Online supplementary:

Figure S1: Literature search and study selection flowchart

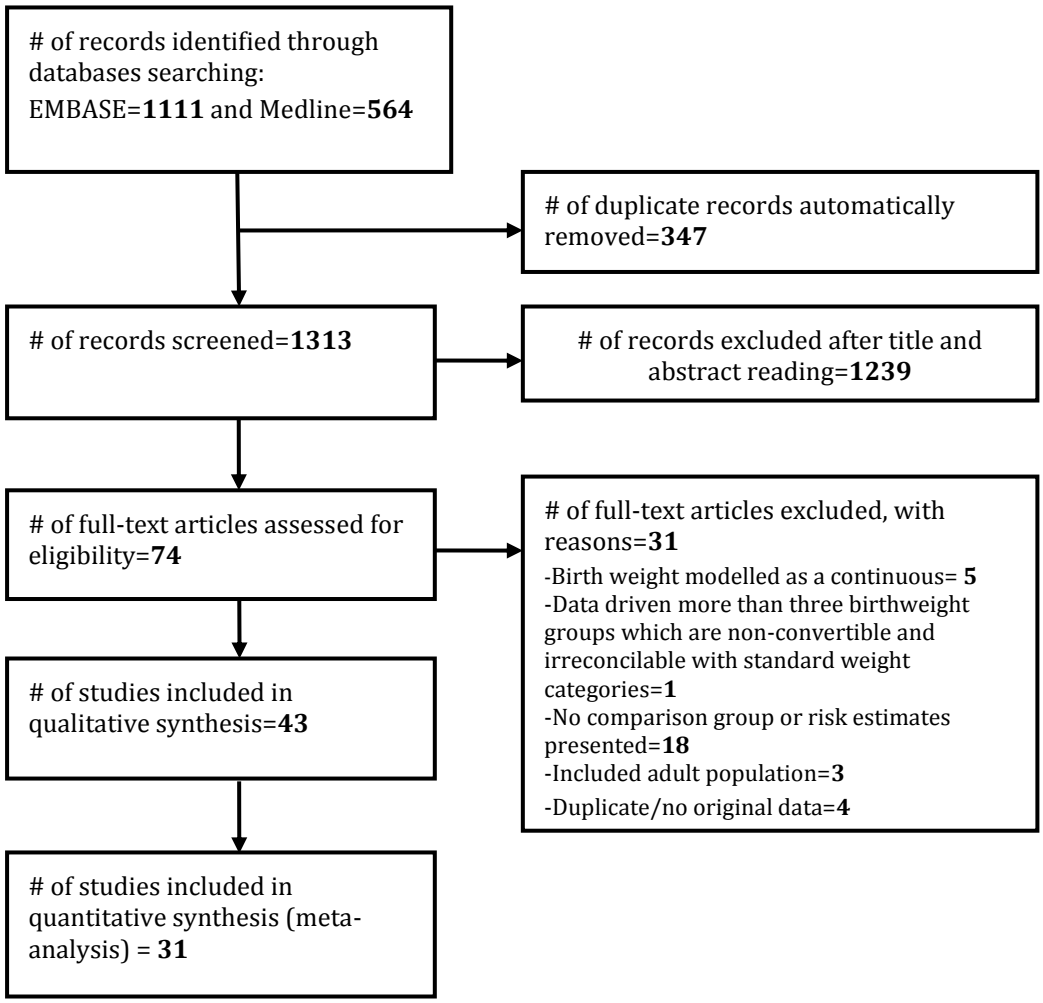


Table S1: Literature search strategies

EMBASE and Medline

Run on	3rd March 2014

1	childhood asthma
2	wheez*
3	wheezing disorders
4	asthm*
5	birthweight
6	low birthweight
7	high birthweight
8	Birth weight
9	low birth weight
10	high birth weight
11	Or/1-4
12	Or/5-10
13	11 and 12
14	limit 13 to English language

