## **Online Appendix**

Management of Asthma in Childhood: Study Protocol of a Systematic Evidence Update by the Pediatric Asthma in Real Life (PeARL) Think Tank.

#### **Search Strategies**

### 1. Overview of SRs evaluating stable asthma treatment

- #1 Asthma [MH]
- #2 Respiratory Sounds[MH]
- #3 Bronchial spasm [MH]
- #4 Bronchial Hyperreactivity [MH]
- #5 Respiratory Hypersensitivity [MH]
- #6 Anti-asthmatic agents[MH]
- #7 Asthma [tiab]
- #8 Wheez\* [tiab]
- #9 Bronchospas\* [tiab]
- #10 Bronchoconstrict\* [tiab]
- #11 Bronch\* [tiab] and (constrict\* [tiab])
- #12 (bronchial\* [tiab] or (respiratory[tiab]) or (airway\* [tiab]) or (lung\* [tiab])) and (hypersensitiv\* [tiab] or (hyperreactiv\* [tiab]) or (allerg\* [tiab]))
- #13 OR / 1-12
- #14 (Steroid\* [tiab] or (corticosteroid\* [tiab]) or (glucocorticoid\* [tiab])) and (inhal\* [tiab])
- #15 Beclomethasone [MH]
- #16 Budesonide [MH]
- #17 Fluticasone [MH]
- #18 Mometasone Furoate [MH]
- #19 Triamcinolone [MH]
- #20 Beclomethasone [tiab]
- #21 Beclometasone [tiab]
- #22 Budesonide [tiab]
- #23 Fluticasone [tiab]
- #24 Ciclesonide [tiab]
- #25 Mometasone [tiab]
- #26 Flunisolide [tiab]
- #27 Triamcinolone [tiab]

