



Supplementary Figure 1 Funnel plot for publication for asthma in children with and without lower respiratory tract infections in infancy. P value = 0.671

Supplementary Table 1 Search strategy in medline (PubMed)

Search	Field	Search terms
#1	Respiratory viruses	HRSV OR RSV OR "human respiratory syncytial virus" OR "respiratory syncytial virus" OR HRSV-A OR HRSV-B OR HMPV OR MPV OR "human metapneumovirus" OR metapneumovirus OR HMPV-A OR HMPV-B OR HAdV OR AdV OR Adenovirus OR Adenovirus Infections, Human OR "Human adenovirus" OR HADV-A OR HADV-B OR HADV-C OR HADV-D OR HADV-E OR HADV-F OR HADV-G OR HBoV OR BoV OR Bocavirus OR Bocavirus Infections, Human OR "Human Bocavirus" OR HCoV OR CoV OR Coronavirus OR Coronavirus Infections, Human OR "Human Coronavirus" OR 229E OR OC43 OR NL63 OR HKU1 OR HCoV-229E OR HCoV-OC43 OR HCoV-NL63 OR HCoV-HKU1 OR HPIV OR PIV OR Parainfluenzavirus OR Parainfluenzavirus Infections, Human OR "Human Parainfluenzavirus" OR PIV-1 OR PIV-2 OR PIV-3 OR PIV-4 OR HPIV-1 OR HPIV-2 OR HPIV-3 OR HPIV-4 OR HEV OR EV OR Enterovirus OR Enterovirus Infections, Human OR "Human Enterovirus" OR HRV OR RV OR Rhinovirus OR Rhinoviruses OR Rhinovirus Infections, Human OR "Human Rhinovirus" OR RV-A OR RV-B OR RV-C OR Influenza OR Inf OR "Influenza virus" OR Influenza, Human OR "Influenza-A virus" OR "Influenza-B virus" OR "Influenza-C virus"
#2	LRTI	bronchiolitis OR "severe acute respiratory infections" OR "severe acute respiratory illness" OR ALRI OR "Acute Lower Respiratory Infections" OR "acute lower respiratory tract infections" OR LRTI OR "Lower

		respiratory tract infections" OR ALRTI OR Croup
#3	Asthma	Asthma OR Asthmatic OR "Atopic asthma" OR "Asthma exacerbation"
#7		#1 AND #2 AND #3

Supplementary Table 2 Items for risk of bias assessment

Newcastle-Ottawa Scale for case cohort studies	One star (1)/No star (0)
Selection	
1) Representativeness of the LRTI cohort	1
2) Selection of the non LRTI cohort	1
3) Ascertainment of LRTI exposition	1
4) Demonstration that asthma was not present at start of study	1
Comparability	
1) Comparability of cohorts on the basis of the design or analysis	2
Outcome	
1) Assessment of asthma	1
2) Was follow-up long enough for asthma to occur	1
3) Adequacy of follow up of cohorts	1
Total score	9
Interpretation of the two risk of bias tools	
6-9: Low risk of bias	
0-5: High risk of bias	

Supplementary Table 3 Main reasons of exclusion of eligible studies

N	Author, Date	Title	Reason of exclusion
1	Amat, 2018	RSV-hRV co-infection is a risk factor for recurrent bronchial obstruction and early sensitization 3 years after bronchiolitis.	Not viral laboratory confirmed LRTI
2	Ardura-Garcia, 2015	Risk factors for acute asthma in tropical America: a case-control study in the City of Esmeraldas, Ecuador.	Not cohort study
3	Bacharier, 2012	Determinants of asthma after severe respiratory syncytial virus bronchiolitis.	No LRTI - group
4	Backman, 2015	Low eosinophils during bronchiolitis in infancy are associated with lower risk of adulthood asthma.	No LRTI - group
5	Backman, 2014	Adults face increased asthma risk after infant RSV bronchiolitis and reduced respiratory health-related quality of life after RSV pneumonia.	Not viral laboratory confirmed LRTI
6	Backman, 2014	Increased asthma risk and impaired quality of life after bronchiolitis or pneumonia in infancy: Asthma Risk After Early Bronchiolitis or Pneumonia	Not viral laboratory confirmed LRTI
7	Balekian, 2017	Cohort Study of Severe Bronchiolitis during Infancy and Risk of Asthma by Age 5 Years.	No LRTI - group
8	Baraldi, 2020	Evidence on the Link between Respiratory Syncytial Virus Infection in Early Life and Chronic Obstructive Lung Diseases.	Review
9	Bergroth, 2020	Rhinovirus Type in Severe Bronchiolitis and the Development of Asthma.	No LRTI - group

10	Biaga, 2020	Rhinovirus Infection in Children with Acute Bronchiolitis and Its Impact on Recurrent Wheezing and Asthma Development.	Review
11	Bisgaard, 2007	Childhood asthma after bacterial colonization of the airway in neonates.	Not cohort study
12	Bizzantino, 2011	Association between human rhinovirus C and severity of acute asthma in children.	Not LRTI
13	Bonnelykke, 2015	Association between respiratory infections in early life and later asthma is independent of virus type.	Not cohort study
14	Broecker, 2020	Detection of respiratory syncytial virus or rhinovirus weeks after hospitalization for bronchiolitis and the risk of recurrent wheezing.	Not cohort study
15	Budakoglu, 2020	Association between respiratory syncytial virus hospitalization in infancy and childhood asthma.	Not viral laboratory confirmed LRTI
16	Calmes, 2021	Asthma and COPD Are Not Risk Factors for ICU Stay and Death in Case of SARS-CoV2 Infection.	Not LRTI
17	Carroll, 2017	Respiratory syncytial virus immunoprophylaxis in high-risk infants and development of childhood asthma.	Not cohort study
18	Cassimos, 2008	Asthma, lung function and sensitization in school children with a history of bronchiolitis.	No LRTI-group
19	Cho, 2016	Association of a PAI-1 Gene Polymorphism and Early Life Infections with Asthma Risk, Exacerbations, and Reduced Lung Function.	Not viral laboratory confirmed LRTI
20	Clark, 2019	Factors Associated With Asthma Diagnosis	No LRTI-