Table S2: Characteristics of studies included descriptive analysis

Author , year, region	Study design	Sample size	Participants' characteristics	Outcome terms used	Outcome ascertainment	Exposure ascertainment	Exposure categories
† Gold et al, 1999, USA	RC	498	1 years mixed	Asthma	Parent	e-records	<3.2kg, 3.2-3.8kg, and >3.8kg
† Yuan et al, 2003, Denmark	RC	9,699	1 year mixed	Asthma	e-records	e-records	<3.2kg, 3.2-3.8kg,and >3.8kg
Sin et al, 2004, Canada	RC	83,595	10 years mixed	Asthma	e-records	e-records	<2.5kg, 2.5-4.5kg, and >4.5kg
Mai et al, 2007, Sweden	PC	2,869	4 years mixed	Wheeze	e-records	e-records	<2.9kg, 2.9-4.2kg, and >4.2kg
Garcia-Marcos et al, 2008, Spain	RC	855	6-8 years mixed	Asthma	Parent	No mention	<2.0kg, 2.0-3.5kg , and >3.5kg
Davidson et al, 2010, UK	RC	248,077	2-11 years mixed	Asthma admission	e-records	e-records	<3.0kg, 3.0-4.0kg, and >4.0kg
Jeong et al, 2010, South Korea	PC	414	3 years mixed	Asthma	parent	e-records	<2.8kg, 2.8-3.3kg, and >3.3kg.
† Mogensen et al 2011, Sweden	PC	1784	8-9 years mixed *	Asthma	Parent	e-records	<2.5kg and ≥2.5kg
† Mogensen et al 2011, Sweden	PC	1784	13-14 years mixed *	Asthma	Parent	e-records	<2.5kg and ≥2.5kg
Brew and Marks, 2012, Australia	PC	450	8 years mixed	Asthma	Parent	e-records	2.1-3.27kg, 3.28-3.70kg, 3.71-5.00kg
Lu et al, 2012, Taiwan	PC	74,180	10-17 years mixed	Asthma	Physician	e-records	<3.0 kg, 3.0-4.0kg, and >4.0kg
Mathew et al, 2012, India	RC	859	5-10 years mixed **	Asthma	Parent	Parent	<2.7kg and >=2.7kg
Mathew et al, 2012, India	RC	754	11-15 years mixed**	Asthma	Parent	Parent	<2.7kg and >=2.7kg
Nuolivirta et al,2012, Finland	PC	127	1-2 years mixed	Wheezing	Physician	No mention	<3.0kg, 3.0–4.0kg, and >4.0kg.

PC=prospective cohort; RC=retrospective cohort; CC=case-control

† = birthweight was regrouped

*= the same children but at different ages

**= different children at different ages

Table S3: Descriptive analysis risk estimates for high and low birthweight on asthma and wheezing disorders for studies used non-standard categories