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#28
       ICS [tiab]
#29
       OR/14-28
#30
       Adrenergic beta-2 receptor Agonists [MH] and (inhal* [tiab])
#31
       Beta-agonist* [tiab] and (inhal* [tiab])
#32
       Salmeterol Xinafoate [MH]
#33
       Formoterol Fumarate [MH]
#34
       Clenbuterol [MH]
#35
       Salmeterol [tiab]
#36
       Formoterol [tiab]
#37
       Vilanterol [tiab]
#38
       Indacaterol [tiab]
#39
       Clenbuterol [tiab]
#40
       Olodaterol [tiab]
#41
       Bambuterol [tiab]
#42
       *formoterol [tiab]
#43
       LABA [tiab]
#44
       OR/30-43
#45
       Muscarinic antagonists [MH] and (inhal* [tiab])
#46
       Tiotropium Bromide [MH]
#47
       Tiotropium [tiab]
#48
       Umeclidinium [tiab]
#49
       GSK573719 [tiab]
#50
       Aclidinium [tiab]
#51
       LAS34273 [tiab]
#52
       Glycopyrronium [tiab]
#53
       NVA237 [tiab]
#54
       LAMA [tiab]
#55
       Muscarinic* [tiab] and (Antagonist* [tiab]) and (inhal* [tiab])
#56
       Antimuscarinic* [tiab]
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#58 Leukotriene Antagonists[MH] #59 Leukotriene* [tiab] AND (Antagonist* [tiab]) #60 Anti-leukotriene* [tiab] #61 Anti-leucotriene [tiab] #62 Montelukast [tiab] #63 Zafirlukast [tiab] #64 Pranlukast [tiab] #65 LTRA [tiab] #66 OR/ 58-65  #67 Biological Factors [MH] #68 Omalizumab [MH] #69 Omalizumab [tiab] #70 Mepolizumab [tiab] #71 Benralizumab [tiab] #72 Reslizumab [tiab] #73 Dupilumab [tiab] #74 OR/ 67-73  #75 meta-analysis [Publication type] HIRU Filter for Systematic Reviews #76 meta-analysis [tiab] #77 meta-analysis [tiab] #78 review [Publication type] #79 search*[tiab] #80 OR/ 75-79  #81 #28 OR #44 OR #57 OR #66 OR #74	#57	OR/ 45-56	
Leukotriene* [tiab] AND (Antagonist* [tiab])  #60 Anti-leukotriene* [tiab]  #61 Anti-leucotriene [tiab]  #62 Montelukast [tiab]  #63 Zafirlukast [tiab]  #64 Pranlukast [tiab]  #65 LTRA [tiab]  #66 OR/58-65   #67 Biological Factors [MH]  #68 Omalizumab [MH]  #69 Omalizumab [tiab]  #70 Mepolizumab [tiab]  #71 Benralizumab [tiab]  #72 Reslizumab [tiab]  #73 Dupilumab [tiab]  #74 OR/ 67-73  #75 meta-analysis [Publication type] HIRU Filter for Systematic Reviews  #76 meta-analysis [tiab]  #77 meta-analysis [tiab]  #78 review [Publication type]  #79 search* [tiab]  #80 OR/ 75-79  #81 #28 OR #44 OR #57 OR #66 OR #74			
#60 Anti-leukotriene* [tiab] #61 Anti-leucotriene [tiab] #62 Montelukast [tiab] #63 Zafirlukast [tiab] #64 Pranlukast [tiab] #65 LTRA [tiab] #66 OR/ 58-65  #67 Biological Factors [MH] #68 Omalizumab [MH] #69 Omalizumab [tiab] #70 Mepolizumab [tiab] #71 Benralizumab [tiab] #72 Reslizumab [tiab] #73 Dupilumab [tiab] #74 OR/ 67-73  #75 meta-analysis [Publication type] HIRU Filter for Systematic Reviews #76 meta-analysis [tiab] #77 meta-analysis [tiab] #78 review [Publication type] #79 search*[tiab] #80 OR/ 75-79  #81 #28 OR #44 OR #57 OR #66 OR #74			
#61 Anti-leucotriene [tiab] #62 Montelukast [tiab] #63 Zafirlukast [tiab] #64 Pranlukast [tiab] #65 LTRA [tiab] #66 OR/ 58-65  #67 Biological Factors [MH] #68 Omalizumab [MH] #69 Omalizumab [tiab] #70 Mepolizumab [tiab] #71 Benralizumab [tiab] #72 Reslizumab [tiab] #73 Dupilumab [tiab] #74 OR/ 67-73  #75 meta-analysis [Publication type] HIRU Filter for Systematic Reviews #76 meta-analysis [tiab] #77 meta-analysis [tiab] #78 review [Publication type] #79 search*[tiab] #80 OR/ 75-79  #81 #28 OR #44 OR #57 OR #66 OR #74	#59		
