Supplementary table 2. Risk Factor Weighting Tables

Notes on this table.

- The study data are grouped by risk factors, so studies with multiple outcomes appear multiple times.
- Within each risk factor, the studies are listed by study design (so cohort studies; case control; cross-sectional), then by quality score and then by size.
- The results are colour coded according to the key below.
- Confidence intervals, odds ratios and P values are as reported in terms of number of significant figures or absolute value or "NS" – not significant.

Risk factor affects risk of exacerbation (either positively or negatively.	
Risk factor null effect.	
Complex or difficult to interpret study – see the comments column. Unexpected results (typically confounded by severity or indication) are indicated in this way.	

Abbreviations used in this table

d	day	ED	Emergency Department	ATAQ	Asthma Therapy Assessment Questionnaire
w	week	FU	Follow up	BMQ	Beliefs about Medicines Questionnaire
m	month				
y	year				
Rx	Therapy	H/O	History of	FEV_1	Forced Expiratory Volume in one second
BD	Bronchodilator	FH	Family History	FVC	Forced Vital Capacity
ICS	Inhaled corticosteroid	AR	Allergic rhinitis	FeNO	Fractional exhaled Nitric Oxide
LABA	Long-acting beta agonist	GORD	Gastro-oesophageal reflux disease	SPT	Skin Prick Test
OCS	Oral corticosteroid course	ETS	Environmental tobacco smoke	BMI	Body mass index
SABA	Short-acting beta agonist				
n	Number of children	NAEPP	National Asthma Education and Prevention Program	PC20	Provocative concentration of methacholine causing a 20% drop in FEV_1
N	Number of centres/sites/schools/practices	NHLBI	National Heart, Lung, and Blood Institute		
x	Number with outcome				
OR	Odds Ratio				
RR	Relative Risk				
GEE	Generalised estimating equations				

Asthma disease status

Previous exacerbation

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Thomas 2005 Cohort, 8/9	UK, n=9,522, General practice, Age 6-15y (mean 10.6y)	OCS use during baseline period (6m)	Hospitalisation	OR	2.24	1.08 to 4.67	No OCS use during baseline period (6mo)	Logistic regression	Multivariable (age, gender, OCS, SABA, dose ICS)	[Reference group assumed - not stated explicitly]
Haselkorn 2009b Cohort, 8/9	US, n=563, Severe/difficult to treat asthma, Age 6-11y	Severe exacerbation in previous 3m	≥1 OCS courses reported during 12m	OR	1.99	1.51 to 2.61	No recent severe exacerbation in previous 3m	Stepwise model	Multivariable (age, sex, race, BMI, allergies, ETS, ICS, control)	TENOR study
Engelkes 2016 Cohort, 7/9	Netherlands, n=14,303, GP records, Age 5-18y	Previous exacerbations	Hospitalisation, ED visit, or OCS course	RR	1.99	1.40 to 2.83	Ref group: no previous exacerbations	Poisson regression	Age, gender	[Model 1]
Tolomeo 2009 Cohort; 7/9	US, n=298, Hospitalised in previous year, Age 2-15y (mean 6.4y) (58% 5+yrs)	Asthma related ED visit in previous 12m	Hospitalisation	OR	3.12	1.12 to 8.33	No asthma related ED visit in previous 12m	Logistic regression	Controlled for 'all variables'	[Likely controlled for age, race, income, sex, insurance, asthma severity]
		Asthma-related ED visit in previous 12m	ED visit	OR	3.32	1.39 to 7.69	No asthma related ED visit in previous 12m	Logistic regression		
Schatz 2003 Cohort, 6/9	US, n=4,197, Age 3-17y (mean age 9.5y (SD 4.1)	Hospitalisation in previous year	Hospitalisation in study year	x/n (%) hospitalised	Hospitalised: 6/57 (10.5%) vs not hospitalised: 50/4140 (1.2%)	P<0.001	No hospitalisation in previous year	Fisher's exact test	'All potential predictors'	
		Hospitalisation in previous year	Hospitalisation in study year	OR	3.37	1.61 to 7.04	No hospitalisation in previous year	Logistic regression		
		ED visits in previous year	Hospitalisation in study year	x/n (%) ED visits	Hospitalised: 10/57 (17.5%) vs Not hospitalised: 23/4140 (6.7%)	P<0.001	No hospitalisation in previous year	Fisher's exact test		
		OCS course in previous year	Hospitalisation in study year	Mean (SD)	Hospitalised: 1.37 (1.68) vs Not hospitalised: 0.55 (0.90)	P<0.001	No hospitalisation in previous year	Wilcoxon rank sum test		

Wu 2011 Cohort, 6/9	US, n=1019, Children Age 5-12y	ED visit or hospitalisation previous 12m	OCS use, ED visit or hospitalisation	Exacerbations in trial year x/n(%)	Prior ED/hospital 197/512 (39%) vs no prior ED/hospital 118/538 (22%)	P<0.0001	Comparison of children with vs without prior event	Multivariate modelling (using GEE)	Age, Use of ICS FEV1/FVC ratio, methacholine response and eosinophil count	CAMP study. Authors give raw beta value as the effect measure
		OCS course in previous 6m			Prior OCS course 154/320 (48%) vs no prior OCS course 159/716 (22%)	P=0.0005				
Zeiger 2012 Cohort, 5/9	US, n=289 Children with severe or difficult-to-treat asthma. Age 6-12y	Exacerbation at baseline	Self-reported (at 3,6 and 12m) hospitalisation, ED visit, or a OCS course	OR	OR 2.94	1.71 to 5.07	No exacerbation at baseline	Multivariable logistic regression	Age groups	Control classified according to NHLBI
Covar 2008 Cohort, 5/9	US, n=285, Mild-moderate persistent asthma Age 6-14y	OCS course in the previous year	OCS use, ED visit or hospitalisation	OR	2.10	1.42 to 3.09	Reference group: no OCS use in the previous year	Multivariate logistic regression (using GEE)	Multivariable	
Forno 2010 Cross-sectional, 7/10	Costa Rica, n=465, Age 6-14y	OCS course in previous year	Hospitalisation or ≥2 ED/urgent care visits in previous year	OR	4.1	2.6 to 6.5	No OCS course in previous year	Multivariate stepwise logistic regression	Age, sex, lung function, SABA, specific IgE, parental education	[Data from 'Model 1']
Quezada 2016 Cross-sectional, 6/10	US, n=200, Exacerbators:110 Non-Exacerbators:185 Age 6-17y (mean 11yrs)	OCS course in previous year	OCS use or urgent care during 24w study	x/n (%)	Exacerbators: 80% (88/110) Non-Exacerbators: 61% (112/185)	P<0.001	No OCS course in previous year	Fisher test	None	Recruited to a trial of proton-pump inhibitors for asthma
		Unscheduled health care visits for asthma in past year	OCS use or urgent care during 24w study	x/n (%)	Exacerbators: 91/110 (83%) Non-Exacerbators: 127/185 (69%)	P<0.01	No unscheduled health care visits for asthma in past year			
Butz 2000 Cross-sectional, 4/10	US, n=686, Inner city, 99% African American, Age 5-12y	Nebuliser use for relief of acute symptoms ≥1d/m in previous 6m)	Hospitalised in previous 6m	x/n(%)	Nebuliser 60/231 (26%) vs no nebuliser 41/455 (9.0%)	P=0.001	No nebuliser use for relief of acute symptoms ≥1d/m in previous 6m)	Chi^2 test	None	
			ED visit ever	x/n (%)	Nebuliser 171/231 (74%) vs no nebuliser 238/455 (52%)	P=0.001				
			OCS course in previous 12m	Mean (SD)	Nebuliser use 3.8 (9.4) Vs no nebuliser 1.3 (6.0)	P<0.001				

Persistent symptoms (Asthma severity/symptom control)

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Robroeks 2012 Cohort study, 9/9	The Netherlands, n=38, Children with severe asthma, Age 6-16y: (mean 10.7y (SD 0.4))	Asthma control score (as used in AIRE survey)	Severe (reduced FEV_1, needing OCS, admitted) Moderate (symptoms but no OCS)	ß: regression coefficient	ß=0.04 SE: 0.02	P=0.007	Asthma control score: continuous variable	Multivariate Cox regression analysis of the time until exacerbation	Multivariable (lung function, control, FeNO)	Intensively monitored cohort.
Haselkorn 2009b Cohort, 8/9	US; n=563, Severe/difficult to treat asthma, Age 6-11y	Very poorly controlled asthma	≥1 OCS courses reported in 12 months	OR	1.40	1.08 to 1.80	Reference group: not well controlled asthma	Stepwise model	Multivariable (age, sex, race, BMI, allergies, ETS, ICS, control)	Control assessed with ATAQ as per 2007 NHLBI guidelines)
		Well controlled asthma	≥1 OCS courses reported in 12 months	OR	0.89	0.45 to 1.75	Reference group: not well controlled asthma			
		Very poorly controlled asthma	≥1 OCS courses reported in 12 months	OR	1.62	1.16 to 2.25	Reference group: not or well controlled asthma			
Kwong 2012 Cohort, 6/9	US, n = 960, Inner city children, Age 2-18y (60% were 6-11y)	Underlying asthma severity: mild intermittent	ED visit or hospitalisation	OR	0.2	0.1 to 0.6	Reference group: severe persistent	Logistic regression	Age, ethnicity, sex, baseline asthma control, clustering effect of site of care	Severity assessed at baseline by NAEPP definitions Control assessed on basis of symptoms, FEV_1, medication use, exacerbations.
			OCS course, ED visit or hospitalisation	OR	0.6	0.4 to 1.0				
		Underlying asthma severity: mild persistent	ED visit or hospitalisation	OR	0.59	0.3 to 1.3	Reference group: severe persistent			
			OCS course, ED visit or hospitalisation	OR	1.20	0.8 to 1.9				
		Underlying asthma severity: moderate persistent	ED visit or hospitalisation	OR	0.58	0.3 to 1.2	Reference group: severe persistent			
			OCS course, ED visit or hospitalisation	OR	1.02	0.7 to 0.6				
		Moderate asthma control	ED visit or hospitalisation	OR	0.96	0.5 to 1.8	Reference group: Difficult to control asthma			
			OCS course, ED visit or hospitalisation	OR	0.74	0.5 to 1.1				

		Well-controlled asthma	ED visit or hospitalisation	OR	0.47	0.2 to 0.9	Reference group: Difficult to control asthma			
			OCS course, ED visit or hospitalisation	OR	0.47	0.3 to 0.7				
Haselkorn 2009a Cohort, 6/9	US, n=82, Severe or difficult to treat asthma: poorly controlled at baseline Age 6-11y	Persistent very poorly controlled asthma	Composite score: hospitalisation/ED visit/OCS course	OR	6.4	1.18 to 34.5	Reference group: improved to not/well controlled asthma	Multivariable analyses: logistic regression	Age, prior ED visits or hospitalisation, controller use, BMI, non/allergic triggers, FVC % predicted, ethnicity	TENOR study Control assessed with ATAQ as per 2007 NHLBI guidelines)
Halterman 2001 Cohort, 5/9	US, n=165, 11 diverse primary care settings, Age 75% 6-12y	Asthma severity: mild intermittent	OCS course during study (3m)	x/n (%)	Mild-intermittent 8/58 (14%) vs Mild-severe persistent 27/107 (25%)	NS	Mild, moderate or severe persistent asthma	Chi^2 test	None	Asthma severity assessed using NHLBI criteria
			ED visit during study (3m)		Mild-intermittent 2/58 (3%) vs Mild-severe persistent 12/107 (11%)	NS				
Lieu 1997 Case-control, 7/9	US, n=1498, (508 cases, 990 controls), Age ≤14y	Parent assessment of severity	Hospitalisation	OR	1.87	1.42 to 2.48	Odds/increase in category (mild, moderate, moderately severe, severe)	Multivariate logistic regression	Income, SABA prescriptions, education status previous ED visits, ICS prescriptions	[Parent assessment of severity may not be robust]
			ED visit	OR	1.93	1.40 to 2.65				
Dales 2002 Cross-sectional, 7/10	Canada; n=2,986 Children from 136 schools, (5-19yrs)	Asthma symptoms daily	ED visit or hospitalisation	OR	2.32	1.70 to 3.17	Reference: no daily symptoms		Outcomes weighted for each student based on probability of the school being sampled and response rates	Statistical adjustment for design effects (including ICC)
		Asthma disturbing sleep	ED visit or hospitalisation	OR	2.38	1.77 to 3.21	Reference: no disturbed sleep			
Stingone 2006a Cross-sectional, 7/10	US, n=530, Inner city minority population, Age 5-12y	Sleep disturbance ≥1d/w	ED visit or hospitalisation in previous 12m	OR	7.84	2.73 to 22.4	Reference group: No sleep disturbance	Multivariate logistic regression	Sex, income, ethnicity, source of usual care, insurance, delaying care, use of controller meds	
		Sleep disturbance <1d/w	ED visit or hospitalisation in previous 12mo	OR	4.91	2.73 to 8.79	Reference group: No sleep disturbance			
Forno 2010 Cross-sectional; 7/10	Costa Rica, n=465, Age 6-14y	Symptoms for ≥3m/y	Hospitalisation or ≥2 ED/urgent care visits in previous year	OR	1.9	1.1 to 3.3	Symptoms for <3m/y	Multivariate stepwise logistic regression	Age, sex, parental education level	[Data from 'Model 1']

