- 1. Should HDM SLIT tablets versus no SLIT tablets be used for treatment in **paediatric** patients with asthma?
 - 1.1. FOREST PLOTS
 - 1.1.1. Critical outcomes
 - 1.1.1.1. Asthma exacerbations

We found no evidence

1.1.1.2. Asthma control

We found no evidence

1.1.1.3. Steroid sparing effect (inhaled steroids) – assessed as use of inhaled steroids (ug budesonide/day)

	HDM SLIT ta	ablets Chi	ldren	Pla	acebo	•		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	ABCDEFG
Pham-Thi 2007	257	232	54	223	270	55	100.0%	34.00 [-60.45, 128.45]		●? ●? ● ●
Total (95% CI)			54			55	100.0%	34.00 [-60.45, 128.45]		
Heterogeneity: Not app	licable									-
Test for overall effect: $Z = 0.71$ (P = 0.48) -200 - 100 0 100 200 HDM SLIT tablets Children Placebo										
Risk of bias legend										
(A) Random sequence	generation (se	election bi	as)							
(B) Allocation concealn	nent (selection	n bias)								
(C) Blinding of particip	ants and pers	onnel (per	formance	bias)						
(D) Blinding of outcom	e assessment	(detection	ı bias)							
(E) Incomplete outcom	e data (attritio	on bias)								
(F) Selective reporting	(reporting bia	s)								
(G) Other bias										

1.1.1.4. Safety (systemic reactions) – assessed as number of patients with at least one reaction

Study or Subgroup	HDM SLIT tablets Children		Place		Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F G	
Pham-Thi 2007	Events	55		10tai 56	weight	Not estimable	M-H, Kandom, 95% CI		
Pham-Thi 2007	0	>>	0	20		Not estimable			
Total (95% CI)		55		56		Not estimable			
Total events	0		0						
Heterogeneity: Not ap	plicable					-	0.005 0.1 1 10 20	<u> </u>	
Test for overall effect:					T tablets Children Placebo	0			
Risk of bias legend									
(A) Random sequence	e generation (selection l	oias)							
(B) Allocation conceal	ment (selection bias)								
(C) Blinding of particip	pants and personnel (p	erformanc	e bias)						
(D) Blinding of outcome assessment (detection bias)									
(E) Incomplete outcome data (attrition bias)									
(F) Selective reporting (reporting bias)									
(G) Other bias									

1.1.2. Important but no critical

1.1.2.1. Symptom score – assessed as asthma symptom score (nocturnal and diurnal)

	HDM SLIT t	ablets Chi	ldren	Pla	acebo			Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEFG
Pham-Thi 2007	-0.04	0.18	54	-0.09	0.15	55	100.0%	0.05 [-0.01, 0.11]		●? •? •••
Total (95% CI)			54			55	100.0%	0.05 [-0.01, 0.11]		
Heterogeneity: Not app	olicable									_
Test for overall effect: $Z = 1.57$ (P = 0.12) HDM SLIT tablets Children Placebo										
Risk of bias legend										
(A) Random sequence	generation (s	election bia	as)							
(B) Allocation conceal	nent (selectio	n bias)								
(C) Blinding of particip	ants and pers	sonnel (per	formance	bias)						
(D) Blinding of outcom	e assessmen	t (detection	ı bias)							
(E) Incomplete outcom	e data (attriti	on bias)								
(F) Selective reporting	(reporting bia	as)								
(G) Other bias										

1.1.2.2. Medication score

We found no evidence

Quality of Life 1.1.2.3.

We found no evidence

Lung function: Small airways (% or absolute improvement of MEF 25, 1.1.2.4. MEF 50, MEF 75)

We found no evidence

1.1.2.5. Lung function: Allergen specific bronchial provocation (ASBP)

We found no evidence

Safety (local reactions) 1.1.2.6.

	HDM SLIT tablets Ch	Placebo			Risk Ratio	Risk Ratio	Risk of Bias	
Study or Subgroup	Events	Total	Events	Events Total		M-H, Random, 95% CI	M-H, Random, 95% CI	ABCDEFG
Pham-Thi 2007	39	55	37	56	100.0%	1.07 [0.83, 1.38]		
Total (95% CI)		55		56	100.0%	1.07 [0.83, 1.38]		
Total events	39		37					
Heterogeneity: Not ap	plicable					-	0.7 0.85 1 1.2	- <u></u>
Test for overall effect:	Z = 0.55 (P = 0.58)					HDM SLI	T tablets Children Placebo	1.5
Risk of bias legend								
(A) Random sequence	generation (selection b	ias)						

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)

(E) Incomplete outcome data (attrition bias)

(F) Selective reporting (reporting bias)

(G) Other bias

1.2. EVIDENCE PROFILE

Author(s): Juan J. Yepes-Nuñez Date: October 2018 Question: HDM SLIT tablets compared to no HDM SLIT tablets for treatment in paediatric patients with asthma Setting: Outpatients