#62 Montelukast [tiab] #63 Zafirlukast [tiab] #64 Pranlukast [tiab] #65 LTRA [tiab] #66 OR/ 58-65  #67 Biological Factors [MH] #68 Omalizumab [MH] #69 Omalizumab [tiab] #70 Mepolizumab [tiab] #71 Benralizumab [tiab] #72 Reslizumab [tiab] #73 Dupilumab [tiab] #74 OR/ 67-73  #75 meta-analysis [Publication type] HIRU Filter for Systematic Reviews #76 meta-analysis (tiab) #77 meta-analysis (tiab) #78 review [Publication type] #79 search*[tiab] #70 OR/ 75-79  #81 #28 OR #44 OR #57 OR #66 OR #74	#60	Anti-leukotriene* [tiab]	
#63 Zafirlukast [tiab] #64 Pranlukast [tiab] #65 LTRA [tiab] #66 OR/ 58-65  #67 Biological Factors [MH] #68 Omalizumab [MH] #69 Omalizumab [tiab] #70 Mepolizumab [tiab] #71 Benralizumab [tiab] #72 Reslizumab [tiab] #73 Dupilumab [tiab] #74 OR/ 67-73  #75 meta-analysis [Publication type] HIRU Filter for Systematic Reviews #76 meta-analysis [tiab] #77 meta-analysis [tiab] #78 review [Publication type] #79 search*[tiab] #80 OR/ 75-79  #81 #28 OR #44 OR #57 OR #66 OR #74	#61	Anti-leucotriene [tiab]	
#64 Pranlukast [tiab] #65 LTRA [tiab] #66 OR/ 58-65  #67 Biological Factors [MH] #68 Omalizumab [MH] #69 Omalizumab [tiab] #70 Mepolizumab [tiab] #71 Benralizumab [tiab] #72 Reslizumab [tiab] #73 Dupilumab [tiab] #74 OR/ 67-73  #75 meta-analysis [Publication type] HIRU Filter for Systematic Reviews #76 meta-analysis [tiab] #77 meta-analysis [tiab] #78 review (Publication type] #79 search*[tiab] #80 OR/ 75-79  #81 #28 OR #44 OR #57 OR #66 OR #74	#62	Montelukast [tiab]	
#65 LTRA [tiab] #66 OR/ 58-65  #67 Biological Factors [MH] #68 Omalizumab [MH] #69 Omalizumab [tiab] #70 Mepolizumab [tiab] #71 Benralizumab [tiab] #72 Reslizumab [tiab] #73 Dupilumab [tiab] #74 OR/ 67-73  #75 meta-analysis [Publication type] HIRU Filter for Systematic Reviews #76 meta-analysis [MH] #77 meta-analysis [tiab] #78 review [Publication type] #79 search*[tiab] #80 OR/ 75-79  #81 #28 OR #44 OR #57 OR #66 OR #74	#63	Zafirlukast [tiab]	
#66 OR/ 58-65  #67 Biological Factors [MH]  #68 Omalizumab [MH]  #69 Omalizumab [tiab]  #70 Mepolizumab [tiab]  #71 Benralizumab [tiab]  #72 Reslizumab [tiab]  #73 Dupilumab [tiab]  #74 OR/ 67-73  #75 meta-analysis [Publication type] HIRU Filter for Systematic Reviews  #76 meta-analysis [MH]  #77 meta-analysis [tiab]  #78 review [Publication type]  #79 search*[tiab]  #80 OR/ 75-79  #81 #28 OR #44 OR #57 OR #66 OR #74	#64	Pranlukast [tiab]	
#67 Biological Factors [MH] #68 Omalizumab [MH] #69 Omalizumab [tiab] #70 Mepolizumab [tiab] #71 Benralizumab [tiab] #72 Reslizumab [tiab] #73 Dupilumab [tiab] #74 OR/ 67-73  #75 meta-analysis [Publication type] HIRU Filter for Systematic Reviews #76 meta-analysis [MH] #77 meta-analysis [tiab] #78 review [Publication type] #79 search*[tiab] #79 OR/ 75-79  #81 #28 OR #44 OR #57 OR #66 OR #74	#65	LTRA [tiab]	
#68 Omalizumab [MH] #69 Omalizumab [tiab] #70 Mepolizumab [tiab] #71 Benralizumab [tiab] #72 Reslizumab [tiab] #73 Dupilumab [tiab] #74 OR/ 67-73  #75 meta-analysis [Publication type] HIRU Filter for Systematic Reviews #76 meta-analysis [MH] #77 meta-analysis [tiab] #78 review [Publication type] #79 search*[tiab] #80 OR/ 75-79  #81 #28 OR #44 OR #57 OR #66 OR #74	#66	OR/ 58-65	