Lasmar 2007 Cross-sectional, 7/10	Brazil, n=126, Persistent asthma, Age 3-17y	Severe persistent asthma	Urgent care	OR	2.09	1.05 to 4.44	Reference: moderate persistent asthma	Logistic regression	Age range, AR, number of exacerbations	Reference group assumed not stated
Canino 2012 Cross-sectional, 2/10	US/Puerto Rico, n=804, White and Hispanic children, Age 7-15y: mean age 10.6y (SD2.5)	Parental perception of severity (very/ mild, moderate, very/ severe)	ED visit	Mean score	Frequent ED use: 3.4 (SD 0.7) vs Infrequent ED use: 2.7 (SD 0.9)	P<0.001	Frequent ED visits (2+ in 12m) Infrequent (0-1 in 12m)	t-test	None	[Unclear scoring Assume: 0 to 5: very mild to very severe]
		Clinician assessed asthma control	ED visit	Mean score (SD)	Frequent ED use: 1.3 (0.7) vs Infrequent ED use: 1.1 (0.7)	P<0.001	Frequent ED visits (2+ in 12m) Infrequent (0-1 in 12m)			Control score based on symptoms, SABA use, lung function

Lung function

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Robroeks 2012 Cohort Study 9/9	The Netherlands, n=38, Children with severe asthma, Age 6-16y: (mean 10.7y (SD 0.4))	FEV_1% predicted at baseline	Severe (reduced FEV1, needing OCS, admitted) Moderate (symptoms but no OCS)	ß: regression coefficient	ß= –0.02 (SE: 0.03)	P=0.43	FEV_1% predicted: continuous variable	Multivariate Cox regression analysis of the time until exacerbation	Multivariable (lung function, control, FeNO)	Intensively monitored cohort.
Wu 2011 Cohort, 6/9	US, n=1019, Children, Age 5-12y	FEV_1/FVC	OCS use, ED visit or hospitalisation	ß: estimate	0.023	-0.040 to -0.006	OR not given	Multivariate modelling (using GEE)	Age, FEV_1/FVC, PC20, eosinophils Use of ICS	CAMP study
		FEV1% predicted	OCS use, ED visit or hospitalisation	ß: estimate		P=0.29				
McCormak 2013 Cohort, 6/9	US, n=150, Persistent asthma with exacerbation in previous 12m, Age 5-17y (mean 11y)	FEV_1/FVC at 3monthly study visits	ED visit in 3m following study visit	OR	1.34	0.98 to 1.83	OR for every 10% decrease in FEV_1/FVC	Logistic regression with generalised estimating equations	Age, sex, FEV_1/FVC	
			Hospitalisation in 3m following study visit	OR	2.23	0.84 to 5.86				
		FEV_1/FVC at 3monthly study visits	Any acute healthcare use in 3m following study visit	OR	1.32	1.01 to 1.72				
Blatter 2016	Puerto Rico, n=304, Urban population,	FEV_1/FVC	≥1 ED visit, hospitalisation or	OR	1.0	0.9 to 1.0	Continuous variable: unclear unit	Stepwise multivariate	Sex and age	

Case-control, 7/9	Age 6-14y		OCS use in previous 12m							
Bacharier 2003 Cross-sectional, 8/10	US, n=1,041, Mild or moderate asthma, Age 5-12y	Greater FEV_1/FVC (pre-BD)	Prior hospitalisation (at at any time during their life).	OR	0.96	0.94 to 0.98	Analysed as a continuous variable	Logistic regression	Clinic, race, income, and gender	CAMP study baseline data.
Forno 2010 Cross-sectional; 7/10	Costa Rica, n=465, Age 6-14y	FEV_1 % change post-bronchodilator	Hospitalisation or ≥2 ED/urgent care visits in previous year	OR	1.03	1.01 to 1.1	Unadjusted OR:	Multivariate stepwise logistic regression	Age, sex, parental education level	[Data from 'Model 1'] [Unadjusted data]
Quezada 2016 Cross-sectional, 6/10	US, n=200 Exacerbators:110 Non-Exacerbators:185, Age 6-17y (mean 11yrs)	Baseline FEV_1/FVC (pre-BD)	OCS use or urgent care during 24w study	Mean ratio %	Exacerbators: 77% (75 to 79%) Non-Exacerbators: 81% (80 to 82%)	P<0.01	Analysed as a continuous variable	Wilcoxon rank-sum test	None	Recruited to a trial of proton-pump inhibitors for asthma
		Baseline PC20 methacoline provocation test	OCS use or urgent care during 24w study	Mean PC20	Exacerbators: 2.8 (1.8 to 3.7) Non-Exacerbators: 3.1 (2.4 to 3.7)	P= 0.55	Analysed as a continuous variable			

Medication use

Sub-optimal regime

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Baltrus 2017 Cohort, 9/9	US,, n=615,432, Children on Medicaid from 28 states,	Low controller/ total medication ratio (<0.5)	ED visit	OR	2.05	2.02 to 2.08	Reference group: no medication	Individual logistic regression	Sex, race, long-term controller medication ratio	County-level data excluded because generalisability concerns
		High controller/ total medication ratio (≥0.5)			1.20	1.16 to 1.24				
Spahn 2009 Cohort, 8/9	US, n=20,084 observations, Health plan, pharmacy claims, Age 4-11y (mean 8.91y)	ICS/LABA use in the summer.	Hospitalisation in the autumn	OR	0.49	0.39 to 0.61	Reference group: No ICS/LABA during the summer	Generalised estimating equations (GEEs)	Adjusted for age, sex, summertime asthma-related ED, hospital visits, OCS use, SABA use	
			ED visit in the autumn	OR	0.60	0.54 to 0.67				
			OCS use in the autumn	OR	0.62	0.57 to 0.67				
Andrews 2013 Cohort, 8/9	US, n=19,512, Medicaid registered, Age 1-18y (mean 8.9y)	Controller/total medication ratio <0.5	ED visits or hospitalisations in subsequent 12m	OR	1.6	1.4 to 1.8	Reference: controller/total ratio >0.5	Logistic regression	Age, gender, race, and rurality	Medication in baseline year with exacerbations in FU year
Zhang 2013 Cohort 8/9	Canada, n=9230, Routine clinical and dispensing data, Age 5-11y	Suboptimal drug regimen (high SABA, low ICS) use over 12m	Hospitalisations	OR	2.2	1.4 to 3.4	Reference group: Optimal regimens	Logistic regression	Gender, socioeconomic status, LABA, prior hospital admission and/or ED visit	See figure 1 for definition of 'appropriate'
Engelkes 2016 Cohort, 7/9	Netherlands, n=14,303, Routine GP records, Age 5-18y	Any previous asthma treatment	Hospitalisation, ED visit, or OCS course	RR	1.16	1.12 to 1.19	Reference group: no asthma treatment	Poisson regression	Age, age^2, gender	[Model 1]
Farber 2004 Cohort, 7/9	US, n=1,504, Routine data: health plan claims data and parental interviews, 2–16y. mean age 8.3y (SD 3.9)	Controller/total medication ratio 0 in baseline 12m	Hospitalisation or ED visit in FU 12m	OR	Intermittent 1.10	0.21 to 5.85	Reference: controller/total medication ratio > 0.5 in baseline 12m	Logistic regression	Child's age, sex, race/ethnicity, parent's education levels, single adult household, and poverty levels	[Comparison of medication in baseline year with exacerbations in FU year]
				OR	Persistent 0.79	0.33 to 1.87				
				OR	Persistent ≥4 SABA 0.75	0 .09 to 6.11				
		Controller/total medication ratio 0.01-0.33 in baseline 12m	Hospitalisation or ED visit in FU 12m	OR	Intermittent 2.06	0.29 to14.82				
				OR	Persistent 0.87	0.28 to 2.70				
				OR	Persistent ≥4 SABA 2.54	0.46 to 14.00				
				OR	Intermittent 1.51	0.27 to 8.47				

		Controller medication ratio 0.34-0.5 in baseline 12m	Hospitalisation or ED visit in FU 12m	OR	Persistent 1.08	0.47 to 2.51				
				OR	Persistent ≥4 SABA 0.60	0.09 to 4.17				
		Controller medication ratio 0.34-0.5 in baseline 12m	ED visits	OR	1.4	1.1 to1.8				
			High use of family practice service (top 5%)	OR	2.3	1.7 to 3.1				
Schatz 2003 Cohort, 6/9	US, n=4,197, Age 3-17y (mean age 9.5y (SD 4.1)	ICS/total medication ratio	Hospitalisation in study year	Mean ICS prescriptions (SD)	Hospitalised: 0.21 (0.24) vs Not hospitalised: 0.26 (0.28)	NS		Wilcoxon rank sum test	'All potential predictors'	
Rust 2013 Cross-sectional, 9/10	US, n=43,156, Children registered on Medicaid, Age 5-12y	Low controller-to-total asthma medication ratio (<0.5)	ED visit in 90d after initiating ICS Rx	OR	1.21	1.14 to 1.27	Reference group: high controller-to-medication ratio (≥0.5)	Logistic regression	Age, gender, race, rural/urban, state, asthma severity, doctor visits, ICS adherence	
			Hospitalisation in 90d after initiating ICS Rx	OR	1.70	1.45 to1.98				
Vernacchio 2013 Cross-sectional, 9/10	US, n=1,562 (in 3 separate year cohorts), Persistent asthma, Age 5-17y	No controller prescriptions	Hospitalisation, ED visit or OCS course	RR 2008 RR 2009 RR 2010	3.35 2.11 2.71	2.24 to 5.00 1.24 to 3.58 1.70 to 4.31	Reference group: ≥1 prescription	Logistic regression	Age and gender	Multiple tests for ICS use: the ones cited are those defined by HEDIS
		50-75% of year covered by ICS prescriptions		RR 2008 RR 2009 RR 2010	0.82 1.01 0.95	0.48 to 1.40 0.62 to 1.6 0.59 to 1.53	>75% of year covered by ICS prescriptions			
		<50% of year covered by ICS prescriptions		RR 2008 RR 2009 RR 2010	1.24 1.16 0.91	0.85 to 1.82 0.79 to 1.69 0.62 to 1.35	>75% of year covered by ICS prescriptions			
		Low controller-to-total asthma medication ratio (<0.5)		RR 2008 RR 2009 RR 2010	1.42 1.67 1.62	0.91 to 2.22 1.14 to 2.46 1.10 to 2.38	Reference: high controller/total medication ratio (≥0.5)			