		Within Five Years of a Bronchiolitis Hospitalization: A Retrospective Cohort Study in a High Asthma Prevalence Population.	group
21	Corne, 2002	Frequency, severity, and duration of rhinovirus infections in asthmatic and non-asthmatic individuals: a longitudinal cohort study.	Not cohort study
22	Costa, 2018	Asthma exacerbations in a subtropical area and the role of respiratory viruses: a cross-sectional study.	Not cohort study
23	Da Silva Sena, 2020	Rhinovirus bronchiolitis, maternal asthma, and the development of asthma and lung function impairments.	No LRTI - group
24	Dabaniyasti, 2020	An investigation into respiratory tract viruses in children with acute lower respiratory tract infection or wheezing.	Not cohort study
25	Dawood, 2011	Children with asthma hospitalized with seasonal or pandemic influenza, 2003-2009.	Not cohort study
26	Del Rosal, 2016	Recurrent wheezing and asthma after bocavirus bronchiolitis.	No LRTI - group
27	Delacourt, 2007	(Sequelae of viral lower respiratory tract infections in children).	Review
28	Ding, 2020	Comparison of clinical features of acute lower respiratory tract infections in infants with RSV/HRV infection, and incidences of subsequent wheezing or asthma in childhood.	No LRTI - group
29	Ding, 2020	Clinical characteristics of acute lower respiratory tract infections according to respiratory viruses in hospitalized children without underlying disease during the last 3	No LRTI - group

		years.	
30	Dixon, 2006	Allergic rhinitis and sinusitis in asthma: differential effects on symptoms and pulmonary function.	No data on outcomes
31	Dumas, 2019	Severe bronchiolitis profiles and risk of recurrent wheeze by age 3 years.	No data on outcomes
32	Dumas, 2021	Severe bronchiolitis profiles and risk of asthma development in Finnish children.	No LRTI - group
33	El-Hajje, 2008	The burden of respiratory viral disease in hospitalized children in Paris.	Not cohort study
34	Eriksson, 2000	Wheezing following lower respiratory tract infections with respiratory syncytial virus and influenza A in infancy.	No data on outcomes
35	Everard, 1999	What link between early respiratory viral infections and atopic asthma?	Review
36	Furuta, 2018	Burden of Human Metapneumovirus and Respiratory Syncytial Virus Infections in Asthmatic Children.	No LRTI - group
37	Garcia-Garcia, 2020	Impact of Prematurity and Severe Viral Bronchiolitis on Asthma Development at 6-9 Years.	Not cohort study
38	Goldstein, 2019	Hospitalizations Associated with Respiratory Syncytial Virus and Influenza in Children, Including Children Diagnosed with Asthma.	Not cohort study
39	Gomez, 2004	Respiratory repercussions in adults with a history of infantile bronchiolitis	Not viral laboratory confirmed LRTI
40	Guibas, 2018	Distinction between rhinovirus-induced acute asthma and asthma-augmented influenza	No LRTI - group

		infection.	
41	Gutierrez, 2021	Lower respiratory tract infections in early life are associated with obstructive sleep apnea diagnosis during childhood in a large birth cohort.	No data on outcomes
42	Heinzmann, 2004	Association study suggests opposite effects of polymorphisms within IL8 on bronchial asthma and respiratory syncytial virus bronchiolitis.	Not LRTI
43	Holster, 2018	IL-17A gene polymorphism rs2275913 is associated with the development of asthma after bronchiolitis in infancy.	Not cohort study
44	Hsu, 2021	Early Life Factors Associated with Preschool Wheezing in Preterm Infants.	No LRTI - group
45	Huang, 2000	(A study on the relationship between viral infections and asthma in adults).	Not LRTI
46	Hyvärinen, 2005	Teenage asthma after severe infantile bronchiolitis or pneumonia.	No LRTI - group
47	Hyvärinen, 2005	Teenage asthma after severe early childhood wheezing: an 11-year prospective follow-up	No LRTI - group
48	Iivan, 2013	(Investigation of the presence of human metapneumovirus in patients with chronic obstructive pulmonary disease and asthma and its relationship with the attacks).	No data on outcomes
49	Jalink, 2019	Severe Respiratory Syncytial Virus Infection in Preterm Infants and Later Onset of Asthma.	No LRTI - group
50	James, 2013	Risk of childhood asthma following infant bronchiolitis during the respiratory syncytial virus season.	No LRTI - group
51	Jartti, 2011	Rhinovirus-associated wheeze during infancy and asthma development.	Review

52	Jartti, 2011	Rhinovirus-induced bronchiolitis and asthma development.	Review
53	Jeng, 2015	A Longitudinal Study on Early Hospitalized Airway Infections and Subsequent Childhood Asthma	Not viral laboratory confirmed LRTI
54	Juntti, 2003	Association of an early respiratory syncytial virus infection and atopic allergy	Not cohort study
55	Kava, 1987	Acute respiratory infection, influenza vaccination and airway reactivity in asthma.	Not LRTI
56	Kennedy, 2014	Comparison of viral load in individuals with and without asthma during infections with rhinovirus.	Review
57	Kneyber, 2000	Long-term effects of respiratory syncytial virus (RSV) bronchiolitis in infants and young children: a quantitative review.	Review
58	Koponen, 2012	Preschool asthma after bronchiolitis in infancy.	No LRTI - group
59	Koponen, 2014	Polymorphism of the rs1800896 IL10 promoter gene protects children from post-bronchiolitis asthma.	No LRTI - group
60	Korppi, 2009	Asthma and lung function at school age after bronchiolitis in infancy.	Comment on an article
61	Korppi, 2013	Post-bronchiolitis asthma risk-hospitalized infants need more precise risk definition.	Comment on an article
62	Korppi, 1994	Bronchial Asthma and Hyperreactivity After Early Childhood Bronchiolitis or Pneumonia: An 8-Year Follow-up Study	Not viral laboratory confirmed LRTI