#68 Omalizumab [MH] #69 Omalizumab [tiab] #70 Mepolizumab [tiab] #71 Benralizumab [tiab] #72 Reslizumab [tiab] #73 Dupilumab [tiab] #74 OR/ 67-73  #75 meta-analysis [Publication type] HIRU Filter for Systematic Reviews #76 meta-analysis [MH] #77 meta-analysis [tiab] #78 review [Publication type] #79 search*[tiab] #80 OR/ 75-79  #81 #28 OR #44 OR #57 OR #66 OR #74			
#69 Omalizumab [tiab] #70 Mepolizumab [tiab] #71 Benralizumab [tiab] #72 Reslizumab [tiab] #73 Dupilumab [tiab] #74 OR/ 67-73  #75 meta-analysis [Publication type] HIRU Filter for Systematic Reviews #76 meta-analysis [MH] #77 meta-analysis [tiab] #78 review [Publication type] #79 search*[tiab] #80 OR/ 75-79  #81 #28 OR #44 OR #57 OR #66 OR #74	#67	Biological Factors [MH]	
#70 Mepolizumab [tiab] #71 Benralizumab [tiab] #72 Reslizumab [tiab] #73 Dupilumab [tiab] #74 OR/ 67-73  #75 meta-analysis [Publication type] HIRU Filter for Systematic Reviews #76 meta-analysis [MH] #77 meta-analysis [tiab] #78 review [Publication type] #79 search*[tiab] #80 OR/ 75-79  #81 #28 OR #44 OR #57 OR #66 OR #74	#68	Omalizumab [MH]	
#71 Benralizumab [tiab] #72 Reslizumab [tiab] #73 Dupilumab [tiab] #74 OR/ 67-73  #75 meta-analysis [Publication type] HIRU Filter for Systematic Reviews #76 meta-analysis [MH] #77 meta-analysis [tiab] #78 review [Publication type] #79 search*[tiab] #80 OR/ 75-79  #81 #28 OR #44 OR #57 OR #66 OR #74	#69	Omalizumab [tiab]	
#72 Reslizumab [tiab] #73 Dupilumab [tiab] #74 OR/ 67-73  #75 meta-analysis [Publication type] HIRU Filter for Systematic Reviews #76 meta-analysis [MH] #77 meta-analysis [tiab] #78 review [Publication type] #79 search*[tiab] #80 OR/ 75-79  #81 #28 OR #44 OR #57 OR #66 OR #74	#70	Mepolizumab [tiab]	
#73 Dupilumab [tiab] #74 OR/ 67-73  #75 meta-analysis [Publication type] HIRU Filter for Systematic Reviews #76 meta-analysis [MH] #77 meta-analysis [tiab] #78 review [Publication type] #79 search*[tiab] #80 OR/ 75-79  #81 #28 OR #44 OR #57 OR #66 OR #74	#71	Benralizumab [tiab]	
#74 OR/ 67-73  #75 meta-analysis [Publication type] HIRU Filter for Systematic Reviews  #76 meta-analysis [MH]  #77 meta-analysis [tiab]  #78 review [Publication type]  #79 search*[tiab]  #80 OR/ 75-79  #81 #28 OR #44 OR #57 OR #66 OR #74	#72	Reslizumab [tiab]	
#75 meta-analysis [Publication type] HIRU Filter for Systematic Reviews  #76 meta-analysis [MH]  #77 meta-analysis [tiab]  #78 review [Publication type]  #79 search*[tiab]  #80 OR/ 75-79  #81 #28 OR #44 OR #57 OR #66 OR #74	#73	Dupilumab [tiab]	
#76 meta-analysis [MH]  #77 meta-analysis [tiab]  #78 review [Publication type]  #79 search*[tiab]  #80 OR/ 75-79  #81 #28 OR #44 OR #57 OR #66 OR #74	#74	OR/ 67-73	
#76 meta-analysis [MH]  #77 meta-analysis [tiab]  #78 review [Publication type]  #79 search*[tiab]  #80 OR/ 75-79  #81 #28 OR #44 OR #57 OR #66 OR #74			
#77 meta-analysis [tiab]  #78 review [Publication type]  #79 search*[tiab]  #80 OR/ 75-79  #81 #28 OR #44 OR #57 OR #66 OR #74	#75	meta-analysis [Publication type]	HIRU Filter for Systematic Reviews
#78 review [Publication type]  #79 search*[tiab]  #80 OR/ 75-79  #81 #28 OR #44 OR #57 OR #66 OR #74	#76	meta-analysis [MH]	
#79 search*[tiab] #80 OR/ 75-79 #81 #28 OR #44 OR #57 OR #66 OR #74	#77	meta-analysis [tiab]	
#80 OR/ 75-79  #81 #28 OR #44 OR #57 OR #66 OR #74	#78	review [Publication type]	
#81 #28 OR #44 OR #57 OR #66 OR #74	#79	search*[tiab]	
	#80	OR/ 75-79	
	#81	#28 OR #44 OR #57 OR #66 OR #74	
#82 #13 AND #80 AND #81	#82	#13 AND #80 AND #81	

