

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	Al-Shawwa et al. 2006.	USA	Prospective/retrospective multicentre study	None	2001-2003	Children <2 years old with a first episode of wheezing and tested for RSV >1 year ago	None	Confirmed RSV infection	155	M 57.8%	6.0 months	Hospitalized patients were more likely to have recurrent wheezing versus non-hospitalized patients (OR 2.84; 95% CI 1.24-6.50). RSV- patients had higher risk of recurrent wheeze than RSV+ patients (OR 6.28; 95% CI 2.84-13.88). No other significant differences between RSV+ and RSV- patients were seen.	Recurrent wheezing within 1 year of first episode of bronchiolitis was higher in RSV- patients and in patients needing hospitalization.	3	11	NA
2	Bacharier et al. 2012.	USA	Prospective single centre study	None	1998-2001	Children hospitalized with bronchiolitis; confirmed RSV infection and physician documented wheezing during acute illness	History of wheezing/asthma; congenital heart or lung abnormalities; CF in patient/family; regular use of anti-gastroesophageal reflux or bronchodilators or anti-inflammatory medication	Confirmed RSV infection	206	Diagnosed asthma by age 7: M 52.6% No asthma by age 7: M 63.5% Active asthma by age 7: M 51.6% No active asthma by age 7: M 63.3%	Diagnosed asthma by age 7: 123 days No asthma by age 7: 147 days Active asthma by age 7: 95 days No active asthma by age 7: 150 days	92% of participants experienced ≥1 additional wheezing episodes before 3 years of age following infantile RSV. 48% of participants were given an asthma diagnosis by age 7, and 35% were classified as having active asthma by age 7. Increased risks included maternal asthma, allergic sensitisation, recurrent wheeze, exposure to dog allergen and increased expression of CCL5 in upper airways.	Severe RSV bronchiolitis in the 1st year of life is followed by a diagnosis of childhood asthma by age 7 in nearly half of children. In addition, the biomarker CCL5 in nasal epithelium during RSV bronchiolitis is strongly predictive of physician-diagnosed asthma.	1	9	NA
3	Backman et al. 2014.	Finland	Prospective single centre study	None	1981-1982 30-year follow-up in 2010	Children <24 months admitted with LRTI	None	Confirmed RSV infection Asthma diagnosed by self/doctor	127	RSV-LRTI group: M 51%	10 months	81/127 (64%) children had confirmed/probable RSV infection based on age, clinical presentation and presence of a community epidemic. 57% of the 81 took part in the 30-year follow-up. 43 formed the RSV study group. Of these, 23-28% (range due to definition variation) had asthma versus 13-17% in the control group. A respiratory health-related QoL questionnaire showed that, on average, RSV patients had lower total scores than controls. Both pre- and post-bronchodilator scores were significantly lower in former RSV patients than controls.	LRTI hospitalization in infants was associated with an increased risk of permanent obstructive lung infection reduction and asthma in adulthood and lower respiratory health related QoL.	1	9	NA

4	Blanken et al. 2013.	Netherlands	Prospective/ retrospective multicentre study	None	2008-2011	Infants 33-35 wGA	Infants with 'gross' abnormalities, DS and those who received palivizumab	Confirmed RSV infection	2442	Derivation cohort: M 55.1% Validation cohort: M 55.2%	NR	RSVH risk in both cohorts was comparable (5.7% vs 4.9%). Four risk factors for RSVH were developed: family atopy (OR 1.9; 95% CI 1.1-3.2), birth period (OR 2.6; 95% CI 1.6-4.2), breastfeeding (OR 1.7; 95% CI 1.0- 2.7) and siblings or day-care attendance (OR 4.7; 95% CI 1.7-13.1). The model showed good discrimination after bootstrapping and external validation.	The risk of RSVH in late preterms is 5.1%. Risk factors can identify infants at increased risk of RSVH who could benefit from preventative measures against RSV infection.	1	11	NA
5	Bloemers et al. 2007.	Netherlands	Prospective/ retrospective multicentre study	DS	1976-2005 2003-2005	Children with DS hospitalized for RSV infection	Palivizumab prophylaxis; death before 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 hsCHD. A further 27.3% had non-significant CHD. RSVH rate was higher in DS/hsCHD children than preterm DS (11.9% vs 9.4%).	hsCHD and prematurity are independent risk factors for RSVH in children with DS (which is itself an independent risk factor).	1	11	NA
6	Bloemers et al. 2010.	Netherlands	Prospective/ retrospective multicentre study	None	1988-2007 2003-2005	Children with DS hospitalized for RSV LTRI	None	Confirmed RSV infection; Physician diagnosed recurrent wheeze	DS+ RSV+: 53 DS+ RSV-: 110 DS- RSV+:48 DS- RSV-: 49	DS+ RSV+: M 60% DS+ RSV-: M 51% DS- RSV+: M 46% DS- RSV-: M 57%	DS+ RSV+: 6 months DS+ RSV-: NR DS- RSV+: 4.5 months DS- RSV-: NR	No significant differences were seen between DS+ RSV+ and DS+ RSV- groups in physician-diagnosed recurrent wheeze (36% vs 30%), parent-reported recurrent wheeze (42% vs 32%) and physician- diagnosed asthma (11% vs 9%)	Children with DS have a high risk of recurrent wheeze independent of a history of severe RSV LRTI.	1	9	NA
7	Bont et al. 2000.	Netherlands	Prospective multicentre study	None	NR	Children <13 months hospitalized with LRTI symptoms and RSV testing	Infants with prior wheezing illness or RSV bronchiolitis	Confirmed RSV infection	Patient: 50 Control: 27	M 58%	Median: 3 months	46/50 infants with RSVH were followed up: 58% had recurrent wheezing episodes. IL-10 levels were significantly higher in patients who developed recurrent wheezing during the year after RSV than in patients without wheezing (p=0.006). IL-10 responses correlated significantly with number of wheezing episodes (r=0.42, n=46, p=0.004).	Monocyte IL-10 production increases during RSV bronchiolitis. Increased IL-10 production is associated with development of recurrent wheezing and physician- diagnosed asthma, indicating that virus-induced changes in monocyte cytokine responses can lead to asthmatic symptoms.	1	11	NA
8	Bont et al. 2004a.	Netherlands	Prospective multicentre study	None	NR	Follow-up of children <13 months hospitalized with LRTI symptoms and RSV testing	None	Confirmed RSV infection; Self-diagnosis of wheezing	140	M 55%	Median: 7 weeks	Follow-up data was available for 106 children. A significant decrease of <50% in wheezing was observed during the first year after RSVH, and the percentage of children with severe wheezing (>5 days/quarter) decreased. In addition, a significant increase in respiratory wheeze occurred during the winter periods in all three study years.	Airway morbidity following RSV LRTI has a seasonal pattern, suggesting that viral upper respiratory tract infections are the predominant trigger for wheezing following RSV LRTI.	1	11	NA