63	Kotaniemi-Syrjänen, 2003	Rhinovirus-induced wheezing in infancy--the first sign of childhood asthma?	No LRTI - group
64	Kusel, 2007	Early-life respiratory viral infections, atopic sensitization, and risk of subsequent development of persistent asthma.	No LRTI - group
65	Lambert, 2018	The role of human rhinovirus (HRV) species on asthma exacerbation severity in children and adolescents.	No LRTI - group
66	Larkin, 2015	Objectives, design and enrollment results from the Infant Susceptibility to Pulmonary Infections and Asthma Following RSV Exposure Study (INSPIRE).	No LRTI - group
67	Larouche, 2000	Asthma and airway hyper-responsiveness in adults who required hospital admission for bronchiolitis in early childhood.	Not viral laboratory confirmed LRTI
68	Lim, 2010	Clinical characteristics of acute lower respiratory tract infections due to 13 respiratory viruses detected by multiplex PCR in children.	No data on outcomes
69	Lin, 2001	Risk factors of wheeze and allergy after lower respiratory tract infections during early childhood.	No LRTI - group
70	Lu, 2016	Predictors of asthma following severe respiratory syncytial virus (RSV) bronchiolitis in early childhood.	No LRTI - group
71	Lukkarinen, 2017	Rhinovirus-induced first wheezing episode predicts atopic but not nonatopic asthma at school age.	No LRTI - group
72	Mak, 2011	Clinical spectrum of human rhinovirus infections in hospitalized Hong Kong	No data on

		children.	outcomes
73	Matsumoto, 1992	(Clinical manifestation and prognosis of respiratory syncytial virus infection in infants).	No LRTI - group
74	McConnochie, 1984	Bronchiolitis as a possible cause of wheezing in childhood: new evidence	Not viral laboratory confirmed LRTI
75	McConnochie, 1985	Predicting clinically significant lower respiratory tract illness in childhood following mild bronchiolitis	Not viral laboratory confirmed LRTI
76	McConnochie, 1989	Wheezing at 8 and 13 years: changing importance of bronchiolitis and passive smoking	Not viral laboratory confirmed LRTI
77	McKenna, 2013	Asthma in patients hospitalized with pandemic influenza A(H1N1)pdm09 virus infection-United States, 2009.	Not cohort study
78	Midulla, 2014	Recurrent wheezing 36 months after bronchiolitis is associated with rhinovirus infections and blood eosinophilia.	No LRTI - group
79	Midulla, 2012	Rhinovirus bronchiolitis and recurrent wheezing: 1-year follow-up.	Not cohort study
80	Mikalsen, 2012	Severe bronchiolitis in infancy: can asthma in adolescence be predicted?	No LRTI - group
81	Mikalsen, 2012	The outcome after severe bronchiolitis is related to gender and virus	Not cohort study
82	Mok, 1982	Outcome of acute lower respiratory tract infection in infants: preliminary report of seven-year follow-up study.	No data on outcomes

83	Mok, 2015	Outcome for acute bronchitis, bronchiolitis, and pneumonia in infancy	Not cohort study
84	Moraes, 2018	Lower respiratory infections in early life are linked to later asthma.	Editorial
85	Morales-Suárez-Varela, 2017	Asthma in older people hospitalized with influenza in Spain: A case-control study.	Not cohort study
86	Moreno-Valencia, 2015	Detection and characterization of respiratory viruses causing acute respiratory illness and asthma exacerbation in children during three different seasons (2011-2014) in Mexico City.	Not cohort study
87	Murray, 1992	Respiratory status and allergy after bronchiolitis	Not viral laboratory confirmed LRTI
88	Nandí-Lozano, 2002	(Acute respiratory infections in children attending a child day care center).	Not cohort study
89	Narita, 2011	Relationship between lower respiratory tract infections caused by respiratory syncytial virus and subsequent development of asthma in Japanese children.	No LRTI - group
90	Nathan, 2014	Clinical risk factors for life-threatening lower respiratory tract infections in children: a retrospective study in an urban city in Malaysia.	No LRTI - group
91	Nhung, 2018	Acute effects of ambient air pollution on lower respiratory infections in Hanoi children: An eight-year time series study.	Not LRTI
92	Nicolai, 1990	Acute viral bronchiolitis in infancy: epidemiology and management.	Review
93	Noble, 1997	Respiratory status and allergy nine to 10 years after acute bronchiolitis	Not viral laboratory

			confirmed LRTI
94	Østergaard, 2012	Childhood asthma in low income countries: an invisible killer?	Review
95	Ozcan, 2011	Evaluation of respiratory viral pathogens in acute asthma exacerbations during childhood.	Not LRTI
96	Panitch, 2007	The relationship between early respiratory viral infections and subsequent wheezing and asthma.	Review
97	Peiris, 2003	Children with respiratory disease associated with metapneumovirus in Hong Kong.	Not cohort study
98	Piedimonte, 2002	Respiratory syncytial virus and subsequent asthma: one step closer to unravelling the Gordian knot?	Editorial
99	Piippo-Savolainen, 2007	Adult asthma after non-respiratory syncytial virus bronchiolitis in infancy: subgroup analysis of the 20-year prospective follow-up study.	No LRTI - group
100	Piippo-Savolainen, 2004	Asthma and Lung Function 20 Years After Wheezing in Infancy: Results From a Prospective Follow-up Study	Not viral laboratory confirmed LRTI
101	Piippo-Savoleinen, 2007	Does blood eosinophilia in wheezing infants predict later asthma? A prospective 18-20-year follow-up.	No LRTI - group
102	Plachco, 2014	The Argentina Premature Asthma and Respiratory Team (APART): objectives, design, and recruitment results of a prospective cohort study of viruses and wheezing in very low birth weight infants.	Not cohort study
103	Poulsen, 2006	Long-term consequences of respiratory	No data

