/360 (11.7%) had died (over half within 28 days of birth).	There is broad variety in CHD severity.	1	10	NA
23	Medrano et al. 2007.	Spain	Prospective multicentre study	None	2004-2005	Children with hsCHD <24 months of age followed through the RSV season	Nosocomial RTI infections; children with HIV; children involved in other studies.	ICD codes for RSV	760	Male RTI 60.8%	6.4 months	79 patients were hospitalized for respiratory infections, with an incidence rate of 21.4/1000 patient-months. Rates were higher in infants <6 months of age. RSV was the most commonly identified viral pathogen (23.8% of cases)	RTI hospitalization in infants with hsCHD is mainly associated with non-cardiac conditions. RSV was the most commonly identified causative agent.	1	10	NA
24	Medrano et al. 2010	Spain	Prospective multicentre study	None	2004-2008	Children < 24 months of age diagnosed with ARI with hsCHD	hnsCHD; HIV; involvement in other clinical trials; nosocomial ARIs	Confirmed RSV infection and physical examination to provide a respiratory score	Total 2613	M: 56.1%	6.72 months	96 patients required RSVH with a 3.8% specific admission rate. RSV was identified in 102 admissions, representing 27.1% of total. CHD was not classified as a risk factor.	Hospital admission rate and severity of ARI are important issues in hsCHD. RSV was the most common etiologic agent found in children requiring hospital admission for ARI.	1	10	NA
25	Pezzotti et al. 2009	Italy	Retrospective multicentre study	None	2000-2006	Cohort of preterm infants (<36 wGA) born in the study catchment area, limited to bronchiolitis admission within first 18 months of life	Death; incomplete records	ICD-9 codes for bronchiolitis	2,407	Bronchiolitis males: 62%	64% < 6 months	137/2407 (5.7%) preterm infants were hospitalized with bronchiolitis by 18 months of age, with an overall incidence rate of 4.70/100 person-years. Bronchiolitis incidence was higher <6 months of age, and through the months of Oct-Apr. The following risk factors were identified: mothers with low education level (≤ 8 years); male gender; low birth weight, <32 wGA; Apgar score ≤7; BPD.	Incidence of hospitalization for bronchiolitis and associated risk factors in Italy are similar to other countries. Highlights need for public health measures to reduce health disparities.	2	11	NA