9	Bont et al. 2004b.	Netherlands	Prospective multicentre study	None	NR	Follow-up of children <13 months hospitalized with LRTI symptoms and RSV testing	Patients with CLD,CHD, immunodeficiency, and prior wheezing	Confirmed RSV infection	Patient: 136 Control: 340	M 56%	Median: 3 years	Health-related QoL was lower in RSV children than in control children for the lung, GI tract and sleeping domains. In addition, QoL in the lung domain was significantly lower during the winter than the summer season.	Post-RSV wheezing has broad implications for long-term well-being. Children with a history of RSVH have lower health-related QoL in several areas, specifically the lung.	1	11	NA
10	Bont et al. 2001.	Netherlands	Prospective multicentre study	None	NR	Follow-up of children <13 months hospitalized with LRTI symptoms and RSV testing	Children with wheezing prior to RSV infection	Confirmed RSV infection	130	M 54.6%	NR	Signs of airflow limitation during RSV were present in 83/130 (64%) infants. During initial RSVH recurrent wheezing was recorded in 10 (21%) infants without signs of airflow limitation and in 51 (61%) with signs of airflow limitation.	Indicators of airflow limitation during RSVH is a primary clinical predictor for subsequent recurrent wheezing	1	11	NA
11	Calvo Rey et al. 2001.	Spain	Prospective study	None	1990-1993	Children <2 years hospitalized for bronchiolitis	NR	Confirmed RSV infection	170	M 58.8%	NR	66.5 % of infants hospitalized with bronchiolitis developed short-term persistent wheezing. 35.3 % developed long-term persistent wheezing. Eosinophil values of >1% were significantly associated with short-term persistent wheezing. Family history of asthma was also significantly associated with development of long-term persistent wheezing.	Eosinophil values of >1% during infantile bronchiolitis was associated with a higher risk of developing persistent wheezing within the first 5 years of life.	3	3*	NA
12	Carbonell-Estrany et al. 2015.	Spain	Prospective multicentre study	None	2005-2006	Birth cohort of healthy preterm infants 32-35 wGA	CLD; CPD; hsCHD; congenital airway abnormalities; neuromuscular disease; immunodeficiency; any condition that would preclude long-term survival; prophylaxis	Confirmed RSV infection	Patient: 113 Control: 321	RSV: M 57.6% Controls: M 56.1%	NR	Up to 6 years of age, incidence of wheezing was significantly higher in RSV cases (46.7%) than controls (27.4%) and occurred significantly earlier (4.69 vs 5.29 years, respectively). Significantly more RSV cases needed outpatient or emergency care up to 6 years of age compared to controls.	The study confirmed that RSV is associated with subsequent wheezing in infants born at 32-35 wGA.	1	11	NA
13	Carroll et al. 2009.	USA	Retrospective multicentre study	None	1995-2000	Cohort of healthy infants enrolled in TennCare within first year of life	Preterm infants; low birthweight infants	ICD-9 code for bronchiolitis and RSV	90,341	M 51%	40 weeks	18% of 90,341 infants had an infant bronchiolitis visit. 22% of infants with bronchiolitis hospitalisation were later diagnosed with early childhood asthma, versus 9% of infants with no visit. No significant association was found of maternal asthma on the relationship between bronchiolitis hospitalization and later asthma diagnosis.	Increased severity of infant bronchiolitis is associated with increased risk of early childhood asthma in a severity-dependent manner. Early childhood asthma following infant bronchiolitis accounts for nearly one-third of early childhood asthma.	2	10	NA

14	Cassimos et al. 2008.	Greece	Retrospective single centre study	None	1996-2001	Follow-up of infants hospitalized for acute bronchiolitis	None	Confirmed RSV infection	189	M 66.7%	6.3 months	57.1% of RSVH infants were later diagnosed as asthmatic. Peak flow measurements for RSVH infants were significantly lower than the control group, regardless of asthma status. Investigation of risk factors showed asthma is independently associated with breast feeding <3 months, ≥1 positive skin prick test, male gender, moisture in the home, and presence of >1 smoker in the household.	Children with a history of RSV-bronchiolitis during infancy have an increased risk for developing asthma in childhood, independent of other risk factors.	3	10	NA
15	Castro et al. 2008.	USA	Prospective single centre study	None	1998-2001	Children ≤12 months old hospitalized for RSV infection with later wheezing	NR	Confirmed RSV infection Physician-diagnosed asthma	206	M 58%	4.3 months	48% of infants with RSVH developed asthma by 6 years old, 48% had eczema by 6 years and 32% developed allergic sensitisation by 3 years. Children with asthma had significantly lower IL-13 expression at 6 years than non-asthmatic children.	Severe RSV infection early in life is associated with a high incidence of childhood asthma and eczema.	1	11	NA
16	del Rosal et al. 2013.	Spain	Prospective single centre study	None	2003-2004 2008-2009	Children ≥4 years hospitalized for viral bronchiolitis	NR	Confirmed RSV infection	144	NR	NR	70/144 cases were caused by RSV infection. RSV+ cases had significantly fewer hospital admissions for respiratory conditions (17% vs 30%), persistent asthmatic symptoms (7% vs 25%) and asthmatic exacerbations in the last year (22% vs 40%), compared to RSV- children.	Respiratory symptoms within 5 years are significantly more frequent after severe non-RSV bronchiolitis compared to controls.	1	3*	NA
17	Drysdale et al. 2014.	UK	Prospective single centre study	None	2008-2009	Infants born ≤36 wGA, prior to the RSV season	NR	Confirmed RSV infection	RSV: 29 Control: 119	RSV: M 48% Control: M 56%	NR	29 infants developed RSV LRTI. 10/29 required RSVH. RSV infants were born at significantly lower wGA, lower birth weight and reduced likelihood of being breastfed. Significantly increased risk of RSV was associated with the C allele of the ADAM33 gene. IL-10 genotype differences were also associated with differences in parent-reported wheeze.	There may be a genetic predisposition to RSV and subsequent respiratory morbidity that is independent of premorbid lung function.	1	10	NA
18	Ehlenfield et al. 2000.	USA	Retrospective single centre study	None	1991-1992	Infants aged 2-18 months hospitalized with acute bronchiolitis	Infants with chronic underlying illnesses; infants receiving corticosteroid therapy	Confirmed RSV infection	43	M 58%	NR	Eosinophil counts during bronchiolitis were greater in subjects with wheezing at 7 years than infants without wheezing up to 3 years of age. Familial asthma, gender, and passive exposure to cigarette smoke were not significant risk factors.	Eosinophilia at the time of bronchiolitis generally predicts the development of wheezing persisting into later childhood.	3	10	NA