		syncytial virus acute lower respiratory tract infection in early childhood in Guinea-bissau	on outcomes
104	Puthothu, 2009	Association of TNF-alpha with severe respiratory syncytial virus infection and bronchial asthma.	Not LRTI
105	Raita, 2021	Integrated omics endotyping of infants with respiratory syncytial virus bronchiolitis and risk of childhood asthma.	No LRTI - group
106	Reijonen, 1998	One-year follow-up of young children hospitalized for wheezing; the influence of early anti-inflammatory therapy and risk factors for subsequent wheezing and asthma	No LRTI - group
107	Riikonen, 2019	Prospective study confirms that bronchiolitis in early infancy increases the risk of reduced lung function at 10-13 years of age.	Not cohort study
108	Rooney, 1971	The relationship between bronchiolitis and subsequent wheezing.	proved viral No LRTI - group
109	Ruotsalainen, 2013	Adolescent asthma after rhinovirus and respiratory syncytial virus bronchiolitis.	No LRTI - group
110	Ruotsalainen, 2010	Adulthood asthma after wheezing in infancy: a questionnaire study at 27 years of age	Not viral laboratory confirmed LRTI
111	Ruotsalainen, 2012	No association between overweight and asthma or allergy in adolescence after wheezing in infancy	Not cohort study
112	Ruotsalainen, 2021	An increased asthma risk continued until young adulthood after early-childhood hospitalisation for wheezing.	Not viral laboratory confirmed LRTI
113	Santos, 2011	Pneumonia in the first 2 years of life, and	Not viral

		asthma in preschool-age children: Early pneumonia and preschool asthma	laboratory confirmed LRTI
114	Sherter, 1981	The relationship of viral infections to subsequent asthma.	Review
115	Simoës, 1999	Respiratory syncytial virus and subsequent lower respiratory tract infections in developing countries: A new twist to an old virus.	Editorial
116	Simões, 2010	The effect of respiratory syncytial virus on subsequent recurrent wheezing in atopic and nonatopic children.	No LRTI - group
117	Sims, 1981	Atopy does not predispose to RSV bronchiolitis or postbronchiolitic wheezing.	No data on outcomes
118	Sims, 1978	Study of 8-year-old children with a history of respiratory syncytial virus bronchiolitis in infancy.	No data on outcomes
119	Sly, 1989	Childhood asthma following hospitalization with acute viral bronchiolitis in infancy.	No LRTI - group
120	Sly, 1984	Factors predisposing to abnormal pulmonary function after adenovirus type 7 pneumonia	No LRTI - group
121	Sokhandan, 1995	The contribution of respiratory viruses to severe exacerbations of asthma in adults.	Not LRTI
122	Stein, 2008	Early-life viral bronchiolitis in the causal pathway of childhood asthma: is the evidence there yet?	Editorial
123	Stein, 2009	Long-term airway morbidity following viral LRTI in early infancy: recurrent wheezing or asthma?	Review
124	Su, 2020	High correlation between human rhinovirus	Not cohort

		type C and children with asthma study exacerbations in Taiwan.	
125	Takeyama, 2014	Clinical and epidemiologic factors related to subsequent wheezing after virus-induced lower respiratory tract infections in hospitalized pediatric patients younger than 3 years.	No LRTI - group
126	Teeratakulpisarnoc , 2014	Rhinovirus infection in children hospitalized with acute bronchiolitis and its impact on subsequent wheezing or asthma: a comparison of etiologies.	No LRTI - group
127	Torgerson, 2015	Pooled Sequencing of Candidate Genes Implicates Rare Variants in the Development of Asthma Following Severe RSV Bronchiolitis in Infancy.	No LRTI - group
128	Törmänen, 2018	Risk factors for asthma after infant bronchiolitis.	Not viral laboratory confirmed LRTI
129	Turner, 2002	Reduced lung function both before bronchiolitis and at 11 years	Not viral laboratory confirmed LRTI
130	Valkonen, 2009	Recurrent wheezing after respiratory syncytial virus or non-respiratory syncytial virus bronchiolitis in infancy: a 3-year follow-up.	No LRTI - group
131	van Meel, 2020	Airway bacterial carriage and childhood respiratory health: A population-based prospective cohort study.	Not viral laboratory confirmed LRTI

132	Verdan, 2018	Association Between Enterovirus Infection and Asthma in Children: A 16-year Nationwide Population-based Cohort Study.	Not LRTI
133	Wang, 1998	Asthma and respiratory syncytial virus infection in infancy: is there a link?	Review
134	Welliver, 1993	The relationship of RSV-specific immunoglobulin E antibody responses in infancy, recurrent wheezing, and pulmonary function at age 7-8 years.	No LRTI - group
135	Wennergren, 2001	Prediction of outcome after wheezing in infancy.	Review
136	Wennergren, 1992	Characteristics and prognosis of hospital-treated obstructive bronchitis in children aged less than two years.	No LRTI - group
137	Wennergren, 2001	Relationship between respiratory syncytial virus bronchiolitis and future obstructive airway diseases.	Review
138	Wenzel, 2002	Respiratory outcomes in high-risk children 7 to 10 years after prophylaxis with respiratory syncytial virus immune globulin.	No data on outcomes
139	Wickman, 1998	Hospitalization for lower respiratory disease during 20 yrs among under 5 yr old children in Stockholm County: a population based survey.	No LRTI - group
140	Williams, 2005	Human metapneumovirus infection plays an etiologic role in acute asthma exacerbations requiring hospitalization in adults.	No LRTI - group
141	Wohlford, 2020	Differential asthma odds following respiratory infection in children from three minority populations.	Not viral laboratory confirmed LRTI

142	Wu, 2008	Evidence of a causal role of winter virus infection during infancy in early childhood asthma.	No LRTI - group
143	Wu, 2011	Evidence for a causal relationship between respiratory syncytial virus infection and asthma.	Review
144	Yamada, 2010	Creola bodies in infancy with respiratory syncytial virus bronchiolitis predict the development of asthma.	No data on outcomes
145	Zheng, 2018	Epidemiological analysis and follow-up of human rhinovirus infection in children with asthma exacerbation.	No LRTI - group
146	Zhou, 2021	Recurrent Wheezing and Asthma After Respiratory Syncytial Virus Bronchiolitis.	No LRTI - group
147	Zhuo, 2015	Pathogenic analysis of acute lower respiratory infections and its correlation with asthma exacerbations.	No LRTI - group

Supplementary Table 4 Baseline characteristics of studies meeting inclusion criteria

Characteristics	N = 18	%
Year of publication	1982-2018	
Period of LRTI	1967-2005	
Period of interview	1992-2011	
Follow-up duration (yr)	3-18	
Study Design		
Cohort	18	100.0
Sampling		
Non probabilistic	16	88.9
Probabilistic	2	11.1
Sampling method		
Consecutive sampling	16	88.9
Simple random sampling	2	11.1
Number of sites		
Monocenter	16	88.9
Multicenter	2	11.1
Timing of exposure collection		
Prospectively	17	94.4
Retrospectively	1	5.6
Countries		
Chile	1	5.6
Denmark	1	5.6
Finland	5	27.8
Netherlands	1	5.6
Norway	1	5.6
Spain	2	11.1
Sweden	4	22.2
United Kingdom	2	11.1

