Supplementary:

Table E1: Search Strategies for the PUBMED, EMBASE and CENTRAL databases

[PUBMED]	[EMBASE]
(Asthma Terms) #1 “Asthma” [Mesh]	(Asthma Terms) #1 exp *Asthma/
(ICS Terms) #2 Inhaled corticosteroid* #3 Inhaled steroid* #4 ICS #5 Fluticasone #6 Budesonide #7 Beclomethasone #8 Triamcinolone #9 Flunisolide #10 Ciclesonide #11 #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10	(ICS Terms) #2 Inhaled corticosteroid*.mp. #3 Inhaled steroid*.mp. #4 ICS.mp. #5 Fluticasone.mp. #6 Budesonide.mp. #7 Beclomethasone.mp. #8 Triamcinolone.mp. #9 Flunisolide.mp. #10 Ciclesonide.mp. #11 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10
(COPD and Lung Function Terms) #12 “Pulmonary Disease, Chronic Obstructive” [Mesh] #13 “Forced expiratory volume” OR “FEV1” #14 “Forced expiratory flow” OR “FEF25-75” #15 “Airflow Obstruction” OR FEV1/FVC #16 “Lung function” AND (Growth OR Decline) #17 "Bronchial Hyperreactivity"[Mesh] #18 #12 OR #13 OR #14 OR #15 OR #16 OR #17	(COPD and Lung Function Terms) #12 exp *Chronic Obstructive Pulmonary Disease/ #13 exp *Forced expiratory volume/ OR exp* FEV1/ #14 exp *Forced expiratory flow/ OR exp* FEF25-75/ #15 exp *Airflow Obstruction/ #16 (Lung function AND (Growth OR Decline)).mp. #17 exp *bronchus hyperreactivity/ #18 12 OR 13 OR 14 OR 15 OR 16 OR 17
(Human Limit) #19 animals [mh] NOT humans [mh]	(Combination) #19 (1 AND 11 AND 18)
(Combination) #20 (#1 AND #11 AND #18) NOT #19	(Human Limit) #20 limit 19 to animal studies #21 19 NOT 20

[CENTRAL]
(Asthma Terms) #1 MeSH Descriptor: [Asthma]
(ICS Terms) #2 Inhaled corticosteroid* #3 Inhaled steroid* #4 ICS #5 Fluticasone #6 Budesonide #7 Beclomethasone #8 Triamcinolone #9 Flunisolide #10 Ciclesonide #11 #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10
(COPD and Lung Function Terms) #12 MeSH Descriptor: [Pulmonary Disease, Chronic Obstructive #13 “Forced expiratory volume” OR “FEV1” #14 “Forced expiratory flow” OR “FEF25-75” #15 “Airflow Obstruction*” OR “FEV1/FVC” #16 “Lung function” AND (Growth OR Decline) #17 MeSH Descriptor: [Bronchial hyperreactivity] #18 #12 OR #13 OR #14 OR #15 OR #16 OR #17
(Combination) #19 (#1 AND #11 AND #18)
(Trial Limit) #20 #19 in Trials

Table E2: List of references assessed in full-text and reasons for exclusion

Reason for Exclusion:	Reference:
1. Not English (n=15)	(1-15)
2. Abstract only (n=59)	(16-74)
3. Review, commentary or protocol (n=39)	(75-113)
4. Not asthma (n=19)	(114-132)
5. No ICS subgroup (n=40)	(133-172)
6. No control/placebo subgroup (n=95)	(173-267)
7. Follow-up < 1 year (n=25)	(268-292)
8. No relevant outcomes (n=35)	(293-327)
Included References: (n=38)	(328-365)