Controller medication use

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Adams 2001 Cohort, 9/9	US, n=11,195, Urban setting, Age 3-15 y	1-5 controller prescriptions	ED visit	RR	0.3	0.3 to 0.4	Reference: no controller use	Multiple logistic regression	Age, gender, frequency of reliever dispensing managed care organisation,	
			Hospitalisation	RR	0.4	0.3 to 0.6				
		>5 controller prescriptions	ED visit	RR	0.7	0.5 to 0.9	Reference: no controller use			
			Hospitalisation	RR	0.5	0.3 to 0.9				
Thomas 2005 Cohort; 8/9	UK, n=9,522, General practice, Age 6-15y (mean 10.6y)	Low dose ICS during baseline period (6m)	Hospitalisation	OR	1.81	1.05 to 3.14	Unclear as to reference group-- assume no use of ICS	Logistic regression	Multivariable (age, gender, OCS, SABA, dose ICS)	Confounding by indication
		High dose ICS during baseline period (6m)	Hospitalisation	OR	5.60	2.11 to14.88				
Engelkes 2016 Cohort, 7/9	Netherlands, n=14,303, Routine GP records, Age 5-18y	Previous ICS prescriptions	Hospitalisation, ED visit, or OCS course	RR	1.25	1.18 to 1.33	Reference group: no ICS prescriptions	Poisson regression	Age, age^2, gender	[Model 1] [Confounding by indication]
Farber 2004 Cohort, 7/9	US, n=1,504, Health plan claims and parental interviews, 2-16y. mean age 8.3y (SD 3.9)	No controller medication in baseline 12m	Hospitalisation or ED visit in FU 12m	OR	Intermittent 0.55	0.19 to 1.63	Controller medication in baseline 12m	Logistic regression	Child's age, sex, race/ethnicity, parent's education levels, single adult household, and poverty levels	[Comparison of medication in baseline year with exacerbations in FU year]
				OR	Persistent 0.72	0.37 to 1.39				
				OR	Persistent ≥4 SABA 0.52	0.10 to 2.55				
Schatz 2003 Cohort, 6/9	US, n=4,197,Age 3-17y (mean age 9.5y (SD 4.1)	ICS prescriptions	Hospitalisation in study year	Mean (SD)	Hospitalised: 1.37 (2.06) vs Not hospitalised: 1.07 (1.67)	NS	NA	Wilcoxon rank sum test	'All potential predictors'	Could be considered clinically relevant
		ICS prescriptions	Hospitalisation in study year	OR	0.73	0.59 to 0.89	Continuous Variable	Logistic regression		
Wu 2011 Cohort, 6/9	US, n=1019, Children, Age 5-12y	ICS use	OCS use, ED visit or hospitalisation	ß: estimate	-0.45	-0.73 to -0.17		Multivariate modelling (using GEE)	Age, FEV_1/FVC, PC20, eosinophils Use of ICS	CAMP study
Vasbinder 2016 Case-control,	Netherlands, n=1,636 included when first prescribed ICS,	ICS adherence ≥80% in 12m before 'event'	'Events' = OCS use or hospital admission	All x/n (%)	Events 14/40 (35%) for vs non-events 322/1,596 (20%)	Not reported	ICS adherence <80% in 12m before 'event'	A variation on Cox proportional	SABA use Matching: on age (incidence density sampling).	Confounding by indication. LABA used as a proxy for asthma

9/9	Age 5-12y (mean 8.1y)	ICS adherence ≥80% in 12m before 'event'	'Events' = OCS use or hospital admission	No LABA use: OR	1.07	0.39 to 2.97	ICS adherence <80% in 12m before 'event'	hazards regression		severity: a strong effect modifier for exacerbations
		ICS adherence ≥80% in 12m before 'event'	'Events' = OCS use or hospital admission	Recent LABA use: OR	4.34	1.20 to 15.64	ICS adherence <80% in 12m before 'event'			
Blatter 2016 Case-control, 7/9	Puerto Rico, n=304, Urban population, Age 6-14y	ICS use in previous 6 m	At least one ED visit or OCS use in past 12 m	OR	4.6	2.3 to 9.0	Reference group: No ICS use	Stepwise multivariate	Sex and age	Confounding by indication
Rust 2013 Cross-sectional, 9/10	US, n=43,156, Children registered on Medicaid, Age 5-12y	<50% of prescription days covered	ED visit	OR	0.93	0.88 to 0.98	Reference: ≥50% of prescription days covered	Logistic regression	Age, gender, race, rural/urban, state, asthma severity, doctor visits, ICS adherence	Confounding by indication
			Hospitalisation	OR	0.62	0.54 to 0.70				
Rosas-Salazar 2013 Cross-sectional, 9/10	Puerto Rico, n=351, Urban children, Age 6-14y	Use of ICS in prior 6m	At least one ED or urgent care visit in past year	OR	2.0	1.2 to 3.3	Reference group: no ICS use in prior 6m	Multivariate stepwise logistic regression	Age, sex, parental numeracy, income, use of ICS, ETS exposure	Likely confounding by indication
Brehm 2012 Cross-sectional, 9/10	Puerto Rico, n=287, Children from households in San Juan, Ages 6-14	ICS in previous year	At least one hospitalisation, ED, urgent care, OCS use	OR	3.3	1.8 to 6.1	Reference group: no ICS use in previous year		Age, sex, income, vit D level, African ancestry, always outside, high vit D intake	
Bacharier 2003 Cross-sectional, 8/10	US, n=1,041, Mild or moderate asthma, Age 5-12y	ICS use in past 6m	Prior hospitalisation (at any time during their life)	OR	1.62	1.16 to 2.26	Reference: No ICS use	Logistic regression	Clinic, race, income, and gender	CAMP study baseline data. [Confounding by indication]
		Cromolyn or nedocromil use in past 6m		OR	1.66	1.15 to 2.39	Reference: No cromolyn/ nedocromil use			
Stingone 2006a Cross-sectional, 7/10	US, n=530, Inner city minority population, Age 5-12y	Controller medication in previous 2w:	ED visit or hospitalisation in previous 12 m	%	Controller in past 2w: 55% vs No controller in past 2w: 44%	Excluded from the final model because reported as 'NS'	No controller medication in previous 2w	Multivariate logistic regression	Sex, income, ethnicity, usual care, delaying care, insurance,	
Forno 2010 Cross-sectional 7/10	Costa Rica, n=465, Age 6-14y	Controller medication	Hospitalisation, ED, urgent visits in previous year	OR	1.90	1.3 to 3.0		Multivariate stepwise logistic regression	Age, sex, parental education level	
Quezada 2016 Cross-sectional, 6/10	US, n=200 Exacerbators:110 Non-Exacerbators:185	Use of ICS	OCS course or urgent care during 24w study	x/n (%)	Exacerbators: 88/ 110 (80%) vs Non-Exacerbators: 112/185 (61%)	P<0.001	No use of ICS	Fisher test	None	[Confounding by indication]

	Age 6-17y (mean 11yrs)	Use of ICS and LABA	OCS course or urgent care during 24w study	x/n (%)	Exacerbators: 71/ 110 (66%) vs Non-Exacerbators: 100/185 (54%)	P=0.04	No use of ICS/LABA			
Canino 2012 Cross-sectional, 2/10	US/Puerto Rico, n=804, White and Hispanic children, Age 7-15y: mean age 10.6y (SD2.5)	Use of ICS	ED visits	x/n (%)	Frequent ED use: 66/255 (26%) vs Infrequent ED use: 170/549 (31%)	P>0.001	Frequent ED visits (2+ in 12m) Infrequent (0-1 in 12m)	Chi^2 test	None	
		Use of any controller medication	ED use	x/n (%)	Frequent ED use: 115/255 (45%) vs Infrequent ED use: 275/549 (50%)	P>0.001	Infrequent ED visit (0-1 in prev. 12 mo) vs frequent (2+)			

Reliever medication use

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Thomas 2005 Cohort; 8/9	UK, n=9,522, General practice, Age 6-15y (mean 10.6y)	Number of SABA prescriptions during baseline period (6m)	Hospitalisation during 12m FU period	OR	1.25	1.13 to 1.39		Logistic regression	Multivariable (age, gender, OCS, SABA, dose ICS)	
Schatz 2003 Cohort, 6/9	US, n=4,197, Age 3-17y (mean age 9.5y (SD 4.1)	SABA use in previous year	Hospitalisation in study year	Mean (SD) number of SABA	Hospitalised: 5.02 (4.58) vs Not hospitalised: 2.61 (3.08)	P<0.001	Number of prescriptions	Wilcoxon rank-sum test	'All potential predictors'	
		SABA use in previous year	Hospitalisation in study year	OR	1.17	1.10 to 1.25	Continuous variable	Logistic regression		
Zeiger 2012 Cohort, 5/9	US, n=289, Severe or difficult-to-treat asthma. Age 6-12y	Very poor control (with SABA use)	Self-reported (at 3,6,12m), OCS course, ED visit, or hospitalisation,	OR	2.03	1.17 to 3.52	Reference Not very poor control	Multivariable logistic regression	Age groups	Control classified according to NHLBI
Lieu 1997 Case-control, 7/9	US, n=1,498 (508 cases, 990 controls), Age ≤14y	Number of SABA prescriptions in past 6m	Hospitalisation	OR	1.31	1.14 to 1.52	Odds/increase in number of SABA prescriptions	Multivariate logistic regression	Income, SABA prescriptions, education status previous ED visits, ICS prescriptions	
Rust 2013			ED visit	OR	1.04	0.98 to 1.10				

Cross-sectional 9/10	US, n=43,156, Medicaid registered, Age 5-12y	Severe asthma (≥2 SABA in the preceding 90d)	Hospitalisation	OR	1.04	0.90 to 1.20	Reference: Not severe asthma (<2 SABA in preceding 90d)	Logistic regression	Age, gender, race, rural/urban, state, asthma severity, doctor visits, ICS adherence	
Vernacchio 2013 Cross-sectional, 9/10	US, n=1,562 (in 3 separate year cohorts), Persistent asthma, Age 5-17y	≥4 SABA prescriptions/y	Hospitalisation, ED visit or OCS course	RR (2008) RR (2009) RR (2010)	1.94 2.05 1.49	1.33 to 2.84 1.34 to 3.12 0.93 to 2.38	Reference group: ≤1 SABA/ye	Logistic regression	Age, gender	[No data for> 3 SABA/yr]
		3 SABA prescriptions/y	Hospitalisation, ED visit or OCS course	RR (2008) RR (2009) RR (2010)	0.99 1.41 1.54	0.62 to 1.58 0.89 to 2.23 0.98 to 2.41	Reference group: ≤1 SABA/y			
		<3 SABA prescriptions/y	Hospitalisation, ED visit or OCS course	RR (2008) RR (2009) RR (2010)	0.83 0.97 1.62	0.46 to 1.47 0.54 to 1.75 0.99 to 2.65	Reference group: ≤1 SABA/y			
Quezada 2016 Cross-sectional, 6/10	US, n=200. Non-exacerbators: 185 Exacerbators:110 Age 6-17y (mean 11y)	Users of SABA >2/w	OCS use or urgent care during 24w study	x/n (%)	Exacerbators: 71/110 (65%) vs Non-exacerbators: 148/185 (80%)	P<0.01		Fisher test	None	Recruited to a trial of proton-pump inhibitors for asthma

Nebuliser use

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Lieu 1997 Case-control, 7/9	US, n=1498 (508 cases, 990 controls), Age ≤14y	Child had a nebuliser	Hospitalisation	OR	2.96	1.41 to 6.23	Reference group: no nebuliser	Multivariate logistic regression	Income, SABA use, education status previous ED visits, ICS prescriptions	Confounding by severity
Butz 2000 Cross-sectional, 4/10	US, n=686, Inner city and 99% African American, Age 5-12yrs	Nebuliser use for relief of acute severe symptoms	Hospitalised in last 6 months:	x/N (%)	Users 60/231 (26%) vs non users 41/455 (9.0%)	P=0.001	Nebuliser users (≥1d/m during last 6m) vs Non-nebuliser users	Chi² test	None	Confounding by severity
			ED visit ever	x/N (%)	Users 171/231 (74%) vs non users 238/455 (52%)	P=0.001				
			OCS courses in last 12m	Mean (SD)	Users 3.8 (SD 9.4) vs non users 1.3 (6.0)	P<0.001				