United States of America	1	5.6
WHO Region		
America	2	11.1
Europe	16	88.9
UNSD Region		
Northern America	1	5.6
Northern Europe	13	72.2
South America	1	5.6
Southern Europe	2	11.1
Western Europe	1	5.6
Country income level		
High-income economies	18	100.0
Age range at recruitment		
< 1 year	9	50.0
< 2 years	7	38.9
< 6 months	1	5.6
< 9 months	1	5.6
Age range at interview		
10-15 years	1	5.6
15-20 years	5	27.8
2-5 years	5	27.8
5-10 years	7	38.9
Hospitalization LRTI +		
Hospitalized	18	100.0
Hospitalization LRTI -		
Ambulatory	9	50.0
Hospitalized	4	22.2
Unclear/Not reported	5	27.8
First episode of LRTI		
No	4	22.2
Unclear/Not reported	3	16.7

Yes	11	61.1
Virus screened for LRTI +		
Human Metapneumovirus (HMPV)	1	5.6
Human Parainfluenza Virus (HPIV),	1	5.6
Human Adenovirus (HAdV), Influenza Virus		
Human Respiratory Syncytial Virus (HRSV)	15	83.3
Rhinovirus (RV)	1	5.6
Sample types		
Nasopharyngeal	9	50.0
Unclear/ Not reported	9	50.0
Detection assays		
Classical RT-PCR	3	16.7
Classical RT-PCR, Immunoflorescent assay	3	16.7
Culture, Immunoflorescent assay	1	5.6
Culture, rapid antigen	1	5.6
ELISA	2	11.1
Immunoflorescent assay	2	11.1
Immunoflorescent assay, Enzyme immunoassay	1	5.6
Unclear/Not reported	5	27.8
Type of LRTI		
Bronchiolitis	15	83.3
Bronchiolitis, Bronchitis, Pneumonia	1	5.6
Bronchiolitis, Pneumonia	1	5.6
LRTI not specified	1	5.6
Type of asthma		
Current asthma	7	38.9
Current medication for asthma	1	5.6
Doctor-diagnosed asthma	10	55.6
Current asthma	8	25.0

Current medication for asthma	4	12.5
Doctor-diagnosed asthma	10	31.3
Night cough	1	3.1
Prolonged cough	1	3.1
Use of inhaled steroid	3	9.4

Supplementary Table 5 Individual characteristics of included studies

Period of interview	Follow-up duration (Years)	Age range at recruitment	Age range at interview	Hospitalization LRTI Pos	Hospitalization LRTI Neg	First episode of LRTI	Virus screened for LRTI Pos	Sample types	Detection assays	Pairing	Type of LRTI	Type of asthma
2010	18	< 2 years	2 15-20 years	Hospitalized	Ambulatory	No	Human Parainfluenza Virus, Human Adenovirus, Influenza Virus	Nasopharyngeal	Classical RT-PCR	Age, Gender	Bronchiolitis	Current asthma
2010	18	< 2 years	2 15-20 years	Hospitalized	Ambulatory	No	Human Respiratory Syncytial Virus	Nasopharyngeal	Classical RT-PCR	Age, Gender	Bronchiolitis	Current asthma
2010	18	< 2 years	2 15-20 years	Hospitalized	Ambulatory	No	Rhinoviruses	Nasopharyngeal	Classical RT-PCR	Age, Gender	Bronchiolitis	Current asthma
Unclear/Not reported	3	< 9 months	9 2-5 years	Hospitalized	Ambulatory	Unclear/Not reported	Human Respiratory Syncytial	Unclear/Not reported	Immunofluorescent assay	Unclear/Not reported	Bronchiolitis	Doctor diagnosed

								Virus					asthma
2000-2004	7	< year	1	5-10 years	Hospitalized	Ambulatory	No	Human Respiratory Syncytial Virus	Nasopharyngeal	Immunofluorescent assay, Enzyme immunoassay	Age	Bronchiolitis	Current asthma
Oct/2005-Dec/2005	5	< years	2	2-5 years	Hospitalized	Hospitalized	Yes	Human Metapneumovirus	Unclear/Not reported	Classical RT-PCR, Immunofluorescent assay	Unclear/Not reported	Bronchiolitis	Doctor diagnosed asthma
Oct/2005-Dec/2005	5	< years	2	2-5 years	Hospitalized	Hospitalized	Yes	Human Respiratory Syncytial Virus	Unclear/Not reported	Classical RT-PCR, Immunofluorescent assay	Unclear/Not reported	Bronchiolitis	Doctor diagnosed asthma
1998-1999	7	< year	1	5-10 years	Hospitalized	Unclear/Not reported	Yes	Human Respiratory Syncytial Virus	Nasopharyngeal	Culture, Immunofluorescent assay	Unclear/Not reported	Bronchiolitis	Doctor diagnosed asthma
2000	8	< years	2	15-20 years	Hospitalized	Unclear/Not reported	Yes	Human Respiratory Syncytial	Unclear/Not reported	Unclear/Not reported	Unclear/Not reported	Bronchiolitis, Pneumonia	Doctor diagnosed

								Virus						asthma
Unclear/Not reported	7.6	< 1 year	1	5-10 years	Hospitalized	Ambulatory	Yes	Human Respiratory Syncytial Virus	Unclear/Not reported	Unclear/Not reported	Age, Gender, Place of residence, Geographical background (rural, urban or rural-urban), monozygotic twin pairs	Bronchiolitis	Current asthma	
Unclear/Not reported	10	< 1 year	1	5-10 years	Hospitalized	Ambulatory	Yes	Human Respiratory Syncytial Virus	Unclear/Not reported	Unclear/Not reported	Age, Gender, social class	Bronchitis, Pneumonia	Current medication for asthma	
Unclear/Not reported	13	< 1 year	1	10-15 years	Hospitalized	Unclear/Not reported	Unclear/Not reported	Human Respiratory Syncytial Virus	Unclear/Not reported	Unclear/Not reported	Unclear/Not reported	Bronchiolitis	Doctor diagnosed asthma	