19	Eriksson et al. 2000.	Sweden	Prospective single centre study	None	1993-1995	Children <3 years old hospitalized with influenza A or RSV during two consecutive seasons	NR	Confirmed RSV and influenza A infection	292	NR	RSV: 2.2 months Influenza A: 11 months	For both RSV and influenza A patients, 60% of patients reported wheezing for >2 weeks following discharge. More than 50% had repeated episodes of wheezing during the first year, and ~15% were hospitalized for wheezing.	Viral infection occurring in infancy is linked to an increased rate of repeated wheezing episodes.	1	11	NA
20	Ermers et al. 2007.	Netherlands	Prospective single centre study	None	1997-1999	Children <13 months with RSVH	Children with wheezing illness before RVS LRTI	Confirmed RSV infection	101	Wheezing at 6 years: M 61.5% No wheezing at 6 years: M 54.5%	Wheezing at 6 years: 3.15 months No wheezing at 6 years: 3.37 months	Distinctive characteristics were determined at age 6 years. Immunologic characteristics of monocyte IL-10 and IL-12 production during RSV LRTI was seen in early but not late wheeze. The IL-13 Gln allele was associated with late wheezing (OR 3.27; 95% CI 1.32-8.06), but it was not associated with early wheezing.	Late wheezing at age 6 years, but not early post-bronchiolitis wheezing, is an asthmatic phenomenon and genetically related to a functional IL-13 polymorphism. Predicting which children are at risk for late asthma could identify children who will benefit from early targeted interventions.	1	11	NA
21	Ermers et al. 2011.	Netherlands	Prospective single centre study	None	1995-1996 2004-2006	Children <13 months with RSVH during winter seasons	History of cardiac and pulmonary disease	Confirmed RSV infection	161	No recurrent wheeze: M 50.6% Recurrent wheeze: M 60.2%	No recurrent wheeze: 10 weeks Recurrent wheeze: 9 weeks	10 SNPs in 9 genes were significantly associated with recurrent wheeze at the genotype level (IL19, IL20, MUC5AC, TNFRSF1B, C3, CTLA4, CXCL9, IL4R, and IL7). Haplotype analysis showed inverse association between the TGG haplotype and recurrent wheeze after RSV. IL19 and IL20 genes were notably associated with recurrent wheeze in infants without asthmatic parents. The association of IL20 SNP rs2981573 with recurrent wheeze was confirmed in a healthy birth cohort.	Genetic variation in adaptive immunity genes and particularly in IL19/IL20 genes is associated with the development of recurrent wheeze after RSV.	1	10	NA
22	Escobar et al. 2013.	USA	Retrospective multicentre study	None	1996-2004	Children born ≥32 wGA	NR	Confirmed RSV infection	72,602	M 50.96%	NR	25.0% of children with RSVH in their first year had recurrent wheezing in the second year of life. These infants were ~3 times as likely to have recurrent wheezing at year 5 than children who did not (12.5% vs. 4.6%), infection. 30%-60% of premature infants 32-36 wGA with RSV infection during the first year of life will have a recurrent wheezing episode by age 5 years; 40% will have >1 episode. Outpatient RSV infection had an adjusted OR of 1.38 (95% CI 1.03-1.85) vs 2.59 (95% CI 1.49-4.50) for prolonged RSVH.	Three important risk factors (RSV disease in first year of life, moderate prematurity, and neonatal exposure to supplemental oxygen) had significant associations with development of recurrent wheezing by year 5. Predictors for recurrent wheezing in the 3rd year of life also predict for recurrent wheezing in the 5th year, of which RSV infection in the first year of life is the most modifiable.	2	10	NA

23	Escobar et al. 2010.	USA	Retrospective multicentre study	None	1996-2002	Children born >32 wGA	NR	Confirmed RSV infection	71,102	M 51.2%	NR	The overall RSV rate was 1.7%. The rate of recurrent wheeze in the 3rd year of life was 16.23% among premature infants with RSV and 6.22% without RSV. The risk of recurrent wheezing increased among infants who had an RSV outpatient encounter (adjusted OR 2.07; 95% CI 1.61-2.67), uncomplicated RSVH (adjusted OR 4.66; 95% CI 3.55-6.12), or prolonged RSVH (adjusted OR 3.42; 95% CI 2.01-5.82) compared with infants without RSV.	RSV infection, prematurity, and exposure to supplemental oxygen during the neonatal period have independent associations with development of recurrent wheezing in the 3rd year of life.	2	10	NA
24	Fauroux et al. 2014.	France	Prospective multicentre study	None	2008-2009	Infants <33 wGA without BPD; infants 39-41 wGA	NR	Confirmed RSV infection	242	M 54%	12.5 months	Preterm infants had significantly increased respiratory morbidity during the follow-up compared to full-terms in terms of wheezing and recurrent wheezing episodes. The 17 infants (14 preterms, 3 full-terms) with RSVH during their first RSV season had significantly more wheezing episodes during the follow-up period than controls (OR 4.72, 95% CI 1.71-13.08).	Male gender, birth weight <3330 g and RSVH during the infant's first RSV season were independent risk factors for the development of wheezing episodes during a subsequent 12-month follow-up period.	NA	12	NA
25	Fjaerli et al. 2005.	Norway	Prospective single centre study	None	1993-1994	Children hospitalized at least once with acute respiratory disease during two consecutive winter seasons	NR	Confirmed RSV infection	57	RSV +: M 57% RSV -: M 54%	RSV+: 5.1 months RSV -: 5.9 months	61% of infants were RSV positive. At 7 years old, children hospitalized for bronchiolitis during infancy had decreased lung function, increased wheezing episodes, and more current medication than the age-matched controls. RSV positive patients also had lower average birth weight and a higher rate of primary family members with asthma.	Children hospitalized for early-life bronchiolitis are susceptible to recurrent wheezing and reduced pulmonary function by 7 years of age.	1	9	NA
26	Frassanito et al. 2015.	Italy	Prospective single centre study	None	2009-2014	Children hospitalized for ARTI	NR	Virologically confirmed RSV infection	273	NR	Median: 2.9 months	RSV was identified as the most common cause of bronchiolitis (118/273). RSV infants had wheezing more frequently than rhinovirus infants. Risk factors for ARTIs were the presence of siblings, parental asthma and smoking cohabitants.	Environmental and genetic factors contribute to ARTIs. RSV infants had more long lasting sequelae.	2	3*	NA