Parental beliefs about medication

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Canino 2012 Cross-sectional, 2/10	US/Puerto Rico, n=804, White and Hispanic children, Age 7-15y: mean age 10.6y (SD2.5)	Parental concerns about medications (BMQ score range 5-25)	Infrequent ED visit (0-1 in previous 12m) vs frequent (2+)	Mean score (SD)	Frequent ED users: 3.1 (SD 0.8) vs infrequent ED users: 2.8 (SD 0.8)	P<0.001	Unclear	t-test	None	[Unclear results – BMQ has a scale of 4-20 except necessity-concerns ratio (single figures)]

Ownership of written asthma management plan

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Lieu 1997 Case-control, 7/9	US, n=1498 (508 cases, 990 controls), Age ≤14y	Had a written asthma action plan	Hospitalisation ED visit	OR	0.54 0.45	0.30 to 0.99 0.27 to 0.76	Reference group: no written asthma management plan	Multivariate logistic regression	Income, SABA prescriptions, education status previous ED visits, ICS prescriptions	
Sunshine 2011 Cross-sectional 7/10	US, n=292, Low income, persistent asthma, Age 3-13y	Written action plan ownership at baseline	Urgent healthcare services for asthma within previous 3m	OR	1.98	1.13 to 3.48	Reference group: non-ownership of action plan	Logistic regression	Ethnicity, primary language, poverty, severity, prior asthma education.	Healthy Homes II RCT Confounded by indication

Allergy/atopy

Co-morbid atopic disease (Asthma, allergic rhinitis, eczema, and food allergy)

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Thomas 2005 Cohort, 8/9	UK, n=9,522, General practice, Age 6-15y (mean 10.6y)	Co-morbid allergic rhinitis	Hospitalisation	OR	2.34	1.41 to 3.91	Reference: asthma only	Logistic regression	Multivariable (age, gender, OCS, SABA, dose ICS)	
			GP visits	Mean (SD)	Allergic rhinitis + asthma 4.4 (4.2) vs asthma 3.4 (3.2)	P<0.0001	Asthma alone			
Engelkes 2016 Cohort, 7/9	Netherlands, n=14,303, Routine GP records, Age 5-18y	Eczema	Hospitalisation, ED visit, or OCS course	RR	0.76	0.42 to 1.36	Reference group: no eczema	Poisson regression	Age, age^2, gender	[Model 1]
		Allergic rhinitis	Hospitalisation, ED visit, or OCS course	RR	0.75	0.47 to 1.21	Reference group: no allergic rhinitis			
		Conjunctivitis	Hospitalisation, ED visit, or OCS course	RR	1.36	0.70 to 2.65	Reference: no conjunctivitis			
Arabkhazaeli 2015 Cross-sectional, 7/10	Netherlands, n=703, Regular users of asthma treatments, Age 4-12y	No allergic history	OCS use	OR	0.5	0.2 to 1.2	Ref group: entire study population	Multivariate analysis	Age, gender	
			ED visit	OR	0.5	0.2 to 1.3				
		Eczema	OCS use	OR	3.0	1.4 to 6.6				
		Eczema	ED visit	OR	2.7	1.2 to 6.0				
		Hay fever (AR)	OCS use	OR	1.4	1.2 to 4.4				
		Hay fever (AR)	ED visit	OR	1.1	0.9 to 3.4				
		Eczema + AR	OCS use	OR	1.8	1.2 to 4.4				
		Eczema + AR	ED visit	OR	1.4	0.9 to 3.4				
		≥2 allergies	OCS use	OR	3.3	1.6 to 6.6				
		≥2 allergies	ED visit	OR	2.3	1.2 to 4.6				
		Food allergy	OCS use	OR	2.3	1.2 to 4.4				
		Food allergy	ED visit	OR	1.8	0.9 to 3.4				
		Food allergy + eczema	OCS use	OR	3.3	1.8 to 6.1				
		Food allergy + eczema	ED visit	OR	2.5	0.9 to 3.4				
		Food allergy + hay fever	OCS use	OR	1.6	0.9 to 3.0				
			ED visit	OR	1.2	0.6 to 2.5				
		Food allergy + AR + eczema	OCS use	OR	1.9	1.0 to 3.6				
		Food allergy + AR + eczema	ED visit	OR	1.5	0.7 to 2.9				

Friedlander 2013 Cross-sectional, 7/10	US, n=300, Inner city, Age 5-13y (mean 7.9y)	Any food allergy	Unscheduled care (previous 12m)	OR	0.77	0.42 to 1.40	Reference group NR: assume no food allergy	Stepwise logistic regression	Age, race, gender, yearly household income, tobacco smoke exposure, eczema history	Multiple allergies were from 2+ distinct food groups
			Hospitalisation in (previous 12m)	OR	1.91	0.68 to 5.38				
		Multiple food allergies	Unscheduled care (previous 12m)	OR	0.76	0.35 to 1.64	Reference group NR: assume no food allergy			
		Multiple food allergies	Hospitalisation in (previous 12m)	OR	3.52	1.12 to11.03				
Lasmar 2007 Cross-sectional, 7/10	Brazil, n=126, Persistent asthma, Age 3-17y	Presence of allergic rhinitis	Emergency care services	OR	2.98	1.10 to 8.06	Reference group: no allergic rhinitis	Logistic regression	Age range, asthma severity classification, number of exacerbations	Reference group assumed not stated
Pinto-Pereira 2010 Cross-sectional, 6/10	Trinidad, n=393, Age 2-17y	Co-morbid allergic rhinitis (AR)	ED visits in previous 12m	x/n (%)	Asthma + AR 154/212 (59%) vs asthma 109/181 (41%)	P<0.01	Chi^2 test	None	None	
				Mean	Asthma + AR 1.75 visits vs asthma 1.36 visits	P<0.04	ANOVA			

Skin prick test (SPT)

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Wu 2011 Cohort, 6/9	US, n=1019, Children, Age 5-12y	Number of positive skin prick tests	OCS use, ED visit or hospitalisation	ß: estimate	-0.019	-0.046 to 0.007	OR not given	Multivariate modelling (using GEE)	Age, FEV_1/FVC, PC20, eosinophils, use of ICS	CAMP study
Blatter 2016 Case-control, 7/9	Puerto Rico, n=304, Urban population, Age 6-14y	Number of positive SPTs to allergens	At least one ED visit or OCS use in previous year	OR	1.0	0.9 to 1.0	Change OR per each positive SPT to allergens	Stepwise multivariate	Sex and age	
Sarpong 1997 Cross-sectional 8/10	US, n=138, Urban area, Mean age 10.1y (SD 2.9)	Positive SPT to cockroach	Hospitalisation	OR	2.18	1.10 to 4.32	Ref: negative SPT cockroach	Univariate log regression	Multivariable (age, sex, race, area of residence, medical insurance)	
		Positive SPT to dust mite	Hospitalisation	OR	0.86	0.44 to 1.68	Ref: negative SPT to dust mite			
		Positive SPT to dog	Hospitalisation	OR	1.66	0.65 to 4.22	Ref: negative SPT to dog			
		Positive SPT to cat	Hospitalisation	OR	2.86	1.29 to 4.29	Ref: negative SPT to cat			

		Positive SPT to cat	Hospitalisation	OR	3.77	1.53 to 9.25	Ref: negative SPT to cat	Stepwise multiple logistic regression	Age, sex, race, area of residence, and type of medical insurance	
Castro-Rodriguez 2007 Cross-sectional, 7/10	Chile, n=237, Age 4-14y	Positive SPT to ≥1 allergens	ED visits	OR	0.85	0.42 to 1.74	Reference group: no positive SPT	Multivariate analysis	Age, dermatitis, passive smokers age of onset, pneumonia, nasal eosinophilia	39 allergens tested
		Positive SPT to ≥1 allergens	OCS course	OR	2.58	1.11 to 5.97				

Animals/allergen in home

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Pongracic 2008 Cohort, 7/9	US, n=937, Moderate/ severe asthma, inner city, Age 5-11y	Mouse allergen in home and positive SPT	Hospitalisation	RR	1.65	1.09 to 2.50	No mouse allergen in home and/or not positive SPT	Poisson regression model	Cockroach sensitivity and exposure	Data from trial of rodent environmental intervention
		Mouse allergen in home and positive SPT	Unscheduled asthma visits	RR	1.05	0.88 to 1.27				
Pongracic 2010 Cohort, 7/9	US, n=937, Moderate to severe asthma, inner city, Age 5-11y	Airborne fungal level	Hospitalisation	Mean (SD)	Positive SPT: 0.2 (0.02) vs Negative SPT: 0.2 (0.02)	P=0.46	Positive vs negative SPT to fungal allergens	Linear mixed-effects Regression Model	Number of positive responses to SPTs to indoor allergens	
			Unscheduled asthma visits		Positive SPT: 0.9 SD 0.1 vs Negative SPT: 0.9 SD 0.1	P=0.73				
		Concentration of indoor fungal allergens	Unscheduled asthma visits	OR	1.22	1.05 to 1.43	Ten-fold increase in concentration	Generalized linear mixed-effects model	Outdoor fungal allergens	Sub-group analysis: children with positive SPT to fungal allergens
Torjusen 2013 Cohort, 5/9	US, n=150, Urban;, persistent asthma, Age 5-17y (median 11y)	Exposed and sensitised to mouse allergen	Unscheduled asthma care	OR	Bed 1.87 Bedroom 1.26 Kitchen 1.37 Air 1.43	1.21 to 2.88 0.91 to 1.73 1.05 to 1.78 1.01 to 2.02	Odds for each 10-fold increase in exposure to mouse allergen.	GEE	Age, gender, total IgE, health insurance	
		Exposed but not sensitised to mouse allergen	Unscheduled asthma care	OR	Bed 1.08 Bedroom 1.07 Kitchen 1.11 Air 1.20	0.71 to 1.64 0.80 to 1.45 0.85 to 1.46 0.84 to 1.73	Odds for each 10-fold increase in exposure to mouse allergen.			
Rabito 2011	US, n=86, Inner city, Age 4-17y	Cockroach allergen exposure>2U/g	Hospitalisation	OR	5.41	1.14 to 25.62	Reference: not exposed	Multivariable logistic regression	Income, insurance status, education,	

Cross-sectional, 7/10									ETS, severity, and adherence	
Dales 2002 Cross-sectional, 7/10	Canada, n=2,986 Children from 136 schools, (5-19yrs)	Cats in home	ED visit or Hospitalisation	OR	0.90	0.71 to 1.14	Reference: no cats in home		Weighted for each student based on probability of the school being sampled and response rates	Statistical adjustment for design effects (including ICC)
		Dogs in home	ED visit or Hospitalisation	OR	0.64	0.51 to 0.80	Reference: no dogs in home			

Serum IgE

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Wu 2011 Cohort, 6/9	US, n=1019, children Age 5-12y	Log_{10} IgE count	OCS use, ED visit or hospitalisation	ß: regression coefficient	0.083	-0.11 to 0.27		Multivariate modelling (using GEE)	Age, Use of ICS FEV1/FVC ratio, PC20, eosinophils	CAMP study Authors give raw beta value as the effect measure.
Forno 2010 Cross-sectional; 7/10	Costa Rica, n=465, Age 6-14y	Positive total serum IgE level, IU/mL	Hospitalisation or 2+ ED/UC visits in previous year	OR	1.5	1.03 to 2.3	Reference: Negative total IgE level	Multivariate stepwise logistic regression	Age, sex, parental education level	[Data from 'Model 1'] [Unadjusted data]

