Supplementary Information: Data Extraction Table

	Study Details	Methodology				Population						Outcomes relating to RSV	Conclusions	Quality Scores		
	Citation	**Country**	**Study Design**	**Intervention**	**Duration**	**Inclusion criteria**	**Exclusion criteria**	**Disease status**	**N**	**Gender**	**Mean age at admission**			**Evidence Level**	**Item Bank**	**JADAD**
1	Arnold et al. 1999.	Canada	Prospective, multi-centre analysis	None	1993-1995	NR	NR	Confirmed RSV infection	159	NR	NR	159 infants of 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
2	Berger et al. 2009.	Switzerland	Prospective, multi-centre study	None	2001-2005	All children <3 years admitted to ICU for RSV-related illness	NR	Confirmed RSV infection	462	NR	89% <12 months	High risk infants (including those with BPD) were hospitalized at a later age, spent more time in hospital for RSV, and required more respiratory support	BPD was associated with a significant increase in relative risk for RSV ICU hospitalization	1	11	NA
3	Berner et al. 2001.	Germany	Retrospective/ prospective, single centre study	None	1988-1999	Specimens taken from children hospitalized with RSV.	None	Confirmed RSV infection	1064	NR	47% <4 months	Overall, RSVH in patients with BPD was 22%. 46/514 premature patients had CLD; of these, 52% had positive diagnosis of RSV. Six RSV patients died, of which 4 had CLD.	Mortality is low, but disease burden is high, particularly in premature infants with CLD	3	11	NA
4	Bonillo Perales et al. 2000.	Spain	Prospective single centre study	None	1997-2000	All neonatal infants	None	Bronchiolitis admission	12,895	NR	Mean 3.1 months	455 of 12,895 neonates (3.52%) were hospitalized for bronchiolitis. Hospitalization rate was 8.6% in preterm infants and 21.1% of preterm infants with neonatal mechanical ventilation. Prematurity also carried increased risk of ICU admission.	Neonatal mechanical ventilation, BPD and CHD are more closely linked to RSV positive bronchiolitis admission than gestational age.	1	10	NA
5	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	An overall rate of 81.6 RSVHs 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 infection	Children <24 months with BPD have high rates of RSVH. After the first year of life, children with CHD or prematurity have similar rates to low risk infants <12 months old.	3	11	NA

6	Broughton et al. 2006.	London	Prospective, single centre study	Lung function	NR	Cohort of infants born <32 wGA born prior to RSV season onset	NR	Confirmed RSV infection	39	M:59%; RSV positive males: 66%	NR	67% (10/15) of preterm infants hospitalized for RSV had BPD	Diminished lung function is likely to be a risk factor for RSV infection in preterm infants	1	11	NA
7	Carbonell-Estrany et al. 2000.	Spain	Prospective multicentre study	None	1998-1999	Preterm infants (≤32 wGA) born and discharged from hospital by March 31, 1999	Prophylaxis	Confirmed RSVH	584	NR	NR	118/584 infants were hospitalized for respiratory infection: 53 children had RSV positive infection. Logistic regression showed gestational age, presence of CLD, and having school-age siblings were all factors for RSVH.	The study enabled definition of the influence of specific risk factors that increase the risk of RSVH in preterm infants.	1	11	NA
8	Deshpande et al. 2003.	UK	Retrospective, multicentre study	None	1996-1999	All children <2 years of age resident within the health authority boundaries with a positive RSV test	Children born in the area that had moved away, and transient residents	Confirmed RSV infection	411	M:F 1.5:1	Median 20.5 weeks	RSV had a rate of 16.3/1000 children. hospitalization rates were higher in preterm infants born <36 weeks and aged <6 months at the start of the RSV season, and children with CLD.	Preterm infants requiring ventilator assistance in the neonatal period, and those discharged on home oxygen therapy are at particular risk of RSVH. Serious adverse outcomes are rare even among high risk infants.	3	11	NA
9	Duppenthaler et al. 2001.	Switzerland	Retrospective, single centre study	Prophylaxis	1998-2000	Children <16 years hospitalised for RSV infection; resident in Canton of Berne	RSV not detected for 72 hours after hospitalization; RSV in absence of respiratory illness	Confirmed RSV infection	242	M: 54.5%	80.6% ≤ 12 months	Overall, 3.7% of patients had CLD; however, all of these were born ≤35 wGA (34.6% of total patients born ≤35 wGA).	RSV course was mild in infants with CLD: median age was 9.3 months; median hospital LOS was 8 days; median duration of oxygen therapy was 4 days. No CLD patients died of RSV	1	11	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	RSV epidemics had a regular biannual pattern. Children with risk factors were older and had longer hospitalization. 76% of patients without risk factors had older siblings. Later hospitalization for wheezing was increased in children with RSVH.	The study found lower population rates of RSVH and complications than previously reported. The seasonal variation and the presence of siblings in the home influenced rates by factors of 2	3	10	NA
11	Flamant et al. 2005.	Paris	Retrospective, single centre study	Ventilation	1996-2003	Ventilated children <1 year hospitalized to PICU for bronchiolitis	Patients requiring chronic ventilation by tracheotomy	Confirmed RSV infection	151	M:F 1.9:1	61.7 days	151 patients received ventilation for severe RSV infection. 9.3% received ECMO, of which BPD was a predictive factor. Diagnosis of BPD did not predict a worse outcome with ECMO	BPD was associated with prolonged mechanical ventilation in RSVH.	3	10	NA