27	Goetghebuer et al. 2004.	UK	Prospective single centre study	None	1992-1998 Follow-up 2001-2002	Children hospitalized for bronchiolitis within the first year of life	NR	Confirmed RSV infection	134	No wheeze : M 47.8% Wheeze: M 50%	No wheeze: 5.5 months Wheeze: 4.9 months	Family-based association showed that the IL-8 variant (IL8 251A allele) was transmitted significantly more in children who wheezed after RSVH. Moreover, the variant was significantly more frequent in post-bronchiolitis wheezes compared with the general population (OR 51.6, 95% CI 1.0-2.6).	The evidence suggests that there is a genetic predisposition to wheeze following severe RSV bronchiolitis, and that this could be IL8-251A.	1	11	NA
28	Greenough et al. 2009.	UK	Prospective/retrospective multicentre study	None	1994-1997	Children born at <32 wGA and admitted during 1st week after birth due to BPD	NR	Confirmed RSV infection	147	NR	NR	Cost of outpatient attendances was significantly higher and total cost of care tended to be higher in the RSV group than in the non-respiratory group. At 8-10 years of age, children with RSVH (n=14) had significantly lower forced expiratory volume, forced vital capacity and flows at 50% and 75% of vital capacity than children hospitalized for non-RSV causes (n=63). Healthcare utilisation decreased with increasing age regardless of RSVH status.	In prematurely born children with BPD, RSVH in the first 2 years is associated with reduced airway function at school age.	2	10	NA
29	Greenough et al. 2004.	UK	Retrospective multicentre study	None	1994-1997	Children born at <32 wGA and admitted during 1st week after birth due to CLD	NR	Confirmed RSV infection	235	NR	NR	Children with RSVH had a greater hospital LOS, more outpatient appointments, significantly more prescriptions for all treatments and respiratory medications, and a greater number had used inhalers. The cost of care of the RSVH group was higher; health-related QoL was lower and associated with increased ongoing morbidity.	Premature children with CHD and an RSVH in the first two years of life required more health care and suffer chronic morbidity.	3	10	NA
30	Greenough et al. 2005.	UK	Retrospective review	None	NR	Preterm infants <35 wGA hospitalized for RSV infection	NR	Confirmed RSV infection	RSV: 33 Non-RSV: 157	NR	NR	RSVH in infants 32-35 wGA or those born more prematurely who developed CLD were associated with increased hospital admissions/LOS, as well as more GP and outpatient visits in the first 2 years after birth. Children born <32 wGA with CLD also used more outpatient visits, prescriptions and respiratory medications between the ages of 2-4 years. Chronic respiratory morbidity occurs in very preterm infants, regardless of whether RSV needs hospitalization.	RSV infection in premature infants is associated with chronic respiratory morbidity.	NA	NA	NA

31	Henderson et al. 2005.	UK	Prospective/ retrospective multicentre study	None	1991-1999	Longitudinal follow-up of children born between April 1991 and December 1992 and hospitalized for bronchiolitis within the first 12 months of life	NR	Confirmed RSV infection	RSV: 150	NR	NR	Wheezing was higher in the RSV groups compared to controls at 30-42 months (28.1% vs 13.1%) and 69-81 months (22.6% vs 9.6%). The cumulative prevalence of asthma at 91 months in the RSV group was 38.4% vs 20.1%. At 7 years of age, 14.6% of the RSV group and 20.7% of controls reported atopy.	RSV bronchiolitis is associated with subsequent wheezing and asthma but not atopy by age 7.	2	10	NA
32	Hyvärinen et al. 2005.	Finland	Prospective single centre study	None	1981-1982	Follow-up of children ages >13 years that were hospitalized in 1981-1982 aged <2 years for bronchiolitis/pneumonia	NR	Confirmed RSV infection	127	NR	NR	98/127 original study subjects were screened at a median age of 14.9 years to assess atopic and asthmatic symptoms. Asthma was present in 14-23% in the original bronchiolitis group and 12-15% in the original pneumonia group. Asthma was present in 8-17% in the RSV group and 16-23% in the non-RSV group. Early predictive factors for asthma were repeated wheezing, atopic dermatitis and elevated blood eosinophils.	An increased risk for asthma persists until the teenage period after bronchiolitis and pneumonia in infancy. The present study was unable to demonstrate an association between early RSV infection and teenage asthma.	2	10	NA
33	Hyvärinen et al. 2007.	Finland	Prospective single centre study	None	1992-1993	2004 follow-up of a 1992-3 study of presence of wheezing and respiratory distress leading to hospital care in children aged 1-23 months	NR	Confirmed RSV infection	81	M 74%	NR	25/81 had RSVH. RSV bronchiolitis and recurrent wheezing were associated with significantly reduced forced vital capacity in 33% of children. Bronchial hyper-responsiveness presented in 26-46% children.	RSV bronchiolitis in infancy was associated with a restrictive pattern of lung function in later childhood.	2	10	NA
34	Jackson et al. 2008.	USA	Prospective multicentre study	None	1998-2000	Cohort of newborns with at least 1 parent with respiratory allergies and/or history of physician diagnosed asthma	NR	Physician-diagnosed allergens and asthma diagnosed	259	NR	NR	454 wheezing illnesses were reported during the first 3 years of life, 21% of which were due to RSV. 48 patients suffered from multi-viruses, of which 42% involved RSV. In the 6th year of life, 73/259 (28%) children had asthma. Children who wheezed with RSV during infancy developed asthma at a rate similar to those who did not wheeze, unlike those with rhinovirus infections. However in children who wheezed only with RSV in year 3 had a significantly increased risk of asthma at age 6 (OR 13.6; 95% CI 3.4-54.0).	Rhinovirus-associated wheezing is a better indicator of asthma risk than RSV-associated wheezing.	1	9	NA

35	James et al. 2013.	USA	Prospective multicentre study	None	1996-2003 (KPNC) 1995-2003 (TennCare)	Infants \geq 32 wGA	Infants with CLD	ICD-9 code for bronchiolitis and asthma	264,010	M 51%	NR	15% of infants had bronchiolitis during the RSV season. The proportion of children diagnosed with asthma among the KPNC and TennCare cohorts was 16%/23%, respectively, for those with a history of bronchiolitis during the RSV season, and 8%/12%, for those <i>without</i> this history.	In the findings, 50% of asthma cases in children with a history of infant bronchiolitis during the RSV season were associated with bronchiolitis. On a population level, 13% of asthma was associated with infant bronchiolitis during the RSV season.	1	10	NA
36	Juntti et al. 2003.	Finland	Prospective single centre study	None	1991-1994 Follow-up 2000-2001	Children hospitalized with RSV during first year of life	Preterm birth (<37 wGA); need for respiratory assistance >6 hours during the neonatal period; CHD; chromosomal abnormality; severe neurological disease	Confirmed RSV infection	76	M 61.8%	4.0 months	Asthma was diagnosed significantly earlier in the RSV subjects than in the controls (mean 3.0 years vs 5.6 years). 8% of RSVH patients and 37% of the controls had at \geq 1 positive skin-prick test for atopy.	An early RSV infection results in reduction of skin prick test positivity but not of occurrence of asthma.	1	11	NA
37	Karaman et al. 2011.	Turkey	Prospective single centre study	None	2006-2008	Children \leq 36 months diagnosed with first incidence of acute bronchiolitis	NR	Confirmed RSV infection	70	M 58.6%	RSV: 6.78 months Non-RSV: 9.53 months	Recurrent wheezing was observed in 35% of RSV patients and 53.3% of non-RSV patients, respectively, although this did not reach significance. Mean serum IFN- γ and IL-4 levels were significantly higher in the non-RSV group. No significant relation was detected between recurrence of wheezing episodes and total eosinophil count, serum IgE, IL-4, IL-13, and IFN- γ levels.	No difference could be detected between RSV and non-RSV bronchiolitis regarding subsequent wheezing episodes. Although serum IL-4 and IFN- γ levels were high her in non-RSV bronchiolitis group, no significant correlation was observed between the separate parameters and recurrence of wheezing episodes.	1	9	NA
38	Kitcharoensakkul et al. 2016.	USA	Prospective single centre study	None	2009-2013	Children <1 year with their first episode of RSVH	NR	Confirmed RSV infection	181	M 58%	4.3 months	41.4% had recurrent wheezing (\geq 3 wheezing episodes); 27.6% had no wheezing. The recurrent wheezing group had significantly higher upper airway plasmacytoid dendritic cells, versus no wheezing. These infants were more likely to be African-American (OR 6.1; 95% CI 1.7-26.0).	Children with recurrent wheezing following severe RSVH may reflect a heightened antiviral response in the airway, leading to subsequent development of asthma.	1	7*	NA
39	Koponen et al. 2012.	Finland	Prospective single centre study	None	2001-2002 2002-2004	Children <6 months hospitalized for bronchiolitis	NR	Confirmed RSV infection Doctor diagnosed asthma	166	M 52%	Current asthma: 113 days No asthma: 77 days	RSV caused 70.25% of bronchiolitis cases. Current asthma was present in 21 (12.7%) children: 8.2% of former RSV patients versus 24% non-RSV patients. 27% children were reported as having ever had asthma. Atopic dermatitis, non-RSV bronchiolitis and maternal asthma were independently significant risk factors for asthma.	The risk of asthma was lower after RSVH than after bronchiolitis caused by other viruses in children hospitalized <6 months of age.	1	11	NA

