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

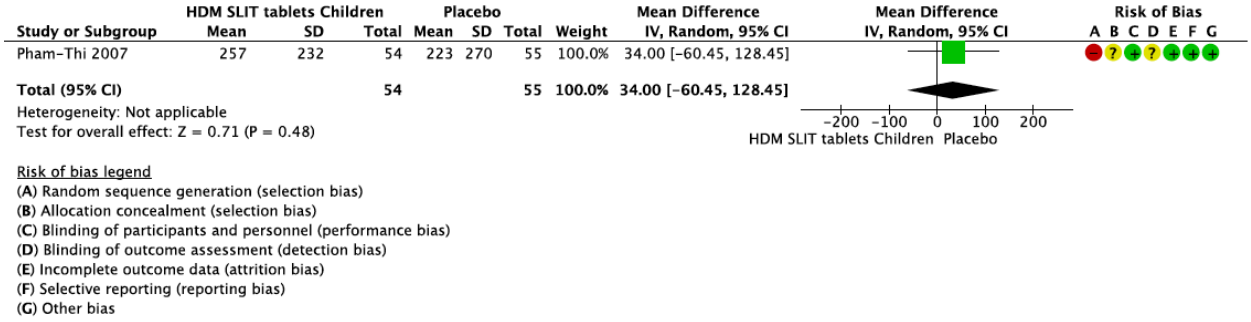
1.1.1.1. Asthma exacerbations

We found no evidence

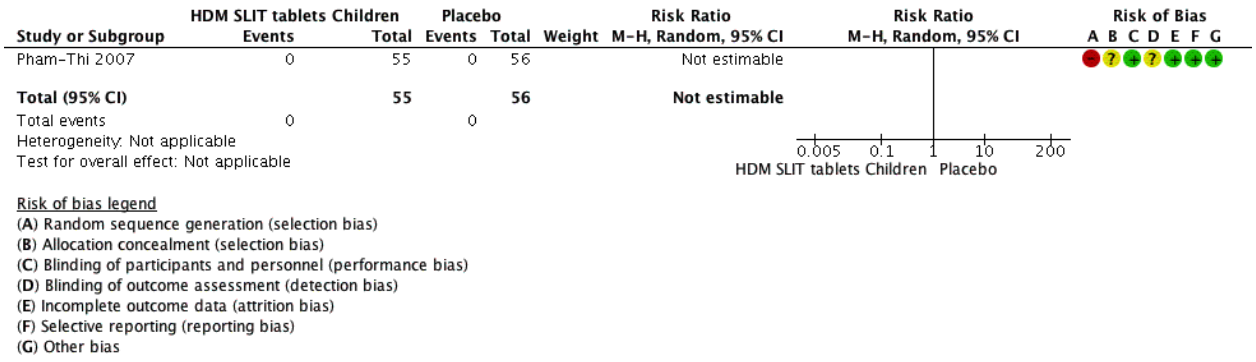
1.1.1.2. Asthma control

We found no evidence

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

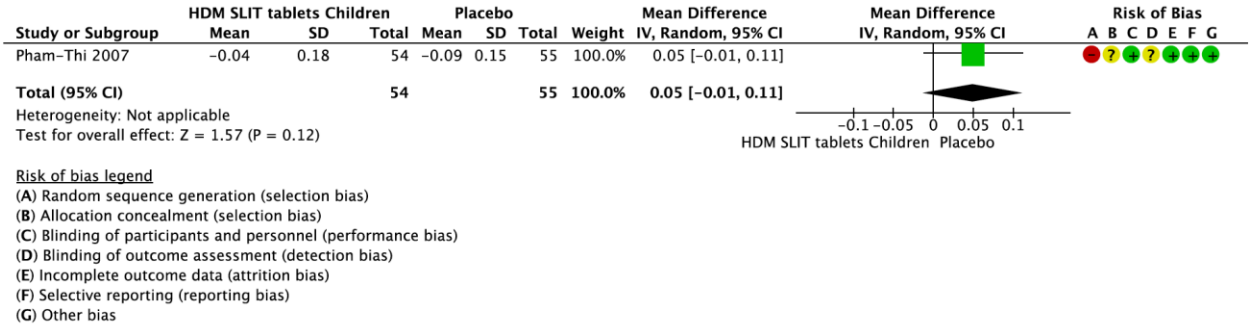


1.1.1.4. Safety (systemic reactions) – assessed as number of patients with at least one reaction



1.1.2. Important but no critical

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



1.1.2.2. Medication score

We found no evidence

1.1.2.3. Quality of Life

We found no evidence

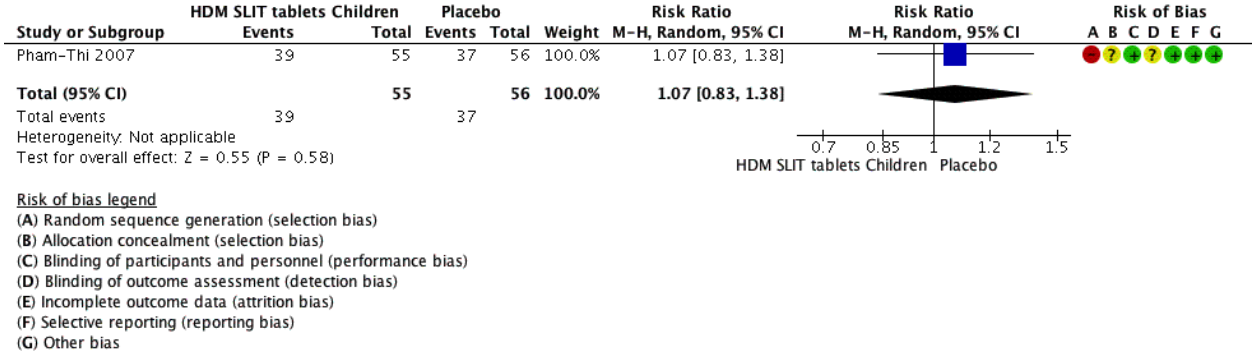
1.1.2.4. Lung function: Small airways (% or absolute improvement of MEF 25, MEF 50, MEF 75)

We found no evidence

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

We found no evidence

1.1.2.6. Safety (local reactions)



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 assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	HDM SLIT tablets	no HDM SLIT tablets	Relative (95% CI)	Absolute (95% CI)		
Asthma exacerbations - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Asthma control - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Corticosteroid use (inhaled steroids) assessed as use of inhaled steroids (ug budesonide/day) (follow up: 18 months)												
1	randomised trials	serious [a]	not serious	serious [b]	very serious [c]	none	54	55	-	MD **34 higher** (60.45 lower to 128.45 higher)	⨁◯◯◯ VERY LOW	CRITICAL
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		⨁⨁◯◯ LOW	CRITICAL
Symptom scores assessed as asthma symptom score (nocturnal and diurnal) (follow up: 18 months)												
1	randomised trials	serious [a]	not serious	not serious	very serious [c]	none	54	55	-	MD **0.05 higher** (0.01 lower to 0.11 higher)	⨁◯◯◯ VERY LOW	IMPORTANT
Medication scores - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Asthma QoL - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Allergen specific bronchial provocation tests (ABPT) - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	HDM SLIT tablets	no HDM SLIT tablets	Relative (95% CI)	Absolute (95% CI)		
Local adverse events (follow up: 18 months)												
1	randomised trials	serious [a]	not serious	not serious	serious [c]	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)	⨁⨁◯◯ LOW	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 effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no HDM SLIT tablets	**Risk with HDM SLIT tablets**				
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 (nocturnal 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)	⨁◯◯◯ VERY 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 effects*** (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no HDM SLIT tablets	**Risk with HDM SLIT tablets**				
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.