12	Frogel et al. 2008.	USA	Prospective, multicentre study	Prophylaxis	2000-2004	Cohort of children receiving ≥1 dose of palivizumab during the RSV season	None	Confirmed RSV infection	19,548 enrolled	NR	NR	38.6% of infants <32 wGA (3023/7826); 8.3% 32-35 wGA (777/9317); and 22.9% >35 wGA (549/2400) had CLD as a risk factor for RSVH. In prophylaxed infants, the overall RSV rate was 1.3%.	Prophylaxis is results in low RSV rates in high risk infants.	3	8	NA
13	Gil-Prieto et al. 2015.	Spain	Retrospective, multicentre study	None	1997-2011	All hospital discharges for bronchiolitis in children <5 years of age	NR	ICD codes for bronchiolitis	Total 326,175	Total Male: 59.2%	Total mean: 5.8 months	Bronchiolitis was the primary cause of hospitalization in 85% of patients. 76% of admissions occurred between November and March. The highest hospitalization rate is shown in the first year of life with a rate of 4136/100,000 children <12 months, which decreases significantly with age. 1% of hospitalized infants had BPD (3114/315872).	The mean hospitalization for congenital cardiopathy, prematurity, and BPD were significantly higher than non–high-risk groups. Costs were also significantly higher in comorbid groups.	3	10	NA
14	Greenough et al. 2001.	UK	Retrospective, single centre study	None	1994-1999	All children ≤32 wGA with CLD followed to 2 years of age	NR	Confirmed RSV infection	235	NR	NR	45 infants (19%) had at least one hospital admission for a proven RSV infection within 2 years of birth. This group spent significantly longer in hospital than non-RSV admissions. The subsequent median admission rate per infant was significantly higher in the RSV group.	Prematurely born CLD infants with RSVH have increased health service utilisation in the first two years after birth	3	11	NA
15	Greenough et al. 2004.	UK	Retrospective, single centre study	None	1994-2002	All children ≤32 wGA with CLD followed to 5 years of age	NR	Confirmed RSV infection	190	NR	NR	33/190 infants experienced RSV infection. At 2–4 years inclusive, the RSV group required more days in hospital and a greater number of outpatient attendances, both overall and for respiratory problems.	In premature infants with CLD, RSVH in the first 2 years of life is associated with chronic morbidity and increased costs of care.	3	11	NA
16	Grimaldi et al. 2002.	France	Retrospective, multicentre study	None	1999-2000	Infants hospitalized for RSV bronchiolitis	NR	Confirmed RSV infection	484	M: 59.6%	5 months	19.6% of infants with RSVH were born preterm (GA <37 weeks). 68.3% were aged <6 months at admission. Duration of hospitalization was a mean 7.3 days. 31 infants (6.4%) were admitted to PICU, 8 (1.7%) needed mechanical ventilation and 1 (0.2%) died.	At risk populations for severe RSV bronchiolitis with PICU admission should include all very preterm infants with respiratory distress syndrome. These epidemiological data could provide indications for RSV immunoprophylaxis	1	8*	NA