40	Korppi et al. 2004.	Finland	Prospective single centre study	None	1981-1982 Follow-up 2000	Children ≤23 months hospitalized with bronchiolitis or pneumonia	NR	Confirmed RSV infection	80	NR	NR	Asthma was present in 17-22% of 36 subjects (depending on definition) compared to 11% of 45 controls. Peak flow measures were lower in patients compared to controls. ≥1 abnormal lung function results were found in 16 (44%) patients versus 5 (11%) controls. 60% of patients had a positive skin prick test. 62% of patients had a significantly abnormal lung function and 67% had significant bronchial reactivity.	RSV infection in infancy is not a significant risk factor for asthma or bronchial reactivity. In young adults, lung function abnormalities may be associated with RSVH in infancy.	1	11	NA
41	Kotaniemi-Syrjänen et al. 2005.	Finland	Prospective single centre study	None	1992-1993	Children <2 years hospitalized for wheezing	Chronic cardiorespiratory disease; preterm infants; infection-related wheezing	Confirmed RSV infection	100	NR	10 months	29% of children hospitalized for wheezing at <2 years were RSV positive. RSV-specific IgG antibody concentrations rose with age, after 1-year follow-up visit, 55/77 of children had RSV-specific IgG. After a 3-year follow-up 66/72 had RSV-specific IgG. 85% of all children were seropositive for RSV by 3 years of age.	Hospitalization for wheezing in infancy is associated with increased risk for later asthma, particularly in children <i>without</i> RSV infection on admission. Children with RSV also have slightly increased risk for asthma, but serological evidence of RSV infection is not associated with development of asthma.	1	11	NA
42	Kotaniemi-Syrjänen et al. 2002.	Finland	Prospective single centre study	None	1992-1993	Children <2 years hospitalized for wheezing	Chronic cardiorespiratory disease; preterm infants; infection-related wheezing	Confirmed RSV infection	82	NR	NR	Children were followed up at a median of 7.2 years. At this time, 40% of children had an asthma diagnosis, of which 91% were on continuous medication. RSV on study entry was significantly associated with low risk of asthma vs RSV-negative or other viral causes.	If hospitalization for wheezing occurs in infancy, >1/3 of children will suffer from asthma at school age. This risk is significantly increased with recurrent wheezing in infancy and development of atopy.	1	11	NA
43	Kristjánsson et al. 2006.	Iceland	Prospective single centre study	None	NR	Children with RSVH	NR	Confirmed RSV infection	17	M 53%	3.3 months	In the RSV group, a relationship was seen between wheezing and urinary eosinophil protein values at inclusion and at 30-month follow-up. Subjects who had experienced wheezing during the 12 months before follow-up had significantly higher urinary eosinophil protein values than non-wheezers, both at inclusion and 30 months later.	RSVH results in significant but transient increase in urinary eosinophil protein. A high urinary eosinophil protein value at baseline appears to increase the risk of future wheezing.	1	11	NA
44	Lauhkonen et al. 2015.	Finland	Prospective single centre study	None	2001-2004	Children hospitalized for bronchiolitis at <6 months	NR	Confirmed RSV infection	103	M 49.5%	NR	62% of subjects had RSV bronchiolitis. In baseline lung-function measurement, resistance (n=8; 7.8%) or reactance (19; 18.4%) at 5 Hz were pathological in 20% of	Though reduced lung function and increased airway reactivity were common, evidence for persistent lung function reduction was rare, <1%, at	1	11	NA

												children versus reference values. Increased bronchial reactivity was present in 16%. Irreversible changes were revealed in only 1 case. Lung function deficit was revealed in 20% and increased airway reactivity in 16% in 5-7 year old children who had been hospitalized for bronchiolitis at <6 months of age.	preschool age in children hospitalized for bronchiolitis at age <6 months.			
45	Murray et al. 2014.	UK	Retrospective multicentre 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-related. Admission rates were higher among preterm infants (47.3/1000 infants vs 22.4/1000 for term infants). DS and cerebral palsy also served as risk factors for bronchiolitis 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.	3	11	NA
46	Nenna et al. 2015.	Italy	Retrospective single centre study	None	NR	Children <1 year with RSVH	NR	Confirmed RSV infection	68	M 63.2%	63.7 days	29 (42.6%) infants with bronchiolitis experienced recurrent wheezing at 36-month follow-up. Eosinophil levels were significantly higher in wheezing-positive than in wheezing-negative children. Children with recurrent wheezing after bronchiolitis showed significantly higher RSV-RNA load and higher IFN- λ 2 and - λ 3 levels than wheezing-negative children	A high RSV-RNA load and IFN- λ activation at the time of admission for bronchiolitis are associated with recurrent wheezing at 36-month follow-up.	2	11	NA
47	Pérez Pérez et al. 2004.	Spain	Prospective single centre study	BPD	1996-2001	Cohort of preterm infants \leq 32 wGA, with or without BPD	NR	Confirmed RSV infection	90	NR	NR	86.2% of preterms with BPD had \geq 1 wheezing episode versus 41.4% of preterms without BPD and 18.8% matched controls. 17 children with BPD were evaluated until age 4. Episodes of wheezing significantly decreased from 88.2% in the 1st year to 41% between the 3rd-4th years. Hospital admissions for respiratory illness decreased from 52.9% in the 1st year to 17.6% in the 2nd year.	During the first 2 years of life, children with BPD have a greater number of wheezing episodes and a greater need for medical treatment. Respiratory morbidity improved with age, with 40% showed recurrent wheezing episodes at the age of 4 years.	1	12	NA
48	Pifferi et al. 2001.	Italy	Prospective single centre study	None	1994	Children <18 months with RSVH	<37 wGA; <2500 g at birth; postnatal respiratory distress	Confirmed RSV infection	48	M 56.25%	153.5 days	Children were re-evaluated 5 years after infant RSVH. Significantly higher serum eosinophil cationic protein levels were seen at enrolment in subjects who developed persistent wheezing compared to subjects who did not. Initial serum eosinophil	Serum eosinophil cationic protein levels in infants with bronchiolitis are useful in predicting risk of developing wheezing in the subsequent 5 years.	1	10	NA