Table E3. Study characteristics of the observational studies included

Study Details	Age Group	Follow-up (Years)	Asthma Definition	Asthma Severity	ICS Intervention	Sample Size	Mean Age (Years)	Female (%)	Pre-BD FEV_1	
									Litres	% Pred.
Observational Studies										
Agertoft (1994) (328)	Children	3-7	Physician-diagnosed asthma	Mild-moderate	ICS use at baseline	216	6.1	31.5	-	81.3
					No ICS use at baseline	62	6.0	25.8	-	79.2
Backman (2018) (329)	Adults	13-28	Self-reported or physician-diagnosed asthma; or asthma-related symptoms with BHR or BDR	No restriction	ICS use within last 12 months	228	-	-	-	-
					No ICS use within last 12 months	1578	-	-	-	-
Boulet* (1994) (332)	Adults	5	Physician-diagnosed asthma; BHR	Mild-moderate	ICS use during follow-up	14	47.0	64.3	2.47	88.0
					No ICS use during follow-up	9	42.7	77.8	2.59	86.0
Bibi* (2006) (331)	Children	5	Physician-diagnosed asthma	No restriction	ICS use during follow-up	148	8.8	-	-	73.0
					No ICS use during follow-up	50	8.5	-	-	85.9
Coumou (2018) (336)	Adults	5	Physician-diagnosed asthma with onset in last 24 months; BHR or BDR	No restriction	ICS use at baseline	118	-	-	-	-
					No ICS use at baseline	23	-	-	-	-
de Marco (2007) (338)	Adults	9	Self-reported asthma	No restriction	ICS use during follow-up	339	34.1	63.7	3.20	95.0
					No ICS use during follow-up	297	33.7	45.4	3.70	101.6
Fujimura (2003) (341)	Adults	5-12	Physician-diagnosed cough-variant asthma; BHR	No restriction	ICS use at baseline	13	-	-	-	-
					No ICS use at baseline	7	-	-	-	-
Grol (1999) (342)	Adults	9-13	Physician-diagnosed asthma	No restriction	ICS use at baseline, follow-up	7	-	-	-	-
					No ICS use at baseline, follow-up	66	-	-	-	-
Konig* (1996) (345)	Children	8.4	Physician-diagnosed asthma; BHR or BDR if participants old enough to be assessed	No restriction	ICS use at baseline	34	-	-	-	92.0
					No ICS use at baseline	84	-	-	-	79.9
Lange (2006) (346)	Adults	10	Self-reported asthma	No restriction	ICS use at baseline, follow-up	44	58.0	75.0%	1.82	65.9
					No ICS use at baseline, follow-up	190	55.0	60.0%	2.63	87.3
Leung (2018) (347)	Children	5	Physician-diagnosed asthma	No restriction	No ICS use at baseline	106	9.8	36.8	-	89.7
					ICS use at baseline	87	9.5	37.9	-	93.2

* Denotes retrospective cohort studies. All others were prospective.

Physician-diagnosed asthma: Asthma reported to be diagnosed by a physician, or according to established clinical guidelines

BHR = Bronchial hyperresponsiveness; BDR = Bronchodilator reversibility

Table E4: Sensitivity analysis for RCTs: according to meta-analysis models and risk of bias (ROB)