26	Resch et al. 2011	Austria	Retrospective single centre study	None	2004-2009	Infants with RSVH	Nosocomial RSV infections	ICD-10 codes and confirmed RSV	388	NR	NR	CHD was a common risk for RSVH in infants, reported in 50/388 (12.9%) patients.	RSVH is linked to greater hospital LOS and oxygen use compared to infants with influenza	2	2*	NA
27	Resch et al. 2016	Austria	Retrospective single centre study	None	2004-2008	Children with CHD	Death, admission for heart surgery, loss to follow up, closure of patient ductus arteriosus during neonatal period	ICD-10 codes	602	M: 53%	Median of 2 months	451/602 (74.9%) of patients had hnsCHD and 151/602 (25.1%) had hsCHD. 58/602 (9.6%) were RSVH with a seasonal peak in January (25.9% of RSVH). hnsCHD were significantly younger than hsCHD. Nearly all RSVH occurred during 1st year of life	RSV burden measured by RSVH was high for both hsCHD and hnsCHD with a more severe course of disease in children with hsCHD. Early surgery reduces RSVH during the 1st RSV season.	1	11	NA
28	Simoes et al. 1998	USA	Prospective multicentre study	None	1992-1995	Children <48 months with CHD or cardio-myopathy	Immuno-deficiency; previous reaction to blood products; poor venous access; renal failure; ventilator dependency, <6 m life expectancy, candidates for heart transplant	Confirmed RSV infection and physical examination to provide a respiratory score	RSV-ISIG: 202 Control Group: 214 Total: 416	Both group-Male: 53%	RSV-ISIG: 9.3 months Control Group: 10.7 months	32/214 (15.0%) in the control group were hospitalized with RSV as compared to 21/202 (10.5%) of the children receiving RSV-IGIV. 26 deaths (13 in each group) occurred during the trial in which there was no statistical significance	No significance of RVS-IGIV in preventing RSVH in children with CHD was seen.	1	13	3
29	Spaeder et al. 2011	USA	Retrospective single centre study	None	2002-2007	<18 years old who had undergone cardiac surgery	Patients who had undergone orthotropic heart or lung transplant.	Confirmed RSV infection	774	Viral season: M - 59% Non-viral season: M-57%	Viral season: 9.5 months Non-viral season: 11 months	13/774 (17.5%) patients had viral respiratory infections, of which 9 occurred in the viral season and 4 during the non-viral season. 5/9 cases in the viral season were due to RSV as well as 1 patient who had RSV and influenza A. Only 1/4 patients had RSV from the non-viral season group	Children with viral respiratory infection have significantly worse outcomes than matched controls. Viral respiratory infection is associated with increased hospital LOS.	3	10	NA
30	Straňák et al. 2016.	Multinational	Prospective multicentre study	None	2013-2014	Preterm infants (33-35 wGA) ≤ 6 months of age at the onset of the RSV season	BPD; CLD; hsCHD; immunopro phylaxis	Confirmed RSV infection	2390	Male RSV: 57.8% Male non-RSV: 63%	NR	204/2390 infants were hospitalized for LRTI during the study. 64/204 infants were RSV positive. The RSVH rate was 4.1%, rising to 6.1% during the RSV season. Family smoking; hnsCHD; maternal age ≤25 years at delivery; low maternal educational level; children aged 4-5 years in the household ; age ≤3 months on 1 October; and paternal atopy were identified as risks for RSVH.	This study adds to evidence from single-country studies regarding RSV risk factors in preterm infants.	1	11	NA

31	Tatochenko et al. 2010	Russia	Prospective multicentre study	None	2008-2009	Children <2 years hospitalized for LRTI	Prophylaxis or participation in a clinical trial	Confirmed RSV infection	519	M: 61%	8.8 months	197/519 (38%) of children tested RSV positive. The RSV season began in late October. Peak activity occurred in early April, when 62% of children tested RSV positive. High risk RSV positive children had increased hospital LOS and oxygen supplementation versus other RSV positive children (28% vs 10%).	The prevalence of serious RSV infections in the Russian Federation is similar to that in other temperate zones of the northern hemisphere.	1	10	NA
32	Thorburn et al. 2004	UK	Prospective single centre study	Strict basic droplet precautions and RSV testing on admission to PICU	2002	All children admitted to PICU	NR	Confirmed RSV infection	154	NR	RSV negative: 2.6 months	54/154 patients were RSV-positive, of which 39 were positive on PICU admission and 15 became RSV positive within PICU. 16/54 RSV-positive patients had CHD with additional diseases such as CLD.	Children with CHD as well as CLD, airway abnormalities and immunosuppression are at increased risk of nosocomial RSV. Basic droplet precautions help control the spread of RSV infection	1	9	NA
33	Thorburn. 2009.	UK	Prospective/ retrospective study	Mortality	1999-2007	Children admitted to the PICU with RSV	NR	Confirmed RSV infection	2009	NR	NR	98.5% of 406 RSV-positive patients admitted to PICU required mechanical ventilation; 35 children died. Overall PICU RSV mortality was 8.6% vs a hospital RSV mortality rate of 1.7%. 18 deaths were directly RSV-related (PICU 4.4%; hospital 0.9%). 17 died from other causes after becoming RSV negative. Mortality risk factors were pre-existing disease (RR 2.36), cardiac anomaly (RR 2.98) and nosocomial RSV (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.	3	8	NA
34	Tulloh et al. 2011	USA	Prospective multicentre trial	None	2003-2005	Children with hsCHD	NR	NR	183	NR	1-10 months	20/183 (10.9%) had an RSV infection and therefore cardiac surgery (shunts, single ventricle physiology or cardiac morphology) was delayed for 6 weeks	RSV infection <6 weeks before cardiopulmonary bypass causes significant morbidity. RSV groups had longer duration of medication, possibly representing respiratory dysfunction several months post-infection	2	7*	2
35	Vo et al. 2012	Canada	Retrospective multicentre study	None	1996-1997	Children <2 years old with CHD	None	ICD code 9	3223	NR	NR	19/3223 (0.6%) had RSVH and 417/3223 (12.9%) LRTI hospitalization before 2 years old. Before age 10, 58.5% of CHD children with LRTI in infancy were diagnosed with chronic respiratory morbidity higher than that of CHD children without LRTI in infancy (31.5%). IRRs were higher for males (2.0) than females (1.6) for chronic respiratory morbidity.	CHD children hospitalized for LRTI in infancy are at almost twice the risk of childhood chronic respiratory morbidity compared to CHD children not hospitalized for LRTI. LRTI hospitalization impact is not limited to perinatal period of CHD infants but impacts throughout childhood.	3	9*	NA