Author and year	Comparison	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Gold et al, 1999	<3.2kg Vs 3.2-3.8kg	1.43 (0.86, 2.39)	
	>3.8kg Vs 3.2-3.8kg	0.61 (0.33, 1.13)	
Yuan et al, 2003	<3.2kg Vs 3.2-3.8kg	1.13 (0.86, 1.49)	
	>3.8kg Vs 3.2-3.8kg	1.00 (0.79, 1.27)	
Sin et al, 2004	<2.5kg Vs 2.5-4.5kg		1.00 (0.90, 1.11)¶
	>4.5kg Vs 2.5-4.5kg		1.16 (1.04, 1.29)¶
Mai et al, 2007	<2.9kg Vs 2.9-4.2kg	1.70 (1.19, 2.43)	1.47 (0.87, 2.49)
	>4.2kg Vs 2.9-4.2kg	1.27 (0.86, 1.87)	1.18 (0.74, 1.87)
Garcia-Marcos et al, 2008	<2.0kg Vs 2.0-3.5kg	0.52 (0.12, 2.22)	
	>3.5kg Vs 2.0-3.5kg	1.04 (0.65, 1.69)	
Davidson et al, 2010	<3.0kg Vs 3.0-4.0kg	1.17 (1.08, 1.26)	1.21 (1.13, 1.30)
	>4.0kg Vs 3.0-4.0kg	1.10 (0.97, 1.24)	1.05 (0.93, 1.18)
Jeong et al, 2010	<2.8kg Vs 2.8-3.3kg	0.29 (0.09, 0.92)	0.56 (0.16, 1.96)
	>3.3kg Vs 2.8-3.3kg	0.45 (0.17, 1.22)	0.29 (0.05, 1.59)
Mogensen et al, 2011 *	<2.5kg Vs ≥2.5kg	1.17 (0.79, 1.75)	
Mogensen et al, 2011 *	<2.5kg Vs ≥2.5kg	1.04 (0.73, 1.49)	
Brew and Marks, 2012	<3.27 kg Vs 3.28-3.7kg		1.95 (1.07, 3.54)
	>3.71kg Vs 3.28-3.7kg		0.91 (0.47, 1.75)
Lu et al, 2012	<3.0 kg Vs 3.0-4.0kg	1.94 (1.78, 2.11)	1.24 (1.16, 1.33)
	>4.0kg Vs 3.0-4.0kg	1.54 (1.33, 1.77)	0.93 (0.82, 1.06)
Mathew et al, 2012 **	<2.7kg Vs >=2.7kg	1.88 (1.08, 3.29)	1.79 (1.08, 2.98)
Mathew et al, 2012 **	<2.7kg Vs >=2.7kg	1.51 (0.94,2.42)	1.09 (0.54, 2.20)
Nuolivirta et al,2012	<3.0kg Vs 3.0–4.0kg	0.65 (0.13, 3.16)	
	>4.0kg Vs 3.0–4.0kg	2.95 (1.04, 8.37)	

¶=Relative risk

*= the same children but at different ages

**= different children at different ages

Table S4: Risk of bias assessment table using Newcastle-Ottawa quality assessment scale for the studies included in the systematic review and meta-analysis

Author , year, region	Study name	Selection [a]	Comparability [b]	Outcome [c]
Seidman et al, 1991, Israel	Is low birth weight a risk factor for asthma during adolescence?	★★	★★	★★★
Lewis et al, 1995, UK	Prospective study of risk factors for early and persistent wheezing in childhood	★★	★★	★★
Lewis et al, 1996, UK	Study of the aetiology of wheezing illness at age 16 in two national British birth cohorts	★★	★★	★
Schaubel et al, 1996, Canada	Neonatal characteristics as risk factors for preschool asthma	★★★	★	★★★
Sears et al, 1996, New Zealnd	Parental and neonatal risk factors for atopy, airway hyper-responsiveness, and asthma	★★	★★	★★★
Fergusson et al, 1997, New Zealand	Perinatal factors and atopic disease in childhood	★★★	★★	★★
Lilljeqvist et al, 1997, Norway	Low birthweight, environmental tobacco smoke, and air pollution: Risk factors for childhood asthma?	★★		★★
Slezak et al, 1998, USA	Asthma prevalence and risk factors in selected Head Start sites in Chicago	★	★★	★
Gold et al, 1999, USA	Predictors of repeated wheeze in the first year of life: the relative roles of cockroach, birth weight, acute lower respiratory illness, and maternal smoking	★★	★★	★
Leadbitter et al, 1999, New Zealand	Relationship between foetal growth and the development of asthma and atopy in childhood	★★	★	★
Rasanen et al,2000, Finland	Perinatal risk factors for asthma in Finnish adolescent twins	★	★★	★
Steffensen et al, 2000, Denmark	Low birth weight and preterm delivery as risk factors for asthma and atopic dermatitis in young adult males	★★★	★★	★★★
Brooks et al, 2001, USA	Impact of low birth weight on early childhood asthma in the United States	★★	★★	★