FeNO

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Robroeks 2012 Cohort, 9/9	The Netherlands, n=38, Children with severe asthma, Age 6-16y: (mean 10.7y (SD 0.4))	FeNO assessed every 2 m	Severe (reduced FEV_1, needing OCS, admitted) Moderate (symptoms but no OCS)	ß correlation coefficient,	ß= 0.01 (SE: 0.01)	P= 0.60		Univariate Cox regression analysis of the time until exacerbation	Multivariable (lung function, control, FeNO)	Intensively monitored cohort.
McCormak 2013 Cohort, 6/9	US, n=150, Persistent asthma with exacerbation in previous 12m, Age 5-17y (mean 11y)	FeNO at 3 monthly visits	ED visit in 3m following study visit	OR	1.09	0.86 to 1.37	OR for every twofold incr. in FeNO level	Logistic regression with GEE	Age, sex, FEV_1/FVC	
			Hospitalisation in 3m following study visit	OR	1.74	0.77 to 3.91				

			Acute care in 3m following study visit	OR	1.08	0.88 to 1.31				
Kelso-Visser 2011 Cohort, 4/9	Netherlands, n=103, Age 6-16y	FeNO at baseline	OCS course in next 12m	Median (!QR)	Exacerbators 41ppb (33-71) vs Non-exacerbators 13ppb (9-21)	P<0.001	OR not given	unclear	none	Significant difference in medians, but 'complete overlap of FeNO measurements in the two groups'

FH atopy

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Wu 2011 Cohort, 6/9	US, n=1019, Children, Age 5-12y	FH asthma	OCS use, ED visit or hospitalisation	ß: estimate	0.18	-0.03 to 0.40		Multivariate modelling (using GEE)	Age, use of ICS, PC20, FEV_1/FVC, eosinophils	CAMP study
Forno 2010 Cross-sectional, 7/10	Costa Rica, n=465, Age 6-14y	Maternal asthma	Hospitalisation, ED or urgent care visits in previous year	x/n (%) of children with risk	Exacerbators 104/324 (32%) vs Non-exacerbators 35/141 (25%)	NS	Comparison exacerbators vs non-exacerbators Puerto-Rican exploratory cohort	Fisher exact tests for categorical variables	Age, sex, lung function, SABA, specific IgE, parental education	CAMP validation: 21% vs 22%
		Maternal hay-fever			Exacerbators 87/324 (27%) vs Non-exacerbators 49/141 (35%)	NS				CAMP validation: 40% vs 39%
		Maternal eczema			Exacerbators 13/324 (4%) vs Non-exacerbators 13/141 (9%)	P<0.05				Not available from CAMP
		Paternal asthma	Hospitalisation, ED or urgent care visits in previous year	Comparison exacerbators vs non-exacerbators	Exacerbators 78/324 (24%) vs Non-exacerbators 24/141 (17%)	NS				CAMP validation: 25% vs 26%
		Paternal hay-fever			Exacerbators 87/324 (27%) vs Non-exacerbators 24/141 (17%)	P<0.05				CAMP validation: 49% vs 47%
		Paternal eczema			Exacerbators 16/324 (5%) vs	NS				Not available from CAMP

					Non-exacerbators 1/141 (1%)					
		Paternal history of hay fever	Hospitalisation, ED or urgent care visits in previous year	OR	1.9	1.02 to 3.7	Reference: no paternal history of hay fever	Multivariate analysis: stepwise logistic regression	Age, sex, parental education level	[Model 1] Validation in CAMP study data

Social context

Poverty

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Schatz 2003 Cohort, 6/9	US, n=4,197, Age 3-17y (mean age 9.5y (SD 4.1)	Family income	Hospitalisation in study year	Mean $ (SD)	Hospitalised: $31,438 (10,205) vs Not hospitalised: $34,733 (10,716)	P<0.05		Wilcoxon rank sum test	'All potential predictors'	
Lieu 1997 Case-control, 7/9	US, n=1498 (508 cases, 990 controls), Age ≤14y	Annual income	Hospitalisation	OR	0.82	0.69 to 0.98	Odds/ $10,000 unit increase in income	Multivariate logistic regression	Income, ED visits, ICS SABA, prescriptions, education,	
Blatter 2016 Case-control, 7/9	Puerto Rico, n=304, Urban population Age 6-14y	Household income (income below $15,000)	At least one ED visit or OCS course in previous year	OR	0.7	0.4 to 1.4	Reference group: income ≥$15,000	Stepwise multivariate	Sex and age	
Rosas-Salazar 2013 Cross-sectional, 9/10	Puerto Rico, n=351, Urban families, Age 6-14y	Household income <$15,000/y	At least one ED or urgent care visit in past year	OR	2.3	1.4 to 3.8	Reference group: income ≥$15,000/y	Multivariate stepwise logistic regression	Age, sex, income, use of ICS, ETS exposure	
Brehm 2012 Cross-sectional, 9/10	Puerto Rico, n=287, Children from San Juan, Age 6-14y	Household income <$15,000/y	At least one ED or urgent visit, OCS course, hospitalisation,	OR	1.3	0.7 to 2.4	Reference group: income above $15,000/y	Stepwise multivariate	Age, sex, vit D level, use of ICS, African ancestry,	
Dales 2002 Cross-sectional, 7/10	Canada, n= 2986, Children from schools, Age 5-19yrs	Annual family income: <$20,000	Hospitalisation	OR	1.75	1.19 to 2.59	Reference group: >$60,000	Weighting based on probability of the school being sampled and response rates	None	Statistical adjustment for design effects (including ICC)
		Annual family income: $20,000-60,000	Hospitalisation	OR	1.27	0.98 to 1.63	Reference group: >$60,000			
Stingone 2006a Cross-sectional 7/10	US, n=530, Inner city minority population, Age 5-12y	<$20,000/y	ED visit or hospitalisation in previous 12m	OR	2.79	1.28 to 6.06	Reference group: ≥$40,000	Multivariate logistic regression	Sex, income, ethnicity, usual care, delaying care, insurance	Poverty associate with increased use of ED/ hospitals
		$20,000 - $39,999/y		OR	2.75	1.27 to 5.92				
Wood 2002	US, n=386, Deprived population,	Denied = had applied but been denied benefits	Parental reported attacks	Incident Rate Ratio (SE)	1.41 (SE 0.13)	P<0.001	Reference: no contact with welfare	Logistic regression	Age, sex,	Denied welfare with increased

Cross-sectional, 5/10	(age 2-12yrs) Classified by welfare status Never 44% Denied 9% Pending 9% Former 25% Current 14%	Pending = application for benefits pending	requiring medical attention		0.94 (SE 0.10)	P=0.57	Reference: no contact with welfare		parent education, quality of care	use of healthcare resources
		Former = benefits in the past,			0.95 (SE 0.07)	P=0.48	Reference: no contact with welfare			
		Current = receiving benefits			1.03 (SE 0.10)	P=0.76	Reference: no contact with welfare			
Canino 2012 Cross-sectional, 2/10	US/Puerto Rico, n=804, White and Hispanic children, Age 7-15y: mean age 10.6y (SD2.5)	% below poverty threshold (derived income-to-needs ratio: annual income/ poverty threshold for family size)	ED visit	% comparison (p-value sig. @ P<0.001)	Frequent ED use: 64% vs Infrequent ED use: 49% Sig	P<0.001	*Infrequent ED visit (0-1 in prev. 12 months) vs frequent (2+)	Chi^2 test	None	
		Neighbourhood risk Index assessing poverty factors (score from 0-8-8 highest risk)	ED visit	Mean score comparison (p-value sig. @ P<0.001)	Freq ED use: 6.1 SD 2.0 vs Infreq ED use: 24.8 SD 2.8	P<0.001	Infrequent ED visit (0-1 in prev. 12 months) vs frequent (2+)	t-test		

Low parent education level

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Lieu 1997 Case-control, 7/9	US, n=1498 (508 cases, 990 controls), Age ≤14y	Father's education level	ED visit	OR	0.55	0.36 to 0.84	Odds/unit increase in education level	Multivariate logistic regression	Income, SABA prescriptions, education status, Previous ED visits, ICS prescriptions	
Quinto 2011 Cross-sectional, 10/10	US, n=32,321, Privately insured, Age 5-17y	Parental education: High School	OCS use	OR	0.97	0.90 to 1.06	Reference: Parental education >High School diploma	Logistic regression	Age, sex, race, parent education, controller use, GORD, diabetes	
		Parental education: High School	Hospitalisation or ED visit	OR	1.08	1.00 to1.17				

Rosas-Salazar 2013 Cross-sectional, 9/10	Puerto Rico, n=351, Urban families, Age 6-14y	Low parental asthma numeracy: no correct answers in ANQ	At least one ED or urgent care visit in past 12m	OR	1.7	1.03 to 2.7	Reference: one or more correct ANQ answers	Multivariate stepwise logistic regression	Age, sex, income, use of ICS, ETS exposure	ANQ = Asthma numeracy questionnaire (math-based questions)
Dales 2002 Cross-sectional, 7/10	Canada, n=2,986 Children from 136 schools, (5-19yrs)	Parental education: Not completed secondary	Hospitalisation	OR	1.85	1.21 to 2.82	Reference group: university degree	Outcomes weighted for each student based on probability of the school being sampled and response rates	None	Statistical adjustment for design effects (including ICC)
		Secondary school completed	Hospitalisation	OR	1.40	1.05 to 1.88	Reference group: university degree			

Ethnicity

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Baltrus 2017 Cohort, 9/9	US ,n=615,432, Children on Medicaid from 28 states,	Black	ED visit	OR	1.97	1.93 to 2.00	Reference group: white	Individual logistic regression	Sex, race, long-term controller medication ratio	
		Hispanic			1.05	1.03 to 1.08				
		Asian			0.73	0.68 to 0.78				
		Other			1.42	1.39 to 1.45				
Stewart 2010 Cohort study, 8/9	US, n=25,138, Children of military personnel, Age 5-10y	Hispanic	Asthma related hospitalisation	OR	1.38	1.02 to 1.87	Reference group: White	Logistic regression	Sex, parent's marital status, military rank, siblings, health care providers used, geographic area, asthma and other drugs	African American at greater risk than Hispanic, and both at greater risk than white.
			Asthma related ED visit	OR	1.24	1.11 to 1.37				
		Black	Asthma related hospitalisation	OR	1.97	1.61 to 2.41				
			Asthma related ED visit	OR	1.62	1.51 to 1.74				
Kwong 2012 Cohort, 6/9	US, n=960, Inner city children, Age 2-18y (60% were 6-11y)	Ethnicity- African American	ED visit or hospitalisation	OR	4.12	1.8 to 9.5	Reference group: Hispanic	Logistic regression	Age, ethnicity, sex, baseline asthma control, clustering effect of site of care	Hispanic 81%; AA 8.5% White 2.4% Other 7.8% African American at greater risk than Hispanic
			OCS course, ED visit or hospitalisation	OR	2.03	1.1 to 3.9				
		Ethnicity-White	ED visit or hospitalisation	OR	1.86	0.5 to 6.8	Reference group: Hispanic			
			OCS course, ED visit or hospitalisation	OR	1.85	0.8 to 4.1				