2007-2008	18	< year	1	15-20 years	Hospitalized	Ambulatory	Unclear/Not reported	Human Respiratory Syncytial Virus	Unclear/Not reported	Unclear/Not reported	Age, Gender, Recruitment hospital	Bronchitis	Current asthma
Unclear/Not reported	7	< year	1	5-10 years	Hospitalized	Hospitalized	Yes	Human Respiratory Syncytial Virus	Nasopharyngeal	ELISA	Age, Gender, Geographical background (rural, urban or rural-urban)	Bronchitis	Doctor diagnosed asthma
Unclear/Not reported	3	< year	1	2-5 years	Hospitalized	Hospitalized	Yes	Human Respiratory Syncytial Virus	Nasopharyngeal	ELISA	Age, Geographical background (rural, urban or rural-urban)	Bronchitis	Doctor diagnosed asthma
Sep/1999-Sep/2001	5	< years	2	5-10 years	Hospitalized	Unclear/Not reported	Yes	Human Respiratory Syncytial Virus	Unclear/Not reported	Culture, rapid antigen	Age, Place of residence, same season	LRTI not specified	Doctor diagnosed asthma
1992	3	< month	6	2-5 years	Hospitalized	Unclear/Not	Yes	Human Respirator	Nasopharyngeal	Immunofluorescent	Age	Bronchitis	Current

		hs				reported		y		assay			asthma
Apr/2010- Nov/2011	10	< 1 year	5-10 years	Hospitalized	Ambulatory	Yes	Human Respiratory Syncytial Virus	Nasopharyngeal	Classical RT-PCR, Immunofluorescent assay	Unclear/Not reported	Bronchitis	Doctor diagnosed asthma	

Supplementary Table 6 Risk of bias assessment

Author, Year of publication	Representativeness of the LRTI Pos	Selection of the LRTI	Ascertainment of LRTI	Demonstration that asthma was present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of asthma	Was long enough for asthma to occur	Follow-up Adequacy of follow-up of cohorts	Risk of bias
Backman, 2018_HPIV, HAdV, Influenza Virus	1	1	1	1	2	1	1	1	Low risk of bias
Backman, 2018_Human Respiratory Syncytial Virus	1	1	1	1	2	1	1	1	Low risk of bias
Backman, 2018_Rhinoviruses	1	1	1	1	2	1	1	1	Low risk of bias
Bertrand, 2015	0	1	1	1	0	1	1	1	Low risk of bias
Fjaerli, 2005	0	0	1	1	1	1	1	1	Low risk of bias

										of bias
Garcia-Garcia, 2007_Human Metapneumovir us	0	0	1	1	0	1	1	1	1	High risk of bias
Garcia-Garcia, 2007_Human Respiratory Syncytial Virus	0	0	1	1	0	1	1	1	1	High risk of bias
Henderson, 2005	0	0	1	1	0	1	1	1	1	High risk of bias
Korppi, 2004	1	1	1	0	0	1	1	1	1	Low risk of bias
Poorisrisak, 2010	1	1	1	1	2	1	1	1	1	Low risk of bias
Pullan, 1982	1	1	1	1	2	1	1	1	1	Low risk of bias
Sigurs, 2005	0	0	1	1	0	1	1	1	1	High risk of

										bias
										Low risk
Sigurs, 2010	0	1	1	1	2	1	1	1	1	of bias
										Low risk
Sigurs, 2000	1	1	1	1	2	1	1	1	1	of bias
										Low risk
Sigurs, 1995	1	1	1	1	2	1	1	1	1	of bias
										Low risk
Singleton, 2003	1	1	1	1	2	1	1	1	0	of bias
Strannegård,										Low risk
1997	1	1	1	1	1	1	1	1	1	of bias
Zomer-										Low risk
Kooijker, 2014	0	1	1	1	0	1	1	1	1	of bias

Supplementary Table 7 P value of Khi-2 and Fisher exact tests for qualitative confounding factors

Author, yr	Qualitative confounding factor	Data extracted from included studies	Number of LRTI with confounding factors	Total number of LRTI +	Total number of LRTI	Total number of LRTI-with confounding factors	Results from this study	P-value Fisher exact test	Status
		<u>Total number of LRTI +</u>					<u>P-value</u>		
		of LRTI +	g factors				Khi-2 test		
Bertrand , 2015	Atopy in parents	14	7	5	2	1	1		Symmetric
Bertrand , 2015	Male gender	14	6	5	3	0.891	0.628		Symmetric
Fjaerli, 2005	Current allergy	35	16	64	33	0.729	0.675		Symmetric
Fjaerli, 2005	Current eczema	35	14	64	28	0.882	0.832		Symmetric
Fjaerli, 2005	Male gender	35	20	64	36	1	1		Symmetric
Fjaerli, 2005	Parental smoking	35	19	64	28	0.428	0.4		Symmetric
Fjaerli, 2005	Siblings in	35	11	64	26	0.492	0.394		Symmetric

2005	the house									
Garcia-	Asthma	in	23	3	30	4	1	1	Symmetric	
Garcia,	Father									
2007										
Garcia-	Asthma	in	32	5	30	4	1	1	Symmetric	
Garcia,	Father									
2007										
Garcia-	Asthma	in	23	6	30	6	0.846	0.743	Symmetric	
Garcia,	Mother									
2007										
Garcia-	Asthma	in	32	6	30	6	1	1	Symmetric	
Garcia,	Mother									
2007										
Garcia-	Asthma	in	23	8	30	4	0.129	0.098	Symmetric	
Garcia,	Siblings									
2007										
Garcia-	Asthma	in	32	5	30	4	1	1	Symmetric	
Garcia,	Siblings									
2007										
Garcia-	Atopy	in	23	6	30	5	0.62	0.501	Symmetric	