17	Grimaldi et al. 2004.	France	Prospective, multicentre study	Prophylaxis	1999-2002	All children ≤32 wGA with BPD hospitalized for RSV infection	Criteria for hospitalization and transfer to PICU were not pre-defined and were the choice of each physician responsible for care.	Confirmed RSV infection	N per season: 123; 144; 154	NR	NR	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%; P<0.01), predominantly due to prophylaxis is later seasons.	The study supports the efficacy of prevention of RSV bronchiolitis by palivizumab in severely premature infants with BPD.	1	9	NA
18	Groothuis et al. 2011.	USA	Retrospective, multicentre study	None	1998-2008	Children <2 years with CLD	NR	ICD codes for RSV	10,622	Male RSV: 65%	RSVH: 45% >6 months	RSVH in children <2 years with CLD steadily decreased over the 11-year study period, while all-cause hospitalization rates remained similar.	Decreased RSVH rates in this high risk population may be related to improved patient management or increased use of prophylaxis.	2	10	NA
19	Heikkinen et al. 2005.	Finland	Retrospective, single centre study	None	1991-2000	Birth cohort of all children born alive in a tertiary care university hospital	Prophylaxis	Confirmed RSV infection	35,811	NR	NR	691 of analysed infants had CLD or were born at ≤ 32 wGA. RSV infection rate was 7.1% in infants born at ≤ 28 wGA and 6.8% in infants born at 29-32 wGA. Children born at ≤32 wGA or had CLD were responsible for 6.6% of all RSV admissions.	The rates of RSVH in preterm infants were substantially lower than reports from other countries.	3	11	NA
20	Impact. 1998.	Multinational	Prospective, multicentre study	Prophylaxis	1996-1997	Cohort of children ≤35 wGA and ≤6 months of age ; or ≤24 months old or younger with a clinical diagnosis of BPD requiring ongoing medical treatment	Current long term hospitalization; mechanical ventilation at the time of entry; life expectancy less than 6 months; RSV infection; other comorbidities; other prophylaxis	Confirmed RSV infection	1,486	Male placebo: 56.8% Male prophylaxis: 56.9%	NR	Prophylaxis resulted in significant reductions in RSVH in both premature infants (78% reduction) and premature infants with BPD (39% reduction).	RSV prophylaxis of preterm infants with CLD significantly decreases RSV infection rates	1	12	3
21	Joffe et al.1999.	USA	Retrospective, multicentre study	None	1992-1996	Cohort of preterm infants ≤36 weeks neonatally discharged from NICU	Diagnosis of CHD; cystic fibrosis; immunodeficiency	ICD-9 codes for respiratory issues with secondary confirmation of RSV	1,721	Male 55.7%	NR	3.2% of infants (55/1721) had RSVH. RSVH infants were more likely to be ≤ 32 wGA at birth; to have required ≥28 days supplemental oxygen in the NICU; to have had a lower birth weight; to have needed more mechanical ventilation in the NICU; and to have been initially discharged from the NICU between September - November.	Most preterm infants in this cohort were at lower risk of RSVH than previous studies in other populations have suggested.	3	11	NA
22	Liese et al. 2003.	Germany	Prospective, multicentre study	Prematurity	1998-2000	Infants with a GA of <35 weeks previously admitted to neonatal intensive care	NR	Confirmed or probable RSV infection	717	M: 52.3%	NR	The risk of subsequent RSV infection in preterm infants released from NICU was 5.2%. This increased to 15% in preterm infants with CLD. Independent risk factors for RSV were male gender, CLD, discharge between October-December, sibling day	Risk of rehospitalization for RSV in preterm infants in Germany is low.	3	11	NA

												care attendance.				
23	Medici et al. 2006.	Italy	Prospective, multicentre study	Seasonality	2000-2004	Children ≤4 years referred to the ED for suspected LRTI	NR	Confirmed RSV infection	Total 2110	Total Male 55%	Total mean: 17 months	433/2110 (20.5%) of bronchiolitis admissions tested positive for RSV. 8% of 2110 infants hospitalized for bronchiolitis had CLD	A significant impact of CLD was recorded, but distribution of 'high risk' factors did not differ across study years.	1	10	NA
24	Murray et al. 2014.	UK	Prospective, multicentre study	None	2007-2008	Birth cohort of all children born across 71 English hospitals	NR	ICD codes for RSV	7189 bronchiolitis admissions	NR	NR	28.0% (2015/7189) of bronchiolitis admissions were coded as RSV. 282 bronchiolitis admissions (5.6%) were in infants with CLD, equal to a rate of 56.2 per 100 infants <1 year	Clinical subgroups are at increased risk of hospital admission, but most bronchiolitis cases in England are in otherwise healthy, term infants	3	11	NA
25	Pedersen et al. 2003.	Denmark	Retrospective, multicentre study	None	1994-1995	Infants born <28 wGA or <1000 g birth weight who were discharged alive and hospitalized during the first 2 years of life.	NR	Confirmed RSV infection	240	RSV positive males: 53.5%	10.5 months	18% (43) of infants analysed were RSV-positive. 16% of infants without CLD and 30% of infants with CLD were RSV positive. 38% of RSV positive infants required ventilator support. Mean RSVH LOS was 10.8 days	The rehospitalization rate in very preterm infants, particularly in infants with CLD, should be used to inform prophylaxis practices.	3	10	NA
26	Pérez Pérez et al. 2004.	Spain	Prospective, single centre study	Prematurity	1996-2001	Cohort of preterm infants (32 wGA) follows for the first 2 years of life	NR	Confirmed RSV infection	Preterm BPD: 29 Preterm no BPD: 29 Matched controls: 32	NR	NR	At least one episode of wheezing occurred in 25 (86.2 %) preterm BPD infants vs. 12 preterm non-BPD children (41.4 %) and 6 (18.8 %) controls.	During the first 2 years of life, children with BPD showed a greater number of admissions and episodes of wheezing and a greater need for medical treatment.	2	10	NA
27	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 hospitalization within the first 18 months of life	Death; incomplete records	ICD-9 codes for bronchiolitis	2,407	Bronchio. males: 62%	64% < 6 months	137/2407 preterm infants were hospitalized with bronchiolitis during the study period, equal to an incidence rate of 4.70/100 person-years. Bronchiolitis incidence was higher <6 months of age, and then decreased with age. The following risk factors were identified: male gender; low birth weight ($p < 0.01$), <32 wGA; Apgar score ≤ 7; BPD.	The incidence rate and risk factors reported here are similar to that reported in other countries.	2	11	NA

