

Material and Methods

In order to obtain relevant publications on long term asthma treatment with oral corticosteroids a systematic literature search in the databases MEDLINE, EMBASE, INAHTA, NHS EED, DARE, and the Cochrane library was conducted. The original search was done in 2016 and was updated in 2018. The search strategy consisted of 3 separate blocks, one block each for intervention, indication, and a filter for treatment-related publications (Table S1, Table S2, Table S3, and Table S4). Only studies reporting primary data on side effects of long term oral corticosteroid exposure in adult asthma patients were included. Because of the broad search, the time frame of the search was limited to the last 5 years (original search in 2016). To ensure the equal consideration of older publications reference lists of all included publications were screened for additional relevant publications. In the first pass, titles and abstracts of all hits from the literature search were analyzed for eligibility. Potential relevant hits were the read as full text (Figure S1). Publications with other indications than asthma or short term use of corticosteroids as topic were excluded as well as publications focusing on special populations like children or pregnant women.

Table S1: Search strategy for MEDLINE

Name of database	MEDLINE	
Search interface	PubMed	
Date of the search	28.05.2018	
Time periode	From 19.01.2011	
Filter	No filter	
Line	Search	Hits
#1	system*[tiab] AND (corticosteroid*[tiab] OR glucocorticoid*[tiab])	34031
#2	OCS[tiab] OR "oral corticosteroid*" [tiab]	7471
#3	"oral glucocorticoid*" [tiab]	265
#4	#1 OR #2 OR #3	41350
#5	asthma[tiab]	134977
#6	Asthma[Mesh]	119318
#7	#5 OR #6	160618
#8	treat*[tiab] OR manage*[tiab] OR therap*[tiab]	6673542
#9	#4 AND #7 AND #10	3066
#10	#9 Publication date from 2011/01/19	1099

Table S2: Search strategy for EMBASE

Name of database	EMBASE	
Search interface	embase.com	
Date of the search	28.05.2018	
Time periode	From 2011	
Filter	No filter	
Line	Search	Hits
#1	system*:ti,ab AND (corticosteroid*:ti,ab OR glucocorticoid*:ti,ab)	49279
#2	OCS:ti,ab or "oral corticosteroid*":ti,ab	11900
#3	"oral glucocorticoid*":ti,ab	1053
#4	#1 or #2 or #3	60281
#5	MeSH descriptor: [Asthma] explode all trees	242460
#6	asthma:ti,ab	192659
#7	#5 or #6	268487
#8	treat*:ti,ab or manage*:ti,ab or therap*:ti,ab	8887658
#9	#4 and #7 and #8	6350
#10	#9 Publication Year from 2011	3149

Table S3: Search strategy for Cochrane Library

Name of database	Cochrane Library	
Search interface	Cochrane Library	
Date of the search	28.05.2018	
Time periode	From 19.01.2011	
Filter	No filter	
Line	Search	Hits
#1	system*:ti,ab AND (corticosteroid*:ti,ab OR glucocorticoid*:ti,ab)	2962
#2	OCS:ti,ab or "oral corticosteroid*":ti,ab	1141
#3	"oral glucocorticoid*":ti,ab	125
#4	#1 or #2 or #3	4009
#5	MeSH descriptor: [Asthma] explode all trees	10310
#6	asthma:ti,ab	21802
#7	#5 or #6	23475
#8	treat*:ti,ab or manage*:ti,ab or therap*:ti,ab	630589
#9	#4 and #7 and #8	947
#10	#9 Publication Year from 2011	416

All Results	416
Cochrane Reviews	60
All	60
Review	58
Protocol	2
Other Reviews	2
Trials	354
Methods Studies	0
Technology Assessments	0
Economic Evaluations	0
Cochrane Groups	0