Outcome or subgroup	Studies	Participants	Statistical Method	Effect Estimate	I^2
Fixed-effects models:					
Δ Pre-BD FEV_1 (% predicted)	8	8332	Mean Diff. (Fixed, 95%CI)	+2.01 (1.46, 2.56)	41%
Adults	5	4181	Mean Diff. (Fixed, 95%CI)	+2.47 (1.64, 3.29)	0%
Children	4	4151	Mean Diff. (Fixed, 95%CI)	+1.65 (0.91, 2.39)	64%
Δ Post-BD FEV_1 (% predicted)	2	7894	Mean Diff. (Fixed, 95%CI)	+0.85 (0.39, 1.31)	71%
Adults	1	3970	Mean Diff. (Fixed, 95%CI)	+1.54 (0.87, 2.21)	-
Children	2	3924	Mean Diff. (Fixed, 95%CI)	+0.21 (-0.43, 0.85)	12%
Random-effects models:					
Δ Pre-BD FEV_1 (% predicted)	8	8332	Mean Diff. (Random, 95%CI)	+2.22 (1.32, 3.12)	41%
Adults	5	4181	Mean Diff. (Random, 95%CI)	+2.47 (1.64, 3.29)	0%
Children	4	4151	Mean Diff. (Random, 95%CI)	+2.08 (0.71, 3.44)	64%
Δ Post-BD FEV_1 (% predicted)	2	7894	Mean Diff. (Random, 95%CI)	+0.61 (-0.31, 1.54)	71%
Adults	1	3970	Mean Diff. (Random, 95%CI)	+1.54 (0.87, 2.21)	-
Children	2	3924	Mean Diff. (Random, 95%CI)	+0.20 (-0.49, 0.90)	12%
All studies included:					
Δ Pre-BD FEV_1 (% predicted)	8	8332	Mean Diff. (Random, 95%CI)	+2.22 (1.32, 3.12)	41%
Adults	3	4181	Mean Diff. (Random, 95%CI)	+2.47 (1.64, 3.29)	0%
Children	4	4151	Mean Diff. (Random, 95%CI)	+2.07 (0.72, 3.42)	64%
Δ Post-BD FEV_1 (% predicted)	2	7894	Mean Diff. (Random, 95%CI)	+0.61 (-0.31, 1.54)	71%
Adults	1	3970	Mean Diff. (Random, 95%CI)	+1.54 (0.87, 2.21)	-
Children	2	3924	Mean Diff. (Random, 95%CI)	+0.20 (-0.49, 0.90)	12%
Studies with ≥1 high ROB excluded:					
Δ Pre-BD FEV_1 (% predicted)	5	8122	Mean Diff. (Random, 95%CI)	+1.95 (0.97, 2.94)	50%
Adults	3	4037	Mean Diff. (Random, 95%CI)	+2.32 (1.47, 3.18)	0%
Children	3	4085	Mean Diff. (Random, 95%CI)	+1.90 (0.41, 3.39)	70%
Δ Post-BD FEV_1 (% predicted)	2	7894	Mean Diff. (Random, 95%CI)	+0.61 (-0.31, 1.54)	71%
Adults	1	3970	Mean Diff. (Random, 95%CI)	+1.54 (0.87, 2.21)	-
Children	2	3924	Mean Diff. (Random, 95%CI)	+0.20 (-0.49, 0.90)	12%

Table E5. Summary of quality assessments for observational studies using the Modified Newcastle-Ottowa Scale

