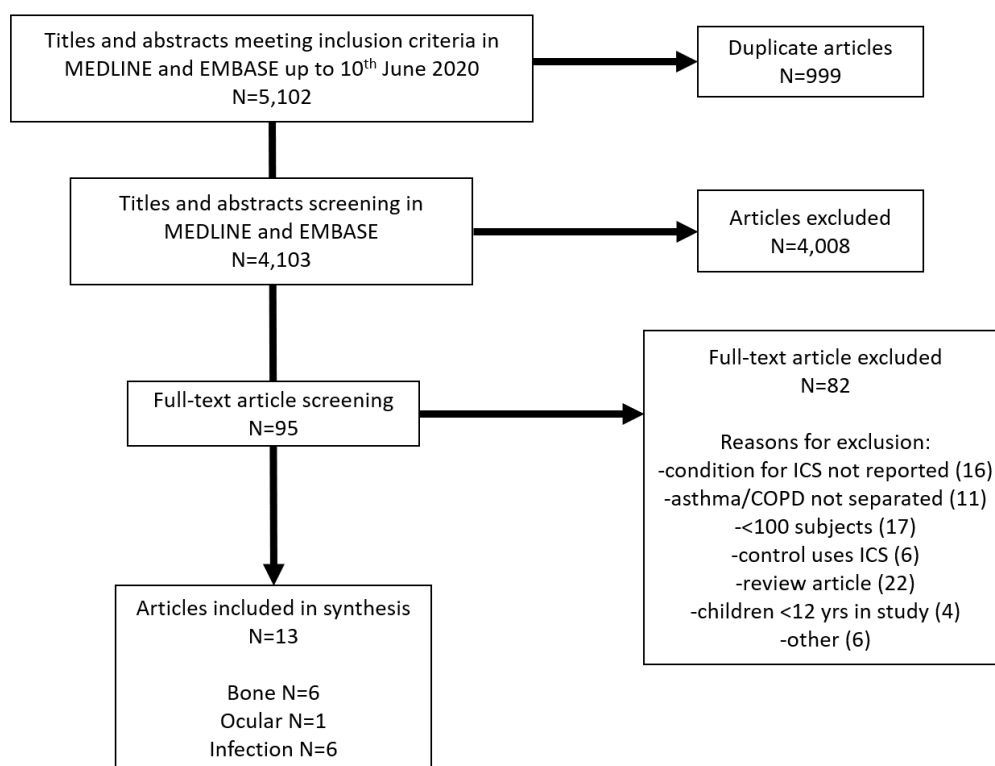


Supplementary Figure 1. PRISMA flowchart illustrating selection process of articles

Supplementary Table 1. Literature search terms

CONCEPTS	Search	search terms
Concept 1: Asthma	1	asthma.mp or Asthma/
Concept 2: Inhaled corticosteroids	2	Inhaled corticosteroid mp.
	3	ics.mp
	4	Inhal\$.mp.
	5	Ciclesonide.mp.
	6	Fluticasone/ or fluticasone.mp.
	7	Beclomethasone/ or beclomethasone.mp.
	8	Budesonide/ or budesonide.mp.
	9	Mometasone furoate/ or mometasone.mp.
	10	4 AND (5 OR 6 OR 7 OR 8 OR 9)
	11	2 OR 3 OR 9
	12	1 AND 10
Concept 3: Adverse effect	13	adverse event\$
	14	adverse effect\$
	15	side effect\$
	16	13 OR 14 OR 15
Concept 4: Bone metabolism	17	bone density.mp or Bone density/
	18	bone mineral.mp or Bone mineral/
	19	osteoporosis.mp or Osteoporosis/
	20	osteopenia.mp or Osteopenia/
	21	fracture.mp or Fracture/
	22	17 OR 18 OR 19 OR 20 OR 21 OR 22
Concept 5: Respiratory infection	23	pneumonia.mp or Pneumonia/
	24	respiratory tract infection.mp or Respiratory tract infection/
	25	tuberculosis.mp or Tuberculosis/
	26	mycobacter\$
	27	Mycobacterium/
	28	23 OR 24 OR 25 OR 26 OR 27
Concept 6: Ocular effects	29	cataract.mp or Cataract/
	30	glaucoma.mp or Glaucoma/
	31	29 OR 30
Concept 7: Diabetes	32	diabetes.mp or Diabetes/
	33	dm.mp
	34	dm\$.mp
	35	17 OR 18 OR 19
Final search	1 AND 2 AND (16 OR 22 OR 28 OR 31 OR 35)	

Supplementary Table 2. The PICO checklist.