		Ethnicity-Other	ED visit or hospitalisation	OR	2.25	0.9 to 5.4	Reference group: Hispanic			
			OCS course, ED visit or hospitalisation	OR	1.80	0.9 to 3.4				
Haselkorn 2009b Cohort, 8/9	US, n=563, Severe/difficult to treat asthma, Age 6-11y	Non-white	At least one OCS course reported in 12m	OR	1.76	1.34 to 2.32	Reference group: White	Stepwise model	Multivariable (age, sex, race, BMI, allergies, ETS, ICS, control)	White 47%; Black 35%; Other 18%
Halterman 2001 Cohort, 5/9	US, n=165, From 11 diverse primary care settings, Age 75% 6-12y	Race	OCS course	x/n (%)	White 16/111 (22%) vs Black: 6/39 (24%) vs Other: 5/15 (46%)	NS		Chi^2 test	None	White (67%) Black (24%) Other (9%)
Quinto 2011 Cross-sectional 10/10	US, n=32,321, Privately insured, Age 5-17y	Hispanic	ED visit or hospitalisation	OR	1.19	1.10 to 1.28	Reference group: non-Hispanic	Logistic Regression	Age, sex, race, parent education, controller use, GORD, diabetes	White 21%; Black 14%; Hispanic 33%
		Hispanic	OCS dispensed	OR	0.89	0.83 to 0.96				
		African American	ED visit or hospitalisation	OR	1.64	1.51 to 1.79	Reference group: non-African American			
		African American	OCS dispensed	OR	0.94	0.87 to 1.03				
		other (white/Asian)	ED visit or hospitalisation	OR	1.52	1.28 to 1.82	Reference group: non-other (white/Asian)			
		other (white/Asian)	OCS dispensed	OR	0.88	0.74 to 1.05				
Rust 2013 Cross-sectional, 9/10	US, n=43,156, Medicaid registered, Age 5-12y	Ethnicity – Black	ED visit in 90d after ICS Rx	OR	1.12	1.05 to 1.19	Reference group: White	Logistic regression	Age, gender, race, rural/urban, state, asthma severity, doctor visits, ICS adherence	White 36%; Black 33%; Hispanic 30% African American at greater risk than White; Hispanic at similar/less risk than white
			Hospitalisation in 90d after ICS Rx	OR	1.36	1.14 to 1.60				
		Ethnicity – Hispanic	ED visit in 90d after ICS Rx	OR	0.71	0.65 to 0.78	Reference group: White			
		Ethnicity – Hispanic	Hospitalisation in 90d after ICS Rx	OR	1.01	0.80 to 1.29				
Brehm 2012 Cross-sectional, 9/10	Puerto Rico, n=287, Children from San Juan, Age 6-14y	Each 20% increase in African ancestry	At least one ED or urgent visit, OCS course, hospitalisation	OR	0.9	0.6 to 1.4		Stepwise multivariate	Age, sex, vitamin D level, use of ICS, African ancestry,	
McCarville 2013	US, n= 466, Inner city low-income,	Hispanic	Number of hospitalisations	Incidence rate ratio	0.75	0.49 to 1.14	Reference group: Black,	Multivariable regression with		White 16%; Black 58%;

Cross-sectional, 8/10	Age 8-14yrs		ED visits, unscheduled care in 12m				White, other non-Hispanic	cotinine as primary predictor	Age, sex, race, BMI, household income,	Hispanic 26% African American at greater risk than Hispanic or White
		White, non-Hispanic	Number of hospitalisations ED visits, unscheduled care in 12m	Incidence rate ratio	0.56	0.35 to 0.90	Reference group: Black			
Sarpong 1997 Cross-sectional, 8/10	US, n=138, Urban area, Mean age 10.1y (SD 2.9)	Race – black	Hospitalisation	OR	3.18	1.35 to 7.49	Reference group: non-Black	Stepwise multiple logistic regression	Age, sex, area of residence, type of medical insurance	
Findley 2003 Cross-sectional, 7/10	US, n=1,615, Inner-city school-based, Mean age 7.4yrs	Ethnicity- Puerto Rican	Parent reported ED visit in past 12m	OR	0.91	0.55 to 1.48	Reference group: non-Puerto Rican	Logistic regression	Controlled for 'other risk factors'	
			Parent reported hospitalisation in past 12m	OR	0.98	0.56 to1.69				
Stingone 2006a Cross-sectional, 7/10	US, n=530, Inner city minority population, Age 5-12y	Dominican	Hospitalisation or ED visit in previous 12m	OR	3.18	1.42 to 7.13	Reference group: White	Multivariate logistic regression	Sex, income, ethnicity, usual care, delaying care, insurance	White 8%; Black 31%; Hispanic 44% African [Americans, Hispanic at greater risk than White]
		Mexican		OR	4.51	0.67 to 29.1				
		Puerto Rican		OR	6.16	2.47 to 15.4				
		Other Latino		OR	3.15	1.17 to 8.45				
		African American		OR	2.87	1.49 to 5.52				
		Asian		OR	1.73	0.85 to 3.54				
		Other		OR	2.36	0.84 to 6.65				
Malhotra 2014 Cross-sectional, 6/10	US, n=155,128, Medicaid, Age 5-12y	Black-white ratio	ED visit	Median Black-White ED visit rate ratio	2.4	Unclear significance	White 26%; Black 45%; Hispanic 21%	Quintile cut-offs and rate ratios	Not applicable	African American at greater risk than White
Quezada 2016 Cross-sectional, 6/10	US, n=200, Non-exacerbators: 185 Exacerbators:110 Age 6-17y (mean 11y)	Race White 43%; Black 47%; Other 11%	OCS use or urgent care during 24w study	x/n (%)	Exacerbators: 43% white, 47% black Non-Exacerbators: 37% white, 51% black	P=0.56		Fisher test	None	Recruited to a trial of proton-pump inhibitors for asthma
Wood 2002 Cross-sectional,	US, n=386, Deprived population, (age 2-12yrs)	Black	Parent reported attack needing medical care	Incident Rate Ratio (SE)	0.85 (SE 0.06)	P=0.02	Reference: Hispanic	Logistic regression	Age, sex, parent education, quality of care	White 27%; Black 24%; Hispanic 65%
		White (non-Hispanic)			0.54 (SE 0.07)	P<0.001	Reference: Hispanic			

5/10		Other			1.34 (SE 0.15)	P=0.01	Reference: Hispanic			
		Parental birthplace: Other	Parent reported attack needing medical care	Incident Rate Ratio (SE)	0.55 (SE 0.06)	P<0.001	Reference: US birthplace			

Access to healthcare

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Halterman 2001 Cohort, 5/9	US, n=165, From 11 diverse primary care settings, Age 75% 6-12y	Medicaid insurance	% with OCS course	x/n (%)	No Medicaid: 19/119 (26%) vs Medicaid: 8/46 (24%)	NS	N/A	Chi^2 test	None	No Medicaid: 72% Medicaid: 28%;
Sarpong 1997 Cross-sectional, 8/10	US, n=138, Urban area, Mean age 10.1y (SD 2.9)	Public aid/ Medicaid/self-pay	Hospitalisation	OR	2.34	1.12 to 4.92	Reference group: commercial insurance	Univariate logistic regression	Multivariable (age, sex, race, area of residence, medical insurance)	
Stingone 2006a Cross-sectional, 7/10	US, n=530, Inner city minority population, Age 5-12y	Stated source of usual care: 'ED'	Hospitalisation or ED visit in previous 12m	OR	4.41	2.27 to 8.58	Reference group: physicians' office	Multivariate logistic regression	Sex, income, ethnicity, usual care, delaying care, insurance	
		'Clinic or health centre'	Hospitalisation or ED visit in previous 12m	OR	1.24	0.814 to 1.90				
		'Other' or 'no usual place'	Hospitalisation or ED visit in previous 12m	OR	2.44	1.21 to 4.93				
		Insurance and healthcare arrangements:	Hospitalisation or ED visit in previous 12m	Excluded from the final model owing to lack of statistical significance			NA	Multivariate logistic regression	Sex, income, ethnicity, usual care, ICS use, sleep disturbance, delaying care	No insurance, Medicaid, child health plus, private, other
		Delaying care					NA			Delay ever: at least once; never
Wood 2002 Cross-sectional, 5/10	US, n=386, Deprived population, Age 2-12y	Insurance status: Intermittent	Parent reported attacks needing medical care	Incident Rate Ratio (SE)	1.00 (SE 0.06)	P=0.98	Reference: continuously insured	Logistic regression	Age, sex, parent education, quality of care	
		No health insurance during past year	Parent reported attacks needing medical care	Incident Rate Ratio (SE)	0.62 (SE 0.11)	P=0.006	Reference: continuously insured			

		Barriers to health care:	Parent reported attacks needing medical care	Incident Rate Ratio (SE)	1.08 (SE 0.02)	P<0.001	For each 1-unit change in score	Logistic regression		
		Quality of health care score	Parent reported attacks needing medical care	Incident Rate Ratio (SE)	1.23 (SE 0.03)	P<0.001	For each 1-unit change in score	Logistic regression		(5 questions based on asthma guidelines)
Canino 2012 Cross-sectional, 2/10	US/Puerto Rico, n=804, White and Hispanic children Age 7-15y: mean age 10.6y (SD2.5)	Public insurance	Frequency of ED visit	x/n (%)	Frequent ED use: 168/255 (66%) vs infrequent ED use: 280/549 (51%)	P<0.001	Frequent (2+) vs infrequent (0-1) ED visit in previous 1y	Chi^2 test	None	
		Lack a usual source of care for breathing problems	Frequency of ED visit	x/n (%)	Frequent ED use: 51/255 (20%) vs infrequent ED use: 44/549 (8%)	P<0.001	Frequent (2+) vs infrequent (0-1) ED visit in previous 1y	Chi^2 test	None	

Care, services

Routine review

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Engelkes 2016 Cohort, 7/9	Netherlands, n=14,303, Routine GP record, Age 5-18y	Specialist visit for asthma	Hospitalisation, ED visit, or OCS course	RR	1.66	1.33 to 2.07	Reference group: No specialist visits	Poisson regression	Age, age^2, gender	[Model 1]
Vernacchio 2013 Cross-sectional, 9/10	US, n=1,562 (in 3 separate year cohorts), Persistent asthma, Age 5-17y	1 routine office visits	Hospitalisation, ED visit, or OCS use	RR for 2008 RR for 2009 RR for 2010	0.79 0.53 0.41	(0.53 to 1.19) (0.34 to 0.85) (0.25 to 0.66)	Reference ≥2 visits	Logistic regression	Age, gender	[Confounding by severity]
		No routine office visits		RR for 2008 RR for 2009 RR for 2010	0.97 0.51 0.69	(0.62 to1.50) (0.29 to 0.90) (0.40 to1.19)	Reference ≥2 visits			
Forno 2010 Cross-sectional, 7/10	Costa Rica, n=465, Age 6-14y	≥4 routine physician visits in the past year	Hospitalisation, ED, urgent visits in previous year	OR	6.8	3.3 to 13.9	Reference: ≤3 physician visits	Multivariate: stepwise logistic regression	Age, sex, lung function, SABA, specific IgE, parental education	[Model 1] [Confounding by severity]

Flu vaccination

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Vernacchio 2013 Cross-sectional, 9/10	US, n=1,562 (in 3 separate year cohorts), Persistent asthma, Age 5-17y	No flu vaccination	Hospitalisation, ED visit, or OCS use	RR for 2008 RR for 2009 RR for 2010	0.95 0.83 0.87	(0.67 to 1.35) (0.57 to 1.21) (0.59 to 1.28)	reference flu vaccination	Logistic regression	Age, gender	

Environment

Environmental tobacco smoke exposure (ETS)