Garcia, 2007	Father									
Garcia- Garcia, 2007	Atopy Father	in 32	4	30	5	0.917	0.728	Symmetric		
Garcia- Garcia, 2007	Atopy Mother	in 23	7	30	6	0.58	0.522	Symmetric		
Garcia- Garcia, 2007	Atopy Mother	in 32	13	30	6	0.138	0.102	Symmetric		
Garcia- Garcia, 2007	Atopy Siblings	in 23	6	30	3	0.239	0.154	Symmetric		
Garcia- Garcia, 2007	Atopy Siblings	in 32	11	30	3	0.047	0.033	Asymmetric		
Garcia- Garcia, 2007	Father smoking	23	8	30	10	1	1	Symmetric		

Garcia- Garcia, 2007	Father smoking	32	18	30	10	0.12	0.081	Symmetric
Garcia- Garcia, 2007	Male gender	23	14	30	13	0.323	0.271	Symmetric
Garcia- Garcia, 2007	Male gender	32	17	30	13	0.605	0.459	Symmetric
Garcia- Garcia, 2007	Mother smoking	23	7	30	12	0.667	0.569	Symmetric
Garcia- Garcia, 2007	Mother smoking	32	21	30	12	0.077	0.074	Symmetric
Garcia- Garcia, 2007	Pets at home	23	7	30	13	0.5	0.4	Symmetric
Garcia- Garcia,	Pets at home	32	8	30	13	0.209	0.18	Symmetric

2007									
Garcia- Garcia, 2007	Prematurity	23	9	30	3	0.029	0.019	Asymmetric	
Garcia- Garcia, 2007	Prematurity	32	6	30	3	0.537	0.475	Symmetric	
Poorisris ak, 2010	History of atopic dermatitis	37	11.1	37	9.99	0.977	1	Symmetric	
Poorisris ak, 2010	Positive airway responsiveness	37	6.29	37	5.18	0.972	1	Symmetric	
Poorisris ak, 2010	Positive skin prick test	37	2.22	37	5.18	0.448	0.43	Symmetric	
Poorisris ak, 2010	Wheeze the first 5 y of life	37	16.28	37	14.43	0.841	0.813	Symmetric	
Pullan, 1982	Father smoking,	130	73	111	45	0.022	0.02	Asymmetric	

	years before								
Pullan, 1982	Father smoking, time of study	130	66	111	45	0.145	0.121	Symmetric	
Pullan, 1982	Mother smoking, 10 years before	130	68	111	46	0.12	0.095	Symmetric	
Pullan, 1982	Mother smoking, time of study	130	68	111	40	0.016	0.014	Asymmetric	
Sigurs, 1995	Asthma in parents	47	0	93	3	0.531	0.551	Symmetric	
Sigurs, 1995	Atopy in parents	47	9	93	18	1	1	Symmetric	
Sigurs, 1995	Family smoking	47	21	93	42	1	1	Symmetric	
Sigurs, 1995	Male gender	47	21	93	42	1	1	Symmetric	
Sigurs, 1995	Pets at home	47	12	93	36	0.173	0.135	Symmetric	

Sigurs, 1995	Single heredity for asthma	47	11	93	19	0.852	0.67	Symmetric
Sigurs, 1995	Single heredity for atopy	47	18	93	34	0.987	0.855	Symmetric
Sigurs, 2000	Asthma in parents	47	16	93	19	0.121	0.099	Symmetric
Sigurs, 2000	Atopy in parents	47	29	93	45	0.19	0.154	Symmetric
Sigurs, 2000	Family smoking	47	20	93	36	0.798	0.716	Symmetric
Sigurs, 2000	Heredity for asthma	47	21	93	27	0.098	0.089	Symmetric
Sigurs, 2000	Heredity for atopy	47	33	93	60	0.628	0.572	Symmetric
Sigurs, 2000	Male gender	47	21	93	42	1	1	Symmetric
Sigurs, 2000	Pets at home	47	21	93	41	1	1	Symmetric

Sigurs, 2005	Asthma parents	in 46	17	92	25	0.327	0.246	Symmetric
Sigurs, 2005	Atopy parents	in 46	28	92	50	0.585	0.585	Symmetric
Sigurs, 2005	Family history of asthma	46	23	92	32	0.124	0.099	Symmetric
Sigurs, 2005	Family history of atopy	46	34	92	68	1	1	Symmetric
Sigurs, 2005	Family smoking	46	16	92	39	0.499	0.462	Symmetric
Sigurs, 2005	Pets at home	46	29	92	68	0.263	0.236	Symmetric
Sigurs, 2010	Asthma parents	in 46	18	92	25	0.217	0.175	Symmetric
Sigurs, 2010	Atopy parents	in 46	30	92	52	0.426	0.362	Symmetric
Sigurs, 2010	Pets at home	46	24	92	56	0.428	0.364	Symmetric

Sigurs, 2010	Smoke exposure	45	19	92	40	1	1	Symmetric
Singleton, 2003	Male gender	95	53	113	57	0.529	0.487	Symmetric
Singleton, 2003	Prematurity	95	13	113	3	0.007	0.004	Asymmetric
Singleton, 2003	Running water	95	39	113	53	0.48	0.405	Symmetric
Singleton, 2003	Smoke exposure	95	45	113	50	0.756	0.677	Symmetric
Stranneg ård, 1997	Family history of asthma	47	0	93	3	0.531	0.551	Symmetric
Stranneg ård, 1997	Family history of atopy	47	9	93	17	1	1	Symmetric
Zomer- Kooijker, 2014	Atopy in Mother	154	66	466	224	0.303	0.266	Symmetric
Zomer-	Day care	155	52	515	227	0.025	0.02	Asymmetric

Kooijker, attendance 2014									
Zomer- Kooijker, 2014	Male gender	159	87	549	265	0.18	0.177	Symmetric	
Zomer- Kooijker, 2014	Pets at home	154	79	475	274	0.196	0.191	Symmetric	
Zomer- Kooijker, 2014	Siblings in the house	155	134	548	297	0	0	Asymmetric	
Zomer- Kooijker, 2014	Smoke exposure	159	42	451	126	0.79	0.757	Symmetric	
Zomer- Kooijker, 2014	Smoking during pregnancy	155	27	548	26	0	0	Asymmetric	

Supplementary Table 8 P value of student test for quantitative confounding factors