Table S4: Search strategy for HTA databases

Name of database	DARE, INAHTA, NHS EED	
Search interface	DIMDI	
Date of the search	28.05.2018	
Time periode	From 2011	
Filter	No filter	
Line	Search	Hits
#1	(system* AND (corticosteroid* OR glucocorticoid)) IN DARE, NHSEED, HTA FROM 2011 TO 2018	348
#2	("oral glucocorticoid*") IN DARE, NHSEED, HTA FROM 2011 TO 2018	4
#3	(OCS OR "oral corticosteroid*") IN DARE, NHSEED, HTA FROM 2011 TO 2018	39
#4	#1 or #2 or #3	361
#5	MeSH DESCRIPTOR Asthma EXPLODE ALL TREES	676
#6	(asthma) IN DARE, NHSEED, HTA FROM 2011 TO 2018	424
#7	#5 or #6	849
#8	(treat* OR manage* OR therap*) IN DARE, NHSEED, HTA FROM 2011 TO 2018	28719
#9	#4 AND #7 AND #8	72

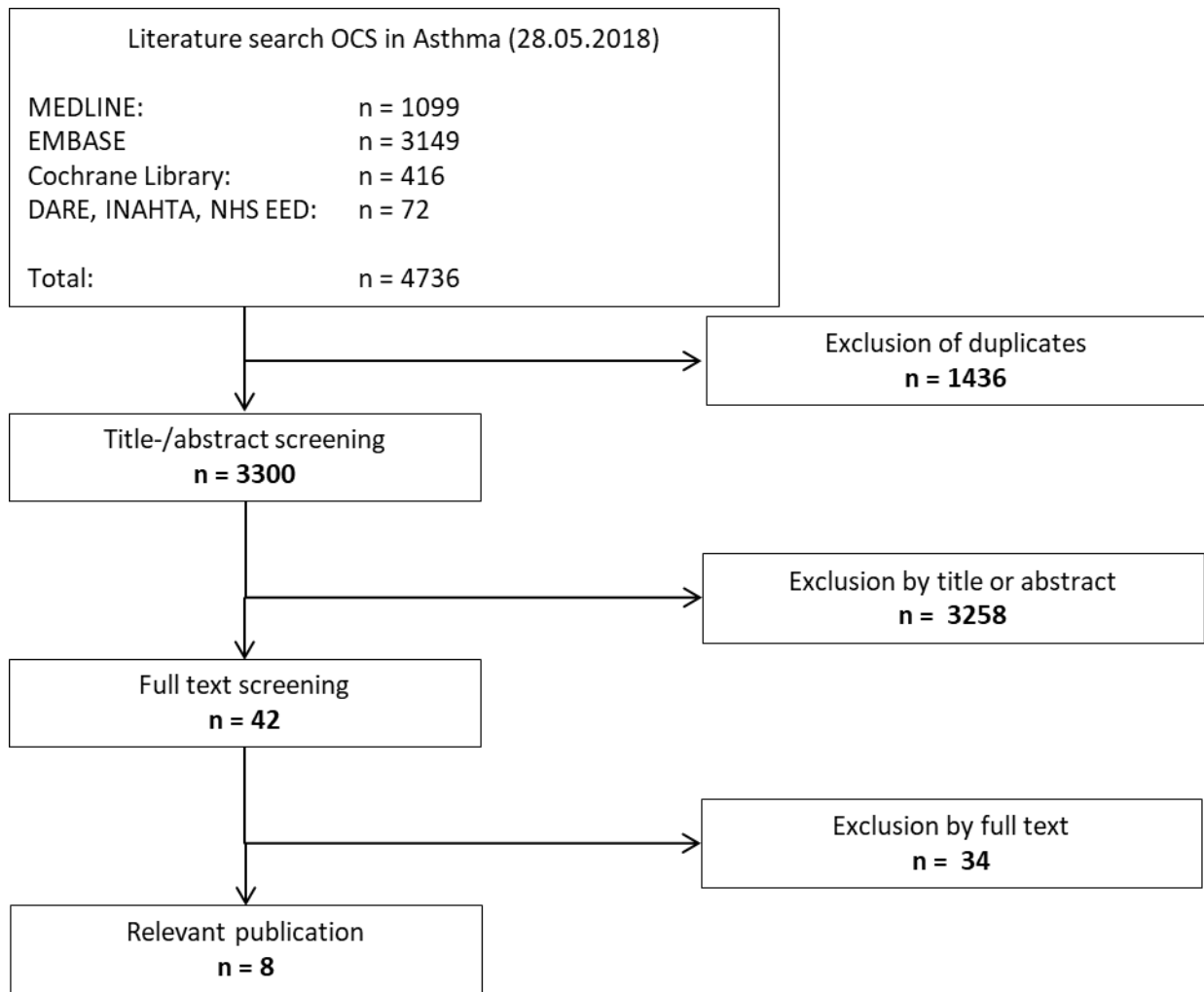


Figure S1: Search flow of the systematic literature search

Overall, the literature search resulted in 4738 hits, of which 1436 publications were duplicates. After title and abstract screening 42 potentially relevant publications remained for a full text review, in which 8 publications were included (Table S5). Because of the limited number of results an additional hand search was performed and 1 additional study was included.

Table S5: List of included publications

No.	Citation
Identified by systematic literature search	
1	Barry LE, Sweeney J, O'Neill C, Price D, Heaney LG. The cost of systemic corticosteroid-induced morbidity in severe asthma: a health economic analysis. <i>Respiratory research</i> 2017; 18(1): 129.
2	Barry LE, O'Neill C, Patterson C, Sweeney J, Price D, Heaney LG. Age and Sex Associations with Systemic Corticosteroid-Induced Morbidity in Asthma. <i>The journal of allergy and clinical immunology In practice</i> 2018.
3	Daugherty J, Lin X, Baxter R, Suruki R, Bradford E. The impact of long-term systemic glucocorticoid use in severe asthma: A UK retrospective cohort analysis. <i>Journal of Asthma</i> 2017: 1-8.