36	von Renesse et al. 2009	Germany	Prospective multicentre study	None	1999-2005	RSV patients	None	Confirmed RSV infection	1541	NR	Median - ventilated mechanically 4.2 months Control group - 4.8 months	1541 patients had 1568 RSV infections. 60% of the group ventilated mechanically had ≥1 additional risk factor for severe infection (prematurity 50%, CLD 20%, CHD 35%, and immunodeficiency 20%)	Children treated by long term mechanical ventilation may acquire RSV infection via transmission by droplets or caregivers and face increased risk of severe course of RSV infections.	1	10	NA
37	Wang et al. 1997.	Canada	Prospective multicentre study	None	1993	Children <2 years with RSVH; any children with RSVH and underlying cardiac or pulmonary disease, or immunosuppr ession	Patients >2 years with only asthma	Confirmed RSV infection	689	NR	9.1 months (median 4.9 months)	Mean LOS for RSVH was 7 days; 110 patients were admitted to ICU, 63 were supported by mechanical ventilation, and 6 died. Aboriginal race (defined by maternal race), history of apnea or respiratory arrest during acute Illness before hospitalization, and pulmonary consolidation as shown at admission were identified as relevant risk factors.	Patients with underlying diseases and, possibly, those of aboriginal race should be targeted for RSV vaccine trials.	1	11	NA
38	Willson et al. 2003	USA	Retrospective multicentre study	None	1995-1996	Infants <1 year hospitalized with bronchiolitis or RSV pneumonia	Cost outliers; transferred patients	ICD-9 codes	684	Male: 58%	Mean 3.4 months	79% of hospitalized infants had ≥1 complication. This increased to 87% in preterm infants, 93% in those with CHD, and 90% in infants with congenital abnormalities relative to those with no risk factors (76%). Infants of 33-35 wGA had the highest complication rate (93%). Complications involved increased LOS, PICU admission, and costs.	Complications, particularly in preterm infants, are common in RSVH and are linked to longer hospitalization outcomes and costs	3	9	NA

* Conference abstract

ARI: acute respiratory infection; BPD: bronchopulmonary dysplasia; CHD: congenital heart disease; CLD: chronic lung disease; hnsCHD: hemodynamically non-significant CHD; hsCHD: hemodynamically significant CHD; DS: Down syndrome; GA: gestational age; HIV: Human Immunodeficiency Virus; ICD: International Classification of Diseases; ICU: intensive care unit: IRR; incidence rate ratio; LOS: length of stay; LRTI: lower respiratory tract infection; OR: odds ratio; PICU: pediatric intensive care until; RR: relative risk; RSV: respiratory syncytial virus; RSVH: respiratory syncytial virus hospitalizations; RSV-IVIG: intravenous RSV immunoglobulin; RTI: respiratory tract infection; wGA: weeks' gestational age