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Rabinovitch 2011 Cohort, 6/9	US, n=44, School for children with moderate/severe asthma, Age 6-15y	ETS (parental report and/or urine cotinine level >ln 3.1 ng/mg)	ED or unscheduled care visits	RR	3.6	1.1 to 11.5	Reference group: not exposed to ETS	2-tailed Fisher exact test	Lung function	[Fewer children in the ETS group were allergic]
Pyle 2015 Case-control, 6/9	US, n=944, Persistent asthma with exacerbation in previous 12m, Age 5-18y; mean 10.2y	Cases (n=236): ETS (parent – reported exposure at home)	ED visit in past 12m	OR	1.121	0.66 to 1.92	Controls (n=708): not exposed to ETS	Logistic regression	Age and sex matched controls	Controls more likely to have had flu vaccination. Cases had greater BMI
			Hospitalisations in past 12m	OR	1.81	0.43 to 7.63				
			OCS use in past 12m	OR	0.91	0.59 to 1.39				
Rosas-Salazar 2013 Cross-sectional, 9/10	Puerto Rico, n=351, Urban children, Age 6-14y	Reported ETS exposure	At least one ED or urgent care visit in past year	OR	0.7	0.5 to 1.1	Reference: no exposure to ETS	Multivariate stepwise logistic regression	Age, sex, income, use of ICS, exposure to ETS	
McCarville 2013 Cross-sectional, 8/10	US, n= 466, Inner city low-income Age 8-14yrs	Cotinine level ≥1 (69.3%)	Number of hospitalisations ED visits, unscheduled care in 12m	Incidence rate ratio, p-value	1.39,	1.08 to 1.78	Cotinine level <1	Multivariable regression	Age, sex, race, BMI, household income,	50.4% households reported ETS; 69.3% of children had cotinine levels ≥1
		Reported household smoking (50.4%)	Number of hospitalisations ED visits, unscheduled care in 12m	Incidence rate ratio, p-value	1.04, NS p-value	0.83 to 1.31	No reported ETS	Multivariable regression		
Dales 2002 Cross-sectional, 7/10	Canada, n=2,986 children from 136 schools, (5-19yrs)	Reported regularly exposed to ETS	ED or Hospitalisation	OR	1.55	1.22 to 1.97	Reference group: no exposure to ETS	Outcomes weighted for each student based on probability of the school being sampled and response rates	None	Statistical adjustment for design effects (including ICC)

Chilmonczyk 1993 Cross-sectional, 7/10	US, n= 199, Age 8m-13y (mean age ~7.5y)	Parent-reported exposure to ETS	Acute exacerbations in previous 12m	RR	1.8	1.4 to 2.2	Reference: highest vs lowest exposure category	Stepwise multivariate linear regression	Mother age & education level, child's age, sex, and day-care attendance	[Exacerbation not defined]
		Urine cotinine measurements			1.7	1.4 to 2.1				
Quezada 2016 Cross-sectional, 6/10	US, n=200, Age 6-17y (mean 11y)	Second hand smoke exposure (yes/no)	OCS use or urgent care during 24week study	x/n (%)	Exacerbators: 34/110 (31%) vs Non-exacerbators: 54/185 (29%)	P= 0.75	ETS exposure Exacerbators vs Non-exacerbators	Fisher test	None	Recruited to a trial of proton-pump inhibitors for asthma
Canino 2012 Cross-sectional, 2/10	US/Puerto Rico, n=804, White and Hispanic children, Age 7-15y: mean age 10.6y (SD2.5)	Reported ETS exposure	ED visit	x/n (%)	Frequent ED use: 97/255 (38%) vs infrequent ED use: 132/549 (24%)	P<0.001	Frequent (2+) vs infrequent (0-1) ED visit in previous 1y	Chi^2 test	None	

Rural/Urban residence

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Halterman 2001 Cohort, 5/9	US, n=165, from11 diverse primary care settings, Age 75% 6-12y	Urban rural location	% with steroid courses	Comparison	Urban: 28% Suburban: 18% Rural/semi-rural : 25% Small town: 31%	NS	N/A	Chi^2 test	None	Urban 33% Suburban 26% Semi/Rural 26% Small town 15%
Blatter 2016 Case-control, 7/9	Puerto Rico, n=304, Urban population Age 6-14y	Residential proximity to a major road, per every 100 m	At least one ED visit or OCS use in previous year	OR	1.2	1.1 to 1.3	Incr. odds per 100 m	Stepwise multivariate	Sex and age	
Rust 2013 Cross-sectional, 9/10	US, n=43,156, Medicaid registered, Age 5-12y	Small metropolitan area	ED visit	OR	0.94	0.88 to1.00	Reference group: large metropolitan area	Logistic regression	Age, gender, race, rural/urban, state, asthma severity, doctor visits, ICS adherence	
			Hospitalisation	OR	1.13	0.95 to1.33				
		Non-metropolitan area	ED visit	OR	0.95	0.95 to1.33				
			Hospitalisation	OR	1.23	0.94 to1.35				
Pesek 2010 Cross-sectional, 8/10	US, n=12,085, Majority African American, Age 4-17yrs	Geographical location: Rural	Emergency health care utilisation	"There were no significant differences in ED visits or hospitalizations between the urban and rural groups"			Reference: urban	Multivariate analysis: logistic regression	Age, race, sex, and type of insurance	OR for exacerbations not reported

Sarpong 1997 Cross-sectional, 8/10	US, n=138, Urban area, Mean age 10.1y (SD 2.9)	Residence – urban	Hospitalisation	OR	1.86	0.80 to 4.29	Reference: Non-urban residence	Univariate logistic regression	Multivariable (age, sex, race, area of residence, medical insurance)	
Brown 2012 Cross-sectional, 7/10	US, n=224, Recruited from urban clinic, Age 6-17y,	Residence <417 metres from major roadway	ED visit	OR	1.86	0.92 to 3.76	Reference group: >417 metres from roadway	Logistic regression	Insurance status, race, FH asthma, ETS exposure, GORD	
		Residence <417 metres from major roadway	Hospitalisation	OR	2.45	1.23 to 4.89				

Demography

Age

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Baltrus 2017 Cohort, 9/9	US, n=615,432, Medicaid children, N=28 states	Age	ED visit	OR	0.99	0.99 to 0.99	Reference group: unknown?	Individual logistic regression	Sex, race, long-term controller medication ratio	County-level data not applicable
Schatz 2003 Cohort, 6/9	US, n=4,197, Age 3-17y (mean age 9.5y (SD 4.1)	Age at hospitalisation	Hospitalisation	Mean age in years (SD)	Not hospitalised: 9.52y (4.10) vs Hospitalised: 7.53y (3.67)	P<0.001	NA	Wilcoxon rank sum test	'All potential predictors'	
		Older age	Hospitalisation in study year	OR	0.84	0.77 to 0.91	Younger age	Logistic regression		
Murray 1997 Cohort, 6/9	US, n=782, Inner-city, Age groups 5-9; 10-14 (and to 34y)	Age 5-9	Hospitalisation	RR	6.09	3.90 to 9.51	Reference age 30+	Kaplan-Meier, log-rank test; Cox regression analysis	Age, duration of treatment	Younger age increases risk of an exacerbation
		Age 10-14	Hospitalisation	RR	4.51	2.86 to 7.11	Reference age 30+			
Sarpong 1997 Cross-sectional, 8/10	US, n=138, Urban area, Mean age 10.1y (SD 2.9)	Age	Hospitalisation in study year	OR	0.77	0.67 to 0.90	Odds per year	Stepwise multiple logistic regression analysis	Sex, race, area of residence, type of medical insurance	Younger age increases risk of an exacerbation
Quezada 2016 Cross-sectional, 6/10	US, n=200, Age 6-17y (mean 11y)	Age	OCS use or urgent care during 24week study	Mean age	Exacerbators: age 10.9y vs Non-exacerbators: 11.6y	P= 0.04	Mean age of exacerbators vs non-exacerbators	Fisher test	None	Recruited to a trial of proton-pump inhibitors for asthma
Wood 2002 Cross-sectional 5/10	US, n=386, Deprived population, Age 2-12y	Child age: for each 1-unit change in score	Parent reported attacks needing medical care	Incident Rate Ratio (SE)	0.95 (SE 0.01)	P=0.001		Logistic regression	Age, sex, parent education, quality of care	Younger age a risk factor for exacerbation

Age onset of asthma

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Quezada 2016	US, n=200, Age 6-17y (mean 11y)	Age at asthma onset	OCS use or urgent care	Mean age of onset	Exacerbators: age 2.9y (2.4-3.4) vs	P= 0.09		Fisher test	None	Recruited to a trial of proton-

Cross-sectional, 6/10			during 24week study		Non-Exacerbators: age 3.7y (3.2-4.1)					pump inhibitors for asthma

Longer duration of asthma

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Haselkorn 2009b Cohort, 8/9	US, n=563, Severe/difficult to treat asthma, Age 6-11y	Duration of asthma	At least one OCS course reported in 12m	OR	1.06	1.01 to 1.12	OR per year increase	Stepwise model	Multivariable (age, sex, race, BMI, allergies, ETS, ICS, control)	TENOR study
Bacharier 2003 Cross-sectional, 8/10	US, n=1,041, Mild or moderate asthma, Age 5-12y	Duration of asthma	Prior hospitalisation (at at any time during their life).	OR	1.93	1.29 to 2.87		Logistic regression	Clinic, race, income, and gender	CAMP study baseline data. [Confounding by duration of outcome]
Quezada 2016 Cross-sectional, 6/10	US, n=200, Age 6-17y (mean 11y)	Number of years with asthma	OCS use or urgent care during 24week study	Mean duration in years	Exacerbators: 8y (7.3 to 8.7) vs Non-Exacerbators: 8y (7.4 to 8.5)	P= 0.98		Fisher test	None	Recruited to a trial of proton-pump inhibitors for asthma

Gender

Male at increased risk of exacerbation	Female at increased risk of exacerbation	No difference between genders

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Baltrus 2017 Cohort, 9/9	US, n=615,432, Children on Medicaid from 28 states	Sex: Male	ED visit	OR	1.14	1.12 to 1.15	Reference group: female	Individual logistic regression	Sex, race, long-term controller medication ratio	County-level data not applicable
Engelkes 2016 Cohort, 7/9	Netherlands, n=14,303, Routine GP record, Age 5-18y	Gender	Hospitalisation, ED visit, or OCS course	RR	1.02	0.69 to 1.50	Reference group: unknown	Poisson regression	Age, age^2	[Model 1]
Kwong 2012	US, n=960, Inner city children	Gender female	ED visit or hospitalisation	OR	0.63	0.4 to 1.1	Reference group: male	Logistic regression	Age, ethnicity, sex, baseline asthma	

Cohort, 6/9	Age 2-18y (60% were 6-11y)		Hospitalisation, ED visit or OCS course	OR	0.73	0.5 to1.0			control, clustering effect of care site	
Schatz 2003 Cohort, 6/9	US, n=4,197, Age 3-17y (mean age 9.5y (SD 4.1)	Gender: female	Hospitalisation in study year	x/n (%) female	Hospitalised: 22/57 (38.6%) vs Not hospitalised: 1564/4140 (37.8%)	Not significant	NA	Fisher's exact test	'All potential predictors'	
Halterman 2001 Cohort, 5/9	US, n=165, From 11 primary care settings, Age 75% 6-12y	Gender	% with OCS courses	x/n (%)	Male 19/61 (31%) Female 8/47 (17%)	NS	Comparison male vs female	Chi^2 test	None	Male (59%) Female (41%)
Quinto 2011 Cross-sectional, 10/10	US, n=32,321, Privately insured, Age 5-17y	Gender male	OCS use	OR	0.86	0.81 to 0.90	Reference group: female	Logistic Regression	Age, sex, race, parent education, controller use, GORD, diabetes	Significant using OCS definition of exacerbation
		Gender male	Hospitalisation or ED visit	OR	1.00	0.94 to 1.06				
Rust 2013 Cross-sectional, 9/10	US, n=43,156, Medicaid registered, Age 5-12y	Gender male	ED visit in 90d after ICS Rx	OR	1.00	0.95 to1.05	Reference group: female	Logistic regression	Age, gender, race, rural/urban, state, asthma severity, doctor visits, ICS adherence	
		Gender male	Hospitalisation in 90d after ICS Rx	OR	0.88	0.77 to1.00				
McCarville 2013 Cross-sectional, 8/10	US, n= 466, Inner city low-income, Age 8-14yrs	Gender: female	Hospitalisations, ED visits, unscheduled care in past 12m	Incidence rate ratio	0.79	0.63 to 0.99	Reference: male	Multivariable regression	Age, sex, race, BMI, household income,	
Sarpong 1997 Cross-sectional, 8/10	US, n=138, Urban area, Mean age 10.1y (SD 2.9)	Gender male	Hospitalisation	OR	1.29	0.64 to 2.60	Reference group: female	Univariate logistic regression	Multivariable (age, sex, race, area of residence, medical insurance)	
Dales 2002 Cross-sectional, 7/10	Canada, n=2,986 children from 136 schools, (5-19yrs)	Gender male	Hospitalisation	OR	1.01	0.78 to 1.30	Reference group: female	Outcomes weighted for each student based on probability of the school being sampled and response rates	None	Statistical adjustment for design effects (including ICC)
Stingone 2006a	US, n=530, Inner city minority population, Age 5-12y	Gender: male	Hospitalisation or ED visit in previous 12m	OR	2.22	1.31 to 3.76	Reference group: female	Multivariate logistic regression	Sex, income, ethnicity, usual care, delaying care, insurance	