[a] Stars awarded for representativeness of the low/high birthweight cohort, Selection of the normal birthweight cohort, ascertainment of low/high birthweight and demonstration that asthma and wheezing disorders were not present at start of study. A maximum of 4 stars to be awarded. [b] Stars awarded for adjustment of gender and age, and additional factors. A maximum of 2 stars to be awarded.
[c] Stars awarded for assessment of asthma and wheezing disorders, length of follow-up, and adequacy of follow-up cohorts. A maximum of 3 stars to be awarded

Author , year, region	Study name	Selection [a]	Comparability [b]	Outcome [c]
Ronmark et al, 2002, Sweden	Incidence rates and risk factors for asthma among school children: A 2-year follow-up Report from the Obstructive Lung Disease in Northern Sweden (OLIN) studies	★★★	★	★★
Anand et al, 2003, UK	Lung function and respiratory health in adolescents of very low birth weight	★★	★	★
Yuan et al, 2003, Denmark	Prenatal factors and use of anti-asthma medications in early childhood: A population-based Danish birth cohort study	★★★	★★	★★★
Benicio et al,2004, Brazil	Wheezing conditions in early childhood: prevalence and risk factors in the city of Sao Paulo, Brazil	★★	★★	★★
Bolte et al, 2004, Germany	The relation of markers of foetal growth with asthma, allergies and serum immunoglobulin E levels in children at age 5-7 years	★★	★★	★★
Sin et al, 2004, Canada	The relationship between birth weight and childhood asthma: a population-based cohort study	★★★	★★	★★★
Al-kubaisy et al, 2005, Iraq.	Risk factors for asthma among primary school children in Baghdad, Iraq	★★★		
Bernsen et al, 2005, Netherlands	Perinatal characteristics and obstetric complications as risk factors for asthma, allergy and eczema at the age of 6 years	★★★	★★	★★★
Nepomnyaschy et al, 2006, USA	Low birthweight and asthma among young urban children	★★★	★★	★★
Kiechl-Kohlendorfer et al,2007, Austria	Neonatal characteristics and risk of atopic asthma in schoolchildren: results from a large prospective birth-cohort study	★★	★★	★★
Mai et al, 2007, Sweden	Birth anthropometric measures, body mass index and allergic diseases in a birth cohort study (BAMSE)	★★★	★★	★

[a] Stars awarded for representativeness of the low/high birthweight cohort, Selection of the normal birthweight cohort, ascertainment of low/high birthweight and demonstration that asthma and wheezing disorders were not present at start of study. A maximum of 4 stars to be awarded. [b] Stars awarded for adjustment of gender and age, and additional factors. A maximum of 2 stars to be awarded.
[c] Stars awarded for assessment of asthma and wheezing disorders, length of follow-up, and adequacy of follow-up cohorts. A maximum of 3 stars to be awarded

Garcia-Marcos et al, 2008, Spain	Percent body fat, skinfold thickness or body mass index for defining obesity or overweight, as a risk factor for asthma in schoolchildren: Which one to use in epidemiological studies?	★★	★★	★

Author , year, region	Study name	Selection [a]	Comparability [b]	Outcome [c]
Remes et al, 2008, Finland	High birth weight, asthma and atopy at the age of 16 yr	★★	★★	★
Ortqvist et al, 2009, Sweden	Familial factors do not confound the association between birth weight and childhood asthma	★★	★★	★
Xu et al, 2009, USA	The effects of birthweight and breastfeeding on asthma among children aged 1-5 years	★★	★★	★
Davidson et al, 2010, UK	Influence of maternal and perinatal factors on subsequent hospitalisation for asthma in children: evidence from the Oxford record linkage study	★★	★★	★★★
Jeong et al, 2010, South Korea	Body weight at birth and at age three and respiratory illness in preschool children	★★★	★★	★
Midodzi et al,2010, Canada	Early Life Factors Associated with Incidence of Physician-diagnosed Asthma in Preschool Children: Results from the Canadian Early Childhood Development Cohort Study	★★★★	★★	★★
Bjerg et al, 2011, Sweden	A strong synergism of low birth weight and prenatal smoking on asthma in schoolchildren	★★	★★	★★
Mogensen et al 2011, Sweden	Association between childhood asthma and ADHD symptoms in adolescence – a prospective population-based twin study	★★★		★
Suglia et al, 2011, USA	Asthma and obesity in three-year-old urban children: Role of sex and home environment	★★★	★★	★★
Brew and Marks, 2012, Australia	Perinatal factors and respiratory health in children	★★	★★	★
Lu et al, 2012, Taiwan	Body mass index may modify asthma prevalence among low-birth-weight children	★★★	★★	★★
Mathew et al, 2012, India	Prevalence and risk factors of asthma in school going children in South India	★★	★★	★