28	Ricart et al. 2012.	Spain	Prospective, single centre study	None	2007-2008	Infants <12 months admitted to the pediatrics ward or PICU	Underlying chronic pulmonary disease other than BPD; recurrent wheezing; apnea secondary to a known disease; respiratory symptoms due to bronchoaspiration.	Confirmed RSV infection	Total 410	Total Male: 57.8%	Median 1.9 months	Of 410 infants hospitalized for bronchiolitis, 10 had BPD. 287/410 infants had virally confirmed RSV. Multivariate logistic regression indicated that BPD was the strongest predictor of severe bronchiolitis	Clinical risk factors have specific weight in predicting bronchiolitis outcome	1	11	NA
29	Rietveld et al. 2004.	Netherlands	Prospective, multicentre study	Costs of RSV	1996-1997 1999-2000	Infants <1 year (<2 years with BPD) hospitalized for severe RSV disease	NR	Confirmed RSV infection	3,458	Male 58.7%	50.2% < 3 months	Of 3548 infants with RSVH, those with prematurity or BPD were significantly more likely to require ICU admission and to receive increased LOS. In all patients, mean hospitalization LOS and the accompanying RSVH costs increased with lower GA (€5555; GA ≤28 weeks), lower birth weight (€3895; birth weight ≤2500 g), BPD (€5785; with BPD) and young age (€4730; first month of life).	RSVH costs are substantial, particularly in high risk groups.	3	10	NA
30	Rossi et al. 2005.	Italy	Prospective, multicentre study	None	2000-2002	Children ≤4 years referred to the ED for suspected LRTI	NR	Virologically confirmed RSV infection	Season 1: 272 Season 2: 756	Male Season 1: 51.8% Male Season 2: 54.8%	Season 1: 15.7 months Season 2: 18.7 months	Of the infants hospitalized for possible RSV infection, 16.5% in season 1 and 7.9% in season 2 had CLD.	Patient characteristics were shown to vary between seasons, but indicated that RSV remains a serious issue in children.	1	10	NA
31	Simon et al. 2008.	Germany	Prospective, multicentre study	None	1999-2005	Children hospitalized with RSV infection	NR	Virologically confirmed RSV infection	1,568	M: 56.7-58.3%	Median 113-160 days	Of the confirmed RSV cases, 6% were nosocomial and 94% were community acquired. A significantly higher proportion in the nosocomial group had additional risk factors e.g. prematurity, CLD, history of mechanical ventilation, CHD, and neuromuscular impairment. 55% of nosocomial infections occurred in preterms. Illness severity and total mortality was significantly higher in the nosocomial group.	This study confirms the increased risk of a severe clinical course in nosocomially acquired RSV infection.	1	11	NA
32	Simon et al. 2007.	Germany	Prospective, multicentre study	None	1999-2005	Preterm infants (<37 wGA) hospitalized with RSV infection	NR	Virologically confirmed RSV infection	406	M: 56.4%	Median 142 days	12.3% (50/406) of preterm infants with RSV had CLD, of which 49 had received treatment within the previous 6 months.	CLD requiring treatment in preterm infants is an independent risk factor for a more complicated disease course.	1	10	NA