												cationic protein values significantly predicted persistent wheezing. Risk of developing respiratory symptoms was 9.73 times higher for infants with serum eosinophil cationic protein levels ≥ 8 micro g/L.				
49	Pooririsak et al. 2010.	USA	Prospective single centre study	None	1994-2003	Monozygotic twin pairs, one of which had RSVH	NR	Confirmed RSV infection and asthma diagnosis	74	NR	10.6 months	The prevalence of asthma among twins was 18%. The twins did not differ by previous RSVH status with respect to current asthma, use of inhaled corticosteroids, atopic dermatitis, fractional exhaled nitric oxide, baseline lung function, bronchial responsiveness, or sensitization.	There was no significant difference on RSVH in infancy on the development of asthma and allergy in monozygotic twins, which argues against a specific viral effect.	1	11	NA
50	Rolfsjord et al. 2015.	Norway	Prospective multicentre study	None	2010-2011	Children <1 year hospitalized for acute bronchiolitis	Other severe or chronic disease; >1 previous episode of obstructive airway disease; use of inhaled corticosteroids within last 4 weeks	NR	Bronchiolitis: 217 Control: 198	Bronchiolitis: M 59.4% Control: M 55.6%	Bronchiolitis: 4.2 months	Questionnaires showed that QoL was lower in children with previous bronchiolitis compared to controls in terms of overall health, general health, and changes in health. Additional risk factors for asthma further decreased scores.	Acute bronchiolitis, atopic eczema and the presence of 3 asthma risk factors is negatively associated with later QoL in early childhood.	1	12	NA
51	Rolfsjord et al. 2016.	Norway	Prospective multicentre study	None	2010-2011	Children <1 year hospitalized for acute bronchiolitis	Other severe or chronic disease; >1 previous episode of obstructive airway disease; use of inhaled corticosteroids within last 4 weeks	NR	Bronchiolitis: 209	M 59.8%	Bronchiolitis: 4.2 months	Increased LOS and use of ventilator assistance during acute bronchiolitis was associated with reduced QoL, physical ability and general health questionnaire responses 9 months later. Bodily pain and discomfort, and change in health were associated with LOS.	Severe bronchiolitis in early infancy is correlated with reduced QoL measures 9 months later.	1	11	NA
52	Romero et al. 2010.	USA	Retrospective multicentre study	None	2001-2004	Infants ≤ 6 months, born at ≤ 36 wGA and/or <2500 g; preterm infants with any medically attended RSV-LRTI	NR	Confirmed RSV infection	RSV: 378 Control: 606	NR	NR	The prevalence of serious early childhood wheezing between 2-3 years was significantly higher in the RSV group vs the control group (16.7% vs 8.6%). Preterm infants with RSV in early life were 2.52-fold (95% CI 1.65-3.85) more likely to present with wheezing between 2-3 years. Wheezing substantially and significantly increased healthcare costs.	RSV in preterm infants was associated with increased prevalence of serious early childhood wheezing between ages 2 and 3 years.	2	12	NA

53	Ruotsalainen et al. 2013.	Finland	Prospective multicentre study	None	1992-1993 Follow-up in adolescence	Children <24 months hospitalized for bronchiolitis	NR	Confirmed RSV infection	67	NR	NR	Doctor-diagnosed asthma was present in 30% of former bronchiolitis patients and in 5% of controls (OR 7.9; 95% CI 3.3-19.3). The respective figures for self-reported asthma were 64% and 11% (OR 14.7; 95% CI 7.2-30.0). Self-reported asthma was more common in former rhinovirus than RSV patients.	Patients hospitalized for RSV and rhinovirus bronchiolitis at <24 months of age have increased asthma risk at 15-18 years of age versus population controls. Within the former bronchiolitis group, risk of self-reported asthma was higher after non-RSV versus RSV and after rhinovirus versus non-rhinovirus bronchiolitis.	1	11	NA
54	Ruotsalainen et al. 2010.	Finland	Prospective single centre study	None	1981-1982 Follow-up >25 years later	Children <24 months with RSVH	NR	Confirmed RSV infection	120	RSV group: M 55%	NR	Doctor-diagnosed asthma and self-reported asthma were present in 13% and 30% of the study subjects, versus 1.3% and 3.8% in the matched population controls. Wheezing symptoms were reported in 35% of cases versus 16.3% controls. Allergic rhinitis was present in 40% of cases versus 30% controls.	RSVH at <24 months of age is, independently from later allergy, smoking and being overweight, a significant risk factor of adulthood asthma at 26-29 years of age. On the contrary, RSV infection in infancy is not a risk factor for allergic rhinitis or conjunctivitis.	1	10	NA
55	Schauer et al. 2002.	Germany	Prospective single centre study	None	1991-2001	Children <1 year with RSVH	Children with neonatal respiratory distress; born <38 wGA	Confirmed RSV infection	42	M 42.9%	16 weeks	A positive test for IgE antibodies was noted in 14/42 (33%) RSV children and in 2/84 (2.3%) non-bronchiolitis controls. RSV bronchiolitis was the most important risk factor for allergic sensitisation. 13 children (15.5%) of the RSV group and 3 controls (3.6%) suffered from recurrent wheezing.	Severe RSVH during the 1st year of life is an important risk factor for the development of recurrent wheezing and sensitisation to common allergens during the subsequent year.	1	11	NA
56	Schuurhof et al. 2011.	Netherlands	Prospective multicentre study	None	2007-2009	Children <13 months with RSVH	Infants with DS, a history of wheezing or cardiac/pulmonary pathology	Confirmed RSV infection	185	M 55.7%	2 months	Local IL-10 levels during RSV infection were significantly higher in infants that later developed wheeze compared to infants without wheeze in the 1st year after RSV infection.	The relationship between high local IL-10 levels during initial RSV infection and physician-diagnosed wheeze shows the importance of the IL-10 response during RSV bronchiolitis.	1	11	NA
57	Sigurs et al. 1995.	Sweden	Prospective single centre study	None	1989-1990	Children <1 year with RSVH	NR	Confirmed RSV infection	RSV: 47 Control: 93	M 45%	3.5 months	89% of the RSV group and 27% of the control group had significant levels of IgG antibodies against RSV at the first follow-up. At the second follow-up, asthma was verified in 11/47 children in the RSV group and 14/44 in the control group.	RSV bronchiolitis is the most important risk factor in the 1st year of life for the development of asthma and sensitisation to common allergies during the subsequent 2 years.	1	11	NA