[a] Stars awarded for representativeness of the low/high birthweight cohort, Selection of the normal birthweight cohort, ascertainment of low/high birthweight and demonstration that asthma and wheezing disorders were not present at start of study. A maximum of 4 stars to be awarded. [b] Stars awarded for adjustment of gender and age, and additional factors. A maximum of 2 stars to be awarded.

[c] Stars awarded for assessment of asthma and wheezing disorders, length of follow-up, and adequacy of follow-up cohorts. A maximum of 3 stars to be awarded.

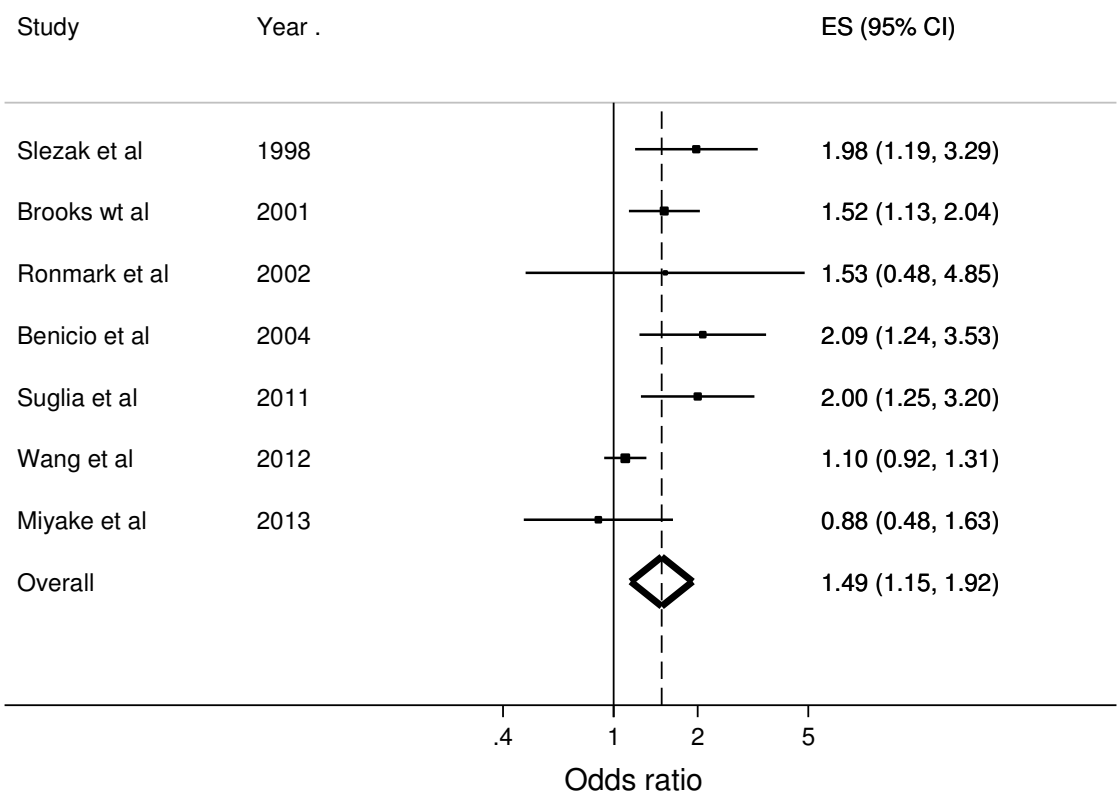
Nuolivirta et al,2012, Finland	Weight gain in infancy and post-bronchiolitis wheezing	★		★★
To et al, 2012, Canada	Is large birth weight associated with asthma risk in early childhood?	★★★	★★	★★★