- #83 children [MH] or (adolescents [MH])
- #84 adults [MH] NOT #75
- #85 Editorial [publication type]
- #86 Letter [publication type]
- #87 #82 NOT (#84 OR #85 OR #86)

# 2. Severe asthma exacerbations treatment: Broad systematic review

- #1 Asthma [MH]
- #2 Severe asthma [MH]
- #3 Brittle asthma [MH]
- #4 Asthma [tiab]
- #5 OR/ 1-4
- #6 Disease Exacerbation [MH]
- #7 Exacerbation [tiab]
- #8 Exacerbation\* [tiab]
- #9 Attack [tiab]
- #10 Acute [tiab]
- #11 OR/ 6-10
- #12 Intensive care [MH]
- #13 Emergency Service, Hospital[MH]
- #14 Severe [tiab]
- #15 Refractory [tiab]
- #16 Near fatal [tiab]
- #17 Life-threatening [tiab]
- #18 Difficult-to-treat [tiab]
- #19 Therapy resistant [tiab]
- #20 Intensive care[tiab]
- #21 Critically ill [tiab]
- #22 ICU [tiab]

#23	Emergency presentation [tiab]
#24	Emergency admission [tiab]
#25	Emergency department [tiab]
#26	OR/ 12-25
#27	(#5 AND #11 AND #26)
#28	Status asthmaticus[MH]
#29	Status asthmaticus[tiab]
#30	(#27 OR #28 OR #29)
#31	(animals [mh] NOT humans [mh])
#32	children [MH] or (adolescents [MH])
#33	adults [MH] NOT #32
#34	adults [MH] NOT #32  Review [publication type]
#34	Review [publication type]
#34 #35	Review [publication type]  Systematic review [publication type]
#34 #35 #36	Review [publication type]  Systematic review [publication type]  Meta-analysis[publication type]

(#30 NOT (#31 OR #33 OR #37 OR #38 OR #39))

## 3. Severe asthma exacerbations treatment: Individual medication meta-analyses

#1 Asthma [MH] #2 Respiratory Sounds[MH] #3 Bronchial spasm [MH] #4 Bronchial Hyperreactivity [MH] #5 Respiratory Hypersensitivity [MH] #6 Anti-asthmatic agents[MH] #7 Asthma [tiab] #8 Wheez\* [tiab]

Bronchospas\* [tiab]

#40

#9

```
#10
       Bronchoconstrict* [tiab]
#11
       Bronch* [tiab] and (constrict* [tiab])
#12
       (bronchial* [tiab] or (respiratory[tiab]) or (airway* [tiab]) or (lung* [tiab])) and
(hypersensitiv* [tiab] or (hyperreactiv* [tiab]) or (allerg* [tiab]))
#13
       OR / 1-12
#14
       Search terms related to the medication under investigation, including MeSH terms and free
       search terms.
#15
       children [MH]
#16
        paediatric*[tiab]
#17
       pediatric* [tiab]
#18
       child* [tiab]
#19
       adolescen* [tiab]
#20
       infant* [tiab]
#21
       toddler* [tiab]
#22
       preschool* [tiab]
#23
       OR/16-22
#24
       #13 AND #14 AND #23
#25
       (animals [mh] NOT humans [mh])
#26
       children [MH] or (adolescents [MH])
#27
       adults [MH] NOT #26
#28
       Review [publication type]
#29
       Systematic review [publication type]
#30
       Meta-analysis[publication type]
#31
        (#28 NOT (#29 OR #30))
#32
       Letter [publication type]
#33
       Editorial [publication type]
```

(#24 NOT (#25 OR #27 OR #31 OR #32 OR #33))

#34