58	Sigurs et al. 2000.	Sweden	Prospective single centre study	None	1989 -1990 Follow-up 1997	Children <1 year with RSVH	Children with concomitant chronic disease	Confirmed RSV infection	RSV: 47 Control: 93	M 45%	116 days	Asthma during the year prior to follow-up was seen in 23% of RSV children and 2% of control subjects. Allergic sensitization was found in 41% of RSV children and 22% of control subjects. RSV had the highest independent risk ratio for asthma (OR 12.7; 95% CI 3.4-47.1) and a significantly elevated independent risk ratio for allergic sensitization (OR 2.4; 95% CI 1.1-5.5).	RSV bronchiolitis in infancy severe enough to require hospitalization was highly associated with development of asthma and allergic sensitization up to age 7.5.	1	12	NA
59	Sigurs et al. 2005.	Sweden	Prospective single centre study	None	1989 -1990 Follow-up 1997 and 2003	Children <1 year with RSVH	Children with concomitant chronic disease	Confirmed RSV infection	RSV: 47 Control: 93	M 45%	116 days	46/47 (RSV) and 92/93 (control) participated in the follow-up. The occurrence of symptoms over the previous 12 months was significantly higher in the RSV group: 43% vs 8% for asthma/recurrent wheezing and 39% vs 15% for allergic rhino conjunctivitis. Sensitization to common inhaled allergens was more frequent in the RSV group than in the control subjects (50% vs 28%).	RSV bronchiolitis in infancy severe enough to cause hospitalization is a risk factor for allergic asthma in early adolescence.	1	12	NA
60	Sigurs et al. 2010.	Sweden	Prospective single centre study	None	1989 -1990 Follow-up 1997, 2003 and 2008	Children <1 year with RSVH	Children with concomitant chronic disease	Confirmed RSV infection	RSV: 47 Control: 93	M 45%	116 days	Increased prevalence of asthma/relapsing wheezing (39% vs 9%), clinical allergy (43% vs 17%) and sensitisation to perennial allergens (41% vs 14%) were present at age 18 in the RSV cohort compared with controls. Persistent/relapsing wheeze associated with early allergic sensitisation predominated in the RSV cohort compared with controls (30%;1.0%).	Severe early RSV bronchiolitis is associated with an increased prevalence of allergic asthma persisting into early adulthood.	1	12	NA
61	Silver et al. 2009.	USA	Prospective single study centre	None	NR	Children <1 year with RSVH	NR	Confirmed RSV infection	206	M 57.4%	4.4 months	45% of participants had physician-diagnosed asthma by 6 years of age. These children had significantly lower plasmacytoid dendritic cell levels than non-asthmatic controls. There were significantly lower numbers of myeloid dendritic cells in children with asthma compared to those without, but this divergence was not significant after adjusting for covariates such as age, gender, smoke exposure etc.	Children who are diagnosed with asthma after severe RSV bronchiolitis appear to have a relative deficiency of plasmacytoid dendritic cells in peripheral blood.	1	12	NA

62	Stein et al. 1999.	USA	Prospective single study centre	None	1980-1984	Follow-up of children with LRTI before 3 years of age	NR	Confirmed RSV infection	472	NR	NR	RSV LRTI was seen in 43.9% of infants. RSV was associated increased risk of infrequent wheeze (OR 3.2; 95% CI 2.0-5.0, p<0.001), and frequent wheeze (4.3; 95% CI 2.2-8.7, p ≤0.001) by age 6. Risk decreased markedly with age and was not significant by age 13. There was no association between RSV and subsequent atopic status. RSV was associated with significantly lower measurements of forced expiratory volume when compared with children with no history of LRTI.	RSV in early childhood is an independent risk factor for subsequent development of wheezing up to age 11 but not by age 13. This association is not caused by increased risk of allergic sensitisation.	1	10	NA
63	Stensballe et al. 2009.	Denmark	Prospective multicentre study	None	1996-2003	Cohort of children with RSV and/or recurrent wheeze	No titre; recurrent wheeze before RSV; not completing all follow-up interviews	Confirmed RSV infection	RSVH: 408 Recurrent wheeze: 408 RSVH and wheeze: 289	NR	NR	Neutralizing antibody levels were inversely associated with RSVH in infants <6 months of age (IRR 0.74; 95% CI 0.62-0.87), and with RSVH in infants with recurrent wheeze (IRR 0.83; 95% CI 0.71-0.97). In contrast, neutralizing antibody levels were directly associated with increased risk of recurrent wheeze in infants <6 months of age (IRR 1.28; 95% CI 1.04-1.57) and recurrent wheeze after RSVH in infants <6 months of age (IRR 1.44; 95% CI 1.10-1.90).	Maternally-derived RSV-neutralizing antibodies protect infants against RSVH and when the infant has recurrent wheeze. However, high maternally derived RSV-neutralizing antibody levels were associated with increased risk of recurrent wheeze.	1	12	NA
64	Stensballe et al. 2009.	Denmark	Prospective multicentre study	None	1994-2003	Twins with RSVH or asthma	Children with chronic disease	Confirmed RSV infection	18,614	M 51%	NR	4.6% (848/18,614) of children had an RSVH within the first 5 years of life. Asthma hospitalization after RSVH was increased by 6-8 fold during the first 2 months after RSVH but was no longer increased 1 year later.	There is a bidirectional association between severe RSV and asthma. Severe RSV is associated with short-term increase in risk of subsequent asthma, suggesting that RSV induces bronchial hyper-responsiveness. Asthma is associated with long-term increased susceptibility for severe RSV, suggesting a host factor is responsible for the severe RSV response.	1	12	NA
65	Strannegård et al. 1997.	Sweden	Prospective single centre study	None	1989-1990	Children <1 year with RSVH	NR	Confirmed RSV infection	RSV: 45 Control: 90	NR	4 months	40/45 infants had IgG antibodies, and 5 had IgA antibodies only against RSV. Anti-RSV IgA antibodies tended to be higher in patients with bronchiolitis. Follow-up at 3 years of age showed that allergic sensitization and asthma occurred more often in	RSV has an unusual propensity to activate the Th2 cell system. RSV bronchiolitis may thus be an important risk factor for later development of atopic disease; however, bronchiolitis may simply serve as a marker	1	11	NA