Author , year, region	Study name	Selection [a]	Comparability [b]	Outcome [c]
Wang et al ,2012, Taiwan	Joint effects of birth outcomes and childhood body mass index on respiratory symptoms	★★★	★★	★★
Kallen et al, 2013, Sweden	Association between preterm birth and intrauterine growth retardation and child asthma	★★★	★★	★★★
Miyake et al, 2013, Japan	Lack of relationship between birth conditions and allergic disorders in Japanese children aged 3 years	★★★	★★	★
Yang et al,2013, USA	Population-based study on association between birth weight and risk of asthma: A propensity score approach	★★★	★★	★★★

[a] Stars awarded for representativeness of the low/high birthweight cohort, Selection of the normal birthweight cohort, ascertainment of low/high birthweight and demonstration that asthma and wheezing disorders were not present at start of study. A maximum of 4 stars to be awarded.[b] Stars awarded for adjustment of gender and age, and additional factors. A maximum of 2 stars to be awarded.

[c] Stars awarded for assessment of asthma and wheezing disorders, length of follow-up, and adequacy of follow-up cohorts. A maximum of 3 stars to be awarded.

Figure S2: Meta-analysis of adjusted ORs of 7 studies that compared the ≥2.5kg (normal) and <2.5kg (low) birthweight categories



Heterogeneity chi-squared = 15 (d.f. = 6, p = 0.02), I^2 = 60% (95% CI: 10% to 82%), and the estimate of between-study variance Tau-squared = 0.06.

Table S5: Meta-regression analysis of 17 studies that presented data on the number of cases and non-cases of asthma in the ≥2.5kg (normal) and <2.5kg (low) birthweight categories.