33	Tatochenko et al. 2010.	Russia	Prospective, multicentre study	None	2008-2009	Children ≤2 years hospitalized for LRTI	Prophylaxis; enrollment in RSV clinical trial within last 100 days	Confirmed RSV infection	519	Male RSV:61%	RSV positive: 7.5 months	38.0% (197/519) children enrolled were RSV positive. The RSV season began in late October and peaked in early April. More high-risk RSV-positive children (i.e. children with CHD, CLD/BPD) required oxygen supplementation than non-high risk children (28% v 10%). No mechanical ventilation, CPAP, or surgeries were required. There were no deaths.	The pattern in the Russian Federation is similar to that identified in other temperate zones in the northern hemisphere.	1	10	NA
34	Thomas et al. 2000.	UK	Retrospective, single centre study	Preterm infants	1995	Neonates <32 wGA admitted for medical neonatal intensive care within the first week of life	Incomplete data	Confirmed RSV infection	82	NR	NR	34/82 preterm infants studied had a diagnosis of CLD. 3/34 were admitted with confirmed RSV. LOS and PICU admission were substantially higher in CLD infants on home oxygen vs non CLD preterms (20 days PICU vs 0 days, respectively).	RSV prophylaxis of infants with CLD on home oxygen would be relatively cost effective compared with other infants	2	10	NA
35	Thorburn. 2009.	UK	Prospective/retrospective cohort study	Mortality	1999-2007	Children hospitalised to the PICU with RSV bronchiolitis	NR	Confirmed RSV infection	2009	NR	NR	98.5% of 406 RSV-positive patients admitted to PICU required mechanical ventilation; 35 children died. The overall PICU RSV mortality was 8.6% with a standardised mortality ratio of 0.76. The hospital RSV 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 negative. 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.	3	8	NA
36	Van de Steen et al. 2016.	Europe	Retrospective, multicentre study	None	2009-2011	Cohort of infants <1 year hospitalized for LRTI	Duplicate records	Confirmed RSV infection	3474	Total Male: 58.3%	Total: 69.1% <6 months	Rapid RSV test was performed in 3354 (96.5%) cases and were positive in 1423 infants (42.4%). Of the RSV-positive, 18.7% were preterm and 72.7% were otherwise healthy term children. Preterm infants had significantly longer hospitalizations than term children, and required more frequent ICU and oxygen support.	RSV is the cause of a substantial burden in European children; preterm birth is a notable risk factor for RSVH	2	11	NA

37	Wang et al. 1995.	Canada	Prospective, multicentre study	None	1993	Children <2 years hospitalised for RSV LRTI; any children hospitalised for RSV LRTI 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 were supported by mechanical ventilation, and 6 died. In addition to previously described risk factors for increased morbidity, aboriginal race (defined by maternal race), a history of apnea or respiratory arrest during the acute Illness before hospitalisation, and pulmonary consolidation as shown on the chest radiograph obtained 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	Weigl et al. 2001.	Germany	Retrospective, multicentre study	None	1996-1999	Children <16 hospitalised for ARTI	NR	Confirmed RSV infection	1,241	NR	74% <1 year	150/1,241 (12.1%) of patients tested positive for RSV. 25% of infected children also had an underlying condition. The cumulative incidence rate was higher in premature infants (1,214/100,000 in infants <32 wGA). Birth at <32 wGA and BPD increased RR to 17.8.	Throughout Germany, approximately 10.000 RSV-related hospitalisations in infants can be expected annually. Prematurity is an effect modifier and BPD a strong risk factor for RSVH in population-based studies.	3	11	NA
39	Zaw et al. 2003.	UK	Retrospective, single centre study	Costs of RSV	1995-1999	Children <2 years of age hospitalised in the Highlands	Children outside region of interest	ICD codes for acute bronchiolitis	507	NR	NR	18/507 children hospitalized for bronchiolitis were preterm at birth (<35 wGA). Four preterm infants had BPD. Their respiratory score at the time of bronchiolitis admission was similar to patients without BPD but median hospitalization LOS was longer (10.5 vs 2.5 days). All BPD infants required supplemental oxygen vs. 28.6% (4/14) non BPD patients. Median duration of oxygen requirement for BPD infants was 7 vs. 2 days for non BPD infants.	The costs of hospital admission of preterm infants (especially <30 wGA) and infants with BPD were high.	2	11	NA

RSV: respiratory syncytial virus; RSVH: RSVH hospitalization; LRTI: lower respiratory tract infection; ICU: intensive care unit; NICU: Neonatal ICU; PICU: pediatric ICU; LOS: length of stay; CHD: congenital heart disease; CLD: chronic lung disease; BPD: bronchopulmonary dysplasia; GA: gestational age; wGA: weeks gestational age; ED: emergency department; ECMO: extracorporeal membrane oxygenation.