												children with past RSV than in controls. Children with past RSV who later developed allergic sensitization had significantly elevated RSV IgA antibody titres at 1 year of age more frequently than non-sensitized children with past RSV.	for later development of atopy.			
66	Szabo et al. 2014.	Canada	Retrospective multicentre study	None	1996-1997	Children <2 years hospitalized for LRTI	NR	Confirmed RSV infection	145,430	M 48.7%	NR	4.9% of the cohort had LRTI. A total of 230 children (0.2% of the birth cohort and 3.2% of the LRTI cohort) were hospitalized for severe RSV. By age 10 years, 52.5% of the LRTI cohort and 27.9% of the non-hospitalized cohort had chronic respiratory morbidity. Male sex, preterm birth, diagnosis of CHD or BPD/CLD before 2 years old, and LRTI hospitalization before 2 years old were identified as significant risks for childhood chronic respiratory morbidity.	Hospitalization of young children for LRTIs is associated with two-fold increased risk of childhood chronic respiratory morbidity, demonstrating the ongoing impact of LRTI in infancy.	2	11	NA
67	Sznajder et al. 2005	France	Retrospective multicentre study	None	1993-1994	Children <12 months who had experienced their first bronchiolitis attack	NR	NR	128	NR	5.1 months	81.2% of subjects had been hospitalized during the first episode of bronchiolitis, but none had been placed in intensive care. A familial history of allergy was found in 71.8% of patients. 40.6% were exposed to tobacco smoke. 75.8% had experienced ≥1 episode of wheezing at some time of their life. 57.4% of children with asthmatic attacks had a history of familial asthma.	High prevalence of asthma and other atopies were seen in children who experienced their first bronchiolitis episode <12 months old. Family history of allergy was the only risk factor for asthma or chest wheezing. There may be an interaction between viral infection and atopic family predisposition on later bronchial hyper-responsiveness.	3	11	NA
68	Thomsen et al. 2009	Denmark	Retrospective multicentre study	None	1994-2000	Infant twins with RSVH	Unknown zygosity twin pairs	Confirmed RSV infection	10,733 (includes 5154 intact twin pairs)	M 51.3%	NR	Of 1019 children with a history of RSVH, 25% had been hospitalized <3 months, 50% <6 months, and 75% <12 months. 95% had been hospitalized <24 months. RSVH and asthma were positively associated, with overlapping genetic determinants. Modelling direction of causation between RSVH and asthma found a model in which asthma “causes” RSVH fitted the data significantly better than a model in which RSVH “causes” asthma.	RSVH does not appear to cause asthma but is an indicator of the genetic predisposition to asthma.	2	12	NA

69	Torgerson et al. 2015	UK	Retrospective multicentre study	None	1998-2001	Children with RSVH in infancy with physician diagnosed wheezing during acute illness	History of previous wheezing/asthma; CF in patient or family; congenital heart/lung abnormalities; regular use of anti-gastroesophageal reflux medication, bronchodilators or anti-inflammatory medication	Confirmed RSV infection	182	M 53.5%	137 days	Four rare nonsynonymous variants significantly associated with asthma were identified following severe RSV bronchiolitis. One of the variants was a highly functional nonsynonymous variant in ADRB2 (rs1800888), which was also nominally associated with asthma and active asthma.	Rare nonsynonymous variants contribute to the development of asthma following severe RSV bronchiolitis in infancy.	1	11	NA
70	Valkonen et al. 2009	Finland	Retrospective single centre study	None	1988-2001	Children <2 years hospitalized with bronchiolitis	History of previous wheezing episodes	ICD code for RSV	416	RSV: M 57.8% Non-RSV: M 70.5%	RSV: 0.34 years Non-RSV: 0.92 years	Within the first year after hospitalization, 16.6% children with non-RSV bronchiolitis developed recurrent wheezing, compared with 2.5% children with RSV (RR 6.6; 95% CI 2.6-16.5). The rates of recurrent wheezing were significantly increased in the non-RSV group within 2 (RR 2.9; 95% CI 1.7-5.1) and 3 years (RR 3.4; 95% CI 2.0-5.7) after hospitalization.	Children hospitalized with bronchiolitis caused by viruses other than RSV develop recurrent wheezing at substantially higher rates during a 3-year follow-up period.	2	11	NA
71	Vo et al. 2012.	Canada	Retrospective multicentre study	None	1996-1997	Children <2 years old with CHD	None	ICD-9 code	3223	NR	NR	19/3223 children with CHD had RSVH and 417/3223 were hospitalized for LRTI <2 years old. Before age 10, 58.5% of children with CHD who were hospitalized for LRTI in infancy were diagnosed with chronic respiratory morbidity, higher than that of CHD children not hospitalized for LRTI in infancy. IRR for chronic respiratory morbidity were higher for males (2.0) than females (1.6).	Children with CHD hospitalized for LRTI in infancy are at almost twice the risk of childhood chronic respiratory morbidity compared to those not hospitalized for LRTI.	3	9*	NA
72	Voraphani et al. 2014	USA	Prospective multicentre study	None	1980-1984	Birth cohort in Tucson	None	Confirmed RSV infection	682	M 48.5%	NR	There was a significant interaction between RSV and active smoking in relation to current asthma and peak flow variability. In subjects with early RSV, those who actively smoked were 1.7 times more likely to have current asthma than non-smokers.	Smoking is associated with increased risk of asthma in young adults who had RSV in early life.	1	11	NA

73	Zomer-Kooijker et al. 2014	Netherlands	Prospective multicentre study	None	2003-2005 2006-2007	Birth cohort of healthy term infants followed through the first year of life	NR	Confirmed RSV infection	2133	M 55.6%	NR	26 infants were hospitalized for bronchiolitis, of which 18 were RSV+. Median neonatal respiratory system compliance was significantly lower and resistance was higher in RSVH patients compared with non-hospitalized patients. Every 10 mLkPa-1 increase in compliance was associated with 55% less post-RSV wheeze, and each kPaL-1 increase in resistance was associated with 42% more post-RSV wheeze.	This cohort study shows that decreased lung function at birth predisposes infants to severe RSV and post-RSV wheeze.	1	11	NA
74	Zomer-Kooijker et al. 2014	Netherlands	Prospective multicentre study	None	2004-2006 Follow-up 2010-2011	Children <13 months and born in term with RSVH	Preterm infants	Confirmed RSV infection	RSV: 159 Control: 549	RSV: M 54.7% Control: M 48.3%	RSV: 2.0 months	A 3.2-fold increased risk of current wheeze and a 3.1-fold increased risk of current asthma in RSVH patients was recorded compared to non-hospitalized children.	RSVH during infancy is associated with increased risk of wheeze, current asthma, and impaired lung function at age 6.	1	10	NA

* Conference abstract

ARTI: acute respiratory tract infection; BPD: bronchopulmonary dysplasia; CF: cystic fibrosis; CHD: congenital heart disease; CI: confidence interval; CLD: chronic lung disease; CPD: chronic pulmonary disease; DS: Down syndrome; GI: gastrointestinal; GP: general practitioner; hsCHD: hemodynamically significant CHD; IFN: interferon; IG: immunoglobulin; IL: interleukin; IRR: incidence rate ratio; LOS: length of stay; LRTI: lower respiratory tract infection; OR: odds ratio; NA: not available; NR: not reported; QoL: quality of life; RNA: ribonucleic acid; RR: relative risk; RSV: respiratory syncytial virus; RSVH: RSV hospitalization; SNP: single nucleotide polymorphism; wGA: weeks' gestational age