4	Lefebvre P, Duh MS, Lafeuille MH, Gozalo L, Desai U, Robitaille MN, Albers F, Yancey S, Ortega H, Forshag M, Lin X, Dalal AA. Acute and chronic systemic corticosteroid-related complications in patients with severe asthma. <i>The Journal of allergy and clinical immunology</i> 2015; 136: 1488-1495.
5	Lefebvre P, Duh MS, Lafeuille MH, Gozalo L, Desai U, Robitaille MN, Albers F, Yancey S, Ortega H, Forshag M, Lin X, Dalal AA. Burden of systemic glucocorticoid-related complications in severe asthma. <i>Current medical research and opinion</i> 2017; 33(1): 57-65.
6	Sweeney J, Patterson CC, Menzies-Gow A, Niven RM, Mansur AH, Bucknall C, Chaudhuri R, Price D, Brightling CE, Heaney LG. Comorbidity in severe asthma requiring systemic corticosteroid therapy: cross-sectional data from the Optimum Patient Care Research Database and the British Thoracic Difficult Asthma Registry. <i>Thorax</i> 2016; 71(4): 339-346.
7	Zazzali JL, Broder MS, Omachi TA, Chang E, Sun GH, Raimundo K. Risk of corticosteroid-related adverse events in asthma patients with high oral corticosteroid use. <i>Allergy and Asthma Proceedings</i> 2015; 36(4): 268-274.
8	Zeiger RS, Schatz M, Li Q, Chen W, Khatry DB, Tran TN. Burden of Chronic Oral Corticosteroid Use by Adults with Persistent Asthma. <i>Journal of Allergy and Clinical Immunology: In Practice</i> 2017; 5(4): 1050-1060.e1059.
Identified by hand search	
9	Dalal AA, Duh MS, Gozalo L, Robitaille MN, Albers F, Yancey S, Ortega H, Forshag M, Lin X, Lefebvre P. Dose-Response Relationship Between Long-Term Systemic Corticosteroid Use and Related Complications in Patients with Severe Asthma. <i>Journal of managed care & specialty pharmacy</i> 2016; 22(7): 833-847.