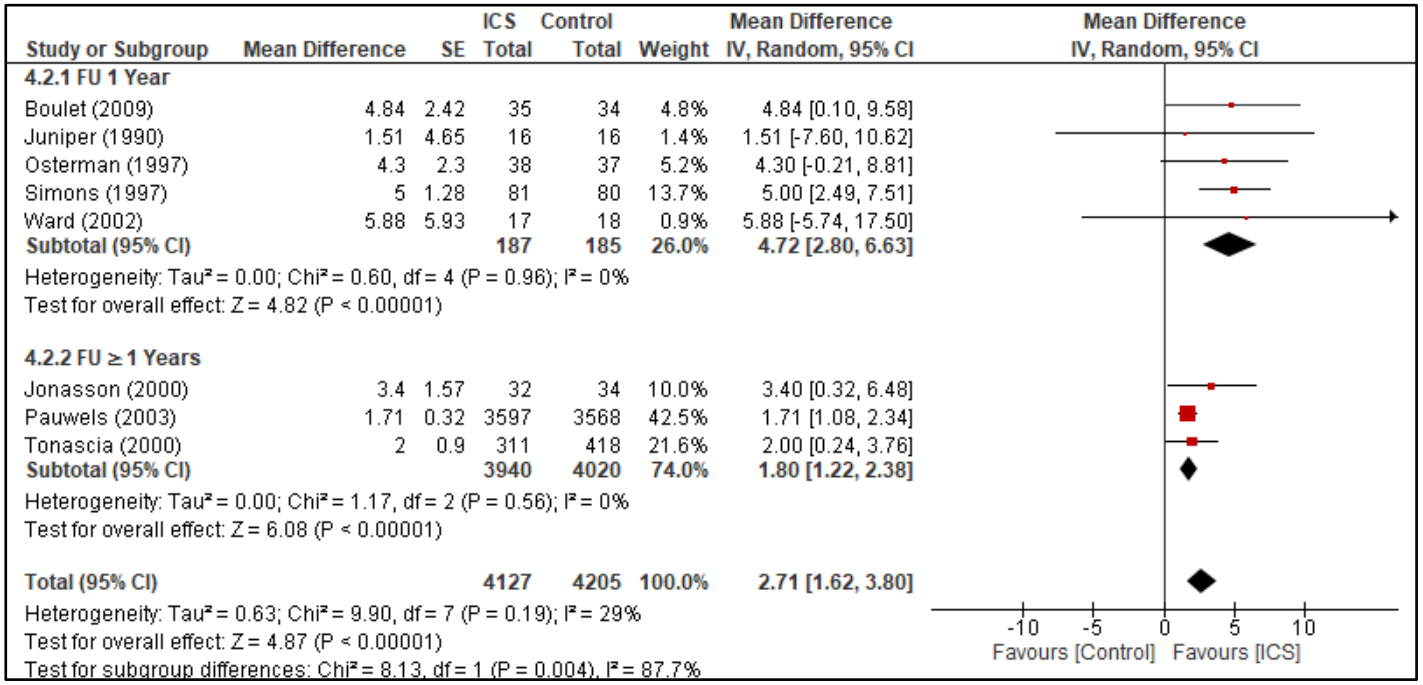
Reference	(1) Representative exposed cohort (Max 1)	(2) Selection of the non-exposed cohort (Max 1)	(3) Ascertainment of exposure (Max 1)	(4) Demonstration that outcome of interest was not present at start of study (Max 1)	(5) Comparability of cohorts on the basis of the design or analysis (Max 3)	(6) Assessment of the outcome (Max 1)	(7) Was follow-up long enough for outcomes to occur (Max 1)	(8) Adequacy of follow up of cohorts (Max 1)	Total (Max 10)
Agertoft (1994)	1	0	1	1	1	1	1	1	7
Backman (2018)	1	1	1	1	0	1	1	0	6
Boulet (1994)	1	1	1	1	0	1	1	0	6
Bibi (2006)	0	0	1	1	0	1	1	0	4
Coumou (2018)	1	1	1	1	0	1	1	1	7
de Marco (2007)	1	1	1	1	3	1	1	0	9
Fujimura (2003)	0	1	1	1	0	1	1	1	6
Grol (1999)	1	1	1	1	2	1	1	0	8
Konig (1996)	1	0	1	1	0	1	1	1	6
Lange (2006)	1	1	1	1	3	1	1	0	9
Leung (2018)	1	1	1	1	2	1	1	1	9

Score classification: Very good = 9-10; Good = 7-8; Satisfactory 5-6; Unsatisfactory 0-4

Table E6: Sensitivity analysis for observational studies: according to meta-analysis models and risk of bias (ROB)