			Certainty a	ssessment			№ of p	atients	Effec	t		
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	HDM SLIT tablets	no HDM SLIT tablets	Relative (95% Cl)	Absolute (95% CI)	Certainty	Importance
Asthma exa	sthma exacerbations - not reported											
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Asthma con	Asthma control - not reported											
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Corticostero	id use (inhaled s	teroids) assessed a	as use of inhaled st	eroids (ug budeson	ide/day) (follow up:	18 months)	1		1			
1	randomised trials	serious a	not serious	serious ^b	very serious °	none	54	55	-	MD 34 higher (60.45 lower to 128.45 higher)		CRITICAL
Systemic ad	Systemic adverse events assessed as number of patients with at least one reaction (follow up: 18 months)											
1	randomised trials	serious ^a	not serious	not serious	serious ^d	none	0/55 (0.0%)	0/56 (0.0%)	not estimable		$\bigoplus_{LOW} \bigcirc \bigcirc$	CRITICAL
Symptom so	cores assessed a	is asthma symptom	score (nocturnal a	nd diurnal) (follow u	ip: 18 months)				L			
1	randomised trials	serious ^a	not serious	not serious	very serious °	none	54	55	-	MD 0.05 higher (0.01 lower to 0.11 higher)		IMPORTANT
Medication	scores - not repo	rted										
-	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Asthma Qol	- not reported		۱ <u>ــــــــــــــــــــــــــــــــــــ</u>	ł	ł	·	·		<u>+</u>			۱ <u>ــــــــــــــــــــــــــــــــــــ</u>
-	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Allergen spe	ecific bronchial pr	rovocation tests (Al	3PT) - not reported	·	·	·	·					·
-	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT

			Certainty a	issessment			Nº of p	atients	Effect	t		
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	HDM SLIT tablets	no HDM SLIT tablets	Relative (95% Cl)	Absolute (95% CI)	Certainty	Importance
Local adver	Local adverse events (follow up: 18 months)											
1	randomised trials	serious ^a	not serious	not serious	serious °	none	39/55 (70.9%)	37/56 (66.1%)	RR 1.07 (0.83 to 1.38)	46 more per 1,000 (from 112 fewer to 251 more)		IMPORTANT

CI: Confidence interval; RR: Risk ratio; MD: Mean difference; SMD: Standardised mean difference

Explanations

a. Serious risk of bias. One study that carried all weight for the effect estimate rated as high risk of bias due to lack of random sequence generation.

b. Serious indirectness. The study used a surrogate outcome to assess HDM SLIT efficacy.

c. Very serious imprecision. 95% CI is consistent with the possibility for important benefit and large harm exceeding a minimal important difference, and no optimal information size criterion met.

d. No optimal information size criterion met.

References

1. Pham-Thi N, Scheinmann P, Fadel R, Combebias A, Andre C. Assessment of sublingual immunotherapy efficacy in children with house dust mite-induced allergic asthma optimally controlled by pharmacologic treatment and mite-avoidance measures. Pediatr Allergy Immunol. 2007;18(1):47-57.

1.3. SOF TABLE

Summary of findings:

HDM SLIT tablets compared to no HDM SLIT tablets for treatment in paediatric patients with asthma

Patient or population: paediatric patients with asthma Setting: Outpatients Intervention: HDM SLIT tablets Comparison: no HDM SLIT tablets

Outcomes	Anticipated absolute e	ffects* (95% CI)	Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence	Comments
	Risk with no HDMRisk with HDM SLITSLIT tabletstablets				(GRADE)	
Asthma exacerbations - not reported	-	-	-	-	-	
Asthma control - not reported	-		-	-	-	
Corticosteroid use (inhaled steroids) assessed as use of inhaled steroids (ug budesonide/day) (follow up: 18 months)	The mean corticosteroid use (inhaled steroids) assessed as use of inhaled steroids (ug budesonide/day) (follow up: 18 months) was 0	The mean corticosteroid use (inhaled steroids) assessed as use of inhaled steroids (ug budesonide/day) (follow up: 18 months) in the intervention group was 34 higher (60.45 lower to 128.45 higher)	-	109 (1 RCT)	VERY LOW a.b.c	
Systemic adverse events assessed as number of patients with at least one reaction (follow up: 18 months)	0 per 1,000	0 per 1,000 (0 to 0)	not estimable	111 (1 RCT)	⊕⊕ ⊖⊖ LOW a.d	
Symptom scores assessed as asthma symptom score (nocturnal and diurnal) (follow up: 18 months)	The mean symptom scores assessed as asthma symptom score (noctumal and diurnal) (follow up: 18 months) was 0	The mean symptom scores assessed as asthma symptom score (nocturnal and diurnal) (follow up: 18 months) in the intervention group was 0.05 higher (0.01 lower to 0.11 higher)	-	109 (1 RCT)	UERY LOW a.c	

Summary of findings:

HDM SLIT tablets compared to no HDM SLIT tablets for treatment in paediatric patients with asthma

Patient or population: paediatric patients with asthma Setting: Outpatients Intervention: HDM SLIT tablets Comparison: no HDM SLIT tablets

Outcomes	Anticipated absolute ef	ffects* (95% CI)	Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence	Comments
	Risk with no HDM SLIT tablets	Risk with HDM SLIT tablets			(GRADE)	
Medication scores - not reported	-	see_comment	-	-	-	
Asthma QoL - not reported	-	see_comment	-	-	-	
Allergen specific bronchial provocation tests (ABPT) - not reported	-	see_comment	-	-	-	
Local adverse events (follow up: 18 months)	661 per 1,000	707 per 1,000 (548 to 912)	RR 1.07 (0.83 to 1.38)	111 (1 RCT)	€ LOW a,c	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk ratio; MD: Mean difference; SMD: Standardised mean difference

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

a. Serious risk of bias. One study that carried all weight for the effect estimate rated as high risk of bias due to lack of random sequence generation.

b. Serious indirectness. The study used a surrogate outcome to assess HDM SLIT efficacy.

c. Very serious imprecision. 95% CI is consistent with the possibility for important benefit and large harm exceeding a minimal important difference, and no optimal information size criterion met.

d. No optimal information size criterion met.