P	Population	Adults with asthma
I	Intervention	Inhaled corticosteroids
C	Comparison	Adults with or without asthma, that do not use inhaled corticosteroids
O	Outcome	1. Respiratory infections (pneumonia or mycobacterial infection) 2. Ocular disorders (cataract or glaucoma) 3. Bone mineral loss (bone density or fracture) 4. Diabetes (new diagnosis or worsening glycaemia)

Supplementary Table 3a. Inclusion and exclusion criteria of trials with bone density as an outcome

Primary author	Tattersfield, A	Kemp, J
Year	2001	2004
Inclusion criteria	<ul style="list-style-type: none"> - relatively mild asthma and pre-bronchodilator FEV1 of 65% predicted or above - taking a B2 agonist only and no corticosteroid treatment (by any route) during the previous 3 months - no more than 1 month of treatment with oral corticosteroids in the previous year or ICS or nasal corticosteroids in the previous 6 months - at least 4 puffs of SABA and showing less than 25% variability in morning PEF during the last 7 days of the run in period with complete data 	<ul style="list-style-type: none"> - not pregnant and non-lactating - premenopausal or using defined contraception - at least 6 month history of stable and mild asthma - normal stimulated cortisol response - normal BMD on screening - absence of glaucoma, posterior subcapsular cataract or blindness - FEV1 of 50%-100% predicted - no CS use for 1 month prior - less than 4 weeks lifetime oral CS use
Exclusion criteria	<ul style="list-style-type: none"> - any other medical conditions - taking drugs known to affect BMD - required more than 2 weeks of bed rest in the previous 6 months - pregnant, lactating or at risk of becoming pregnant 	<ul style="list-style-type: none"> - excluded medications - presence of glaucoma, posterior subcapsular cataract or blindness - reversal of normal nocturnal sleeping hours - alterations in body weight (anorexia; morbid obesity; recent unexplained weight loss of >25%) - substance abuse

Supplementary Table 3b. Inclusion and exclusion criteria of observational studies with bone density as an outcome

Primary author	Sasagawa, M	Sosa, M	Langhammer, A	Israel, E
Year	2011	2006	2004	2001
Inclusion criteria	-Bronchial asthma -Hospital patient	Cases: - women - bronchial asthma -treated with ICS ≥ 1 year Controls: - weight-matched women	-Self reported previous or current asthma -Use of asthma medication -Asthma-related symptoms during the last 12 months	Physician diagnosed asthma ≥ 10 menstrual periods in the preceding year.
Exclusion criteria	Oral steroid use	Cases: - not received oral or parenteral steroids. Controls: - no asthma - no steroids of any form - weight matched to cases	N/A	- men - disease affecting bone turnover - taking any drugs known to influence bone metabolism - smoked in the preceding year - abnormal serum thyrotropin concentrations - low 25-hydroxyvitamin D concentrations - high serum parathyroid hormone concentrations - high serum follicle-stimulating hormone concentrations - 24-hour urinary calcium excretion of more than 250 mg (6.2 mmol) or low bone density (z score, -2 or less) - received >2 short courses of oral or parenteral glucocorticoids in the preceding year or any oral or parenteral glucocorticoids in the preceding three months

Supplementary Table 3c. Inclusion and exclusion criteria of observational studies with respiratory infection as an outcome

Primary author	McKeever, T	Qian, C. J	Ekbom, E	Kim M-H	Lee, C. H	Brode, S. K
Year	2013	2017	2019	2019	2013	2017
Inclusion criteria	Recorded diagnosis after Jan 2004	>1 prescription for a respiratory medication between Jan 1990-Dec 2007	Responded to RHINE II survey	- at least 2 outpatient visits - treated with asthma medications or received inpatient care - using more than 1 systemic corticosteroid and at least 1 asthma medication at the time of the outpatient clinic visits.	-Prescriptions for inhaled respiratory medications for >30 days -No history of recent TB	- >1 prescription for any inhaled B-agonist, inhaled anticholinergic, ICS, oral corticosteroid or methylxanthine during study period
Exclusion criteria	Cases: - COPD, bronchiectasis - changed inhaler in previous 90 days - prescribed >1 type of ICS inhaler on same day Controls: - COPD	-Prevalent users of respiratory medications -Less than 1 year of RAMQ drug coverage prior to cohort entry -Hospital admission for COPD -Data inconsistencies	N/A	N/A	-Previous prescriptions for inhaled medication for >30 days during the year prior to initiation date -Any ICD-10 diagnosis of TB within 1yr of index date -No matched controls -Age unknown	N/A

Supplementary Table 3d. Inclusion and exclusion criteria of observational studies with an ocular disorder as an outcome

Primary author	Smeeth, L
Year	2003
Inclusion criteria	-First diagnosis of cataracts while registered with a practice participating in CPRD -Date of first diagnosis of cataract was the index date -All participants have at least 180 days of observation period before the index date
Exclusion criteria	Diagnosis of congenital or traumatic cataracts