Author, year	Quantitative confounding factors	Data extracted from included studies						Results from this study	
		Total number of LRTI +	Mean for LRTI +	SD for LRTI +	Total number of LRTI -	Mean for LRTI -	SD for LRTI -	P-value for Student Test with Unequal Variance	Status
Bertrand , 2015	Age at interview (Years)	14	2.6	2.6	5	2.1	1.4	0.301	Symmetric
Garcia-Garcia, 2007	Age at recruitment (months)	23	3.7	0.92	30	3.9	0.61	0.187	Symmetric
Garcia-Garcia, 2007	Age at recruitment (months)	32	4.03	0.65	30	3.9	0.61	0.21	Symmetric
Sigurs, 1995	Birth weight (grams)	47	3314	556	93	3520	657	0.027	Asymmetric
Sigurs, 1995	Gestational age (weeks)	47	38.9	2	93	39.8	1.6	0.004	Asymmetric
Sigurs, 1995	Number of siblings	47	1.3	0.9	93	1.1	1	0.117	Symmetric
Sigurs, 1995	Weight at interview (Kg)	47	15.6	1.8	93	15.4	1.8	0.268	Symmetric
Sigurs, 2000	Height at interview (cm)	47	126	6.58	93	127	5.22	0.183	Symmetric
Sigurs, 2000	Number of siblings	47	1.8	0.97	93	1.78	1.1	0.456	Symmetric
Sigurs, 2000	Weight at interview (Kg)	47	27	4.63	93	27.1	4.21	0.451	Symmetric
Sigurs, 2005	Height at interview (cm)	46	160.3	8.8	92	162.3	8.3	0.102	Symmetric
Sigurs, 2005	Weight at interview (Kg)	46	52.2	10.6	92	52.9	11.2	0.36	Symmetric

Sigurs, 2010	Height at interview (cm)	46	174	10	92	174	10	0.5	Symmetric
Sigurs, 2010	Weight at interview (Kg)	46	65	12	92	70	13	0.014	Asymmetric
Zomer-Kooijker, 2014	Age at interview (Years)	159	5.9	0.4	549	6.1	1.9	0.046	Asymmetric
Zomer-Kooijker, 2014	Birth weight (grams)	159	3416.7	374.1	549	3559.0	446.0	0	Asymmetric
Zomer-Kooijker, 2014	Gestational age (weeks)	159	39.9	1.2	549	40.0	1.3	0.115	Symmetric
Zomer-Kooijker, 2014	Height at age 6 (cm)	159	118.8	9.8	549	118.1	5.6	0.207	Symmetric
Zomer-Kooijker, 2014	Weight at age 6 (Kg)	159	21.7	4.5	549	21.8	3.2	0.397	Symmetric

Supplementary Table 9 Subgroup analyses of asthma in children with viral lower respiratory tract infection in infancy and control without respiratory diseases

	OR (95%CI)	95% Prediction interval	N Stu dies	N LRTI cases	N contr ols	H (95%CI)	I² (95%CI)	P heterog eneity	P-value subgroup difference
Sampling									0.048
Non probabilistic	4.5 (3-6.8)	(1.2-17)	16	851	9572	1.5 (1.2-2)	58.1 (27.1-75.9)	0.002	
Probabilistic	12.5 (4.9-31.9)	NA	2	55	60	1	0	0.741	
Timing of exposure collection									0.104
Prospectively	5.3 (3.5-8.2)	(1.3-22.3)	17	871	9568	1.6 (1.2-2)	59.3 (30.6-76.1)	0.001	
Retrospectively	2.3 (0.9-5.8)	NA	1	35	64	NA	NA	1	
Countries									< 0.001
Chile	1.1 (0.1-13.8)	NA	1	14	5	NA	NA	1	
Denmark	1.2 (0.4-4)	NA	1	37	37	NA	NA	1	
Finland	6.7 (3.3-13.7)	(1.1-42.2)	5	122	317	1.3 (1-2.2)	43.3 (0-79.2)	0.133	
Netherlands	5.2 (3.4-8)	NA	1	158	517	NA	NA	1	
Norway	2.3 (0.9-5.8)	NA	1	35	64	NA	NA	1	
Spain	12.5 (4.9-31.9)	NA	2	55	60	1	0	0.741	

interview								
2-5 years	12.4 (5.9-26.4)	(3.7-42.3)	5	163	249	1.1 (1-2.4)	16.5 (0-82.6)	0.309
5-10 years	3.1 (2-4.7)	(1-9.2)	7	575	8974	1.6 (1.1-2.4)	61.6 (12.5-83.2)	0.016
10-15 years	11.7 (3.1-43.6)	NA	1	46	92	NA	NA	1
15-20 years	6.1 (3.3-11.2)	(1.6-23.3)	5	122	317	1.3 (1-2)	36.1 (0-76.1)	0.181
Hospitalization LRTI								
–								
Ambulatory	3.9 (2.3-6.6)	(0.9-16.4)	9	460	1006	1.5 (1-2.2)	55.6 (6.2-79)	0.021
Hospitalized	14.2 (6.7-30.1)	(2.8-73.5)	4	149	246	1 (1-2.6)	0 (0-84.7)	0.898
Virus screened for								
LRTI Pos								
Human	14.9 (3.7-58.9)	NA	1	23	30	NA	NA	1
Metapneumovirus								
Human Respiratory	4.2 (2.8-6.3)	(1.2-14.8)	15	857	9482	1.5 (1.2-2)	57.7 (24.9-76.2)	0.003
Syncytial Virus								
Rhinovirus	13.6 (3.5-52.5)	NA	1	14	60	NA	NA	1
Type of LRTI								
Bronchiolitis	6.1 (3.9-9.4)	(1.5-24.2)	15	645	9363	1.6 (1.2-2.1)	58.5 (26.5-76.6)	0.002
LRTI not specified	3.9 (1.8-8.6)	NA	1	95	113	NA	NA	1
Type of asthma								

Current asthma	5.4 (2.7-10.7)	(0.8-35.6)	7	205	464	1.5 (1-2.4)	58.2 (3.4-81.9)	0.026
Current medication for asthma	1.2 (0.4-3.9)	NA	1	130	111	NA	NA	1
Doctor diagnosed asthma	5.3 (3.3-8.6)	(1.4-19.7)	10	571	9057	1.6 (1.1-2.2)	59.3 (18.4-79.7)	0.008