Outcome or subgroup	Studies	Participants	Statistical Method	Effect Estimate	I^2
Fixed-effects models:					
Δ Pre-BD FEV_1 (% predicted)	1	190	Mean Diff. (Fixed, 95%CI)	+0.81 (0.01, 1.61)	-
Adults	0	0	Mean Diff. (Fixed, 95%CI)	Not estimable	-
Children	1	190	Mean Diff. (Fixed, 95%CI)	+0.81 (0.01, 1.61)	-
Δ Pre-BD FEV_1 (ml)	3	939	Mean Diff. (Fixed, 95%CI)	+9.24 (3.76, 14.73)	59%
Adults	3	939	Mean Diff. (Fixed, 95%CI)	+9.24 (3.76, 14.73)	59%
Children	0	0	Mean Diff. (Fixed, 95%CI)	Not estimable	-
Random-effects models:					
Δ Pre-BD FEV_1 (% predicted)	1	190	Mean Diff. (Random, 95%CI)	+0.81 (0.01, 1.61)	-
Adults	0	0	Mean Diff. (Random, 95%CI)	Not estimable	-
Children	1	190	Mean Diff. (Random, 95%CI)	+0.81 (0.01, 1.61)	-
Δ Pre-BD FEV_1 (ml)	3	939	Mean Diff. (Random, 95%CI)	+14.09 (1.77, 26.42)	59%
Adults	3	939	Mean Diff. (Random, 95%CI)	+14.09 (1.77, 26.42)	59%
Children	0	0	Mean Diff. (Random, 95%CI)	Not estimable	-
All studies included (including those with NOS score <7):					
Δ Pre-BD FEV_1 (% predicted)	2	468	Mean Diff. (Random, 95%CI)	+2.33 (-1.65, 6.32)	70%
Adults	0	0	Mean Diff. (Random, 95%CI)	Not estimable	-
Children	2	468	Mean Diff. (Random, 95%CI)	+2.33 (-1.65, 6.32)	70%
Δ Pre-BD FEV_1 (ml)	4	959	Mean Diff. (Random, 95%CI)	+9.54 (2.42, 16.65)	47%
Adults	4	959	Mean Diff. (Random, 95%CI)	+9.54 (2.42, 16.65)	47%
Children	0	0	Mean Diff. (Random, 95%CI)	Not estimable	-
Studies with NOS score <7 excluded:					
Δ Pre-BD FEV_1 (% predicted)	2	468	Mean Diff. (Random, 95%CI)	+2.33 (-1.65, 6.32)	70%
Adults	0	0	Mean Diff. (Random, 95%CI)	Not estimable	-
Children	2	468	Mean Diff. (Random, 95%CI)	+2.33 (-1.65, 6.32)	70%
Δ Pre-BD FEV_1 (ml)	3	939	Mean Diff. (Random, 95%CI)	+14.09 (1.77, 26.42)	59%
Adults	3	939	Mean Diff. (Random, 95%CI)	+14.09 (1.77, 26.42)	59%
Children	0	0	Mean Diff. (Random, 95%CI)	Not estimable	-

Figure E1: Forest plot comparison (RCTs): Change in Pre-BD FEV_1 (% predicted) stratified by follow-up



Methods E1: Modified Newcastle-Ottowa Scale template

Selection	Score	Notes
1) Representativeness of the exposed cohort: a) Truly representative of the average patient in the community * b) Somewhat representative of the average patient in the community * c) Selected group of individuals d) No description of the derivation of the cohort	/1	
2) Selection of the non-exposed cohort: a) Drawn from the same community as the exposed cohort * b) Drawn from a different source c) No description of the derivation of the non-exposed cohort	/1	
3) Ascertainment of exposure: a) Secure records * b) Structured interview * c) Written self-report d) No description	/1	
4) Demonstration that outcome of interest was not present at start of study: † a) Yes * b) No	/1	
Comparability		
*1) Comparability of cohorts on the basis of the design or analysis: (Max ***)* a) Study controls for asthma severity * and smoking status*; b) Study controls for socioeconomic status or education*	/3	
Outcome		
1) Assessment of the outcome a) Independent blind assessment. * b) Record linkage. * c) Self report. d) No description.	/1	
2) Was follow-up long enough for outcomes to occur ‡ a) Yes (select an adequate follow up period for outcome of interest) * b) No	/1	
3) Adequacy of follow up of cohorts § a) Complete follow up or all subjects accounted for. * b) Subjects lost to follow up unlikely to introduce bias * c) High loss-to-follow-up and no description of those lost, or no statement	/1	
Comments:		
Total score (Max = 10)		

Score classifications: Very good = 9-10; Good = 7-8; Satisfactory = 5-6; Unsatisfactory = 0-4.
* Indicates criteria for which the score is increased by 1 if fulfilled by the study being assessed

Scoring Information:
† Demonstrates outcome not present at start of study: Studies assessing only continuous lung function automatically received a score for this criteria. Studies assessing fixed airflow obstruction needed to demonstrate that fixed airflow obstruction was not present at baseline. ‡ Duration of follow-up: All included studies, having a follow-up duration of one or more years, automatically received a score for this criteria. § Adequacy of follow-up: Assessments of 'high loss to follow-up' were subjective and relative to the duration of the specific study. Those with a shorter durations required higher rates of retention to score (e.g. 80% for 1 year follow) compared to those with longer follow-up (e.g. 60% for 10 years). Studies which provided evidence that loss to follow-up was unlikely to introduce bias still received a score.

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