Cross-sectional, 7/10										
Akinbami 2009 Cross-sectional, 6/10	US, n≈ 6.7million, census survey data, Age 5-10y and 11-17y	Gender (M/F)	ED visits	x per 10,000 children with current asthma	M: 988 (SE 157) F: 1,296 (SE 243)	95%CI included 1.0		At-risk analysis	'When higher asthma prevalence among boys was accounted for, the differences between boys and girls diminished. The RR for boys compared with girls for ED visits, hospitalisations, and death had 95%CI that included 1.0	
			Hospitalisations	x per 10,000 children with current asthma	M: 313 (SE 51) F: 244 (SE 39)	95%CI included 1.0		At-risk analysis		
Quezada 2016 Cross-sectional, 6/10	US, n=200, Age 6-17y (mean 11y)	Gender	OCS use or urgent care during 24w study	x boys (%)	Exacerbators: 73 boys (66%) vs Non-Exacerbators: 110 boys (59%)	P= 0.24	Comparison exacerbators vs non exacerbators	Fisher test	None	Recruited to a trial of proton-pump inhibitors for asthma
Canino 2012 Cross-sectional, 2/10	US/Puerto Rico, n=804, White and Hispanic children, Age 7-15y:	Gender	ED use	x girls (%)	Frequent ED use: 112 (44%) vs infrequent ED use: 236 (43%)	NS	Frequent (2+) vs infrequent (0-1) ED visit in previous 1y	Chi^2 test	None	

Other health conditions

Obesity

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Peters 2011 Cohort, 8/9	US, n=473, Deprived area, Aged 5-17y (mean age 9.5yrs)	BMI percentiles <85th >85th- <95th >95th	Hospitalisation, ED visits, UC visits	No data, but the statement is made 'In children, there was no relationship between BMI and hospital admissions, ED visits, unscheduled office visits or overall healthcare utilisation (>0.19 – 0.79)				Chi² test	None	
Black 2013 Cohort, 8/9	US, n=623,358, Private insurance, Aged 6-19y	Underweight: BMI <5th percentile	ED visit and/or OCS use	Adjusted prevalence ratio	1.10	0.98 to 1.24	Reference: normal BMI	Prevalence ratios from Poisson regression models	Age, sex and insurance payer	Normal Weight defined as (BMI ≥ 5th to <85th percentiles)
		Overweight (BMI 85 to 95th percentile or BMI>25)	ED visit and/or OCS use	Adjusted prevalence ratio	1.08	1.03 to 1.14	Reference: normal BMI			
		Moderately obese (BMI >95th percentile or BMI>30)	ED visit and/or OCS use	Adjusted prevalence ratio	1.16	1.10 to 1.23	Reference: normal BMI			
		Extremely obese (BMI >1.2 x 95th percentile or BMI >35)	ED visit and/or OCS use	Adjusted prevalence ratio	1.15	1.07 to1.23	Reference: normal BMI			
Wu 2011 Cohort, 6/9	US, N=1019, Children age 5-12y	BMI z score	OCS use, ED visit or hospitalisation	β estimate	-0.039	-0.14 to 0.07	OR not given	Multivariate modelling using GEE	Age, FEV_1/FVC Use of ICS, PC20, eosinophils	
Schatz 2013 Cohort, 7/9	US, n=4,197, Age 3-17y (mean age 9.5y (SD 4.1)	Overweight (BMI 85th to 94th percentile); Obese ≥95th percentile	OCS course	RR	1.17	1.07 to 1.29	Reference group: normal BMI	A GEE model	Sex, education	46% overweight or obese
Quinto 2011 Cross-sectional, 10/10	US, n=32,321, Privately insured Age 5-17y	Overweight	OCS use	OR	1.21	1.13 to 1.29	Reference group: normal BMI	Logistic Regression	Age, sex, race, parent education, controller use, GORD, diabetes	Weight defined as: Obese (BMI >95th percentile) Overweight (BMI 85th -94th percentile)
		Overweight	Hospitalisation or ED visit	OR	1.07	0.99 to 1.15				
		Obese	OCS use	OR	1.28	1.21 to 1.36	Reference group: normal BMI			
		Obese	Hospitalisation or ED visit	OR	1.04	0.98 to 1.11				

Lang 2012 Cross-sectional, 8/10	US, n=10,599, 5-11yrs	Underweight (BMI <5th percentile)	Exacerbation (visit to asthma specialist)	OR	3.79	0.22 to 64.18	Reference: normal BMI	Multivariate logistic regression	Gender, race, age group, insurance status, asthma severity. FVC, FEV_1; ICS	Normal Weight defined as (≥ 5th to <85th percentiles)
		Obese (BMI >95th percentile)	Exacerbation (specialist visit)	OR	1.41	0.64 to 3.11	Reference: normal BMI			
Mahut 2012 Cross-sectional, 7/10	France, n=491, Age 6-15y	BMI BMI z-score	OCS use or ED visit		BMI BMI z-score:	P=0.90 P=0.34		ANOVA (unclear)	None	
Wiesenthal 2016 Cross-sectional, 7/10	US, n=472, Children with persistent asthma, Age 3-10y	Overweight/ obese BMI >85th percentile	≥2 ED visits, urgent care or hospitalisations, in the past year	OR	1.3	0.87 to 1.93	Reference group: normal BMI	Logistic regression	Race, ethnicity, caregiver age and screen time	Baseline data from an trial.
Stingone 2011 Cross-sectional, 6/10	US, n=264, Urban, Aged 5-12y	Underweight: <5th centile Normal: 5th to 84.9th centile Overweight/ obese: >85th centile	ED visit in previous 12m	% with ED visit	Underweight 36.3% Normal 30.5% Overweight 49.2%	P<0.05	Prevalence of events by BMI groups		Gender, parent education, household income, ethnicity, ETS	
			Hospitalisation in previous 12m	% hospitalised	Underweight 24.7% Normal 4.9% Overweight 6.8%	P<0.05				
Quezada 2016 Cross-sectional, 6/10	US, n=200, Age 6-17y (mean 11y)	BMI (kg/m^2)	OCS use or urgent care during 24week study	Mean BMI	Exacerbators: 22.4 kg/m^2 vs Non-exacerbators: 22.5 kg/m^2	P=0.48	Comparison exacerbators vs non-exacerbators	Fisher test	None	Recruited to a trial of proton-pump inhibitors for asthma

IQ/special needs

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Bacharier 2003 Cross-sectional, 8/10	US, n=1,041, Mild or moderate asthma, Age 5-12y	IQ (Not stated, but presumably a continuous variable)	Prior hospitalisation (at any time during their life)	OR	0.98	0.97 to 0.99	Lower IQ = higher odds of prior hospitalisation	Logistic regression	Clinic, race, income, and gender	CAMP study baseline data
Stingone 2006b	US, n=530, Inner city minority population,	Special education classes	Hospitalisation in previous 12m	% hospitalised,	Special education: 18.3% vs General education: 6.9%	P<0.05	Prevalence of events by	Chi^2 test	Sociodemographic factors	

Cross-sectional, 7/10	Age 5-12y	Special education	ED visit in previous 12m	% with ED visit	Special education: 54.9% vs General education: 44.1%	P<0.10	education class			

Parental health

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Wood 2002 Cross-sectional, 5/10	US, n=386, Deprived population, Age 2-12y	Parental mental health	Parent reported attacks needing medical care	Incident Rate Ratio (SE)	0.99 (SE 0.001)	P<0.001	For each 1-unit change in 5-item Mental Health scale (SF-36)	Logistic regression	Age, sex, parent education, quality of care	

Parent marital status

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Dales 2002 Cross-sectional, 7/10	Canada, n=2,986 children from 136 schools, Age 5-19yrs	Parent marital status- single, never married	Hospital admission	OR	1.92	1.18 to 3.12	Reference group: married	Outcomes weighted for each student based on probability of the school being sampled and response rates	None	Statistical adjustment for design effects (including ICC)
		Separated, divorced, widowed	Hospital admission	OR	0.96	0.67 to 1.36				
Wood 2002 Cross-sectional, 5/10	US, n=386, Deprived population, Age 2-12y	Marital status: single	Parent reported attacks needing medical care	Incident Rate Ratio (SE)	0.90 (SE 0.06)	P=0.12	Reference group: married	Logistic regression:	Age, sex, parent education, quality of care	
		Marital status: single with partner	Parent reported attacks needing medical care	Incident Rate Ratio (SE)	1.16 (SE 0.09)	P=0.08	Reference group: married			

Co-morbidities

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Quinto 2011	US, n=32,321, Privately insured,	Diagnosis of GORD	OCS use	OR	1.08	0.96 to 1.21		_Hlk349690904	Age, sex, race, parent education,	

Cross-sectional 10/10	Age 5-17y	Diagnosis of GORD	Hospitalisation or ED visit	OR	1.58	1.41 to 1.77	Reference: no diagnosis of GORD		controller use, GORD, diabetes	
		Diagnosis of diabetes	OCS use	OR	0.79	0.58 to 1.07	Reference: no diagnosis of diabetes			
		Diagnosis of diabetes	Hospitalisation or ED visit	OR	1.59	1.19 to 2.13				

Nutritional deficiencies

Study ID Design, Quality score	Country, Sample size, Population, Ages	Risk factor definition	Exacerbation definition	Effect measure	Effect measure value	95%CI or significance	Reference group or comparator	Analysis used	Adjustments or variables	Comments [Reviewers' interpretation]
Brehm 2010, Cohort, 7/9	US, n=1024, CAMP study, Age 5-12y	Vitamin D insufficiency (≤30ng/ml)	ED visit or hospitalisation in 4 years of study	OR	1.4	1.0 to 1.9	Reference: Vitamin D sufficient group	Multivariate logistic regression	Age, sex, BMI, race, income, treatment group, season, severity,	Deficiency: <30 ng/ml
Blatter 2016 Case-control, 7/9	Puerto Rico, n=304, Urban population, Age 6-14y	Folate deficiency	At least one ED visit or OCS use in previous year	OR	2.20	1.1 to 4.6	Reference: normal folate	Stepwise multivariate	Sex and age	Deficiency <20 ng/ml
		Vitamin D insufficiency	At least one ED visit or OCS use in previous year	OR	2.8	1.5 to 5.2	Reference: no vitamin D insufficiency			Deficiency: <30 ng/ml
Brehm 2012 Cross-sectional, 9/10	Puerto Rico, n=287, Children from San Juan, Age 6-14y	Vitamin D insufficiency	At least one ED or urgent visit, OCS course, hospitalisation	OR	2.6	1.5 to 4.7	Reference: no vitamin D insufficiency	Stepwise multivariate	Age, sex, vitamin D level, use of ICS, African ancestry,	Deficiency: <30 ng/ml
		High vitamin D intake (diet or supplements)	At least one ED or urgent visit, OCS course, hospitalisation	OR	1.1	0.6 to 1.9	Reference group: unknown			
Searing 2010 Cross-sectional, 5/10	US, n=100, Age 0-18y	Vitamin D level	OCS use	Median (IQR)	OCS use: 25 (18-30) vs no OCS use: 32 (25-40)	P=0.02	Comparison of vitamin D level in group with vs no OCS use	Wilcoxon test with Chi^2 approximation	None	[only 14 children had OCS use]

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