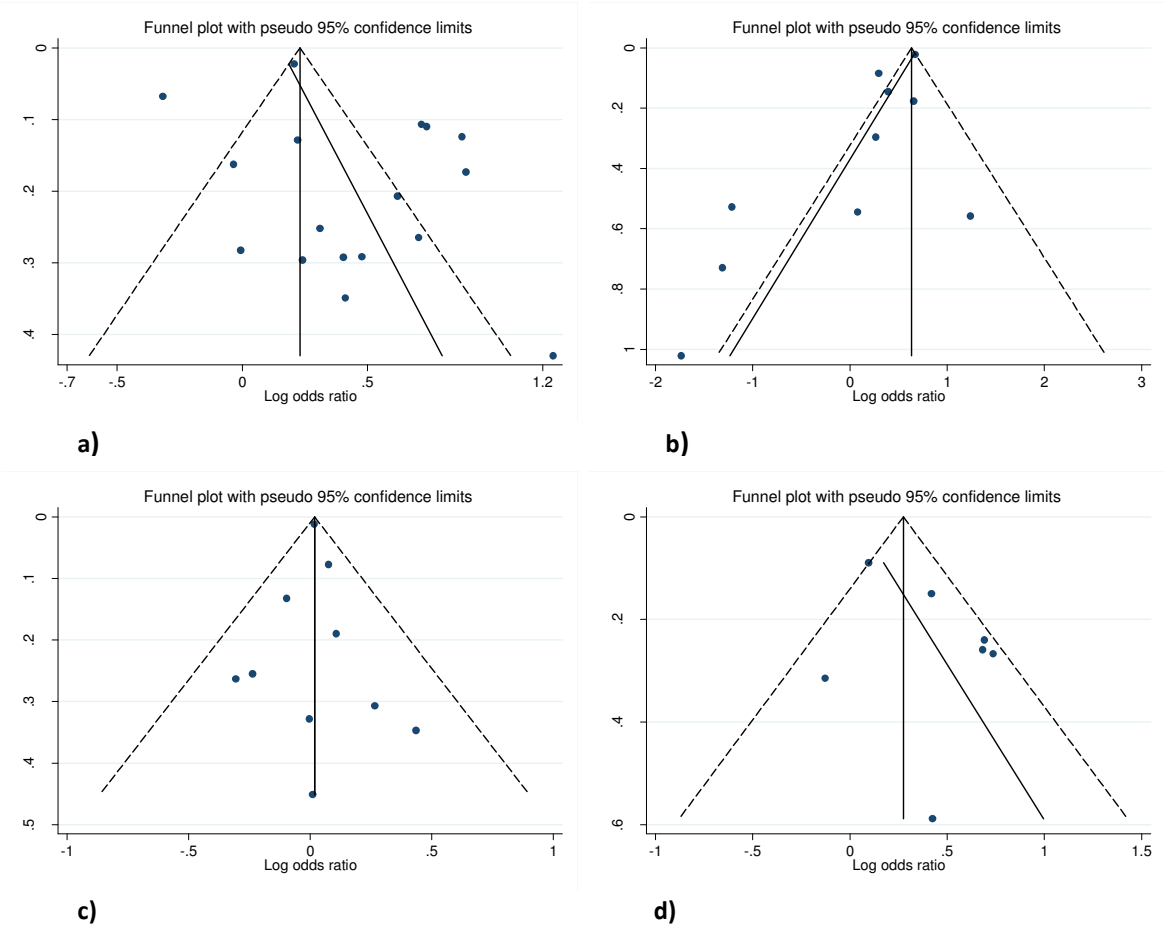
	OR (95% CI)	P-value
Outcome terms used (ref=Asthma)	1.1 (0.75, 1.61)	0.60
Outcome ascertainment (ref=Physician)	0.86 (0.60, 1.23)	0.36
Exposure ascertainment (ref=E-records)	1.1 (0.79, 1.50)	0.54
Age during diagnosis (ref=Five-and-above)	1.27 (0.94 ,1.72)	0.11
Sample size (ref=less than 1000)	0.36 (0.11, 1.21)	0.09
Study period (ref=before 2000)	0.86 (0.48, 1.53)	0.56
Study type (ref=cohort)	2.04 (0.96, 4.36)	0.06
Overall		0.19

Table S6: Meta-regression analysis of 10 studies that presented data on the number of cases and non-cases of asthma in the 2.5-4.0kg (normal) and <2.5kg (low) birthweight categories.

	OR (95% CI)	P-value
Outcome ascertainment (ref=Physician)	2.37 (0.66, 8.57)	0.12
Exposure ascertainment (ref=E-records)	0.64 (0.13, 3.08)	0.44
Age during diagnosis (ref=Five-and-above)	1.69 (0.25 ,11.18)	0.44
Gender (ref=mixed)	3.37 (0.12, 90.9)	0.33
Sample size (ref=less than 1000)	0.99 (0.07, 14.52)	0.99
Study period (ref=before 2000)	1.22 (0.16, 10.16)	0.79
Overall		0.42

Note: The covariate "Diagnosis terms used" was automatically dropped due to collinearity.

Figure S3: Egger's funnel plots of birthweight and wheezing disorder studies



a) <2.5kg (low) versus ≥2.5kg (normal) birthweight **b)** <2.5kg (low) versus 2.5-4.0kg (normal) birthweight **c)** >4.0kg (high) versus 2.5-4.0kg (normal) birthweight **d)** <2.5kg (low) versus ≥2.5kg (normal) birthweight risk estimate funnel plots. Unadjusted risk estimates in a, b, and c, and adjusted risk estimates in d. In all funnel plots: the middle solid line is the summary OR estimate and the two diagonal dotted lines are the 95% confidence limits around the summary OR, and the slant solid lines in figures a, b, d and are the fitted regression lines for Egger's small-study effect test. Note that the fitted regression line in c is exactly aligned to and obscured by the middle solid line.